Cost-effectiveness analyses (CEAs) of CAR-T therapies over the past four years: what's new?

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INTRODUCTION

- The Chimeric antigen receptor (CAR) T-cell therapy is a personalized gene therapy that consists in collecting T cells from the patient's own blood, via a process known as apheresis, and to genetically modify and multiply them in laboratory before infusing them back to the patient[3].
- CAR-T cell therapies have improved outcomes for people living with hematological cancers and seemed to present better clinical performance in comparison to standard treatments[1,4,5]
- Nevertheless, with list prices of approximately 373,000 dollars USD (346,700 EUR) in the United States and 320,000 EUR in Europe, CAR T-cell therapies belong with the most expensive cancer treatments[2]
- Due to the specificities surrounding these treatments and their clinical potential, their evaluation requires special attention notably regarding their economic viability and value for money, both for patients and for health systems.
- This systematic literature review (SLR) of health economic evaluations of CAR-T therapies aimed to understand all the implications of the economic evaluation of these treatments as well as the challenges and criticisms identified in the evaluations

OBJECTIVE

The objective of this systematic literature review was to identify the standard health economic methods used, methodological challenges associated with the assessment of these treatments, and the critiques made by the HTA agencies.

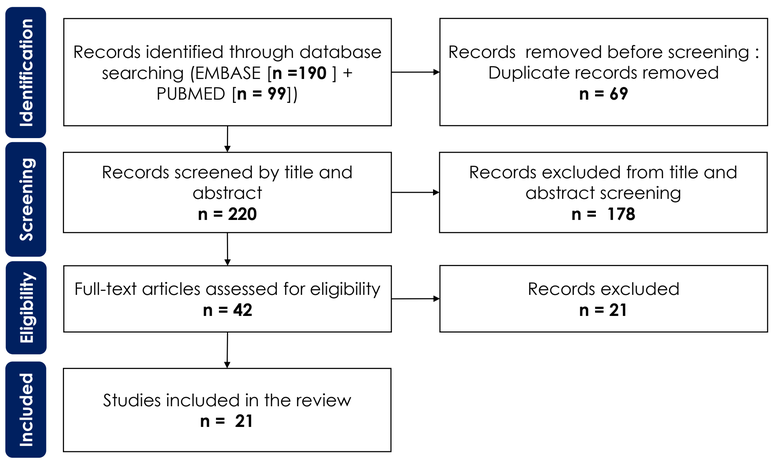
METHODS

- The study question was formalized according to the PICOS framework (Population, Interventions, Comparisons, Outcome[s] and Study design), in line with the PRISMA guidelines **(Figure 1)**:
  - **Population :** Adults, adolescents, and children treated by CAR-T therapy
  - **Intervention :** Approved CAR-T therapies
  - **Comparators:** No restriction
  - **Outcomes :** incremental cost-effectiveness ratio (ICER), incremental cost-utility ratio (ICUR), Quality-adjusted life years (QALYs) and/or life years, costs
  - **Study type :** economic evaluations (Cost-consequence, cost-minimization, cost-effectiveness, cost-utility, cost-benefit)
- Letters, editorials, and other publications not reporting on an original study were excluded.
- Structured search terms have been developed for three different databases: EMBASE (via EMBASE.com), MEDLINE (via EMBASE.com) on May 31st, 2022, and MEDLINE in Process (via pubmed.com) on 26th May 2022.
- Title and abstract screening and full-text screening were conducted independently by two reviewers. Discrepancies were resolved by discussion.

Results

- Twenty-one publications were included, assessing tisagenlecleucel (n=12), axicabtagene ciloleucel (n=5), and brexucabtagene autoleucel (n=3) and both tisagenlecleucel and axicabtagene independently (1) **(see Figure 2)**.
- Two studies compared two CAR-T therapies, and 19 assessed a CAR-T treatment vs. the standard of care (SoC).

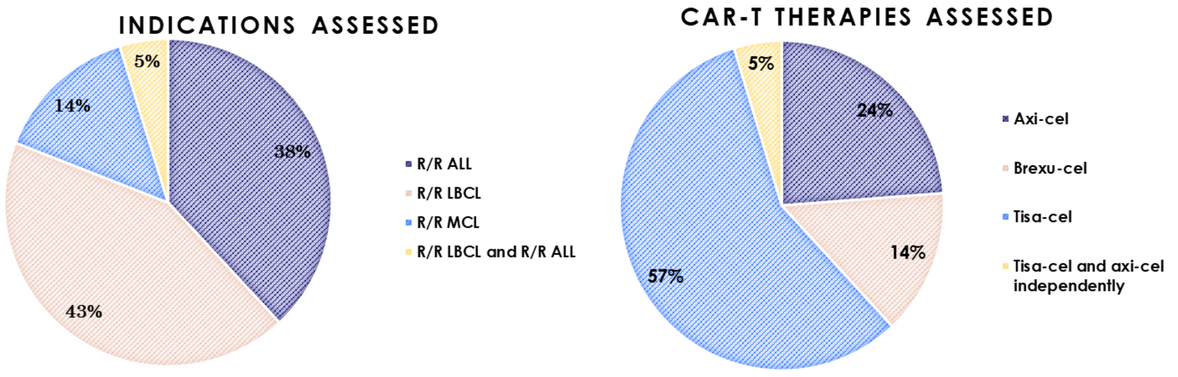
Figure 1. PRISMA diagram for study selection



Abbreviations: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

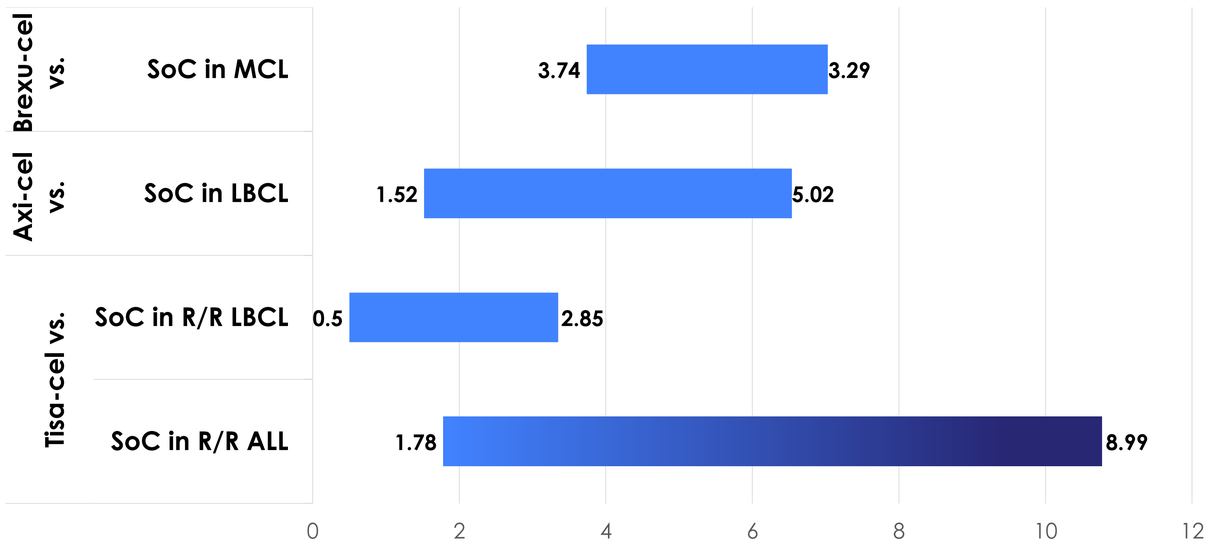
- Studies related to large B-cell lymphoma (LBCL, n=9), acute lymphoblastic leukemia (ALL, n=8), and mantle cell lymphoma (MCL, n=3). One study investigate CAR-T in both LBCL and ALL.
- The studies identified covered several countries including the United States (n=10), Canada (n=2), Japan (n=2), Singapore (n=2), the United Kingdom, Spain, China, the Netherlands, and Switzerland (n=1 for each).
- Most studies relied on partitional survival models (n=16), and six were based on semi-Markov models (2 microsimulations, 4 cohort models).
- Survival extrapolation mostly rely on mixture cure models (n=17). 3 studies used standard parametric functions and 1 study opposed scenarios with different methods including spline models, parametric functions and mixture cure model .
- Main limitations highlighted in the studies were the lack of head-to-head comparative data, short follow-up data, small numbers of patients, and uncertainty in long-term extrapolation

Figure 2. Characteristics of included studies



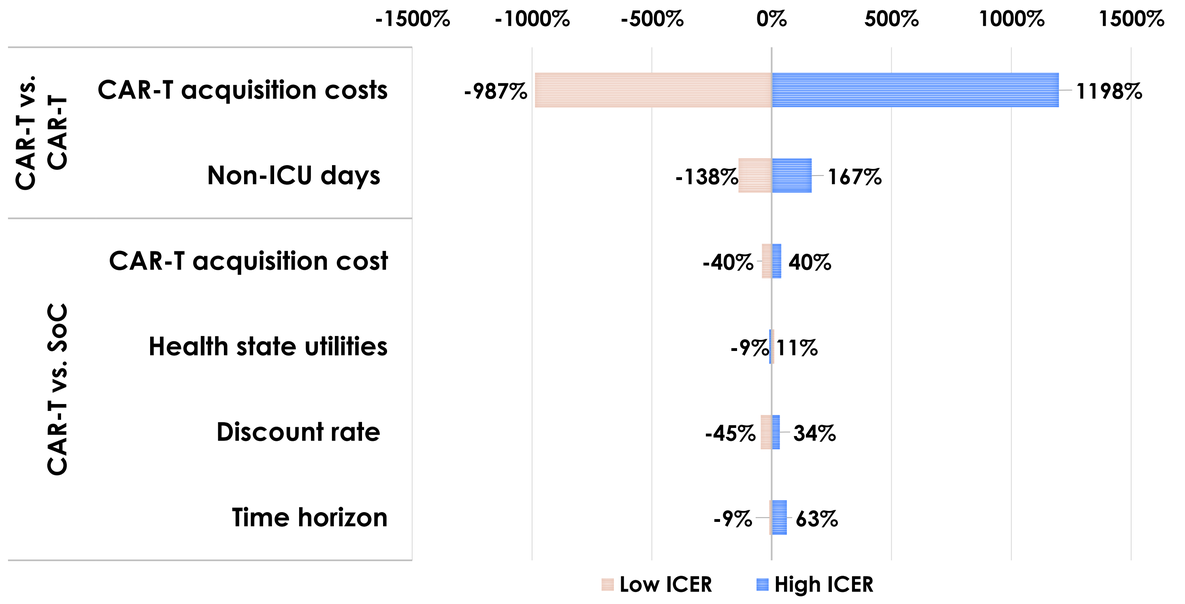
- Incremental LYs and QALYs ranged between 0.807 – 13.27 and 0.509 - 10.77, respectively, for studies comparing tisagenlecleucel vs. SoC (n=10). For studies comparing axicabtagene ciloleucel vs. SoC (n=3), LYs were 1.89 - 6.9 and QALYs 1.52 - 6.54 **(see Figure 3)**.
- Drivers of the CAR-Ts comparison were the acquisition cost and pre-progression utility while other tested factors had a limited impact. For studies comparing CAR-Ts to SoC, the most influential parameters included discount rate (n=10), health states utilities (n=10), cost of CAR-T therapies (n=9) and time horizon (n=4) **(see Figure 4)**.
- Studies comparing CAR-Ts to SoC would mostly consider CAR-T cost-effective (n=18)

Figure 3. Incremental QALYs range by type of comparison



Abbreviations: R/R : Relapse/Refractory; ALL : Acute lymphoblastic leukemia; LBCL: Large B-cell lymphoma; MCL :Mantle cell lymphoma; Tisa-cel Tisagenlecleucel; Axi-cel : Axicabtagene ciloleucel ; Brexu-cel : Brexucabtagene autoleucel

Figure 4. Main drivers' impact on Cost per QALY gained (in % of variation)



Abbreviations: CAR : Chimeric Antigen Receptor; ICU: Intensive Care Unit; SoC : Standard of care

Conclusions

- Over the past four years, CEAs have expanded to the comparison of CAR-T therapies and further work has been conducted to better understand the CEA drivers
- Mixture cure models (MCMs) seems to be the more appropriate method for CAR-Ts survival extrapolation
- Overall, CAR-T therapies seemed to be associated with positive outcomes and were considered as a potential cost-effective option by most of the studies (n=18).
- Real world evidence and long-term data are needed to confirm these assessments.

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