Poster 562

A United States (US) Cost-Effectiveness Analysis of Axicabtagene Ciloleucel Compared to Odronextamab in Third Line or Later (3L+) Diffuse Large B-Cell Lymphoma

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INTRODUCTION

- Patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) historically carry a poor prognosis. [1]
- Axicabtagene ciloleucel (axi-cel), the first autologous chimeric antigen receptor T-cell (CAR-T) therapy approved for patients with third line or beyond (3L+) R/R DLBCL in 2017, offers curative potential and has since also been approved for the treatment of second line (2L) R/R DLBCL in 2022. [2]
- The treatment landscape continues to evolve with odronextamab, a novel bispecific antibody, positioned for regulatory approval in the United States (US) following its approval by the European Medicines Agency for patients with 3L+ R/R DLBCL. [3]

OBJECTIVE

- To assess the relative cost-effectiveness of axi-cel versus odronextamab in patients with R/R 3L+ DLBCL.

METHODS

Model overview

- A discrete event simulation (DES) model, which simulates patients across 1L, 2L, and 3L treatment in DLBCL, previously evaluated cost-effectiveness of axi-cel versus glofitamab and epcoritamab. [4,5]
- This model was adapted to assess the cost-effectiveness of axi-cel versus odronextamab in patients with R/R 3L DLBCL from a US payer perspective.
  - Scenario analyses addressed the impact of uncertainty of odronextamab's cost and efficacy.

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

- To estimate quality-adjusted life years (QALYs), baseline sex- and age-matched utilities were adjusted by applying utility decrements for treatment-specific pre-progression (on and off treatment), post-progression, and death health states.
- Treatment data and costs were sourced from the literature and Micromedex, adjusted to 2023 US dollars (USD) (Table 1).
- Since odronextamab lacks a publicly available list price, its cost was benchmarked against epcoritamab, given similar treat-to-progression regimens.
  - In scenario analyses, the odronextamab price was reduced by 20-80% and the maximum treatment duration capped at 2 years.
- Costs and utilities were discounted at 3.0% annually, per US modeling guidelines. [6]

Table 1. Key cost inputs and sources

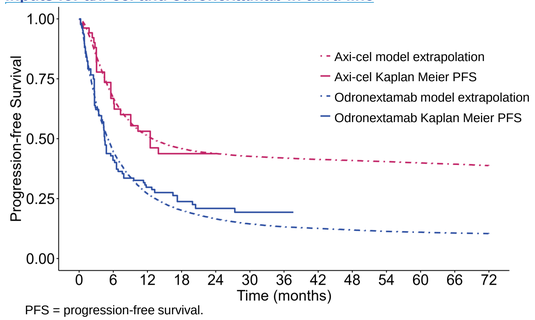
Model Input	Value	Source
Axi-cel drug acquisition costs, incl. chemotherapy and leukapheresis	$470,018	[7,8]
Axi-cel drug administration & safety management costs	$74,069	[8]
Odronextamab drug acquisition costs (cycle 1 / cycle 2-9 months / 9 months+), per cycle†	$2,350 / $45,677 / $22,838	[7]
Odronextamab drug administration costs (cycle 1 / cycle 2-9 months / 9 months+), per cycle†	$7,298 / $4,802 / $2,401	[7]
Odronextamab 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, ordronextamab was modeled as treat-to-progression.
‡ Safety management costs are assumed to incur in cycle 1 and are applied as one-off costs. Due to a lack of adverse event data for odronextamab, it was assumed to incur the same cost as epcoritamab as informed in [11].

Progression-free and overall survival inputs

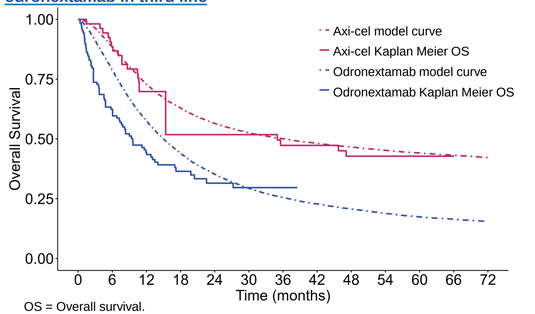
- Clinical data was leveraged from Phase 2 trials for axi-cel (ZUMA-1 [13]) and odronextamab (ELM-2 [14]). The base case analysis relied on progression-free survival (PFS) data derived from a matching-adjusted indirect treatment comparison (MAIC) (Figure 1). [15]
  - A scenario analysis was also performed using naïve data from these trials.
- Given uncertainty about the durability of response for odronextamab, a 10% cure fraction was assumed in the base case, consistent with analyses for epcoritamab and glofitamab. [4,5]
  - A scenario analysis tested a cure fraction of 15%, based on the proportion of ELM-2 patients with sustained complete response for 24 months.
- Survival after progression in 3L was modeled using the ZUMA-1 OS data, assumed representative of 3L post-progression patients across all treatments in the DLBCL setting.
  - Model fit was validated with MAIC-adjusted overall survival (OS) data and was satisfactory, being conservative for axi-cel (Figure 2). [15]

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



PFS = progression-free survival.

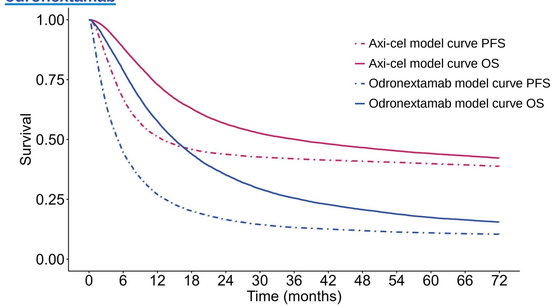
Figure 2. Kaplan Meier curves and modeled overall survival for axi-cel and odronextamab in third line



OS = Overall survival.

RESULTS

Figure 3. Progression-free and overall survival outputs for axi-cel and odronextamab



OS = Overall survival, PFS = progression-free survival.

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

	Axi-cel	Odronextamab	Incremental
Life years (LY)	7.46	3.27	4.19
Quality-adjusted life years (QALY)	5.85	2.25	3.60
Costs	$603,310	$1,134,778	-$531,468
Treatment costs	$470,018	$948,640	-$478,622
Administration & safety management	$111,345	$151,383	-$40,038
Post-progression & palliative care	$21,947	$34,755	-$12,808
ICER (axi-cel vs. odronextamab)			**Dominates***

ICER = incremental cost-effectiveness ratio, LY = Life years, MAIC = matching adjusted indirect comparison, QALY = Quality-adjusted life years.
* Expression refers to axi-cel being both more effective (higher QALY gains) and less costly.

Table 3. Cost-effectiveness results (discounted) for axi-cel versus odronextamab in scenario analyses, 2023 USD

Scenario	LYs	QALYs	Cost, $	ICER, $/QALY
Axi-cel				
Base case results (same as in Table 2)	*7.46*	*5.85*	*$603,310*	*Dominates**
Axi-cel naïve comparison (no MAIC adjustment)	6.86	5.38	$599,476	Dominates*
Odronextamab				
Base case results (same as in Table 2)	*3.27*	*2.25*	*$1,134,778*	*Dominates**
Odro cure fraction increased to 15%	3.90	2.80	$1,145,231	Dominates*
Odro price reduced to 80% of base case	3.27	2.25	$925,671	Dominates*
Odro price reduced to 60% of base case	3.27	2.25	$719,660	Dominates*
Odro price reduced to 40% of base case	3.27	2.25	$507,458	$26,626 / QALY
Odro price reduced to 20% of base case	3.27	2.25	$298,352	$84,711 / QALY
Max odro treatment time reduced to 2 years	3.27	2.25	$651,336	Dominates*

ICER = incremental cost-effectiveness ratio, LY = life year, MAIC = matching adjusted indirect comparison, Max = maximum, Odro = odronextamab, QALY = quality-adjusted life year.
* Expression refers to axi-cel being both more effective (higher QALY gains) and less costly.

- In the base case analysis, patients in the axi-cel arm had discounted costs of $603,310 versus $1,134,778 for patients in the odronextamab arm (Table 2). Projected PFS and overall survival were higher in the axi-cel arm, resulting in 7.46 life years (LYs) versus 3.27 LYs for odronextamab. QALYs were also higher for axi-cel compared to odronextamab (5.85 versus 2.25).
  - Axi-cel is therefore a dominant treatment option, meaning it is more efficacious and less costly than odronextamab.
- The 5-year PFS was estimated as 39.6% for axi-cel and 10.7% for odronextamab, with a median PFS of 1.05 and 0.40 years, respectively (Figure 3).
- Scenario analyses analyzed the impact of varying key parameters (Table 3):
  - Using unadjusted efficacy sources (i.e., no MAIC) produced very similar results, with axi-cel remaining the dominant treatment option.
  - Increasing the odronextamab cure fraction to 15%, improved survival with odronextamab, though axi-cel remained dominant (Table 3).
  - At reduced odronextamab costs of 80% and 60%, axi-cel was still dominant. For the 20% and 40% scenarios, the axi-cel incremental cost effectiveness ratios of $84,711 and $26,626 respectively, would still be considered cost-effective by prevailing US thresholds of $150,000/QALY.
  - Limiting the maximum treatment duration for odronextamab to 2 years lowered discounted costs in the odronextamab arm to $651,366, with axi-cel remaining the dominant treatment strategy.

CONCLUSIONS

- Results suggest that axi-cel is highly cost-effective compared to odronextamab for patients in a R/R 3L+ DLBCL setting in the US.
- Due to lower PFS with odronextamab, more patients require subsequent treatment, leading to higher downstream costs. Combined with a treat-to-progression strategy, this results in higher costs over a patient's lifetime compared to the upfront costs of axi-cel, while still resulting in inferior long-term clinical outcomes.
- These results reinforce the cost-effectiveness of axi-cel compared to all regulatory approved bispecific antibodies for patients with R/R 3L+ DLBCL to date.
- Future research is needed to confirm these findings when long-term survival and the published price of odronextamab become available.

LIMITATIONS

- There is no publicly available list price for odronextamab in the US, therefore it was benchmarked to that of epcoritamab. This assumption was tested by reducing the odronextamab cost by up to 20%.
- Median follow-up was much longer in the axi-cel trial (ZUMA-1; 63.1 months) [5] compared to the odronextamab trial (ELM-2; 32.8 months) [6]. Furthermore, patients were considerably younger in ZUMA-1 (median age: 58 year) compared to ELM-2 (median age: 67 years). The MAIC adjustment addresses these inter-trial differences, and the analysis was also run with no MAIC adjustment to assess its impact on the results.

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