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

by Wendy Osborne, Euan Haynes, William Wilson, Kushani Ediriwickrema, James Paterson, Tobias Menne, Dima El-Sharkawi, Li Yuan Chan, Sunil Iyengar, Andrew J. Davies, Hwai Jing Hiew, Edward Kanfer, David Foldes, Sridhar Chaganti, Henry Crosland, Mary Owen, George Follows, Anna Santarsieri, Sarah Lawless, Matthew Wilson, Pam McKay, Robert Osborn, David Tucker, Cristina M. Thiebaud, Christopher P. Fox, Harriet Ambrose, Mary Gleeson, Jeff Lam, Angus Broom, Jeffery Smith, Matthew Wells, Laura Oldham, Kim Linton, Lisa Jeffers, Andrea Kuhnl, Graham Collins, Janine Qasim, Nimish Shah, Rory McCulloch, Mahina Baloch, Catherine Cox, David Lewis, Abigail Martin, Kyaw Zin Dino Maw, Jane Norman, Vismay Deshani, Victoria Stables, Gavin Preston, Dominic Culligan, John Willan, Matthew Ahearne, Rishabh Motiwale, Laura Dunning, Joanna Fawcett, Philippa Kelsey, Caroline Besley, Sanne Lugthart, Jack Easton, Sudarshan Gurung, Desmond Ojie, Susanna Mathew, Rebecca Auer and William Townsend

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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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- Study conduct: W.T., W.O., W.W., E.H.

- Data collection: All authors
- Data analysis: W.T., W.O., W.W., E.H.
- Data interpretation: W.T., W.O., W.W., E.H.
- Manuscript review/approval and agreement to be accountable for the contents: W.T., W.O., W.H., E.H.

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Data sharing agreement

The data that support the findings of this article are available from the corresponding author upon reasonable request. A data sharing agreement will be required, and data will be provided in de-identified form to protect patient confidentiality.

Running heads

Glofitamab and Epcoritamab for LBCL: Real world UK analysis

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Key points

In a real-world high-risk cohort, the Complete Response Rate (CRR) was 24%. For patients who met trial eligibility criteria, the CRR is comparable to that seen in the registration trials (43%) while the 12-month duration of CR is 88% in all patients.

Encouraging safety data with 12% of patients having G≥2 CRS.

Very poor outcomes and short survival were observed for those patients who are unable to complete cycle 2, highlighting the need for improving patient selection.

High pre-treatment LDH, refractory to the prior line of treatment, bendamustine within 6 months and poor performance status were all associated with inferior PFS

Abstract

Glofitamab and epcoritamab are CD3xCD20 bispecific antibodies licensed for relapsed/refractory large B cell lymphoma (RR LBCL), yet real-world data are limited. Data were collected from 332 patients (219 glofitamab, 113 epcoritamab) across 34 UK centres (November 2023-May 2025). This high-risk cohort had median 2 prior lines of treatment; 179 (55%) primary refractory disease; 81 (25%) ECOG ≥2; 152 (50%) prior Chimeric Antigen Receptor T-cell therapy; and 232 (78%) pivotal-trial ineligible. 7 patients died before treatment initiation, 1 patient was yet to start treatment, of 324 treated patients, 28% had cytokine release syndrome (CRS), predominately grade 1/2 (82/90). Overall response rate (ORR) and complete response rate (CRR) were 43% and 24%, respectively, while for trial-eligible patients the CRR was 43%. At a median 10.0 months follow-up (IQR 5.3-15.0), median progression-free survival (PFS) was 3.1 months (95% confidence interval [CI], 2.5-4.2), median overall survival (OS) was 6.9 months (95% CI, 4.9-10.8). For patients not completing cycle 2, 6-month OS was 4% (95% CI 1-11%). Median duration of complete response was not reached. Refractoriness to prior line of treatment (HR 2.89, 95% CI 1.73-4.81, p=0.007), elevated LDH (HR 2.62, 95% CI 1.74-3.93. p=0.001), bendamustine exposure within 6 months (HR 1.62, 95% CI 1.14-2.30, p=0.007) and ECOG 1 (HR 2.70, 95% CI 1.52-4.79, p=0.001) or 2 (HR 6.49, 95% CI 3.47-12.01, p<0.001) were associated with inferior PFS. This analysis shows both glofitamab and epcoritamab are effective treatment options in RR LBCL with durable complete responses achieved while underscoring the importance of improved patient selection.

Introduction

The treatment of relapsed/refractory Large B Cell Lymphoma (RR LBCL) has been transformed by chimeric antigen receptor T-cell therapy (CAR-T)[1-5]. However, patients with RR LBCL who are unsuitable for, unable to access, or who relapse after CAR-T have poor outcomes[6, 7]. In recent years, following positive results from single-arm phase I/II trials, the CD3xCD20 bispecific antibodies (BsAbs) glofitamab and epcoritamab, have been rapidly integrated into clinical practice in the UK for patients with two or more prior lines of therapy, as permitted by regulatory licensing and reimbursement frameworks[10, 11]. Epcoritamab and glofitamab are both routinely commissioned in the UK following approval by the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC) in the publicly funded National Health Service which is free at point of access for patients. Odronextamab is licensed but is not currently commissioned in the UK[8, 9].

In registration trials, both glofitamab and epcoritamab demonstrated complete response rates (CRR) of approximately 40% in heavily treated patients, many of whom had refractory disease and approximately 1/3rd of patients had previously received CAR-T[10, 11]. Follow-up analyses show high durability of response for both antibodies, with median duration of complete response (DoCR) of 29.8 months and 32 months for glofitamab and epcoritamab respectively[12, 13]. Some real-world data on BsAbs have been published already[14, 15], but additional large cohort real world data are needed.

Several disease-specific and patient characteristics have been shown to be associated with poorer outcomes following CAR-T, including poor ECOG performance status, elevated pre-treatment LDH, extranodal involvement and high tumour volume[16-20]. To date, there is a paucity of data to guide prognosis and identify risk factors for response to BsAbs in 3rd line LBCL. A sub analysis of the glofitamab registration study demonstrated that tumour metabolic volume is predictive of PFS [13], a real world data series identified CD20 negativity as predictive of poor outcomes but other pre-treatment predictors of response have not been identified[14].

This UK real world study aims to characterize patients treated with glofitamab and epcoritamab, assess safety and efficacy in the current treatment landscape and to investigate factors influencing outcomes so we can better understand treatment sequencing and patient selection.

Methods

A retrospective analysis of anonymized consecutive patient data from 34 UK centers. Patients received glofitamab or epcoritamab outside of clinical trials between November 2023 and May 2025. Follow-up data were collected until July 2025. Data were collected from electronic records at local centers as part of a national service evaluation with local audit approval at individual sites. As a service evaluation, all data collection and handling respected the ethical standards set out in the UK. UK BsAb delivery spans academic and community hospitals, and step-up dosing—initially concentrated in tertiary centers—is now routinely undertaken in community sites consistent with the British Society for Haematology (BSH) BsAb guidance [21].

Response assessments were performed locally, with positron emission tomography (PET)/computed tomography (CT) or with plain CT imaging as per local guidelines. Cytokine

Release Syndrome (CRS) and Immune Cell Associated Neurotoxicity Syndrome (ICANS) were graded against ASTCT consensus criteria[22], treatment for CRS and ICANS followed local protocols. Other toxicities were retrospectively graded according to CTCAE v5.0. All patients were managed in accordance with the respective summary of product characteristics including at least one overnight admission for CRS monitoring during cycle 1.

Statistical considerations

All patients commencing BsAb are included in the safety and efficacy evaluable populations. Baseline characteristics, safety data and response rates were compared between treatment groups using chi-squared and Wilcoxon rank-sum tests for categorical and continuous variables, respectively. Duration of response (DoR) and duration of complete response (DoCR) were measured from the date of best response. Progression-free survival (PFS) and overall survival (OS) were measured from the date of first BsAB dose. DoR, DoCR, PFS and OS were assessed using Kaplan-Meier survival analysis and compared between treatment groups using Cox regression. Two separate multivariable analyses were performed to evaluate predictors of progression-free survival and complete response (CR) rate. PFS was analysed using Cox regression and CR rate using logistic regression. To avoid overfitting, forward stepwise variable selection (p-value for inclusion 0.05) was used. Missing data were handled using complete case analysis, whereby observations with missing values for a given variable were excluded from analyses involving that variable.

Results

Baseline characteristics:

332 patients were intended to receive either epcoritamab (n=113) or glofitamab (n=219) from 34 hospitals in the UK between November 2023 and May 2025 (supplementary table 1). Most patients received treatment on a nationally commissioned basis but 96 (29%) received treatment via compassionate access schemes prior to routine commissioning.

Baseline characteristics are described in table 1. The median number of lines of prior therapy was 2 (range 1-7) with 47% receiving BsAb in 4th line or beyond. Of all patients, 80% were refractory (defined as disease that did not respond to, or that progressed within 6 months after completing a line of therapy) to their last line of therapy, while 55% were refractory to their first line of therapy. 60% of patients had a histological diagnosis of DLBCL NOS with transformed follicular lymphoma (FL) the 2nd commonest diagnosis (18%), a wider range of other NHL subtypes were treated than were included in the pivotal trials (table1). Baseline characteristics were compared to the inclusion criteria for the registrational glofitamab trial[11]. Of the 299 patients where data allowed comparison, 26% (50/196) of glofitamab treated patients and 17% (17/103) of epcoritamab treated patients met eligibility criteria. Reasons for not meeting eligibility criteria included cytopenias (n=144), ECOG performance status (PS) ≥2 (n=81), specific co-morbidities (n=51), active or recent infection requiring hospital admission (n=49), and histological diagnosis (n=38).

Important differences in the baseline characteristics of patients who received epcoritamab or glofitamab were identified. Patients treated with epcoritamab were more likely to have an ECOG Performance Score of 2 or more (40% vs 17%, p<0.001) and were less likely to have previously received CAR-T cell therapy (37% vs 56%, p=0.002).

Treatment received:

The median follow-up was 10.0 months (IQR 5.3-15.0), data cut-off date was 29/08/2025. Of 332 patients intended for treatment, 8 did not commence BsAb (see flowchart) and so are excluded from subsequent analyses, 212 and 112 patients in the glofitamab and epcoritamab respectively were included in the treatment efficacy and safety analysis.

The median number of full cycles of glofitamab completed was 3 (range 0-12), 31 (16%) did not complete the 2nd cycle of treatment. For patients completing the 2nd cycle, the median number of cycles completed was 4 (2-12). The commonest reason for terminating treatment was progression of disease (65%). 40/194 (21%) patients completed 12 cycles of fixed duration treatment with 18 still ongoing at time of analysis.

The median number of full cycles of epcoritamab completed was 2 (range 0-25), 46 (47%) did not complete cycle 2 of treatment. For patients completing the 2nd cycle, the median number of cycles completed was 4 (2-25). Progression was the most common reason for termination (79%), 15 patients were still on treatment at time of analysis, 4 (4%) received at least 12 cycles.

Safety:

Safety data are presented in supplementary table 2. For patients receiving glofitamab, any grade CRS occurred in 59/212 (28%), the maximum grade was 1 in 30 (14%), grade 2 in 22 (10%), and grade ≥3 in 7 patients (3%), there were no grade 4 events reported. One patient had a fatal grade 5 CRS event, at the onset of CRS a clinical decision was taken not to escalate their care to the intensive care unit (ICU) due to concurrent disease progression and poor performance status (see additional information in supplementary data). Tocilizumab was administered in 32/195 (16%) patients, only 1 dose was required in 22/32 (69%) cases. Any grade ICANS occurred in 9/212 (4%) patients treated with glofitamab (grade 1- 3% (6), grade 2- <1% (1), grade ≥3- <1% (1)). ICU admission was required in 10/208 (5%) patients receiving glofitamab, primarily for CRS or sepsis management. Infections were reported in 102/212 (48%) patients (G≥3 57/212, 27%), grade ≥3 neutropenia was observed in 51/208 (25%). Treatment delays (most commonly due to slow count recovery or infections) were required in 61/204 (30%) patients.

For patients receiving epcoritamab, any grade CRS occurred in 31/112 (28%), the maximum grade was 1 in 21 (19%), grade 2 in 9 (8%), and there was 1 (1%) grade 3 event. ICANS was reported in 6/112 (5%) patients treated with epcoritamab (grade 1- 3% (3), grade 2- 1% (1), grade 3- 2% (2)), tocilizumab was administered in 14/107 (13%) with 10/14 (71%) requiring only one dose and 5/106 (5%) needed ICU admission, most commonly with sepsis or for CRS management. Infections were reported in 62/112 (55%) patients (G≥3 36/112, 32%). Treatment delays were required in 47/110 (43%) patients primarily due to infection or cytopenias.

Immunoglobulin replacement was administered to 29 patients (9%) in the whole cohort, predominantly in CAR-T exposed patients (n=21). Antimicrobial prophylaxis was employed in 322/324 (99%) patients, predominately with co-trimoxazole and aciclovir as per BSH BsAb guidance [21].

Efficacy:

For glofitamab treated patients the overall response rate (ORR) was 48%, CR 27% (table 2). For patients who completed cycle 2, 31% achieved CR and for the subset of patients who would have met the trial inclusion criteria 47% achieved CR. The median duration of response was 18.8 months (8.1-NA) (figure 1), the median DoCR has not yet been reached, the 12-month DoCR was 84% (66-93%). Median PFS was 3.4 months (2.5-5.5) with 12-

month PFS 31% (24-39), median PFS was 5.5 months (3.2-8.9) for those completing cycle 2 and was 8.9 months (4.3-21.2) for those who were trial eligible (supplementary table 3 and supplementary figure 1). Median OS was 10.0 months (6.2-12.9) with 12-month OS 46% (38-53%), for trial-eligible patients, median OS was 20.3 months (13.3-N/A) (supplementary figure 2).

For epcoritamab treated patients the ORR was 33%, CR 17%, for patients who received ≥2 cycles the ORR and CR were 53% and 30% and for those who would have been trial eligible ORR 44%, CR 31%. The median duration of response was not reached, the 12-month DoR was 71% (45-86%) with 12-month DoCR 100%. Median PFS was 2.9 months (1.7-4.3) (supplementary table 3 and figure 3), median OS 4.7 months (2.9-6.8) (supplementary figure 4). For those starting cycle 2, median PFS was 6.8 months (5.0-NA) and median OS not yet reached.

The 3-month and 6-month OS for patients who did not complete cycle 2 with either BsAb were 13% (95% CI 6-21) and 4% (95% CI 1-11) respectively (figure 2).

In multivariable analysis of factors influencing CR, LDH>ULN (OR 0.35, 95% CI 0.18-0.68, p=0.002), refractoriness to the prior line of therapy (OR 0.23, 95% CI 0.11-0.46, p<0.001) and exposure to bendamustine within 6 months (OR 0.42, 95% CI 0.19-0.94, p=0.03) were independently associated with a lower probability of achieving CR (supplementary table 4). Baseline characteristics by prior bendamustine exposure are detailed in supplementary table 5.

In multivariable analysis of factors associated with PFS (table 3), patients with transformed FL had a significantly better outcome (HR 0.40 (0.24-0.68, p=0.001). Factors associated with inferior PFS were LDH>ULN (HR 2.62, 95% CI 1.74-3.93, p<0.001), refractoriness to the prior line of therapy (HR 2.89, 95% CI 1.73-4.81, p<0.001), ECOG 1 (HR 2.70, 95% CI 1.52-4.79, p=0.001) or ECOG 2 (HR 6.49, 95% CI 3.47-12.01, p<0.001), and exposure to bendamustine within 6 months (HR 1.62, 95% CI 1.14-2.30, p=0.007). A univariate analysis restricted to patients receiving BsAb within 6 months of previous therapy (n=213) also found that patients who received bendamustine within 6 months of BsAb had poorer PFS (HR <6 months vs Never = 1.58, 95% CI 1.12-2.23, p=0.01).

Prior CAR-T exposure was not independently associated with inferior PFS or CRR on multivariate analysis. 1-year PFS was 38% (95% CI 29-47) in CAR-T naïve and 22% (95% CI 15-30) in exposed patients (HR 1.31, 95% CI 0.98-1.74, p=0.07) (supplementary figure 5). CRR was 27% (95% CI 42-60) in CAR-T naïve and 22% (95% CI 16-30) in exposed patients (p=0.3). 1-year OS was 50% (95% CI 40-59) in CAR-T naïve and 38% (95% CI 29-47) in exposed patients (HR 1.15, 95% CI 0.84-1.59, p=0.4) (supplementary figure 6).

Of the 107 patients (82 glofitamab, 25 epcoritamab) who had received CAR-T as the prior treatment line before BsAb, shorter time from CAR-T infusion to BsAb start was associated with inferior PFS both as a continuous variable (HR for 1 month increase= 0.94, 95% CI 0.89-1.00, p=0.05) and when early CAR-T failure occurred (<3 months from infusion) (HR=0.51, 95% CI 0.32-0.83, p=0.005) (supplementary figure 7) which was also associated with inferior OS (HR=0.46, 95% CI 0.26-0.79, p=0.005) (supplementary figure 8). Time to CAR-T failure was significantly associated with best response both as a continuous variable for CR (HR for one month increase=1.13, 95% CI 1.03-1.25, p=0.01) and OR (HR for one month increase=1.19, 95% CI 1.06-1.35, p=0.005), as well as in early CAR-T failure, CR (HR 2.53, 95% CI 1.01-6.33, p=<0.001), OR (HR 2.93, 95% CI 1.29-6.65, p=0.01). CAR naïve patients were more likely to be older, have higher IPI, fewer prior lines, not refractory to first line and less likely to have received prior bendamustine.

Predictive factors associated with not completing cycle 2 included ECOG >1 OR 0.09 (0.02-0.42, p=0.002), bendamustine within 6 months OR 0.48 (0.24-0.99, p=0.05), LDH >ULN OR 0.15 (0.05-0.43, p<0.001), epcoritamab treatment OR 0.27 (0.14-0.53, p=<0.0.01).

Of 7 patients with a diagnosis of T-cell/histiocyte rich LBCL (6 glofitamab, 1 epcoritamab) none responded to treatment with best responses being progressive disease (6/7) and stable disease (1/7).

Of 14 patients with active CNS involvement at the time of BsAb treatment initiation. CR was reached in 4/14 (29%) and PR in a further 5/14 (36%) with progressive disease in 5/14 (36%).

Discussion

We report here a retrospective real-world series of 324 patients treated with epcoritamab or glofitamab for RR LBCL in the UK. This is the largest series of comprehensive, real-world data on patients treated with BsAbs for RR LBCL published to date. We demonstrate a similar toxicity profile to the published trials, high efficacy with durable remissions, and identify factors influencing response and informing treatment decisions.

In this series, most patients had high-risk features with nearly half of the patients receiving treatment in 4th line or beyond, and 50% having received prior CAR-T, a high-risk population for whom life expectancy would be anticipated to be short in the absence of effective therapy. Furthermore, 78% would not have met trial eligibility criteria.

It is important to highlight that there were significant differences in baseline characteristics between those treated with the two BsAbs. Patients treated with epcoritamab were more likely to have higher ECOG performance score, and less likely to have previously received CAR-T than patients treated with glofitamab. Reasons for these differences may include a more permissive ECOG for epcoritamab approval and reimbursement but other reasons impacting choice of BsAb were not formally investigated. Both drugs are routinely commissioned and reimbursed in the UK for patients with RR LBCL and 2 or more lines of therapy. More patients were treated with glofitamab possibly reflecting earlier reimbursement and availability. Commissioning in the UK permits ECOG 0-2 for epcoritamab whereas glofitamab is restricted to ECOG 0-1 as per the registration trials and this may have influenced the use of epcoritamab in a frailer cohort that were less likely to have been CAR-suitable. The inherent differences in the populations treated in this study prevents any comparison of efficacy and safety between the two products.

The safety data presented here closely mirror the clinical trials despite being used in predominantly trial-ineligible patients. The rate of any grade CRS was 28% for both antibodies with G≥2 in about 13% of patients for both. ICANS events were rare. Only 5% of patients needed care on ICU during treatment with either drug. Infections were the commonest reported toxicity in this heavily pre-treated population highlighting the need to be vigilant in monitoring for infections and ensuring adequate vaccination and antimicrobial prophylaxis. Overall, these safety data confirm that BsAbs can be delivered safely in a wide range of hospitals. The geographical spread of units and community hospitals offering BsAbs emphasises deliverability in hospitals close to patient's homes. This is important for patient experience and is a key difference between delivery of BsAbs and CAR-T, which remains restricted to larger hospitals.

Achieving CR is important in LBCL and the registration trials have focused on CR rate and durability of these remissions. The overall CR rate in this study of 24% is inferior to the published trial data but when considering use as monotherapy in such a heavily pre-treated, refractory population for whom there are very few other treatment options, BsAB represents an effective treatment choice. When analysis is restricted to patients who would have met trial eligibility criteria, the CR rate is comparable to that seen in the registration trials (43%).

We identified that a proportion of patients did not complete the 2nd cycle of BsAb most commonly due to progression of disease and clinical deterioration during cycle 1. Numerically more patients treated with epcoritamab were unable to complete cycle 2 than glofitamab again reflecting differences in these populations. Outcomes for these patients were very poor, with 3 month OS 13% (95% CI 6-21). We performed an exploratory analysis of outcomes for patients completing cycle 2 and identified outcomes that were close to the published trial data for these patients. Our finding that up to 47% of patients do not complete cycle 2 indicates we need to improve patient selection or investigate ways to improve responses for high-risk patients. Compared to delivery of CAR-T cell therapy, BsAbs are available immediately with no requirement to wait for funding approvals, apheresis slots and manufacturing timelines. This difference in patient pathway may lead to differences in patients being selected for each approach and may explain why real-world efficacy data for CAR-T infused patients is closer to the trial data than we see in this and other series of patients treated with BsAbs in the real-world setting[14, 16, 23].

In a multivariate analysis of factors impacting CR, refractoriness to last line of therapy and elevated LDH were independently associated with reduced chance of attaining CR. Patients with a diagnosis of transformed FL were significantly more likely to achieve CR. These findings are similar to predictive factors identified in real world CAR-T studies[16, 24].

Durability of remissions was very high in our cohort with median DoCR not reached for either antibody and 12-month DoCR of 88% overall. This is an important finding and although follow-up is too short at present to understand the curative potential of these drugs in the real-world setting, it is encouraging that few relapses have been observed to date in those who achieve CR.

Survival data in our series show median PFS of 3.4 and 2.9 months for glofitamab and epcoritamab respectively with median OS of 10 and 4.7 months respectively. Given the differences in the patient populations we are unable to interpret any differences in survival data between the two antibodies. Median PFS and OS for patients who completed cycle 2 and those who were trial-eligible were superior to the whole population, again highlighting a need to improve patient selection and explore alternative strategies for those most likely to progress prior to completing cycle 2.

In a multivariate analysis of risk factors for PFS, transformed FL was associated with improved PFS, refractoriness to last line of therapy, higher ECOG, elevated LDH and prior bendamustine were independently associated with inferior PFS.

Whereas previous studies, including the epcoritamab NHL1 study, did not identify prior bendamustine as a risk factor for impaired response[10, 14, 15, 25, 26], we have identified this in our larger cohort in which 160 (48%) patients had previously been exposed to bendamustine, HR 1.69 (1.18-2.41 p=0.004). Patients who had bendamustine within 6 months of BsAb had an inferior PFS and reduced chance of attaining CR. This novel finding

should be interpreted with caution and we have been unable to explore reasons for poor response in bendamustine-exposed patients which may include impaired T-cell fitness or confounding factors.

The PFS for patients previously treated with CAR-T was numerically lower than for CAR-naive patients but did not reach significance (HR 1.40, 95% CI 1.00-1.97, p = 0.051). Previous trial data have indicated similar outcomes for CAR-exposed patients[11, 27, 28]. Similar to other series, timing of relapse post CAR-T appears to be prognostic with shorter time to CAR-T failure associated with inferior response rates[29], PFS and OS. Better treatments are needed for patients with early relapse post CAR-T.

The strengths of our study are that it is a large cohort that captures most patients treated in the UK in the early years of BsAb availability including data from both larger academic hospitals and smaller community hospitals. As with all retrospective series, the main weaknesses are that it is hard to capture complete and detailed safety data, we were unable to conduct central review of histology or collect data on CD20 status which has previously been identified as an important risk factor for response and responses could not be verified by central imaging review.

Conclusions

These data further confirm that epcoritamab and glofitamab monotherapies are effective treatments in relapsed LBCL, with high durability of remissions in those who attain CR even in this high-risk population. Unlike other published data, efficacy was impacted by prior bendamustine and this may have implications for sequencing decisions. Safety data closely mirrored trial data. Outcomes were very poor for those unable to complete cycle 2. It is important to improve identification of those at high-risk of failure so these patients can be offered other management options which may include clinical trials or no further treatment.

CD3xCD20 BsAbs are being explored in numerous trials in earlier lines of therapy and in novel combinations with data demonstrating that higher response rates can be achieved, and it is hoped that such strategies will lead to better options for patients with RR LBCL in the near future[30-32].

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Tables

	All N=332	Glofit N=219	Epcor N=113	p-value
Age, median (range) (IQR)	68 (18-93) (58-76)	68 (18-90) (57-76)	68 (34-93) (59-76)	0.8
Sex				
Female	119 (36%)	77 (35%)	42 (37%)	0.7
Male	213 (64%)	142 (65%)	71 (63%)	
ECOG				
0	51 (15%)	41 (19%)	10 (9%)	<0.001
1	198 (60%)	140 (65%)	58 (51%)	
2	74 (22%)	34 (16%)	40 (35%)	
3	5 (2%)	2 (1%)	3 (3%)	
4	2 (1%)	0	2 (2%)	
Unknown (excluded from denominator)	2	2	0	
Diagnosis				
DLBCL	198 (60%)	129 (59%)	69 (61%)	0.07
T-FL	61 (18%)	43 (20%)	18 (16%)	
HGBCL	27 (8%)	15 (7%)	12 (11%)	
T-MZL	12 (4%)	11 (5%)	1 (1%)	
T cell/histiocyte rich large b cell lymphoma	7 (2%)	6 (3%)	1 (1%)	
Richter’s	6 (2%)	5 (2%)	1 (1%)	
FL	6 (2%)	2 (1%)	4 (4%)	
T-LPL	5 (2%)	2 (1%)	3 (3%)	
Primary mediastinal b cell lymphoma	2 (1%)	2 (1%)	0	
PTLD	5 (2%)	1 (<1%)	4 (4%)	
Burkitt lymphoma	1 (<1%)	1 (<1%)	0	
Grey zone lymphoma	1 (<1%)	1 (<1%)	0	
Unknown (excluded from denominator)	1	1	0	
IPI				
0	4 (1%)	4 (2%)	0	0.8
1	32 (10%)	20 (10%)	12 (11%)	
2	100 (31%)	65 (31%)	35 (32%)	
3	94 (29%)	62 (30%)	32 (29%)	
4	78 (24%)	51 (24%)	27 (24%)	
5	13 (4%)	8 (4%)	5 (5%)	
Unknown (excluded from denominator)	11	9	2	
Bulk (>7.5cm)				
Yes	85 (26%)	51 (24%)	34 (30%)	0.2
No	245 (74%)	166 (77%)	79 (70%)	
Unknown (excluded from denominator)	2	2	0	
No. prior lines, median (range) (IQR)	2 (1-7) (2-3)	2 (1-7) (2-3)	2 (1-5) (2-3)	0.5
Refractory to first line				
Yes	179 (55%)	116 (54%)	63 (56%)	0.7
No	148 (45%)	99 (46%)	49 (44%)	
Unknown (excluded)	5	4	1	
Refractory to most recent line				
Yes	264 (80%)	177 (82%)	87 (77%)	0.3
No	65 (20%)	39 (18%)	26 (23%)	
Unknown (excluded from denominator)	3	3	0	
Prior CAR-T				
Yes	152 (50%)	115 (56%)	37 (37%)	0.002
No	155 (50%)	92 (44%)	63 (63%)	
Unknown (excluded from denominator)	25	12	13	
Prior bendamustine				
Yes	160 (48%)	106 (48%)	54 (48%)	0.9

	All N=332	Glofit N=219	Epcor N=113	p-value
No	172 (52%)	113 (52%)	59 (52%)	
Lymphocyte count, median (range)	0.62 (<0.1-18.97)	0.61 (0.1-18.97)	0.62 (<0.1-16.7)	0.4
<0.5	128 (39%)	83 (41%)	45 (43%)	0.7
≥0.5	180 (54%)	121 (59%)	59 (57%)	
Unknown (excluded)	24	15	9	
LDH, median (range)	323 (78-19065)	325 (78-19065)	311 (149-17789)	0.6
≤ULN	75 (27%)	48 (26%)	27 (28%)	0.7
>ULN	208 (74%)	140 (74%)	68 (72%)	
Unknown (excluded)	49	31	18	
Trial eligible				
Yes	67 (22%)	50 (26%)	17 (17%)	0.08
No	232 (78%)	146 (75%)	86 (84%)	
Unknown (excluded from denominator)	33	23	10	

Table 1. Baseline Characteristics

All patients	**All N=324**	**Glofit N=212**	**Epcor N=112**	**Glofit vs Epcor**
Best response				
CR/CMR	73 (24%)	55 (27%)	18 (17%)	
PR/PMR	58 (19%)	41 (20%)	17 (16%)	
SD	8 (3%)	3 (1%)	5 (5%)	
PD	157 (51%)	97 (48%)	60 (57%)	
Died before assessment	10 (3%)	5 (2%)	5 (5%)	
Unknown (excluded)	18	11	7	
Overall response rate (95% CI)	43% (37-49)	48% (41-55)	33% (24-43)	p=0.02[1]
Complete response rate (95% CI)	24% (19-29)	27% (21-34)	17% (10-26)	p=0.05[1]
Median DoR (95% CI), months	18.8 (18.3-N/A)	18.8 (8.1-N/A)	Not reached	HR=1.12 (95% CI 0.46-2.72), p=0.8
12-month DoR rate	63% (51-73)	61% (47-72)	71% (45-86)	
Median DoCR (95% CI), months	Not reached	Not reached	Not reached	p=0.2[2]
12-month DoCR	88% (73-95)	84% (66-93)	100% (N/A)	
Started cycle 2	**All N=243**	**Glofit N=179**	**Epcor N=64**	**Glofit vs Epcor**
Best response				
CR/CMR	72 (31%)	54 (32%)	18 (30%)	
PR/PMR	55 (24%)	41 (24%)	14 (23%)	
SD	5 (2%)	1 (1%)	4 (7%)	
PD	97 (42%)	73 (43%)	24 (40%)	
Died before assessment	1 (1%)	1 (1%)	0	
Unknown (excluded)	13	9	4	
Overall response rate (95% CI)	55% (49-62)	56% (48-63)	53% (40-66)	p=0.7[1]
Complete response rate (95% CI)	31% (25-38)	32% (25-39)	30% (19-43)	p=0.8[1]
Median DoR (95% CI), months	18.8 (18.3-N/A)	18.8 (8.7-N/A)	Not reached	HR=1.27 (95% CI 0.48-3.33), p=0.6
12-month DoR rate	64% (52-74)	62% (48-73)	73% (46-88)	
Median DoCR (95% CI), months	Not reached	Not reached	Not reached	p=0.3[2]
12-month DoCR	90% (74-96)	86% (67-95)	100% (N/A)	
Trial eligible	**All N=67**	**Glofit N=50**	**Epcor N=17**	**Glofit vs Epcor**
Best response				
CR/CMR	27 (43%)	22 (47%)	5 (31%)	
PR/PMR	11 (17%)	9 (19%)	2 (13%)	
SD	3 (5%)	1 (2%)	2 (13%)	
PD	22 (35%)	15 (32%)	7 (44%)	
Unknown (excluded)	4	3	1	
Overall response rate (95% CI)	60% (47-72)	66% (51-79)	44% (20-70)	p=0.1[1]
Complete response rate (95% CI)	43% (30-56)	47% (32-62)	31% (11-59)	p=0.3[1]
Median DoR (95% CI), months	18.3 (6.0-N/A)	18.3 (6.0-N/A)	4.2 (2.4-N/A)	HR=0.49 (95% CI 0.10-2.38), p=0.4
12-month DoR rate	68% (48-82)	71% (48-N/A)	FU too limited	
Median DoCR (95% CI), months	18.8 (18.3-N/A)	18.8 (18.3-N/A)	Not reached	p=0.5[2]
12-month DoCR	83% (56-94)	81% (51-93)	FU too limited	

Table 2. Response data

Variable	N	Univariable HR (95% CI), p-value	Multivariable (N=252[1]) HR (95% CI), p-value	Multivariable (N=256[2]) HR (95% CI), p-value
Treatment (glofit vs epcor)	324	0.85 (0.64-1.13), p=0.3	-	-
Age (5 year increase)	324	0.97 (0.92-1.02), p=0.2	-	-
Sex (M vs F)	324	1.31 (0.98-1.76), p=0.07	-	-
Stage 3 vs 1-2 4 vs 1-2	323	1.16 (0.70-1.94), p=0.6 1.60 (1.09-2.34), p=0.02	- 1.59 (1.12-2.26), p=0.01	0.94 (0.51-1.75), p=0.9 1.54 (0.99-2.38), p=0.05
Diagnosis (T-FL vs all others)	323	0.55 (0.36-0.83), p=0.005	0.40 (0.24-0.67), p=0.001	0.40 (0.24-0.67), p=0.001
IPI 2 vs 0-1 3 vs 0-1 4-5 vs 0-1	314	1.55 (0.88-2.73), p=0.1 1.85 (1.04-3.26), p=0.04 2.82 (1.61-4.93), p<0.001	-	-
Bulk (Yes vs No)	323	1.64 (1.21-2.22), p=0.001	-	-
No. prior lines 3 vs <3 4 vs <3 ≥5 vs <3	324	1.20 (0.88-1.64), p=0.2 1.03 (0.68-1.57), p=0.9 0.87 (0.44-1.72), p=0.7	-	-
ECOG 1 vs 0 ≥2 vs 0	323	1.77 (1.12-2.79), p=0.02 3.78 (2.33-6.14), p<0.001	2.72 (1.51-4.91), p=0.001 6.52 (3.47-12.25), p<0.001	2.70 (1.52-4.79), p=0.001 6.46 (3.47-12.01), <0.001
Refractory to most recent line	322	2.81 (1.83-4.31), p<0.001	2.58 (1.57-4.22), p<0.001	2.89 (1.73-4.81), p<0.001
Prior CAR-T	299	1.31 (0.98-1.74), p=0.07	1.40 (1.00-1.95), p=0.05	1.40 (1.00-1.97), p=0.05
Last bendamustine >6 months vs Never ≤6 months vs Never	318	1.01 (0.67-1.52), p=0.9 1.93 (1.42-2.62), p<0.001	- 1.53 (1.10-2.14), p=0.01	1.23 (0.72-2.10), p=0.4 1.62 (1.14-2.30), p=0.007
Bendamustine cycles (1 cycle increase)	296	1.05 (0.98-1.11), p=0.2	-	-
LDH>ULN (Yes vs No)	279	2.32 (1.59-3.39), p<0.001	2.68 (1.78-4.03), p<0.001	2.62 (1.74-3.93), p<0.001
Lymphocytes<0.5x10^9/L (Yes vs No)	324	1.48 (1.13-1.96), p=0.005	-	-

[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

Table 3. Multivariate analysis of PFS

Figure legend

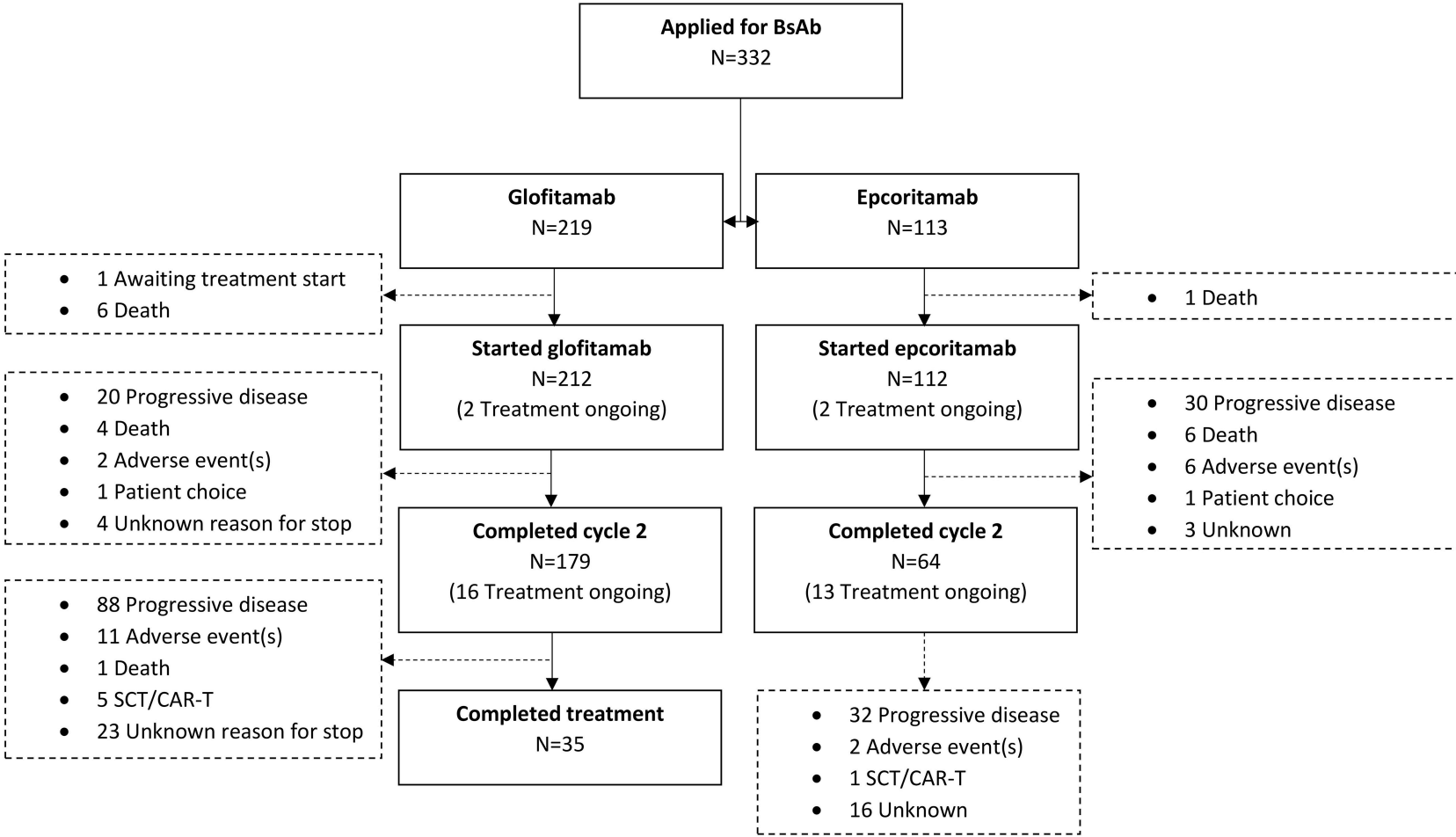
Figure 1. Flow Chart

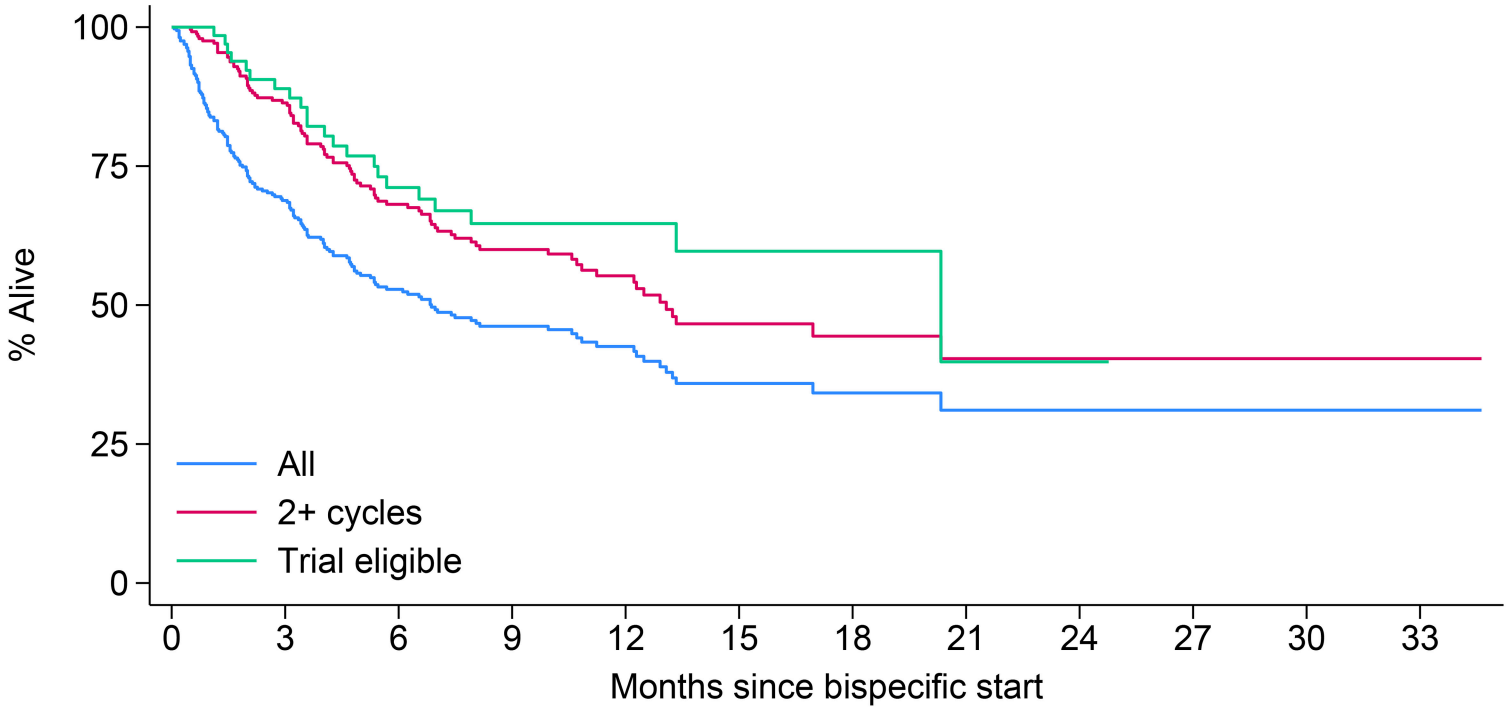
Figure 2. All patients Progression Free Survival (PFS)

Figure 3. All patients Overall Survival (OS)

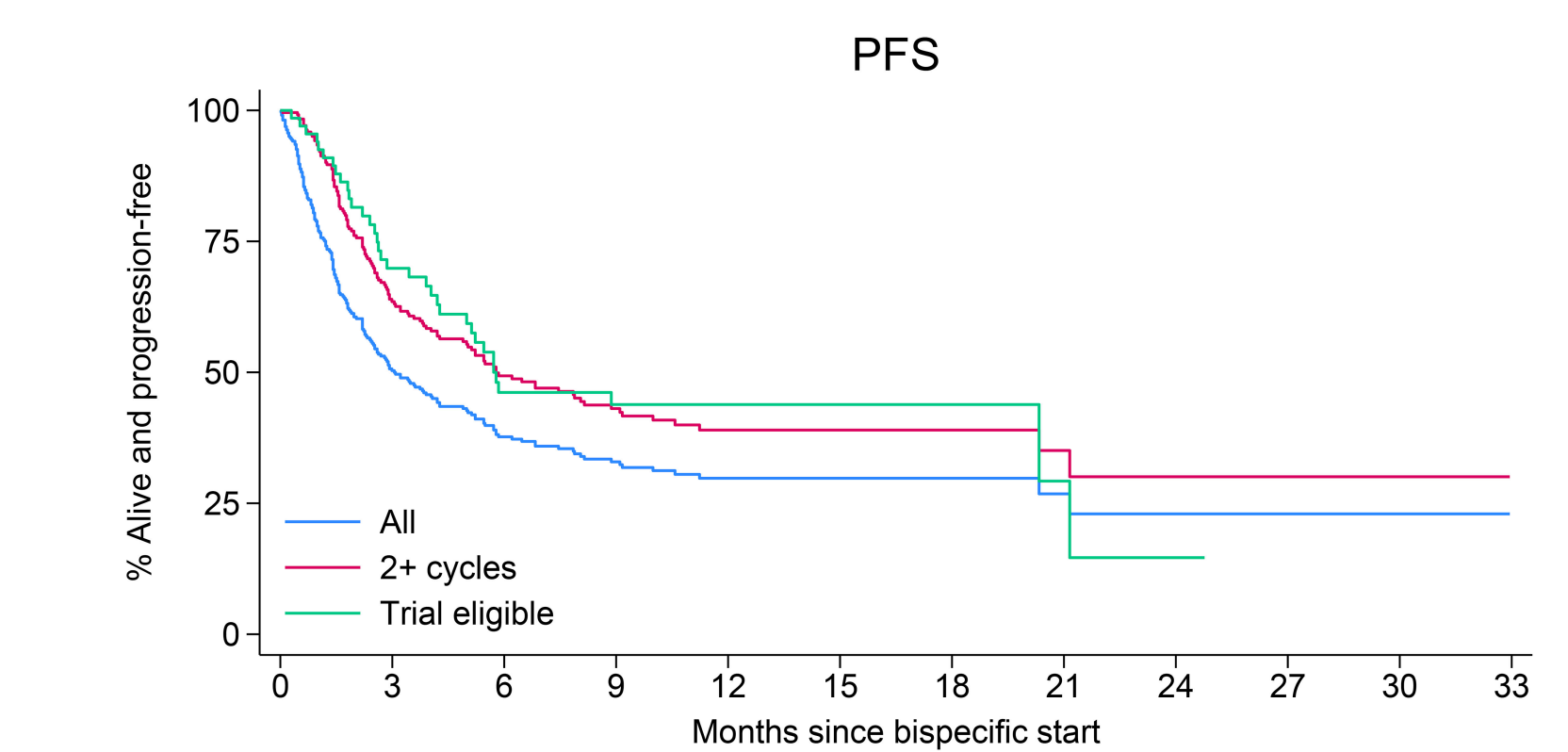
Figure 4. All patients Duration of Complete Response (DoCR)

Figure 5. Patients completing less than 2 cycles Overall Survival (OS)

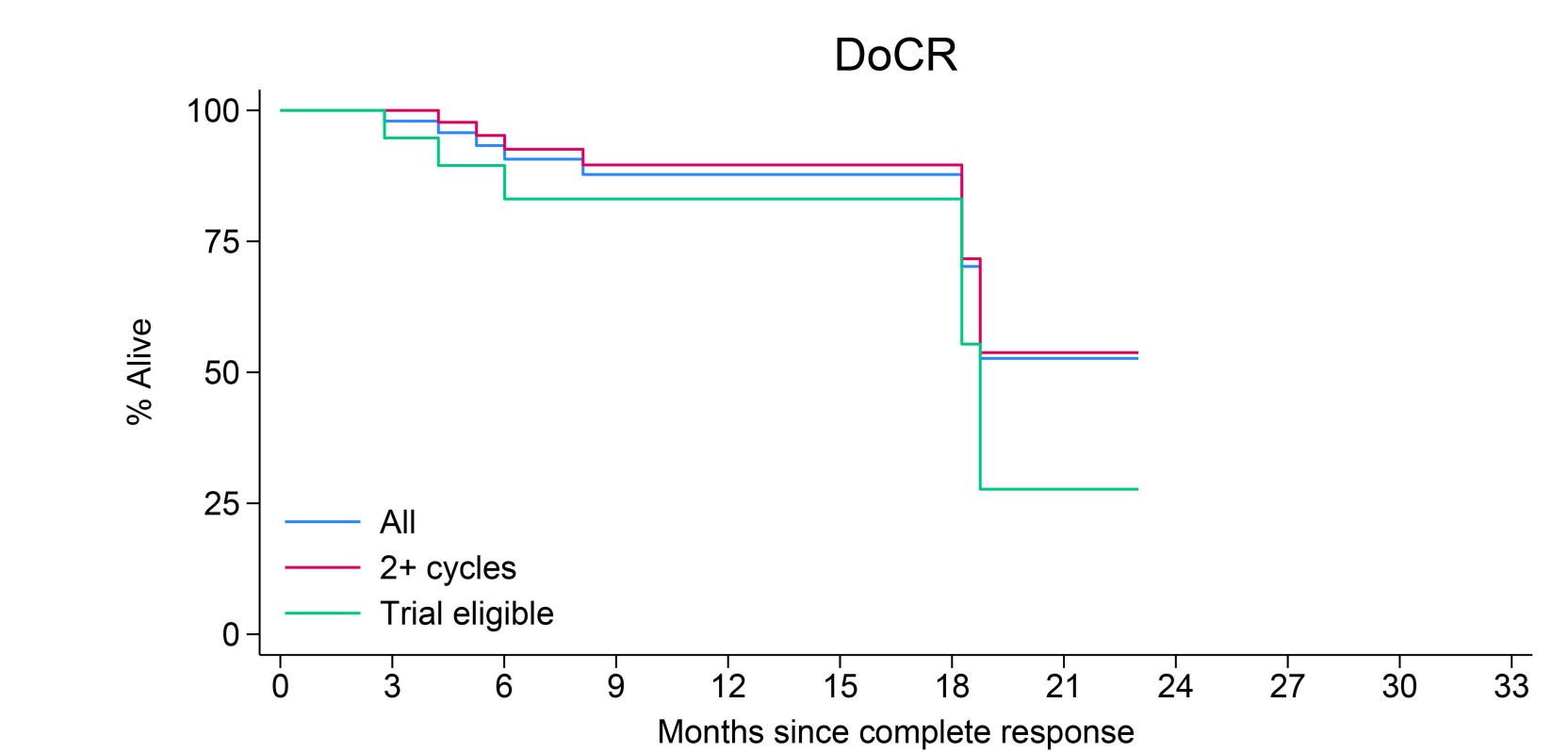

Applied for BsAb
N=332
Glofitamab
N=219
Epcoritamab
N=113
1 Awaiting treatment start
6 Death
1 Death
Started glofitamab
N=212
(2 Treatment ongoing)
Started epcoritamab
N=112
(2 Treatment ongoing)
20 Progressive disease
4 Death
2 Adverse event(s)
1 Patient choice
4 Unknown reason for stop
30 Progressive disease
6 Death
6 Adverse event(s)
1 Patient choice
3 Unknown
Completed cycle 2
N=179
(16 Treatment ongoing)
Completed cycle 2
N=64
(13 Treatment ongoing)
88 Progressive disease
11 Adverse event(s)
1 Death
5 SCT/CAR-T
23 Unknown reason for stop
Completed treatment
N=35
32 Progressive disease
2 Adverse event(s)
1 SCT/CAR-T
16 Unknown



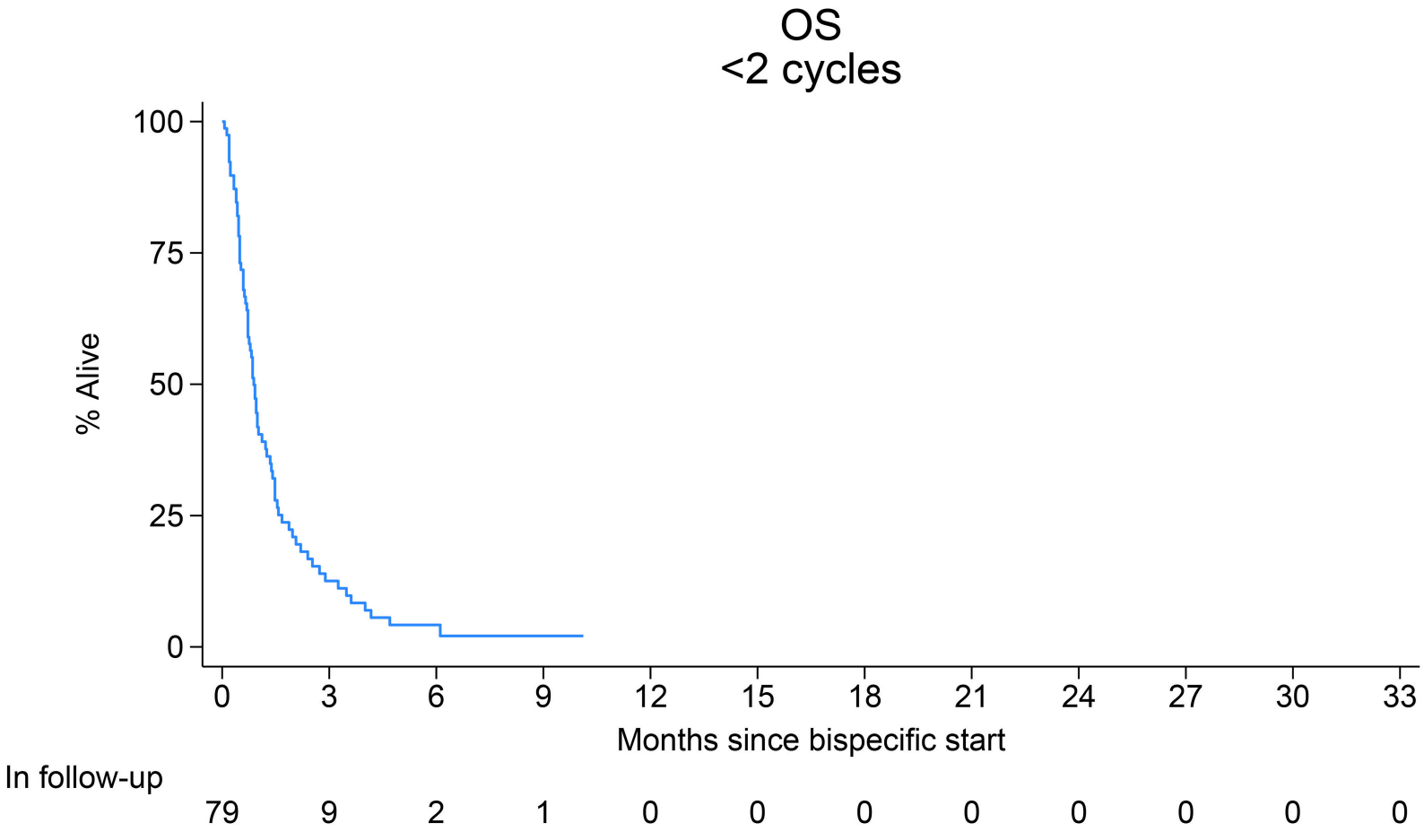
In follow-up												
All	324	199	119	82	50	30	16	8	5	2	2	1
2+ cycles	243	189	117	81	50	30	16	8	5	2	2	1
Trial eligible	67	53	36	25	15	10	5	2	1	0	0	0



In follow-up												
All	324	145	87	61	37	26	15	7	4	1	1	0
2+ cycles	243	139	87	61	37	26	15	7	4	1	1	0
Trial eligible	67	42	24	18	12	9	5	2	1	0	0	0



In follow-up												
All	73	47	36	27	19	11	5	1	0	0	0	0
2+ cycles	72	47	36	27	19	11	5	1	0	0	0	0
Trial eligible	27	18	14	11	8	6	3	1	0	0	0	0


OS
<2 cycles
100
75
50
25
0
% Alive
0
3
6
9
12
15
18
21
24
27
30
33
Months since bispecific start
In follow-up
79
9
2
1
0
0
0
0
0
0
0
0

Supplementary Data

	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	

Supplemental Table 1. Safety data (treated patients)

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

Supplemental Table 2. Contributing sites and authors

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)	
Started 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	

Supplemental Table 3. 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

Supplemental Table 4. Multivariate Analysis of CR

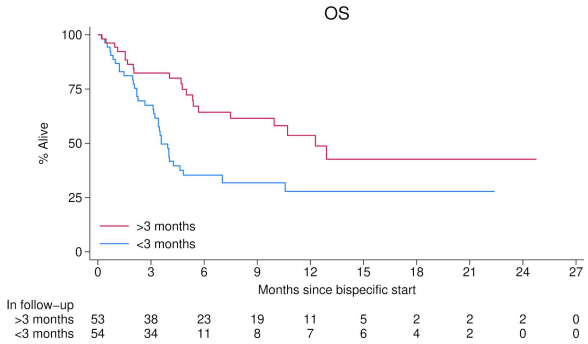
	Never had bendamustine N=171	Bendamustine ≤6 months N=62	p-value vs Never	Bendamustine >6 months N=92	p-value vs Never
Age, median (range) (IQR)	67 (25-90)(59-76)	68.5 (27-89)(57-76)	0.9	68 (18-93)(50.5-78)	0.8
Sex					
Female	60 (35%)	23 (37%)	0.9	34 (37%)	0.8
Male	111 (65%)	39 (63%)		58 (63%)	
ECOG					
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%)	

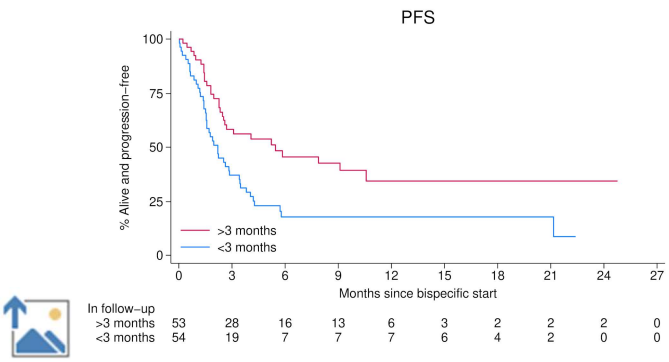
Supplemental Table 5. Baseline characteristics by prior bendamustine exposure

Grade 5 CRS event

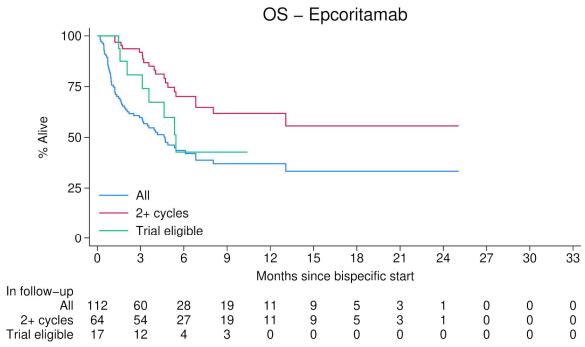
A single grade 5 cytokine release syndrome event was observed following one dose of glofitamab. The patient experienced rapid disease progression between treatment planning and treatment initiation. Consequently, a deliberate decision was made not to pursue intensive care unit admission, with both progressive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



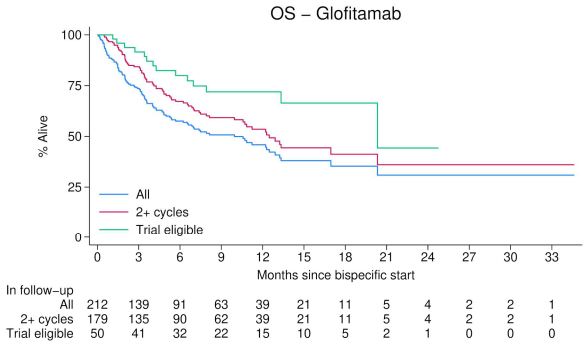
Supplemental figure 1. Overall Survival (OS) by time to CAR-T failure



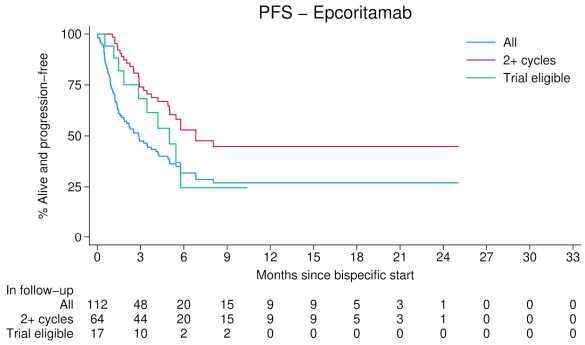
Supplemental figure 2. Progression Free Survival (PFS) by time to CAR-T failure



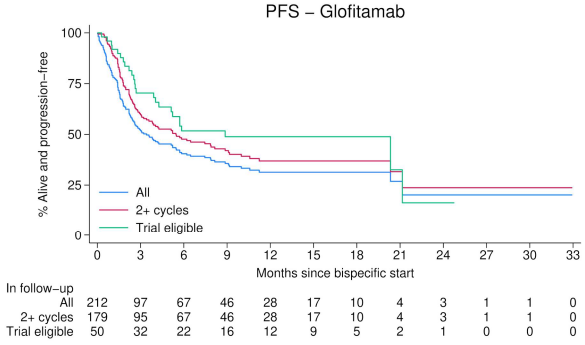
Supplemental figure 3. Epcoritamab Overall Survival (OS)



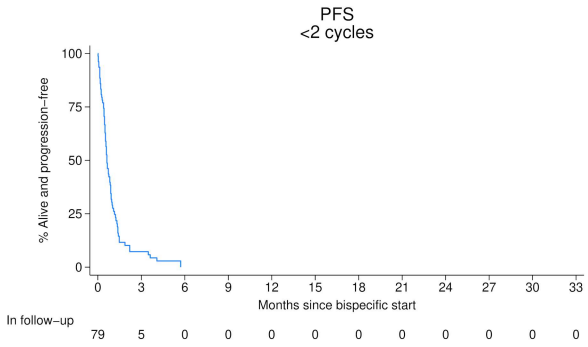
Supplemental figure 4. Glofitamab Overall Survival (OS)



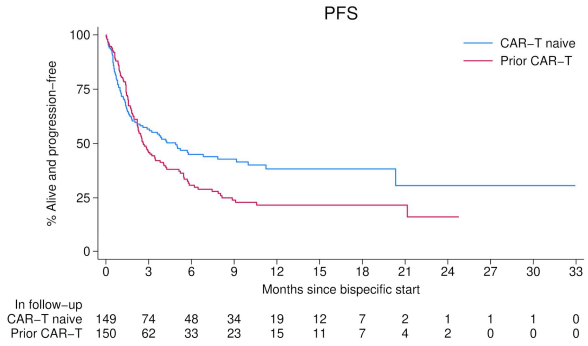
Supplemental figure 5. Epcoritamab Progresion Free Survival (PFS)



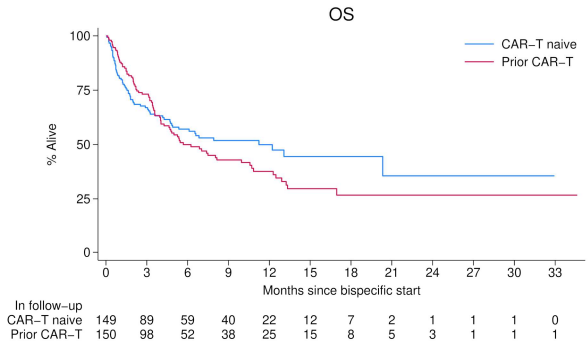
Supplemental figure 6. Glofitamab Progression Free Survival (PFS)



Supplemental figure 7. Patients completing <2 cycles of BsAb Progression Free Survival (PFS)



Supplemental figure 7. Progression Free Survival (PFS) by prior CAR-T exposure



Supplemental figure 8. Overall Survival (OS) by prior CAR-T exposure