Poster EE403

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

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is a CD19-directed genetically modified autologous T cell immunotherapy,[1] approved by the European Commission for adult patients with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) that relapses within 12 months from completion of, or is refractory to, first-line chemoimmunotherapy.[2]
- 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 and autologous stem cell transplantation in responders) in patients who were refractory to or had relapsed no more than 12 months after completion of first-line chemoimmunotherapy (2L r/r).[3]
- Additionally, axi-cel has been proven cost-effective and has been recommended for reimbursement in the treatment of 2L r/r DLBCL 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.[4 - 6]

OBJECTIVE

- The objective of this study was to estimate the cost-effectiveness of axi-cel versus SOC in 2L DLBCL from a German health care 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 trial (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).
- 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 extrapolations based on expert opinion.
- General population mortality rates to which a standardised mortality ratio (SMR) 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.
- Acquisition cost of considered treatments were sourced from the Lauer-Taxe. Subsequent treatment costs were considered and were obtained from the literature. Subsequent treatment patterns were based on the ZUMA-7 trial. In the absence of German-specific data for costs of managing adverse events, purchasing power parity for the UK and for Germany were used to convert 2023 UK costs.
- Health-state utility values were estimated from EuroQoL five-dimensions five-levels (EQ-5D-5L) data collected in ZUMA-7 and ZUMA-1 (3L+ LBCL) for the pre-event and post-event health state, respectively.
- Patients who remained in the EFS state after 5 years were assumed to have achieved long-term remission, do not require subsequent treatment, and revert to general population utility.
- The analysis used a lifetime time horizon (50 years), costs and utilities were discounted at 3% annually from a health care perspective.
- Deterministic and probabilistic sensitivity analyses were conducted on the incremental cost-effectiveness ratio (ICER) to assess the robustness of the results.

Table 1. Key model parameters

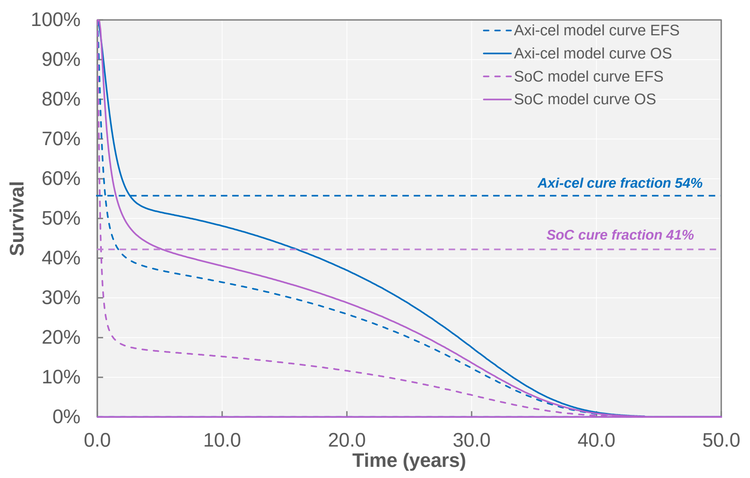
Model parameter	Base case
SMR to general population multiplier	1.09[7]
Utility on-treatment with axi-cel	0.781
Utility on-treatment with SoC	0.770
Utility off-treatment pre-event	0.786
Utility post-event	0.722

SMR, standardized mortality rate; SoC, standard of care.

RESULTS

- Axi-cel treatment of patients with DLBCL was associated with a per patient incremental QALY gain of 1.64 and incremental costs of € 85,255 compared to SoC. As a result, axi-cel was cost-effective based on commonly cited willingness-to-pay thresholds in Germany with an ICER of € 51,830 per QALY gained versus SoC.
- The difference in 5-year projected OS was 9.2% (51.6% vs. 42.5% for axi-cel and SoC, respectively)
- The model estimated 5-year EFS to be 37.0% and 16.5% for axi-cel and SoC, respectively.

Figure 1. Modelled extrapolated survival



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

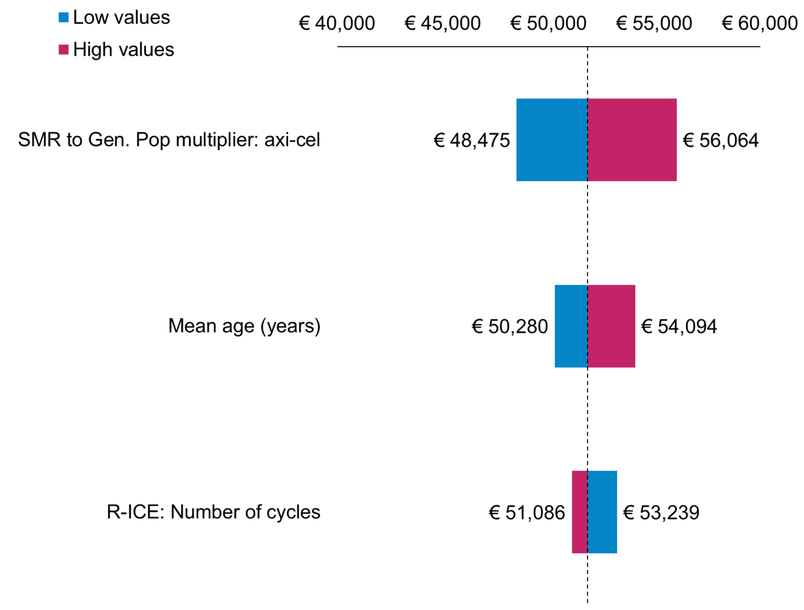
Table 2. Base case incremental outcomes

	Axi-cel	SoC	Difference
Total discounted LYs	**9.42**	**7.68**	**1.74**
Event-free	6.65	3.08	3.57
Post-event	2.77	4.61	-1.83
Total discounted QALYs	**7.41**	**5.76**	**1.64**
Event-free	5.46	2.52	2.94
Post-event	1.95	3.24	-1.29
Total discounted costs	**€ 312,999**	**€227,744**	**€ 85,255**
2L treatment costs	€ 266,375	€ 25,018	€ 241,357
3L+ CAR T treatment costs	€ 3,179	€ 163,823	-€ 160,644
3L+ other treatment costs	€ 26,701	€ 21,170	€ 5,531
Disease management costs	€12,938	€ 12,447	€ 491
Adverse event costs	€ 823	€ 2,090	-€ 1,267
Terminal care costs	€ 2,983	€ 3,196	-€ 213
ICER, axi-cel versus SoC			**€ 51,830**

LY, life year; QALY, quality-adjusted life year; 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.

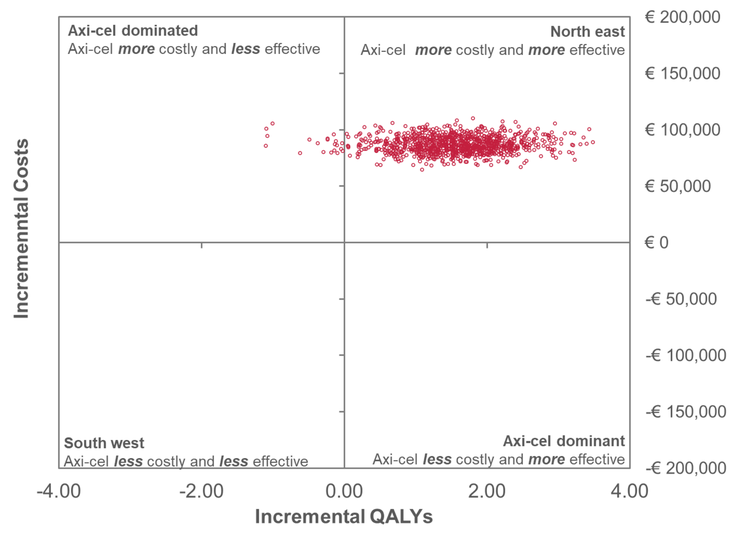
Figure 2. Deterministic sensitivity analysis



SMR, standardised mortality ratio; R-ICE, rituximab, ifosfamide, carboplatin, and etoposide

- Deterministic sensitivity analyses found that the ICER was most sensitive to the SMR applied to the general population mortality for long-term survivors for axi-cel, mean age, and the number of cycles of chemotherapy regimen R-ICE **(Figure 2).**
- Results from PSA **(Figure 3)** showed that the model was robust to joint parameter uncertainty as the probabilistic mean ICER was closely in line with the deterministic base case (€ 51,830 vs € 56,128).

Figure 3. Probabilistic sensitivity analysis



QALY, quality-adjusted life year.

CONCLUSIONS

- Over a lifetime horizon of 50 years, with an ICER of € 51,830 per QALY, treatment of 2L DLBCL (early relapses and refractory disease) with axi-cel is cost-effective considering commonly cited willingness-to-pay thresholds.
- In this study, this is primarily because by treating in the 2L setting, patients experience a survival benefit and a better 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 adult patients with 2L DLBCL in Germany. Hence, axi-cel use in 2L r/r DLBCL can be considered an efficient use of resources in Germany.
- Ongoing challenges include minimizing delays and barriers to access, as well as improving patient awareness of CAR T therapies.

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DISCLOSURES

FK has consulted and reports honoraria for Kite and Gilead; AE, LR, RW, SV, and BD 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.

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