Poster # 501

A cost-effectiveness analysis of axicabtagene ciloleucel versus glofitamab 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]
- Glofitamab, a CD3xCD20 BsAb, received accelerated FDA approval in 2023 for patients with R/R DLBCL not otherwise specified or large B-cell lymphoma (LBCL) arising from follicular lymphoma and at least two prior systemic therapies. [3]
- The objective of this study was to compare the cost-effectiveness of axi-cel versus glofitamab in third line (3L) DLBCL in the United States.

METHODS

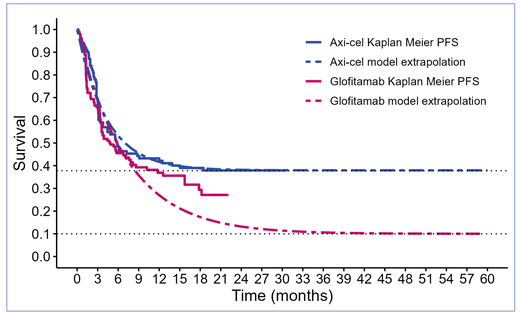
Model overview

- 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 glofitamab 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 glofitamab treatments, mixture cure models (MCM) were used in a naïve comparison to extrapolate 3L progression-free survival from ZUMA-1 [4] and NCT03075696 [5] (***Figure 1***).
- Considerable uncertainty surrounds the durability of response for glofitamab in NCT03075696. Therefore, the glofitamab 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 NCT03075696.
- A scenario analysis using a standard parametric model and no cure assumption for the glofitamab patients was explored.
- 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 glofitamab 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]
Glofitamab drug acquisition costs (cycle 1 / cycle 2+), per cycle*	$ 20,549 / $ 30,657	[7]
Glofitamab drug administration costs (cycle 1 / cycle 2+), per cycle*	$ 6,098 / $ 1,201	[7]
Glofitamab safety management costs‡	$ 23,569	[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, it was assumed that treatment continued until progression or up to a maximum of 12 cycles.
‡ Safety management costs are assumed to incur in cycle 1 and are applied as one-off costs.

REFERENCES

[1] KITE PRESS RELEASE, 2017; [2] GENENTECH PRESS RELEASE 2023; [3] KITE PRESS RELEASE, 2022; [4] LOCKE ET AL., *LANCET ONCOL*, 2019; [5] DICKINSON ET AL., *N ENG J MED*, 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

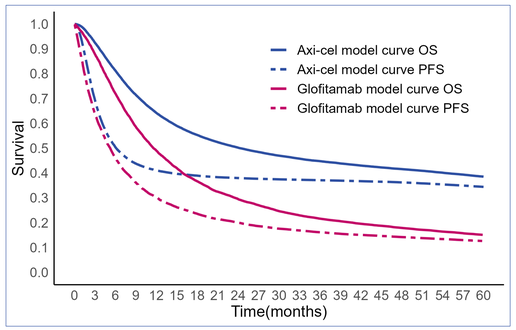
Table 2. Cost-effectiveness results (discounted) for axi-cel versus glofitamab in the base case, 2023 USD

	Axi-cel	Glofitamab	Incremental
Life years	5.45	2.64	2.81
Quality-adjusted life years (QALY)	4.15	1.87	2.28
Costs	$ 545,685	$ 272,311	$ 273,374
• Treatment costs	$ 447,146	$ 210,427	$ 236,719
• Administration & safety management	$ 75,374	$ 39,736	$ 35,638
• Post-progression & palliative care	$ 23,165	$ 22,148	$ 1,017
ICER (axi-cel vs. glofitamab)			$ 119,901

ICER = Incremental cost-effectiveness ratio, QALY = Quality-adjusted life years.

- In the base case analysis, the axi-cel arm of the model had discounted costs of $545,685 compared to the glofitamab arm's $272,311 (***Table 2***). The cost of treating with glofitamab varied as some patients with fast progression had lower treatment costs while patients with longer response received the full 12 cycles of treatment at a high cost.
- 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 glofitamab (4.15 versus 1.87).
- **The incremental cost effectiveness ratio (ICER) for axi-cel versus glofitamab was $119,901 per QALY, indicating that axi-cel would be considered cost-effective in the US payer setting.**
- The 2-year PFS in the model was estimated as 38% for axi-cel and 19% for glofitamab (***Figure 2***) with a median PFS of 0.51 and 0.41 years for axi-cel and glofitamab, respectively.
- In a scenario analysis with a standard parametric model for glofitamab, the ICER for axi-cel decreased to $103,891 suggesting that the relative durability of treatment response is a key model driver.

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

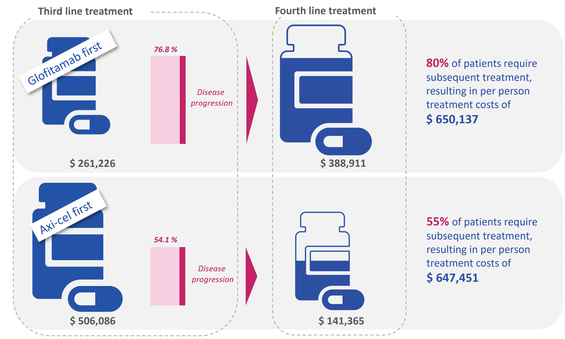


OS = Overall survival, PFS = Progression-free survival

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.
- **Analysis results suggest that a treatment sequence with axi-cel first, followed by glofitamab, leads to overall cost savings (*Figure 3*).**
- Despite lower average costs per patients starting treatment with glofitamab, the higher proportion of patients progressing from glofitamab, and requiring subsequent treatment makes a glofitamab first treatment sequence more costly compared to axi-cel in 3L with glofitamab as subsequent therapy.

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



CONCLUSIONS

- Based on extrapolation of the pivotal trial data, this simulation suggests that axi-cel is cost-effective compared to glofitamab in a 3L DLBCL setting at the commonly-cited $150,000 per QALY willingness-to-pay threshold for the US.
- Findings were driven by the projected survival and progression-free survival benefits of axi-cel, leading to QALY gains.
- 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, Gerson 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.