# 5037 Estimating the Impact on Survival of Not Receiving CAR T Therapy Despite Being Eligible in Relapsed or Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) Patients in Germany

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## Abstract

**Introduction:**

The treatment paradigm of R/R DLBCL 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 (pts) with early R/R DLBCL. Following the results of these trials and the confirmatory real-world evidence (RWE), the German Society of Haematology and Medical Oncology (DGHO) revised its guidelines in 2024. In this updated guideline, second line (2L) R/R DLBCL pts are stratified based on their CAR T eligibility and axicabtagene ciloleucel (axi-cel) or lisocabtagene maraleucel (liso-cel) are recommended for pts with refractory disease and early relapse. Pts with late relapse are still evaluated for HDT+ASCT and considered for CAR T in the third line plus setting (3L+). In addition, bispecific antibodies (BsAb) glofitamab and epcoritamab have been approved and are also recommended for use in the 3L+ setting. Despite these recommendations, due to a misinterpretation of eligibility and non-clinical barriers, some pts may still not receive CAR T therapy and are misallocated to different pathways which may affect their outcomes. In this study we examine the cumulative effect of this misallocation by modelling survival outcomes for pts who do not follow their intended pathway based on the DGHO guideline.

**Methods:**

A patient-level simulation model based on the DGHO guideline was built using data from over 18 sources (including trials and RWE) to simulate lifetime health outcomes of various R/R DLBCL treatment pathways. As per the guideline, we simulated three treatment pathways for CAR T eligible patients: 1) 2L CAR T for early R/R pts followed by 3L BsAb; 2) 2L HDT+ASCT for late relapses, then 3L CAR T; 3) 2L chemoimmunotherapy for ASCT ineligible late relapses and 3L CAR T. In the alternative scenario, CAR T eligible pts are misallocated to treatments according to the CAR T ineligible pathway of the DGHO guideline. Long-term outcomes were extrapolated using validated statistical models. Finally, we estimated the impact on survival if an increasing proportion of CAR T eligible pts follow the alternative CAR T ineligible pathway due to misallocation or suboptimal referral by assigning a varying probability of misallocation.

**Results:**

In the base case, we estimate the misallocation rate of 21% based on a chart review of 126 German pts from 50 physicians. An additional sensitivity analysis using 10% and 30% misallocation rates was explored given the uncertainty of this parameter. Based on 2,191 pts with DLBCL in Germany who are R/R after 1L therapy and CAR T eligible, a misallocation rate of 21% equated to 460 pts being misallocated to the CAR T ineligible pathway. In terms of outcomes, the estimated 5-year overall survival were projected to be 52%, 57% and 48% for pathways 1-3 respectively, and 34% for those who follow the CAR T ineligible pathway. Therefore, misallocation is estimated to decrease life expectancy by over 8 months per pt on average. If this applies to the whole German DLBCL incident population, we can expect 83 lives lost at 5 years. In the sensitivity analysis, the estimated number of lives lost at 5 years was between 40 and 120.

**Conclusions:**

Our comprehensive treatment sequencing model in DLBCL is based on 18 compelling data sources including clinical trials and RWE. Using simulation modelling, we show that misallocation of CAR T eligibility due to clinical and non-clinical reasons leads to pts receiving alternative sequence of treatments which is 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 pts. Nonetheless, greater efforts are needed to ensure that CAR T eligible pts are identified systematically, and referral pathways are optimized to ensure all eligible pts receive CAR T therapy.

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