THE COST-EFFECTIVENESS OF AXICABTAGENE CILOLEUCEL VERSUS STANDARD OF CARE AS SECOND-LINE THERAPY IN PATIENTS WITH LARGE B-CELL LYMPHOMA IN SWITZERLAND

Abstract category: Clinical hemato-oncology

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is a CD19-directed genetically modified autologous T cell immunotherapy, approved by Swissmedic for adult patients with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy.[1]
- In the pivotal phase 3, open-label, randomized controlled trial ZUMA-7 (NCT03391466), axi-cel demonstrated a clinically meaningful and statistically significant benefit versus standard of care (SoC; salvage chemoimmunotherapy followed by high-dose therapy with autologous stem cell rescue for responders) in patients with LBCL who were refractory to or had relapsed no more than 12 months after completion of first-line chemoimmunotherapy (2L DLBCL).[2]
- Additionally, axi-cel has been proven cost-effective and has been recommended for reimbursement by leading health technology agencies, including the National Institute for Health and Care Excellence in the United Kingdom and the Medical Services Advisory Committee in Australia.[3 - 5]

OBJECTIVES

- The objective of this study was to estimate the cost-effectiveness of axi-cel versus SOC in 2L DLBCL from the Swiss compulsory health insurance system perspective.

METHODS

- A partitioned survival model comprising the health states ‘event-free’, ‘post-event’, and ‘death’ was developed to model the costs and effects of axi-cel and SoC in 2L DLBCL patients.
- Time-to-event data were obtained from ZUMA-7 (primary OS analysis [Jan 2023 data cut]). Event-free survival (EFS), time-to-next therapy (TTNT) and overall survival (OS, median follow-up 47.2 months) were extrapolated beyond the trial follow-up period using mixture cure models (MCMs) (**Figure 1**).
- Model selection was based on statistical fit (using Akaike’s and Bayesian Information Criteria [AIC and BIC, respectively]) and the clinical plausibility of long-term extrapolation based on expert opinion.
- General population mortality rates to which a standardised mortality ratio (SMR) of 1.09[6] was applied were used to model mortality among the fraction of patients who were considered cured in the MCMs to reflect potentially higher rates of death in the long-term for all patients.
- Medical resource use and unit costs were sourced from the Swiss analysis & specialty lists (AL & SL), TARMED and Swiss DRG tariffs. Subsequent treatment costs were considered and were obtained from public sources. Subsequent treatment patterns were based on the ZUMA-7.

METHODS

- Health-state utility values were estimated from EuroQoL five-dimensions five-levels (EQ-5D-5L) data collected in ZUMA-7[7] and ZUMA-1[8] (3L+ DLBCL) for pre-event (0.892) and post-event (0.874), respectively.
- Patients who remained in the EFS state after 5 years were assumed to have achieved long-term remission, not require subsequent treatment, and revert to general population utility.
- The analysis used a health care perspective and a lifetime time horizon (50 years); costs and utilities were discounted at 3% per annum.
- Deterministic sensitivity and probabilistic sensitivity analyses were conducted to test the robustness of results.

RESULTS

- Axi-cel treatment of patients with DLBCL was associated with a per patient incremental QALY gain of 1.57 and incremental costs of 71,084 CHF compared to SoC (**Table 1**). As a result, axi-cel was cost-effective based on commonly cited willingness-to-pay thresholds (WTP) in Switzerland with an ICER of 45,228 CHF per QALY gained versus SoC.
- The difference in 5-year projected OS was 9.4% (52.5% vs. 43.1% for axi-cel and SoC, respectively).
- The model estimated 5-year EFS to be 37.6% and 16.8% for axi-cel and SoC, respectively.

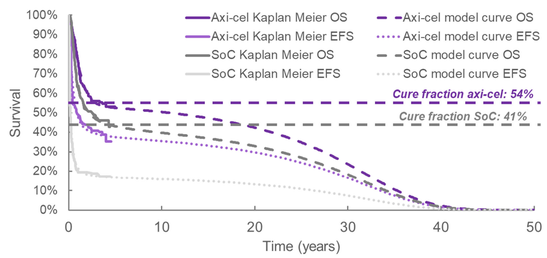
Table 1. Base case incremental outcomes

	Axi-cel	SoC	Difference
Total discounted LYs	**10.28**	**8.33**	**1.95**
Event-free	7.24	3.32	3.92
Post-event	3.05	5.01	-1.96
Total discounted QALYs	**8.65**	**7.08**	**1.57**
Event-free	6.04	2.77	3.26
Post-event	2.61	4.30	-1.29
Total discounted costs	**414,444 CHF**	**343,360 CHF**	**71,084 CHF**
2L treatment	318,199 CHF	49,786 CHF	268,412 CHF
3L+ CAR T treatment	-	209,937 CHF	-209,937 CHF
3L+ other treatment	44,035 CHF	35,084 CHF	8,951 CHF
Disease management	21,999 CHF	18,374 CHF	3,625 CHF
Adverse event	6,330 CHF	4,330 CHF	2,000 CHF
Terminal care	23,881 CHF	25,848 CHF	-1,967 CHF
ICER, axi-cel versus SoC			**45,228 CHF**

Axi-cel, axicabtagene ciloleucel; LY, life year; QALY, quality-adjusted life year; SoC, standard of care.

RESULTS

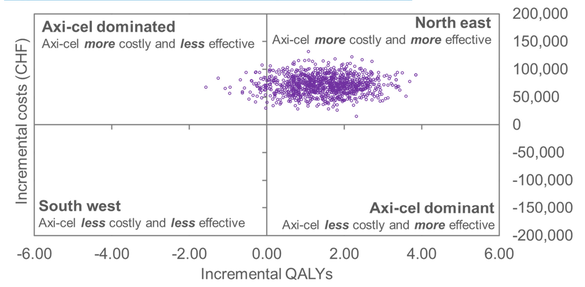
Figure 1. Modelled extrapolated survival



Axi-cel, axicabtagene ciloleucel; EFS, event-free survival; OS, overall survival; SoC, standard of care.

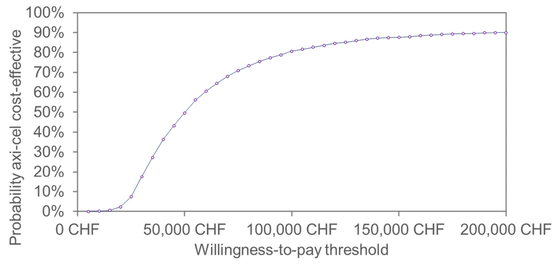
- The results were driven by better long-term survival of patients in the axi-cel arm, more time spent in the event-free state, and the avoidance of subsequent lines of CAR T.

Figure 2. Probabilistic sensitivity analysis (PSA)



Axi-cel, axicabtagene ciloleucel; QALY, quality-adjusted life year.

Figure 3. Cost-effectiveness acceptability curve



- Deterministic sensitivity analyses found that the ICER was most sensitive to CAR T therapy costs, the mean age at which patients enter the model and the utility post-progression**.**
- Results from PSA **(Figure 2)** showed that the model was robust to joint parameter uncertainty as the probabilistic mean ICER was closely in line with the deterministic base case (50,049 CHF vs 45,228 CHF).
- The probability of axi-cel being cost-effective is reported across an array of willingness-to-pay (WTP) thresholds in **Figure 3.**

CONCLUSIONS

- Over a lifetime horizon of 50 years, with an ICER of 45,228 CHF per QALY, treatment of patients with 2L DLBCL with axi-cel is cost-effective according to commonly cited WTP thresholds in Switzerland.
- This is because by treating in the 2L setting with axi-cel, patients experience a survival benefit and a better quality of life (QoL) in the long-term, whilst avoiding 3L+ use of CAR T which off-sets incremental costs.
- Axi-cel is a cost-effective alternative compared to SoC for treating adult patients with 2L DLBCL in Switzerland. Hence, axi-cel use in 2L DLBCL can be considered an efficient use of resources in Switzerland.

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DISCLOSURES

AG, BD, OE, and SV are employees and hold stocks of Gilead, the parent company of Kite. YRG, FvH, NJS, and RB are employees of the Maple Health Group, who received consulting fees from Kite and Gilead for this work.