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Cost-Effectiveness of Chimeric Antigen Receptor (CAR) T-Cell Therapies for Blood Cancers: A Systematic Review

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Background

Chimeric antigen receptor (CAR) T-cell therapy is an area of rapid development, showing the promise of curing blood cancers. Since 2017, six CAR T-cell therapy products have been granted recommendation for use in patients with (i) B-cell acute lymphoblastic leukaemia (ALL) (ii) diffuse large B-cell lymphoma (DLBCL) (iii) mantle cell lymphoma and (iv) multiple myeloma. Implementation of these products includes complex and novel engineering, manufacturing, and delivery processes, which means very high costs per patient and a threat to the sustainability of healthcare systems. While health gains may justify such high costs, it is currently unclear the extent to which the overall cost-effectiveness of these therapies is determined by the cost of drug acquisition, magnitude of health benefits or cost-effectiveness threshold.

Aim

The aim of this systematic review is to summarize the evidence on the cost-effectiveness of CAR T-cell therapies and to identify the cost drivers across different international jurisdictions.

Methods

Search Strategy

- A search strategy was developed from March to November 2022 to include all CAR T-cell therapies granted market authorisation, using PubMed, Scopus and Ovid.
- The review was conducted using the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022).

Inclusion and Exclusion Criteria

- Medical subject headings (MeSH) definitions and free-text searches were conducted to identify relevant peer-reviewed studies.
- Studies were included if they were full economic cost-effectiveness/cost-utility studies of CAR T-cell therapies.
- Abstract only, unavailable full-text, commentaries, editorials, cost only, reviews, budget impact analysis, partial economic evaluations, reports, guidance, and non-English studies were excluded from the search.

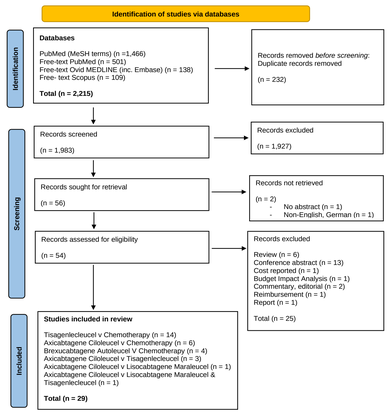
Data extraction

- Full-text copies of relevant studies were retrieved and assessed against inclusion/exclusion.
- 10% of the final abstracts of were independently considered and any disagreements were resolved through discussion.

Assessment of Study quality

- Consolidated Health Economic Evaluation Reporting Standards (CHEERS 2022) checklist was used to assess the methodological quality of each study included at the end of the selection process. The CHEERS checklist (14) included 28 items, and the recommendations were subdivided into seven categories: (1) title, (2) abstract, (3) introduction, (4) methods, (5) results, (6) discussion, and (7) other relevant information.

Figure 1: PRISMA Statement Flow Diagram

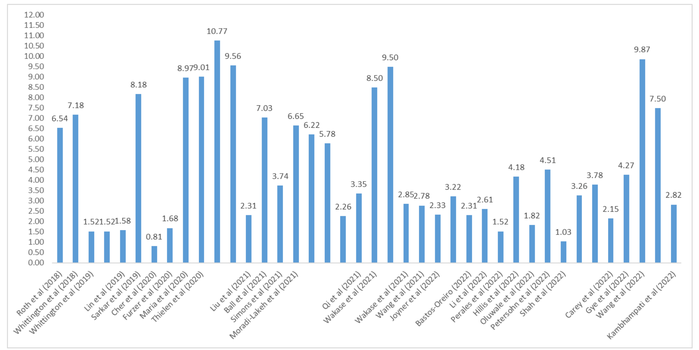


- The search yielded 2,215 studies.
- A total of 56 potentially relevant studies were identified as relevant for full-text screening. After full text screening, a further 25 studies were excluded.
- Reasons for exclusion: absence of abstract (n=1), non-English study (n=1), review (n=6), abstract only (n=13), cost study (n=1), budget impact analysis (n=1), commentary/editorial (n=2), reimbursement (n=1), report (n=1).
- A total of 29 out of 56 studies were included in the review.
- Most studies (n =24, 83%) included three-state partitioned survival model, with parameter estimates derived from previously published randomised controlled trials and other literature.

Results

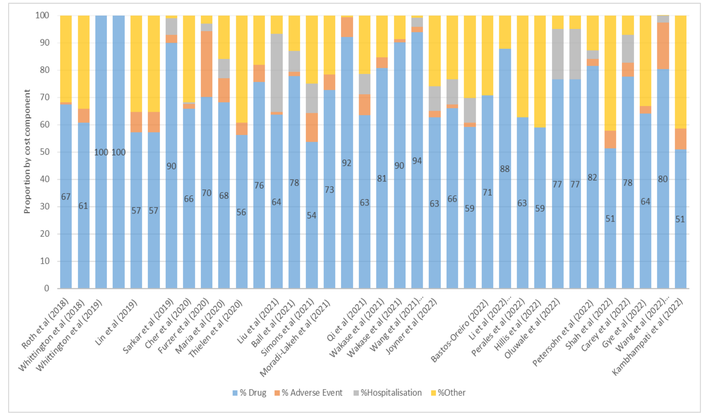
- 29 studies extended across 10 countries: United States of America (US), Singapore, Canada, Spain, Netherlands, Switzerland, Japan, China, Ireland and United Kingdom (UK). The most represented country was the US, with 14 studies (48.3%), followed by Canada, (3 studies; 10.3%), Singapore (3 studies; 10.3%), Spain (2 studies; 6.7%), Japan (2 studies; 6.7%) and China (1 study; 3.4%), Netherlands (1 study; 3.4%), Switzerland (1 study; 3.4%), Ireland (1 study; 3.4%) and UK (1 study; 3.4%).
- CAR T-cell therapies recovered from published studies evaluated tisagenlecleucel (n = 14 studies; 48%) axicabtagene ciloleucel (n = 6 studies; 21%), axicabtagene ciloleucel with tisagenlecleucel (n = 3 studies; 10%), Brexucabtagene Autoleucel (n = 4 studies; 14%), axicabtagene ciloleucel with lisocabtagene maraleucel with (n = 1 study; 3%) and axicabtagene ciloleucel with lisocabtagene maraleucel and tisagenlecleucel and (n = 1 study; 3%).
- All studies included the cost of drug acquisition (n = 29, 100%) and more than half reported the cost of adverse events (21/29; 72%). Adverse events accounted for 10% - 24% of total cost in three studies. The largest cost component of for CAR T-cell therapies is the cost of drug acquisition, which is responsible for 51 % - 100% of total costs.

Figure 2: Incremental quality adjusted life years (QALYs)



- Incremental costs varied considerably between $US6,277 and $US443,619, and QALYs gained ranged from 0.81 to 16.76 over a lifetime horizon.
- The highest incremental QALYs were reported for tisagenlecleucel in the Netherlands, Singapore and Japan; 10.77, 9.87 and 9.50 for use in paediatric, relapsed/refractory B-cell acute lymphoblastic leukaemia (ALL).
- The highest incremental cost was reported for axicabtagene ciloleucel therapy in Canada for diffuse large B-cell lymphoma (DLBCL); $US606,010 and for brexucabtagene autoleucel for mantle cell lymphoma; US$471,879.
- Cost-per-QALY ratios ranged from -US$609 to US$1,615,000.
- At a willingness-to-pay threshold between US$23,592 and US$570,444, there was a 16% - 100% probability, CAR T-cell therapies were cost effective

Figure 3: CAR T-cell therapy spending by cost component (%)



Conclusion

To our knowledge, this is the most up-to-date literature review on the cost-effectiveness of the six CAR T-cell therapies. This review highlights the need for robust evidence to address considerable uncertainty in the cost and effectiveness data given the magnitude of differences in cost-effectiveness estimates. Furthermore, this review provides some evidence on the variation in cost-effectiveness of the CAR T-cell therapies, in particular the willingness to pay threshold (WTP).

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