UCSF Helen Diller Family Comprehensive Cancer Center

Bispecific antibodies for lymphoma: updates and practical considerations

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UCSF Helen Diller Family Comprehensive Cancer Center

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Outline

- Recent updates in bispecifics for FL and DLBCL
- Practical considerations in use of bispecifics

Bispecific antibodies for lymphoma

Indication	Regimen	Phase	N	CR Rate	PFS	Median Follow Up	Approval Status	Reference
DLBCL 1st line	Epcoritamab + R-CHOP	Phase 1b/2	47	85.0%	NR	38.8 mo	Not approved; not included in NCCN	EPCORE-NHL-2. Falchi et al. Blood (2025) 146 (Supplement 1): 1955.
	Glofitamab + Pola-R-CHOP	Phase 2	80	98.0%	86% (2-y)	20.7 mo	Not approved; not included in NCCN	COALITION: Minson et al. J Clin Oncol. 2025 Aug 10;43(23):2595-2605.
	Mosunetuzumab	Phase 2	49	59.2%	68.8% (1-y)	12.5 mo	Not approved; not included in NCCN	MorningSun: Sharman et al. Blood (2025) 146 (Supplement 1): 62.
DLBCL 2nd line	Glofitamab + GemOx	Phase 3	183	58.5%	13.8 mo	20.7 mo	Not approved; included in NCCN	STARGLO: Abramson et al. Lancet. 2024 Nov 16;404(10466):1940-1954.
	Epcoritamab + GemOx	Phase 1b/2	103	61.2%	44% (1-y)	13.2 mo	Not approved; included in NCCN	EPCORE NHL-2: Brody et al. Blood. 2025 Apr 10;145(15):1621-1631.
	Mosunetuzumab + Polatuzumab	Phase 3	138	55.1%	11.5 mo	23.2 mo	Not approved; included in NCCN	SUNMO: Budde et al. J Clin Oncol. 2025 Dec 20;43(36):3799-3811.
	Glofitamab + Polatuzumab	Phase 1b/2	129	59.7%	12.3 mo	25.5 mo	Not approved; included in NCCN	Hutchings et al. J Clin Oncol. 2025 Dec 20;43(36):3788-3798.
DLBCL 3rd line	Glofitamab	Phase 1/2	154	39.0%	37% (1-y)	12.6 mo	Accelerated approval; included in NCCN	Dickinson et al. N Engl J Med. 2022 Dec 15;387(24):2220-2231.
	Epcoritamab	Phase 1/2	157	38.9%	4.4 mo	10.7 mo	Accelerated approval; included in NCCN	EPCORE NHL-1: Thieblemont et al. J Clin Oncol. 2023 Apr 20;41(12):2238-2247.
FL 1st line	Mosunetuzumab	Phase 2	43	81.0%	Not reported	6 mo	Not approved; not included in NCCN	Falchi et al. Blood (2023) 142 (Supplement 1): 604.
FL 2nd line	Epcoritamab + R2	Phase 3	243	83.0%	85.5% (16-mo)	14.8 mo	Approved; included in NCCN	EPCORE FL-1: Lancet. 2026 Jan 10;407(10524):161-173.
FL 3rd line	Epcoritamab	Phase 1/2	128	62.5%	49.4% (18-mo)	5.7 mo	Accelerated approval; included in NCCN	EPCORE NHL-1: Linton et al. Lancet Haematol. 2024 Aug;11(8):e593-e605.
	Mosunetuzumab	Phase 2	90	60.0%	17.9 mo	18.3 mo	Accelerated approval; included in NCCN	Budde et al. Lancet Oncol. 2022 Aug;23(8):1055-1065.
MCL 2nd line	Glofitamab	Phase 1/2	60	78.3%	16.8 mo	19.6 mo	Not approved; included in NCCN	Phillips et al. J Clin Oncol. 2025 Jan 20;43(3):318-328.
	Mosunetuzumab + Polatuzumab	Phase 2	42	79.0%	19 mo	Not reported	Not approved; included in NCCN	MCL-1493: Wang et al. Clinical Lymphoma, Myeloma and Leukemia, 25S858
MZL 1st line	Mosunetuzumab	Phase 2	36	61.0%	Not reported	11.3 mo	Not approved; not included in NCCN	Burke et al. EHA 2025

Bispecific antibodies for hematologic malignancies

Bi-Specific Antibody	Targets	Design	Ig Fragment Formats	Ref.
blinatumomab	**CD19 x CD3**		• two murine scFv joined by a glycine-serine linker • monovalent CD19 and monovalent CD3 binding • cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs	1, 2, 3
mosunetuzumab	**CD20 x CD3**		• humanized mouse heterodimeric IgG1-based antibody • monovalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding	4
glofitamab	**$(CD20)_2$ x CD3**		• humanized mouse IgG1-based antibody • bivalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding	5
odronextamab	**CD20 x CD3**		• fully human IgG4-based heterodimeric antibody • monovalent CD20 and monovalent CD3ε binding • Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding • common κ light chain from anti-CD3ε mAb	6
epcoritamab	**CD20 x CD3**		• humanized mouse IgG1-based heterodimeric antibody • monovalent CD20 and monovalent CD3 binding • IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield	7

Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

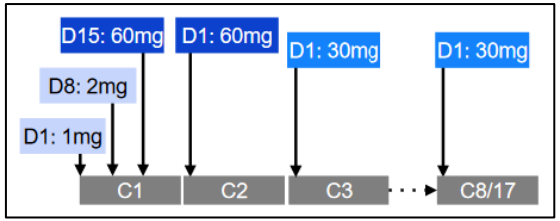
[1]Dufner V, *et al*. Blood Adv (2019) 3:2491; [2]Goebeler ME, *et al*. J Clin Oncol (2016) 34:1104; [3]Viardot *et al*. Blood (2016) 127(11):1410; [4]Schuster SJ, *et al*. ASH 2019, Plenary Abstract 6; [5]Hutchings M, *et al*. ASH 2020, Abstract 403; [6]Bannerji R, *et al*. ASH 2020, Abstract 400; [7]Hutchings M, *et al*. ASH 2020, Abstract 406

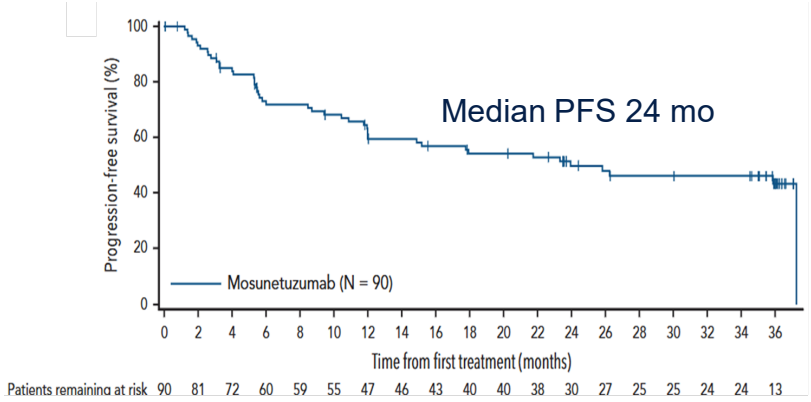
Schuster et al. Hematol Oncol 2021

Follicular lymphoma

FL: Mosunetuzumab IV

- Single-arm study of mosunetuzumab monotherapy in 3rd or subsequent line
  - Median 3 prior lines of therapy, POD24 52.2%





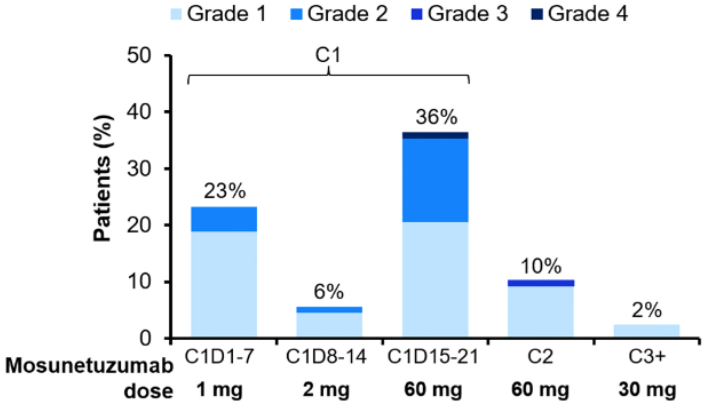
INV-assessed efficacy end points	Mosunetuzumab (N = 90)
ORR* % (95% CI)	77.8 (67.8-85.9)
CR* % (95% CI)	60.0 (49.1-70.2)
Time to first response, mo, median (range)	1.4 (1-11)
Time to first CR, mo, median (range)	3.0 (1-19)
DOR, mo, median (95% CI) (n = 70)	35.9 (20.7-NE)
30-mo remission rate, % (95% CI)	56.6 (44.2-68.9)
DOCR, mo, median (95% CI) (n = 54)	NR (33.0-NE)
30-mo remission rate, % (95% CI)	72.4 (59.2-85.6)
PFS, mo, median (95% CI)	24.0 (12.0-NE)
36-mo PFS rate, % (95% CI)	43.2 (31.3-55.2)
OS, mo, median (95% CI)	NR (NE-NE)
36-mo OS rate, % (95% CI)	82.4 (73.8-91.0)
TTNT, mo, median (95% CI)	37.3 (18.0-NE)
36-mo TTNT rate, % (95% CI)	51.8 (40.8-62.8)

Sehn et al. Blood 2024

FL: Mosunetuzumab IV

- Single-arm study of mosunetuzumab monotherapy in 3rd or subsequent line
  - Median 3 prior lines of therapy, POD24 52.2%
- ORR 78%, CRR 60%

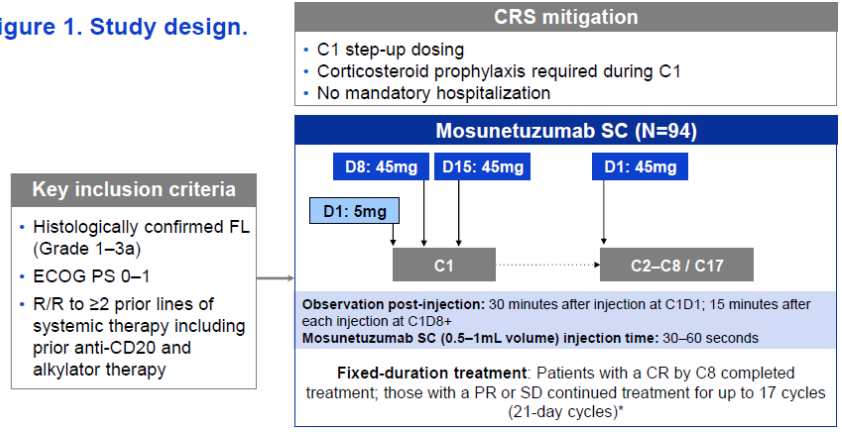
	Grade 1–2	Grade 3	Grade 4
Cytokine release syndrome	38 (42%)	1 (1%)	1 (1%)
Fatigue	33 (37%)	0	0
Headache	27 (30%)	1 (1%)	0
Neutropenia or decreased neutrophil count	2 (2%)	12 (13%)	12 (13%)
Pyrexia	25 (28%)	1 (1%)	0
Hypophosphataemia	9 (10%)	15 (17%)	0
Pruritus	19 (21%)	0	0
Hypokalaemia	15 (17%)	2 (2%)	0
Cough	16 (18%)	0	0
Constipation	16 (18%)	0	0
Diarrhoea	15 (17%)	0	0
Nausea	15 (17%)	0	0
Rash	13 (14%)	1 (1%)	0
Dry skin	14 (16%)	0	0
Anaemia	5 (6%)	7 (8%)	0
Chills	11 (12%)	1 (1%)	0
Hypomagnesaemia	11 (12%)	0	0
Increased alanine aminotransferase	6 (7%)	4 (4%)	1 (1%)
Insomnia	11 (12%)	0	0
Arthralgia	10 (11%)	0	0
Peripheral oedema	10 (11%)	0	0
Abdominal pain	8 (9%)	1 (1%)	0
Back pain	8 (9%)	1 (1%)	0
Dizziness	9 (10%)	0	0
Urinary tract infection	8 (9%)	1 (1%)	0
Skin exfoliation	9 (10%)	0	0
Thrombocytopenia or decreased platelet count	5 (6%)	0	4 (4%)



Sehn et al. Blood 2024

FL: Mosunetuzumab SC

Figure 1. Study design.



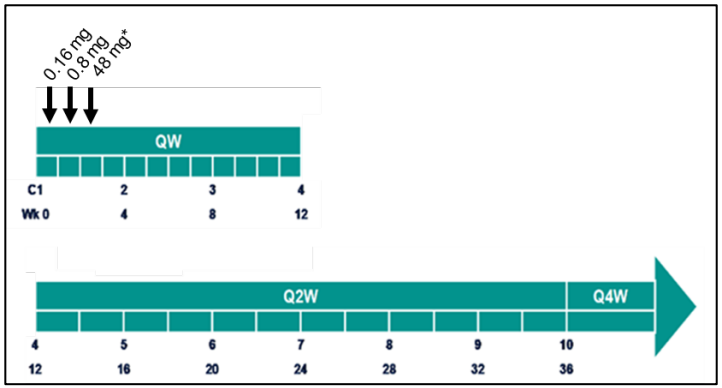
	Overall population (N=94)	Patients with CR (n=59)	POD24 (n=40)	Bulky disease (>7cm) (n=22)
ORR, n (%)	70 (74.5)	59 (100)	28 (70.0)	15 (68.2)
CR, n (%)	59 (62.8)	59 (100)	23 (57.5)	12 (54.5)
Median DOR, months (95% CI)	25.1 (21.0–39.2)	33.6 (22.6–NE)	34.6 (21.0–NE)	NR (21.8–NE)
Median DOCR, months (95% CI)	33.6 (21.8–NE)	33.6 (21.8–NE)	34.6 (21.0–NE)	NR (21.8–NE)
Median PFS, months (95% CI)	18.5 (11.3–28.3)	35.9 (25.3–NE)	15.7 (5.8–NE)	28.3 (5.7–NE)
30-month PFS, % (95% CI)	37.3 (26.8–47.8)	55.5 (41.7–69.3)	41.1 (25.3–56.9)	42.1* (18.3–65.9)

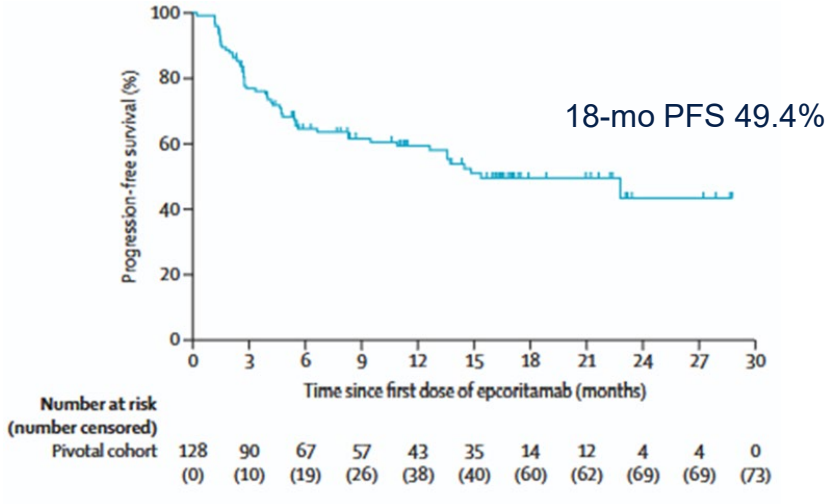
n (%) unless stated	Mosunetuzumab SC (N=94)
AE	93 (98.9)
Grade 3/4 AE	46 (48.9)
Serious AE	37 (39.4)
Grade 5 (fatal) AE	5 (5.3)*
AE leading to Mosun SC discontinuation	7 (7.4)
Any grade CRS by ASTCT	28 (29.8)
Grade 1	19 (20.2)
Grade 2	7 (7.4)
Grade 3	2 (2.1)
Any grade infections	52 (55.3)
Grade 1	13 (13.8)
Grade 2	21 (22.3)
Grade 3/4	15 (16.0)
Grade 5	3 (3.2)

Assouline et al. ASH 2025

FL: Epcoritamab

- Single-arm study of epcoritamab monotherapy in 3rd or subsequent line
  - Median 3 prior lines of therapy, POD24 42%
- ORR 82%, CRR 62.5%

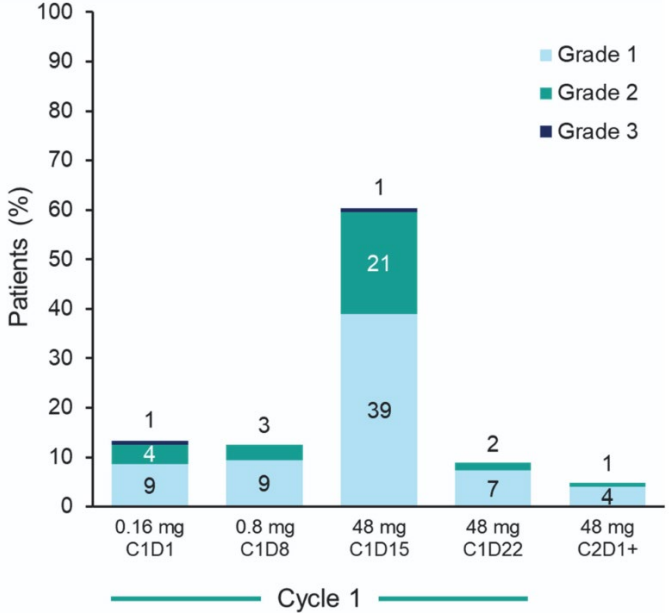




Linton et al. Lancet Haematol 2024

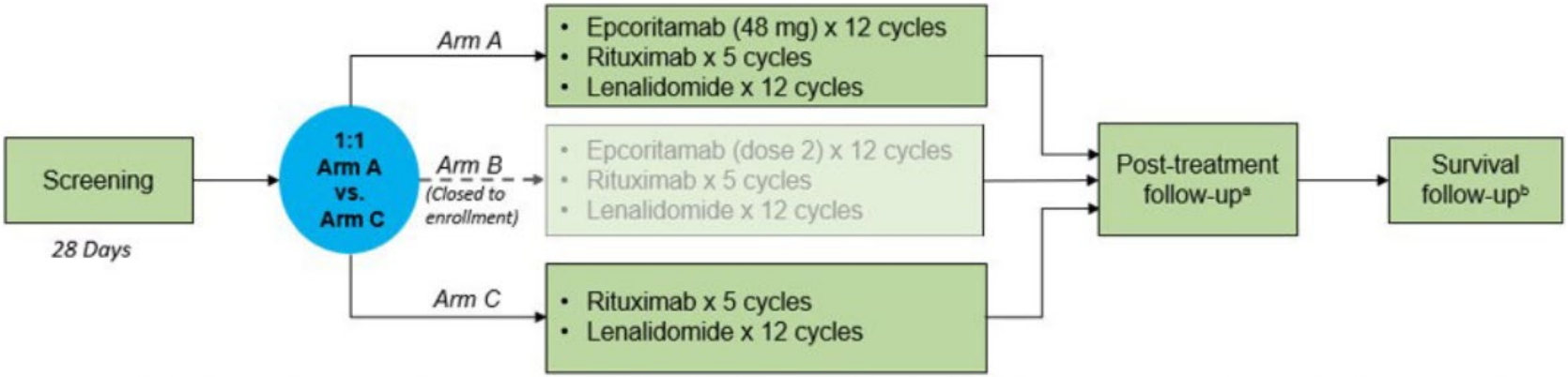
FL: Epcoritamab

	Grade 1–2	Grade 3	Grade 4	Grade 5
Pivotal cohort (n=128)				
Cytokine release syndrome	83 (65%)	2 (2%)	0	0
Injection-site reaction*	73 (57%)	0	0	0
COVID-19*	27 (21%)	18 (14%)	0	6 (5%)
Fatigue	36 (28%)	3 (2%)	0	0
Neutropenia*	4 (3%)	16 (13%)	16 (13%)	0
Diarrhoea	32 (25%)	2 (2%)	0	0
Pyrexia	29 (23%)	3 (2%)	0	0
Headache	25 (20%)	0	0	0
Cough	22 (17%)	0	0	0
Nausea	22 (17%)	0	0	0
Constipation	20 (16%)	0	0	0
Anaemia*	11 (9%)	8 (6%)	0	0
Arthralgia	17 (13%)	1 (1%)	0	0
Peripheral oedema	18 (14%)	0	0	0
Dyspnoea†	17 (13%)	0	0	0
Upper respiratory tract infection	17 (13%)	0	0	0
Insomnia	16 (13%)	0	0	0
Lymphopenia*	2 (2%)	5 (4%)	9 (7%)	0
Thrombocytopenia*	9 (7%)	2 (2%)	5 (4%)	0
Back pain	14 (11%)	1 (1%)	0	0
Dizziness	14 (11%)	0	0	0
Urinary tract infection	8 (6%)	5 (4%)	0	0



Linton et al. Lancet Haematol 2024

FL: Epcoritamab + R2



After initial step-up dosing during cycle 1, epcoritamab will be administered weekly in cycles 2-3, then Q4W in cycles 4-12.

Falchi et al. ASH 2023

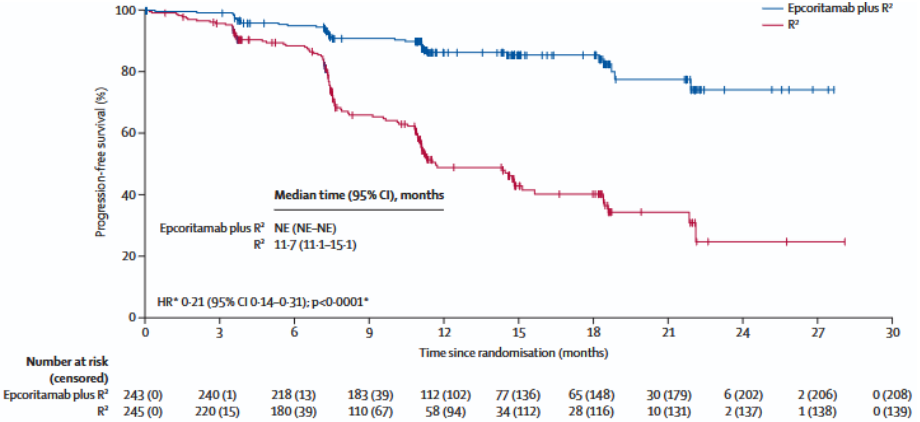
FL: Epcoritamab + R2

- Median 1 prior line of therapy
- 54% stage IV, 38-44% POD24

	Epcoritamab plus R² (n=243)		R² (n=238)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse event	242 (>99%)	219 (90%)	235 (99%)	161 (68%)
Adverse event related to study drug	236 (97%)	203 (84%)	213 (90%)	129 (54%)
Serious adverse event	135 (56%)	--	69 (29%)	--
Adverse event leading to treatment discontinuation	46 (19%)	--	29 (12%)	--
Epcoritamab	21 (9%)	--	--	--
Rituximab	7 (3%)	--	12 (5%)	--
Lenalidomide	45 (19%)	--	29 (12%)	--
Adverse event of special interest ≥20%				
Infections*	188 (77%)	81 (33%)	125 (53%)	37 (16%)
Neutropenia	180 (74%)	167 (69%)	123 (52%)	100 (42%)
Cytokine release syndrome	85 (35%)	0	1 (<1%)	0
Anaemia	68 (28%)	19 (8%)	41 (17%)	11 (5%)
Thrombocytopenia	67 (28%)	23 (9%)	44 (18%)	15 (6%)
Pyrexia	58 (24%)	1 (<1%)	33 (14%)	3 (1%)
Rash	58 (24%)	19 (8%)	53 (22%)	9 (4%)
COVID-19	54 (22%)	7 (3%)	32 (13%)	4 (2%)

Data are n (%). The safety population consisted of all participants who received at least one dose of the study drug.
*Events were in the MedDRA system organ class "Infections and Infestations".

	Epco-R2 (N=243)	R2 (N=245)
Median follow up	14.8 mo	14.6 mo
ORR	95%	79%
CRR	83%	50%
12-mo DoCR	91.20%	56%
16-mo PFS	85.50%	40.20%
16-mo OS	95.80%	88.80%



Falchi et al. Lancet 2026

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Summary of approved bispecifics in FL

3rd line

	Mosunetuzumab (Sehn et al. 2024)	Epcoritamab (Linton et al. 2024)
Treatment	C1: weekly C2-17: q3 weeks	C1-C3: weekly C4-C9: q2 weeks C10+: q4 weeks
Treatment duration	CR: 8 cycles PR/SD: 17 cycles	Indefinite
Route of admin	IV or SQ	SQ
Patients	90	128
Median prior lines	3	3
POD24	52%	42%
ORR	78%	82%
CRR	60%	63%
PFS	24 mo (median)	49.4% (18 mo)
CRS (Gr 1-2)	42%	2%
CRS (Gr 3-4)	65%	2%

2nd line

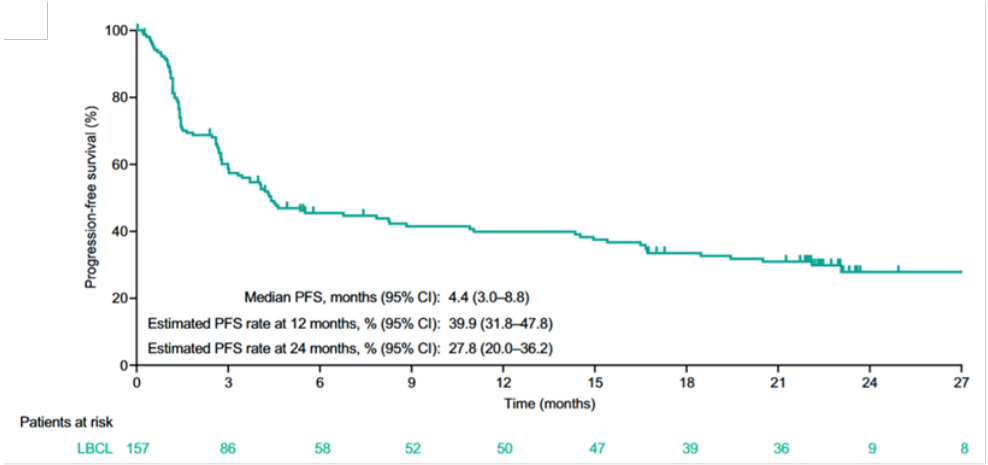
	Epcor + R2 (Falchi et al. 2026)
Treatment	C1-3: weekly C4-12: q4 weeks
Treatment duration	12 cycles
Route of admin	SQ
Patients	243
Median prior lines	1
POD24	44%
ORR	95%
CRR	83%
PFS	Median NR
CRS (Gr 1-2)	35%
CRS (Gr 3-4)	0%

Large B-cell lymphoma

DLBCL: Epcoritamab

- Single-arm phase 2 study of epcoritamab monotherapy in 3rd+ line of therapy
- 61% stage IV, 39.5% >=4 prior lines of therapy, 39% prior CAR T

Endpoint	LBCL (*N* = 157)
Best overall response	
Overall response, No. (%) [95% CI][a]	99 (63.1) [55.0–70.6]
CR	63 (40.1) [32.4–48.2]
PR	36 (22.9) [16.6–30.3]
SD, No. (%)	5 (3.2)
PD, No. (%)	37 (23.6)
Nonevaluable,[b] No. (%)	16 (10.2)
PFS,[c] months, median (range) [95% CI]	4.4 (0.0+ to 29.0+) [3.0–8.8]
OS,[c] months, median (range) [95% CI]	18.5 (0.3 to 32.7+) [11.7–27.7]

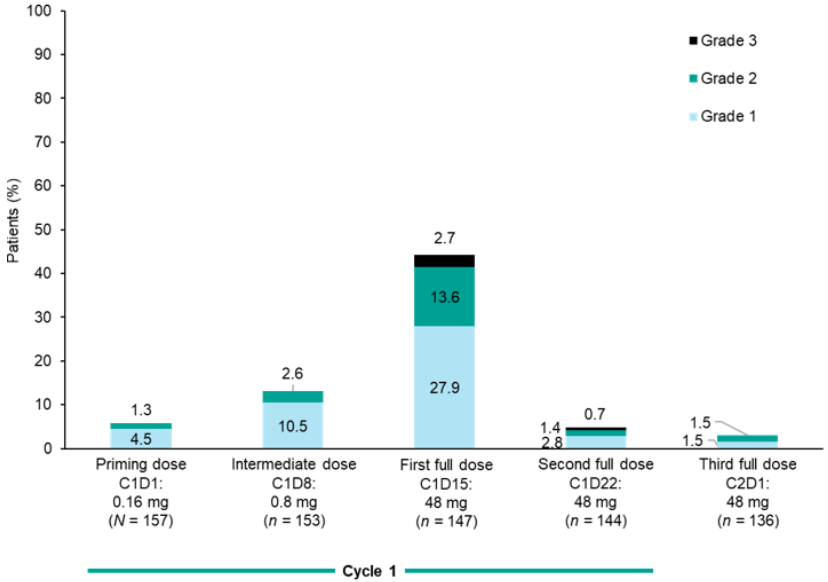


Thieblemont et al. Leukemia 2024

DLBCL: Epcoritamab

- Single-arm phase 2 study of epcoritamab monotherapy in 3rd+ line of therapy
- 61% stage IV, 39.5% >=4 prior lines of therapy, 39% prior CAR T

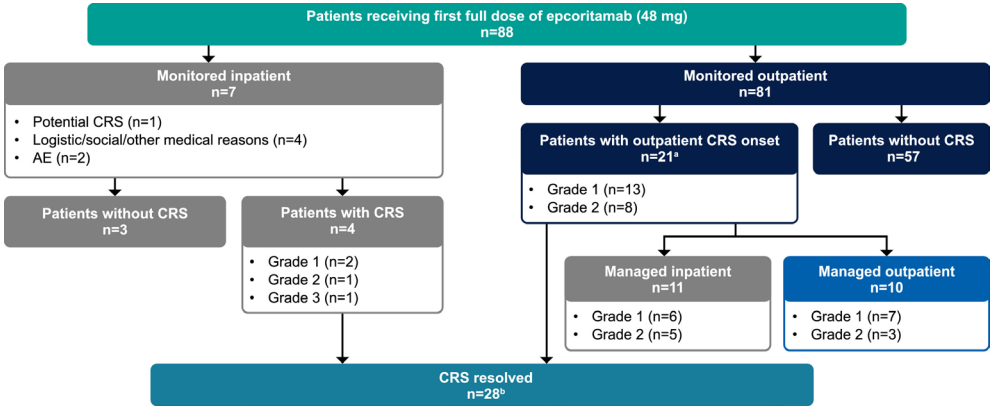
Adverse events*	Any grade (*N* = 157) No. (%)	Grade ≥3 (*N* = 157) No. (%)
CRS	80 (51.0)	5 (3.2)
Injection-site reaction	31 (19.7)	0
Neutropenia	29 (18.5)	18 (11.5)
Fatigue	22 (14.0)	1 (0.6)
Pyrexia	16 (10.2)	1 (0.6)
Injection-site erythema	15 (9.6)	0
Nausea	11 (7.0)	1 (0.6)
Anemia	10 (6.4)	4 (2.5)
Decreased neutrophil count	10 (6.4)	8 (5.1)
ICANS†	10 (6.4)	1 (0.6)
Diarrhea	9 (5.7)	0
Headache	8 (5.1)	0

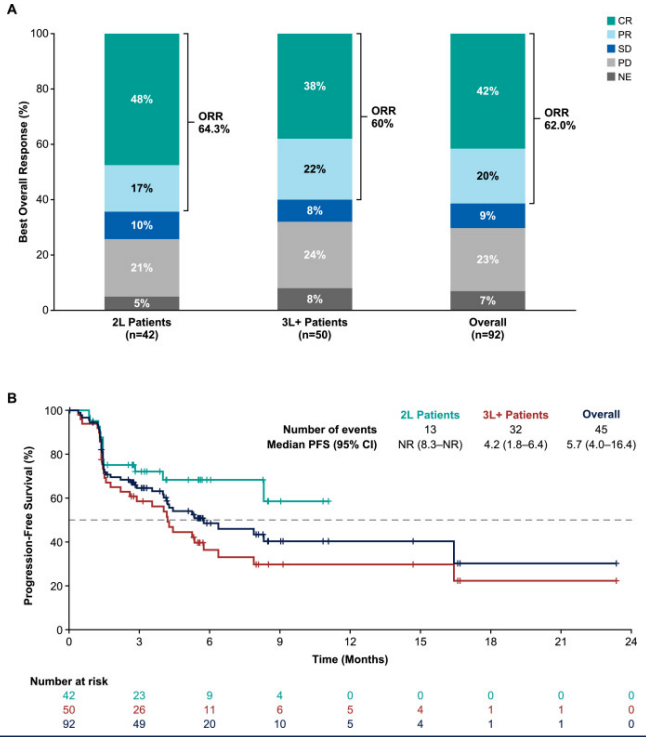


Thieblemont et al. Leukemia 2024

DLBCL: Epcoritamab outpatient

- Single-arm study of epcoritamab monotherapy in 2nd or subsequent line with outpatient monitoring



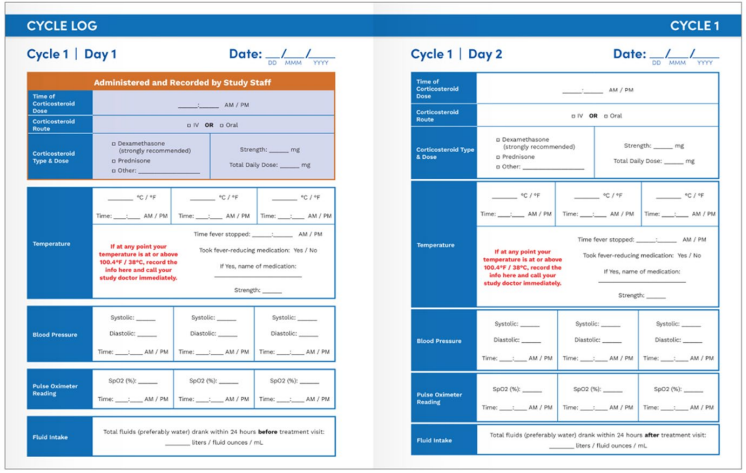


Andorsky et al. Clin Lymphoma Myeloma Leuk 2026

DLBCL: Epcoritamab outpatient

The following steps should be taken to ensure appropriate evaluation and management:

- Measure vital signs, including temperature, blood pressure, pulse, and oxygen saturation by pulse oximetry.
- Check immediately: complete blood count (CBC) with differential and biochemistry including potassium, phosphate, calcium, uric acid, lactate dehydrogenase and creatinine
- Check immediately C-reactive Protein (CRP) and ferritin
- A simultaneous workup (i.e., blood cultures, chest x-ray) should be completed to rule out symptoms that are due to infection.
- The following signs and symptoms may quickly increase in severity and should be managed urgently:
  - For CRS: early signs and symptoms of CRS include fever ≥ 38.0°C (100.4°F), hypotension, and hypoxia. Manage initially with parenteral fluids and oxygen supplementation. Initial management may include, but should not be limited to, anti-pyretics, IV fluids, oxygen supplementation, anti-cytokine therapy, and/or corticosteroid therapy.
  - For ICANS: Early multiple signs and symptoms include disorientation, trouble naming objects, following commands, inability/difficulty writing, and attention deficit, seizure, motor weakness and intracranial pressure elevation/ or cerebral edema. When exhibiting any of these symptoms, a neurological assessment including an ICE score evaluation is recommended. Initial management may include, but should not be limited to, corticosteroid therapy.
- It is important to immediately call the study doctor (or covering physician) at:


CYCLE LOG

CYCLE 1

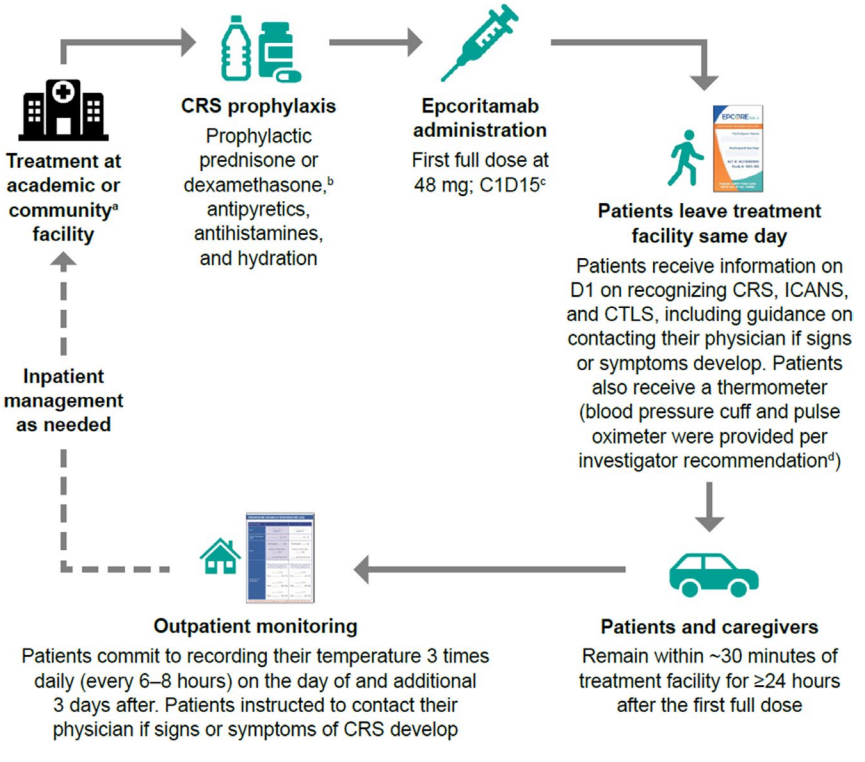
Cycle 1 | Day 1 — Date: __/__/__ (DD MMM YYYY)

Administered and Recorded by Study Staff

Time of Corticosteroid Dose	____:____ AM / PM
Corticosteroid Route	☐ IV OR ☐ Oral
Corticosteroid Type & Dose	☐ Dexamethasone (strongly recommended) ☐ Prednisone ☐ Other: _____ — Strength: ____ mg — Total Daily Dose: ____ mg
Temperature	____ °C / °F — Time: ____:____ AM / PM — If at any point your temperature is at or above 100.4°F / 38°C, record the info here and call your study doctor immediately. — Time fever stopped: ____:____ AM / PM — Took fever-reducing medication: Yes / No — If Yes, name of medication: _____ — Strength: _____
Blood Pressure	Systolic: _____ Diastolic: _____ — Time: ____:____ AM / PM
Pulse Oximeter Reading	SpO2 (%): _____ — Time: ____:____ AM / PM
Fluid Intake	Total fluids (preferably water) drank within 24 hours before treatment visit: _____ liters / fluid ounces / mL

Cycle 1 | Day 2 — Date: __/__/__ (DD MMM YYYY)

Time of Corticosteroid Dose	____:____ AM / PM
Corticosteroid Route	☐ IV OR ☐ Oral
Corticosteroid Type & Dose	☐ Dexamethasone (strongly recommended) ☐ Prednisone ☐ Other: _____ — Strength: ____ mg — Total Daily Dose: ____ mg
Temperature	____ °C / °F — Time: ____:____ AM / PM — If at any point your temperature is at or above 100.4°F / 38°C, record the info here and call your study doctor immediately. — Time fever stopped: ____:____ AM / PM — Took fever-reducing medication: Yes / No — If Yes, name of medication: _____ — Strength: _____
Blood Pressure	Systolic: _____ Diastolic: _____ — Time: ____:____ AM / PM
Pulse Oximeter Reading	SpO2 (%): _____ — Time: ____:____ AM / PM
Fluid Intake	Total fluids (preferably water) drank within 24 hours after treatment visit: _____ liters / fluid ounces / mL

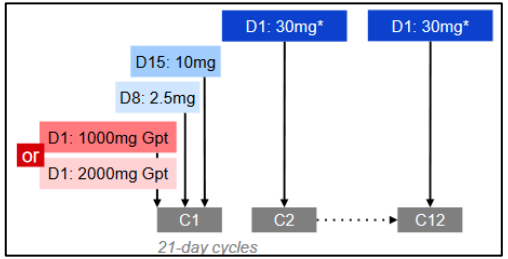


Andorsky et al. Clin Lymphoma Myeloma Leuk 2026

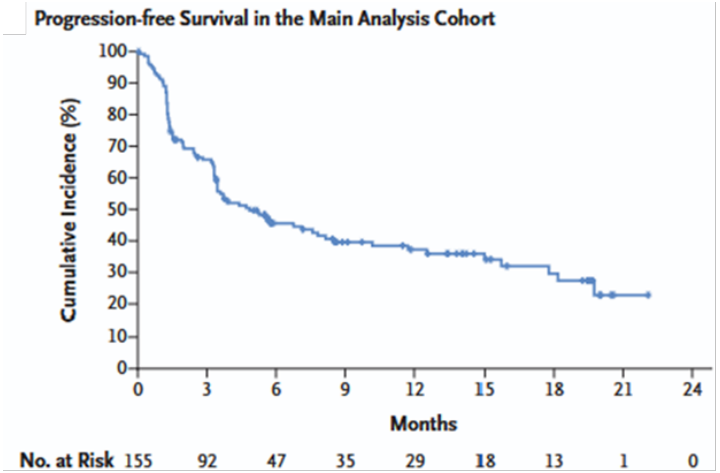
UCSF Helen Diller Family Comprehensive Cancer Center

DLBCL: Glofitamab

- Single-arm phase 1/2 study of glofitamab in 3rd+ line of therapy
- 55% stage IV, 60% >=3 prior lines of therapy, 33% prior CAR T



	Glofitamab (N=155)
Median follow up	12.6 mo
ORR	52%
CRR	39%
12-mo DoCR	78%
12-mo PFS	37%
12-mo OS	50%



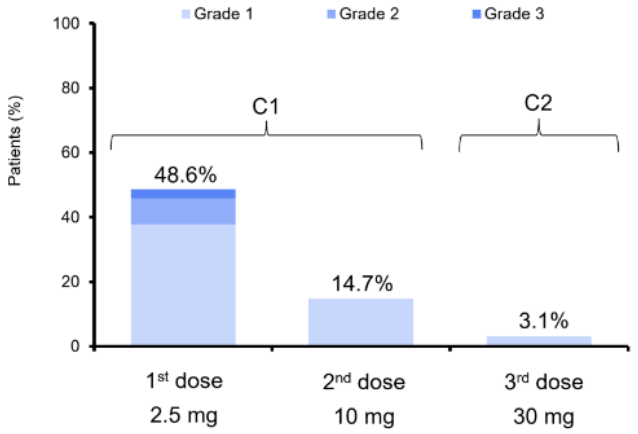
Dickinson et al. N Engl J Med 2022

UCSF Helen Diller Family Comprehensive Cancer Center

DLBCL: Glofitamab

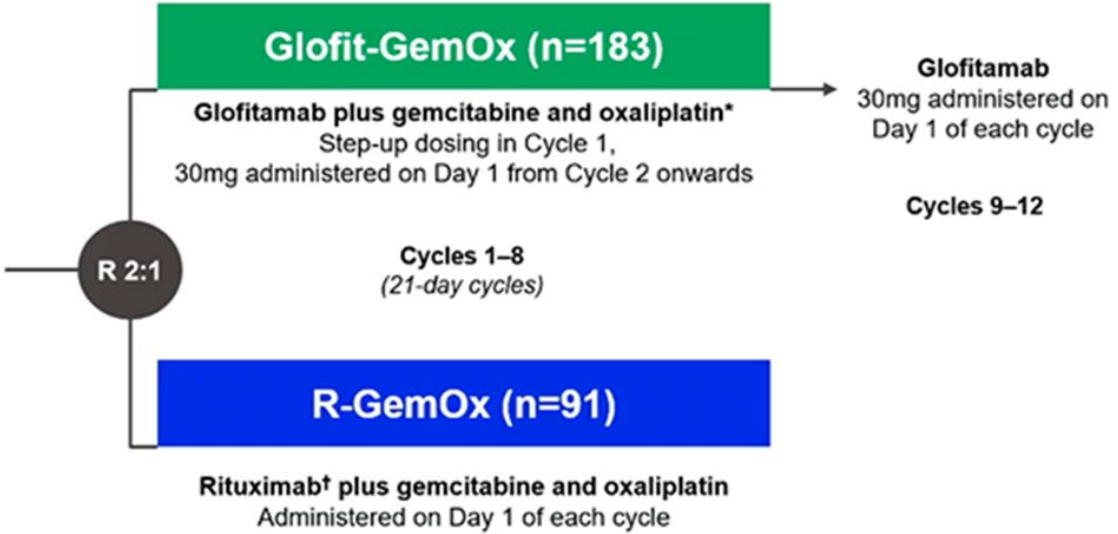
No. (%) of Patients with ≥1 Adverse Event	All Grades N=154	Grade 3 N=154	Grade 4 N=154
Cytokine release syndrome (ASTCT grade)	97 (63.0)	4 (2.6)	2 (1.3)
Cytokine release syndrome (Lee grade)	101 (65.6)	2 (1.3)	2 (1.3)
Neutropenia*	58 (37.7)	26 (16.9)	15 (9.7)
Anemia	47 (30.5)	10 (6.5)	0
Thrombocytopenia†	38 (24.7)	9 (5.8)	3 (1.9)
Pyrexia	28 (18.2)	0	0
Hypophosphatemia	27 (17.5)	8 (5.2)	1 (0.6)
Hypomagnesemia	21 (13.6)	0	0
Constipation	21 (13.6)	0	0
Hypocalcemia	19 (12.3)	0	0
Diarrhea	18 (11.7)	0	0
Fatigue	18 (11.7)	1 (0.6)	0
Hypokalemia	17 (11.0)	2 (1.3)	0
Tumor flare	17 (11.0)	4 (2.6)	0
Back pain	16 (10.4)	2 (1.3)	0

Adverse events of special interest	
Cytokine release syndrome, grade ≥2 per ASTCT	24 (16)
Cytokine release syndrome, grade ≥2 per Lee et al.[28]	28 (18)
Infection, any grade	59 (38)
Neurologic event, grade ≥2	23 (15)
Event grade consistent with ICANS, any grade§	12 (8)
Tumor flare, grade ≥2	11 (7)
AST, ALT, or total bilirubin elevation, grade ≥2	11 (7)
Febrile neutropenia, grade ≥3	4 (3)
Tumor lysis syndrome, grade ≥3	2 (1)



Dickinson et al. N Engl J Med 2022

DLBCL: Glofitamab + GemOx



Patients R/R DLBCL (N=274)

- R/R DLBCL NOS after ≥1 prior systemic therapy
- Patients with one prior line must be transplant ineligible
- ECOG PS 0–2

Stratification factors

- Relapsed vs refractory disease‡
- 1 vs ≥2 prior lines of therapy

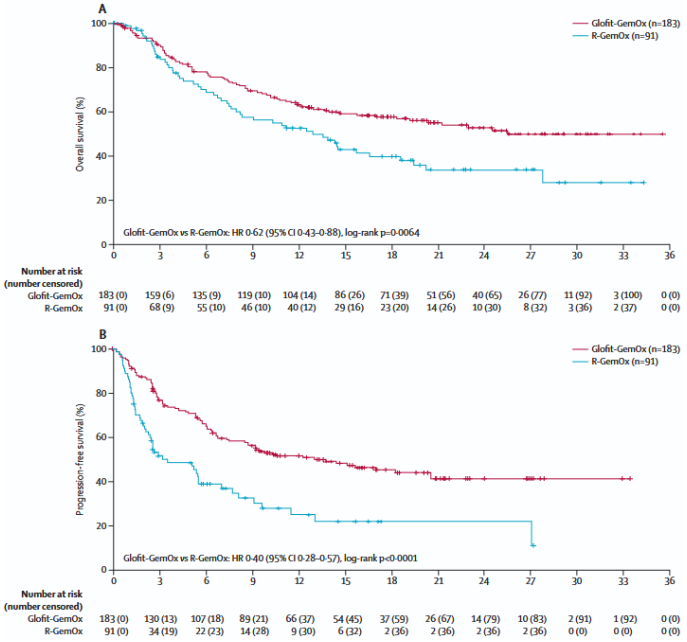
*Gemcitabine 1000mg/m² and oxaliplatin 100mg/m². In C1, Gpt administered on D1, GemOx on D2, followed by glofit 2.5mg on D8 and glofit 10mg on D15; in C2–8, glofit 30mg and GemOx are administered on D1. †Rituximab 375mg/m². ‡Relapsed disease: recurrence following a response that lasted ≥6 months after completion of the last line of therapy; refractory disease: disease that did not respond to, or that progressed <6 months after, completion of the last line of therapy. ASCT, autologous stem cell transplant; C, cycle; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; Gpt, obinutuzumab pre-treatment; NOS, not otherwise specified; R 2:1, patients randomized in a 2:1 ratio.

Abramson et al. EHA 2024

DLBCL: Glofitamab + GemOx

- Median 1 prior line of therapy
- 67-77% stage IV, 19-21% IPI 4-5, 7-9% prior CAR T

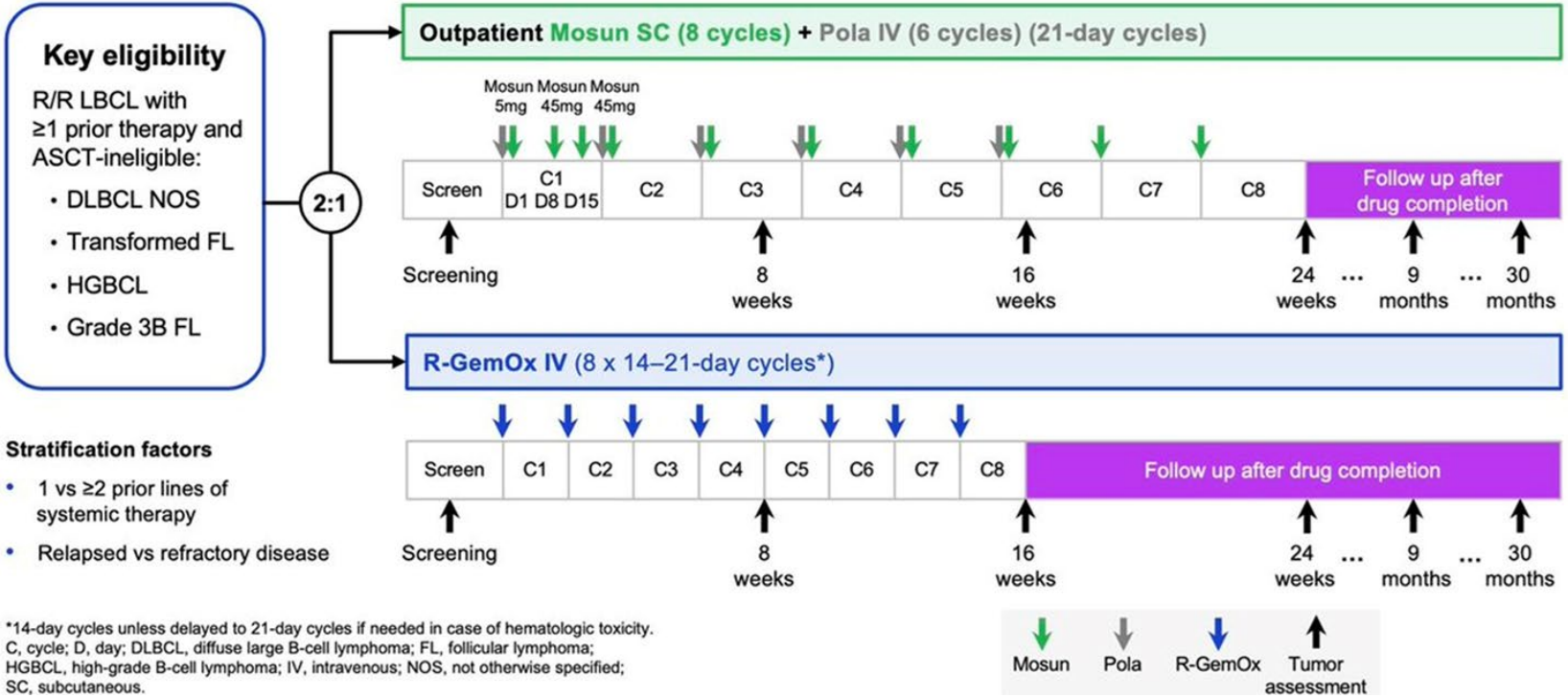
	Glofit-GemOx (N=183)	R-GemOx (N=91)
Median follow up	11.3 mo	11.3 mo
ORR	68%	41%
CRR	59%	25%
Median DoCR	NR	24.2 mo
Median PFS	14.4 mo	2.7 mo
Median OS	25.5 mo	12.9 mo



	R-GemOx (n=88)	Glofit-GemOx (n=180)
Any adverse event	84 (96%)	180 (100%)
Most common adverse event (≥30% patients in either group)		
Thrombocytopenia*	42 (48%)	87 (48%)
CRS†	NA	76 (44%)†
Neutropenia‡	27 (31%)	76 (42%)
Anaemia	19 (22%)	73 (41%)
Nausea	35 (40%)	71 (39%)
Peripheral neuropathy§	23 (26%)	64 (36%)
Diarrhoea	24 (27%)	62 (34%)
Aspartate transferase increased	17 (19%)	59 (33%)
Alanine transaminase increased	19 (22%)	57 (32%)
Any glofitamab-related or rituximab-related adverse event	58 (66%)	149 (83%)
Any grade ≥3 adverse event	36 (41%)	140 (78%)
Any glofitamab-related or rituximab-related grade ≥3 adverse event	20 (23%)	85 (47%)
Any serious adverse event	15 (17%)	98 (54%)
Any glofitamab-related or rituximab-related serious adverse event	7 (8%)	62 (34%)
Any adverse event of special interest	69 (78%)	176 (98%)
CRS†	NA	76 (44%)†
Grade 1	NA	54 (31%)†
Grade 2	NA	18 (11%)†
Grade 3	NA	4 (2%)†
Neurological adverse event (grade ≥2)	11 (13%)	55 (31%)
Serious infections	11 (13%)	46 (26%)
Febrile neutropenia	1 (1%)	6 (3%)
Tumour flare (grade ≥2)	1 (1%)	1 (1%)
Any grade 5 adverse event	4 (5%)	15 (8%)
COVID-19-associated grade 5 adverse event	0	7 (4%)¶
COVID-19	0	4 (2%)
Respiratory tract infection	0	1 (1%)
Neutropenic sepsis	0	1 (1%)
Acute respiratory distress syndrome	0	1 (1%)
Other grade 5 adverse event		
Pneumonia	3 (3%)	1 (1%)
Multiple organ dysfunction syndrome	1 (1%)	1 (1%)
Pneumonitis	0	2 (1%)
Cerebral haemorrhage	0	1 (1%)
Cardiac arrest	0	1 (1%)
Septic shock	0	2 (1%)
Any glofitamab-related or rituximab-related grade 5 adverse event‖	1 (1%)	5 (3%)

Abramson et al. Lancet 2024

DLBCL: Mosunetuzumab + Polatuzumab

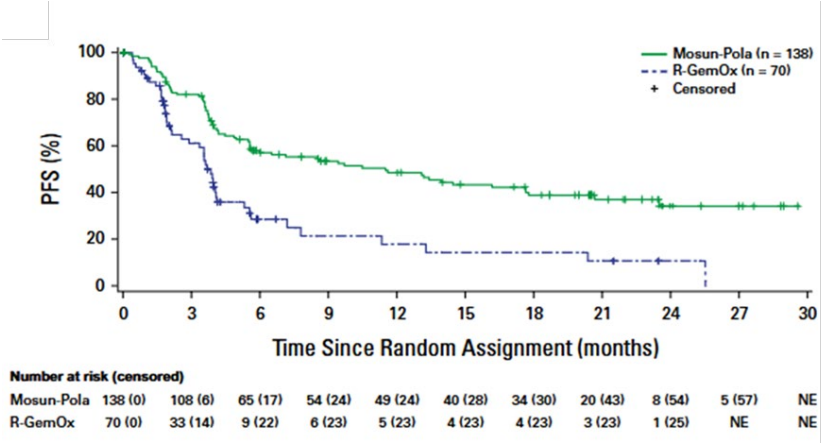


*14-day cycles unless delayed to 21-day cycles if needed in case of hematologic toxicity.
C, cycle; D, day; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IV, intravenous; NOS, not otherwise specified; SC, subcutaneous.

Westin et al. ICML 2025

DLBCL: Mosunetuzumab + Polatuzumab

- Median 2 prior lines of therapy
- 75-80% stage III/IV, 49-51% IPI 3-5, 2.2% (MP) vs 7.1% prior CAR T, 4.3% (MP) vs 14% prior ASCT
- ORR 70% vs 40%, CRR 51% vs 24%
- mPFS 11.5 mo vs 3.8 mo
- mOS 18.7 mo vs 13.6 mo



	Mosun-Pola (n = 135), No. (%)		R-GemOx (n = 64), No. (%)	
Adverse Event	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any adverse event	131 (97)	86 (64)	61 (95)	41 (64)
Most common adverse event (≥20%)				
Injection site reaction	71 (53)	0	0	0
Neutropenia[a]	62 (46)	45 (33)	35 (55)	20 (31)
Anemia[a]	41 (30)	8 (5.9)	27 (42)	12 (19)
Cytokine response syndrome	35 (26)	1 (0.7)	0	0
Peripheral neuropathy[b]	33 (24)	0	27 (42)	0
Fatigue	21 (16)	2 (1.5)	13 (20)	1 (1.6)
Nausea	17 (13)	0	17 (27)	1 (1.6)
Diarrhea	14 (10)	0	15 (23)	1 (1.6)
Thrombocytopenia[a]	12 (8.9)	3 (2.2)	42 (66)	23 (36)
Infusion-related reaction	10 (7.4)	2 (1.5)	13 (20)	1 (1.6)
Adverse event of special interest for mosunetuzumab				
Cytokine release syndrome[c]	35 (26)		0	
Grade 1	29 (21)		0	
Grade 2	5 (3.7)		0	
Grade 3	1 (0.7)		0	
Hemophagocytic lymphohistiocytosis	0		0	
Infections	69 (51)		20 (31)	
Serious infections	22 (16)		9 (14)	
Grade ≥3 infections	21 (16)		9 (14)	
Febrile neutropenia	3 (2.2)		2 (3.1)	
Pneumonitis/interstitial lung disease	7 (5.2)		0	
Tumor flare	9 (6.7)		0	
Tumor lysis syndrome	1 (0.7)		0	

Budde et al. J Clin Oncol 2025

Summary of approved bispecifics in DLBCL

3rd line

	Epcoritamab (Thieblemont et al. 2024)	Glofitamab (Dickinson et al. 2022)
Treatment	C1-3: weekly C4-9: q2 weeks C10+: q4 weeks	C1: weekly C2-12: q3 weeks
Treatment duration	Indefinite	12 cycles
Route of admin	SQ	IV
Patients	157	155
Prior lines of therapy	40% >=4	60% >=3
ORR	63%	52%
CRR	40%	39%
PFS	4.4 mo (median)	4.9 mo (median)
CRS (Gr 1)	48%	47%
CRS (Gr 2-4)	3%	16%
ICANS (any grade)	6.4%	8%

2nd line

	Epco + GemOx (Brody et al. Blood 2025)	Glofit + GemOx (Abramson et al. Lancet 2024)	Mosun + Pola (Budde et al. 2025)
Treatment	C1-3: weekly C4-9: q2 weeks C10+: q4 weeks GemOx: q2 weeks x8	C1: weekly C2-12: q3 weeks GemOx: q3 weeks x8	C1: weekly C2-8: q3 weeks Pola: q3 weeks C1-6
Eligibility	1 prior LOT Transplant ineligible or relapsed after transplant	1 prior LOT (transplant ineligible) 2 prior LOT (transplant eligible)	1 prior LOT Transplant ineligible
Treatment duration	Indefinite	12 cycles	8 cycles
Route of admin	SQ + IV	IV	SQ + IV
Patients	103	183	138
Prior lines of therapy	2	1	2
ORR	85%	68%	70%
CRR	61%	59%	51%
PFS	11.2 mo (median)	14.4 mo (median)	11.5 mo (median)
CRS (Gr 1-2)	51.4%	42%	24.7%
CRS (Gr 3-4)	1%	2%	0.7%
ICANS (Gr 1-2)	1.9%	2%	0%
ICANS (Gr 3-4)	1%	1%	0%

Practical considerations

Dosing schedules

	Cycle 1 Step-Up Dosing Schedule (to minimize CRS)				Subsequent Dosing
Mosunetuzumab IV (FL)	**Day 1**	**Day 8**	**Day 15**		**Day 1 (21-day cycle)**
(flat dose)	1 mg	2 mg	60 mg		C2: 60 mg--> C3+: 30 mg
	Dex 20 mg (C1-2)	Dex 20 mg	Dex 20 mg		CR: stop after C8. PR/SD: stop after C17
Mosunetuzumab SQ (FL, DLBCL)	**Day 1**	**Day 8**	**Day 15**		**Day 1 (21-day cycle)**
(flat dose)	5 mg	45 mg	45 mg		C2: 45 mg
	Dex 20 mg (C1)	Dex 20 mg	Dex 20 mg		CR: stop after C8. PR/SD: stop after C17
Epcoritamab SQ (FL)	**Day 1**	**Day 8**	**Day 15**	**Day 22**	**C2-3: Day 1, 8, 15, 22; C4-9: Day 1, 15; C10+: Day 1**
(flat dose)	0.16 mg Dex 15 mg x4 days	0.8 mg Dex 15 mg x4 days	3 mg Dex 15 mg x4 days	48 mg Dex 15 mg x4 days	Monotherapy: indefinite. With R2: 12 cycles
Epcoritamab SQ (DLBCL)	**Day 1**	**Day 8 (+/- inpt)**	**Day 15**	**Day 22**	**C2-3: Day 1, 8, 15, 22; C4-9: Day 1, 15; C10+: Day 1**
(flat dose)	0.16 mg Dex 15 mg x4 days	0.8 mg Dex 15 mg x4 days	48 mg Dex 15 mg x4 days	48 mg Dex 15 mg x4 days	Indefinite
Glofitamab IV	**Day 1**	**Day 8 (inpt)**	**Day 15**		**Day 1 (21-day cycle)**
(flat dose)	Obinutuzumab 1000 mg	2.5 mg	10 mg		30 mg
	Dex 20 mg (C1-3)	Dex 20 mg	Dex 20 mg		Stop after C12

Eligibility and management

CRS risk

- At-home dexamethasone for epcoritamab
- Topical steroids for epcoritamab or mosunetuzumab sc
- 24-hour inpatient monitoring for first step-up dose glofitamab
- Consider inpatient monitoring for first full dose epcoritamab for high-risk patients with DLBCL
- Full-time caregiver for step-up doses
- Home vital sign monitoring
- Dexamethasone at home PRN per on-call instructions

Infection risk

- HBV screening prior to treatment
- HSV/VZV prophylaxis
- PJP prophylaxis
- GCSF for grade ≥3 neutropenia (avoid with step-up doses)
- IVIG as needed for hypogammaglobulinemia with recurrent infections

Dose management

- Withhold dose and give GCSF for ANC <0.5
- Withhold dose if concerned for active infection
- Step-up doses may need to be repeated for prolonged dose delays (>2 weeks)

Trials at UCSF

- SWOG S2114
  - Randomized trial of mosunetuzumab, polatuzumab vedotin, both, or observation (control) as early consolidation in patients after CAR T-cell therapy for DLBCL

- Glofitamab + pirtobrutinib in relapsed/refractory mantle cell lymphoma
  - Single-arm phase 2 trial of glofitamab and pirtobrutinib for patients with relapsed/refractory MCL
  - Limited-duration MRD-guided study

Questions?