SUPPLEMENTARY APPENDIX

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Inclusion/Exclusion criteria

Inclusion criteria

Patients are eligible to be included in the study only if all of the following criteria apply:

1. Able and willing to provide written informed consent and to comply with the study protocol and protocol mandated hospitalisations according to International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use and local regulations. Patient must also be willing to comply with all study-related procedures

2. Age ≥18 years

3. Histologically confirmed hematologic malignancy that is expected to express CD20:

   - Relapsed after or refractory to at least one (>1) prior systemic therapy
   - No available treatment options that are expected to prolong survival (e.g. standard chemotherapy or autologous stem cell transplant [SCT]) or patients refusing chemotherapy or autologous SCT

   A) Dose-Escalation Part

   - Eligible patients include: grades 1–3b relapsed/refractory (R/R) follicular lymphoma (FL) or marginal zone lymphoma (nodal; extra-nodal; or splenic), diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), high-grade B-cell lymphoma (HGBCL) with MYC and BCL2 and/or BCL6 rearrangements (double-hit lymphoma), HGBCL not otherwise specified (NOS). Based on emergent risk/benefit considerations, the Sponsor retains the right to further restrict the inclusion of specific non-Hodgkin lymphoma (NHL) histologies

   B) Expansion Part

   - R/R DLBCL, including DLBCL NOS, DLBCL arising from FL (transformed FL), PMBCL, HGBCL with MYC and BCL2 and/or BCL6 rearrangements (i.e. double-hit and triple-hit lymphomas), and HGBCL NOS. Based on emergent benefit-risk considerations, the Sponsor retains the right to further restrict the inclusion of specific NHL histologies
   - R/R disease, defined as follows:
     - Relapsed: disease that has recurred following a response that lasted ≥6 months after completion of the last line of therapy
     - Refractory: disease that did not respond to or that progressed <6 months after completion of the last line of therapy

   The Sponsor retains the option to limit the expansion part to one or more specific histologies among the approved histologies in Part II

4. At least one measurable target lesion, measurable as defined by Lugano classification (node: >1.5 cm longest transverse diameter; extra-nodal: >1 cm longest transverse diameter) by computerised tomography (CT) scan. The following lesions should not be counted as target lesions:

   - Previously irradiated lesions
   - Lesions that are intended to be used to collect tissue samples for biopsy
   - Bone lesions

Note: In case patient has just one target lesion, no baseline and/or on-treatment biopsy is required as this would exclude the patient from study participation.

5. Tumour tissue:

   - Able to provide a pretreatment biopsy collected during the screening period

   If a pretreatment biopsy cannot be safely taken per Investigator's determination, provide a

previously archived biopsy that is preferably not older than 6 months and preferably not confounded by major events (e.g. treatment or progression since the biopsy was taken), if available. A formalin fixed paraffin embedded (FFPE) block is preferred. If an FFPE block is not available, 20 slides containing unstained, freshly cut serial sections should be submitted along with an associated pathology report prior to enrolment. Note: If an archival biopsy cannot be provided, please contact the Medical Monitor.

- Willingness to provide biopsies

6. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2
7. Life expectancy (in the opinion of the Investigator) of ≥12 weeks
8. Adequate liver function:
    - Total bilirubin ≤1.5 × upper limit of normal (ULN; ≤3 × ULN in patients with Gilbert's syndrome)
    - Aspartate aminotransferase (AST)/alanine aminotransferase (ALT), alkaline phosphatase (ALP) ≤3 × ULN
        - Patients with bone marrow or liver involvement: ALP ≤5 × ULN
        - Patients with documented liver involvement: AST and/or ALT ≤5 × ULN
    - Albumin ≥2.5 g/dL
9. Adequate hematological function:
    - Neutrophil count of ≥1.5 × 10^9 cells/L (1.500/µL)
    - Platelet count of ≥75 × 10^9 cells/L (75,000/µL)
    - Haemoglobin (Hb) ≥9.0 g/dL
        - Platelet and haemoglobin transfusion free within 1 week prior to obinutuzumab pretreatment (Gpt)

    Note: In case screening procedures are leading to situations that would exclude the patient from study participation (such as Hb value below entry criteria or blood transfusion given within 1 week prior to therapy due to a bleeding event caused by the screening biopsy), the patient may still be enrolled into the trial after consultation with the Medical Monitor.
    - For patients not receiving therapeutic anti-coagulation: international normalized ratio (INR) or activated partial thromboplastin time (aPTT) ≤1.5 × ULN
10. Adequate renal function:
    - Creatinine ≤1.5 × ULN

or

    - Creatinine clearance calculated by Cockroft–Gault formula of ≥ 50 mL/min for patients in whom, in the Investigator's judgement, serum creatinine levels do not adequately reflect renal function
11. Negative serologic and/or polymerase chain reaction (PCR) test results for acute or chronic hepatitis B virus (HBV) infection. Note: patients whose HBV infection status cannot be determined by serologic test results [https://www.cdc.gov/hepatitis/hbv/pdfs/serologicchartv8.pdf] must be negative for HBV by PCR to be eligible for study participation
12. Negative test results for hepatitis C virus (HCV) and HIV. Note: patients who are positive for HCV antibody must be negative for HCV by PCR to be eligible for study participation
13. Negative HIV test at screening, with the following exception:
    - Individuals with a positive HIV test at screening are eligible provided they are stable on antiretroviral therapy for at least 4 weeks, have a CD4 count ≥200 mL, have an undetectable viral load, and have not had a history of opportunistic infection attributable to AIDS within the last 12 months
    - Participants with positive HIV at screening should be monitored while receiving study

treatment. HIV viral load will be performed every 3 months (± 4 weeks) in the first 6 months and subsequently every 6 months (± 4 weeks) until end of study treatment. If HIV viral load is detected (positive), the patient should be treated per local institutional standards, and the Medical Monitor should be notified. Testing may be performed at the local institution. If local laboratory assessments are not available for testing, local laboratory collections may be waived only if samples are collected for central laboratory assessments of viral infections

14. Male and female patients

The contraception and abstinence requirements are intended to prevent exposure of an embryo to the study treatment. The reliability of sexual abstinence for male and/or female enrolment eligibility needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the patient. Periodic abstinence (e.g. calendar, ovulation, symptothermal, or post-ovulation methods) and withdrawal are not acceptable methods of contraception

a) Female Patients

A female patient is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies:

- Women of non-childbearing potential (WONCBP)

or

- Women of childbearing potential (WOCBP) who:
    - Have a negative serum pregnancy test within 7 days prior to study treatment. WONCBP, i.e., who are considered to be post-menopausal (≥12 months of non-therapy amenorrhoea) or surgically sterile (absence of ovaries and/or uterus) are not required to have a pregnancy test
    - Agree to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of <1% per year during the treatment period and for at least:
    - 18 months after pretreatment with obinutuzumab
    - 2 months after the last dose of glofitamab
    - 5 months after the last dose of atezolizumab
    - 9 months after the last dose of polatuzumab vedotin
    - 3 months after the last dose of tocilizumab (if applicable), whichever is longer

    Examples of contraceptive methods with a failure rate of <1% per year include bilateral tubal occlusion, male sterilisation, established proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices and copper intrauterine devices
    - Refrain from donating ova during the same period described above

b) Male Patients

- During the treatment period and for at least:
    - 3 months after pretreatment with obinutuzumab
    - 2 months after the last dose of glofitamab
    - 6 months after the last dose of polatuzumab vedotin
    - 2 months after the last dose of tocilizumab (if applicable), whichever is longer

Agreement to:

- Remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom plus an additional contraceptive method that together result in a failure rate of <1% per year, with partners who are WOCBP
- With pregnant female partners, remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom to avoid exposing

the embryo

- Refrain from donating sperm during this same period

Exclusion criteria

Patients are excluded from the study if any of the following criteria apply:

1. Patients with chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL) (including CD20+ ALL), lymphoblastic lymphoma, Richter's transformation, Burkitt lymphoma, or lymphoplasmacytic lymphoma
2. Patients with known active infection, or reactivation of a latent infection, whether bacterial (e.g. tuberculosis), viral (including, but not limited to severe pneumonia, symptomatic COVID-19, Epstein-Barr virus, cytomegalovirus, hepatitis B, and hepatitis C), fungal, mycobacterial, or other pathogens (excluding fungal infections of nail beds) or any major episode of infection requiring hospitalization or treatment with intravenous (IV) antibiotics (for IV antibiotics this pertains to completion of last course of antibiotic treatment) within 4 weeks prior to Gpt infusion

   Note: patients receiving prophylactic antibiotics (e.g. to prevent a urinary tract infection or chronic obstructive pulmonary disease exacerbation) are eligible for the study

   Exclusion of patients with mycobacterial infections on the basis of chest X-ray or CT or on the basis of a positive Quantiferon or Mantoux test
3. Current grade >1 peripheral neuropathy (only for patients being treated in the polatuzumab vedotin arm)
4. Patient with history of confirmed progressive multifocal leukoencephalopathy
5. History of leptomeningeal disease
6. Current or past history of central nervous system (CNS) lymphoma
7. Current or past history of CNS disease, such as stroke, epilepsy, CNS vasculitis, or neurodegenerative disease

   Note: patients with a history of stroke who have not experienced a stroke or transient ischemic attack in the past 2 years and have no residual neurologic deficits, as judged by the Investigator, are allowed
8. Major surgery or significant traumatic injury ≤28 days prior to Gpt infusion (excluding biopsies) or anticipation of the need for major surgery during study treatment

   Note: Placement of central venous access catheter (e.g. port or similar) is not considered a major surgical procedure and is therefore permitted
9. Patients with another invasive malignancy in the last 2 years (with the exception of basal cell carcinoma and tumours deemed by the Investigator to be of low likelihood for recurrence), with the exception of malignancies with a negligible risk of metastasis or death (e.g. 5-year overall survival [OS] rate ≥90%), such as adequately-treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localised prostate cancer, ductal carcinoma in situ, or stage 1 uterine cancer
10. Significant or extensive history of cardiovascular disease (such as New York Heart Association class ≥2 cardiac disease, congestive heart failure, myocardial infarction or cerebrovascular accident within the past 3 months, unstable arrhythmias, or unstable angina or history of multiple cardiovascular events) or significant pulmonary disease (including obstructive pulmonary disease and history of bronchospasm)
11. Active or history of autoimmune disease or immune deficiency, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, *granulomatosis with polyangiitis*, Sjögren syndrome, Guillain–Barré syndrome, or multiple sclerosis, with the following exceptions:

- Patients with a history of autoimmune-related hypothyroidism who are on thyroid replacement hormone are eligible for the study
- Patients with controlled Type 1 diabetes mellitus who are on an insulin regimen are eligible for the study
- Patients with eczema, psoriasis, lichen simplex chronicus, or vitiligo with dermatologic manifestations only (e.g. patients with psoriatic arthritis are excluded) are eligible for the study provided all the following conditions are met:
    - Rash must cover <10% of body surface area
    - Disease is well controlled at baseline and requires only low-potency topical corticosteroids
    - No occurrence of acute exacerbations of the underlying condition requiring psoralen plus ultraviolet A radiation, methotrexate, retinoids, biologic agents, oral calcineurin inhibitors, or high-potency or oral corticosteroids within the previous 12 months

12. Uncontrolled tumour-related pain
    - Patients requiring pain medication must be on a stable regimen at study entry
    - Symptomatic lesions (e.g. bone metastases or metastases causing nerve impingement) amenable to palliative radiotherapy should be treated prior to treatment. Patients should be recovered from the effects of radiation. There is no required minimum recovery period
    - Asymptomatic lesions whose further growth would likely cause functional deficits or intractable pain (e.g. epidural lymphoma that is not currently associated with spinal cord compression) should be considered for loco-regional therapy, if appropriate, prior to enrolment
13. Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (once monthly or more frequently)

    Note: patients with indwelling catheters (e.g. PleurX®) are allowed
14. Uncontrolled or symptomatic hypercalcaemia (ionised calcium >1.5 mmol/L, calcium >12 mg/dL or corrected serum calcium >ULN)
15. History of idiopathic pulmonary fibrosis, organising pneumonia (e.g. bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan

    Note: history of radiation pneumonitis in the radiation field (fibrosis) is permitted.
16. Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results, including diabetes mellitus, history of relevant pulmonary disorders (bronchospasm, obstructive pulmonary disease), and known autoimmune diseases
17. Any other diseases, metabolic dysfunction, physical examination finding, mental status or clinical laboratory finding giving reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
18. Treatment with any other standard anti-cancer radiotherapy/chemotherapy, including investigational therapy (defined as treatment for which there is currently no regulatory authority approved indication) within 4 weeks prior to Gpt infusion
19. Prior solid organ transplantation
20. Prior allogeneic stem cell transplantation (SCT)
21. Autologous SCT within 100 days prior to Gpt infusion
22. Documented refractoriness to an obinutuzumab-monotherapy regimen
23. Prior treatment with targeted anti-cancer/lymphoma therapies (e.g. tyrosine kinase inhibitors, systemic immunotherapeutic/immunostimulating agents, including, but not limited to, CD137

agonists or immune checkpoint blockade therapies, including anti-CTLA-4, anti-PD1, and anti-PDL1 therapeutic antibodies, radio-immunoconjugates, antibody-drug conjugates (ADCs), immune/cytokines, and monoclonal antibodies) within 4 weeks or five half-lives of the drug, whichever is shorter, prior to Gpt infusion

24. Prior treatment with chimeric antigen receptor (CAR) T-cell therapy within 30 days before first study treatment administration
25. Toxicities from prior anti-cancer therapy including immunotherapy that did not resolve to grade 1 or better with the exception of alopecia, endocrinopathy managed with replacement therapy and stable vitiligo
26. Any history of immune-related grade ≥3 AE with the exception of endocrinopathy managed with replacement therapy
27. Ongoing corticosteroid use >25 mg/day of prednisone or equivalent within 4 weeks prior and during study treatment
    - Patients who received corticosteroid treatment with ≤25 mg/day of prednisone or equivalent must be documented to be on a stable dose of at least 4-week duration prior to day (D)7 of cycle (C)1
    - Patients may have received a brief (<7 days) course of systemic steroids (≤100 mg prednisone equivalent per day) prior to initiation of study therapy for control of lymphoma-related symptoms
28. Treatment with systemic immunosuppressive medication (including, but not limited to, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumour necrosis factor [TNF] agents) within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during study treatment, with the following exceptions:
    - Patients who received mineralocorticoids (e.g. fludrocortisone), corticosteroids for chronic obstructive pulmonary disease or asthma, or low-dose corticosteroids for orthostatic hypotension or adrenal insufficiency are eligible for the study
29. Administration of a live, attenuated vaccine within 4 weeks prior to Gpt infusion or anticipation that such a live, attenuated vaccine will be required during the study or within 5 months after last dose of study treatment

    Notes:

    Influenza vaccination should be given during influenza season only. Patients must not receive live, attenuated influenza vaccine (e.g. Flumist®) at any time during the study treatment period

    Investigators should review the vaccination status of potential study patients being considered for this study and follow local disease control and prevention guidelines for adult vaccination with any other non-live vaccines intended to prevent infectious disease prior to study entry
30. History of illicit drug or alcohol abuse within 12 months prior to screening, in the Investigator's judgement
31. History of severe allergic anaphylactic reactions to chimeric or humanised monoclonal antibodies or recombinant antibody-related fusion proteins. Please consult Medical Monitor if the patient has documented history of cytokine release syndrome (CRS) or hemophagocytic lymphohistiocytosis at previous treatments

    Note: patients with infusion-related reactions are in general not excluded, only in the case if IRR was accompanied by documented tryptase elevation
32. Known hypersensitivity to Chinese hamster ovary cell products or to any component of the atezolizumab, polatuzumab vedotin, and/or glofitamab formulation and/or to the contrast agents used in the study
33. Positive SARS-CoV-2 test within 7 days prior to enrolment. Rapid antigen test result is also acceptable

Supplementary methods

Mandatory hospitalization
Due to the risk of potential treatment-emergent toxicities, hospitalization was required for all patients for a minimum of 24 hours following the completion of the first dose of glofitamab at C1D8. Hospitalization for patients that experience cytokine release syndrome (any grade) during C1 and/or C2 may require hospitalization for subsequent cycles.

Efficacy definitions
Progression-free survival (PFS) was defined as the time from the first study treatment to the first occurrence of disease progression or death from any cause, whichever occurs first. Event-free survival (EFS) was defined as the time from first study treatment to the first occurrence of disease progression or relapse, initiation of new anti-lymphoma therapy, or death from any cause, whichever occurs first. Both PFS and EFS were determined by the investigator (INV) and the independent review committee (IRC).

Duration of complete response (DOCR) was defined as the time from the first documented complete response to disease progression or death from any cause, whichever occurred first, as assessed by both INV and the IRC. Duration of response (DOR) was defined as the time from the first documented objective response (complete or partial) to disease progression or death from any cause, whichever occurred first, also as assessed by the INV and IRC. OS was defined as the time from the first dose of study treatment to death from any cause.

Central biomarker assessment
MYC, BCL2, and BCL6 rearrangements were examined by fluorescent in situ hybridization (FISH) using Vysis locus-specific identifier MYC, BCL2, and BCL6 Dual Color Break apart Probes, respectively (CellCarta).

Flow cytometry of peripheral blood T/B/natural killer (NK) cells, and activated and proliferating T cells were evaluated by using validated flow cytometry analyses (Q2 Solutions). CD19+ B cells at baseline, end of treatment (EOT) and follow up period were from local laboratory assessment. Plasma samples were collected for cytokine (interleukin [IL]-6, interferon-ɣ [IFN-ɣ], tumor necrosis factor-α) analysis using validated multiplex immunoassays on a ProteinSimple Ella platform (Microcoat Biotechnologie GmbH).

Modified continual reassessment method for dose escalation guidance
A modified continual reassessment method was used to guide dose escalation in C2 after step-up dosing in C1. The dose-determining population was used to recommend the next dose-level and included all patients from the safety population who received glofitamab and underwent the scheduled safety evaluations.

Measures taken during COVID-19 pandemic
During the study, if a patient developed a SARS-CoV-2 infection, study treatment was interrupted, and the infection was managed according to local or institutional guidelines. Treatment was resumed only after the infection was fully resolved, and investigators ruled out active infection, reassessing the benefit-risk balance. COVID-19 vaccinations were recommended for all patients.

Supplementary results

Efficacy of patients in the second-line (2L) and third-line or later (3L+) setting, and patients who were primary refractory
Among patients who received one prior line of therapy (2L; n=53) or two or more prior lines (3L+; n=76), the overall response rates (ORRs) were 79.2% and 81.6% and the complete response (CR) rates were 66.0% and 59.2%, respectively. The ORR and CR rate for patients who were primary refractory to the first-line (1L) of therapy (n=80) were 76.2% (95% CI, 65.4–85.1) and 52.5% (95% CI, 41.0–63.8).

Peripheral neuropathy events
Time to first peripheral neuropathy event from the first glofitamab dose was a median of 1 day and the median duration of the event was 15 days. Twenty-two (22/37 [59.5%]) events recovered with 14 (37.8%) not recovered and one (2.7%) event with unknown status at the EOT. Median time to resolution was 97.5 days (range, 1.0–784.0) for patients who received any treatment. No events of peripheral neuropathy led to the discontinuation of glofitamab but three events led to polatuzumab vedotin treatment discontinuation.

New anti-lymphoma therapy (NALT) following progressive disease or completion of glofitamab in combination with polatuzumab vedotin
Forty-nine of 129 patients received NALT after glofitamab in combination with polatuzumab vedotin (Glofit-Pola), 41 with progressive disease (PD) and 8 without PD. Eleven received CAR T-cell therapy post PD and 7 of these remained alive at the time of the clinical cut-off date (CCOD). Ten patients received allogeneic SCT, 4 patients after PD, and 6 patients received allogeneic SCT as consolidative therapy post EOT with Glofit-Pola after achieving a complete response (CR). Seven of the 10 patients remain alive at the time of the CCOD. The rest of the patients received varied chemoimmunotherapy regimens (n=15, 1/15 without an overall survival [OS] event), radiotherapy (n=2, 1 patient with a partial response [PR] at EOT remained alive at the time of CCOD) and 11 received a variety of non-chemotherapy-based regimens (2/11 without an OS event; 1 patient with a PR was treated with the novel cereblon E3 Ligase Modulator [CC-99282]1). No patients received polatuzumab vedotin as a part of NALT. Median time to NALT was 12.9 months (95% CI, 9.9–24.0).

Supplementary Table 1: *Patient demographics in the 2L and 3L+ setting*

n (%) unless otherwise stated	2L N=53	3L+ N=76
Median age (range), years	73 (26–84)	64 (23–82)
Male	31 (58.5)	51 (67.1)
ECOG PS		
0–1	49 (92.5)	73 (96.1)
2	4 (7.5)	3 (3.9)
Ann Arbor stage		
I/II	10 (18.9)	20 (26.3)
III/IV	43 (81.1)	56 (73.7)
Bulky disease		
>6 cm	21 (39.6)	32 (42.1)
>10 cm	8 (15.1)	11 (14.5)
Disease type		
DLBCL	21 (39.6)	36 (47.4)
HGBCL	24 (45.3)	20 (26.3)
DH	14 (58.3)	9 (45.0)
TH	1 (4.2)	5 (25.0)
trFL	7 (13.2)	19 (25.0)
PMBCL	1 (1.9)	1 (1.3)
Median time from last therapy (range), months	4.4 (0.8–52.8)	3.9 (-9.3–67.7)
Prior CAR T-cell therapy	1 (1.9)	27 (35.5)
Refractory to prior CAR T-cell therapy	1 (1.9)	21 (27.6)

2L, second-line; 3L+, third-line and later; CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; trFL, transformed follicular lymphoma.

Supplementary Table 2: **Best overall response (INV- and IRC-assessed)**

Response rate, n (%) unless otherwise specified	**All patients (n=129)**		**Prior CAR T-cell (n=28)**	**DLBCL NOS (n=57)**	**HGBCL (n=44)**	**trFL (n=26)**	**PMBCL (n=2)**
	INV	**IRC**	**INV**	**INV**	**INV**	**INV**	**INV**
ORR	104 (80.6)	101 (78.3)	21 (75.0)	48 (84.2)	35 (79.5)	19 (73.1)	2 (100)
CR	80 (62.0)	77 (59.7)	14 (50.0)	35 (61.4)	29 (65.9)	14 (53.8)	2 (100)
PR	24 (18.6)	24 (18.6)	7 (25.0)	13 (22.8)	6 (13.6)	5 (19.2)	0
SD	6 (4.7)	7 (5.4)	2 (7.1)	1 (1.8)	2 (4.5)	3 (11.5)	0
PD	16 (12.4)	16 (12.4)	4 (14.3)	7 (12.3)	6 (13.6)	3 (11.5)	0
NE	0	1 (0.8)	0	0	0	0	0
ND*	3 (2.3)	4 (3.1)	1 (3.6)	1 (1.8)	1 (2.3)	1 (3.8)	0

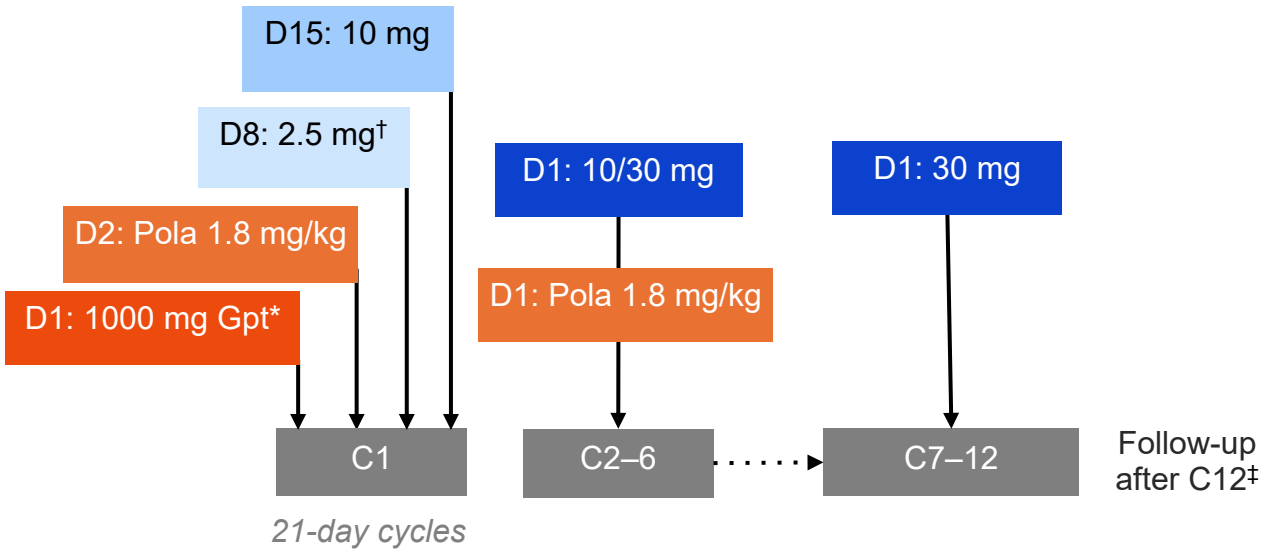
*Missing or not done. CAR, chimeric antigen receptor; CR, complete response; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; INV, investigator. IRC, independent review committee; ND, missing or not done; NE, not evaluable; NO, not otherwise specified; ORR, overall response rate; PD, progressive disease; PMBCL, primary mediastinal large B-cell lymphoma; PR, partial response; SD, stable disease; trFL, transformed follicular lymphoma.

***Supplementary Table 3**:* **Efficacy summary**

	Patients receiving any treatment	
	N=129	
	INV	**IRC**
Median time to first response, months (range)	1.3 (1–14)	1.3 (1–12)
Median DOR, months (95% CI)	24.3 (15.0–37.8)	26.4 (10.9–44.3)
Event free rate, % (95%)		
12 months	62.4 (52.5–72.2)	59.9 (49.5–70.2)
24 months	50.5 (39.6–61.4)	51.9 (40.8–63.0)
Median time to first CR, months (range)	1.3 (1–24)	2.1 (1–24)
Median DOCR, months (95% CI)	31.8 (21.9–NE)	37.8 (24.1–NE)
Event free rate, % (95%)		
12 months	75.1 (65.1–85.2)	74.1 (63.4–84.8)
24 months	59.9 (47.5–72.3)	63.9 (51.4–76.4)
Median PFS, months (95% CI)	15.5 (8.8–25.7)	12.3 (8.8–27.7)
Event free rate, % (95%)		
12 months	51.6 (42.7–60.6)	50.5 (41.2–59.7)
24 months	42.3 (32.9–51.7)	41.8 (32.2–51.5)
Median OS, months (95% CI)	33.8 (20.6–NE)	
Event free rate, % (95%)		
12 months	69.6 (61.6–77.7)	
24 months	54.3 (45.3–63.4)	

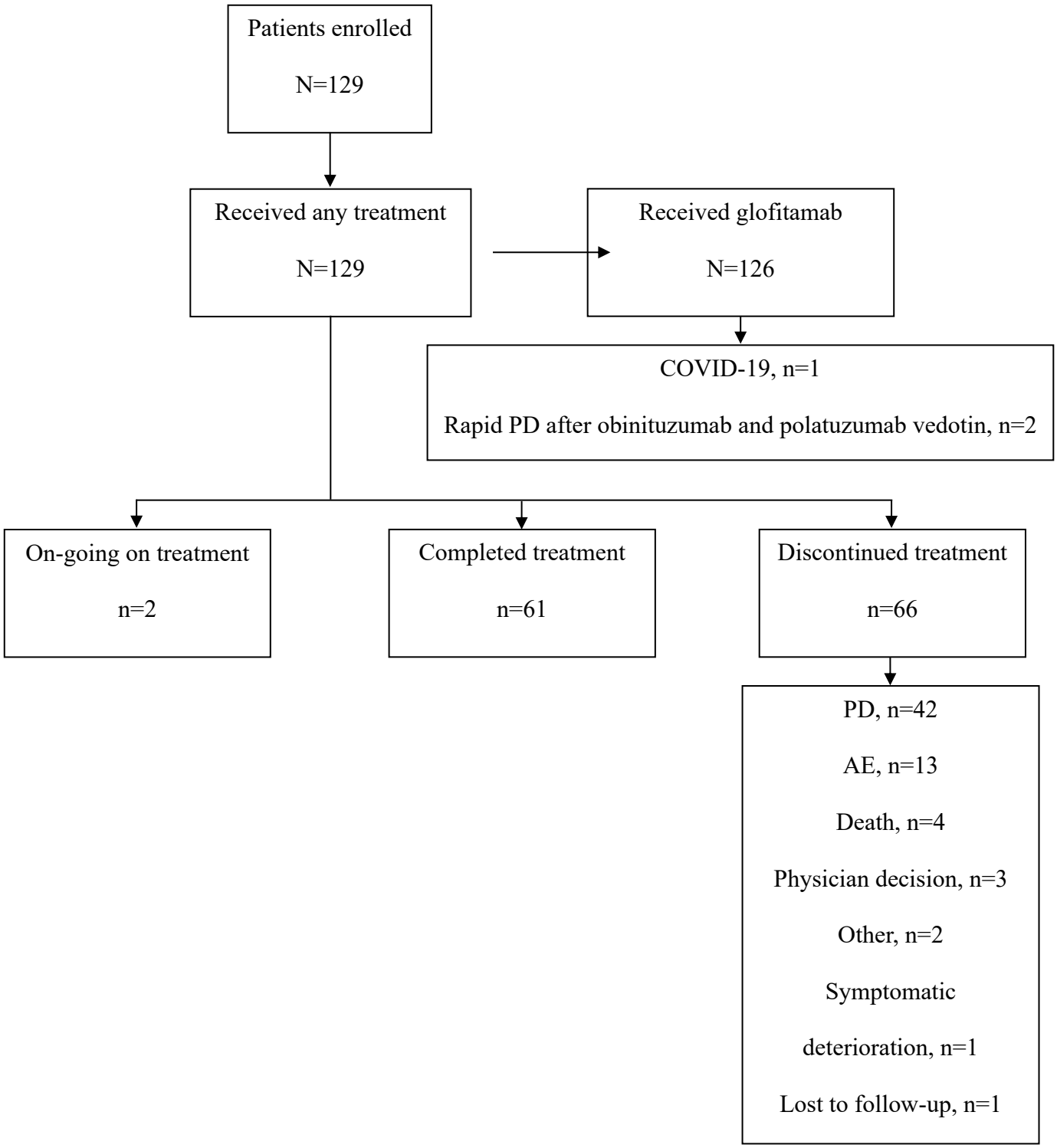
CI, confidence interval; CR, complete response; DOCR, duration of complete response; DOR, duration of response; Glofit-Pola, glofitamab plus polatuzumab vedotin; INV, investigator; IRC, independent review committee; NE, not estimable; OS, overall survival; PFS, progression-free survival.

Supplementary Figure 1: **Study design (online only)**



*Patients received obinutuzumab 1000 mg on D1 of the first 21-day cycle to mitigate risk of CRS. †Mandatory 24-hour hospitalization for first glofitamab infusion. ‡Patients with CR, PR, or SD were followed until disease progression, those with PD had an end of study visit then were followed for survival.
C, cycle; CR, complete response; CRS, cytokine release syndrome; D, day; Gpt, obinutuzumab pretreatment; PD, progressive disease; Pola, polatuzumab vedotin; PR, partial response; SD, stable disease.

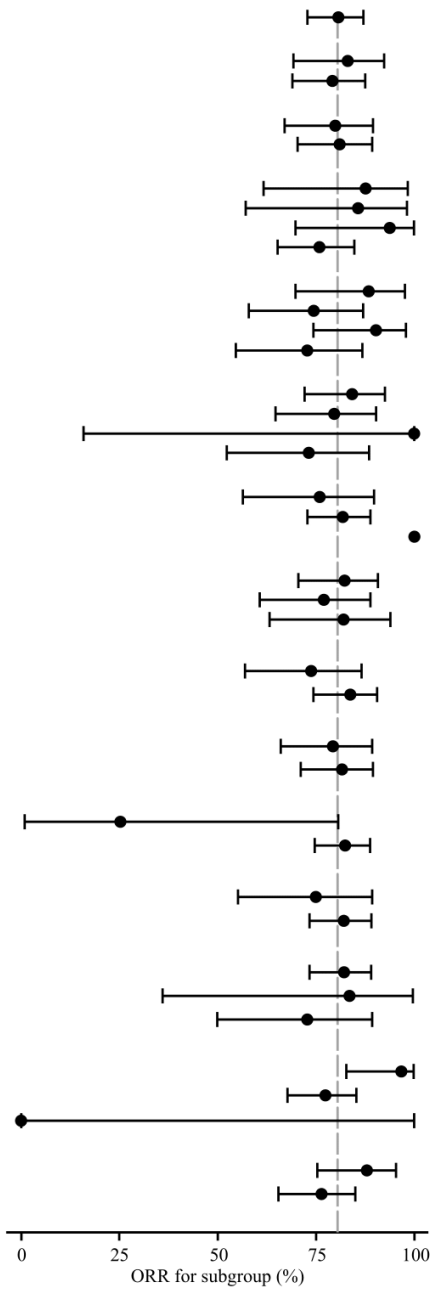
Supplementary Figure 2: **Patient disposition (online only)**



AE, adverse events; PD, progressive disease.

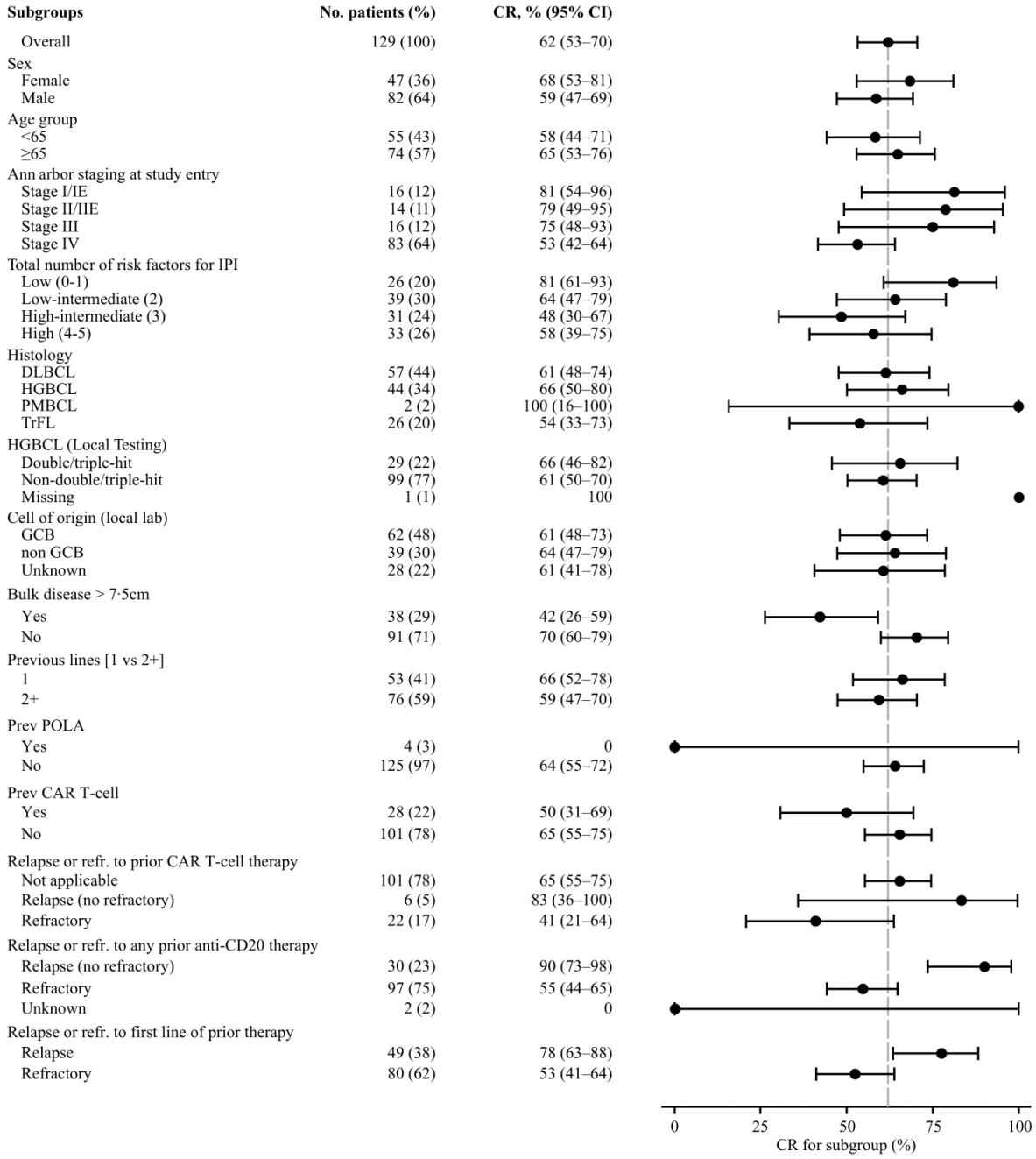
Supplementary Figure 3: **Forest plot of overall response rate per subgroup (INV-assessed; online only)**

Subgroups	No. of patients (%)	ORR, % (95% CI)
Overall	129 (100)	81 (73–87)
Sex		
Female	47 (36)	83 (69–92)
Male	82 (64)	79 (69–87)
Age group		
<65	55 (43)	80 (67–90)
≥65	74 (57)	81 (70–89)
Ann arbor staging at study entry		
Stage I/IE	16 (12)	88 (62–98)
Stage II/IIE	14 (11)	86 (57–98)
Stage III	16 (12)	94 (70–100)
Stage IV	83 (64)	76 (65–85)
Total number of risk factors for IPI		
Low (0-1)	26 (20)	88 (70–98)
Low-intermediate (2)	39 (30)	74 (58–87)
High-intermediate (3)	31 (24)	90 (74–98)
High (4-5)	33 (26)	73 (54–87)
Histology		
DLBCL	57 (44)	84 (72–93)
HGBCL	44 (34)	80 (65–90)
PMBCL	2 (2)	100 (16–100)
TrFL	26 (20)	73 (52–88)
HGBCL (Local Testing)		
Double/triple-hit	29 (22)	76 (56–90)
Non-double/triple-hit	99 (77)	82 (73–89)
Missing	1 (1)	100
Cell of origin (local lab)		
GCB	62 (48)	82 (70–91)
non GCB	39 (30)	77 (61–89)
Unknown	28 (22)	82 (63–94)
Bulk disease > 7·5cm		
Yes	38 (29)	74 (57–87)
No	91 (71)	84 (74–90)
Previous lines [1 vs 2+]		
1	53 (41)	79 (66–89)
2+	76 (59)	82 (71–90)
Prev POLA		
Yes	4 (3)	25 (1–81)
No	125 (97)	82 (75–89)
Prev CAR T-cell		
Yes	28 (22)	75 (55–89)
No	101 (78)	82 (73–89)
Relapse or refr. to prior CAR T-cell therapy		
Not applicable	101 (78)	82 (73–89)
Relapse (no refractory)	6 (5)	83 (36–100)
Refractory	22 (17)	73 (50–89)
Relapse or refr. to any prior anti-CD20 therapy		
Relapse (no refractory)	30 (23)	97 (83–100)
Refractory	97 (75)	77 (68–85)
Unknown	2 (2)	0
Relapse or refr. to first line of prior therapy		
Relapse	49 (38)	88 (75–95)
Refractory	80 (62)	76 (65–85)



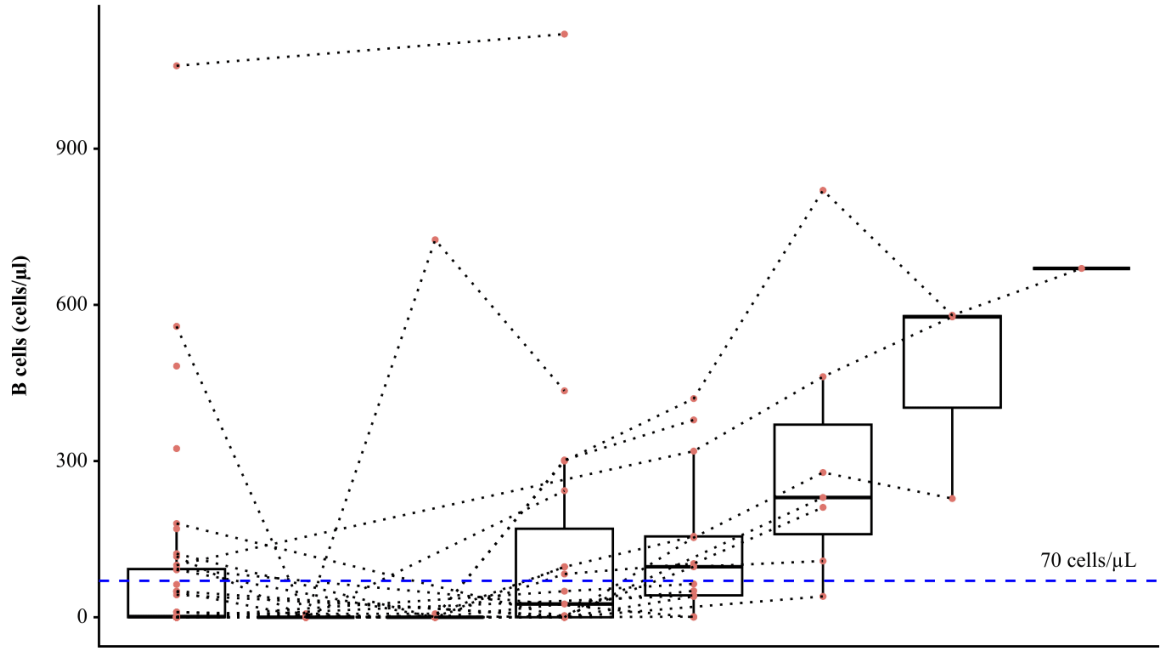
CAR, chimeric antigen receptor; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; GCB, germinal centre B-cell; HGBCL, high-grade B-cell lymphoma; INV, investigator; IPI, International Prognostic Index; ORR, overall response rate; PMBCL; primary mediastinal large B-cell lymphoma; POLA, polatuzumab vedotin; refr, refractory; trFL, transformed follicular lymphoma.

Supplementary Figure 4: **Forest plot of complete response per subgroup (INV-assessed; online only)**



CAR, chimeric antigen receptor; CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; GCB; germinal centre B-cell; HGBCL, high-grade B-cell lymphoma; INV, investigator; IPI, International Prognostic Index; PMBCL, primary mediastinal large B-cell lymphoma; POLA, polatuzumab vedotin; refr, refractory; trFL, transformed follicular lymphoma.

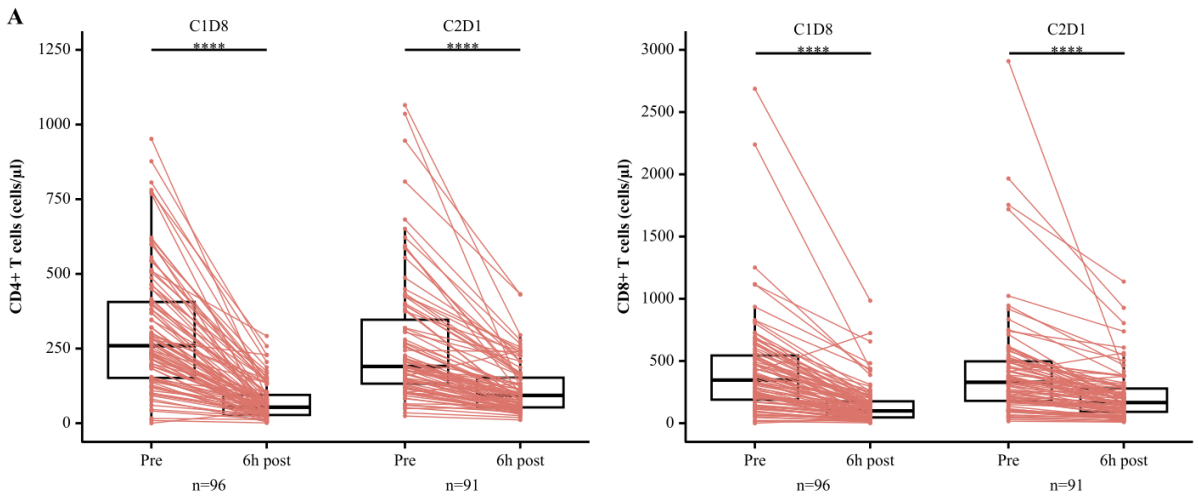
Supplementary Figure 5: **B-cell recovery over time (online only)**



	C1D1	EOT	EOT-FU 6mo	FU 6−12mo	FU 12−18mo	FU 18−24mo	FU 24−30mo	FU 30−36mo
>70cells/ul	11/38	0/18	1/17	8/19	7/13	6/7	3/3	1/1

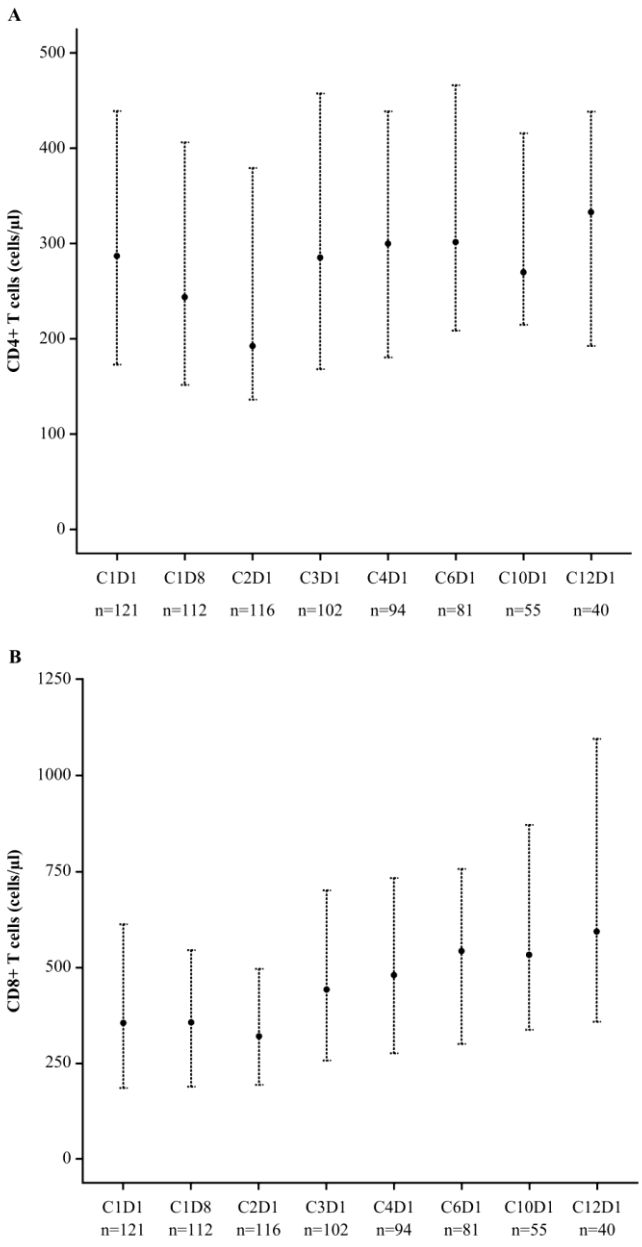
One patient was removed from analysis due to abnormally high (>5000 cells/ul) B cell count confirmed by site. No other clinical abnormalities were observed and patient is still in remission.
Each dot represents a patient, and the horizontal dashed blue line represents lower limit of normal (70 cells/ul).
C, cycle; D, day; EOT, end of treatment; FU, follow-up; mo, months.

Supplementary Figure 6: **Absolute counts of CD4+ and CD8+ T cells pre- and post-glofitamab treatment at C1D8 and C2D1 (online only)**



P-values (****, p≤0.0001) represent pairwise two-sided Wilcox test against pre-glofitamab treatment. C, cycle; D, day; h, hour.

Supplementary Figure 7: **Median ± interquartile range of absolute counts of A) CD4+ T cells and B) CD8+ T cells (online only)**



C, cycle; D, day.

References

1. Carrancio S, Groocock L, Janardhanan P, et al. CC-99282 is a novel cereblon (CRBN) E3 ligase modulator (CELMoD) agent with enhanced tumoricidal activity in preclinical models of lymphoma. *Blood* 2021; **138**:1200.