EE513

Cost-Effectiveness of Axicabtagene Ciloleucel and Tisagenlecleucel for Relapsed or Refractory Large B-Cell Lymphoma – Exploring the Impact of Country Settings and Performance-Based Managed Entry Agreements

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INTRODUCTION

- Patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) used to have a poor prognosis[1]. Chimeric Antigen Receptor T-cell (CAR-T) therapy is a promising treatment option for these patients, demonstrating high response rates and durable remissions.
- In August 2018 the EMA approved the first two CAR-T products, axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel), to treat adult patients with R/R LBCL after ≥2 lines of systemic therapy, based on the results of the pivotal phase 2 trials ZUMA-1 and JULIET.[2,3]
- In the UK and the Netherlands axi-cel and tisa-cel have become standard of care for patients with R/R LBCL after ≥2 lines of systemic therapy.[4,5]
- Indications are rapidly expanding and moving to earlier lines and new products are becoming available.
- However, the high costs of CAR-T (list price of ±€ 320 000 per product) raise concerns and strategies to improve affordability are needed.

AIM

To evaluate the cost-effectiveness of two CD19-directed CAR-T products, axi-cel and tisa-cel, compared to the prior standard of care for R/R LBCL after ≥2 lines of systemic therapy, and the impact of country settings and performance-based managed entry agreements (MEAs)

METHODS

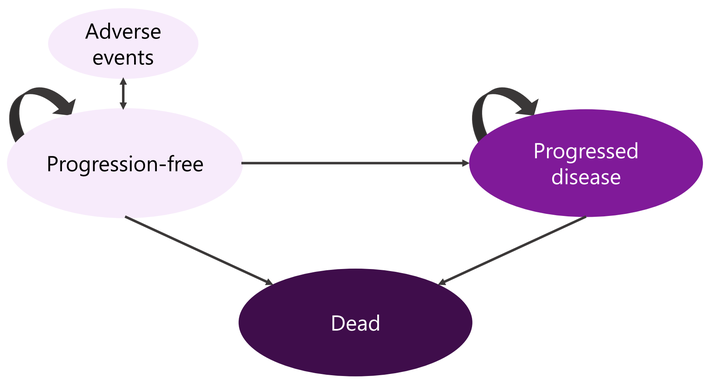
- Decision-analytic modeling was used to compare the cost-effectiveness of axi-cel and tisa-cel with the prior standard of care (pSoC) for adult patients with R/R LBCL after ≥2 lines of systemic therapy from 2 perspectives:

The Dutch healthcare setting (societal perspective)

The UK* healthcare setting (healthcare perspective)

** England*

- Total costs, effects (life years and quality-adjusted life years (QALYs)) and incremental cost-effectiveness ratios (ICERs) were estimated using a partitioned survival model* with three health states:



**The model was developed using R software (Version 4.2.2)*

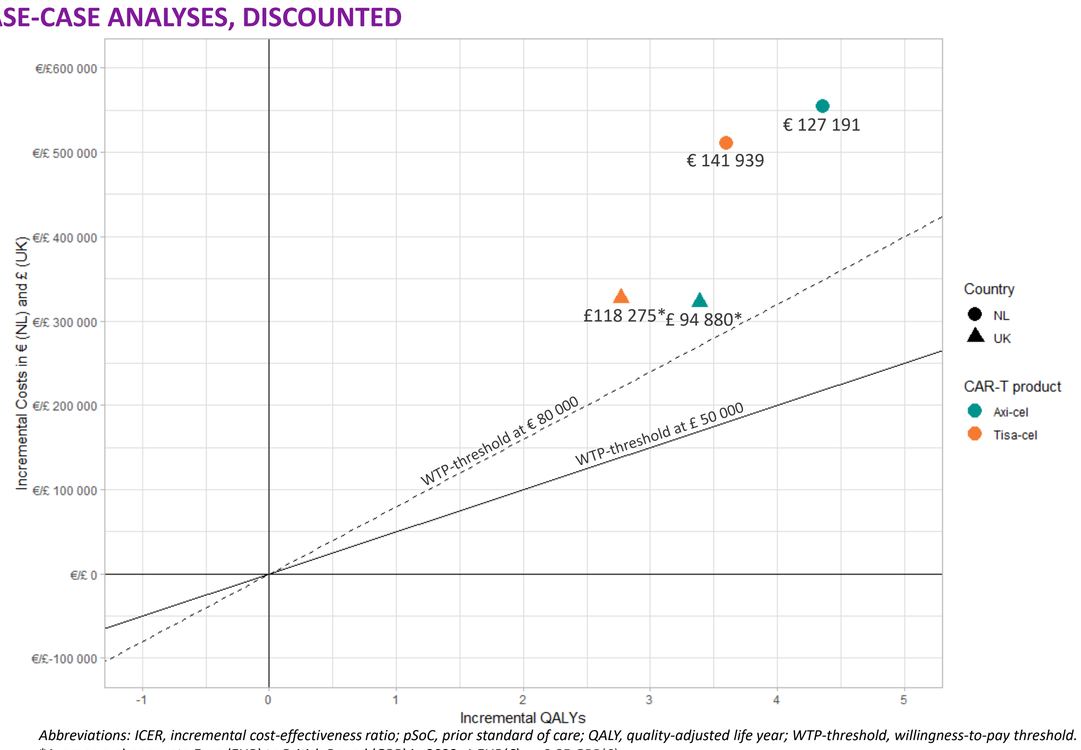
- Sensitivity and scenario analyses were conducted to assess uncertainties and the impact of two performance-based MEAs:

Performance-based MEA: **PARTIAL REFUND**	Performance-based MEA: **PAYMENT IN INSTALLMENTS**
Partial refund of 50% of acquisition costs	Payment in 3 installments (acquisition costs divided in 3 equal parts)
Condition: Refund for a patient who died within the first year after CAR-T infusion	**Condition:** Payment conditional on if a patient is alive and progression-free
Timepoint: M12 after CAR-T infusion	**Timepoint:** D0, M6 and M12 after CAR-T infusion

RESULTS

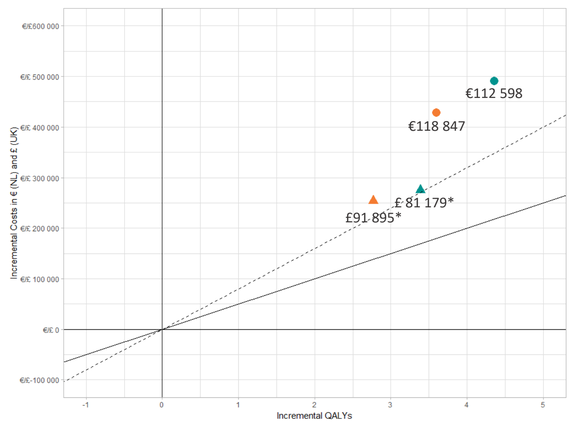
Incremental costs, QALYs and ICERs of axi-cel and tisa-cel compared to pSoC in the UK and the Netherlands

BASE-CASE ANALYSES, DISCOUNTED

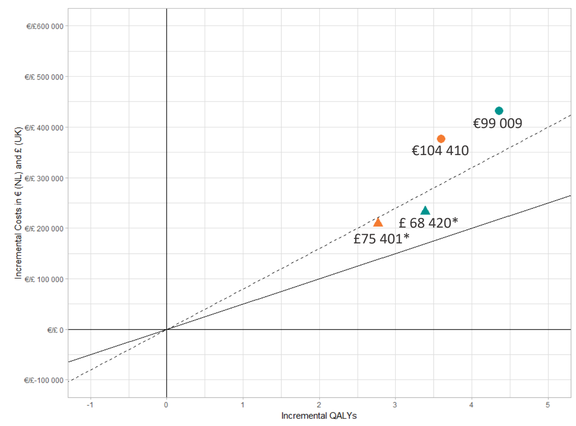


Abbreviations: ICER, incremental cost-effectiveness ratio; pSoC, prior standard of care; QALY, quality-adjusted life year; WTP-threshold, willingness-to-pay threshold.
*Average exchange rate Euro (EUR) to British Pound (GBP) in 2022: 1 EUR(€) = ±0.85 GBP(£)

PERFORMANCE-BASED MEA: PARTIAL REFUND



PERFORMANCE-BASED MEA: PAYMENT IN INSTALLMENTS



CONCLUSION

- Both CAR-T products were not cost-effective mainly due to their high costs.
- Axi-cel resulted in a lower ICER compared to tisa-cel due to greater health benefits.
- By incorporating performance-based MEAs the ICER for axi-cel and tisa-cel in both countries decreased, but both axi-cel and tisa-cel were still not cost-effective.
- Differences among countries were primarily influenced by differences in discount rates and perspectives (healthcare vs societal).
- Next steps include validating the input and assumptions with clinical experts.

REFERENCES

1. Crump M, Neelapu SS, Farooq U, et al. Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. *Blood* 2017; 130(16): 1800–1808.; 2. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): A single-arm, multicentre, phase 1–2 trial. *Lancet Oncol* 2019; *20*: 31–42.; 3. Schuster SJ, Tam CS, Borchmann P, et al. Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): A multicentre, open-label, single-arm, phase 2 study. *Lancet Oncol.* **2021**; *22*: 1403–1415.; 4. Kuhnl A, Roddie C, Kirkwood AA, et al. A national service for delivering CD19 CAR-T in large B-cell lymphoma–The UK real-world experience. *Br. J. Haematol* **2022;** *198*: 492–502.; 5. Spanjaart AM, Pennings ERA, Mutsaers PGNJ, et al. The Dutch CAR-T Tumorboard Experience: Population-Based Real-World Data on Patients with Relapsed or Refractory Large B-Cell Lymphoma Referred for CD19-Directed CAR T-Cell Therapy in The Netherlands. *Cancers* 2023; 15.17: 4334.

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