EUROPEAN HEMATOLOGY ASSOCIATION

INTRODUCTION

Large B-cell lymphoma (LBCL) is the most common histological subtype of non-Hodgkin lymphoma.¹ About 40% LBCL patients become refractory or relapse (R/R) following first-line (1L) treatment and for nearly 30 years, the standard-of-care (SOC) for these patients has been platinum-based chemotherapy ideally followed by high-dose therapy plus autologous stem-cell transplantation (ASCT).² However, not all R/R LBCL patients are eligible for SOC and among those who respond, only a small proportion have sustained remission.³

In the ZUMA-7 phase III clinical trial, axicabtagene ciloleucel (axi-cel) demonstrated statistically significant survival benefits over SOC.⁴ However, its economic value to Singapore's multi-payer healthcare system is currently unknown.

AIM

- Assess cost-effectiveness of axi-cel versus SOC for treatment of adults with R/R LBCL from Singapore's healthcare system perspective.
- Estimate net financial implication to the Singapore healthcare system from introducing axi-cel as a treatment for adults with R/R LBCL within 12 months of 1L chemoimmunotherapy.

METHOD

Cost-effectiveness analysis

- A mixture-cure partition survival model was developed to evaluate the costeffectiveness of axi-cel vs SOC over a lifetime horizon. The model, with monthly duration cycles, comprised three mutually exclusive health states: event-free, post-event and death.
- Clinical outcomes data were from ZUMA-7 trial (47.2-months follow up).⁴ \bullet
- Utility values were sourced from literature, with discount rate of 3% applied to all costs and health outcomes in line with Singapore ACE guideline.⁵
- Healthcare resource utilization and direct medical costs included conditioning chemotherapy, hospitalization, drugs, and management of adverse events (costs presented in 2023 Singapore dollars [S\$]; where applicable, exchange rate of US\$1 = S\$1.367 [spot rate at time of analysis: Sep 2023] was used)⁶
- Outcomes considered include life years (LYs), quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs).
- Parameter uncertainty was assessed using deterministic and probabilistic sensitivity analyses.
- In absence of a formal willingness-to-pay (WTP) threshold in Singapore, the cost-effectiveness threshold suggested by the World Health Organization (WHO), based on gross domestic product (GDP) per capita, was used.⁷ A treatment strategy in Singapore can be considered highly cost-effective at an ICER less than 1 × GDP per capita (S\$113,779 [US\$83,238]).⁸

Budget impact analysis

Financial implications of introducing axi-cel into Singapore's healthcare system was analysed over a 5-year period. Patient numbers were projected based on epidemiology data, published literature and clinical expert opinions.

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RESULTS

Outcomes, costs and ICER

• In the base case analysis over a lifetime horizon, axi-cel generated 1.72 incremental QALYs at an incremental cost of S\$130,433 (US\$95,423). (Table 1). The resultant ICER is S\$75,910 (US\$55,534) per QALY gained, which is below WHO's WTP threshold of 1 × GDP per capita for a treatment strategy to be considered highly cost effective.

Table 1: Base case results (discounted)

	Axi-cel	SOC	Difference
Life Years (Total)	9.96	8.49	1.46
Event-free	7.03	3.31	3.72
Post-event	2.93	5.18	-2.25
Quality-adjusted life years (Total)	8.24	6.52	1.72
Event-free	6.19	2.89	3.30
Post-event	2.05	3.64	-1.58
Total costs	S\$569,652	S\$439,219	S\$130,433
Second-line treatment-related	S\$505,050	S\$63,303	S\$441,747
Subsequent treatment-related	S\$33,092	S\$344,516	-S\$311,423
Disease management	S\$28,343	S\$22,012	S\$6,331
Other costs	S\$3,166	S\$9,388	-S\$6,222
ICER, axi-cel versus SOC	S\$75,910 (US\$55,534) per QALY		

Sensitivity analysis

Base case results were sensitive to patients receiving axi-cel in third line (3L) treatment setting. (Figure 1).

Figure 1: Sensitivity analysis

Low values	High values		ICER [S\$/QALY; WT
		S\$ 40,000	S\$ 60,00
3L SoC arm: %	receiving Yescarta (67%, 74%	ő, 81%)	S\$ 57,398
	Utility: post event (0.65, 0.72	2, 0.79)	
SMR to Gen. Po	p multiplier: axi-cel (1.01, 1.09	9, 1.17)	
Utility: off-t	reatment pre event (0.74, 0.82	2, 0.90)	
3L axi-cel arm: 9	% receiving Allo-SCT (3%, 8%	ő, 13%)	
SMR to Gen. F	Pop multiplier: SoC (1.01, 1.09	9, 1.17)	
3L axi-cel arm: %	receiving Auto-SCT (5%, 11%	ő, 17%)	
3L SoC arm:	% receiving Allo-SCT (1%, 4	%, 7%)	
3L SoC arm:	% receiving Auto-SCT (1%, 4	%, 8%)	
3L SoC arm: %	% receiving Pola-BR (8%, 13%	ő, 19%)	
3L – third line treatme Singapore dollars	ent; SCT – stem cell transplant; OS – o	overall survival; MC	CM - Mixture cure model; SO

CONCLUSION

At WTP thresholds recommended by WHO, results of this analysis suggest that axi-cel can be considered a highly cost-effective allocation of healthcare resources in Singapore with manageable budget impact compared to SOC in patients with LBCL refractory to or relapsing within 12 months of 1L chemoimmunotherapy.

Disclaimer: Product registration conditions differ internationally. Axicabtagene ciloleucel is approved for the treatment of R/R diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) in Singapore.⁹

Cost-effectiveness and Budget Impact Analyses of Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma in Singapore

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Budget impact analysis

- increasing to 30 patients in year 5.
- (Figure 2B)

Figure 2: Budget impact analysis (Total impact and impact of subsequent treatment)

A) Total budget impact of current vs future practice





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• 19 patients were estimated to be treated with axi-cel in second-line (2L) setting Year 1,

• At these patient numbers, introducing axi-cel to Singapore's public healthcare system for 2L LBCL is expected to increase annual expenditure by ~17% from S\$21.7 million (US\$15.9 million; without axi-cel) to S\$25.4 million (US\$18.6 million; with axi-cel) in Year 5. (Figure 2A) with projected annual net budget impact ranging from S\$2.5 million (US\$1.8 million) to S\$ 3.7 million (US\$2.7 million) during the first 5 years of introduction of axi-cel (Figure 2A).

• The SOC 'current practice' scenario showed higher increasing subsequent treatment costs, increasing from S\$15.3 million (US\$11.2 million) to S\$17.1 million (US\$12.5 million) per year over 5 years, whereas 2L axi-cel treatment showed a reduction in 3L treatment costs from S\$9.7 million (US\$7.1 million) to S\$7.8 million (US\$5.7 million) per year over the 5 years.

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