Glofitamab and epcoritamab for large B cell lymphoma: a real-world retrospective UK analysis of efficacy, tolerability, and impact of treatment sequencing

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Supplementary data

Site	No. of Patients	Investigators
University College Hospital London	34	William Townsend, James Paterson
Freeman Hospital, Newcastle Upon Tyne NHS Foundation Trust	28	Wendy Osborne, Euan Haynes, Tobias Menne
The Royal Marsden NHS Foundation Trust	27	Dima El-Sharkawi, Li Yuan Chan, Sunil Iyengar
University Hospital Southampton NHS Trust	17	Andrew John Davies, Hwai Jing Hiew
Imperial College Healthcare NHS Trust	16	Edward Kanfer, David Foldes
University Hospitals Birmingham	15	Sridhar Chaganti, Henry Crosland
Leeds Teaching Hospitals NHS Trust	15	Mary Owen
Cambridge University Hospitals	14	Kushani Ediriwickrema, George Follows, Anna Santarsieri
Belfast City Hospital	14	Sarah Lawless
Beatson West of Scotland Cancer Centre, Glasgow	13	Matthew Wilson, Pam McKay, Robert Osborn
Royal Cornwall Hospital	13	David Tucker, Cristina M. Thiebaud
Nottingham University Hospital NHS Trust	10	Christopher P. Fox, Harriet Ambrose
Guy's and St Thomas' NHS Foundation Trust	9	Mary Gleeson, Jeff Lam
Edinburgh Cancer Centre	9	Angus Broom
Clatterbridge Cancer Centre, Liverpool,	8	Jeffery Smith, Matthew Wells, Laura Oldham
The Christie NHS Foundation Trust, Manchester,	8	Kim Linton, Lisa Jeffers
King's College Hospital NHS Foundation Trust	8	Andrea Kuhnl
Cancer and Haematology Centre, Churchill Hospital, Oxford	8	Graham Collins, Janine Qasim
Norfolk and Norwich University Hospital, Norwich	7	Nimish Shah
Gloucester Royal Hospital, Gloucestershire Hospitals NHS Foundation Trust	6	Rory McCulloch, Mahina Baloch
St Georges Hospital, London	6	Catherine Cox
University Hospitals Plymouth NHS Trust, Plymouth	6	David Lewis, Abigail Martin
James Paget Hospital, Norfolk,	5	Kyaw Zin Dino Maw
Manchester Royal Infirmary, Manchester	5	Jane Norman, Vismay Deshani
Maidstone and Tunbridge Wells NHS Trust , Kent,	5	Victoria Stables
Aberdeen Royal Infirmary, Aberdeen,	4	Gavin Preston, Dominic Culligan
Frimley Health NHS Foundation Trust, Wexham,	4	John Willan

University Hospitals of Leicester NHS Trust	4	Matthew Ahearne, Rishabh Motiwale
James Cook University Hospital, South Tees Hospitals NHS Foundation Trust	4	Laura Dunning, Joanna Fawcett
Sheffield Teaching Hospitals NHS Foundation Trust	3	Philippa Kelsey
Bristol Haematology and Oncology Centre, Bristol,	2	Caroline Besley, Sanna Lugthart, Jack Easton
Medway Maritime NHS Trust, Kent	2	Sudarshan Gurung, Desmond Ojie
Sunderland Royal Hospital, Sunderland	2	Susanna Mathew
St Bartholomew's Hospital, *Bart's Health NHS Trust*	1	Rebecca Auer

Online Supplementary Table S1. Contributing sites and authors

	All N=324	Glofit N=212	Epcor N=112	p-value
CRS				
No	234 (72%)	153 (72%)	81 (72%)	>0.9
Yes	90 (28%)	59 (28%)	31 (28%)	
1	*51 (16%)*	*30 (14%)*	*21 (19%)*	
2	*31 (10%)*	*22 (10%)*	*9 (8%)*	
3	*7 (2%)*	*6 (3%)*	*1 (1%)*	
5	*1 (<1%)*	*1 (<1%)*	*0*	
ICANS				
No	309 (95%)	203 (96%)	106 (95%)	0.7
Yes	15 (5%)	9 (4%)	6 (5%)	
1	*9 (3%)*	*6 (3%)*	*3 (3%)*	
2	*2 (1%)*	*1 (<1%)*	*1 (1%)*	
3	*3 (1%)*	*1 (<1%)*	*2 (2%)*	
4	*1 (<1%)*	*1 (<1%)*	*0*	
Tocilizumab				
No	256 (85%)	163 (84%)	93 (87%)	0.4
Yes	46 (15%)	32 (16%)	14 (13%)	
1 dose per cycle	*32 (11%)*	*22 (11%)*	*10 (9%)*	
2 doses per cycle	*7 (2%)*	*4 (2%)*	*3 (3%)*	
3 doses per cycle	*3 (1%)*	*3 (2%)*	*0*	
>3 doses per cycle	*3 (1%)*	*3 (2%)*	*0*	
Unknown doses per cycle	*1 (<1%)*	*0*	*1 (1%)*	
Unknown (excluded)	22	17	5	
Infection				
No	160 (49%)	110 (52%)	50 (45%)	0.2
Yes	164 (51%)	102 (48%)	62 (55%)	
ICU admission				
No	299 (95%)	198 (95%)	101 (95%)	>0.9
Yes	15 (5%)	10 (5%)	5 (5%)	
Unknown (excluded)	10	4	6	
Grade ≥3 neutropenia				
No	250 (79%)	157 (75%)	93 (87%)	0.02
Yes	65 (21%)	51 (25%)	14 (13%)	

Unknown (excluded)	9	4	5	
Treatment delay				
No	206 (66%)	143 (70%)	63 (57%)	0.02
Yes	108 (34%)	61 (30%)	47 (43%)	
Infection	*87 (28%)*	*49 (25%)*	*38 (35%)*	*0.05*
Count recovery	*22 (7%)*	*16 (8%)*	*6 (5%)*	*0.4*
Other	*24 (8%)*	*10 (5%)*	*14 (13%)*	*0.01*
Unknown (excluded)	10	8	2	

Online Supplementary Table S2. Safety data (treated patients)

All patients	**All N=324**	**Glofit N=212**	**Epcor N=112**	**Glofit vs Epcor**
Median PFS (95% CI), months	3.1 (2.5-4.2)	3.4 (2.5-5.5)	2.9 (1.7-4.3)	HR=0.85 (95% CI 0.64-1.13), p=0.3
12-month PFS	30% (24-36)	31% (24-39)	27% (18-37)	
Median OS (95% CI), months	6.9 (4.9-10.8)	10.0 (6.2-12.9)	4.7 (2.9-6.8)	HR=0.71 (95% CI 0.52-0.97), p=0.03
12-month OS	43% (36-49)	46% (38-53)	37% (27-47)	

Completed cycle 2	**All N=243**	**Glofit N=179**	**Epcor N=64**	**Glofit vs Epcor**
Median PFS (95% CI), months	5.8 (4.3-8.9)	5.5 (3.2-8.9)	6.8 (5.0-N/A)	HR=1.42 (95% CI 0.94-2.14), p=0.1
12-month PFS	39% (32-46)	37% (29-45)	45% (30-58)	
Median OS (95% CI), months	13.1 (10.7-N/A)	12.5 (10.0-20.3)	Not reached	HR=1.33 (95% CI 0.81-2.18), p=0.3
12-month OS	55% (47-62)	54% (45-62)	62% (46-74)	

Trial eligible	**All N=67**	**Glofit N=50**	**Epcor N=17**	**Glofit vs Epcor**
Median PFS (95% CI), months	5.8 (4.2-21.2)	8.9 (4.3-21.2)	5.0 (1.8-N/A)	HR=0.60 (95% CI 0.28-1.28), p=0.2
12-month PFS	44% (31-56)	49% (33-63)	FU too short	
Median OS (95% CI), months	20.3 (13.3-N/A)	20.3 (13.3-N/A)	5.5 (3.1-N/A)	0.35 (0.14-0.87), p=0.02
12-month OS	65% (50-76)	72% (56-83)	FU too short	

Online Supplementary Table S3. Survival data

Variable	N	Univariable OR (95% CI), p-value	Multivariable (N=181[1]) OR (95% CI), p-value	Multivariable (N=256[2]) OR (95% CI), p-value
Treatment (glofit vs epcor)	306	1.82 (1.00-3.30), p=0.05	-	-
Age (5 year increase)	306	1.09 (0.98-1.21), p=0.1	1.23 (1.05-1.43), p=0.009	1.13 (0.99-1.29), p=0.08
Sex (M vs F)	306	1.04 (0.60-1.80), p=0.9	-	-
Stage 3 vs 1-2 4 vs 1-2	305	 0.56 (0.23-1.36), p=0.2 0.50 (0.26-0.94), p=0.03	-	-
Diagnosis (T-FL vs all others)	305	1.83 (0.95-3.53), p=0.07	-	-
IPI 2 vs 0-1 3 vs 0-1 4-5 vs 0-1	296	 0.65 (0.28-1.52), p=0.3 0.48 (0.20-1.16), p=0.1 0.26 (0.10-0.66), p=0.005	-	-
Bulk (Yes vs No)	305	0.38 (0.18-0.77), p=0.008	-	-
No. prior lines 3 vs <3 4 vs <3 ≥5 vs <3	306	 1.02 (0.56-1.87), p=0.9 1.33 (0.60-2.93), p=0.5 1.36 (0.40-4.58), p=0.6	-	-
ECOG 1 vs 0 ≥2 vs 0	305	 0.98 (0.49-1.95), p>0.9 0.03 (0.004-0.22), p=0.001	-	-
Refractory to most recent line	304	0.17 (0.09-0.32), p<0.001	0.14 (0.06-0.34), p<0.001	0.23 (0.11-0.46), p<0.001
Prior CAR-T	283	0.75 (0.43-1.28), p=0.3	-	-
Last bendamustine >6 months vs Never ≤6 months vs Never	300	 1.28 (0.66-2.48), p=0.5 0.37 (0.18-0.76), p=0.007	 - 0.37 (0.16-0.87), p=0.02	 1.18 (0.54-2.59), p=0.7 0.42 (0.19-0.94), p=0.03
Bendamustine cycles (1 cycle increase)	279	0.91 (0.79-1.04), p=0.2	-	-
LDH>ULN (Yes vs No)	264	0.32 (0.18-0.59), p<0.001	0.43 (0.20-0.90), p=0.03	0.35 (0.18-0.68), p=0.002
Lymphocytes ($1x10^9$/L increase)	306	0.52 (0.29-0.92), p=0.02	-	-

[1]Only includes patients that have complete data for every variable in the table except bendamustine cycles which was excluded due to strong correlation with timing of last bendamustine

[2]Only includes patients that have complete data for the variables selected by forward stepwise selection

Online Supplementary Table S4. Multivariable Analysis of CR

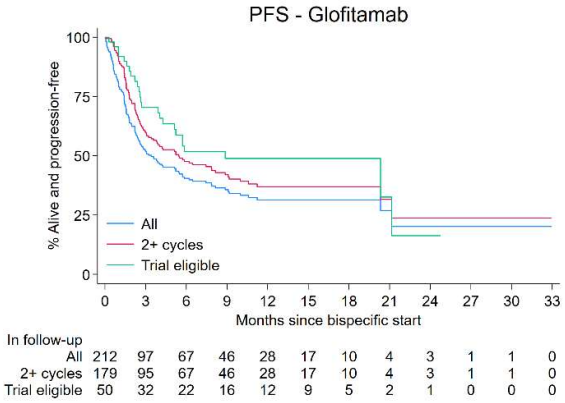
	Never had bendamustine N=171	Bendamustine ≤6 months N=62	p-value vs Never	Bendamustine >6 months N=92	p-value vs Never
Age, median (range) (IQR)	67 (25-90)(59-76)	68.5 (27-89)(57-76)	0.9	68 (18-93)(50.5-78)	0.8
Sex					
Female	60 (35%)	23 (37%)	0.9	34 (37%)	0.8
Male	111 (65%)	39 (63%)		58 (63%)	
ECOG					
0	31 (18%)	9 (15%)		11 (12%)	
1	94 (55%)	40 (66%)		58 (63%)	
2	41 (24%)	12 (20%)	0.7	20 (22%)	0.4
3	2 (1%)	0		3 (3%)	
4	2 (1%)	0		0	
Unknown (excluded from denominator)	1	1		0	
Diagnosis					
DLBCL	106 (62%)	28 (46%)		60 (65%)	
T-FL	29 (17%)	19 (31%)		10 (11%)	
HGBCL	15 (9%)	3 (5%)		9 (10%)	
T-MZL	3 (2%)	1 (2%)		8 (9%)	
T cell/histiocyte rich large b cell lymphoma	2 (1%)	2 (3%)		3 (3%)	
Richter's	5 (3%)	1 (2%)	0.03	0	0.09
FL	3 (2%)	3 (5%)		0	
T-LPL	1 (1%)	4 (7%)		0	
Primary mediastinal b cell lymphoma	1 (1%)	0		1 (1%)	
PTLD	4 (2%)	0		1 (1%)	
Burkitt lymphoma	1 (1%)	0		0	
Grey zone lymphoma	1 (1%)	0		0	
Unknown (excluded from denominator)	0	1		0	
IPI					
0	4 (2%)	0		0	
1	17 (10%)	8 (13%)		7 (8%)	
2	46 (28%)	16 (26%)	0.9	34 (37%)	0.5
3	51 (31%)	21 (34%)		21 (23%)	
4	41 (25%)	14 (23%)		22 (24%)	
5	3 (2%)	2 (3%)		7 (8%)	
Unknown (excluded from denominator)	9	1		1	
Bulk					
Yes	40 (24%)	18 (30%)	0.4	26 (28%)	0.4
No	130 (76%)	43 (70%)		66 (72%)	
Unknown (excluded from denominator)	1	1		0	
No. prior lines, median (range) (IQR)	2 (1-5)(2-3)	3 (1-6)(2-4)	<0.001	3 (1-7)(2-4)	<0.001
Refractory to first line					
Yes	87 (51%)	24 (40%)	0.1	63 (68%)	0.01
No	82 (49%)	36 (60%)		29 (32%)	
Unknown (excluded)	2	2		0	
Refractory to most recent line					
Yes	138 (81%)	39 (65%)	0.01	82 (89%)	0.09
No	32 (19%)	21 (35%)		10 (11%)	
Unknown (excluded from denominator)	1	2		0	
Prior CAR-T					
Yes	63 (39%)	35 (64%)	0.002	49 (58%)	0.006
No	97 (61%)	20 (36%)		36 (42%)	
Unknown (excluded from denominator)	11	7		7	
Lymphocyte count, median (range)	0.79 (<0.1-16.7)	0.52 (0.04-18.97)	0.02	0.42 (0.02-8.00)	<0.001
<0.5	55 (35%)	24 (43%)	0.3	48 (55%)	0.002
≥0.5	104 (65%)	32 (57%)		39 (45%)	

	Never had bendamustine N=171	Bendamustine ≤6 months N=62	p-value vs Never	Bendamustine >6 months N=92	p-value vs Never
Unknown (excluded)	12	6		5	
LDH, median (range)	323 (78-17789)	279 (149-2864)	0.3	345 (119-5504)	0.3
≤ULN	45 (31%)	13 (27%)	0.6	16 (20%)	0.07
>ULN	101 (69%)	36 (73%)		65 (80%)	
Unknown (excluded)	25	13		9	
Trial eligible					
Yes	36 (24%)	10 (18%)	0.3	20 (23%)	0.9
No	114 (76%)	46 (82%)		66 (77%)	
Unknown (excluded from denominator)	21	6		6	
Treatment received					
Glofitamab	112 (66%)	38 (61%)	0.6	62 (67%)	0.8
Epcoritamab	69 (35%)	24 (39%)		30 (33%)	

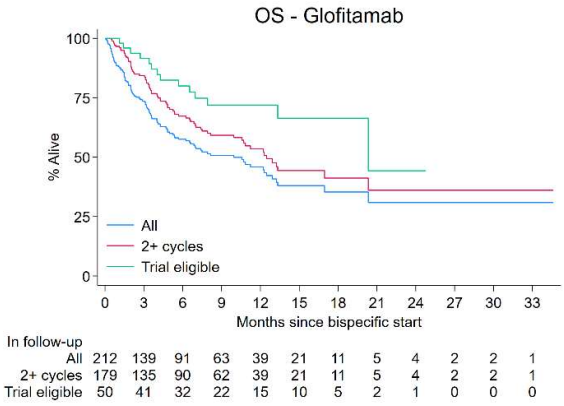
Online Supplementary Table S5. Baseline characteristics by prior bendamustine exposure

Grade 5 CRS event

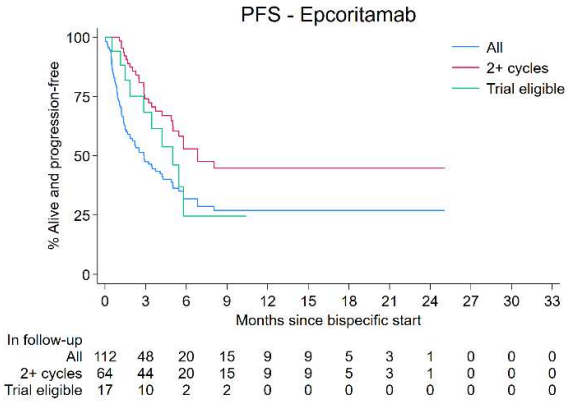
A single grade 5 cytokine release syndrome event was observed following one dose of glofitamab. The patient experienced rapid disease progression between treatment planning and treatment initiation. Consequently, a deliberate decision was made not to pursue intensive care unit admission, with both progressive disease and cytokine release syndrome documented as equally contributing causes of death.



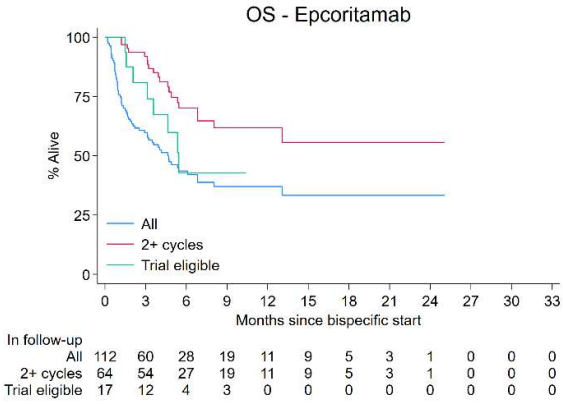
Online Supplementary Figure S1. Glofitamab progression free survival



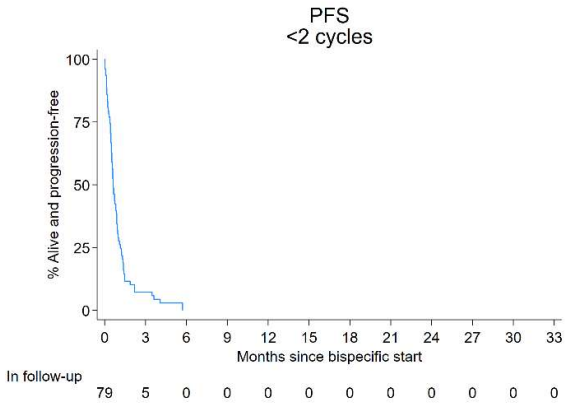
Online Supplementary Figure S2. Glofitamab overall survival



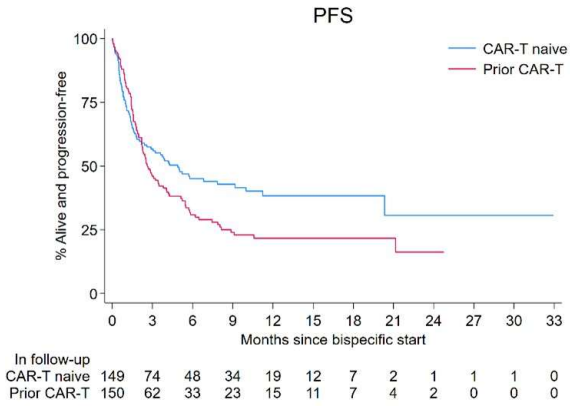
Online Supplementary Figure S3. Epcoritamab progression free survival



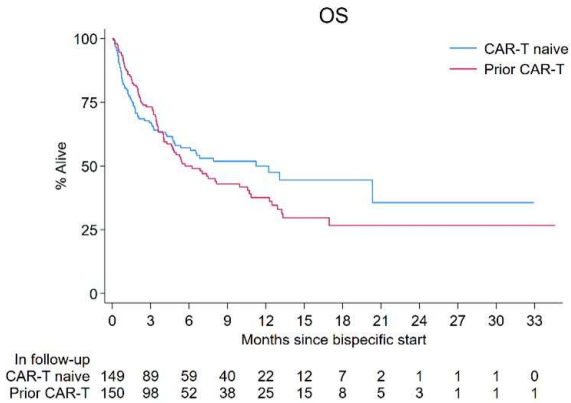
Online Supplementary Figure 4. Epcoritamab overall survival



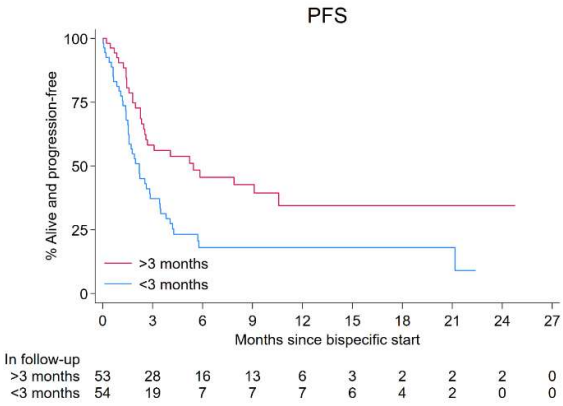
Online Supplementary Figure 5. Patients completing <2 cycles progression free survival



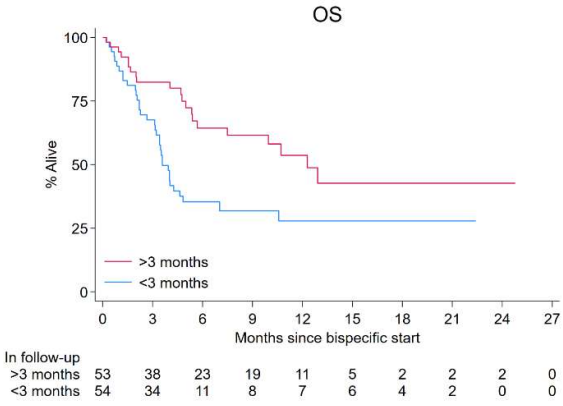
Online Supplementary Figure 6. Progression free survival by prior CAR-T exposure



Online Supplementary Figure 7. Overall survival by prior CAR-T exposure



Online Supplementary Figure 8. Progression free survival by time to CAR-T failure



Online Supplementary Figure 9. Overall survival by time to CAR-T failure