

LETTER TO THE EDITOR OPEN ACCESS

Polatuzumab Vedotin and Glofitamab for Relapsed/Refractory Diffuse Large B-Cell Lymphoma in the Compassionate Use Program in Italy

Pier Luigi Zinzani^{1,2} | Giulia Dell'Omo³ | Letizia Fusco³ | Ilaria Peduto³ | Carlotta Galeone⁴ | Federica Cavallo^{5,6} | Giuseppe Gritti⁷

¹IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy | ²Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna, Bologna, Italy | ³Roche S.p.A., Monza, Italy | ⁴Bicocca Applied Statistics Center (BASC), Università degli Studi di Milano-Bicocca, Milan, Italy | ⁵Department of Molecular Biotechnologies and Health, University of Torino, Torino, Italy | ⁶Hematology U, AOU "Città della Salute e della Scienza di Torino", Torino, Italy | ⁷Hematology and BMT Unit, ASST Papa Giovanni XXIII, Bergamo, Italy

Correspondence: Carlotta Galeone (carlotta.galeone@unimib.it)

Received: 26 August 2025 | **Revised:** 5 December 2025 | **Accepted:** 11 December 2025

Keywords: compassionate use programs | diffuse large B-cell lymphoma | glofitamab | polatuzumab vedotin | real world evidence | treatment pathways

To the Editor,

Compassionate Use Programs (CUP) offers patients with severe diseases, early access to promising new drugs outside of clinical trial and prior to marketing approval. Data arising from CUP provides valuable insights on treatment pathways. In the last few years, the treatment landscape for relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL) has rapidly evolved based on the approval of several novel therapies, resulting in changing treatment patterns which benefit from assessment of modern retrospective data.

To address this, we retrospectively evaluated data of two large patient cohorts of r/r DLBCL within the polatuzumab vedotin and glofitamab Roche Global CUP opened in Italy [1], as was done in similar studies from other European countries [2, 3]. In fact, this analysis did not evaluate the effectiveness of the two products, that has been recently reported for polatuzumab vedotin [4].

The polatuzumab vedotin-rituximab +/- bendamustine CUP cohort included r/r DLBCL patients after at least 2 lines of treatment; with 208 patient requests received from 92 national centers between May 2019 and April 2020. The glofitamab CUP cohort included patients with r/r DLBCL, high-grade B-cell lymphoma (HGBCL) or primary mediastinal B cell lymphoma (PMBCL) after at least 3 lines of previous treatments; with 145 patient requests received from 59 national centers between

March 2022 and April 2024. Cohort characteristics were compared using the Chi-square or Fisher's exact test for categorical data, and the Wilcoxon rank-sum test for continuous data.

Clinical characteristics of the patient population are summarized in Table 1. Both cohorts showed a prevalence of males. The median age (minimum-maximum range) at diagnosis was higher in the polatuzumab vedotin-rituximab +/- bendamustine cohort (63 years; range: 24–84 years) compared to the glofitamab cohort (60 years; range: 17–82 years, p -value = 0.002). Similarly, the median age at CUP request was higher in the polatuzumab vedotin-rituximab +/- bendamustine (67 years; range: 25–85 years) than in the glofitamab cohort (62 years; range: 19–85 years, p -value < 0.001). The median duration from diagnosis to CUP request was comparable in the two cohorts (median 2 years, range 0–22). In the polatuzumab vedotin cohort, 78% patients were previously treated with 2 (49%) or 3 (29%) lines of treatment, whereas the glofitamab cohort had 79% of patients previously treated with 3 (34%) or 4 (45%) lines of treatment (p -value = 0.004).

Treatment courses experienced by patients across the two cohorts are depicted in Figure 1. In the polatuzumab vedotin-rituximab +/- bendamustine cohort (Figure 1A), the most frequent frontline regimen was R-CHOP (66%), followed by R-CHOP like (e.g., R-COMP, R-COMP + rituximab, R-BENDA,

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2025 The Author(s). *Hematological Oncology* published by John Wiley & Sons Ltd.

TABLE 1 | Baseline characteristics of the population, overall and in CUP strata (polatuzumab vedotin and glofitamab).

		Total N = 353	Polatuzumab vedotin N = 208	Glofitamab N = 145	p-value^a
Sex					
Female	N (%)	140 (39.7%)	84 (40.4%)	56 (38.6%)	0.824
Male	N (%)	213 (60.3%)	124 (59.6%)	89 (61.4%)	
Age at CUP request (years) ^b					
	N	353	208	145	
	Mean (SD)	62.6 (13.3)	65.1 (11.8)	59.2 (14.4)	
	Median (IQR)	64 (56–73)	67 (57–75)	62 (51–69)	0.0001
	Min-max	19–85	25–85	19–85	
Disease histology					
DLBCL	N (%)	—	208 (100%)	—	
DLBCL NOS (including HGL)	N (%)	—	—	139 (95.9%)	
PMBCL	N (%)	—	—	6 (4.1%)	
No. lines of previous treatment					
1L	N (%)	—	—	—	
2L	N (%)	102 (28.9%)	102 (49.0%)	—	
3L	N (%)	110 (31.2%)	60 (28.8%)	50 (34.5%)	0.004 ^c
4L	N (%)	98 (27.8%)	33 (15.9%)	65 (44.8%)	
5L	N (%)	37 (10.5%)	12 (5.8%)	25 (17.2%)	
6L+	N (%)	6 (1.7%)	1 (0.5%)	5 (3.5%)	
Age at diagnosis (years)					
	N	336	191	145	
	Mean (SD)	59.6 (13.3)	61.8 (12.1)	56.7 (14.4)	
	Median (IQR)	62 (52–70)	63 (55–71)	60 (49–67)	0.0015
	Min-max	17–84	24–84	17–82	
Time from diagnosis to CUP request (years)					
	N	336	191	145	
	Mean (SD)	2.7 (3.0)	2.9 (3.4)	2.5 (2.4)	
	Median (min-max)	2 (0–22)	2 (0–22)	2 (0–15)	0.788
First line regimen (1L)					
R-CHOP dose dense chemotherapy	N (%)	56 (15.9%)	21 (10.5%)	35 (24.1%)	0.001
R-CHOP	N (%)	223 (63.2%)	138 (66.0%)	85 (58.6%)	
R-CHOP like	N (%)	74 (20.9%)	49 (23.4%)	25 (17.2%)	
Second line regimen (2L)					
Immune-chemotherapy	N (%)	27 (7.7%)	20 (9.6%)	7 (4.8%)	0.001 ^d
Chemo free-regimen	N (%)	21 (5.9%)	10 (4.8%)	11 (7.6%)	
Other	N (%)	60 (17.0%)	48 (23.1%)	12 (8.3%)	
High dose chemotherapy and stem cell transplantation ^e	N (%)	239 (67.7%)	130 (62.5%)	109 (75.2%)	
Polatuzumab-vedotin	N (%)	6 (4.1%)	—	6 (4.1%)	

(Continues)

TABLE 1 | (Continued)

		Total N = 353	Polatuzumab vedotin N = 208	Glofitamab N = 145	p-value ^a
Third line regimen (3L)					
Immune-chemotherapy	N (%)	19 (7.6%)	14 (13.2%)	5 (3.5%)	
Chemo free-regimen	N (%)	50 (19.9%)	28 (26.4%)	22 (15.2%)	
Other	N (%)	41 (16.3%)	34 (32.1%)	7 (4.8%)	
High dose chemotherapy and stem cell transplantation	N (%)	52 (20.7%)	30 (28.3%)	22 (15.2%)	
Polatuzumab-vedotin	N (%)	48 (19.1%)	—	48 (33.1%)	
CAR-T	N (%)	41 (16.3%)	—	41 (28.3%)	
Fourth line regimen (4L)					
Immune-chemotherapy	N (%)	7 (5.0%)	3 (6.5%)	4 (4.2%)	
Chemo free-regimen	N (%)	20 (14.2%)	11 (23.9%)	9 (9.5%)	
Other	N (%)	30 (21.3%)	23 (50.0%)	7 (7.4%)	
High dose chemotherapy and stem cell transplantation	N (%)	15 (10.6%)	9 (19.6%)	6 (6.3%)	
Polatuzumab-vedotin	N (%)	35 (24.8%)	—	35 (36.8%)	
CAR-T	N (%)	34 (24.1%)	—	34 (35.8%)	
Fifth line regimen (5L)					
Immune-chemotherapy	N (%)	2 (4.7%)	1 (7.7%)	1 (3.3%)	
Chemo free-regimen	N (%)	13 (30.2%)	6 (46.2%)	7 (23.3%)	
Other	N (%)	8 (18.6%)	3 (23.1%)	5 (16.7%)	
High dose chemotherapy and stem cell transplantation	N (%)	8 (18.6%)	3 (23.1%)	5 (16.7%)	
Polatuzumab-vedotin	N (%)	5 (16.3%)	—	5 (16.7%)	
CAR-T	N (%)	7 (11.6%)	—	7 (23.3%)	

^aChi-square test or Fisher's exact test if counts are less than five. Wilcoxon rank-sum test for age comparisons.

^bCUP = compassionate use program.

^cThe comparison between cohorts does not include the 2L.

^dp-value calculated excluding polatuzumab vedotin treatment from the glofitamab cohort.

^eIncluding R-DHAOX, R-DHAP, R-DHAP + ASCT, R-IEV, R-ICE, R-MICMA, R-CODOX-M/IVAC, R-HYPER C-VAD, DHAOX, ICE and other regimens.

etc; 23%) and by R-CHOP dose-dense chemotherapy (e.g., DA-EPOCH-R, MACOP-B, etc; 10%). The corresponding distribution in the glofitamab cohort (Figure 1B) was 59%, 17% and 24%, respectively. In both cohorts the use of R-CHOP dose-dense chemotherapy was more frequent in younger patients (median age: 51 years, range: 33–78 years in the polatuzumab vedotin-rituximab +/- bendamustine cohort; median age: 54 years, range: 17–72 years in the glofitamab cohort) as compared to R-CHOP standard-dose regimen (median age: 63 years, range: 24–83 years in the polatuzumab vedotin-rituximab +/- bendamustine cohort; median age: 59 years, range: 17–83 years in the glofitamab cohort).

In second line, in the polatuzumab vedotin-rituximab +/- bendamustine cohort, we observed that 63% of patients were treated with high dose chemotherapy and stem cell transplantation (SCT), at a median age of 61 years (range: 24–78 years), whereas in the glofitamab cohort the corresponding percentage was 75% and the median age was 57 years (range: 18–76 years). In both cohorts, the use of second-line chemo-free regimens was limited (< 10%) and was mainly reserved for older patients, with a

median age of 73 years in both the polatuzumab vedotin-rituximab +/- bendamustine (range: 60–82 years) and glofitamab cohorts (range: 18–84 years).

Third line treatment significantly differed in the two cohorts due to the different period observed that is, 2019–20 in the polatuzumab vedotin-rituximab +/- bendamustine and 2022–24 in the glofitamab cohort. In the polatuzumab vedotin-rituximab +/- bendamustine cohort, 28% of cases were treated with high dose chemotherapy and SCT, and 26% with chemo-free regimens, while in the glofitamab cohort 33% of patients were treated with polatuzumab vedotin, 28% with CAR-T therapy, and 15% each with high dose chemotherapy and SCT or chemo-free regimens.

The two CUPs generated data to observe the treatment pathways of r/r DLBCL in Italy in two different time periods. A significant shift toward use of novel immunotherapies (primarily, polatuzumab vedotin and CAR-T), particularly after two lines of treatment, emerged in the descriptive analyses of the two cohorts. Earlier Italian data from the STRIDER study which evaluated first and second line therapy in DLBCL patients from

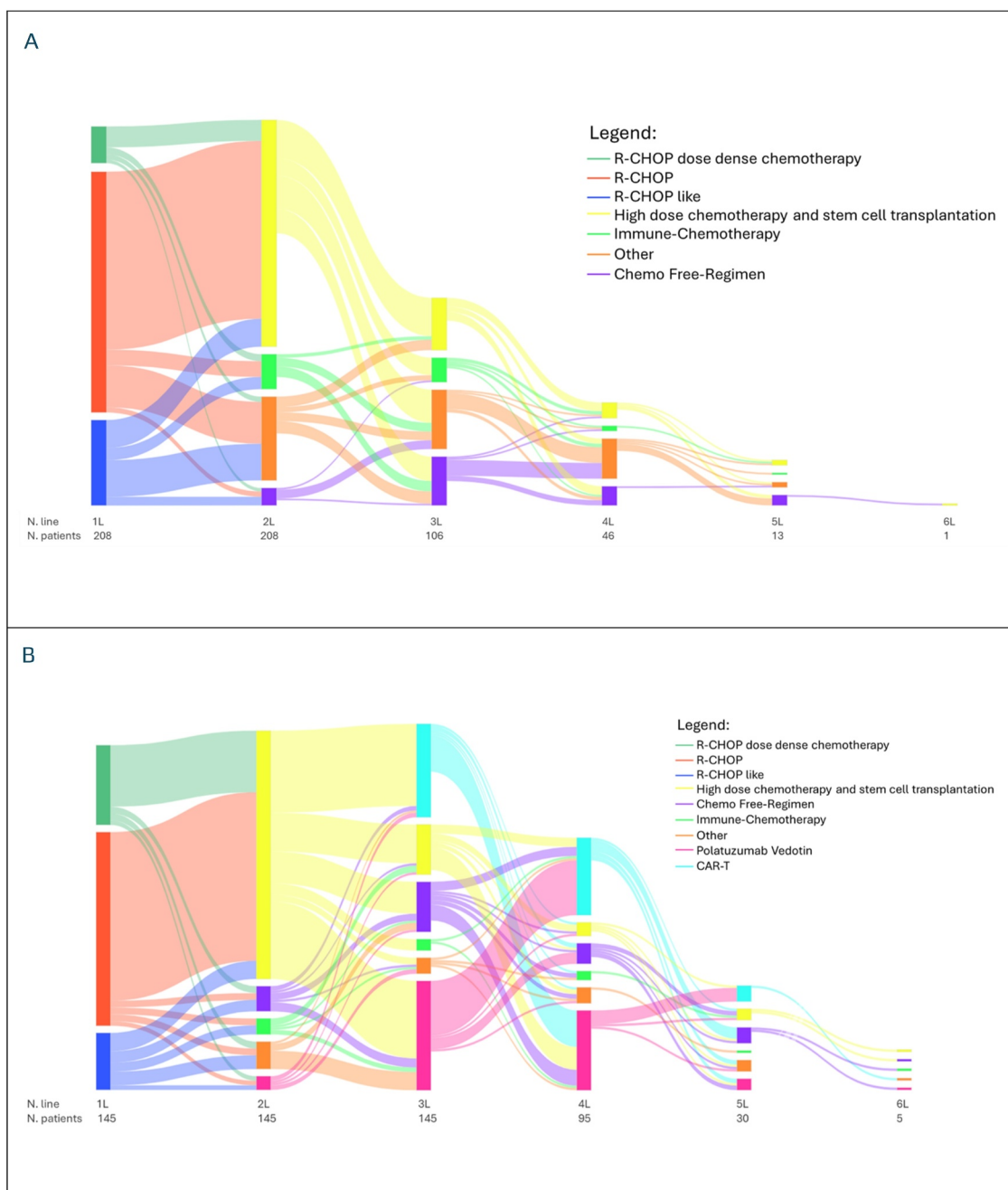


FIGURE 1 | Sankey diagram reporting treatment flow of patients before entering polatuzumab vedotin (Panel A) and glofitamab (Panel B) compassionate use programs.

2010–2019 reported use of lenalidomide, platinum-based regimens, investigational drugs and other various regimens in third line of treatment [5], highlighting the urgency for widespread approval of novel treatments such as CAR-T cells and bispecific antibodies as second-line to improve r/r DLBCL patients outcomes. Moreover the commercial availability of CAR-T cell therapy (November 2019 Yescarta) and polatuzumab vedotin (January 2022) has been captured our observation (Sankey Diagram, Figure 1). Consistent with what was observed in the glofitamab cohort, recent data from the European transplant registry confirms that the use of high dose chemotherapy and SCT is progressively declining with the availability of new immunotherapies [6]. The current therapeutic landscape is also

rapidly evolving, with second-line CAR-T therapy and first-line pola-R-CHP now established standards of care. Due to the temporal constraints of our cohorts and the requirement of ≥ 3 prior treatment lines for CUP eligibility, our dataset cannot yet reflect the impact of these recent advances on treatment sequencing, thus limiting the relevance of the observed sequencing in the current clinical practice.

In conclusion, it provided insights into the evolving treatment pathways in Italy across two distinct time periods, showing the shift toward earlier use of novel immunotherapies. This approach may serve as a valuable complement to traditional data-generation methods, enhancing the understanding of treatment

sequencing in patients with r/r DLBCL within a rapidly evolving therapeutic landscape.

Acknowledgments

The authors gratefully acknowledge Pier Luigi Zinzani, Federica Cavallo and Giuseppe Gritti for their valuable contribution of expertise and time towards the interpretation of the results and the critical review of this manuscript without financial compensation.

Funding

The retrospective analysis was sponsored by Roche SpA.

Conflicts of Interest

Pier Luigi Zinzani: Consultant for MSD, Takeda, Recordati, Novartis, Speakers bureau for Sobi, Kite-Gilead, Janssen, BMS, MSD, AstraZeneca, Takeda, Roche, Recordati, Kyowa Kirin, Novartis, Incyte, Beigene, Advisory Board for Sobi, Kite-Gilead, Janssen, BMS, MSD, AstraZeneca, Takeda, Roche, Recordati, Kyowa Kirin, Novartis, ADC Therap., Incyte, Beigene; Giulia Dell'Omo, Letizia Fusco and Ilaria Peduto are employees of Roche SpA; Carlotta Galeone performed statistical analysis for Roche; Federica Cavallo: Advisory Board for Roche, Speakers fee and Research grant from Roche; Giuseppe Gritti: Advisory Board for Abbvie, Roche, Takeda, Kite-Gilead, Genmab, Speaker's bureau for Takeda, Ideogen, Genmab, Support for attending meetings from Kite-Gilead, Janssen, Research support from Ideogen.

Data Availability Statement

The datasets generated and/or analyzed are available from the corresponding author on reasonable request. For up-to-date details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related documents, see here: go.roche.com/data_sharing.

Pier Luigi Zinzani
Giulia Dell'Omo
Letizia Fusco
Ilaria Peduto
Carlotta Galeone
Federica Cavallo
Giuseppe Gritti

References

1. D. Pilunni and P. Navarra, "Compassionate Drug Uses in Italy: Analysis of Regional and Local Diffusion," *Annali dell'Istituto Superiore di Sanita* 59, no. 1 (2023): 43–50, https://doi.org/10.4415/ANN_23_01_07.
2. N. Liebers, J. Duell, D. Nörenberg, et al., "Polatuzumab Vedotin in Relapsed and Refractory (r/r) Large B-Cell Lymphoma (LBCL): Real-World Data of the German National Compassionate Use Program (CUP)," Supplement, *Blood* 136, no. S1 (2020): 11–13, <https://doi.org/10.1182/blood-2020-136539>.
3. M. Northend, W. Wilson, W. Osborne, et al., "Results of a United Kingdom Real-World Study of Polatuzumab Vedotin, Bendamustine, and Rituximab for Relapsed/Refractory DLBCL," *Blood Advances* 6, no. 9 (2022): 2920–2926, <https://doi.org/10.1182/bloodadvances.2021005953>.
4. L. Argnani, A. Broccoli, C. Pellegrini, et al., "Real-World Outcomes of Relapsed/Refractory Diffuse Large B-Cell Lymphoma Treated With Polatuzumab Vedotin-Based Therapy," *HemaSphere* 6, no. 12 (2022): e798, <https://doi.org/10.1097/hs9.0000000000000798>.

5. I. Dogliotti, V. Peri, M. Clerico, et al., "Real Life Clinical Outcomes of Relapsed/Refractory Diffuse Large B Cell Lymphoma in the Rituximab Era: The STRIDER Study," *Cancer Medicine* 13, no. 14 (2024): e7448, <https://doi.org/10.1002/cam4.7448>.

6. J. R. Passweg, H. Baldomero, F. Ciceri, et al., "Hematopoietic Cell Transplantation and Cellular Therapies in Europe 2022: CAR-T Activity Continues to Grow; Transplant Activity Has Slowed: A Report From the EBMT," *Bone Marrow Transplantation* 59, no. 6 (2024): 803–812, <https://doi.org/10.1038/s41409-024-02248-9>.