OVERALL SURVIVAL OF PATIENTS WITH LARGE B CELL LYMPHOMAS IN POLAND AFTER CHIMERIC ANTIGEN RECEPTOR T CELL (CAR-T) THERAPIES COMPARED TO THE REAL-WORLD EVIDENCE FROM OTHER COUNTRIES

ACCEPTANCE CODE: **CO151**

Książek Paweł[1], Kręcisz Monika[1], Bronikowska Małgorzata[2], Pruszko Cezary[1,2], Jachimowicz Michał[1,2], Binowski Grzegorz[2].

[1]MAHTA, Warsaw, Poland, [2]MAHTA Intl., Warsaw, Poland

INTRODUCTION

Large B-cell lymphomas (LBCL) are a heterogeneous group of aggressive B-cell lymphomas and represent one of the more frequently diagnosed groups among non-Hodgkin's lymphomas (NHL) worldwide[1].

Adult patients with relapsed and refractory (R/R) LBCL after two or more lines of systemic therapy in Poland can be treated one of the two modern, high-costly CAR-T therapies - axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel). Therapies are reimbursed since May 2022 in the Polish clinical setting under the Drug Programme's limited eligibility criteria[2]. According to the National Health Fund (NHF) data, from the start of reimbursement until the end of May 2024, CAR-T therapy was reported for 180 patients in Poland. The total reported reimbursement value of the therapy was PLN 250 million[3]. The NHF has provided survival data for the group of patients who have received CAR-T therapies until January 2024[3].

OBJECTIVES

The aim of this study is to establish differences in the efficacy of available CAR-T therapies in Poland in patients with LBCL and compare them with available real-world evidence from other countries.

METHODS

The NHF report on CAR-T therapy was used to compare the efficacy of available therapies for patients with R/R LBCL - axi-cel and tisa-cel in terms of overall survival (OS). The systematic literature review (SLR) was performed in Medline from 2020 to identify observational studies describing the outcomes in patients with R/R LBCL treated with any CAR-T therapy. The outcome of interest was overall survival (OS). During the study selection process the publication *Jacobson et al. 2024*[4] has been identified. This review aims to comprehensively describe the clinical outcomes of approved CAR-T therapies in patients with R/R LBCL, using the abundance of available real-world evidence (RWE). Together with SLR a comparative meta-analysis was conducted to characterise the real-world safety and efficacy of these products including 14 patient cohorts in the US and Europe for quantitative evidence synthesis. Survival outcomes reported by NHF were then compared with key findings from a meta-analysis of RWE.

Pseudo-individual patient data (IPD) were generated from available data - NHF report and RWE using a direct digitisation process and Guyot's algorithm[5]. All analyses were performed using R software.

Patient characteristics were also analysed to compare differences between treated populations, however few data were available for the Polish population.

Figure 1. Age and sex distribution in the analysed population of patients given axi-cel (n=57) as part of the Drug Programme for the treatment of patients with B-cell lymphoma in Poland

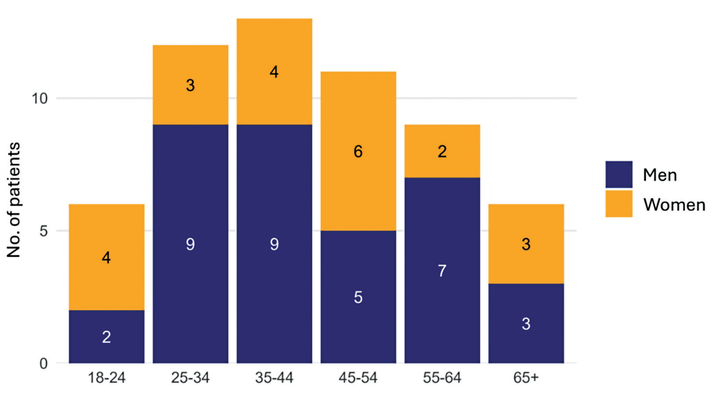


Figure 2. Age and sex distribution in the analysed population of patients given tisa-cel (n=53) as part of the Drug Programme for the treatment of patients with B-cell lymphoma in Poland

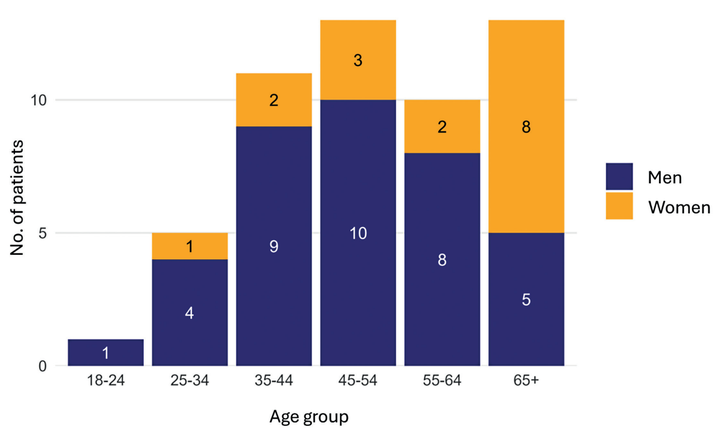


Table 1. Key baseline characteristics in the axi-cel and tisa-cel patient cohorts

PARAMETER	AXI-CEL		TISA-CEL	
	NHF DATA	JACOBSON ET AL. 2024	NHF DATA	JACOBSON ET AL. 2024
Age, yr	43.7*	60.6 (59.7 – 61.6)	51.8*	64.3 (62.8 – 65.8)
Male, %	61	64.8 (62.9 – 66.6)	70	60.1 (58.0 – 62.3)
ECOG PS ≥2, %	0	9.1 (6.2 – 12.1)	0	9.1 (3.4 – 14.8)
CRS, %	45	86.3 (any grade) 8.2 (grade ≥ 3)	36	70.6 (any grade) 8.9 (grade ≥ 3)

*not precisely defined, average from age ranges was used

ECOG PS, Eastern Cooperative Oncology Group Performance Status; CRS, cytokine release syndrome

RESULTS

Comparative analysis of axi-cel and tisa-cel in the Polish clinical setting showed hazard ratios (HR) for OS of 0.81 (95% confidence interval [CI], 0.46 to 1.44) and HR of 0.80 (0.44 – 1.47), depending on the method of IPD generation - direct digitisation process (Figure 3a) and Guyot's algorithm (Figure 3b).

Figure 3a. Comparative effectiveness of axi-cel vs tisa-cel in terms of OS based on survival data provided by Polish NHF – direct digitisation process

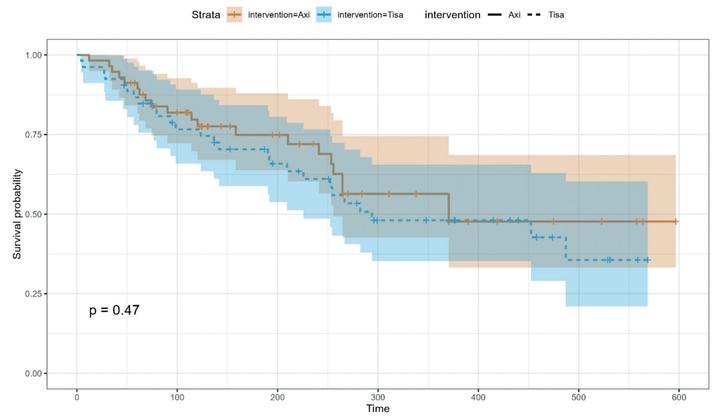
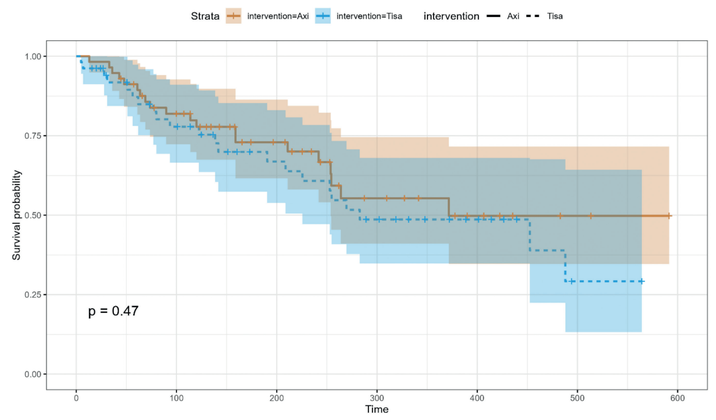


Figure 3b. Comparative effectiveness of axi-cel vs tisa-cel in terms of OS based on survival data provided by Polish NHF – Guyot's algorithm



Both results, regardless of the method used, show comparable survival for axi-cel and tisa-cel (not statistically significant, p>0.05), but with the direction favouring axi-cel.

Whereas, RWE shows significant improvements in OS for axi-cel compared with tisa-cel – adjusted HR in the primary OS model was 0.60 (95% CI, 0.47 to 0.77). The sensitivity analysis incorporating HRs derived from KM curves or using Cox proportional hazard (PH) regression with pseudo-IPD showed comparable findings.

A comparison of each therapy between the Polish and RWE data shows lower median survival (12.4 months in the Polish setting vs. 19.5 months according to RWE for axi-cel and 9.4 vs. 11.7 for tisa-cel, respectively). Overall survival is slightly better in countries other than Poland for both therapies - HR of 1.21 (95% CI, 0.77 to 1.88) and HR of 1.07 (0.69 – 1.64) for axi-cel and tisa-cel, respectively, but the difference is not statistically significant (Figure 4a, Figure 4b).

Figure 4a. Comparative effectiveness of axi-cel in terms of OS between Polish NHF data and RWE data from Jacobson et al. 2024 – Guyot's algorithm

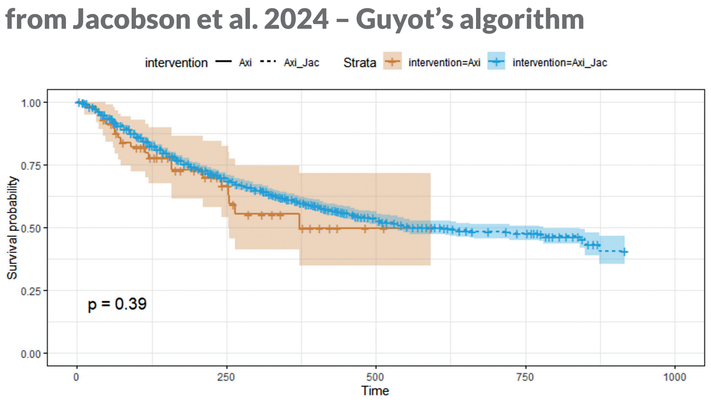
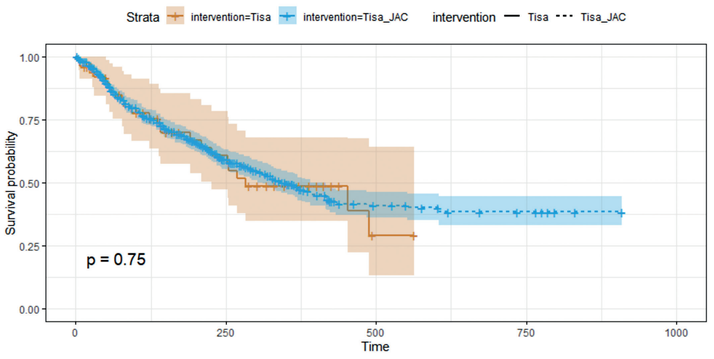


Figure 4b. Comparative effectiveness of tisa-cel in terms of OS between Polish NHF data and RWE data from Jacobson et al. 2024 – Guyot's algorithm



CONCLUSIONS

The RWE shows that axi-cel is superior to tisa-cel therapy, while the Polish data suggest that there is a slightly, not statistically significant, advantage in favour of axi-cel over tisa-cel. Slightly lower median survival were reported in Poland compared to the RWE data.

The lower mean age of the patients in the Polish cohort according to the NHF data and the eligibility criteria for therapy taking into account lower ECOG performance status (0-1) could suggest a better treatment effect. However, there is a lack of detailed data on the Polish cohort of characteristics, including important information of type of prior bridging therapy, number of previous therapy lines, LBCL type or apheresis-to-infusion time, which may also affect mortality and the variation between the efficacy of the two therapies. In addition, the small sample size of the Polish cohort is also a limitation.

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CONTACT INFORMATION: Grzegorz Binowski: grzegorz.binowski@mahta.pl