Poster 5037

Estimating the survival impact of not receiving CAR T therapy while being eligible for treatment in relapsed or refractory diffuse large B-cell lymphoma (DLBCL) patients in Germany

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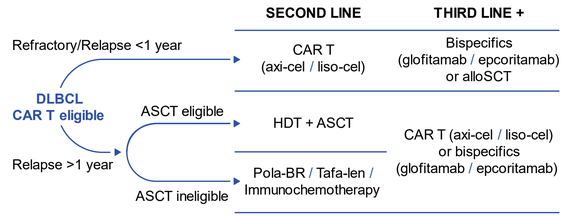
BACKGROUND

Relapsed/Refractory diffuse large B-cell lymphoma (DLBCL) historically carried a poor prognosis from the second line of therapy onwards (2L+). The treatment paradigm was revolutionized based on the results of two recently published phase III trials where chimeric antigen receptor T-cell (**CAR T**) therapy showed significant benefit over high-dose chemotherapy and autologous stem-cell transplant (HDT+ASCT) for patients with early relapsed/refractory DLBCL. [1,2] Following the trial results and the confirmatory real-world evidence, the German Society of Haematology and Medical Oncology (DGHO) revised its **guidelines** in 2024 (Figure 1). [3]

Figure 1. DHGO Guideline



Despite these recommendations, due to a misinterpretation of eligibility and non-clinical barriers, some patients may still not receive CAR T therapy and are **misallocated** to different pathways which may affect their outcomes.

OBJECTIVES

To examine the impact of misallocation of CAR T-eligible patients by modeling survival outcomes considering their adherence to or deviation from the pathway recommended by DGHO guideline.

METHODS

A patient-level discrete event simulation model, which uses parametric survival modelling to simulate first line, second line, and third line treatment in DLBCL, was previously published and evaluated the cost-effectiveness of axi-cel versus glofitamab and epcoritamab. [4,5] This **model** was extended to the fourth line of treatment and was adapted to simulate lifetime health outcomes of German patients across various relapsed/refractory DLBCL treatment pathways based on the DGHO guideline.

As per the guideline [3], we simulated three **treatment pathways** for CAR T eligible patients (Figure 2):

- **Pathway 1**: 2L CAR T for early relapsed/refractory patients followed by 3L BsAb if patients progress
- **Pathway 2**: 2L HDT+ASCT for late relapses followed by 3L CAR T if patients progress
- **Pathway 3**: 2L chemoimmunotherapy for ASCT ineligible late relapses followed by 3L CAR T if patients progress

In an alternative scenario, **CAR T eligible** patients were **misallocated** to treatments according to the **CAR T ineligible** pathway of the DGHO guideline.

MODEL INPUTS

Clinical data was leveraged from pivotal trials and real-world evidence for each of the included treatments. [1, 6-11] Long-term outcomes were extrapolated using validated statistical mixture cure models.

Survival after progression in 3L was modeled using the OS data of the ZUMA-1 study; The proportion of ASCT eligible patients was informed by age and comorbidity thresholds of ALYCANTE, a DLBCL trial of CAR T eligible but ASCT ineligible patients. [12-14]

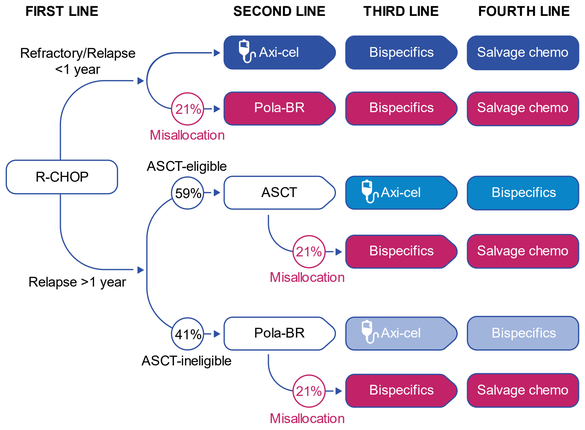
The proportion of relapsed/refractory versus late relapse individuals entering 2L is not a model input and is rather determined at the time of 1L progression for each patient (i.e., relapsed/refractory if they progressed <1 year after treatment start, otherwise late relapse).

The base case **misallocation** rate was estimated to be 21% based on a **chart review** of 126 German patients from 50 physicians (January - September 2023). Post initial analysis, a subsequent chart review of 232 German patients was conducted during the period between November 2023 and July 2024, and the observed misallocation proportion amounted to 27%. [15] Sensitivity analysis using 10%, 27% and 30% misallocation rates was explored given the uncertainty of this parameter.

RESULTS

Based on 2,191 incident patients with DLBCL in Germany who are relapsed/refractory after 1L therapy and CAR T eligible a misallocation rate of 21% equated to 460 patients being misallocated to the CAR T ineligible pathways. [16-18] In terms of outcomes, Figure 3 presents the estimated 5-year overall survival for each pathway, along with the number of misallocated patients, lives lost, and reduction in life expectancy for both the base case misallocation rate and the rates tested through the sensitivity analysis.

Figure 2. Treatment sequence

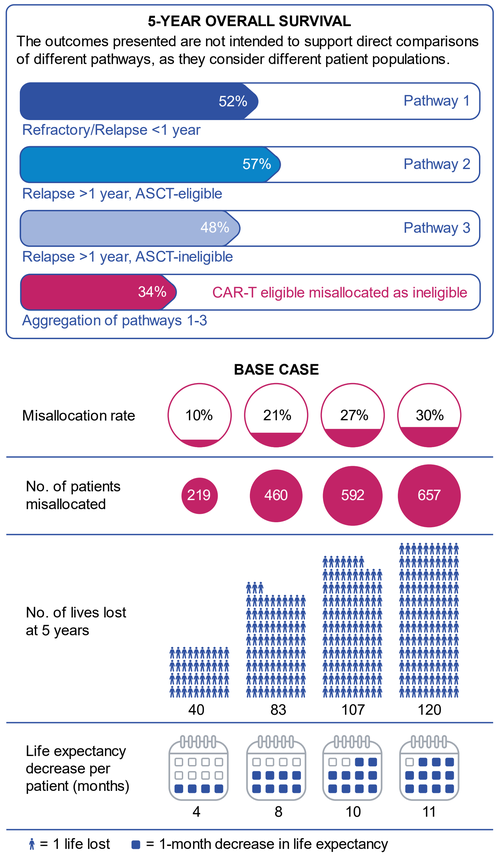


CONCLUSIONS

Using simulation modelling, we showed that misallocation of CAR T eligibility due to clinical and non-clinical reasons leads to patients receiving alternative sequence of treatments that are likely to reduce the overall survival, resulting in suboptimal outcomes at population level. Our results hold true over a range of misallocation rates.

We acknowledge that clinical practice is variable, and guidelines may not be appropriate for all patients. Nonetheless, greater efforts are needed to ensure that CAR T eligible patients are identified systematically, and referral pathways are optimized to ensure all eligible patients receive CAR T therapy.

Figure 3. Results



LIMITATIONS

Except for the outcomes for axi-cel and ASCT in 2L, which were assessed head-to-head in ZUMA-7 [1], the survival data used in the model were compared naively.

The treatment sequence pathways served as a simplification of the German DGHO guidelines and are not inclusive of every possible treatment sequence. Axi-cel is representative of all CAR T treatments approved in relapsed/refractory CAR T-eligible DLBCL (i.e., axi-cel, lisocabtagene maraleucel, and tisagenlecleucel). Pola-BR is representative of all chemotherapy/immunotherapy regimens in relapsed/refractory CAR T-eligible DLBCL (i.e., Rituximab with gemcitabine and oxaliplatin [R-GemOx], tafasitamab with lenalidomide [tafa-len]).

ABBREVIATIONS AND ACRONYMS

ASCT = autologous stem-cell transplant
Axi-cel = axicabtagene ciloleucel
BsAb = bispecific antibodies
CAR T = chimeric antigen receptor T-cell
DGHO = German Society of Haematology and Medical Oncology
DLBCL = diffuse large B-cell lymphoma
HDT = high-dose chemotherapy
L = Line of therapy
Lisa-cel = lisocabtagene maraleucel
No. = Number

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