The young side of
LYMPHOMA

gli under 40 a confronto

Verona, Centro Congressi Camera di Commercio
26-27 settembre 2025

Nuove Terapie nel paziente con DLBCL R/R

Beatrice Casadei

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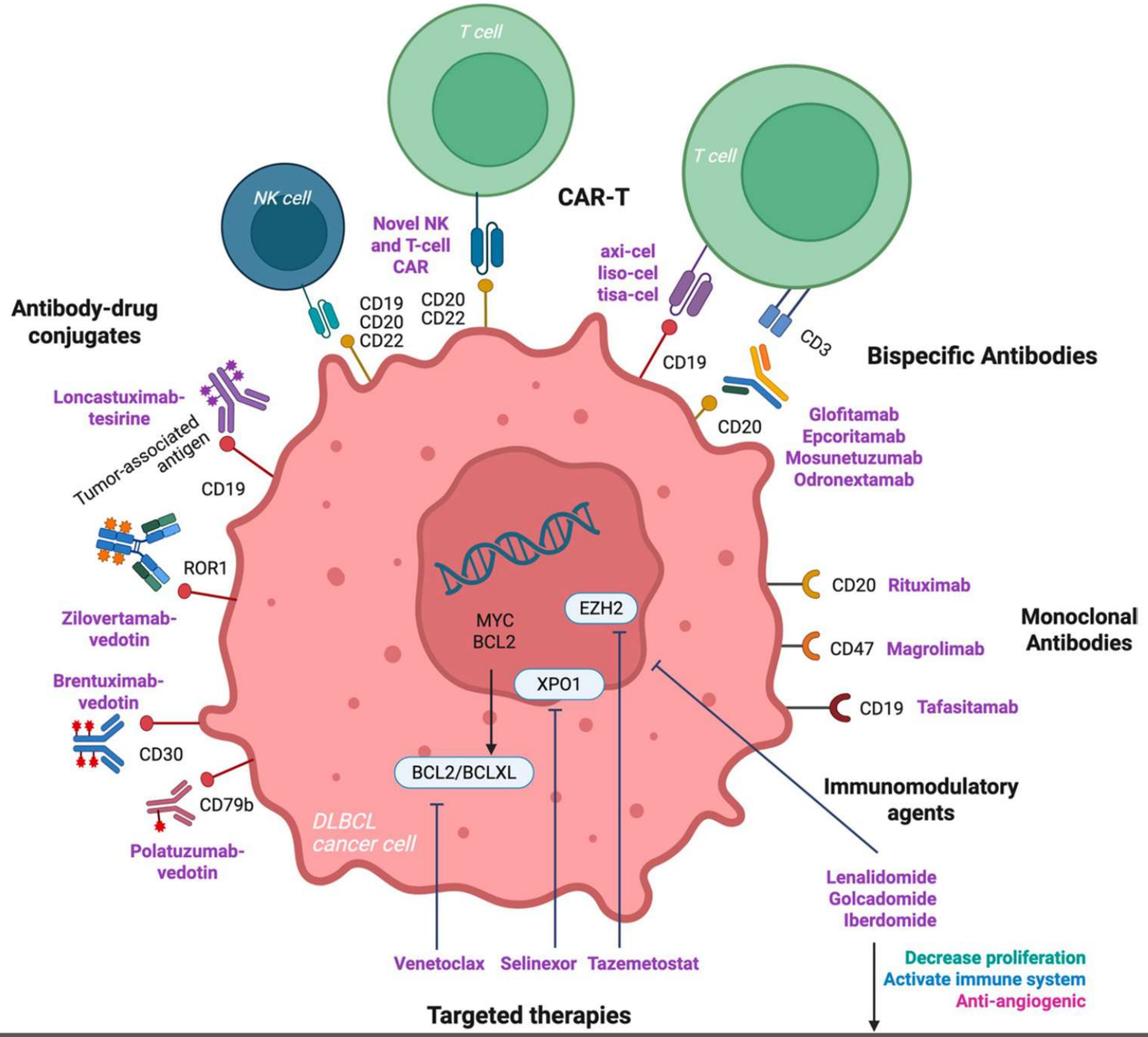
Disclosures of Beatrice Casadei

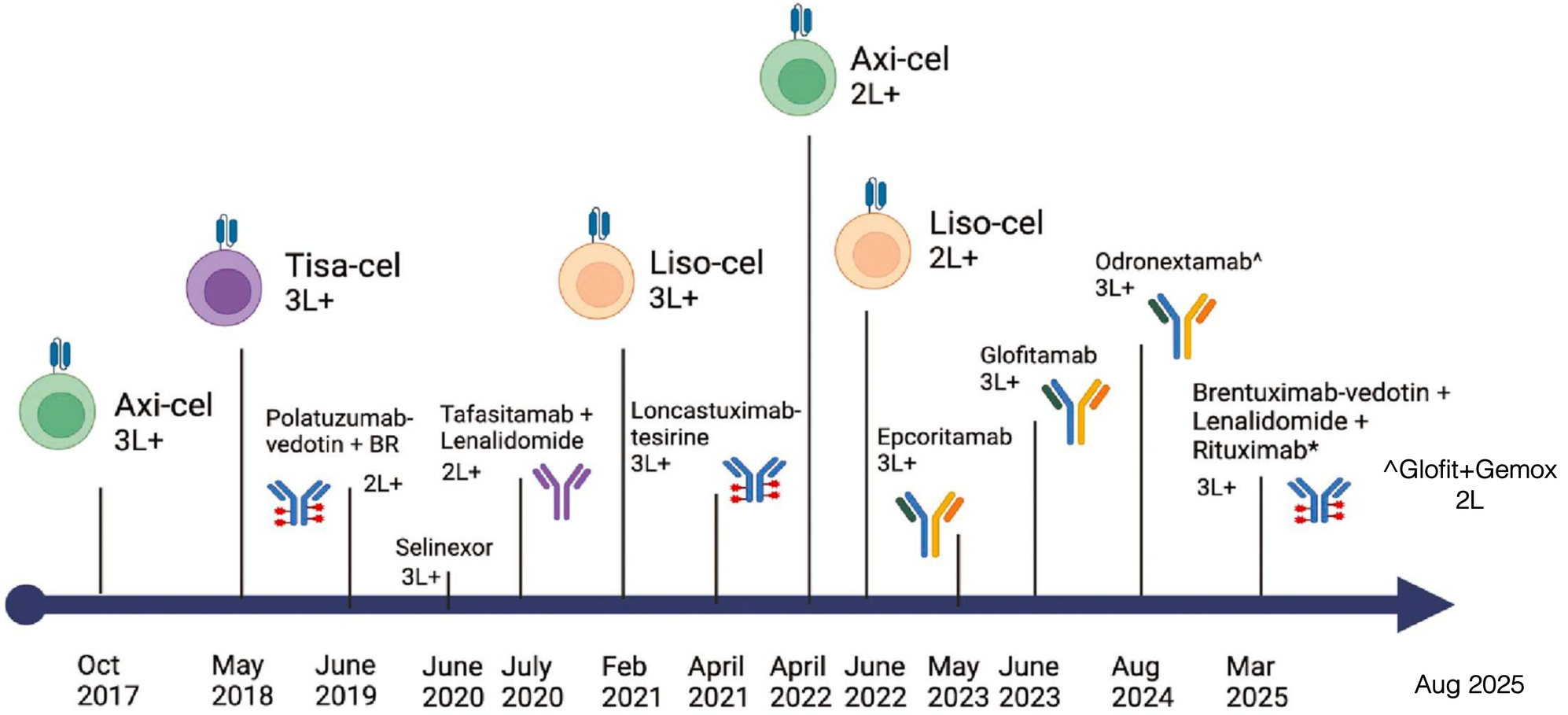
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Kite-Gilead					x	x	
Novartis					x		
Celgene-BMS						x	
Abbvie					x	x	
Janssen					x	x	
Lilly					x		
Beigene						x	
Roche					x	x	
Incyte					x		
Takeda						x	

RR DLBCL: Treatment Scenario between Approved and Experimental Agents



Bock and Epperla Journ of Hematology and Oncology 2025

RR DLBCL: FDA and EMA Approved Treatments



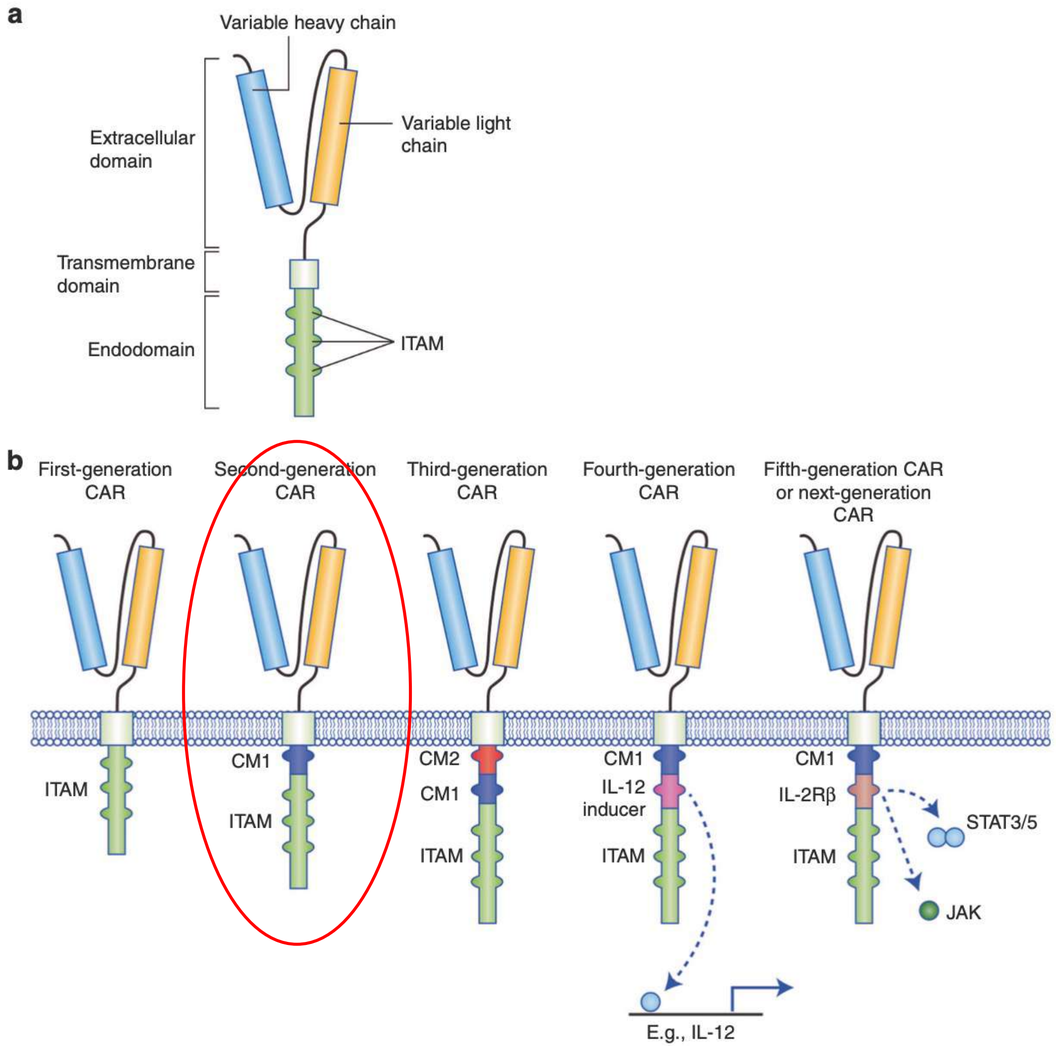
Abbreviations: axi-cel, Axicabtagene ciloleucel; liso-cel, Lisocabtagene maraleucel; tisa-cel, Tisagenlecleucel. 2L+, second line or later; 3L+, third line or later. *FDA approval only, ^EMA approval only.

Fig. 1 FDA and EMA approved novel treatments and cellular therapies for relapsed/refractory DLBCL

Modified from Bock and Epperla Journ of Hematology and Oncology 2025

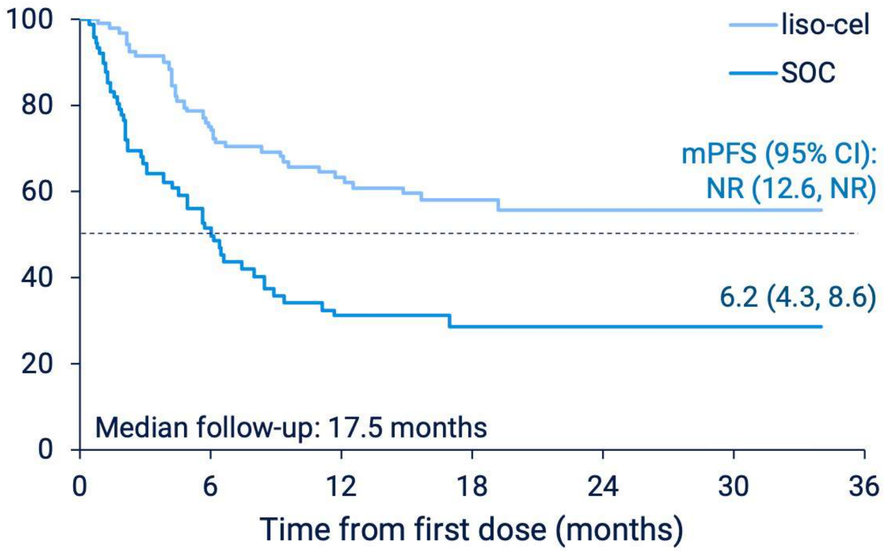
Cell Based Immunotherapy: CAR T-cell

- Patient's own T cells are engineered to express an **anti-CD19 CAR** using a viral vector (gamma retrovirus or lentivirus);
- The **target-binding domain** identifies and binds to the CD19 surface antigen of B cells;
- Upon binding, the **CD3ζ activation** and **CD28 (axi-cel and brexu-cel) or 41BB (tisa-cel and liso-cel) costimulatory domains** activate the CAR T cells;
- Activated CAR T cells release inflammatory cytokines and chemokines and destroy the CD19-expressing B cells.



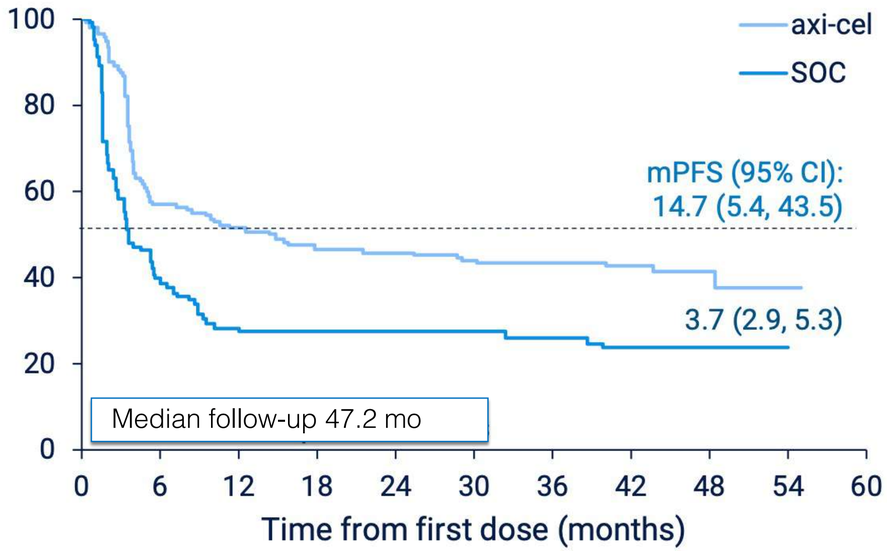
CAR T-cell has Improved Outcomes over SOC in Refractory DLBCL

PFS: Ph3 TRANSFORM (liso-cel 2L)[1]



Response	Liso-cel (n = 92)	SOC (n = 92)
ORR	**87%**	**49%**
CR	74%	43%

PFS: Ph3 ZUMA-7 (axi-cel 2L)[2]

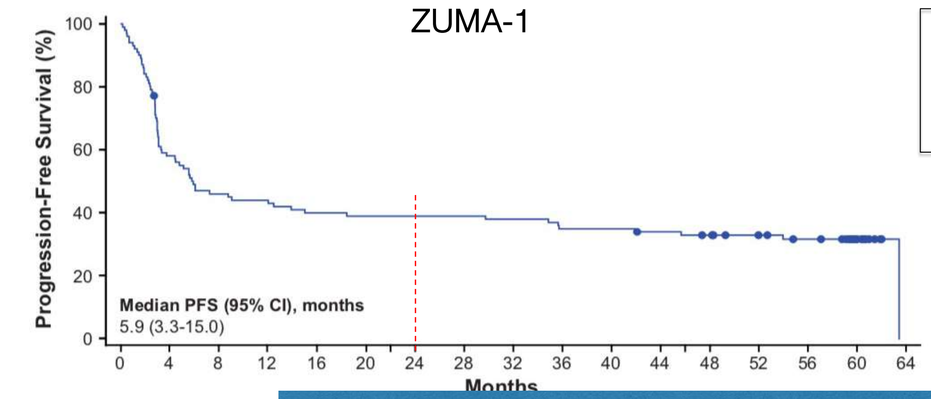


Response	Axi-cel (N=180)	SOC (N=179)
ORR	**83%**	**45%**
CR	61%	34%

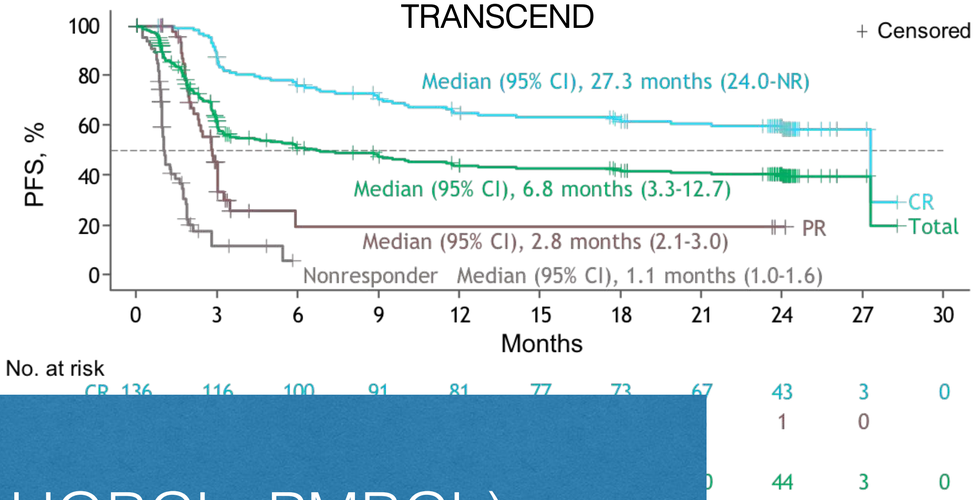
2L; primary refractory or relapsed ≤ 12 mo
LBCL (DLBCL NOS, HGBCL)

Abramson JS, et al. Blood (2023) 141 (14): 1675–1684.; Westin J, et al. N Engl J Med 2023; 389:148-157.

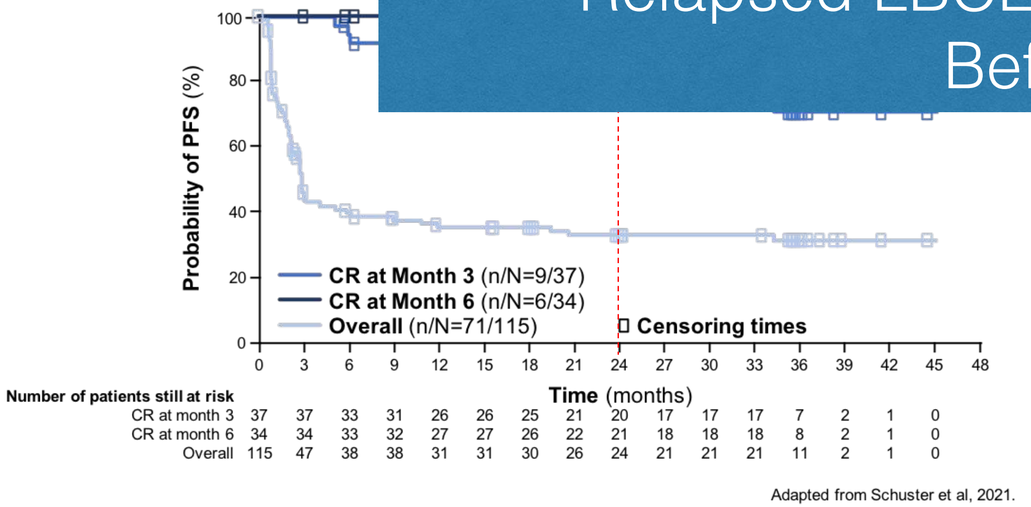
CAR T-cell has Improved Outcome in RR (3L+) DLBCL



BEST ORR: 50-80%
BEST CR: 39-58%



3L
Relapsed LBCL (DLBCL NOS, HGBCL, PMBCL)
Before or After BsAbs?



Adapted from Schuster et al, 2021.

			TRANSCEND
		.8)	23.9 (23.7-24)
Median DOCR, mo (range)	62.2 (12.9-NE)	NR	26.1 (23.1-NR)
Median PFS, mo (range)	5.9 (3.3-15)	2.9 (2.3-5.2)	6.8 (3.3-12.7)
PFS at 2 years, %	32 (at 5 years)	NA	40.6
Median OS, mo (range)	25.8 (12.8-NE)	11.1 (6.6-23.9)	27.5 (16.2-47.3)
OS at 5 years, %	42.6 (64.4% for those in CR)	NA	38 (56% for those in CR)

Abramson JS, et al. Blood. 2024; Abramson JS, et al. Blood. 2019; Neelapu SS, et al. Blood 2023; Locke FL, et al. Lancet Oncol. 2019; Neelapu SS, et al. N Engl J Med. 2017; Schuster SJ et al, Lancet 2021; Schuster SJ, et al. N Engl J Med. 2019; Schuster SJ, et al. N Eng J Med 2017

Emerging CAR T-cell Treatment

Table 3 Investigative novel CAR treatments for R/R DLBCL

Treatment	NCT#	Target	Phase	Sample size	Median prior LOT	Median follow up (months)	ORR% (CRR%)	Median PFS (months)	PFS estimate	OS estimate	CRS Any grade, % (Grade ≥ 3, %)	ICANS Any grade, % (Grade ≥ 3, %)	Neutropenia Any grade, % (Grade > 3, %)	Thrombocytopenia any grade, % (Grade ≥ 3, %)	Other notable treatment emergent adverse events, %
Zamto-cel	04792489	Auto CD20/ CD19	1	27	2	NR	50 (38)	NR	NR	NR	14 (5)	15 (4)	NR	NR	NR
Rap-cabtagene autoleucel	03960840	Auto CD19	2	63	2	16.4	88 (65)	11.9	12 month PFS of 48%	NR	43 (6)	6 (3)	62% G3	25% G3	Infections (G3, 27%)
firicabtagene autoleucel	04088890; 05972720	Auto CD22	1, 2	38	4	36.7	68 (53)	3	3 year PFS of 30%	3 year OS of 47%	93 (0)	10 (0)	100 (100)	86 (52)	second primary malignan-cies (MDS/ AML, 11%), infection, hypogam-maglobu-linemia
Tak-007	03056339	Allo NK CAR19/ IL15	1,2	37	4	12	89 (83)	NR	NR	NR	2.7 (0)	0 (0)	100 (34)	89 (27)	asthenia (35%), dysrhythmia (19%), rash (11%)
CB-010	04637763	Allo CAR19/ PD-1 knockout	1	16	2	NR	94 (69)	NR	NR	NR	44 (0)	25 (13)	NR (G3 56)	NR (69)	CRS, ICANS, thrombo-cytopenia, neutropenia, anemia. No GVHD
FT596	04245722	iPSC-derived NK CAR19	1	20	4	NR	52 (64)	NR	NR	NR	10 (0)	0 (0)	85 (NR)	40 (NR)	nausea (75%), peripheral edema (35%). No GVHD
LY007	06279611	Auto CD20	1	9	3	NR	89 (78)	NR	88.9% at 6 months	100% at 6 months	66 (0)	0 (0)	77% G3	0 (0)	cytopenias
Cemacabta-gene anseg-edleucel (501/501 A)	03939026 (ALLO-501); 04416984 (ALLO-501 A)	Allo CAR19	1,2	33	4	7.1	67 (58)	NR	NR	NR	24 (0)	0 (0)	NR	NR	prolonged G3 or greater cytopenia (12%), infec-tion, infusion reaction. No GVHD

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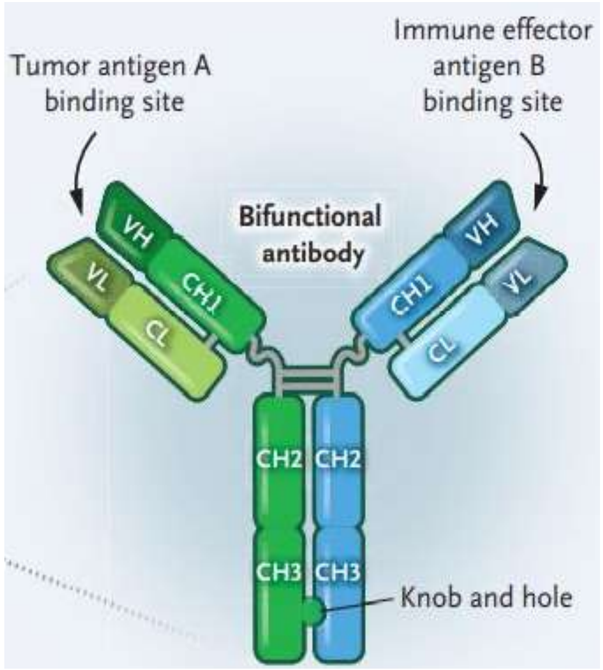
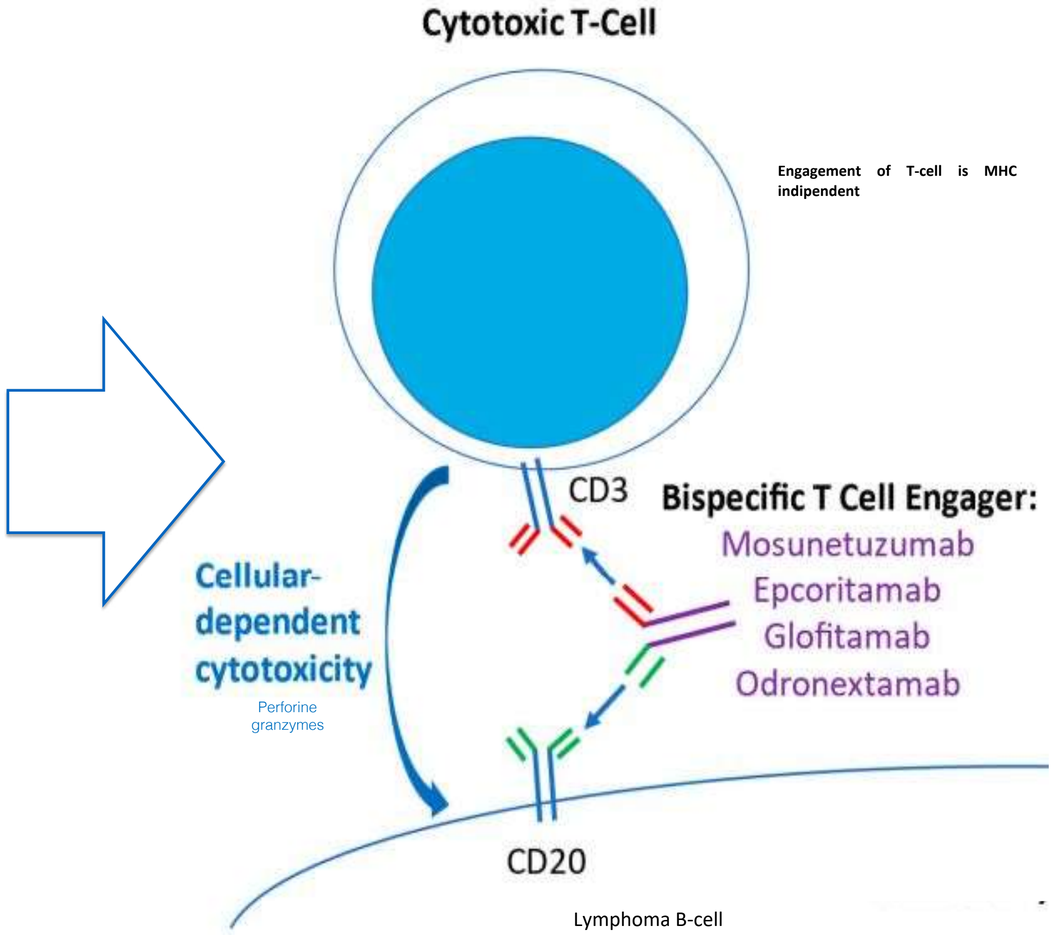
Bispecific Antibodies: CD20xCD3





Longo D.L. New Eng J Med 2022; Falchi L. et al. Blood 2023.

Drug	Mosunetuzumab[3]	Epcoritamab[4]	Glofitamab[5]	Odronextamab[6,7]
Structure	Fully humanized IgG1 CD3×CD20 BsAb with 1:1 CD3:CD20 ratio of Fab arms	IgG-like anti-CD3×CD20 BsAb. Proprietary format, with point mutations in the Fab portion of the Fc of the antibody and heterodimerization.	Humanized mouse-derived BsAb with 1:2 CD3:CD20 ratio of Fab arms	Fully humanized IgG4 anti-CD3×CD20 BsAb developed using an Fc domain with a mutation in the protein A of the Fc portion
Route of administration	IV	SC	IV	IV
Dosing schedule	C1: days 1, 8, 15; C2+: day 1, every 21 d, for up to 8 cycles in CR or up to 17 cycles for PR or SD	C1-3: days 1, 8 ,15, and 22; C4-9: days 1 and 15; C10+: day 1, every 28 d until progression	C1: obin, day 1; glofit, days 8 and 15; C2-12: day 1, every 21 d	C1: days 1, 2, 8, 9, 15, 16 of a 21-d cycle; C2-4: days 1, 8, 15 of a 21-d cycle; C5+: day 1, every 14 d; If CR for at least 9 mo: day 1, every 28 d
CRS mitigation				
Step-up dosing	C1D1: 1 mg C1D8: 2 mg C1D15: 60 mg C2D1: 60 mg C3+D1: 30 mg	C1D1: 0.16 mg C1D8: 0.8 mg C1D15: 48 mg C1D22: 48 mg C2D1+: 48mg	C1D1: obin 1000 mg C1D8: 2.5 mg C1D15: 10 mg C2D1+: 30 mg	C1D1: 0.2 mg C1D2: 0.5 mg C1D8: 2 mg C1D9: 2 mg C1D15: 10 mg C1D16: 10 mg C2-C4: 80 mg (FL) or 160 mg (DLBCL) C5+: 160 mg (FL) or 320 mg (DLBCL)
Premedications	(1) A/P 500-1000 mg, 30 min prior, for C1 and C2 (2) Diphenhydramine 50-100 mg, 30 min prior, for C1 and C2 (3) Dexamethasone 20 mg or methylprednisolone 80 mg, 1 h prior, for C1 and C2. Continue all premedications if CRS with prior dose.	(1) A/P 650-1000 mg, 30-120 min before C1 treatments (2) Diphenhydramine 50 mg, 30-120 min before C1 treatments (3) Dexamethasone 15 mg, 30-120 min before C1 treatments and for 3 consecutive days after. Continue dexamethasone thereafter if G2 or G3 CRS with prior dose.	(1) A/P 500-1000 mg, 30 min before all treatments (2) Diphenhydramine 50 mg, 30 min before all infusions (3) Dexamethasone 20 mg, 1 h before treatment on C1D8, C1D15, C2D1, and C3D1. Continue if CRS with prior dose.	(1) A/P 650 mg, 30-60 min prior, during step-up dosing, continue if IRR or CRS with prior dose (2) Diphenhydramine 25 mg, 30-60 min prior during step-up dosing, continue if IRR or CRS with prior dose (3) Dexamethasone 10 mg orally, 12-24 h before split dose, 20 mg IV on day of dosing, 10 mg orally on the day after step-up dosing. Following first full dose, dexamethasone 10 mg before dosing; continue if CRS with prior dose.
Hospitalization	Optional	C1D15: 24-h admission	C1D8: 24-h admission	Performed during step-up dosing
CRS occurrence	G1: 26%; G2: 17%; G3: 1%; G4: 1%; G5: 0%	G1: 34%; G2: 15%; G3: 3%; G4: 0%; G5: 0%	G1: 47%; G2: 12%; G3: 3%; G4: 1%; G5: 0%	G1: 35%-39%; G2: 13% (DLBCL); G3: 0%; G4: 0%; G5: 0%
	Time course for CRS onset: C1D1: 23.3% C1D8: 5.6% C1D15: 36.4% C2D1: 10.3% C3+D1: 2.4%	Time course for CRS onset: C1D1: 5.8% C1D8: 11.8% C1D15: 42.8% C1D22: 4.9% C3+ 3%	Time course for CRS onset: C1D8: 42.8% C1D15: 25.2% C2: 26% C3+: 0.9%	Time course for CRS onset: C1D1/2: 22%-24% C1D8/9: 27%-32% C1D15/16: 21%-35% C2D1: 14%-17% C2D8+: 9%-14%
	Median time (h) to CRS onset: C1D1: 5 C1D8: 20 C1D15: 27 C2D1: 38	Median time (h) to CRS onset: All doses: 24 C1D15: 20	Median time (h) to CRS onset: C1D8: 13.5 (range: 6-52)	Median time (h) to CRS onset: All doses: 18-20
Median duration of CRS	3 d (1-29 d)	2 d (range: 1-27 d)	30.5 h (range, 0.5-317 h)	8-10 h (range, 0.1-190 h)
Neurotoxicity	G 1-2: 3%; G3: 0%; G4: 0%; G5: 0%	G1: 4.5%; G2: 1.3%; G3: 0%; G4: 0%; G5: 0.6%	G 1-2: 5%; G 3-4: 3%; G5: 0%	G 1-2: 4% (DLBCL); G 3-4: 0%; G5: 0%

Crombie JL et al, Blood 2024

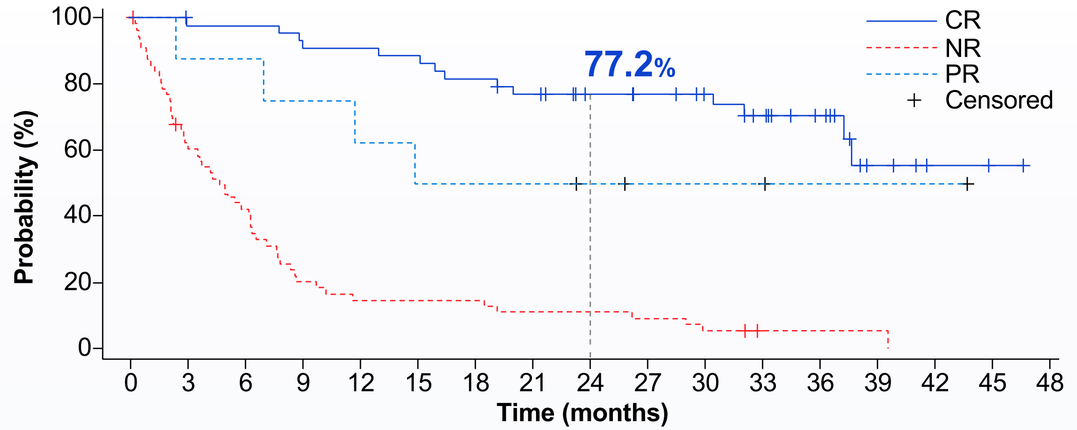
BsAbs CD20xCD3: Summary from Clinical Trials and RWE

Agent and trial	Ph	Route	Pts n	Prior tx median (range)	Primary ref. %	Prior CART, %	ORR/CR %	Median Follow-up, mo	Median DoR/CR mo	Median PFS, mo	Median OS, mo	CRS (any/gr ≥3), %	ICANS (any/gr ≥3) %
Glofitamab[1,2]	I/II	EV, fixed duration	155	3 (2-7)	58	33	52/40	32.1	18.4/29.8	4.9	11.5	63/4	8/3
Epcoritamab[3,4]	I/II	SC, Until PD	148	3 (2-11)	61	38	59/41	31	20.8/36.1	4.4	NR	52/3	6/0.6
Odronextamab[5]	II	EV, Until PD	127	2 (2-8)	55	0	52/31.5	29.9	10.2/17.9	4.4	10.5	53/1.7	0
REALBiTE[6]	RWE	EV/SC	245	3 (1-10)	52	60	52/25	6.3	10 (epco), NR (glofit)	2.5	7.8	39.5/7.7	11/6

1 Dickinson M et al, Blood 2024; 2 Dickinson M. et al, NEJM 2022; 3. Thieblemont C. et al. JCO 2022; 4. Vose JM et al, Blood 2024; 5 Kim WE et al, Nat Cancer 2025; 6 Brooks TR et al, Blood 2025; .

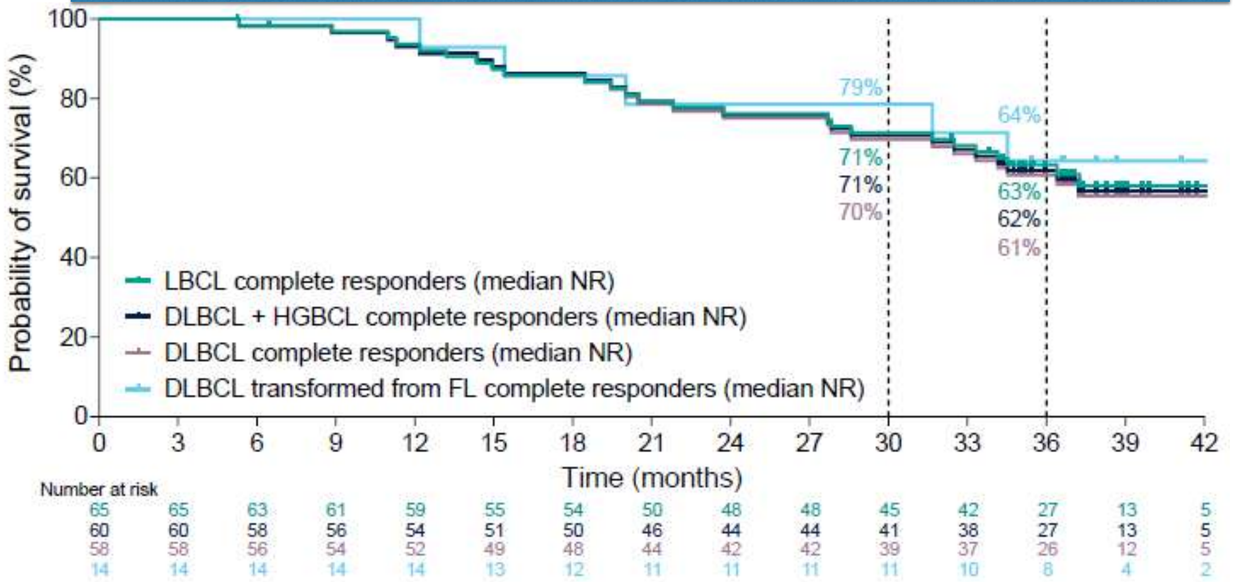
Glofit and Epco: Long Term PFS and OS benefits with CR

OS with Glofi for CR pts



- Among complete responders (n=62), median PFS was NR (95% CI, 20-NR)
- Median OS for the overall population (n=154) was 11.5 mo, among CR was NR (77% at 24 mo in LBCL)

OS with Epco for CR pts



- Among complete responders (n=65), median PFS was 37.3 mo (95% CI, 26-NR)
- Median OS for the overall population (n=157) was 18.5 mo, among CR was NR (63% at 36 mo in LBCL)

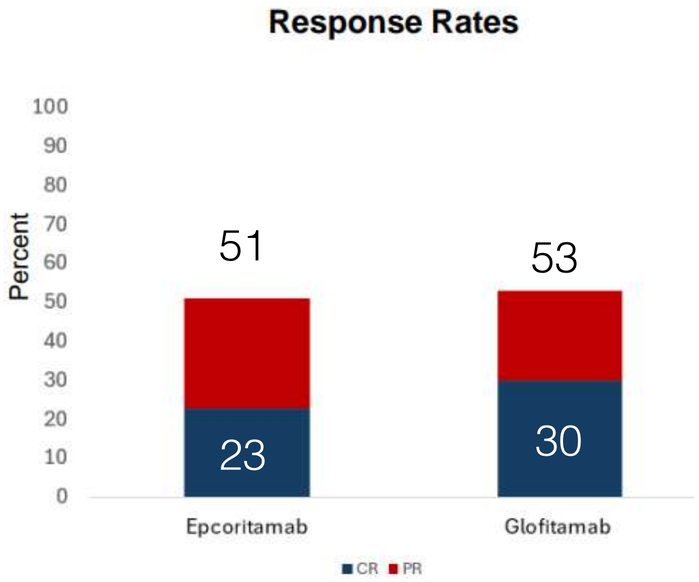
. Dickinson M, et al. ASH 2024; oral presentation (abstract #865 ; Vose JM et al. ASH 2024; Dec 2024; P4480, San Diego, Virtual

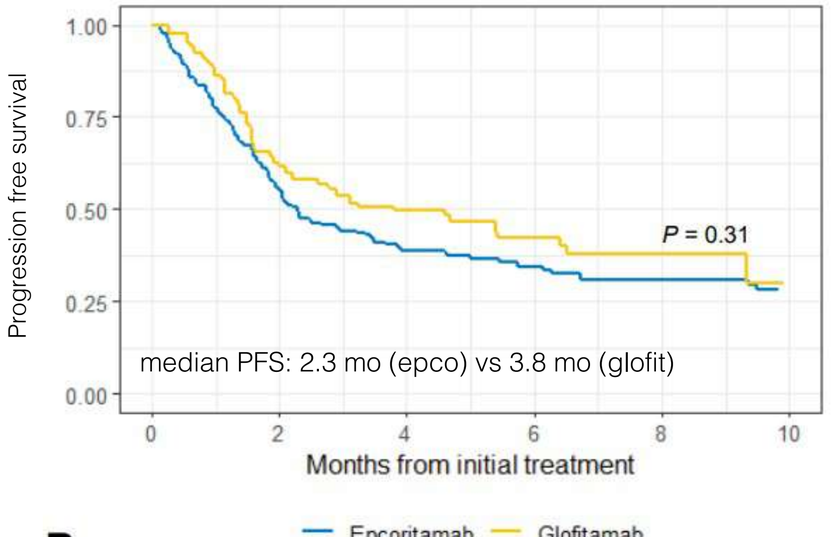
BsAbs CD20xCD3: Summary from Clinical Trials and RWE

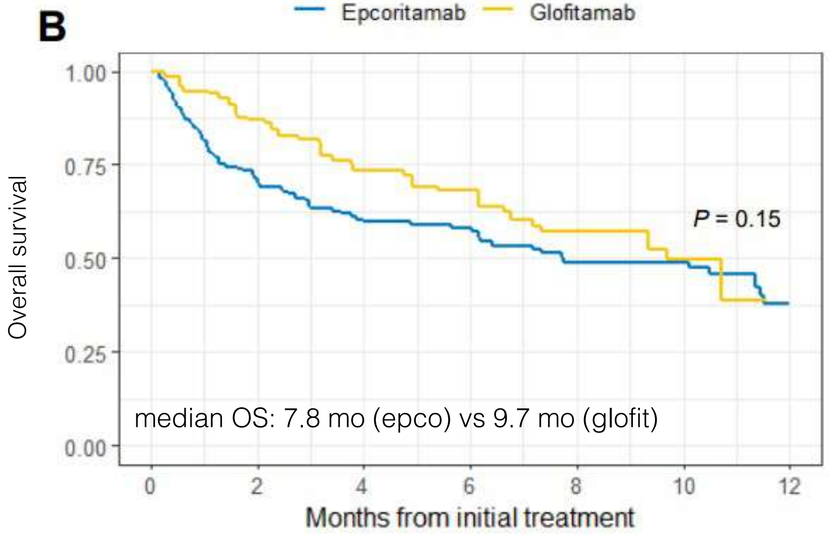
Agent and trial	Ph	Route	Pts n	Prior tx median (range)	Primary ref. %	Prior CART, %	ORR/CR %	Median Follow-up, mo	Median DoR/CR mo	Median PFS, mo	Median OS, mo	CRS (any/gr ≥3), %	ICANS (any/gr ≥3) %
Glofitamab[1,2]	I/II	EV, fixed duration	155	3 (2-7)	58	33	52/40	32.1	18.4/29.8	4.9	11.5	63/4	8/3
Epcoritamab[3,4]	I/II	SC, Until PD	148	3 (2-11)	61	38	59/41	31	20.8/36.1	4.4	NR	52/3	6/0.6
Odronextamab[5]	II	EV, Until PD	127	2 (2-8)	55	0	52/31.5	29.9	10.2/17.9	4.4	10.5	53/1.7	0
REALBiTE[6]	RWE	EV/SC	245	3 (1-10)	52	60	52/25	6.3	10 (epco), NR (glofit)	2.5	7.8	39.5/7.7	11/6

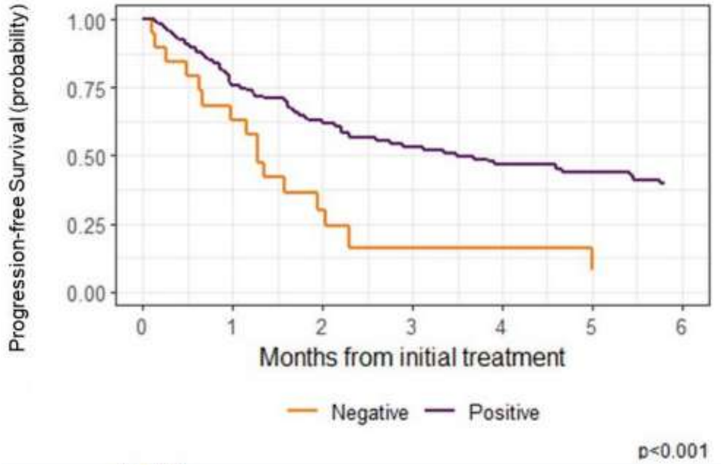
1 Dickinson M et al, Blood 2024; 2 Dickinson M. et al, NEJM 2022; 3. Thieblemont C. et al. JCO 2022; 4. Vose JM et al, Blood 2024; 5 Kim WE et al, Nat Cancer 2025; 6 Brooks TR et al, Blood 2025; .

RWE: Similar Response but Shorter Survival in Comparison to Pivotal Trials

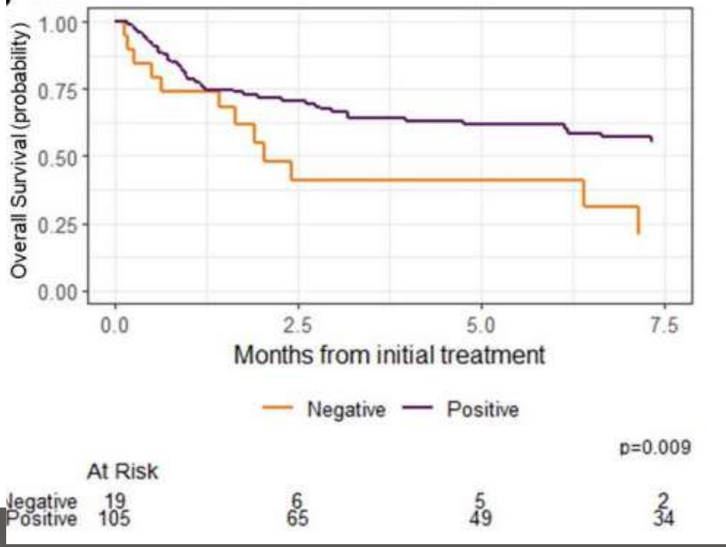








CD20 loss before BsAb = shorter survival



Brooks TR et al, Blood 2025.

BsAb: Infections are the First Cause of NRM

Table 1. **Summary of included clinical trials by malignant target and bispecific product**

Malignant target	BsAb	No. of trials	Lymphoma subtype (no. of trials)	No. of patients	All-grade infection, % (95% CI)	Median length of follow-up, mo (IQR)
CD20	Epcoritamab	7	Aggressive (5), indolent (1), and B-cell NHL NOS (1)	470	39 (29-47)	11.4 (6.1-17.1)
	Glofitamab	7	Aggressive (6) and B-cell NHL NOS (1)	618	42 (30-53)	10.6 (6-15)
	Mosunetuzumab	6	Aggressive (3), indolent (2), and B-cell NHL NOS (1)	599	43 (47-50)	12.5 (8-28.5)
	Odronextamab	3	Aggressive (1), indolent (1), and B-cell NHL NOS (1)	414	59 (48-69)	21 (NR)

NR, not reported; NHL, non-Hodgkin lymphoma; NOS, not otherwise specified.

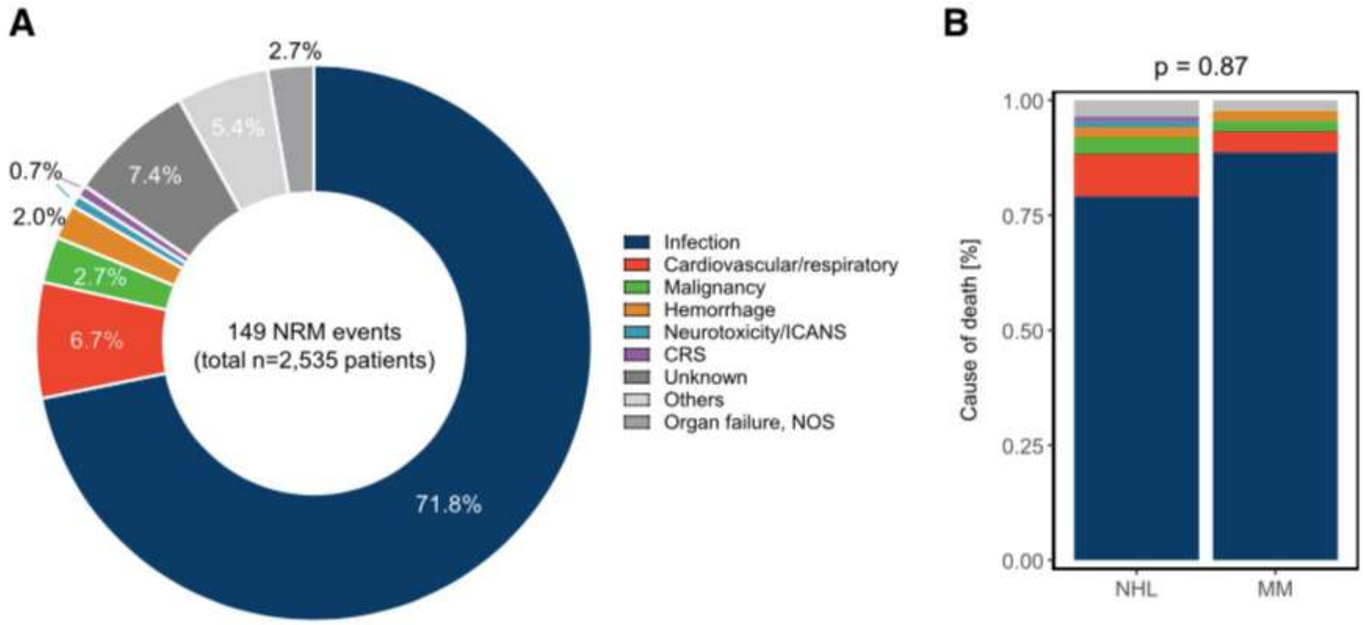


Table 2. **Etiology of fatal infections**

	n
Fatal infections	79
Microbiologically confirmed	**42 (53% of fatal infections)**
Viral	32 (41% of fatal infections)
SARS-CoV-2	>29*
EBV	1
CMV	1†
PML	1
Bacterial	4 (5% of fatal infections)
Gram-negative bacteremia	4
Fungal	5 (6% of fatal infections)
Candidemia	1
Pneumocystis jirovecii pneumonia	3
Systemic mycoses	1
Protozoan	
Toxoplasmosis	1
Clinically diagnosed	**12 (15% of fatal infections)**
Sepsis	4
Pneumonia	8
Etiology not reported	25 (32% of total infections)

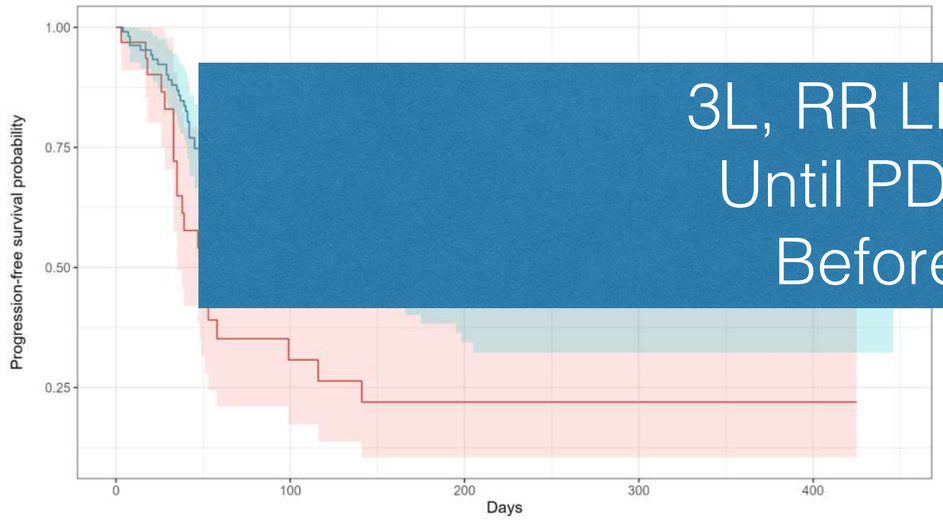
Reynolds GK et al, Blood Adv 2024; Tix T. et al, Molecular Therapy 2025

Does Prior CAR T-Cell Treatment Have an Impact on BsAb Efficacy?

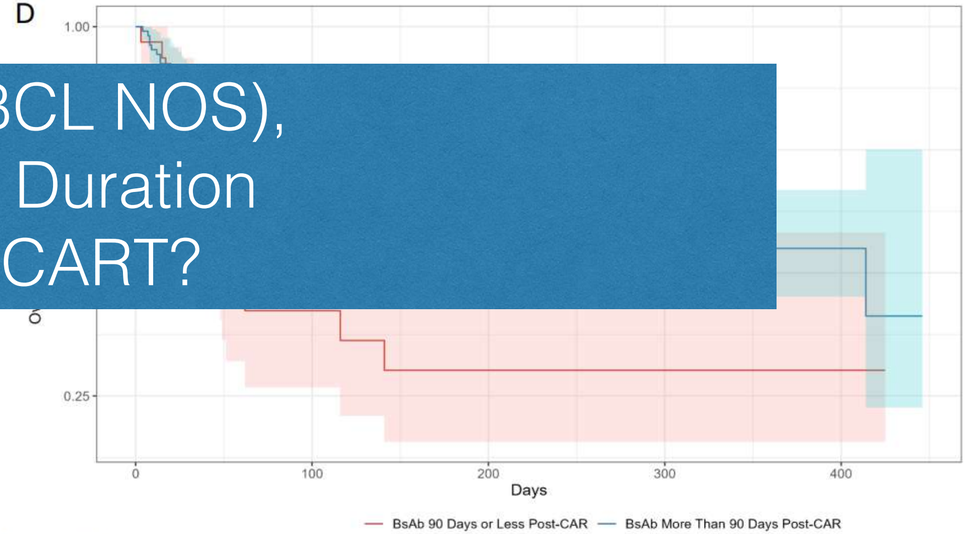
Patients with DLBCL Who Received BsAbs Early Versus Late Following CAR T

	Overall N = 139/147	BsAb ≤90 Days Post-CAR T N = 32	BsAb ≥90 Days Post-CAR T N = 107
Best response to bispecific, No. (%)			
Overall response of CR or PR, No. (%)	60 (43)	9 (35)	51 (48)
CR	31 (22)	4 (15)	27 (30)
PR	29 (21)	5 (19)	24 (27)
SD	7 (5)	1 (3)	6 (7)
PD	48 (35)	16 (62)	32 (36)
Not evaluable	24 (17)	6 (19)	18 (17)

3L, RR LBCL (DLBCL NOS),
Until PD vs Fixed Duration
Before or After CART?



CAR to BsAb less than 90 days					
At Risk	32	7	5	3	1
Events	0	19	21	21	21
CAR to BsAb more than 90 days					
At Risk	107	48	23	13	4
Events	0	36	47	48	48

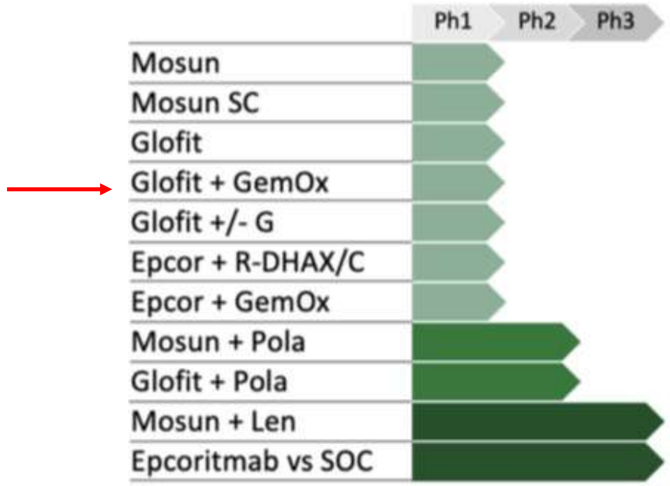


CAR to BsAb less than 90 days					
At Risk	32	7	5	3	1
Events	0	16	18	18	18
CAR to BsAb more than 90 days					
At Risk	107	48	23	13	4
Events	0	36	41	41	41

Brooks TR et al, Blood 2025.

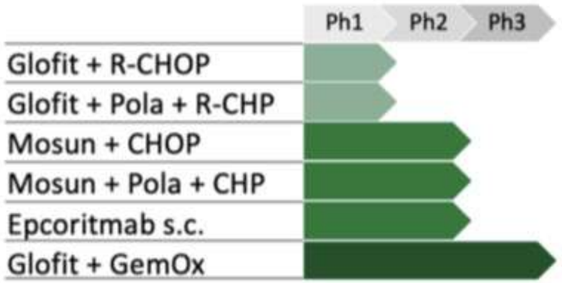
What's Next?

R/R DLBCL



AZD0486 (CD19xCD3)
FS118 (tetravalent: PDL1XLAG3XCD3)

1st Line DLBCL



Elderly/Unfit DLBCL

STARGLO: Glofit+Gemox vs R-Gemox (2L+)

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

R 2:1

Glofit-GemOx (n=183)
Glofitamab plus gemcitabine and oxaliplatin*
Step-up dosing in Cycle 1,
30mg administered on Day 1 from Cycle 2 onwards

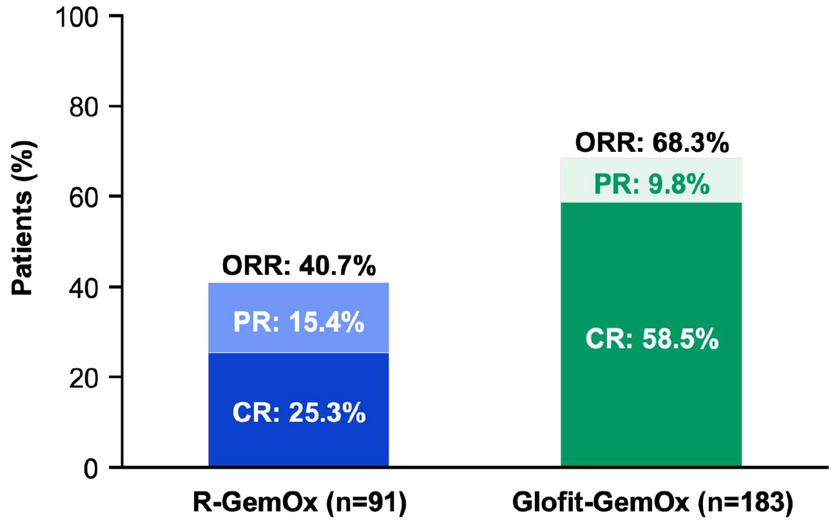
Cycles 1–8
(21-day cycles)

Glofitamab
30mg administered on Day 1 of each cycle

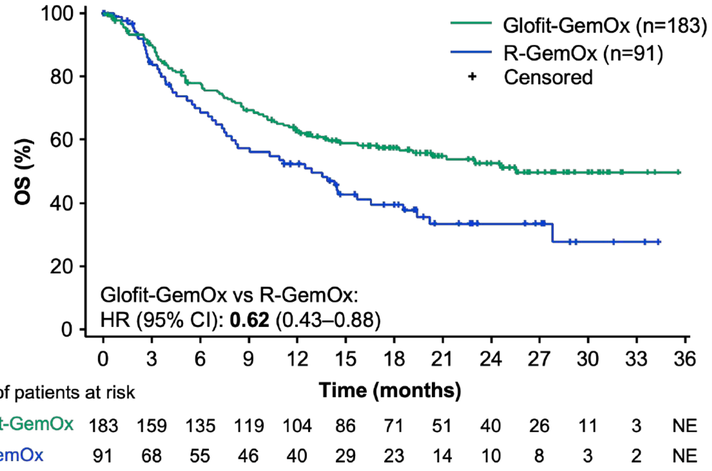
Cycles 9–12

R-GemOx (n=91)
Rituximab† plus gemcitabine and oxaliplatin
Administered on Day 1 of each cycle

Response rates at the updated analysis



Updated analysis



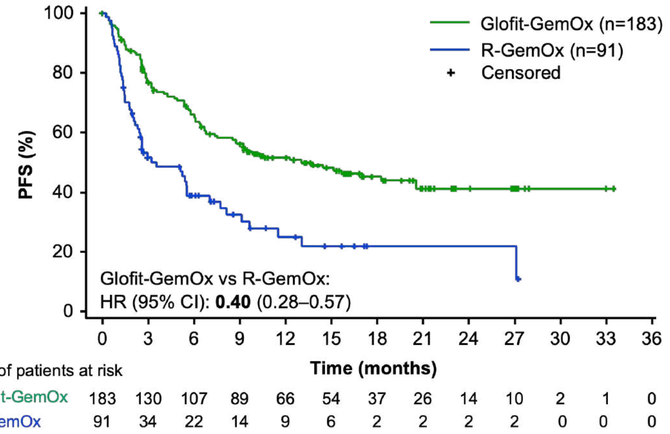
No. of patients at risk

Glofit-GemOx	183	159	135	119	104	86	71	51	40	26	11	3	NE
R-GemOx	91	68	55	46	40	29	23	14	10	8	3	2	NE

	R-GemOx (n=91)	Glofit-GemOx (n=183)
Primary analysis (median follow-up: 11.3 months)		
OS, median (95% CI); months	9 (7.3–14.4)	NE (13.8–NE)
HR (95% CI)	**0.59** (0.40–0.89)	
p-value*	0.011	
Updated analysis (median follow-up: 20.7 months)		
OS, median (95% CI); months	12.9 (7.9–18.5)	25.5 (18.3–NE)
HR (95% CI)	**0.62** (0.43–0.88)	
p-value*	0.006	
24-month OS (95% CI)	33.5% (22.2–44.9)	52.8% (44.8–60.7)

- Statistically significant and clinically meaningful **OS benefit for Glofit-GemOx** versus R-GemOx

Updated analysis



No. of patients at risk

Glofit-GemOx	183	130	107	89	66	54	37	26	14	10	2	1	0
R-GemOx	91	34	22	14	9	6	2	2	2	2	0	0	0

	R-GemOx (n=91)	Glofit-GemOx (n=183)
Primary analysis (median follow-up: 9.6 months)		
PFS, median (95% CI); months	3.3 (2.5–5.6)	12.1 (6.8–18.3)
HR (95% CI)	**0.37** (0.25–0.55)	
p-value*†	<0.000001	
Updated analysis (median follow-up: 16.1 months)		
PFS, median (95% CI); months	3.6 (2.5–7.1)	13.8 (8.7–20.5)
HR (95% CI)	**0.40** (0.28–0.57)	
p-value*†	<0.0001	
12-month PFS, % (95% CI)	25.2 (13.6–36.9)	51.7 (44.0–59.4)

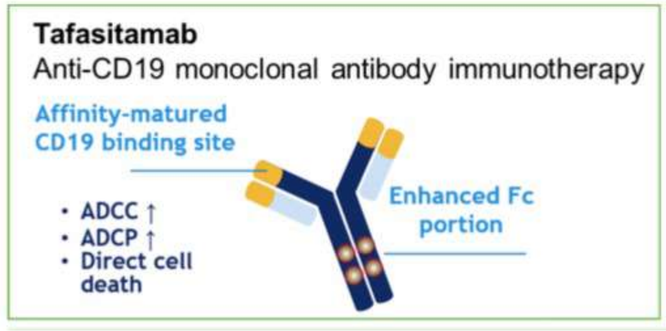
Statistically significant and clinically meaningful PFS benefit for Glofit-GemOx versus R-GemOx

Abramson JS, et al. EHA 2024; Oral presentation abstract#LB3438

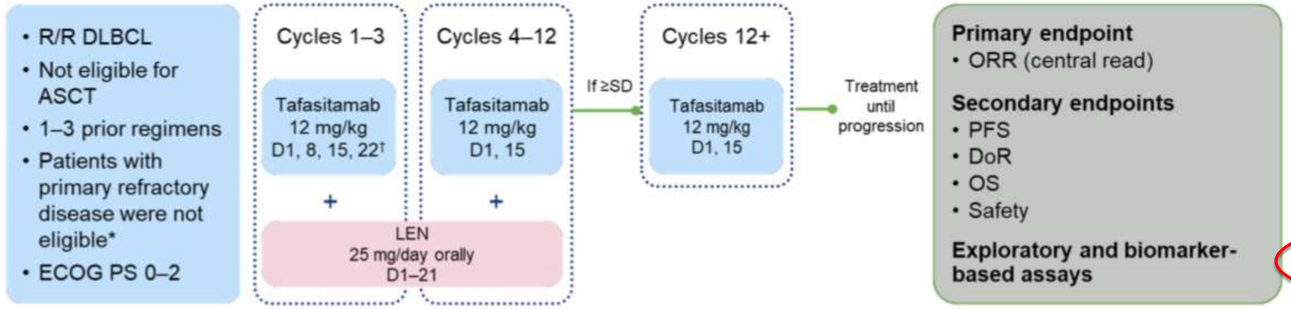
Treatment	NCT#	Phase	Sample size	Median prior LOT	Median follow up (months)	ORR, % (CR, %)	Median PFS (months)	PFS estimate	OS estimate	CRS Any grade, % (Grade ≥ 3, %)	ICANS Any grade, % (Grade ≥ 3, %)	Neutropenia any grade, % (Grade ≥ 3, %)	Thrombocytopenia any grade, % (Grade ≥ 3, %	Notable Treatment emergent adverse events, (%)	Reference
Epcoritamab + R-DHAX	04663347	1/2	29	2	27.5	100 (86)	NR	24 month PFS of 60%	24 month OS of 86%	45 (0)	3.4 (0)	48 (NR)	76 (NR)	No new safety signals	[141]
Epcoritamab + GemOx	04663347	1/2	103	2	13.2	85 (61)	11.2	12 month PFS of 44%	12 month OS of 59%[a]	51 (1)	2 (1)	65 (57)	73 (59)	infections (72%)	[142]
Mosunetuzumab + polatuzumab vs R-Polatuzumab	03671018	2	79	2	23.9	78 (58)	11.4	12 month PFS of 64.2%	12 month OS of 73.8%	10 (0)	2.5 (0)	40 (30)	25 (4)[b]	injection site reactions (55%), peripheral neuropathy (27.5%), tumor flare (7.5%)	[143]
Glofitamab + Polatuzumab	03533283	1b/2	129	2	28.2	78.3 (59.7)	12.3	24 month PFS of 41.8	24 month OS of 54.3	44 (1.6)	3.8 (0.8)	42 (33)	15 (10)[b]	peripheral neuropathy (24%), tumor flare (7%)	[144]
Glofitamab + R-ICE	05364424	1b	41	1	NR	83.3 (66.7)	NR	NR	NR	49 (0)	0 (0)	35.7 (28.6)	52.4 (26.8)	Infections (G3, 5%), TLS (G3, 5%)	[145]
Glofitamab + GemOx vs GemOx	04408638	3	274	1	20.7	68.3 (58.5)	13.8	12 month PFS of 51.7%c	24 month OS of 52.8	44 (2)	2 (1)	42 (NR)	48 (NR)	Nausea (49%), peripheral neuropathy (36%)	[146]
Loncastuximab + Venetoclax	05053659	1/2	16	4	NR	57 (43)	NR	NR	NR	-	-	45 (25)	10 (0)	ALT/AST increased (12%), atrial fibrillation 12.5%), elevated bilirubin (18%)	[147]
Zanubrutinib + Lenalidomide	04436107	1	66	2	16.5	58 (42)	5.5	12 month PFS of 34%	median OS not reached	-	-	57 (NR)	15 (NR)	hypokalemia (11%)	[148]
Gloftamab + Englumafusp alpha	04077723	1/2	134	3	16.2	68.6 (56.6)	9.7	1 year PFS of 82.6	median OS of 20.4 months	55.2 (0.7)	0.7 (0)	41 (30)[b]	30.6 (20)[b]	Infections (64%), hepatotoxicity (21%)	[149]

Bock and Epperla Journ of Hematology and Oncology 2025

L-MIND: Tafasitamb + Lenalidomide for Transplant Inelegible RR DLBCL



Open-label, single-arm, multicenter, global, Phase II study; **N=81**



NCT02399085[1]

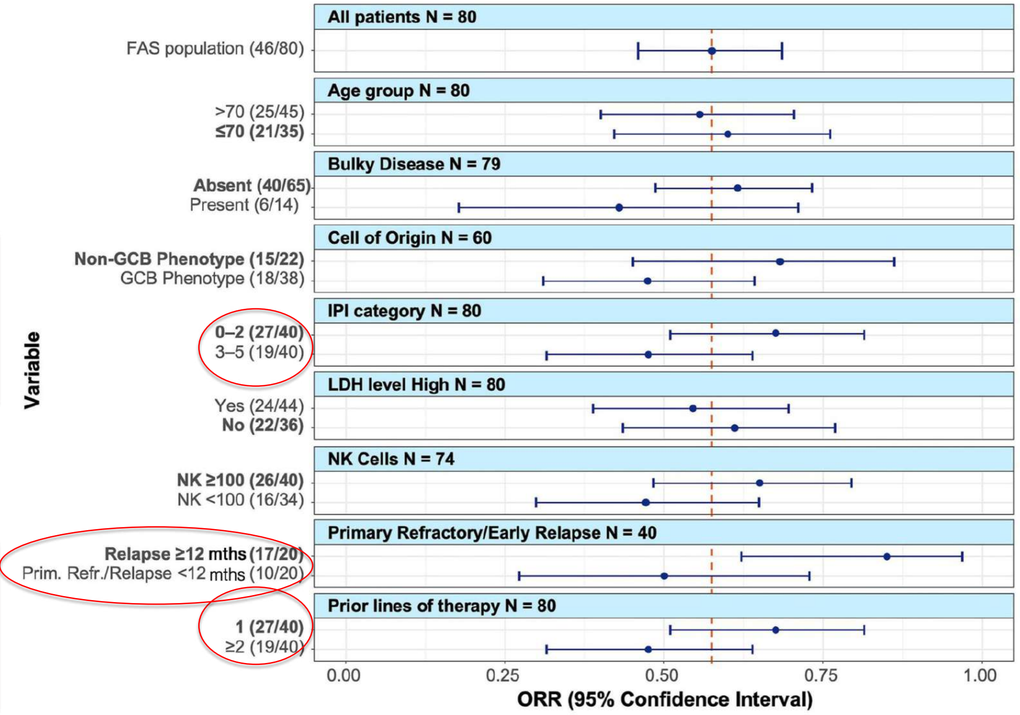
*Primary refractory is defined as no response to, or progression/relapse during/within 6 months of, front-line therapy; 15 patients with refractory disease were included under an early version of the protocol.

Characteristics	All patients: full analysis set	1 prior line of therapy	≥2 prior lines of therapy
N	80	40	40
Age in years, median (range)	72.0 (41.0-86.0)	72.0 (53.0-86.0)	70.5 (41.0-82.0)
Age >70 years, N (%)	45 (56.3)	25 (62.5)	20 (50.0)
Sex, N (%)			
Female	37 (46.3)	19 (47.5)	18 (45.0)
Male	43 (53.8)	21 (52.5)	22 (55.0)
Ann Arbor stage, N (%)			
I-II	20 (25.0)	11 (27.5)	9 (22.5)
III-IV	60 (75.0)	29 (72.5)	31 (77.5)
IPI score, N (%)			
0-2	40 (50.0)	25 (62.5)	15 (37.5)
3-5	40 (50.0)	15 (37.5)	25 (62.5)
Elevated LDH, N (%)			
Yes	44 (55.0)	18 (45.0)	26 (65.0)
No	36 (45.0)	22 (55.0)	14 (35.0)
Prior lines, N (%)			
1	40 (50.0)	-	-
2	34 (42.5)	-	-
3	5 (6.3)	-	-
4	1 (1.3)	-	-
Primary refractory*, N (%)			
Yes	15 (18.8)	6 (15.0)	9 (22.5)
No	65 (81.3)	34 (85.0)	31 (77.5)
Refractory to previous line of therapy, N (%)			
Yes	35 (43.8)	6 (15.0)	29 (72.5)
No	45 (56.3)	34 (85.0)	11 (27.5)
Prior ASCT, N (%)			
Yes	9 (11.3)	2 (5.0)	7 (17.5)
No	71 (88.8)	38 (95.0)	33 (82.5)
Cell of origin (by IHC), N (%)			
GCB	38 (47.5)	16 (40.0)	22 (55.0)
Non-GCB	22 (27.5)	14 (35.0)	8 (20.0)
Unknown/NE	20 (25.0)	10 (25.0)	10 (25.0)

Duell J, et al. Haematologica . 2024

L-MIND: Tafasitamb + Lenalidomide for Transplant Inelegible RR DLBCL

Characteristics	Primary analysis	3-year follow-up	Final 5-year data	5-year data for patients with 1 prior line of therapy, N=40	5-year data for patients with ≥2 prior lines of therapy, N=40
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022	Nov 14, 2022	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6-46.5]
PR rate, N (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
Median DoR in months [95% CI]	21.7 [21.7-NR]	43.9 [26.1-NR]	NR [33.8-NR]	NR [9.1-NR]	NR [26.1-NR]
Median PFS in months [95% CI]	12.1 [5.7-NR]	11.6 [6.3-45.7]	11.6 [5.7-45.7]	23.5 [7.4-NR]	7.6 [2.7-45.5]
Median OS in months [95% CI]	NR [18.3-NR]	33.5 [18.3-NR]	33.5 [18.3-NR]	NR [24.6-NR]	15.5 [8.6-45.5]



2L DLBCL, non transplant and CAR-T elegible,
IPI 0-2, relapsed
Until PD

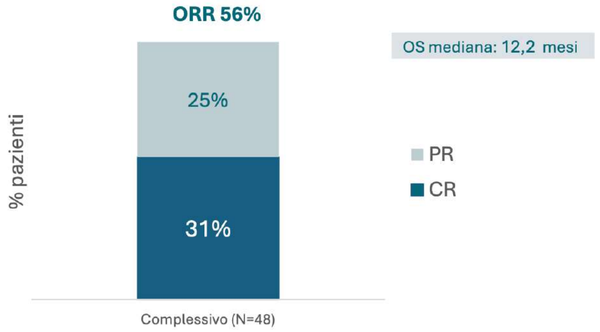
Duell J, et al. Haematologica . 2024

RWE of Tafa- Lena Show Similar Efficacy in Comparison to Pivotal Trial

	Qualls et al, 2023[1,2]	Saverno et al, 2024	Brisou et al, 2025 (EarlyMIND,	Gutiérrez et al, 2025 (GELTAMO)[5]	Duell et al, 2024 (L-MIND)[6,7]
Patient characteristics					
Number of patients	178	181[c]	186	83[e]	80
mFU (months)	NA	14.7	8.2	21.6	65.6
ORR (%)	31	73.5	46.8[d]	61	57.5
CR (%)	19	23.2	29	42	41.3
mPFS (months)	1.9	11.3	4.7	10.9	11.6
mOS (months)	6.5	24.8	10	21.8	33.5
mDoCR (months)	NA	19.2	Not Reached	Not Reached	Not Reached

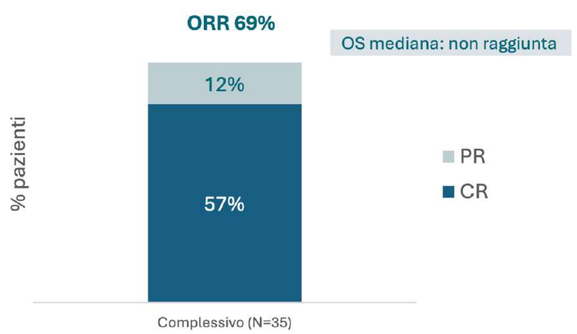
Risultati nel paziente Primary Refractory: 31% CR

Tasso di risposta nei pazienti *primary refractory*

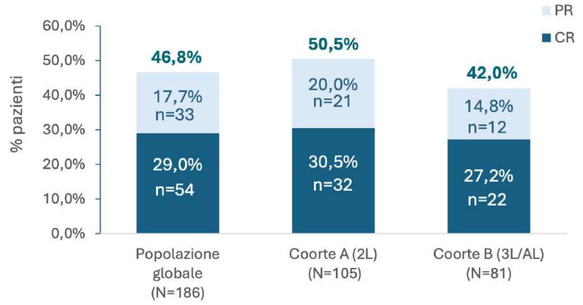


Risultati nel paziente Ricaduto: 57% CR

Tasso di risposta nei pazienti ricaduti

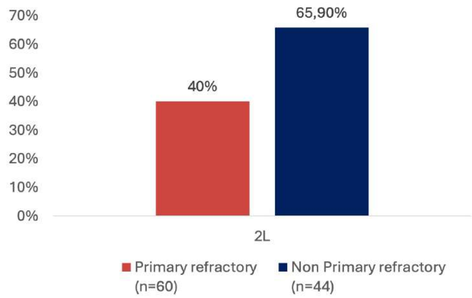


BOR nella popolazione complessiva E per linea terapeutica (%)



Elaborazione grafica di dati da testo

BOR in pazienti in 2L sulla base della refrattarietà



Elaborazione grafica di dati da testo

Tempo mediano alla CR: 4 cicli (15.3 settimane)

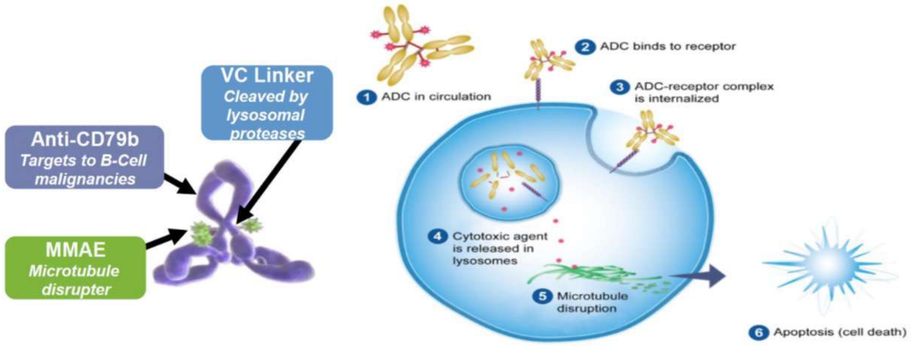
Nei pazienti con CR: PFS, OS e DOR non raggiunte.

1. Qualls DA, et al. Blood . 2023;; 2. Qualls DA, et al. Blood . 2023; 3. Saverno K, et al. Poster presentation at: The 66th ASH [Abstract 2375]; 4. Brisou G, et al. Haematologica . 2025; 5. Gutierrez A, et al. Blood Advances. 2025. 6. Duell J, et al. Haematologica . 2024; 7. Salles G, et al. Lancet Oncol . 2020;

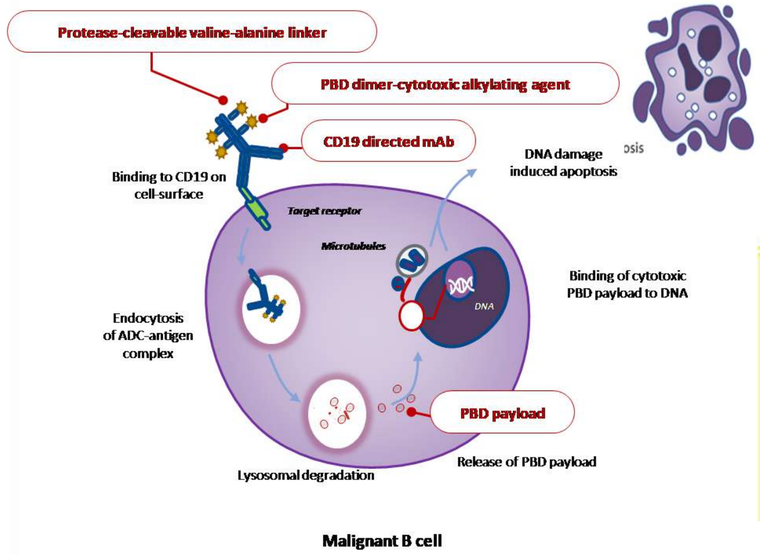
Antibody-drug Conjugates: PV, Loncastuximab and BV

Polatuzumab Vedotin (anti CD79b ADC)

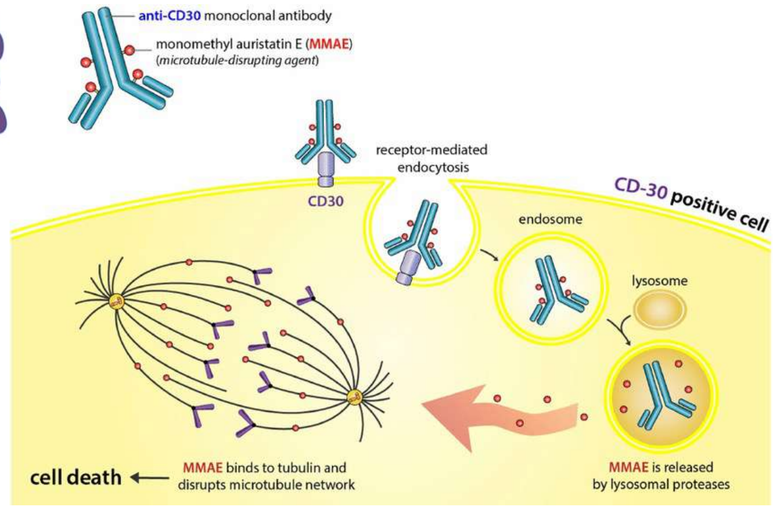
- Microtubule inhibitor MMAE conjugated to CD79b monoclonal antibody via a protease-cleavable peptide linker



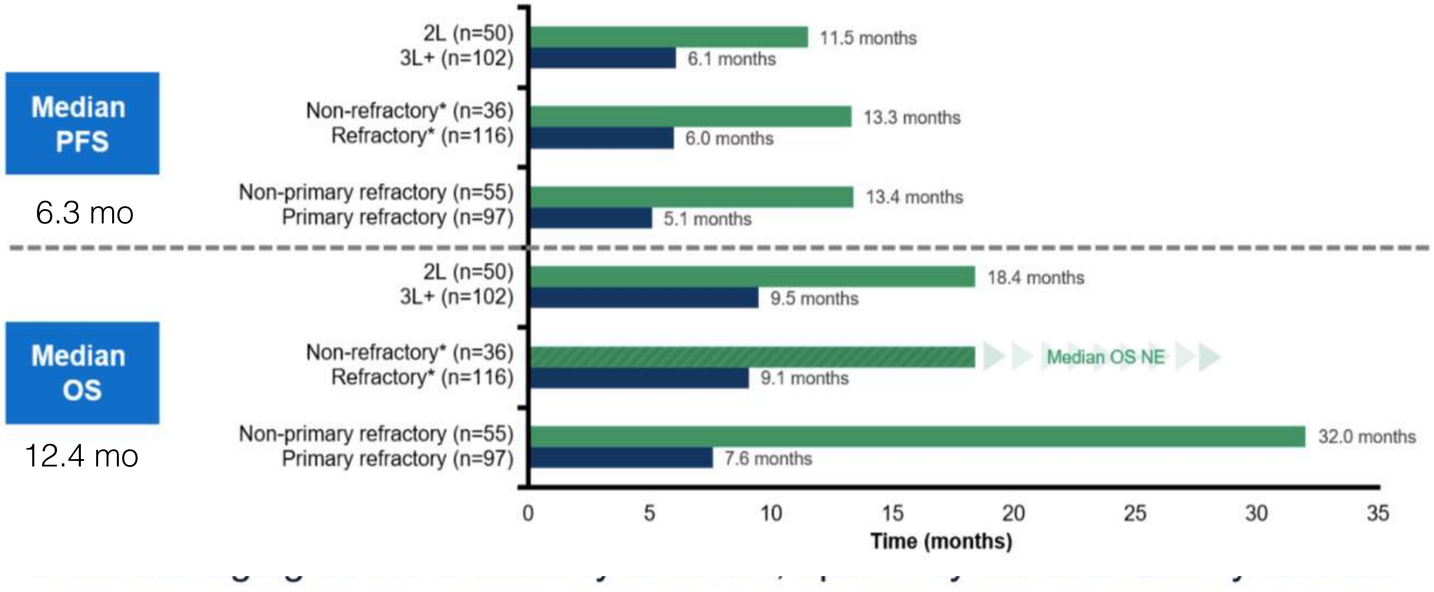
Loncastuximab Teserine (anti CD19 ADC)

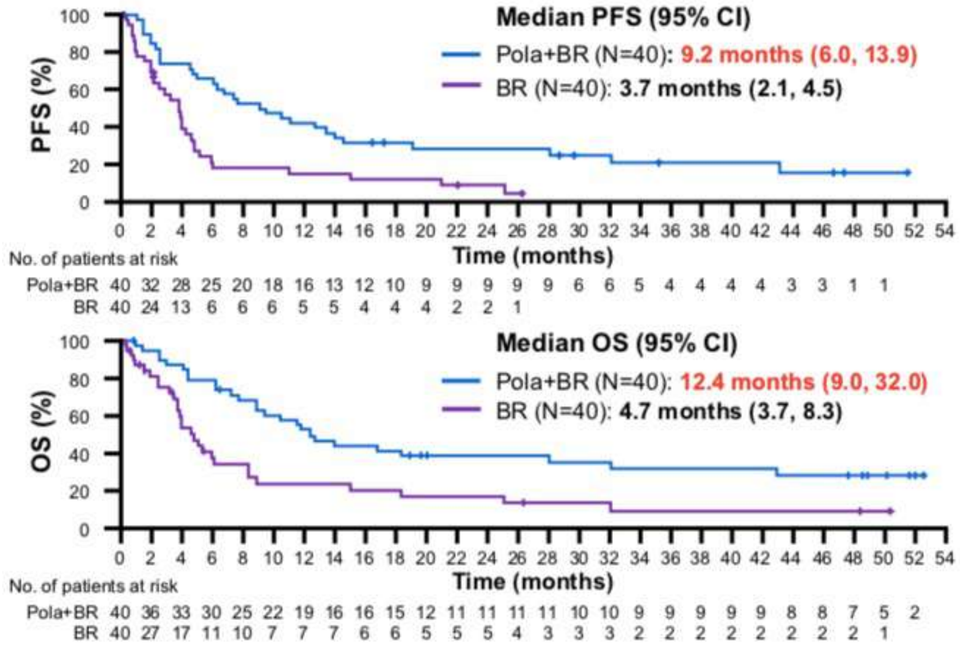


Brentuximab Vedotin (anti CD30 ADC)



Polatuzumab + R-Bendamustine for Transplant Inelegible RR DLBCL

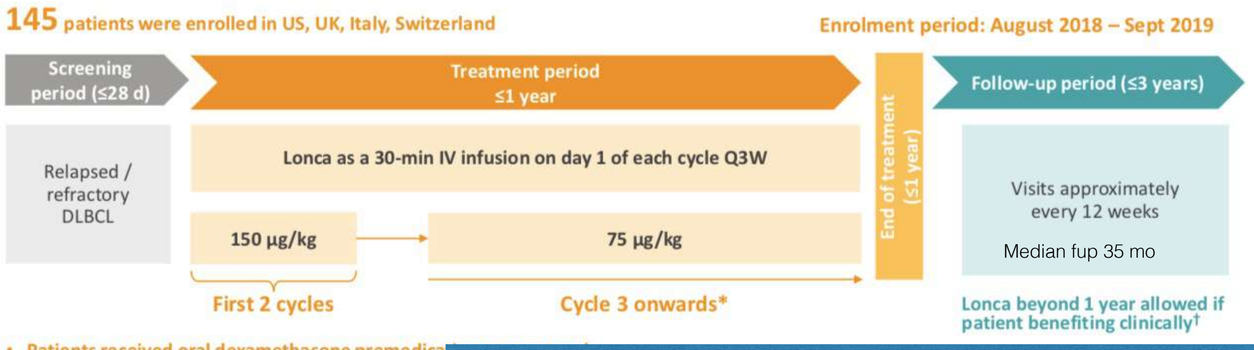


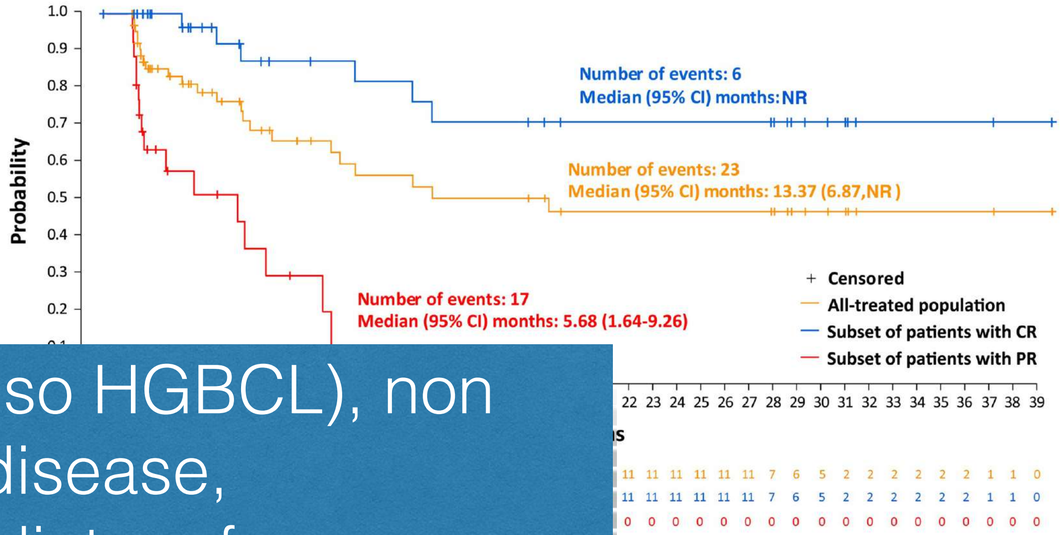


2L DLBCL, non GCB, non transplant elegible, non refractory disease
Fixed Duration

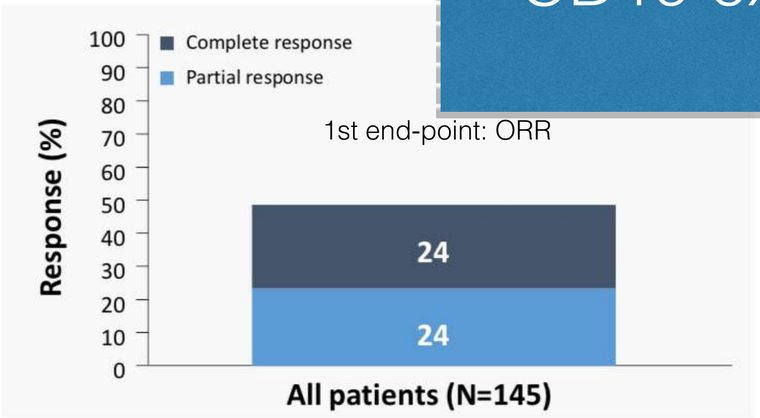
Shen L et al, JCO 2020; Shen L et al, Blood Adv 2022; Cliff ERS Blood 2024

LOTIS-2: Loncastuximab Teserine as 3rd Line Therapy for RR DLBCL





3L+ (also CART), DLBCL (also HGBCL), non primary refractory disease,
CD19 expression is not a predictor of response
Until PD



1st end-point: ORR

(95% CI, 39.9-56.7)

Median time to first response
41.0 days
(IQR, 38-44)

		Best response CR (38)
Median PFS, mo 24 mo PFS, %	4.4. 25.9	NR 72.5
Median OS, mo 24 mo OS, %	9.5 29.5	NR 68.2

Caimi PF et al, Hematologica 2024

LOTIS-2: Treatment Emergent Adverse Events

Non-haematological TEAE	Patients, n (%) All grades	Patients, n (%) Grades 3 or 4
Fatigue	40 (27)	2(1)
Nausea	34 (23)	0 (0)
Cough	32 (22)	1 (1)
Peripheral oedema	**29 (20)**	**2 (1)**
Pyrexia	28 (19)	2 (1)
Diarrhoea	25 (17)	3 (2)
Decreased appetite	22 (15)	0 (0)
Vomiting	19 (13)	0 (0)
Rash	**19 (13)**	**1 (1)**
Pruritus	18 (12)	0 (0)
Constipation	17 (12)	0 (0)
Insomnia	16 (11)	0 (0)
Abdominal pain	16 (11)	4 (3)
Dyspnoea	17 (11)	2 (1)
Headache	15 (11)	1 (1)
Erythema	**15 (11)**	**1 (1)**
Pleural effusion	**15 (10)**	**3 (2)**
Photosensitivity reaction	**15 (10)**	**3 (2)**

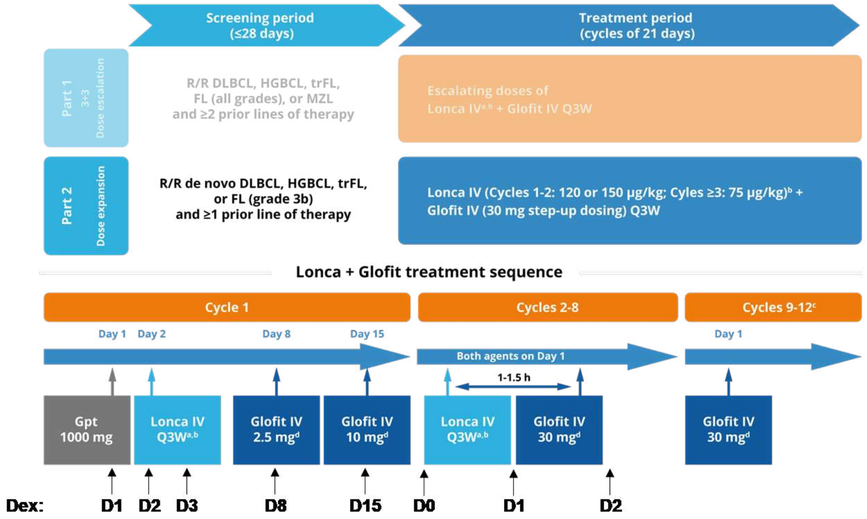
Haematological TEAE	Patients, n (%) All grades	Patients, n (%) Grades 3 or 4
Neutropenia	57 (40)	37 (26)
Thrombocytopenia	48 (33)	26 (18)
Anaemia	38 (26)	15 (10)
Leukopenia	21 (14)	13 (9%)
Febrile neutropenia	5 (3)	5 (3)

Laboratory TEAE	Patients, n (%) All grades	Patients, n (%) Grades 3 or 4
GGT increase	**59 (40)**	**24 (16)**
ALP increase	29 (20)	1 (1)
AST increase	23 (16)	1 (1)
ALT increase	23 (16)	4 (3)

TEAE (GGT, edema and effusions) leading to treat-ment discontinuation occurred in 24.8% of patients in the all-treated population

Caimi PF et al, Hematologica 2024

LOTIS 7 a Phase 1b Study of Lonca + Glofit in RR DLBCL



Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

Endpoints

- **Primary**: safety and tolerability; MTD and/or RDE
- **Secondary**: ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory**: Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

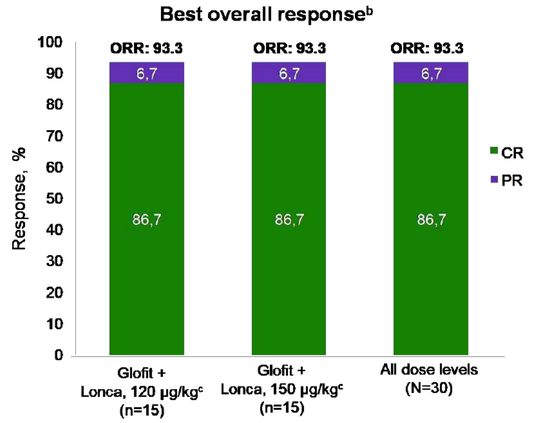
	Glofit + Lonca, 120 µg/kg[a] (n=20)	Glofit + Lonca, 150 µg/kg[a] (n=21)	All dose levels (N=41)
Age, median (range), y	70 (50-82)	74 (26-85)	71 (26-85)
Male sex, n (%)	11 (55.0)	12 (57.1)	23 (56.1)
ECOG PS score, n (%)			
0	9 (45.0)	14 (66.7)	23 (56.1)
1	10 (50.0)	7 (33.3)	17 (41.5)
2	1 (5.0)	0	1 (2.4)
Ann Arbor disease stage, n (%)			
Stage I/II	3 (15.0)	3 (14.3)	6 (14.6)
Stage III/IV	17 (85.0)	18 (85.7)	35 (85.4)
IPI score, n (%)			
0-2	9 (45.0)	10 (46.7)	19 (46.3)
3-5	11 (55.0)	11 (52.4)	22 (53.7)
Bulky disease, n (%)	2 (10.0)	2 (9.5)	4 (9.8)
LDH levels high, n (%)	11 (55.0)	10 (47.6)	21 (51.2)
LBCL histology, n (%)			
de novo DLBCL	13 (65.0)	17 (81.0)	30 (73.2)
HGBCL	4 (20.0)	2 (9.5)	6 (14.6)
trFL	2 (10.0)	2 (9.5)	4 (9.8)
FL grade 3b	1 (5.0)	0	1 (2.4)
DH or TH, n (%)	3 (15)	5 (23.8)	8 (19.5)
DLBCL subtype, n (%)			
GCB	10 (50.0)	11 (52.4)	21 (51.2)
NGC	5 (25.0)	8 (38.1)	13 (31.7)
Number of prior LOT			
Median (range)	2 (1-4)	2 (1-5)	2 (1-5)
1, n (%)	10 (50.0)	10 (47.6)	20 (48.8)
≥2, n (%)	10 (50.0)	11 (52.4)	21 (51.2)
Refractory status, n (%)			
Refractory to primary therapy	8 (40.0)	13 (61.9)	21 (51.2)
Refractory to last prior therapy	7 (35.0)	13 (61.9)	20 (48.8)
Prior CAR-T therapy, n (%)	4 (20.0)	4 (19.0)	8 (19.5)

Alderuccio JP et al, Oral Presentation at 18-ICML

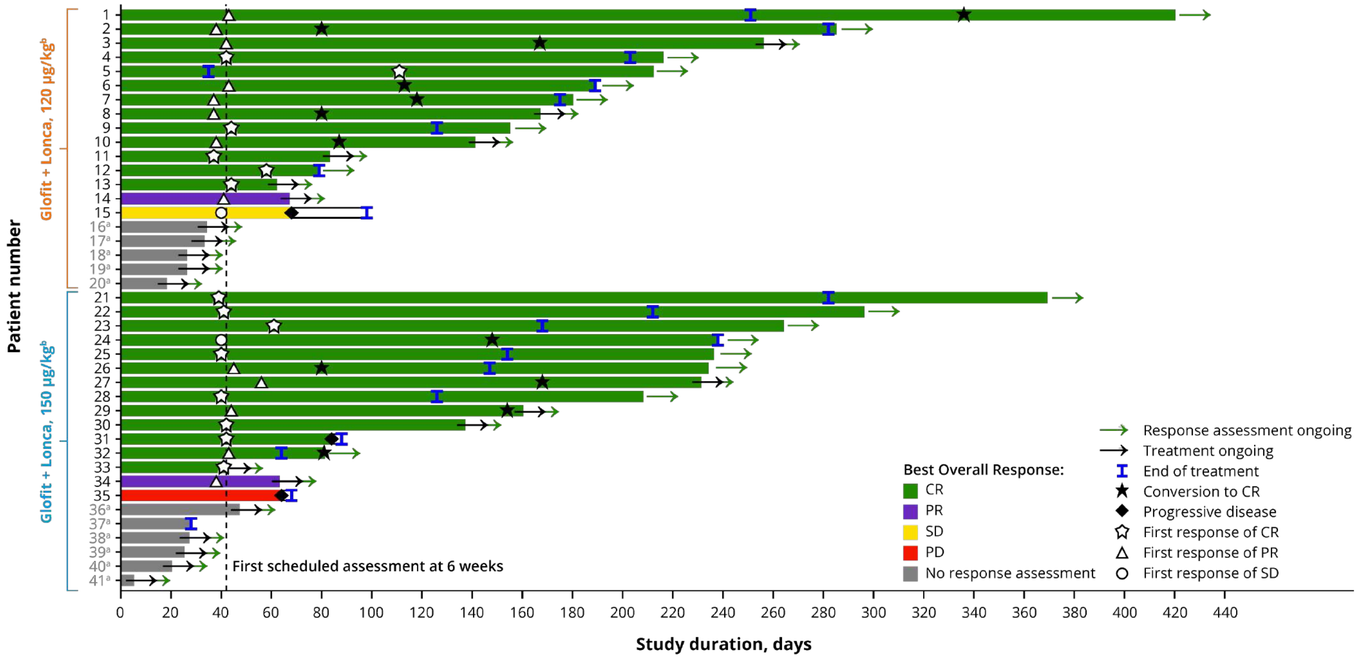
LOTIS 7 a Phase 1b Study of Lonca + Glofit in RR DLBCL

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Grade 3/4 TEAEs (> 5% of patients)[a]	**11 (55%)**	**12 (57.1%)**	**23 (56.1%)**
Neutropenia	4 (20%)	6 (28.6%)	10 (24.4%)
Anemia	1 (5%)	3 (14.3%)	4 (9.8%)
AST increased	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)

Neutropenia was the most common TEAE leading to dose delay of Lonca (12.2%) and Glofit (17.1%); there was only 1 patient who had a dose reduction of Lonca



	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Cytokine Release Syndrome[a]			
Any grade	11 (55%)	5 (23.8%)	16 (39.0%)
Grade 1	7 (35%)	5 (23.8%)	12 (29.3%)
Grade 2	3 (15%)	0	3 (7.3%)
Grade 3	1 (5%)	0	1 (2.4%)
Grade 4/5	0	0	0
ICANS[a]			
Any grade	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 1	1 (5%)	0	1 (2.4%)
Grade 2	1 (5%)	1 (4.8%)	2 (4.9%)
Grade ≥ 3	0	0	0



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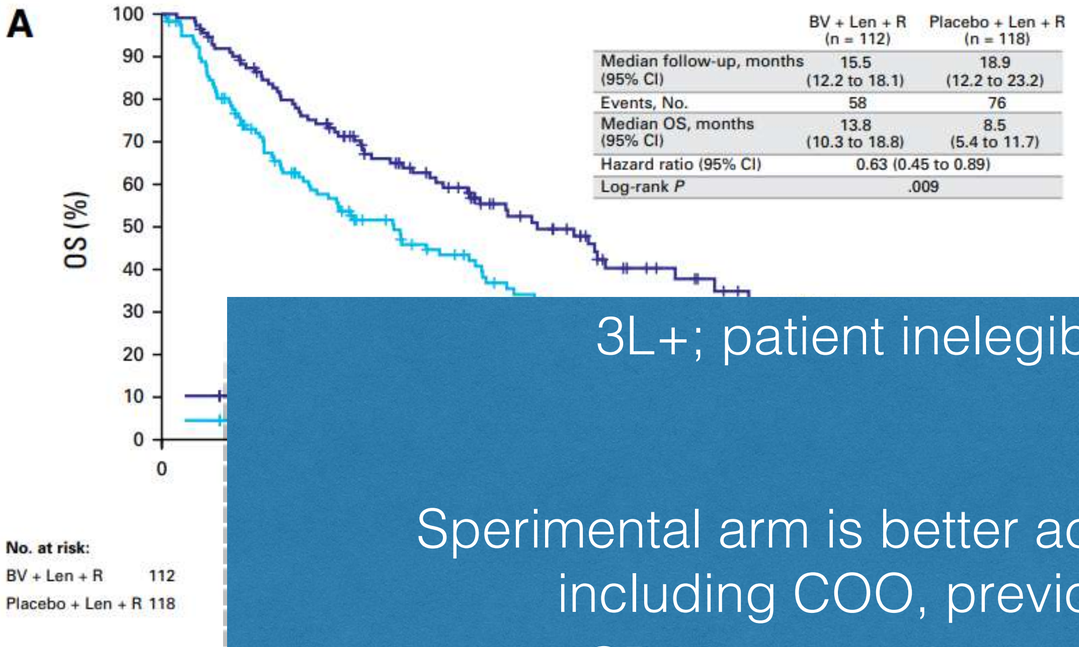
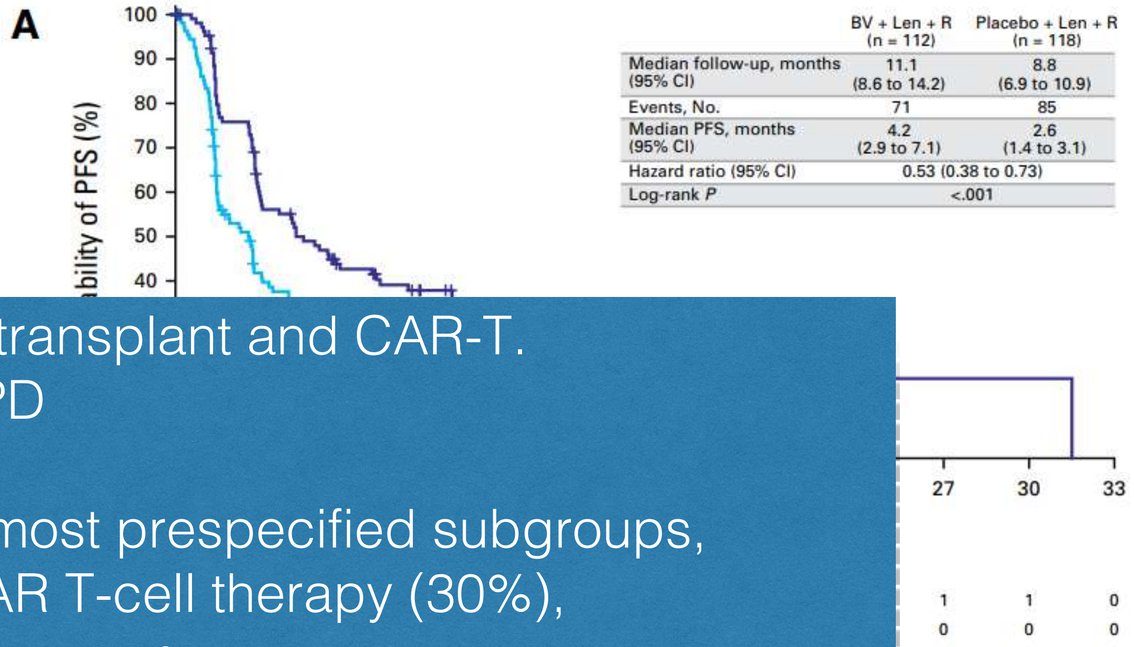
ECHELON-3 Trial: BV+Lena-R vs R-Lena-Placebo



	BV + Len + R (n = 112)	Placebo + Len + R (n = 118)
Median follow-up, months (95% CI)	15.5 (12.2 to 18.1)	18.9 (12.2 to 23.2)
Events, No.	58	76
Median OS, months (95% CI)	13.8 (10.3 to 18.8)	8.5 (5.4 to 11.7)
Hazard ratio (95% CI)	0.63 (0.45 to 0.89)	
Log-rank *P*	.009	



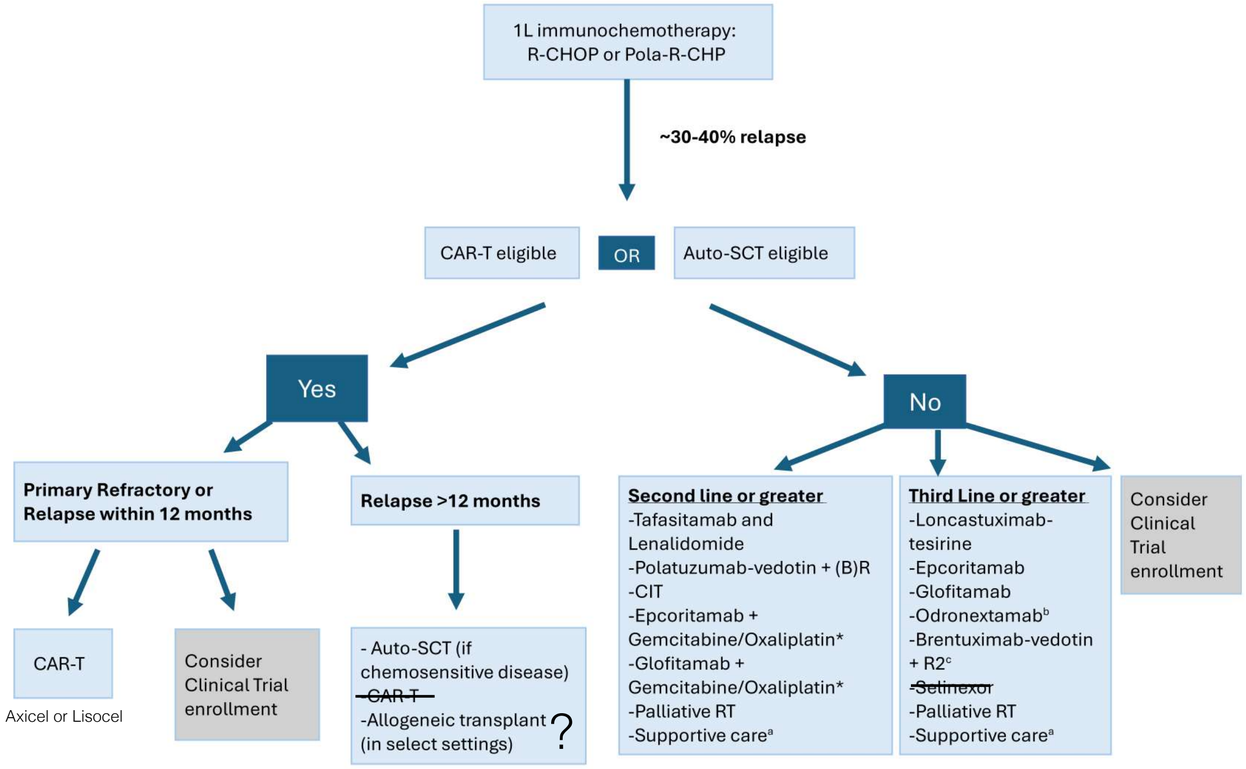
	BV + Len + R (n = 112)	Placebo + Len + R (n = 118)
Median follow-up, months (95% CI)	11.1 (8.6 to 14.2)	8.8 (6.9 to 10.9)
Events, No.	71	85
Median PFS, months (95% CI)	4.2 (2.9 to 7.1)	2.6 (1.4 to 3.1)
Hazard ratio (95% CI)	0.53 (0.38 to 0.73)	
Log-rank *P*	<.001	

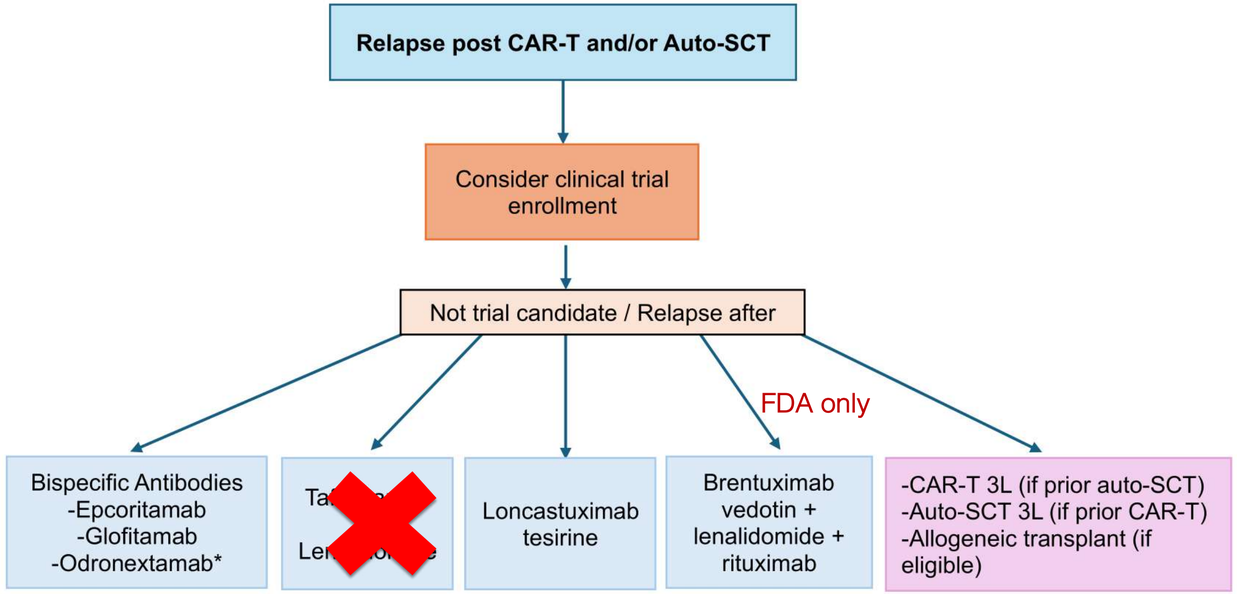
3L+; patient inelegibile to transplant and CAR-T.
Until PD
+
Sperimental arm is better across most prespecified subgroups, including COO, previous CAR T-cell therapy (30%), CD30 expression, and primary refractory disease

	BV+R	Placebo+R2
ORR,% CR,%	64 40	42 19
Median DoR, mo Median DoCR, mo	8.3 18.9	3 NE

Bartlett NL et al, JCO 2025

RR DLBCL: Treatment Algorithm





Abbreviations: DLBCL: diffuse large B-cell lymphoma, CAR-T, chimeric antigen receptor T-cell therapy, Auto-SCT: autologous stem cell transplant, 3L: third line. *EMA approval only

Abbreviations: 1L: first line, R/R: relapsed/refractory, DLBCL: diffuse large B-cell lymphoma, CAR-T, chimeric antigen receptor T-cell therapy, Auto-SCT: autologous stem cell transplant, BR: bendamusine and rituximab, R2: rituximab and lenalidomide, RT: radiation therapy
*Anticipate FDA approval in summer 2025
[a]Do not recommend unless ineligible for therapeutic options or patient preference, [b]Approval by EMA only, [c]Approval by FDA only.

> 3L: consolidation with allogenic transplant?

Modified from Bock and Epperla Journ of Hematology and Oncology 2025