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# The cost-effectiveness of axicabtagene ciloleucel versus standard of care as second-line therapy in patients with large B-cell lymphoma in Sweden

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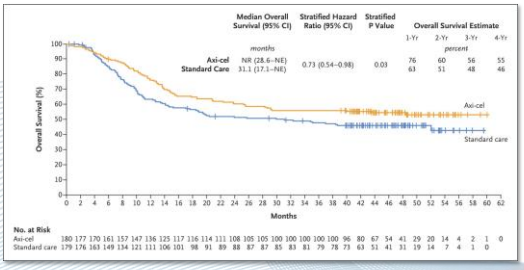
# Declaration of interests

- Viktor Hedlöf Kanje is an employee of Gilead Sciences and holds stock in Gilead Sciences


These are my disclosures

# This analysis was based on ZUMA-7: a phase III, international multicentre open-label clinical trial (NCT03391466)

**Axicabtagene ciloleucel (axi-cel) demonstrated a clinically meaningful and significantly improved event-free survival** (EFS) and **overall survival** (OS) versus standard of care (SoC) over a median follow up time of 47.2 months **in R/R large B-cell lymphoma** (LBCL), with a manageable safety profile.




Driven by its superior clinical benefit, **axi-cel has been recommended** as a **cost-effective treatment for 2L LBCL** in several countries:

- CADTH
- DMC
- HAS (based on CEESP assessment)
- NT Council (based on TLV assessment)
- NICE
- NoMA

***Source:*** Westin et al (2023). N Engl J Med.

***Abbreviations***: 2L = second line; axi-cel = axicabtagene ciloleucel; CADTH = Canadian Agency for Drugs and Technologies in Health; CEESP = Economic and Public Health Evaluation Committee; DMC = Danish Medicines Council; HAS = High Health Authority; LBCL = large B-cell lymphoma; R/R = relapsed or refractory; NICE = National Institute for Health and Care Excellence; NoMA = Norwegian Medicines Agency; NT = New Therapies; SoC = standard of care; TLV = The Swedish Dental and Pharmaceutical Benefits Agency.

# The presented analysis is based on the primary OS analysis from ZUMA-7, while the original HTA submission to TLV (and published manuscript) was based on interim data

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ORIGINAL RESEARCH

OPEN ACCESS

**Axicabtagene ciloleucel compared to standard of care in Swedish patients with large B-cell lymphoma: a cost-effectiveness analysis of the ZUMA-7 trial**

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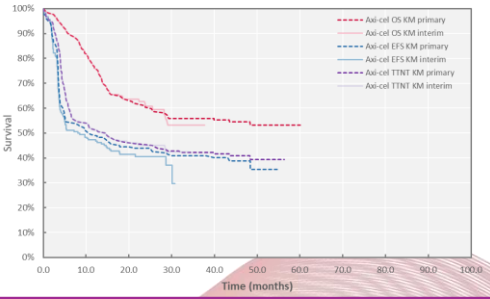
A **cost-effectiveness analysis based on interim data** (median follow up of **24 months**) showed that **axi-cel is cost-effective from a Swedish health care perspective compared to SoC in 2L LBCL** as the incremental cost-effectiveness ratio was well below the established willingness-to-pay threshold of SEK 1,000,000 in Sweden[1]

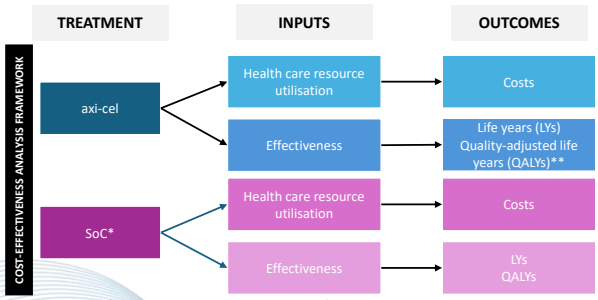



Longer-term follow-up (median 47.2 months) has resulted in **reduced uncertainty in long-term extrapolations**[2] and **confirms findings**[3] from previous analyses based on interim data

***Source:*** 1. Loftager et al (2023). J. Med. Econ.; 2. Patel et al (2023). Blood; 3. Oluwole et al (2024). J. Med. Econ.
***Abbreviations***: 2L = second line axi-cel = axicabtagene ciloleucel; LBCL = large B-cell lymphoma; OS = overall survival; SoC = standard of care; TLV = The Swedish Dental and Pharmaceutical Benefits Agency.

OBJECTIVE

# The objective of this study was to estimate the cost-effectiveness of axi-cel versus SoC in 2L LBCL from the Swedish healthcare perspective




*SoC was defined as salvage chemoimmunotherapy, followed by high-dose therapy with autologous stem cell transplant for responders
** A QALY combines both quality of life and life expectancy into a single index.

**ANALYSIS**

Incremental cost-effectiveness Ratio (ICER)

$$ICER = \frac{Costs_{axi-cel} - Costs_{SoC}}{QALYs_{axi-cel} - QALYs_{SoC}}$$

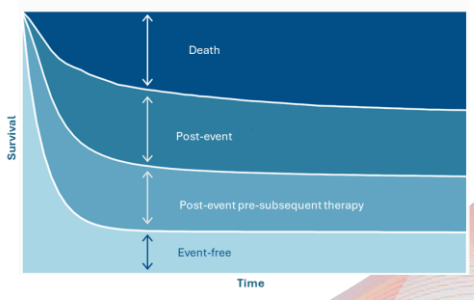
The cost-effectiveness analysis was conducted in **accordance with the Swedish recommended reference case** inclusive of an outcome (costs and benefits) **discount rate of 3% per year**

***Abbreviations***: 2L = second line; axi-cel = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; LBCL = large B-cell lymphoma; QALY = quality adjusted life years; LY = life year; SoC = standard of care.

# A 4-state partitioned survival model was developed to estimate costs and outcomes over a life-time time horizon

**Clinically validated mixture cure models** (MCM) were used to **extrapolate** ZUMA-7 time-to-event data: event free survival (**EFS**), time-to-next treatment (**TTNT**) and overall survival (**OS**) of axi-cel and SoC.

The **proportion of patients** in each health state is **defined by portioning survival** projections of **the EFS, TTNT**, and **OS curves**.

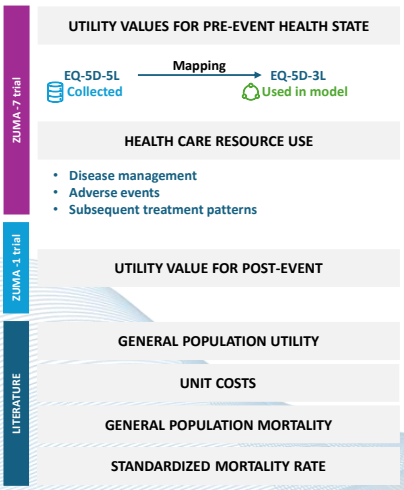



**MCMs are used to estimate the proportion of patients** for whom **mortality matches that of the general population** and the **proportion of patients** with a poor prognosis for whom **parametric extrapolation is performed**



***Abbreviations***: axi-cel = axicabtagene ciloleucel; EFS = event free survival; MCM = mixture cure model; OS = overall survival; SoC = standard of care; TTNT = time to next treatment.

# Health care resource use was collected in the ZUMA-7 trial, adapted to a Swedish healthcare setting, and validated by a Swedish clinical expert

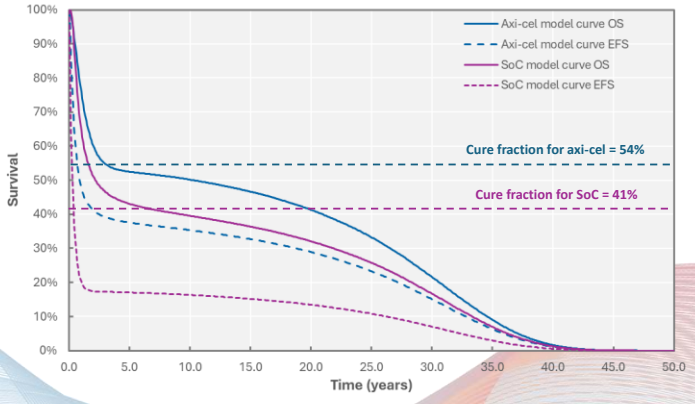



The **cost of axi-cel** was the **list price/pharmacy purchase price** (SEK 3,380,000)

| KEY MODEL PARAMETERS | BASE CASE ANALYSIS |
|---|---|
| SMR to general population multiplier | 1.09 |
| 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 |

***Abbreviations:*** axi-cel = axicabtagene ciloleucel; SoC = standard of care; EFS = event-free survival; SMR = standardized mortality rate.

# Results of the MCM-based extrapolation showed axi-cel led to a substantial survival benefit compared to SoC over a life-time horizon



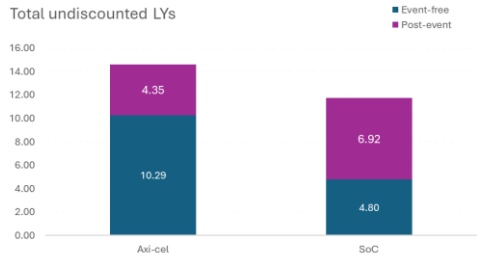

The **difference in 5-year projected OS was 9.4%** (52.5% vs. 43.1% for axi-cel and SoC, respectively). The model estimated **5-year EFS to be 37.5% and 17.0% for axi-cel and SoC**, respectively.

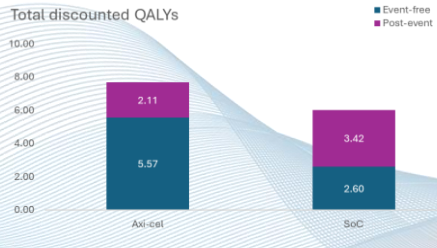


***Abbreviations***: axi-cel = axicabtagene ciloleucel; EFS = event free survival; MCM = mixture cure model; OS = overall survival; SoC = standard of care.

CLINICAL RESULTS

# 2L treatment of LBCL patients with axi-cel was associated with an undiscounted LY and discounted QALY gain of 2.90 and 1.65 compared to SoC



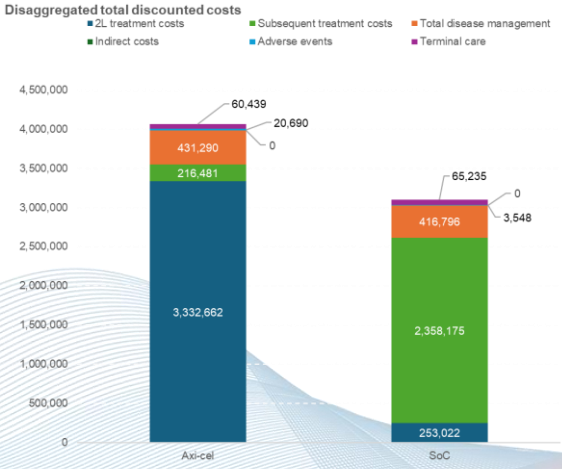




| | Axi-cel | SoC | Difference |
|---|---|---|---|
| **Total undiscounted LYs** | **14.63** | **11.73** | **2.90** |
| Event-free | 10.29 | 4.80 | 5.48 |
| Post-event | 4.35 | 6.92 | -2.58 |
| **Total discounted QALYs** | **7.68** | **6.03** | **1.65** |
| Event-free | 5.57 | 2.60 | 2.96 |
| Post-event | 2.11 | 3.42 | -1.32 |



***Abbreviations***: 2L= second-line; 3L+ = third-line; axi-cel = axicabtagene ciloleucel; LBCL = large B-cell lymphoma; LY = life year; QALY = quality-adjusted life year; SoC = standard of care.

# Axi-cel is associated with an incremental cost of SEK 964,786; the 2L treatment costs of axi-cel are offset by the substantial use of 3L+ CAR T therapy in the SoC arm




| | Axi-cel | SoC | Difference |
|---|---|---|---|
| **Total discounted costs** | **SEK 4,061,652** | **SEK 3,096,776** | **SEK 964,786** |
| 2L treatment costs | SEK 3,332,662 | SEK 253,022 | SEK 3,079,640 |
| Subsequent 3L+ CAR T therapy costs | - | SEK 2,157,533 | SEK -2,157,533 |
| Other subsequent treatment costs | SEK 216,481 | SEK 200,642 | SEK 15,839 |
| Disease management costs | SEK 431,290 | SEK 416,796 | SEK 14,494 |
| Adverse event costs | SEK 20,690 | SEK 3,548 | SEK 17,142 |
| Terminal care costs | SEK 60,439 | SEK 65,235 | SEK -4,797 |

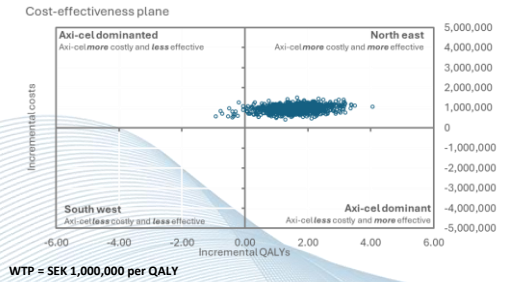


***Abbreviations***: 2L= second-line; 3L+= third-line plus; axi-cel = axicabtagene ciloleucel; CAR T = chimeric antigen receptor T-cell; SoC = standard of care.

# Axi-cel is cost-effective with an ICER of SEK 585,663 per QALY gained versus SoC

**The results** were **driven** by **better long-term survival with axi-cel**, with its **upfront costs offset by the use of 3L+ CAR T in the SoC arm**

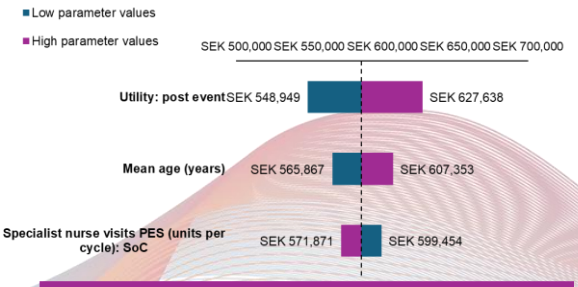
## PROBABILISTIC SENSITIVITY ANALYSIS




**WTP = SEK 1,000,000 per QALY**

At a willingness-to-pay of **SEK 1,000,000 per QALY gained, axi-cel is 84% likely to be cost-effective.**

## DETERMINISTIC SENSITIVITY ANALYSIS




Deterministic sensitivity analyses found that the **ICER was most sensitive** to the **utility value in the post event health state**, the **mean age** at the model start and the **number of specialist nurse visits** for SoC

***Abbreviations***: 2L= second-line; axi-cel = axicabtagene ciloleucel; CAR T = chimeric antigen receptor T-cell; QALY = quality adjusted life year; SoC = standard of care; WTP = willingness to pay

CONCLUSIONS

# Axi-cel is a cost-effective treatment compared to SoC for adult patients with 2L R/R LBCL and leads to an efficient use of resources in Sweden

The **ZUMA-7 trial demonstrated significantly improved event-free survival and overall survival for axi-cel** compared with **SoC in 2L LBCL**, with a manageable safety profile

Treatment with axi-cel is a **cost-effective strategy** in the **2L treatment of LBCL in Sweden** as the **ICER of SEK 585,663 (~€50,000) is well below** the established willingness to pay threshold of **SEK 1 million/QALY gained**

**Results are driven** by **longer survival and a better quality of life in patients treated with axi-cel** in 2L, whilst **avoiding use of subsequent CAR T-cell therapy**, which off-sets incremental costs

**The results** are **robust as demonstrated in the scenario and sensitivity analyses**, also **confirmed by the TLV assessment**, and **recommendation for use by the NT-council**

Driven by its superior clinical benefit, **axi-cel has been recommended** as a **cost-effective treatment for 2L LBCL** in several countries such as **Canada**, **Denmark**, **France**, **Norway** and **England** and **Wales**

***Abbreviations***: 2L= second-line; 3L+ = third-line plus; axi-cel = axicabtagene ciloleucel; CAR T = chimeric antigen receptor T-cell; ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life years; LY = life year; SoC = standard of care; NT = New Therapies; TLV = The Swedish Dental and Pharmaceutical Benefits Agency.

# Acknowledgements


- We would like to thank the patients of the ZUMA-7 trial, their caregivers, and families as well as the clinical trial investigators and their team members
- This study was sponsored by Gilead Sciences