Axicabtagene Ciloleucel As Second-Line Treatment For Relapsed/ Refractory Large B-Cell Lymphoma In Spain: A Cost-Effectiveness Analysis

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INTRODUCTION

- At least 40% of treated patients with diffuse large-B cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBCL) do not respond or develop relapsed disease (R/R) after first-line treatment[1].
- Axicabtagene ciloleucel (axi-cel), an anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, has been approved by the European Medicines Agency for the second-line treatment of adult patients with refractory or early relapsed DLBCL and HGBL, based on the results observed in ZUMA-7[2,3].

OBJECTIVE

- This study aimed to assess the cost-effectiveness of axi-cel versus standard of care (SoC) for the treatment of DLBCL and HGBCL in patients who are relapsed or refractory to first-line treatment in Spain.

METHODS

- A partitioned survival mixture cure model (PS-MCM) comprising three health states (event-free, post-event and death) was used to estimate, in monthly cycles, the costs and outcomes in terms of life-years gained (LYG) and quality-adjusted life-years (QALY), accumulated over a lifetime horizon.
- The model compared axi-cel with salvage chemotherapy followed by high-dose chemotherapy and autologous stem-cell transplantation (ASCT), and subsequent treatments.
- Long-term survival was extrapolated using a Log-logistic and Gamma MCMs distributions for axi-cel and SoC event free survival (EFS) curves, respectively, while the OS curve was adapted to a Generalised Gamma MCM distribution for both therapies. The cure fraction was estimated using logistic regression.
- The time to next treatment (TTNT) curve was used to estimate the initiation of subsequent treatment and was extrapolated using a Log-logistic MCM distribution for both therapies.
- The efficacy data for axi-cel and SoC was extracted from the ZUMA-7 clinical trial[3], using the interim EFS, OS and TTNT data (18 Mar 2021 cut-off).
- The utility values assigned for each health state were obtained from literature (Table 1)[4,5].
- The perspective of the analysis was the Spanish healthcare system.
- Direct healthcare costs (€, 2022) considered in the model were: axi-cel and SoC related costs, subsequent treatment costs, disease management costs, adverse event (AE) management costs and palliative care (Table 1). Axi-cel related costs included leukapheresis (97% of patients), bridging therapy (36.1%), lymphodepleting chemotherapy (91%), CAR T acquisition (90%) and CAR T administration and monitoring (90%). SoC related costs included drug acquisition, drug administration, leukapheresis (50%), high dose chemotherapy (35.8%) and ASCT (34.6%).
- Only cytokine release syndrome and neurological events, grade 3 or higher, were considered as AEs in the axi-cel arm[3].
- Drug acquisition costs were calculated based on public ex-factory prices[6], with national mandatory deduction applied (4%)[7]. Unit costs were derived from local cost databases[6,8].
- An expert panel in the haemato-oncology field was consulted to establish healthcare resource consumption.
- An annual discount rate of 3% was applied to costs and health outcomes[9].
- In order to test the model's robustness, probabilistic sensitivity analysis (PSA) was performed.

Table 1. Model inputs

Costs (€/2022)	
Axi-cel related costs[6,7,8]	
Acquisition cost	€313,920*
Leukapheresis	€1,025
Bridging therapy	€2,599
Lymphodepleting chemotherapy	€1,249
Administration and monitoring	€9,794
SoC related costs[6,7,8,10]	
Chemotherapy (19% R-DHAP, 42% R-ESHAP, 31% R-GDP, 8% R-ICE)	€4,063
Administration	€2,443
High dose chemotherapy	€9,205
ASCT (procedure and annual monitoring)	€79,358
Subsequent treatment total cost[6,7]	
After axi-cel	€32,754
After SoC	€233,412
Health states management costs[8]	
Event free with axi-cel (€/month)	€305
Event free with SoC (€/month)	€527
Post-event with axi-cel (€/month)	€537
Post-event with SoC (€/month)	€352
Adverse event grade ≥3 management costs[8]	
Cytokine release syndrome	€2,077
Neurological events	€24
Palliative care costs[10]	€6,267
Utility values[4,5]	
Event free: on treatment with axi-cel	0.74
Event free: on treatment with SoC	0.67
Event free: off treatment	0.82
Post-event	0.71

**Axi-cel cost was based on list price with a 4% of mandatory deduction applied[6,7].*
AE, adverse event; ASCT; autologous stem-cell transplantation; axi-cel, axicabtagene ciloleucel; R-DHAP, (rituximab, dexamethasone, high doce cytarabine, cisplatin); R-ESHAP (rituximab, etoposide, methylprednisolone, cisplatin, cytarabine); R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin); R-ICE (rituximab, ifosfamide, carboplatin, etoposide). SoC, standard of care.

RESULTS

- Axi-cel yielded 10.00 LYG and 7.85 QALY per patient compared with SoC which provided 8.28 LYG and 6.04 QALY per patient (Table 2).
- In terms of costs, axi-cel accrued an additional €85,587 per patient compared to SoC (Table 2).
- Subsequent treatment costs were higher among those patients receiving SoC in the second-line, because a high proportion of patients were treated with CAR T therapies in following lines (Table 2).
- The incremental cost-effectiveness ratio of axi-cel versus SoC was €49,627/LYG and the incremental cost-utility ratio was €47,309/QALY.
- PSA results were consistent with the results from the base case in terms of total costs and QALYs (Figure 1).

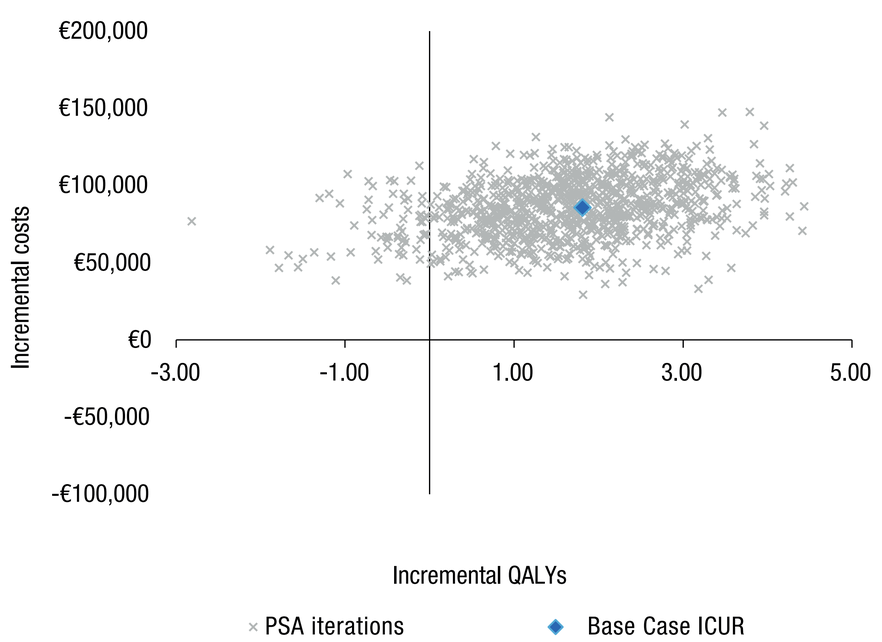
Table 2. Base case results

	Axi-cel	SoC	Incremental
Total LYG	**10.00**	**8.28**	**1.72**
Total QALYs	**7.85**	**6.04**	**1.81***
Total costs per patient	**€343,581**	**€257,994**	**€85,587**
Axi-cel related costs	€294,326	€0	€294,326
SoC related costs	€0	€40,889	-€40,889
Subsequent treatment	€18,598	€184,632	-€166,034
CAR T related	€0	€179.988	-€179.988
Salvage chemotherapy	€18,598	€4.643	€13.954
Health state management	€26,112	€27,748	-€1,636
AEs management	€140	€0	€140
Palliative care	€4,406	€4,726	-€319
ICER (axi-cel vs SoC)	**€49,627/LYG**		
ICUR (axi-cel vs SoC)	**€47,309/QALY**		

**Incremental QALYs are larger than incremental LYGs because QALYs in the SoC arm are largely accrued in the post-event health state.*

Axi-cel, axicabtagene ciloleucel; CAR T, chimeric antigen receptor T-cell; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio; LYG, life years gained; QALY, quality-adjusted life year; SoC, standard of care.

Figure 1. Probabilistic sensitivity analysis results



ICUR, incremental cost-utility ratio; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year.

CONCLUSIONS

- Compared to SoC, axi-cel has shown an improvement in health outcomes in terms of LYG and QALY.
- Axi-cel is a potentially cost-effective alternative to SoC for the treatment of adults with R/R LBCL in Spain.

REFERENCES

1. Tilly H, et al. Ann Oncol. 2015;26:116-25.
2. EMA. https://www.ema.europa.eu/en/documents/product-information/yescarta-epar-product-information_en.pdf
3. Locke FL, et al. N Engl J Med. 2022;386(7):640-54.
4. Roth JA, et al. J Med Econ. 2018;21(12):1238-45.
5. NICE. https://www.nice.org.uk/guidance/ta567
6. Bot Plus 2.0. https://botplusweb.portalfarma.com/
7. Real Decreto-Ley 8/2010. http://www.boe.es/boe/dias/2010/05/24/pdfs/BOE-A-2010-8228.pdf
8. eSalud. http://www.oblikue.com/bddcostes/
9. López-Bastida J, et al. Eur J Health Econ. 2010;11:513–20
10. Ortega M. http://digibug.ugr.es/handle/10481/40272

DISCLOSURES

- Martín García-Sancho A. has received honoraria from Roche, BMS/Celgene, Janssen, Gilead/kite, Takeda, Eusa Pharma and Novartis; conference and consulting fees from Roche, BMS/Celgene, Kyowa Kirin, Clinigen, Eusa Pharma, Novartis, Gilead/Kite, Incyte, Lilly, Takeda, ADC Therapeutics America, Miltenyi, Ideogen, Abbvie.
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- Pardo C. and Martín-Escudero V. are employees of Gilead Sciences Spain.