Poster 14

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

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- Axicabtagene ciloleucel (axi-cel) is a CD19-directed genetically modified autologous T cell immunotherapy,[1] approved in Australia for patients with relapsed or refractory (r/r) large B-cell lymphoma (LBCL) and patients with r/r follicular lymphoma (FL) after two or more lines of systemic therapy.[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 with autologous stem cell rescue for responders) in patients who were refractory to or had relapsed no more than 12 months after completion of first-line chemoimmunotherapy (2L LBCL)).[3]
- 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 and the Medical Services Advisory Committee.[4 - 6]

- The objective of this study was to estimate the cost-effectiveness of axi-cel versus SOC in 2L LBCL from an Australian health care perspective.

- 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 LBCL 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).
- 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.
- A standardised mortality ratio (SMR) was applied to survival estimates to increase the hazard of death compared to the general population of the cure fraction in MCM and to reflect potentially higher rates of death in the long-term for all patients.
- Acquisition cost of considered treatments were sourced from Australian price databases. Subsequent treatment costs were considered and were obtained from public sources. Subsequent treatment patterns were based on the ZUMA-7. The cost of treatments not recommended were not included.
- 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 pre-event and post-event, 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 lifetime time horizon (30 years), costs and utilities were discounted at 5% annually from a health care perspective.
- Deterministic sensitivity analysis was conducted on the incremental cost-effectiveness ratio (ICER) and was presented as the percentage change from the base case.

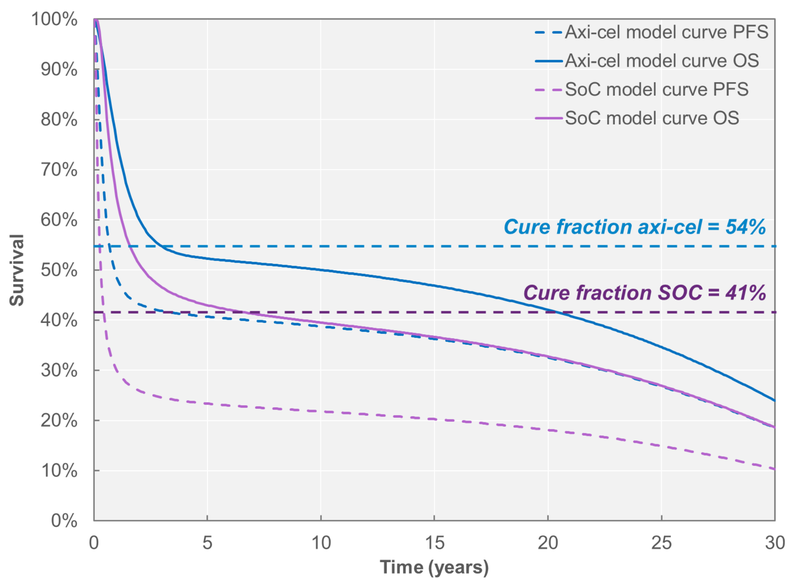
Table 1. Key model parameters

Model parameter	Base case
SMR to general population multiplier	1.09[7]
Utility on-treatment with axi-cel	0.883
Utility on-treatment with SOC	0.879
Utility off-treatment pre-event	0.891
Utility post-event	0.818

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

- Axi-cel treatment of patients with LBCL was associated with a per patient incremental QALY gain of 1.33. As a result, axi-cel was cost-effective with an ICER below $100,000 per QALY gained versus SOC.
- The difference in 5-year projected OS was 9.3% (52.3% vs. 43.0% % for axi-cel and SOC, respectively)
- The model estimated 5-year EFS to be 40.7% and 23.4% for axi-cel and SOC, respectively.

Figure 1. Modelled extrapolated survival



Axi-cel, axicabtagene ciloleucel; PFS, progression-free survival; OS, overall survival; SOC, standard of care.

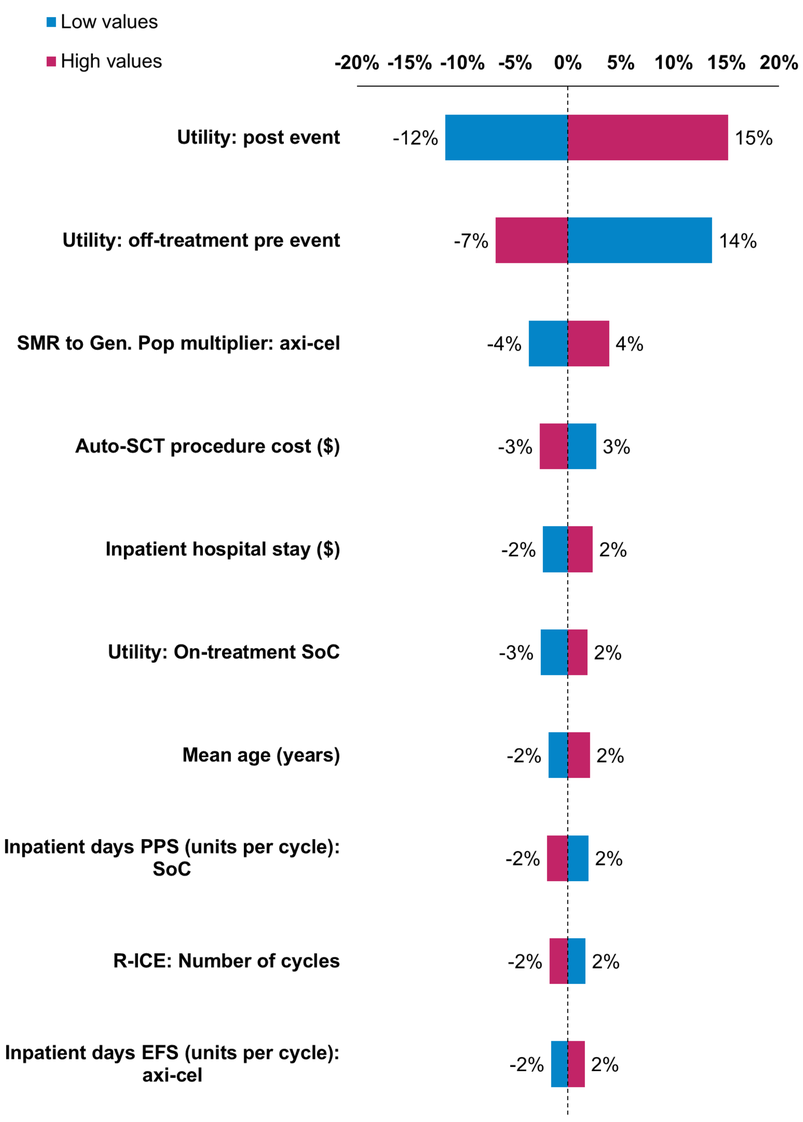
Table 2. Base case incremental outcomes

	Axi-cel	SOC	Difference
Total discounted LYs	**7.95**	**6.52**	**1.43**
Event-free	6.07	3.56	2.52
Post-event	1.88	2.97	-1.09
Total discounted QALYs	**6.82**	**5.49**	**1.33**
Event-free	5.31	3.11	2.20
Post-event	1.51	2.38	-0.87

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 in the SOC arm.

Figure 2. Deterministic sensitivity analysis



3L; third line treatment; auto-SCT, autologous stem-cell transplantation; axi-cel, axicabtagene ciloleucel; EFS, event-free survival; R-ICE, rituximab, ifosfamide, carboplatin, etoposide, SMR, standardized mortality rate; SOC, standard of care.

- Deterministic sensitivity analyses found that the ICER was most sensitive to the utility values of post and pre-event off treatment health states, the SMR applied to the general population mortality for long-term survivors for axi-cel, and the cost of autologous stem cell transplantation **(Figure 2)**.

- Over a lifetime horizon of 30 years, with an ICER well below $100,000 per QALY, treatment of 2L LBCL with axi-cel can be considered cost-effective.
- This is 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 can be considered cost-effective alternative compared to SOC for adult patients with 2L LBCL in Australia. Hence, axi-cel use in 2L LBCL can be considered an efficient use of resources in Australia.
- Reducing delays and barriers to access and increasing patient awareness of CAR T therapies are remaining challenges to address.

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DISCLOSURES

MA has consulted and reports honoraria for Kite/Gilead; AE, BN, 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/Gilead for this work.

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