Poster
ABCL-1076

Estimating the survival impact of not receiving CAR T-cell (CAR T) therapy when eligible in Relapsed or Refractory (R/R) Diffuse Large B-cell Lymphoma (DLBCL) patients in the United States (US)

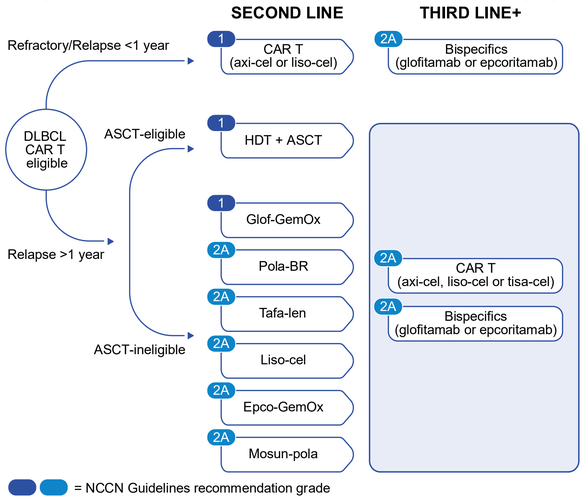
Jason R Westin[1]*, Bradley Kievit[2], Genevieve Meier[3], Rob Blissett[2], Hil Hsu[4], Marco Caterino[2], Timothy Best[4], Markqayne Ray[4], Olalekan O Oluwole[5]

Presenting author 1. University of Texas MD Anderson Cancer Center, Houston, TX, USA; 2. Maple Health Group, New York, NY, USA; 3. Aesara Inc., Chapel Hill, NC, USA; 4. Kite, a Gilead Company, Santa Monica, CA, USA; 5. Vanderbilt University Medical Center, Nashville, TN, USA.

INTRODUCTION

Relapsed/Refractory (R/R) diffuse large B-cell lymphoma (DLBCL) has historically carried a poor prognosis from the second line of therapy onwards (2L+).[1] The treatment landscape for R/R DLBCL in the United States (US) has evolved with the introduction of chimeric antigen receptor T-cell (CAR T) therapy and bispecific antibodies (BsAb).[2] This led to regulatory approval and endorsement by the National Comprehensive Cancer Network (NCCN) of BsAbs as a treatment option in R/R 3L+ DLBCL[3,4] and CAR Ts over high-dose chemotherapy (HDT) with autologous stem cell transplant (ASCT) for patients relapsing within 12 months of ending first-line therapy,[5] with the latter only being recommended for late-relapsing patients.[6] More recently, the BsAb glofitamab, in combination with gemcitabine and oxaliplatin (Glof-GemOx), was recommended by NCCN for patients ineligible for CAR T and ASCT in R/R 2L DLBCL (Figure 1).[6] Despite these novel advances in the R/R DLBCL therapeutic space, a significant proportion of CAR T-eligible patients are misallocated or not receiving treatment in accordance with NCCN guideline recommendations, due to various clinical and non-clinical barriers.[7,8]

Figure 1. Therapies recommended by NCCN for R/R DLBCL (US).[6]



Acronyms and abbreviations: ASCT = autologous stem-cell transplant, CAR T = chimeric antigen receptor T-cell, DLBCL = diffuse large B-cell lymphoma, HDT = high-dose chemotherapy, NCCN = National Comprehensive Cancer Network, R/R = Refractory/Relapse.

OBJECTIVES

To evaluate how deviations from NCCN-recommended treatment pathways affect survival outcomes among CAR T-eligible patients with R/R DLBCL.

METHODS

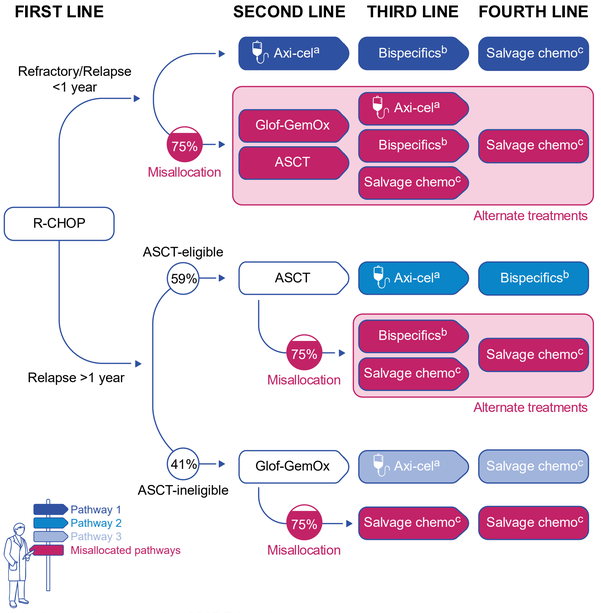
A patient-level discrete event simulation model, which used parametric survival modelling to simulate the first through third lines of treatment (1-3L) in R/R DLBCL, was previously published and evaluated the cost-effectiveness of CAR T therapy in various lines of treatment in the US.[9] This model was expanded to include a fourth line of treatment and the comparator, Glof-GemOx, and adapted to simulate lifetime health outcomes of US patients based on NCCN guideline pathways (Figure 2):

- **Pathway 1**: 2L CAR T for early R/R patients followed by 3L bispecific antibodies if patients progress.
- **Pathway 2**: 2L HDT+ASCT for late relapses followed by 3L CAR T if patients progress.
- **Pathway 3**: 2L Glof-GemOx for ASCT-ineligible late relapses followed by 3L CAR T if patients progress.

CAR T-eligible patients were misallocated and instead received treatments that are not recommended in NCCN guidelines. The impact of misallocation on overall survival, quality of life, and statistical cure rate (i.e., remission followed by non-DLBCL mortality) was analyzed for up to 75% of CAR T-eligible patients being misallocated to non-preferred pathways. The misallocation rate and alternate treatments received were informed by data from real-world practice.[7]

In **scenario analysis #1**, the impact of reducing the misallocation rate (i.e., 15%) was explored. Since mean age in the base case aligned with that of the real-world study used to inform misallocation rates and treatments (61 years)[7], **scenario analysis #2** explored the impact of patients age and aligned with the sourced clinical trial containing the oldest cohort (i.e., STARGLO; 68 years).[10]

Figure 2. Treatment sequence assumed for each of the modeled pathways.



[a] Axi-cel assumed representative of CAR T therapies.
[b] Bispecifics refer to a mixture of glofitamab and epcoritamab monotherapy.
[c] Salvage chemo refers to a basket of five R-chemotherapies (R-DHAP, R-ESHAP, R-ICE, R-GDP and R-GemOx).
Acronyms and abbreviations: ASCT = autologous stem-cell transplant, chemo = chemotherapy.

MODEL INPUTS

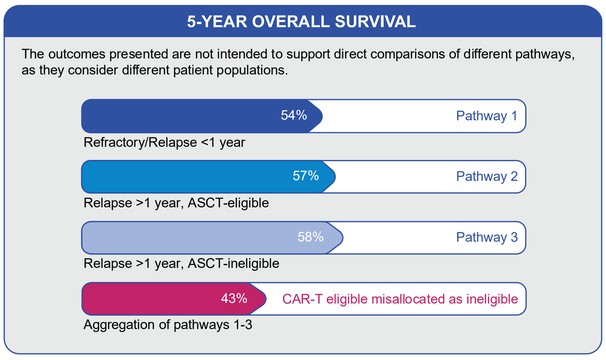
Overall survival (OS) and progression-free survival (PFS) endpoints were leveraged from pivotal trials and real-world evidence for each of the included treatments[2,9-15] and long-term outcomes were extrapolated using validated statistical mixture cure models.[16] Survival curves were modeled from the time of infusion. Survival after progression in 4L was modeled using the OS data of the ZUMA-1 study.[12] The proportion of ASCT-eligible patients was informed by age and comorbidity thresholds of ALYCANTE (age ≥ 65 years and/or comorbidity index (CI) ≥ 3), a DLBCL trial of CAR T-eligible but ASCT-ineligible patients.[2,17,18] The proportion of early (<12 months) versus late relapse individuals entering 2L is not a model input and is rather determined at the time of 1L progression for each patient as per published PFS curves from Sehn et al. (i.e., R/R if they progressed <1 year after treatment start, otherwise late relapse).[19] The base case (61 years) matched the real-world study informing misallocation rates and treatments[7], and the age-associated scenario aligned with the oldest sourced clinical trial (STARGLO; 68 years).[10] Patient health-related quality of life (HRQoL) was explored by assigning a baseline utility for each patient based on their age and sex as described elsewhere.[9] Utility decrements were then applied to this to reflect on/off-treatment and pre/post-progression health states.

RESULTS

At the given rate of 75% of misallocation, among an annual estimate of 8,399 CAR T-eligible patients after first-line relapse in the US,[20] up to 6,299 would be misallocated to suboptimal pathways. Figure 3 presents the estimated 5-year overall survival for each pathway, while Figure 4 shows the number of misallocated patients, mean life years (LYs) and quality-adjusted LYs (QALYs) lost, lives lost, statistical cures foregone, and reduction in life expectancy.

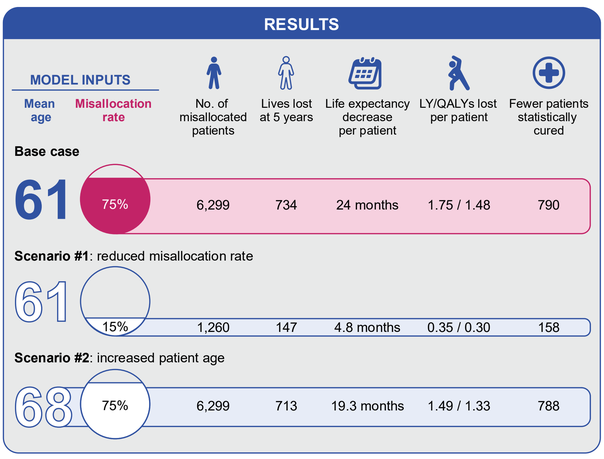
Both scenario analyses, one with minimized misallocation rates (**scenario analysis #1**) and one with an older cohort (**scenario analysis #2**), still demonstrate that misallocation adversely affects patient outcomes. The impact was reduced in Scenario #1 because more patients received optimal treatment, and only modestly reduced in Scenario #2 because older patients had a higher risk of death from causes other than misallocation.

Figure 3. Resulting overall survival for each of the modeled pathways.



Acronyms and abbreviations: ASCT = autologous stem-cell transplant, CAR T = chimeric antigen receptor.

Figure 4. Results of the base case and scenario analyses.



Acronyms and abbreviations: LY = Life year, No. = Number, QALY = Quality-adjusted life year.

CONCLUSIONS

In this simulation model, patients with R/R DLBCL have superior health outcomes when treated with CAR T therapy as recommended compared to other treatments, further supporting its NCCN category 1 classification. Further, it demonstrates that not following NCCN-recommended guidelines for CAR T-eligible R/R DLBCL patients may substantially reduce survival outcomes. These results hold true over a range of misallocation rates and patient ages. We acknowledge that the definition of CAR T eligibility is not limited to clinical criteria alone but also includes social and logistical aspects. Given that real-world treatment patterns show upwards of 75% non-adherence to guidelines in CAR T-eligible R/R DLBCL patients, it is likely that at least some barriers to appropriate care are surmountable.[7,8] Addressing these are essential to ensuring that eligible patients have optimal access to CAR T therapy, which is a proven effective treatment option in R/R 2L+ DLBCL.

Limitations

- All survival data used in the model were compared naively, apart from the outcomes for axi-cel and ASCT in 2L, which were assessed head-to-head in ZUMA-7.[2]
- The treatment sequence pathways served as a simplification of the NCCN-recommended R/R DLBCL treatment landscape and are not inclusive of every possible treatment sequence.[6]
- Similarly, treatments in the misallocated pathways are a simplification of those reported in Perales et al. (2025).[7]

Plain language summary

- Many patients with 2L DLBCL who are eligible for CAR T therapy do not receive it, despite NCCN treatment guidelines recommending its use.
- Real-world data in the US show that upwards of 75% of these patients receive non-CAR T treatments, which are projected to lead to reduced survival and lower life expectancy.
- This trend affects thousands of patients annually in the US, with meaningful implications for outcomes at both the individual and population level.

Acronyms and abbreviations

ASCT = autologous stem-cell transplant; BsAb = bispecific antibodies; CAR T = chimeric antigen receptor T-cell; Chemo = chemotherapy; CI = Comorbidity index; DLBCL = diffuse large B-cell lymphoma; HDT = high-dose chemotherapy; HRQoL = Health-related quality of life; L = Line of therapy LY = Life year; NCCN = National, Comprehensive Cancer Network; No. = Number; OS = Overall survival PFS = Progression-free survival; QALY = Quality-adjusted life year; R = rituximab; R/R = Refractory/Relapse; US = United States.

References

1. Sarkozy C et al. Ann Lymphoma. 2019;3:1–19.
2. Westin JR et al. N Engl J Med 2023; 389(2): 148-57.
3. U.S. Food and Drug Administration. Silver Spring, MD: FDA; June 15, 2023. Available at FDA's news release.
4. U.S. Food and Drug Administration. Silver Spring, MD: FDA; May 19, 2023. Available at FDA's news release.
5. U.S. Food and Drug Administration. Silver Spring, MD: FDA; April 1, 2022. Available at FDA's news release.
6. National Comprehensive Cancer Network Inc. NCCN Clinical Practice Guidelines in Oncology for B-Cell Lymphomas. V.1.2025. 2025.
7. Perales M-A et al. Transplant Cell Ther 2025; 31(2, Suppl): S391.
8. Kaltwasser J. Targeted Oncology 2022.
9. Patel AP et al. MDM Policy Pract 2025; 10(1).
10. Abramson JS et al. J Clin Oncol 2025; 43 (16 suppl).
11. Van Imhoff GW et al. J Clin Oncol 2017; 35(5): 544-51.
12. Locke FL et al. Lancet Oncol 2019; 20(1): 31-42.
13. Dickinson MJ et al. N Engl J Med 2022; 387(24): 2220-31.
14. Thieblemont C et al. Leukemia 2024; 38(12): 2653-62.
15. Crump M et al. Blood 2017; 130(16): 1800-8.
16. Vadgama S et al. Value Health. 2022;25:1010–7.
17. Vic S et al. Eur J Cancer 2022; 175: 246-53.
18. Kittai AS et al. Transplant Cell Ther 2021; 27(1): 46-52.
19. Sehn LH et al. Blood 2007; 109(5): 1857-61.
20. Kanas G et al. Leuk Lymphoma 2022; 63(1): 54-63.

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