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CURRENT USE OF SALVAGE 2ND LINE TREATMENT IN PATIENTS WITH RELAPSED/REFRACTORY AGGRESSIVE B-CELL LYMPHOMA AND KEY DRIVERS FOR SELECTING THERAPY WITH CAR-T CELLS. DATA FROM REAL-WORLD STUDY IN EU5

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BACKGROUND

Aggressive B-cell lymphomas encompass a spectrum of subtypes, including high grade B-cell lymphoma (HGBCL), diffuse large B-cell lymphoma (DLBCL) and primary mediastinal B-cell lymphoma (PMBCL).
These subsets, particularly DLBCL, exhibit significant genomic heterogeneity. Most patients (55%) present with advanced disease (Ann Arbor stage III/IV) at a median age of diagnosis of 66 years (1, 2).
Rituximab-based immunochemotherapy with R-CHOP remains the standard of care in first line for all eligible patients but approximately 20%-30% of them fail first-line therapy (3).
Treatment within this subset remains challenging, particularly early relapses and primary refractory disease and management of those patients rely currently on CAR-T cells as new SoC with an improvement in survival data with both axicabtagene ciloleucel (axi-cel, ZUMA-7 clinical trial) and lisocabtagene maraleucel (liso-cel, TRANSFORM clinical trial) (4, 5).

AIMS

Identify treatment patterns and key drivers for selecting CAR-T treatment vs. alternative treatment options in 2nd line patients with aggressive B-cell lymphoma in EU5 countries based on real-world patient data.

METHODS

Anonymous patient charts were provided by onco-haematologists treating patients with aggressive B-cell lymphoma in EU5 countries: France (FR), Germany (DE), Spain (ES), Italy (IT) and UK were analyzed.
A total of 804 unique patient charts were included in the analysis, from October to December 2023. The analysis focused specifically on the 2nd line of therapy for different subsets of aggressive B-cell lymphoma (HGBCL, DLBCL and PMBCL) based on the treatment receiveds: CAR-T cells vs. non-CAR-T therapies.
A total of 122 patients received CAR-T cell therapy, while 682 received other treatments (immunochemotherapy, stem cell transplant, or targeted therapy).

RESULTS

Median age was 65 years in the overall population, 66 years in the non-CAR-T and 62 years in the CAR-T subgroup. As expected, a higher proportion of patients were younger than 65 in the CAR-T subgroup (55%) as compared to the non-CAR-T population (44%). No difference in patient age was observed between countries in the two subsets. See Figure 2 for age comparison between CAR-T and non-CAR-T patients.

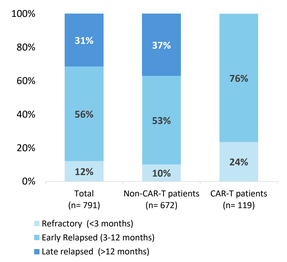

Fig 1. Comparison of time from 1st line to relapse between CAR-T and non-CAR-T populations

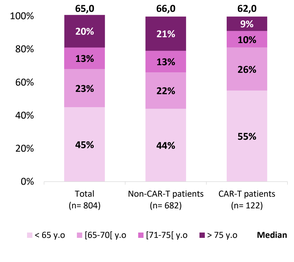

Fig 2. Patients' age in both CAR-T and non-CAR-T populations in EU5 countries

ECOG score at 2nd line treatment initiation was 0-1 in 71% in the non-CAR-T group and 78% in the CAR-T population. A slightly higher proportion of patients (27%) had ECOG 2-3 in the non-CAR-T group vs. 19% in the CAR-T population. Analysis of the IPI score breakdown revealed no significant difference between the two groups across the entire range and within intermediate/high- and high-risk subsets. Patients' ECOG scores at initial diagnostic and at 2nd line initiation is described in Table 1.

	Total	NON-CAR-T PATIENTS	CAR-T PATIENTS
ECOG SCORE AT DIAGNOSIS STAGE	(n= 798)	(n= 676)	(n= 122)
ECOG 0	**26%**	**25%**	**30%**
ECOG 1	**52%**	**52%**	**51%**
ECOG 2	**18%**	**19%**	**16%**
ECOG 3+	**4%**	**4%**	**3%**
ECOG SCORE AT 2L TREATMENT INITIATION	(n= 794)	(n= 675)	(n= 119)
ECOG 0	**21%**	**22%**	**20%**
ECOG 1	**52%**	**51%**	**60%**
ECOG 2	**22%**	**22%**	**17%**
ECOG 3+	**5%**	**5%**	**3%**

Table 1. ECOG score at diagnosis and at 2nd line treatment initiation for CAR-T vs. non-CAR-T patients

In the non-CAR-T subgroup, 43% of patients were considered to be CAR-T ineligible and 57% were CAR-T eligible and not treated. When analyzing delay of relapse after 1st line in the non-CAR-T subgroup, 63% of this population relapse within one year and 57% were considered to be CAR-T eligible but finally did not receive this treatment. Delay between 1st line and relapse in both CAR-T and non-CAR-T population is detailed in Figure 1.

Assessment of genetic abnormalities in the two groups did not reveal any significant difference with a slight over-representation of double hit subset in the CAR-T group (13%) as compared to non-CAR-T (9%). Details regarding the main genetic alterations are described in Figure 4. IPI score breakdown in both CAR-T and non-CAR-T populations is also provided in Figure 3.

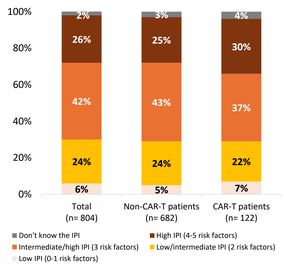

Fig 3. IPI score at diagnosis in both CAR-T and non-CAR-T patients

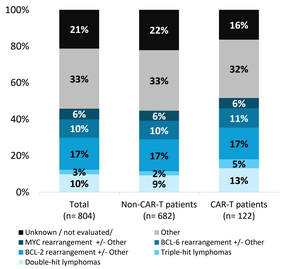

Fig 4. Main genetic alterations at disease diagnosis between CAR-T and non-CAR-T patients

Among the two CAR-T products, axi-cel was the most frequently used agent for majority of patients, especially in Spain (80%), the UK (82%) and France (79%). Use of the two products is more balanced in Germany (44% axi-cel vs. 56% liso-cel) and Italy (50% axi-cel vs. 50% liso-cel). Details are provided in Figure 5.

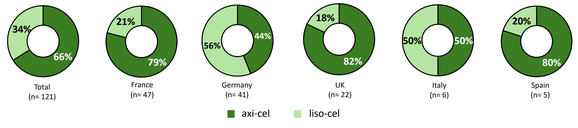

Fig 5. Breakdown of axi-cel and liso-cel by country

Analysis of treatment in the non-CAR-T subgroup revealed that auto SCT was proposed in 47% of patients. Salvage rituximab-based immunochemotherapy was used in 17% of patients and 17% received polatuzumab + rituximab +/- bendamustin regimen. Details for salvage regimens used in the non-CAR-T population are given in Figure 6 as well as the different bridging regimens used prior to CAR-T treatment in Figure 7.

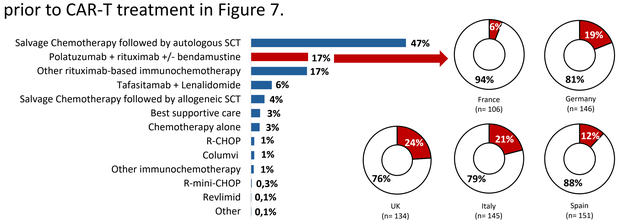

Fig 6. Different salvage regimens used in the non-CAR-T population with a focus in polutuzumab vedotin-based combinations by country (Total n= 682)

Fig 7. Different bridging regimens used prior to CAR-T treatment (Total n= 804)

Consistent with expectations, analysis of co-morbidities demonstrated a slightly higher prevalence of hypertension, cardiovascular conditions, and renal impairment in the non-CAR-T group (see Figure 8).

	Total (n= 804)	NON-CAR-T PATIENTS (n= 682)	CAR-T PATIENTS (n= 122)
None	**28%**	**26%**	**37%**
Hypertension	53%	54%	44%
Other cardiovascular condition	6%	6%	5%
Neurological condition	2%	2%	2%
Pulmonary condition	2%	2%	2%
Renal condition	1%	2%	0%
Obesity	3%	3%	2%
Autoimmune condition	2%	2%	4%
Hepatic condition	1%	1%	2%
Retinopathy	0%	0%	1%

Fig 8. Main co-morbidities among CAR-T and non-CAR-T populations

CONCLUSION

This real-world study highlights that treatment options in 2nd line aggressive B-cell lymphoma rely mainly on CAR-T products, salvage chemotherapy followed by auto SCT and other rituximab-based immunochemotherapy.
In this series, all patients receiving CAR-T cells were in early relapse or with a refractory disease and eligible to intensive treatment (based on design of ZUMA-7 and TRANSFORM trials).
In patients not receiving any CAR-T treatment, a mix is observed between patients not eligible and patients eligible but not treated due to delay of relapse or no potential eligibility to SCT.
Current approval by EMA of axi-cel and liso-cel in early relapse and refractory disease and more extensive real-world data should enhance their use as a new standard of care in aggressive B-cell lymphoma.

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