Poster # 499

A cost-effectiveness analysis of axicabtagene ciloleucel versus epcoritamab in third-line diffuse large B-cell lymphoma patients in the United States

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BACKGROUND & OBJECTIVE

- New immunotherapies have been introduced over recent years that have improved the outlook for relapsed and refractory (r/r) diffuse large B-cell lymphoma (DLBCL). Two classes of these new treatments include chimeric antigen receptor T-cell (CAR-T) therapies and the T-cell engaging bispecific antibodies (BsAbs).
- Axicabtagene ciloleucel (axi-cel), a CAR-T, was granted approval for treatment of r/r DLBCL in patients with at least two prior systemic therapies in 2017, making it the first FDA-approved CAR-T therapy for this indication. [1] Since 2022, it is further approved for the treatment of r/r DLBCL after first-line chemoimmunotherapy. [2]
- Epcoritamab, a CD3xCD20 BsAb, received accelerated FDA approval in 2023 for patients with R/R DLBCL not otherwise specified and at least two prior systemic therapies. [3]
- The objective of this study was to compare the cost-effectiveness of axi-cel versus epcoritamab in third line (3L) DLBCL in the United States.

METHODS

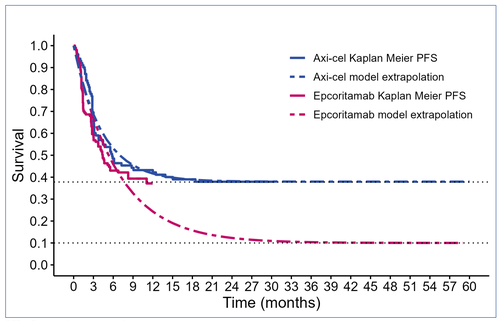
Model overview

- We developed a novel treatment sequencing model that simulates first line, second line, and third line treatment in DLBCL.
- This model was used to assess the cost-effectiveness of axi-cel versus epcoritamab in third line therapy.
- We also assessed the cost impact of a 3L treatment, followed by a subsequent treatment with the respective other therapy upon progression.

Progression-free and overall survival inputs

- For both axi-cel and epcoritamab treatments, mixture cure models (MCM) were used in a naïve comparison to extrapolate 3L progression-free survival from ZUMA-1 [4] and EPCORE NHL-1 [5] (***Figure 1***).
- Considerable uncertainty surrounds the durability of response for epcoritamab in EPCORE NHL-1. Therefore, the epcoritamab modeled cure fraction was assumed to be 10% and was chosen such that the predicted overall survival data best fit the overall survival data from EPCORE NHL-1 .
- Survival after progression in 3L was modeled using the OS data of the ZUMA-1 study; it was assumed that this data was representative of 3L post-progression patients across all treatments in the DLBCL setting.

Figure 1. Kaplan Meier curves and extrapolated progression-free survival for axi-cel and epcoritamab in third line



PFS = Progression-free survival

Health-related quality of life (HRQoL) and cost inputs

- To estimate quality-adjusted life years (QALYs), we used health state utilities derived from the literature.
- Baseline sex- and age-matched utilities were adjusted by applying utility decrements for pre-progression (on and off treatment, by treatment), post-progression, and death health states.
- A United States (US) payer perspective was used to estimate costs. Treatment information and costs were sourced from the available literature and Micromedex and inflated to 2023 US prices.
- Costs and utilities were discounted at 3.0% annually, with reference to the time of initiation of 1L treatment, according to US modeling guidelines. [6]

Table 1. Key cost inputs and sources

MODEL INPUT	VALUE	SOURCE
Axi-cel drug acquisition costs, incl. chemotherapy and leukapheresis	$ 470,017	[7], [8]
Axi-cel drug administration & safety management costs	$ 74,069	[8]
Epcoritamab drug acquisition costs (cycle 1 / cycle 2-3 / cycle 4-9 / cycle 10+), per cycle*	$ 31,720 / $ 60,902 / $ 30,451 / $ 15,225	[7]
Epcoritamab drug administration costs (cycle 1 / cycle 2-3 / cycle 4-9 / cycle 10+), per cycle*	$ 7,298 / $ 4,802 / $ 2,401 / $1,201	[7]
Epcoritamab safety management costs‡	$ 23,204	[9]
HCRU, pre-progression / post-progression, per month	$ 2,253 / $ 2,463	[10], [11]
HCRU, in remission (in % of pre-progression costs), per month	50%	Assumption
Palliative care costs (one-time costs)	$ 19,696	[12]

HCRU = Healthcare resource use.
* In line with the label, epcoritamab was modeled as treat-to-progression.
‡ Safety management costs are assumed to incur in cycle 1 and are applied as one-off costs.

REFERENCES

[1] KITE PRESS RELEASE, 2017; [2] ABBVIE PRESS RELEASE; [3] KITE PRESS RELEASE, 2022; [4] LOCKE ET AL., *LANCET ONCOL*, 2019; [5] THIEBLEMONT ET AL., J CLIN ONCOL, 2022; [6] INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW, 2020; [7] IBM MICROMEDEX, REDBOOK, 2023; [8] OLUWOLE ET AL., *J MED ECON*, 2022; [9] MAHMOUDJAFARI ET AL., ASH POSTER, 2023; [10] PERALES, *TRANSPLANT CELL THER*, 2020; [11] CENTERS FOR MEDICARE & MEDICAID SERVICES, PHYSICIAN FEE SCHEDULE, 2023; [12] KUTIKOVA ET AL., *MED DECIS MAKING*, 2006.

RESULTS

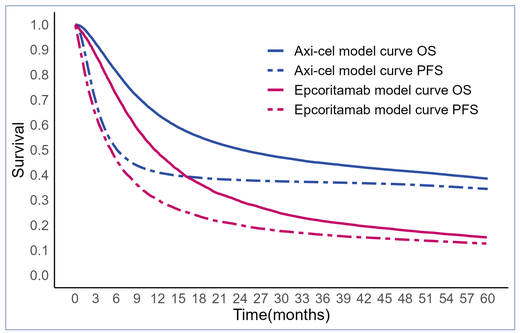
Table 2. Cost-effectiveness results (discounted) for axi-cel versus epcoritamab in the base case, 2023 USD

	Axi-cel	Epcoritamab	Incremental
Life years	5.45	2.47	2.98
Quality-adjusted life years (QALY)	4.15	1.69	2.46
Costs	$ 545,685	$ 581,778	- $ 36,093
• Treatment costs	$ 447,146	$ 495,619	- $ 48,473
• Administration & safety management	$ 75,374	$ 66,963	$ 8,411
• Post-progression & palliative care	$ 23,165	$ 19,196	$ 3,969
ICER (axi-cel vs. epcoritamab)			dominates*

ICER = Incremental cost-effectiveness ratio, QALY = Quality-adjusted life years.
* Expression refers to a treatment which is both more effective (higher QALY gains) and less costly.

- In the base case analysis, the axi-cel arm of the model had discounted costs of $545,685 compared to the epcoritamab arm's $581,778 (***Table 2***).
- Due to the higher projected overall survival and duration of progression-free disease in the axi-cel arm, QALYs were also higher for axi-cel compared to epcoritamab (4.15 versus 1.69).
- **Axi-cel is therefore both more effective and less costly than epcoritamab, making axi-cel a dominant treatment option.**
- The 2-year PFS in the model was estimated as 38% for axi-cel and 18% for epcoritamab (***Figure 2***) with a median PFS of 0.51 and 0.40 years for axi-cel and epcoritamab, respectively.
- In a scenario analysis, the maximum treatment duration for epcoritamab was restricted to 2 years, which led to lower average lifetime costs with epcoritamab, while costs for axi-cel remained the same. This resulted in an incremental cost effectiveness ratio for axi-cel of $89,240, which is well below common cost-effectiveness thresholds in the US, indicating that axi-cel is still cost-effective in this scenario.

Figure 2. Modeled extrapolated survival of axi-cel and epcoritamab

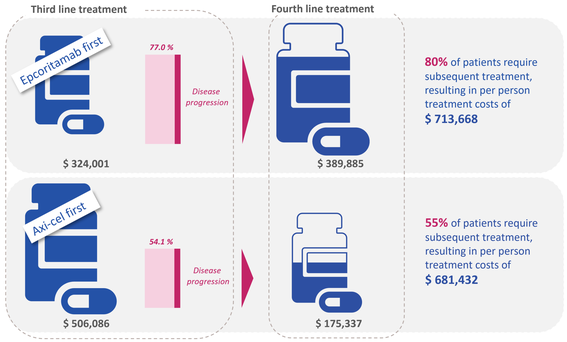


OS = Overall survival, PFS = Progression-free survival

Budget impact analysis

- To estimate the cost impact of different 3L and subsequent 4L treatment strategies, average treatment costs per patient treated in 3L with either agent were extracted from the cost-effectiveness model.
- The analysis assumed that patients progressing beyond third line would incur costs for a fourth line treatment with the therapy not received in 3L.
- Included costs were drug acquisition and administration costs, adverse event costs, and healthcare resource use while in a pre-progression health state.
- The maximum treatment duration for epcoritamab was restricted to 2 years.
- **Analysis results suggest that a treatment sequence with axi-cel first, followed by epcoritamab, leads to overall cost savings** (***Figure 3***).
- Despite lower average costs per patients starting treatment with epcoritamab, the higher proportion of patients who progress from epcoritamab and require subsequent treatment makes an 'epcoritamab first' treatment sequence more costly compared to axi-cel in 3L with epcoritamab as subsequent therapy.

Figure 3. Budget impact of treatment sequences with axi-cel or epcoritamab as 3L treatment.



CONCLUSIONS

- This simulation suggests that axi-cel is highly cost-effective compared to epcoritamab in a 3L DLBCL setting based on extrapolation of the pivotal trial data.
- The higher lifetime treatment cost with epcoritamab suggests a treat-to-progression strategy would result in higher costs over time than the upfront costs of axi-cel and still result in inferior long-term clinical outcomes overall.
- Future research is needed to confirm these findings in larger samples with longer follow-up.

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Conflict of interest statements: A. R. Patel, M. Ray, and K. Hasegawa are employees of Kite, A Gilead Company. S. Hofmann, B. Kievit, and R. Blissett are employees of Maple Health Group, who were contracted by Kite, A Gilead Company, to conduct the work contained in this study. F. Locke received consulting fees from Kite, A Gilead Company, Cowen, BMS/Celgene, EcoR1, Legend Biotech, CERo Therapeutics, Imedex, Allogene, Cellular Biomedicine Group, Calibr, Wugen, Janssen, bluebird bio, Umoja, Caribou, Novartis, Gersson Lehrman Group, Aptitude Health, Takeda, Daiichi Sankyo, Emerging Therapy Solutions, Iovance, Amgen, GammaDelta Therapeutics, Sana, institutional support from Society for Immunotherapy of Cancer, Leukemia and Lymphoma Society, National Cancer Institute, and several patents held by the institution in my name (unlicensed) in the field of cellular immunotherapy.