Poster
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Cost-Effectiveness of Axicabtagene Ciloleucel (axi-cel) vs Standard of Care for Adult Patients with Relapsed or Refractory Follicular Lymphoma as 4th or Later Line Treatment in Sweden

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BACKGROUND

- Follicular lymphoma (FL) is an indolent non-Hodgkin lymphoma with an annual incidence of around 250 patients in Sweden [1]. Patients who relapse or are refractory (r/r) after three or more lines of therapy (4L+) have a reported median survival of 32.2 months on standard of care (SoC) [2].
- Axicabtagene ciloleucel (axi-cel) is an autologous single infusion anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved in the EU for large B-cell lymphoma and follicular lymphoma [3].
- ZUMA-5 is a single arm, multicentre, phase 2 trial investigating use of axi-cel in adult patients with histologically confirmed indolent non-Hodgkin lymphoma, including follicular and marginal zone lymphomas, previously treated with two or more lines of therapy [4]. In the EU, axi-cel is approved for 4L+ FL, corresponding to a subset [N=75] of the enrolled ZUMA-5 ITT population [3].
- SCHOLAR-5 is a multi-country retrospective observational cohort comprised of r/r FL patients sourced from real-world clinical sites to enable comparisons versus ZUMA-5 [5].

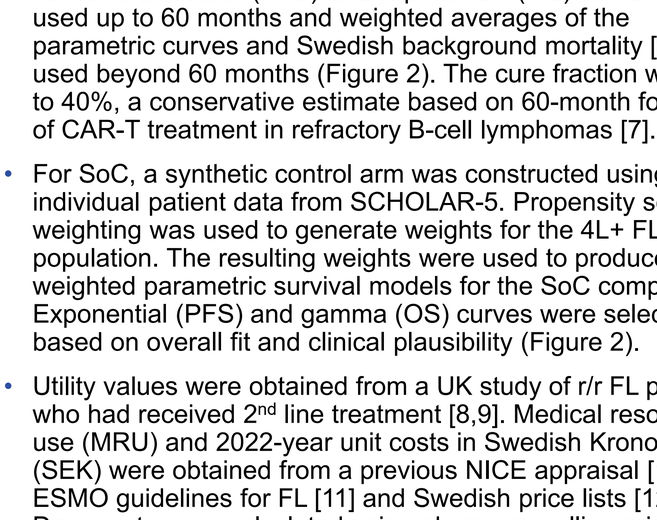
OBJECTIVES

- To estimate the cost-effectiveness of axi-cel as 4L+ treatment for r/r FL versus SoC in Sweden.

METHODS

- A de novo partitioned-survival model (Figure 1), consisting of three mutually exclusive health states: progression-free survival (PFS), progressed disease (PD) with sub-states for on- and off-treatment, and death was developed in Microsoft Excel®.
- State transitions were determined based on independently fitted parametric models of PFS and OS using 36-month and 24-month data from the ZUMA-5 and SCHOLAR-5 ITT populations. Parametric model selection was guided by statistical and visual fit, and by clinical plausibility.
- To capture the potential for long-term survivors, a piecewise cure model was used to extrapolate PFS and OS for the axi-cel cohort. Weibull (PFS) and exponential (OS) curves were used up to 60 months and weighted averages of the parametric curves and Swedish background mortality [6] were used beyond 60 months (Figure 2). The cure fraction was set to 40%, a conservative estimate based on 60-month follow-up of CAR-T treatment in refractory B-cell lymphomas [7].
- For SoC, a synthetic control arm was constructed using individual patient data from SCHOLAR-5. Propensity score weighting was used to generate weights for the 4L+ FL population. The resulting weights were used to produce weighted parametric survival models for the SoC comparator. Exponential (PFS) and gamma (OS) curves were selected based on overall fit and clinical plausibility (Figure 2).
- Utility values were obtained from a UK study of r/r FL patients who had received 2nd line treatment [8,9]. Medical resource use (MRU) and 2022-year unit costs in Swedish Kronor (SEK) were obtained from a previous NICE appraisal [10], ESMO guidelines for FL [11] and Swedish price lists [12-14]. Drug costs were calculated using pharmacy selling prices [15-17]. Treatment mix for the SoC basket was based on market research conducted on behalf of Kite Pharma [18] (Table 1).
- The patients entered the model at a mean age of 59.8 years and 37% were female based on an interim analysis of ZUMA-5 [19]. Model outcomes in terms of costs in SEK, life-years (LY) and quality-adjusted life-years (QALYs) were estimated over a life-time horizon of 40 years and discounted at the recommended annual rate of 3% using a Swedish healthcare perspective [20].

Figure 1. CE model structure



Tx: treatment

Figure 2. axi-cel and SoC OS curves

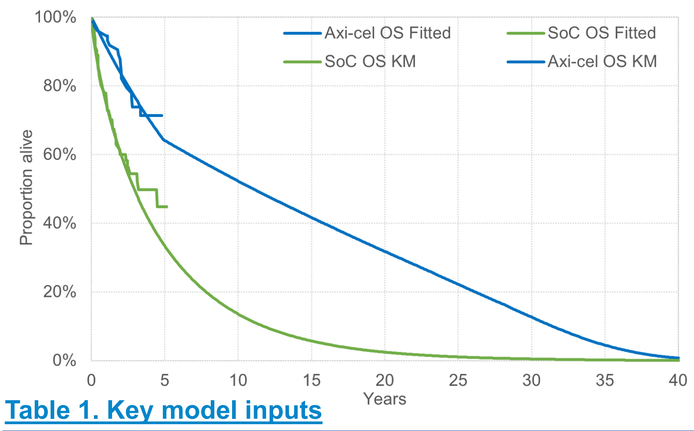


Table 1. Key model inputs

	Input	Source
axi-cel costs		
Leukapheresis	SEK 23,447	[14]
Drug acquisition	SEK 3,380,000	[17]
Conditioning chemo (3 days)	SEK 36,948	[3,12]
CAR-T infusion	SEK 1,757	[13]
Hospitalization (10.4 days)	SEK 107,567	[12]
Total axi-cel*	SEK 3,461,562	
SoC costs (tx % weight / tx dur months)		
R-lena (26.4% / 11.04)	SEK 128,311	[15,18,21]
Allo-SCT (22.3% / N/A)	SEK 739,018	[12,18]
R-benda (21.4% / 5.52)	SEK 174,844	[15-16,18,22]
R mono (12.4% / 1.15)	SEK 145,554	[15,18,21]
ASCT (7.3% / N/A)	SEK 251,763	[12,18]
O-benda (6.4% / 5.52)	SEK 409,184	[15-16,18,23]
R-borte (3.2% / 5.75)	SEK 351,198	[15,18,24]
R-CVP (0.3% / 5.52)	SEK 189,132	[15-16,18,25]
R-CHOP (0.3% / 5.52)	SEK 233,542	[15-16,18,25]
Total SOC basket (100% / 4.81)*	SEK 311,373	
Monthly administration of SoC drugs	SEK 7,678	[13]
Other costs		
Monitoring (freq per year induc / main / PD)		
Hematologist visit (12 / 4 / 12)	SEK 3,560	[10-12]
Diagnostic tests (12 / 4 / 12)	SEK 562	[10-12]
CT scans (2 / 1 / 2)	SEK 1,484	[10-12]
AE management* (axi-cel)	SEK 44§	[14,18,24-29]
AE management* (SoC)	SEK 19,332	[14,18,24-29]
PD treatments, incl admin* (axi-cel)	SEK 271,193	[13,15-16,18,21-26]
PD treatments, incl admin* (SoC)	SEK 271,193	[13,15-16,18,21-26]
End of life care*	SEK 77,794	[30]
Health-state utility values		
Progression-free	0.805	[8-9]
Progressed disease, on Tx	0.620	[8-9]
Progressed disease, off Tx	0.736	[8-9]

*One-off cost in the model, §All axi-cel AEs except hypogammaglobulinemia were assumed to be covered by the hospitalization cost.

RESULTS

- In the base case scenario, the incremental cost-effectiveness ratio (ICER) was SEK 680,001 (Table 2). Axi-cel and SoC were associated with 7.85 and 2.99 QALYs respectively, resulting in an incremental QALY gain of 4.87 in favor of axi-cel. Total costs for axi-cel and SoC amounted to SEK 4,263,520 and SEK 952,663 respectively, resulting in total incremental costs of SEK 3,310,856. Treatment costs were the largest cost items alongside monitoring costs for both axi-cel and SoC.
- The ICER was most sensitive to mean patient age, progression-free utility, piecewise cure fraction, choice of parametric distribution for OS and a shorter time horizon (Table 3 and Figure 3). The likelihood of axi-cel being cost-effective compared to SoC was 99% at the relevant 1 million SEK willingness-to-pay threshold for r/r FL in Sweden (Figure 4) [31].

Table 2. Cost-effectiveness results (axi-cel vs SoC)

	axi-cel	SoC	Incremental results
Health outcomes			
Total life-years	**10.18**	**4.17**	**6.00**
LYs in PFS	7.10	0.78	6.31
LYs in PD	3.08	3.39	-0.31
Total QALYs	**7.85**	**2.99**	**4.87**
QALYs in PFS	5.71	0.63	5.08
QALYs in PD	2.14	2.36	-0.22
Cost outcomes (SEK)			
Total PF costs	**3,833,701**	**441,724**	**3,391,978**
Total treatment costs*	3,461,562	311,373	3,150,189
Administration	0	72,131	-72,131
Monitoring	372,095	38,887	333,208
Adverse events	44	19,332	-19,288
Total PD costs	**429,818**	**510,940**	**-67,172**
Treatment	186,439	230,780	-44,341
Administration	27,585	34,146	-6,561
Monitoring	161,541	177,813	-16,271
End-of-life costs	54,253	68,202	-13,949
Total costs	**4,263,520**	**952,663**	**3,310,856**
Cost-effectiveness (SEK)			
Cost per LY gained			**551,483**
Cost per QALY gained (ICER)			**680,001**

All costs and health outcomes were discounted at 3% per annum.
*Axi-cel treatment costs includes leukaphereses, acquisition, conditioning, infusion and hospitalization

Table 3. Scenario analyses (axi-cel vs SoC)

Parameter	Base case	Scenario	ICER (SEK/QALY)
Base case	-	-	**680,001**
Starting age	60 yrs	70 yrs	874,649
Time horizon	40 yrs	5 yrs	3,159,004
		10 yrs	1,464,637
		15 yrs	1,006,584
		20 yrs	822,546
		30 yrs	696,950
PFS distribution for axi-cel	Piecewise Weibull	Exponential	681,993
		Gompertz	663,164
		Log-logistic	675,174
		Log-normal	671,078
		Gen gamma	662,863
		Gamma	682,033
OS distribution for axi-cel	Piecewise Exponential	Gompertz	709,283
		Log-logistic	688,588
		Log-normal	666,009
		Weibull	699,470
		Gen gamma	700,552
		Gamma	696,006
PFS distribution for SoC	Exponential	Gompertz	679,998
		Log-logistic	675,819
		Log-normal	676,744
		Weibull	679,996
		Gen gamma	676,987
		Gamma	679,998
OS distribution for SoC	Gamma	Exponential	640,880
		Gompertz	1,512,371
		Log-logistic	790,518
		Log-normal	800,545
		Weibull	708,978
		Gen gamma	1,162,491
Discount rates	Cost: 3%, QALYs 3%	Costs 5%; QALYs 5%	786,216
		Costs 5%; QALYs 0%	416,184
Population	ITT	mITT	1,159,808
Drug wastage	Yes	No	642,232
Frequency treatment cost accrual	One-off lump sum	Monthly	607,031
Include AE disutility	Yes	No	640,859

Scenarios for axi-cel PFS and OS distributions assume piecewise model with 40% cure fraction at 60 months. Scenarios for SoC PFS and OS distributions assume standard parametric models.

Figure 3. One-way sensitivity analysis (axi-cel vs SoC)

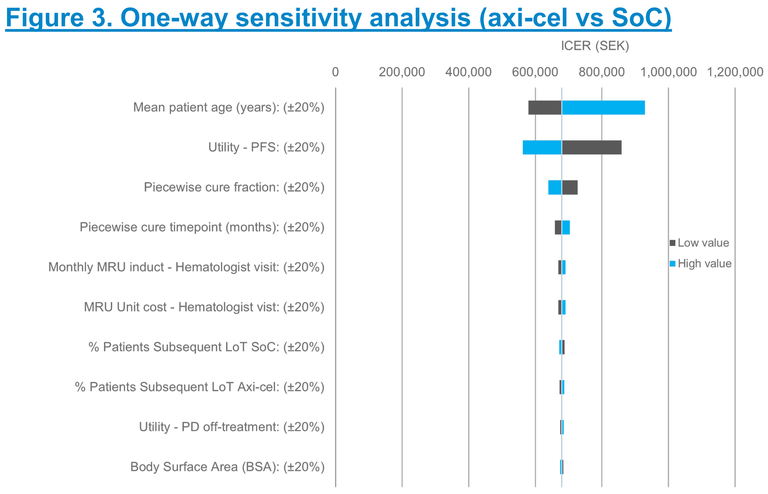
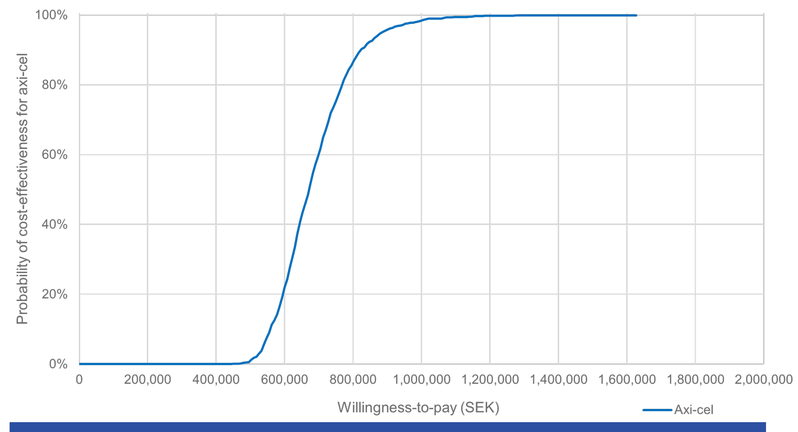


Figure 4. Cost-effectiveness acceptability curve for axi-cel



CONCLUSIONS

- Axi-cel is a cost-effective 4L+ treatment alternative to SoC for adults with r/r FL in Sweden. Cost-effectiveness results were similar to another axi-cel indication assessed by the Swedish HTA agency in 2018 (3rd line treatment for diffuse large B-cell lymphoma: company base case ICER of SEK 657,112/QALY gained) [30].
- Uncertainty around long-term survival and the potential for cure will decrease with longer follow-up in ZUMA-5.

DISCLOSURES

O.E., V.H.K., B.D., K.C. are paid employees of Gilead Sciences & Kite pharma.

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