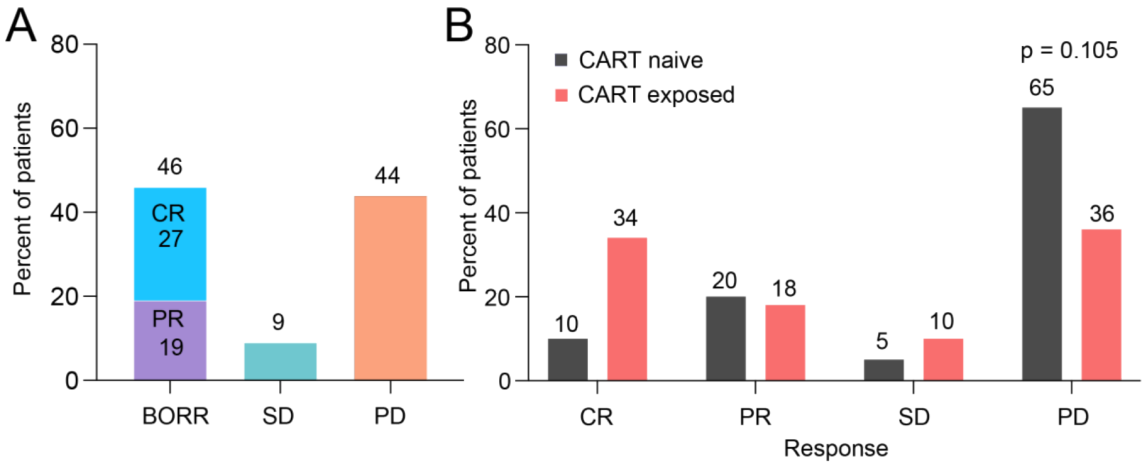
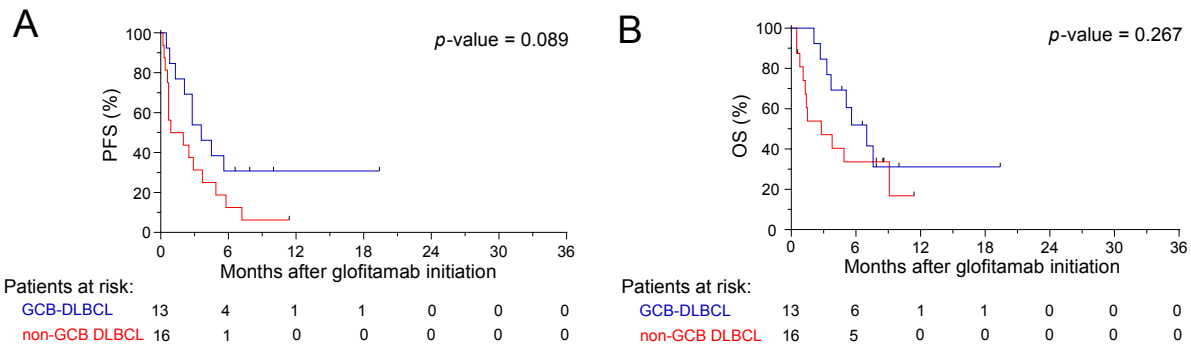
Supplementary Information

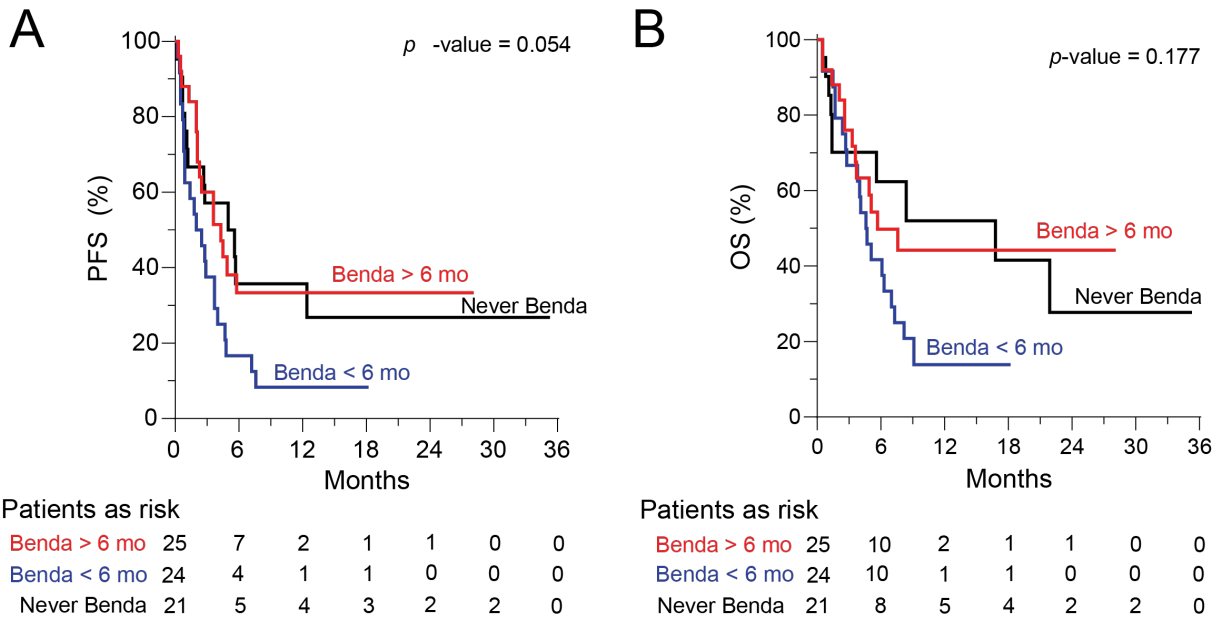
Supplementary Figures



Supplemental Figure S1. Response assessment following glofitamab. (A) Response rates in all patients (n=70); BORR, best overall response rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease. **(B)** Responses separately for CAR-T-naive and CAR-T-exposed patients. The p-value was obtained using a Fisher's Exact t-test.



Supplemental Figure S2. Survival following glofitamab stratified by cell-of-origin subtypes. (A,B) PFS (A) and OS (B) for patients treated with glofitamab in GCB-DLBCL (blue) and non-GCB-DLBCL (red). The p-values are obtained using a logrank test and patients at risk are highlighted below the Kaplan-Meier plot.



Supplemental Figure S3. Survival following glofitamab stratified by prior exposure to bendamustine. (A,B) PFS (A) and OS (B) for patients treated before glofitamab with bendamustine-containing regimes (red, > 6 months; blue, ≤ 6 months; black, never exposed to bendamustine). The p-values are obtained using a logrank test and patients at risk are highlighted below the Kaplan-Meier plot.

Supplementary Tables

Treatment	Number of Patients (n=70), %
Ongoing glofitamab treatment	9 (13%)
No further treatment after glofitamab	35 (50%)
Further treatment after glofitamab*	26 (37%)
Allo SCT	3 (12%)
CAR-T	3 (12%)
Ibrutinib	1 (4%)
Loncastuximab-tesirine	5 (20%)
Pola-BR	3 (12%)
Radiation	1 (4%)
Tafasitamab-Lenalidomide	4 (16%)
VIPOR	3 (12%)
Salvage Chemotherapy (R-ICE, R-DHAP, R-GemOx)	3 (12%)

Supplementary Table S1. Treatments applied after glofitamab. Summary of the subsequent treatments administered to patients following glofitamab. The number of patients per treatment category and the respective percentages are shown. * first treatment after glofitamab is shown, 5 patients received a further therapy thereafter

Parameters	DACH cohort	Dickinson et al	Atesoglu et al
Patient number, %	70	154	43
Age at lymphoma diagnosis (R)	62 (23-94)	66 (21-90)	54 (20-81)
Gender, n (%)			
Male	41 (59%)	100 (65%)	28 (65.1%)
Female	29 (41%)	54 (35%)	15 (34.9%)
Lymphoma types			
- DLBCL *de novo*, n (%)	40 (57%)	110 (71%)	41 (95.4%)
- GCB	13 (19%)	66 (43%)	19 (44.2%)
- Non-GCB	16 (23%)	51 (33%)	11 (25.6%)
- NOS	11 (16%)	38 (25%)	13 (30%)
DLBCL trans. from Ig-NHL, n (%)	18 (26%)	27 (18%)	2 (4.6%)
HGBCL w/ MYC & BCL2/BCL6 rearr., n (%)	9 (13%)	11 (7%) (double hit lymphoma)	*
HGBCL, NOS, n (%)	2 (3%)	*	*
TCRLBCL, n (%)	1 (1%)	*	*
Median time from dx to glo, mo (R)	20 (7-295)	*	*
Therapies prior to glo			
Median therapy lines prior glo, n (R)	4 (2-14)	3 (2-7)	4 (3-6)
Anti-CD20/anthra-based reg., n (%)	67 (96%)	anti- CD20: 154 Antracycline: 149	*
Platinum-based salvage reg., n (%)	63 (90%)	*	*
Benda/ritux +/- polatuz. ved., n (%)	49 (70%)	*	*
Benda w/in last 6 mo prior to glo, n (%)	24 (34%)	*	*
Tafasitamab/lenalidomide, n (%)	24 (34%)	*	*
PD-1 inhibitor, n (%)	6 (9%)	*	*
Ibrutinib, n (%)	4 (6%)	*	*
Prior autologous SCT, n (%)	22 (31%)	28 (18 %)	20 (47.6%)
Prior allogeneic SCT, n (%)	7 (10%)	*	*

Bulky dz (>7.5 cm) prior to glo, avail. for 69/70 pts	22 (32%)	> 6 cm: 64 >10 cm: 18	> 5 cm: 13
Extranodal lesions prior to glo, avail. for 64/70 pts	23 (36%)	95 (62%)	*
Median LDH U/l prior to glo, n (R)	400 (157-1799)	*	*
IPI prior to glo, avail. for 63/70 pts			
IPI low (0-1)	8 (13%)	*	*
IPI low-int. (2)	9 (14%)	*	*
IPI high-int. (3)	26 (41%)	*	*
IPI high (4-5)	20 (32%)	*	*
Dx confirming bx prior to glo, n (%)	38 (54%)	*	*
CD20 positivity by IHC prior to glo		*	*
CD20 + lymphoma	35/38 (92%)	*	*
CD20 - lymphoma	3 (8%)	*	*

Supplementary Table 2. Comparison of patient characteristics between DACH cohort, Phase II trial (Dickinson et al) & Turkish cohort (Atesoglu et al). CAR-T, chimeric antigen receptor T-cells; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B-cell like-type; lg-NHL, low-grade Non-Hodgkin Lymphoma; HGBCL, High-Grade B-Cell Lymphoma; w/, with; rearr. rearrangement; NOS, not otherwise specified; TCRLBCL, T-cell/Histiocyte-Rich Large B-Cell Lymphoma; R, range; glo, glofitamab; anthra-based, anthracycline based; reg., regimen; Benda, bendamustine; ritux, rituximab; polatuz. Ved, polatuzumab vedotin; dz, disease; avail, available; SCT, stem cell transplantation; Dx, diagnosis; bx, biopsy; IHC, immunohistochemistry; int., intermediate; NOS, not otherwise specified; LDH, lactate dehydrogenase; IPI, international prognostic index; +, positive; -, negative; tx, therapy.

Parameters	DACH cohort	Dickenson et al	Atesoglu et al
Patients number, %	70 (100%)	154	43
Median number of glofitamab cycles administered, n (range)	4 (1-12)	5 (1-13)	4 (1-12)
CRS after glofitamab, n (%)			
Any grade CRS	28 (40%)	97 (63%) (ASTCT)	12 (28%)
Grade 0	42 (60%)	57 (37%)	31(72%)
Grade 1	17 (24%)	47%[1]	*
Grade 2	9 (13%)	12%[1]	*
Grade 3	1 (1%)	3%[1]	4 (9%) (≥ III°)
Grade 4	1 (1%)	1%[1]	
Grade 5	0	0	1
ICANS after glofitamab, n (%)			
Any grade ICANS	8 (11%)	12 (8%)	3 (7%)
Grade 0	62 (89%)	*	*
Grade 1	4 (6%)	*	*
Grade 2	3 (4%)	*	*
Grade 3	1 (1%)	3%[1](≥ III°)	*
Grade 4	0		*
Grade 5	0		*
Treatment of CRS (available for 24/28 cases)			
symptomatic, n (%)	10 (36%)	*	*
steroids only, n (%)	1 (4%)	27 (28%)	*
steroids/tocilizumab, n (%)	11 (39%)	16 (16.5%)	*
tocilizumab only, n (%)		31 (32%)	
steroids/tocilizumab/vasopressor, n (%)	2 (7%)	6 (6%)	*
Treatment of ICANS (available for 6/8 cases)			
symptomatic, n (%)	2 (33%)	*	*
steroids only, n (%)	2 (33%)	*	*
steroids/tocilizumab, n (%)	1 (17%)	*	*
steroids/tocilizumab/vasopressor, n (%)	1 (17%)	*	*
Admission to IMC/ICU due to CRS and/or ICANS, n (%)	7 (10%)	7 (7%)	*

Infection incidence under glofitamab, n (%)	22 (31%)	59 (38%)	* 8 (19%) (febrile neutropenia)
Infection type under glofitamab, n (%)			
bacterial	9 (13%)	*	*
fungal	2 (3%)	*	*
viral non-SARS-CoV-2	7 (10%)	*	*
SARS-CoV-2	4 (6%)	9 (6%)	9 (21%)
Infection grade (CTCAE) under glofitamab, n (%) (n=21)			
Grade 1	8 (11%)	*	*
Grade 2	5 (7%)	*	*
Grade 3	6 (9%)	1 (1%)	*
Grade 4	-	3 (2%)	*
Grade 5	2 (3%)	2 (1%)	*
Tumor lysis syndrome under glofitamab, n (%)	2 (3%)	2 (1%) (≥ III°)	*
Median time to best response, days (range)	54 (6-337)	42	84
Best response under glofitamab, n (%)			
Overall response rate (%)	**33 (47%)**	80 (52%) (objective response rate)	14 (37%) (response CR/PR)
CR	19 (27%)	61 (39%)	8 (21%)
PR	20 (20%)	19 (12%)	6 (16%)
SD	6 (9%)	*	3 (8%)
PD	31 (44%)	*	21 (55%)
Median duration of response, months, range	3.2 (0.4-34)	*	*
Reason for ending glofitamab			
Progressive disease	45 (64%)	63 (41%)	*
EOT	9 (13%)	34 (22%)	8 (19%)
Hypersensitivity pneumonitis	1 (1%)	0	0
Death due to non-lymphoma reason	3 (4%)	*	*
Consolidation of PR by allo-SCT	3 (4%)	*	3 (7%)
Ongoing	9 (13%)	12 (8%)	4 (9%)
Median time follow-up from glofitamab initiation, months (range)	5 (0.5-35)	12.6 (0-22)	5.7 (0.3-14.19)

Remission status at last follow-up (available for 69/70 cases)			
CR	16 (23%)	61 (39%) (at median follow up of 12.6 ms)	8 (21%)
PR	8 (12%)	19 (13%) (at median follow up of 12.6 ms)	6 (16%)
SD	4 (6%)	*	*
r/r disease	41 (59%)	*	*
Consolidative therapy following glofitamab			
Allogeneic SCT, n (%)	4 (6%)	7 (22%)	6 (14%)
Survival status at last follow-up			
alive	27 (39%)	50 (32%) (at 12 months)	16 (37%)
dead	43 (61%)	105 (68%) (at 12 months)	27 (63%)
Mortality reasons			
r/r lymphoma	39 (56%)	97 (63%)	16 (37%)
non-lymphoma reasons	4 (6%)	8 (5%) (any grade 5 adverse events)	11 (26%)
- infection	2 (3%)	7 (5%)	7 (16%)
- other reasons	2 (3%)	1 (1%)	4 (9%)

Supplementary Table 3. Comparison of adverse effects and outcomes of glofitamab therapy between DACH cohort, Phase II trial (Dickenson et al) and Turkish cohort (Atesoglu et al). CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IMC, intermediate care; ICU, intensive care unit; CTCAE, Common Terminology Criteria for Adverse Events; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; EOT, end of treatment; allo-SCT, allogeneic stem cell transplantation; r/r, refractory/relapsed; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; [1] absolute number not reported in publication; * not stated in publication

Parameters at initiation of glo	**DLBCL NOS, N=11**	**HGBL, N=11**	**Transformed DLBCL, n=18**	***p*-value**
IPI prior to glo (for 34/40 cases available)				
IPI low (0-1)	1 (14%)	2 (20%)	3 (19%)	1.000
IPI low-int. (2)	0 (0%)	3 (30%)	2 (13%)	0.171
IPI high-int. (3)	2 (25%)	3 (30%)	8 (50%)	0.474
IPI high (4-5)	5 (62%)	2 (20%)	3 (19%)	0.097
Bulky disease (for 39/40 cases available)	3 (27%)	5 (45%)	3 (18%)	0.325
Extranodal lesions (for 35/40 cases available), n (%)	3 (37%)	4 (36%)	1 (6%)	0.091
Median LDH U/l, range	429 (267-1644)	442 (287-1154)	350 (157-512)	0.054
Median therapy lines prior glo, n (range)	4 (2-11)	4 (2-8)	4 (3-9)	0.708
Benda within 6 mo prior glo, n (%)	4 (36%)	4 (36%)	5 (28%)	0.832
Refractory to last tx, n (%)	8 (73%)	8 (73%)	13 (72%)	1.000
CAR-T treatment prior glo, n (%)	7 (63%)	8 (73%)	13 (72%)	0.910

Supplemental Table 4. Patient characteristics at initiation of glofitamab among transformed DLBCL, DLBL NOS and HGBL (n=9).

Parameters at initiation of glo	**Benda within 6 mo. prior glo, n=24**	**No benda within 6 mo. prior glo, n=25**	***p*-value**
IPI prior to glo (for 44/49 cases available)			
IPI low (0-1)	1 (5%)	3 (13%)	0.340
IPI low-int. (2)	4 (19%)	5 (22%)	0.825
IPI high-int. (3)	10 (48%)	10 (43%)	0.783
IPI high (4-5)	6 (29%)	5 (22%)	0.601
Bulky disease (for 48/49 cases available)	11 (46%)	7 (29%)	0.233
Extranodal lesions (for 44/49 cases available)	7 (33%)	10 (43%)	0.409
Median LDH U/l	465 (1-1607)	379 (1-1799)	0.506
Refractory to last tx , %	19 (79%)	16 (64%)	0.206

Supplementary Table 5. Patient characteristics depending on the timepoint of bendamustine pretreatment (≤6 vs. >6 mo.). IPI, International Prognostic Index; LDH, lactate dehydrogenase; tx, treatment; glo, glofitamab; int., intermediate; mo, months.