Biespecíficos: una luz en la oscuridad para LATAM

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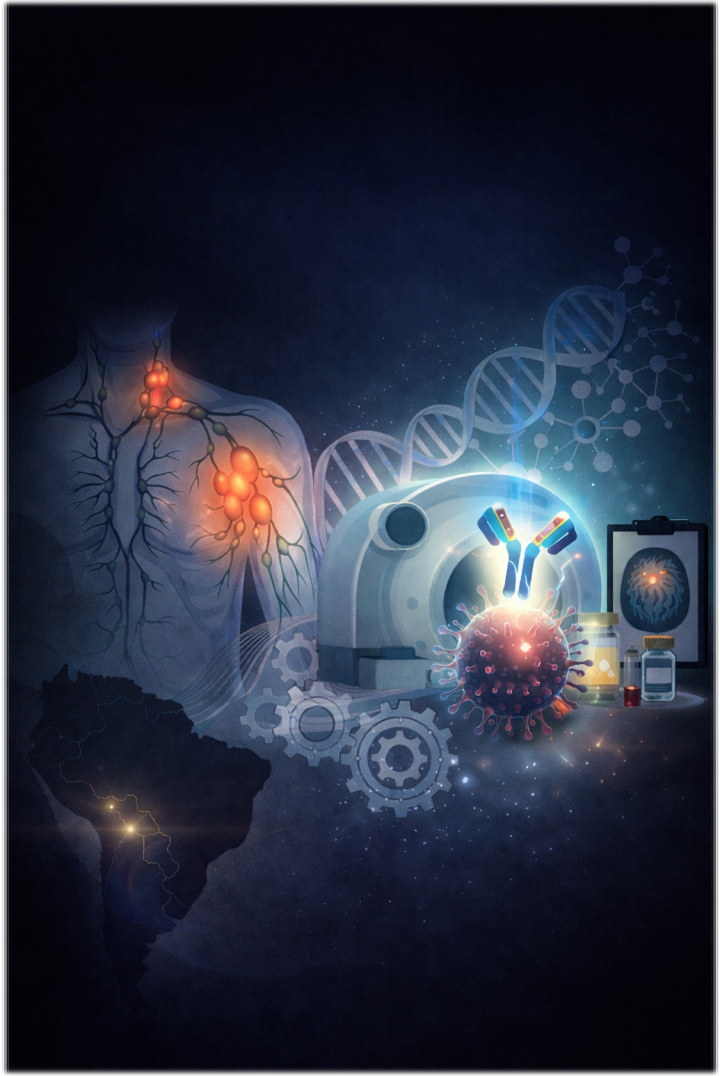

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- Travel & Accommodations:
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The darkness of R/R DLBCL

The gap between what we know and LATAM can offer

Access gaps across 73 centers in 16 countries | GELL Survey 2025

DIAGNOSTIC GAPS

21%
of centers lack immunohistochemistry

56%
wait ≥3 weeks for pathology report

41%
have access to PET-CT

15%
have next-generation Sequencing (NGS)

DRUG ACCESS

65%
restricted access to polatuzumab vedotin

80%
highly restricted access to tafasitamab

35%
access to clinical trials

36%
partial or restricted rituximab access

ADVANCED THERAPIES

Only Brazil
has approved CAR-T in the region

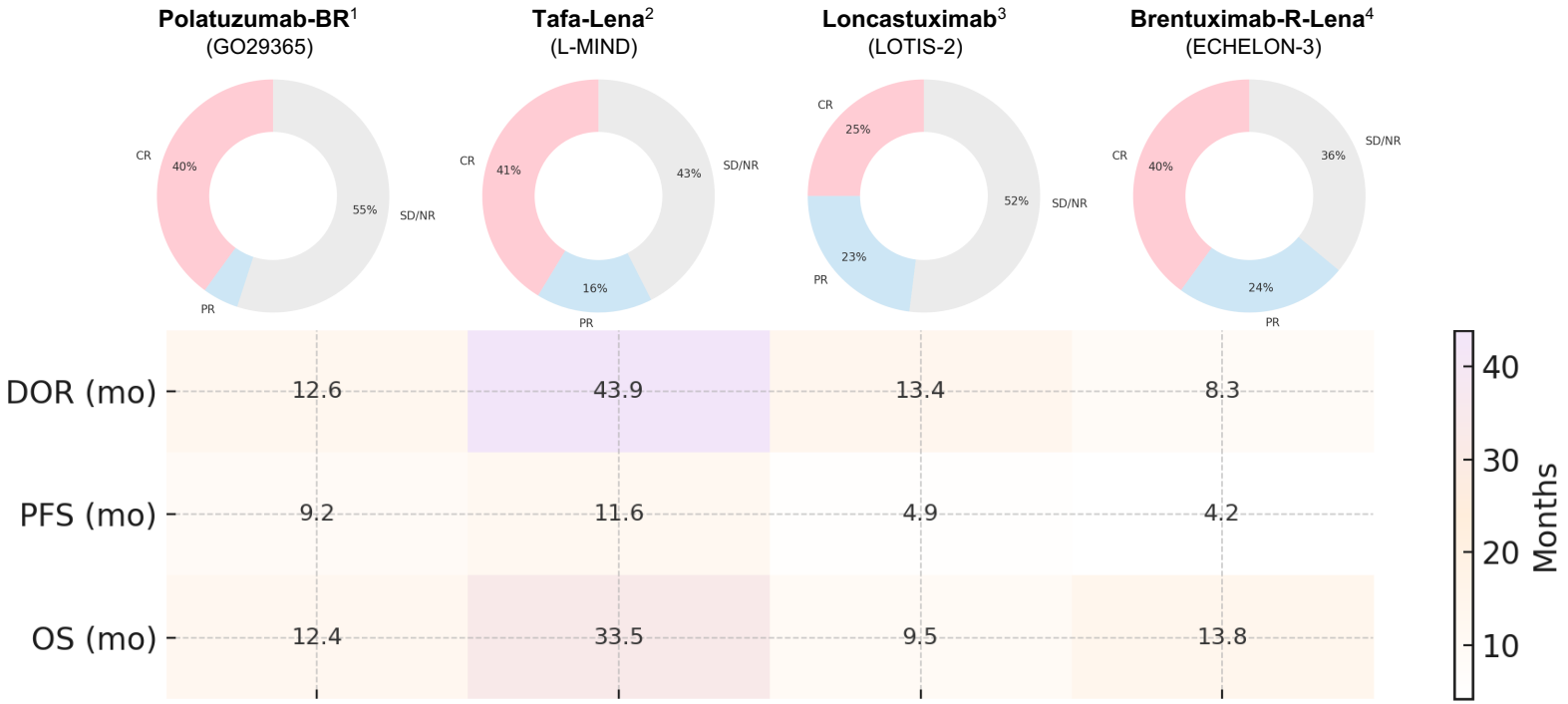
73%
highly restricted access to glofitamab

73%
highly restricted access to epcoritamab

~0%
commercial CAR-T outside Brazil

Colunga-Pedraza PR, et al. Blood 2025;146(Suppl 1):6193

The promise
Outcomes from pivotal trials of novel agents for R/R DLBCL



Inter-trial comparisons should not be made because differences in study design, patient populations, and treatment interventions, among others. We cannot make direct comparisons or draw conclusions from one trial to another. Efficacy results for each of the studies are listed only for descriptive purposes.

CR: complete response; DOR: duration of response; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; PR: partial response; SD/NR: stable disease / non-response

1. Sehn L, et al. Blood Adv 2022;6:533–43
2. Duell J, et al. Haematologica 2024;109:553–66
3. Caimi PF, et al. Haematologica 2024;109:1184–93
4. Bartlett NL, et al. J Clin Oncol 2025;43:1061–72

The fine print
Patient characteristics in pivotal trials

	N	Median age Age ≥ 65y	Prior therapies	Primary refractory	Refractory to last LoT	Prior ASCT
Pola-BR[1] GO29365	152	69 (24-94) 103 (68%)	2 (1-7)	64%	76%	18%
Tafa-Lena[2] L-MIND	81	72 (62-76) 45 (56%)*	2 (1-4)	19%	44%	11%
Loncastuximab[3] LOTIS-2	145	66 (23-94) 80 (55%)	3 (2-7)	20%	61%	17%
BV + R-Lena[4] ECHELON-3	230	74 (29-87) 79 (71%)	3 (2-8)	57%	88%	9%

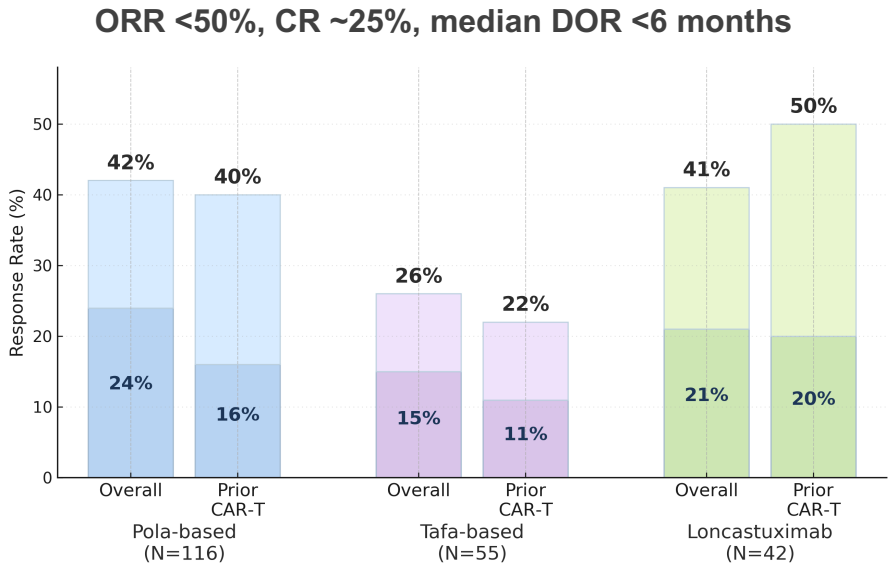
* Age > 70 years

1. Sehn L, et al. Blood Adv 2022;6:533–43
2. Duell J, et al. Haematologica 2024;109:553–66
3. Caimi PF, et al. Haematologica 2024;109:1184–93
4. Bartlett NL, et al. J Clin Oncol 2025;43:1061–72

Novel agents for R/R DLBCL: RWE
LEO Consortium of Real-World Evidence (CReWE)

	Pola-based regimens	Tafa-based regimens	Lonca-T
n	116	55	42
Median age	66 (29-91)	74 (44-88)	68 (21-87)
Prior LoT - 1 line - 2 lines - ≥ 3 lines	 17% 30% 53%	 44% 22% 34%	 7% 29% 64%
Primary refractory	**73%**	**58%**	**71%**
Prior CART	**43%**	**33%**	**48%**

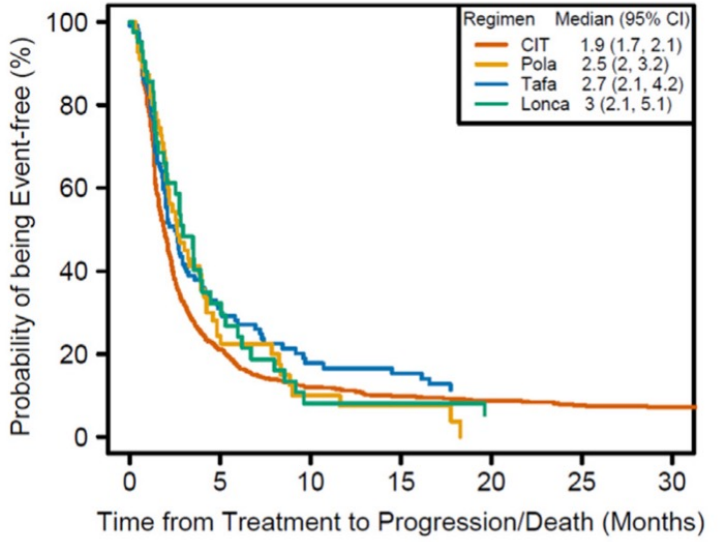
Responses (ORR & CR) by regimen and CAR-T status



Adapted from Nastoupil LJ, et al. Clin Lymphoma Myeloma Leuk 2025;25:e183-e199.e8

The trial-to-reality gap
Novel agents for R/R DLBCL: RWE (CReWE)

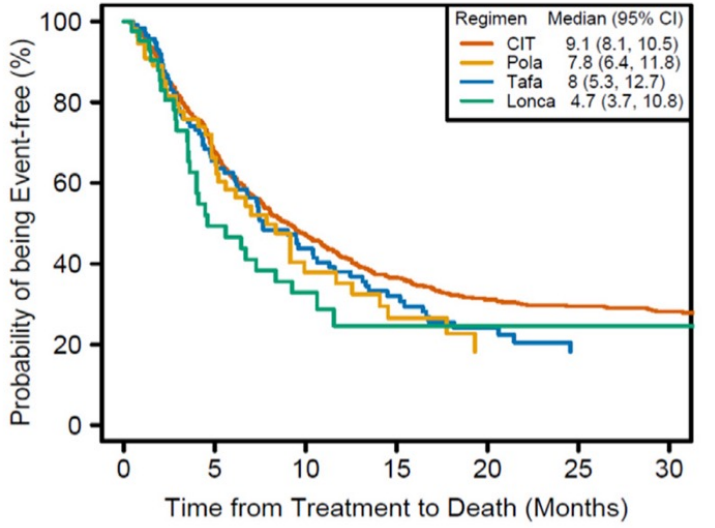
Progression-free survival



Number at Risk

CIT	653	137	75	57	49	42	38
Pola	116	33	16	13	NR	NR	NR
Tafa	55	15	5	4	NR	NR	NR
Lonca	42	13	4	4	NR	NR	NR

Overall survival



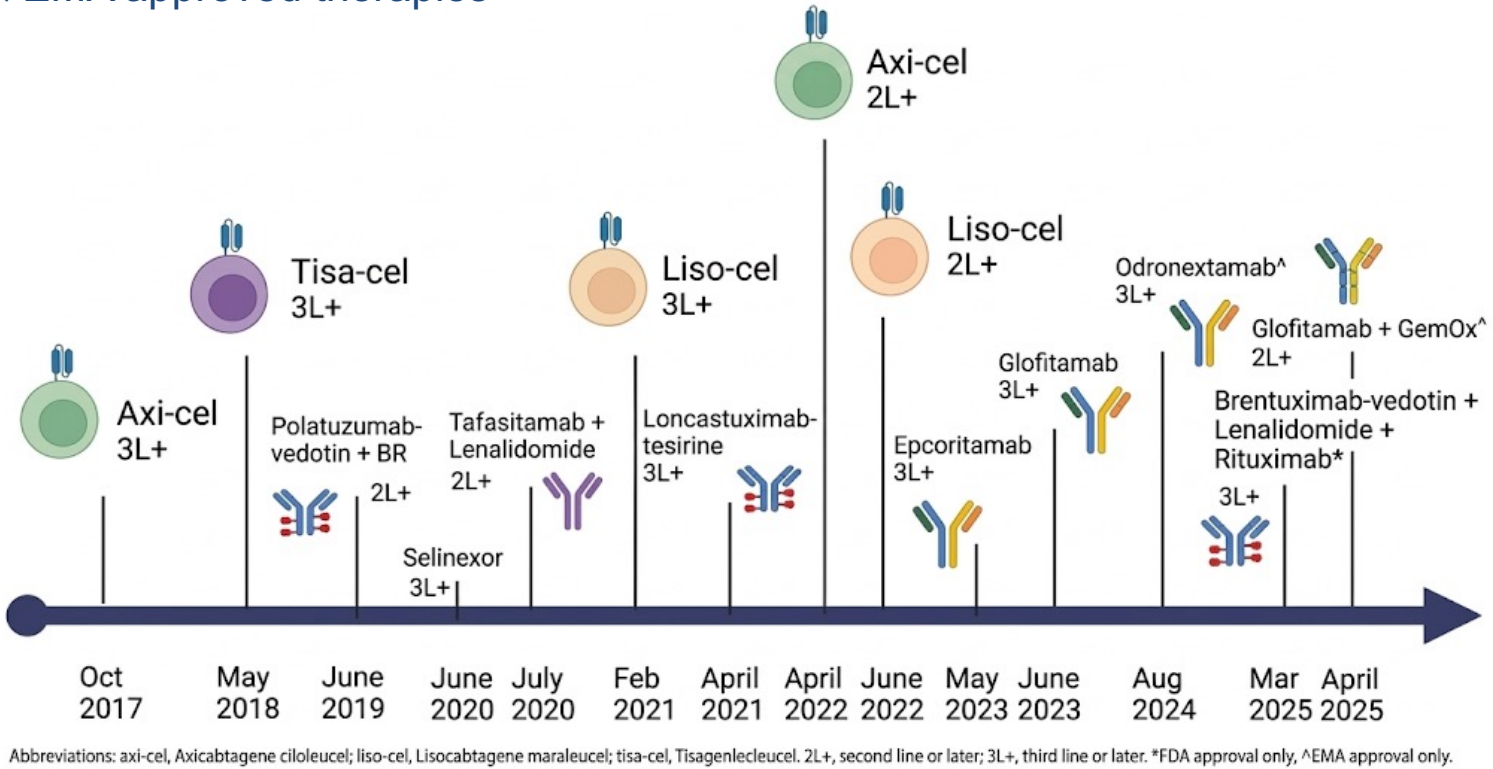
Number at Risk

CIT	653	436	289	209	165	142	122
Pola	116	69	39	27	17	NR	NR
Tafa	55	37	16	10	NR	NR	NR
Lonca	42	19	13	7	7	7	7

Nastoupil LJ, et al. Clin Lymphoma Myeloma Leuk 2025;25:e183-e199.e8

Navigating the “paradox of choice”
Practice changing treatments for 2L / 3L+ DLBCL

FDA & EMA approved therapies



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.

Modified from Bock AM, Epperla N. J Hematol Oncol 2025;18:68

What to expect from CAR-T in 3L+ DLBCL

	ZUMA-1 Axi-cel n = 101	JULIET Tisa-cel n = 115	TRANSCEND Liso-cel n = 269
ORR	83%	53%	73%
CR rate	58%	39%	53%
5-yr OS	42.6%	—	—
Estimated cure rate	~40%	~30-35%	~35%

Inter-trial comparisons should not be made due to differences in study design, patient populations, and treatment interventions.

Neelapu SS, et al. Blood 2023;141:2307–15
Schuster SJ, et al. Lancet Oncol 2012;22:1403–15
Abramson JS, et al. Lancet 2020;396:839–52

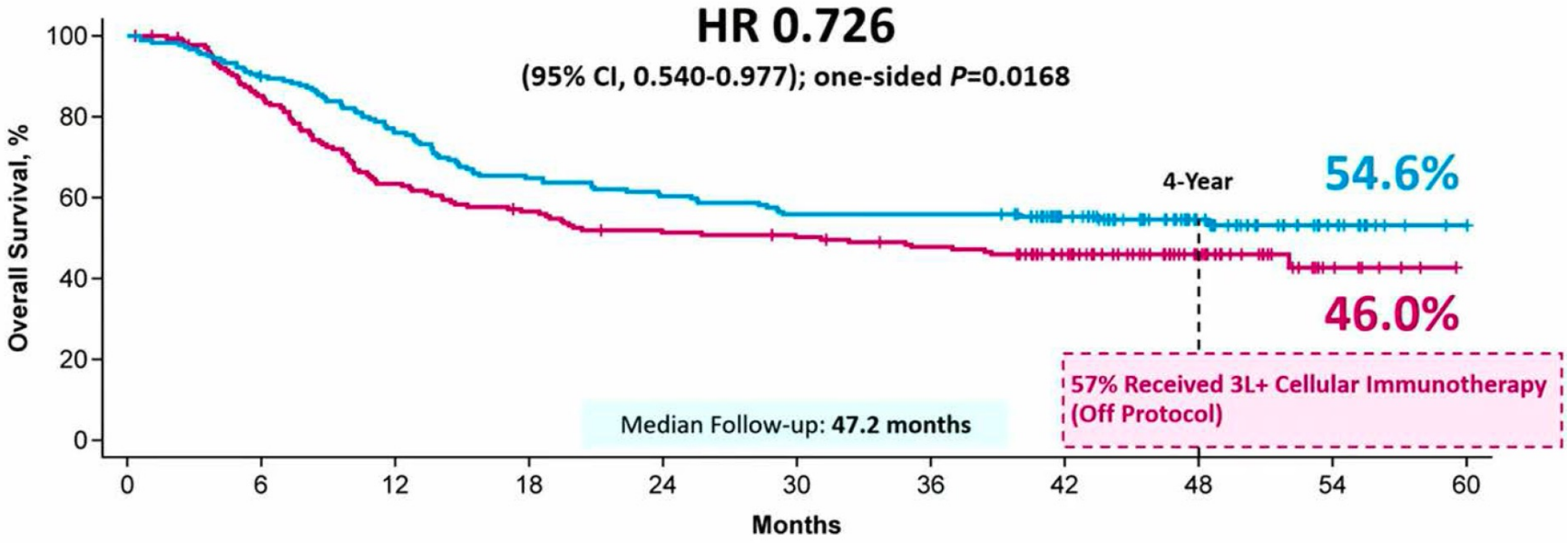
The paradigm shift in the 2L setting
CAR-T for early relapsed and primary refractory patients

	ZUMA-7 [1,2] Median f/u 47.2 mo		TRANSFORM [3] Median f/u 33.9 mo	
Patients, ITT set	**Axi-cel (n=180)**	**SOC (n=179)**	**Liso-cel (n=92)**	**SOC (n=92)**
CAR-T infusion (%)	94	N/A	98	N/A
ASCT (%)	N/A	36	N/A	47
Crossover to CAR-T (%)	N/A	56	N/A	63
ORR / CR (%)	**83 / 65**	**50 / 32**	**87 / 74**	**49 / 43**
Median EFS (mo)	**10.8**	**2.3**	**29.5**	**2.4**
Median PFS (mo)	**14.7**	**3.7**	NR	**6.2**
Median OS (mo)	NR	31.1	NR	NR

SOC = salvage chemoimmunotherapy ± ASCT. NR = not reached. N/A = not applicable. ITT = intent-to-treat.

1. Locke FL, et al. N Engl J Med 2022;386:640–54
2. Westin JR, et al. N Engl J Med 2023;389:148–57
3. Kamdar M, et al. J Clin Oncol 2025;43:2671–8

ZUMA-7
Axi-cel improved overall survival vs. SoC



Westin JR, et al. N Engl J Med 2023;389:148–57

Why CAR-T may not be the answer

$373K - $475K

Cost per patient

Product only — excludes hospitalization, ICU, bridging

3-5 weeks

Manufacturing time

Requires leukapheresis, shipping, production, quality control

Only Brazil

Approved in LATAM

No commercial CAR-T outside Brazil in the region

60-80%

Never receive CAR-T

Of eligible R/R DLBCL patients do not access therapy (EU/US data)

Accredited centers required

Specialized infrastructure

ICU, multidisciplinary team, CRS/ICANS management capacity

~60%

Relapse post CAR-T

Median OS <6 months after CAR-T failure

The unmet need:

What happens to patients who never receive CAR-T — and the ~60% who fail it?

Abramson JS, et al. Blood 2022;140:2527–9
Canales MA, et al Front Med 2023;10:1128295
Hoffmann MS, et al. Transplant Cell Ther 2023;29:440–8

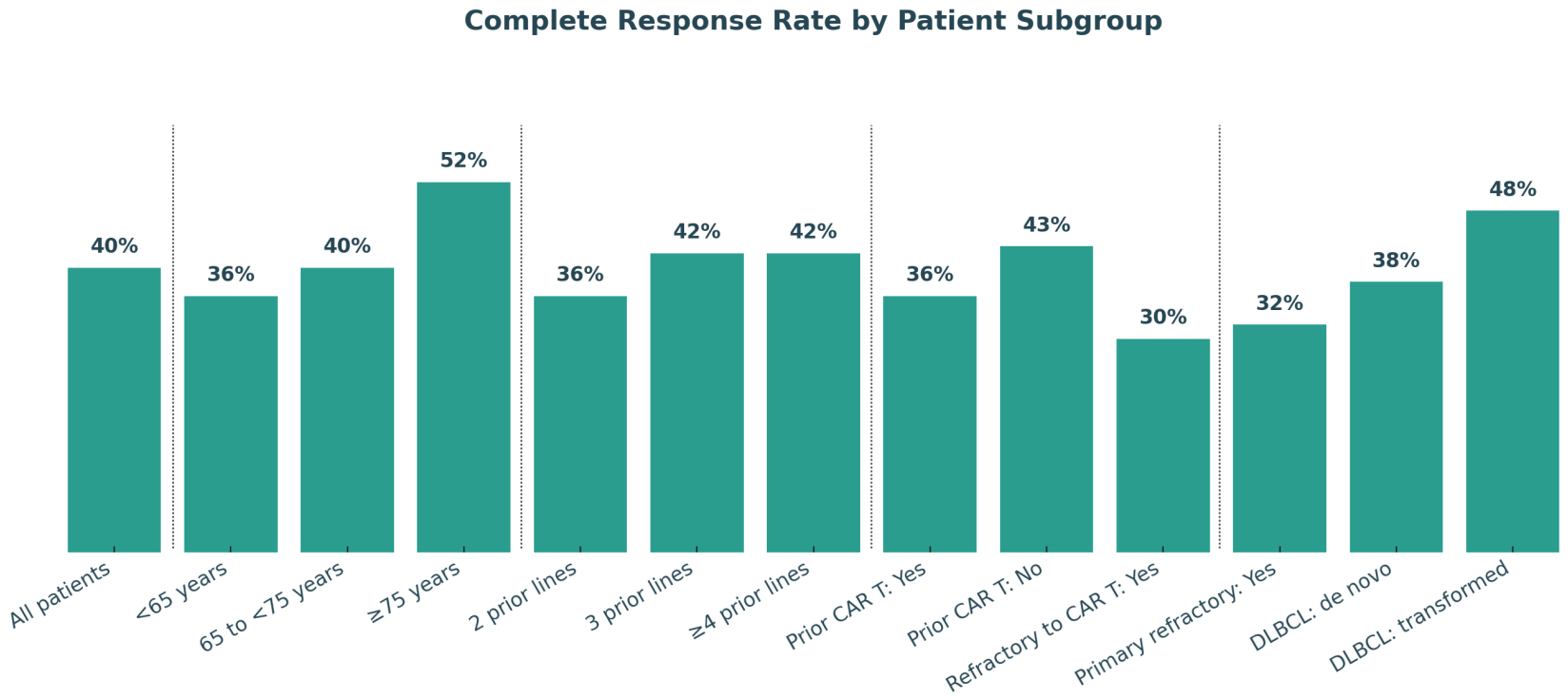
The players
CD20×CD3 bispecific antibodies in 3L+ DLBCL

Bispecific antibody	N	ORR	CR	CR after CART	CRS (%) All / G3+	ICANS (%) All / G3+
Glofitamab[1] (NP30179) Median follow-up 37.7 mo	155	52%	40%	35%	64 / 4	8 / 3
Epcoritamab[2] (EPCORE NHL-1) Median follow-up 37.1 mo	157	59%	41%	36%	51 / 2.5	6 / 0.6
Odronextamab[3] (ELM-2) Median follow-up 29.9 mo	127	52%	31.5%	-	55 / 5	0 / 0

Inter-trial comparisons should not be made because differences in study design, patient populations, and treatment interventions, among others. We cannot make direct comparisons or draw conclusions from one trial to another. Efficacy results for each of the studies are listed only for descriptive purposes.

1. Dickinson M, et al. Blood 2024;144(Suppl 1):865
2. Cheah CY, et al. EHA 2025:PF920 (abstract)
3. Kim WS, et al. Nat Cancer 2025;6:528–39

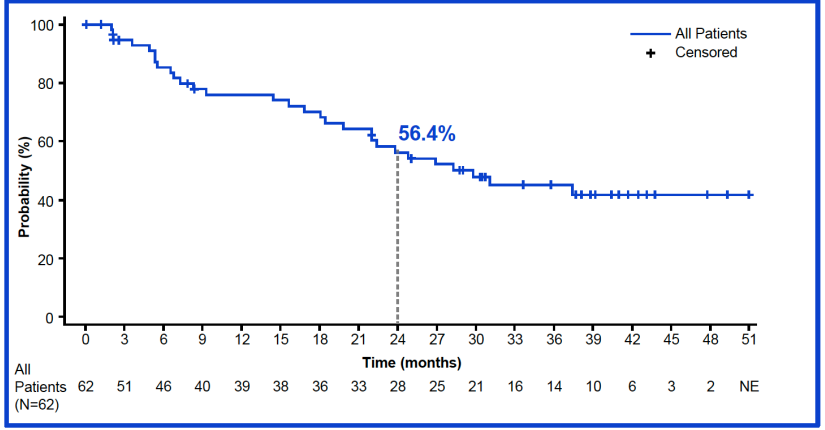
Epcoritamab (EPCORE NHL-1)
Consistent efficacy across key subgroups



Thieblemont C, et al. Leukemia 2024;38:2653–62

Glofitamab (NP30179)
Complete responses remain durable

DoCR by IRC

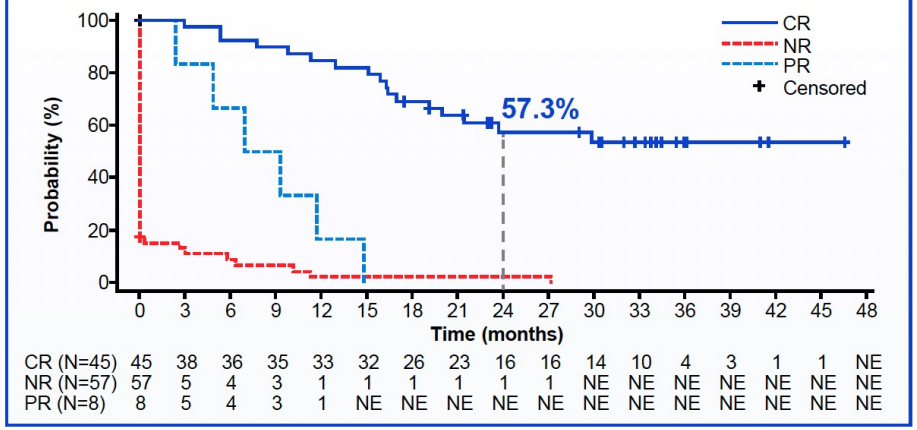


29.8 months	56.4%	53.2%
Median DoCR	24-month DoCR	Ongoing CRs
(95% CI: 22.0–NE)	(95% CI: 42.9–69.8)	33/62 patients

77.2% of CR patients at EOT alive at 24 months

Median time on study: 41.0 months (range: 0–52)

PFS



Landmark PFS from EOT in patients with CR at EOT*	N=45
Median PFS, months (95% CI)	NE (20.0–NE)
24-month PFS rate, % (95% CI)	57.3 (41.2–73.4)

Dickinson M, et al. Blood 2024;144(Suppl 1):865

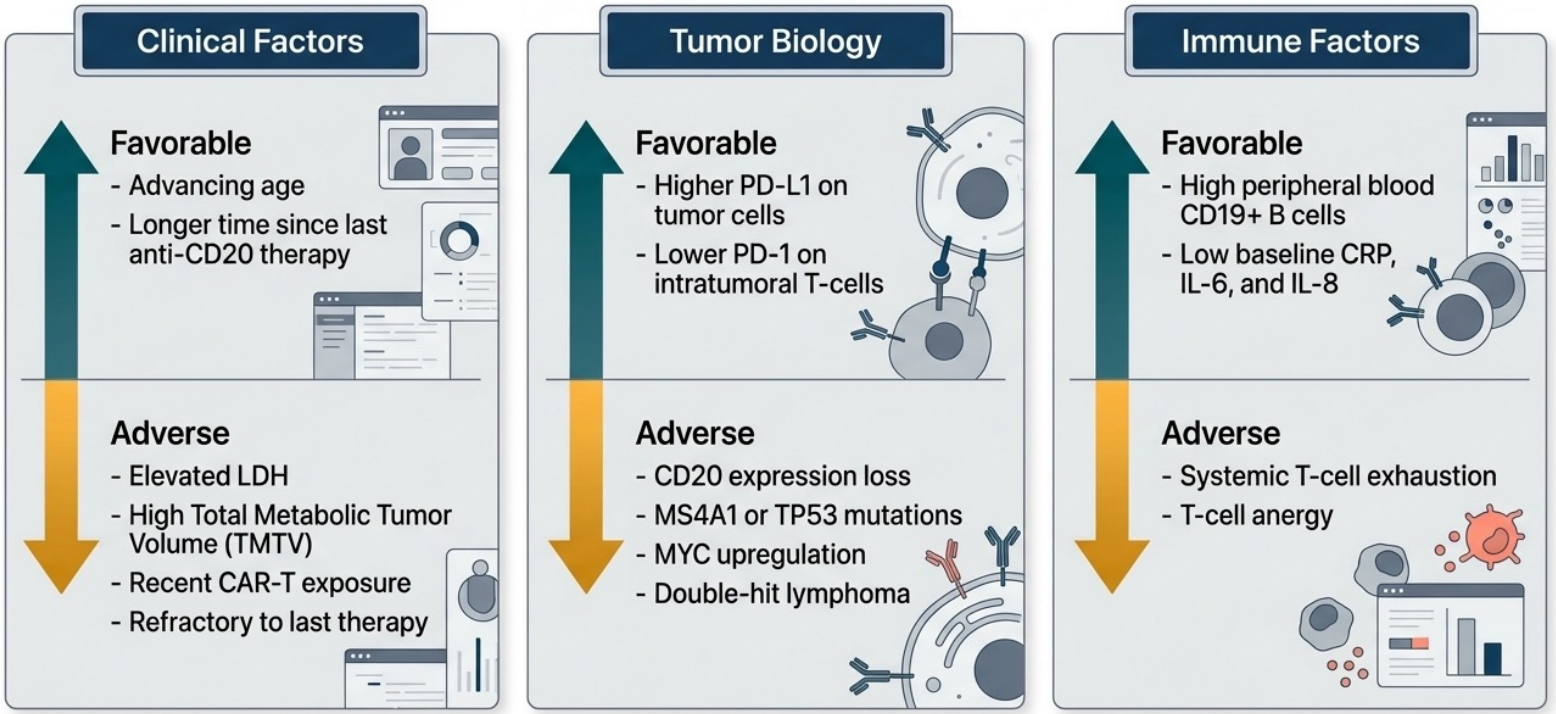
Beyond the trials
CD20×CD3 BsAbs in heavily pretreated patients (RWE)

Study	N	Median age	Prior lines	Prior CAR-T	ORR	CR
US multicenter (REALBiTE)[1] 21 centers | Epco + Glofit	331	68	3	~57%	**54%**	**33%**
UK multicenter[2] 31 centres | Glofit n=211 + Epco n=108	288*	68 IQR 57-76	2 (1-7)	55% Glofit 38% Epco	**52%** **54%**	**30%** **27%**
DE/AT/CH Region[3] 20 centers | Glofit CUP	70	62 (23-94)	4 (2-14)	71%	**46%**	**27%**
DE/AT/CH Post-CAR-T[4] 24 centers | Glofit n=85 + Epco n=6	92	61 (20-78)	4 (2-9)	100%	**43%**	**22%**

*N=319, 288 evaluable patients, 210 patients completing ≥2 cycles (Glofit n=158 + Epco n=52).
60–74% of patients would have been ineligible for registrational trials.

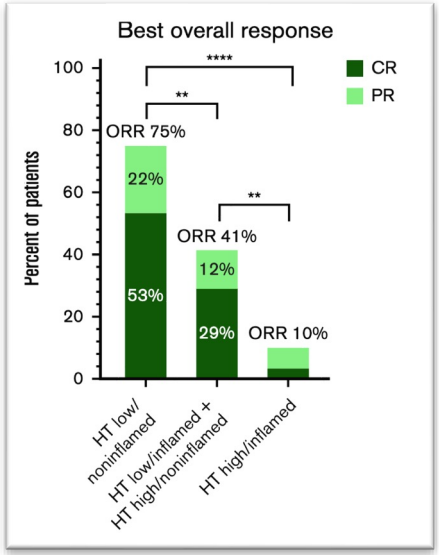
1. Brooks T, et al. Blood 2025;146(Suppl 1):4499
2. Haynes E, et al. Hematol Oncol 2025;43(S3):e326
3. Shumilov E, et al. Blood Adv 2025;9:3865–77
4. Shumilov E, et al. Blood Adv 2025;9:3955–66

Forces driving BsAb efficacy and resistance



Adapted from Lewis CS, et al. Blood 2025;145:1850–7

Zomming in
Impact of pretreatment inflammation scores (HT & Inflamix)

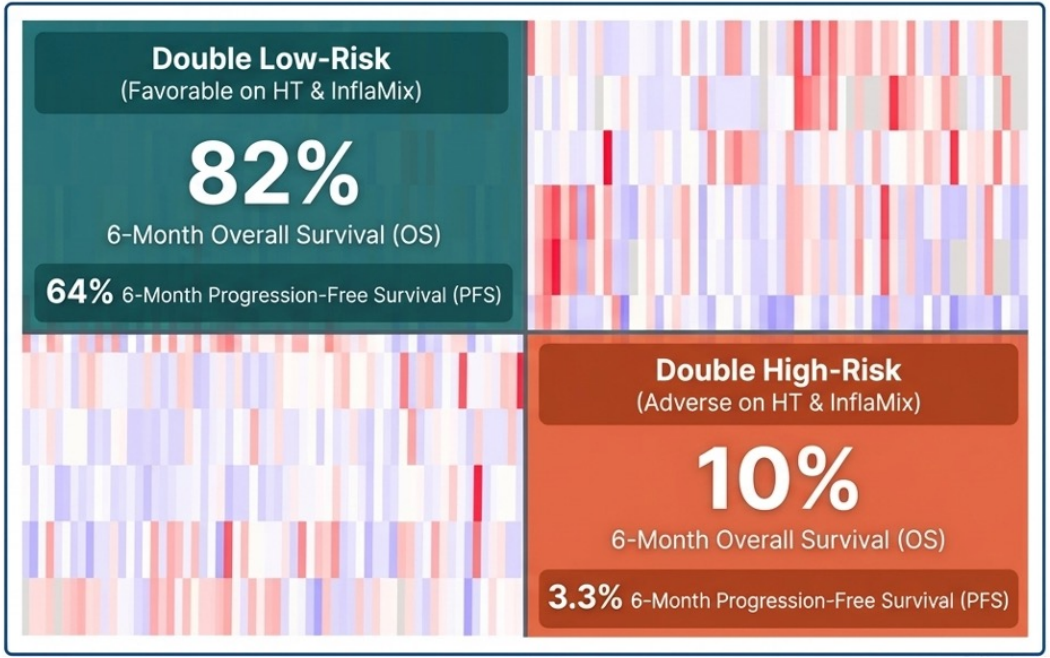


CAR-HEMATOTOX (HT) ≥3

Measures hematopoietic reserve and inflammation (ANC, hemoglobin, platelets, CRP, ferritin).

InflaMix (Inflammatory Cluster)

Integrates markers of organ function and systemic hyperinflammation.



*InflaMix: https://ssraj017.github.io/inflamix_app_prod/

*Raj SS, et al. Nat Med 2025;31:1183–94
Adapted from Magno G, et al. Blood Adv 2025;10:1675–86

Shaping 2L therapy beyond CAR-T

	STARGLO	EPCORE DLBCL-1	OLYMPIA-4	SUNMO	POLARGO	LOTIS-5	MK-2140-003
	R/R DLBCL transplant ineligible (N=270)	R/R DLBCL transplant ineligible (N=552)	R/R aNHL transplant eligible (N=216)	R/R aNHL transplant ineligible (N=222)	R/R DLBCL transplant ineligible (N=270)	R/R DLBCL (N=350)	R/R DLBCL (N=290)
	Glofit + GemOx → Glofit mono vs R-GemOx	**Epcoritamab** vs INV choice (R-GemOx, BR)	**Odronextamab** vs SOC (R-ICE, -GDP, or -DHAP + ASCT)	**Mosun SC + Pola** vs R-GemOx	**Polatuzumab + R-GemOx** vs R-GemOx	**Lonca-R** vs R-GemOx	**Zilovertamab + R-GemOx** vs R-GemOx
	OS	OS	EFS	ORR and PFS	OS	PFS (by IRC)	PFS (by IRC)
	April 2025	April 2028	May 2027	November 2027	Completed Nov 2024	June 2025	June 2027

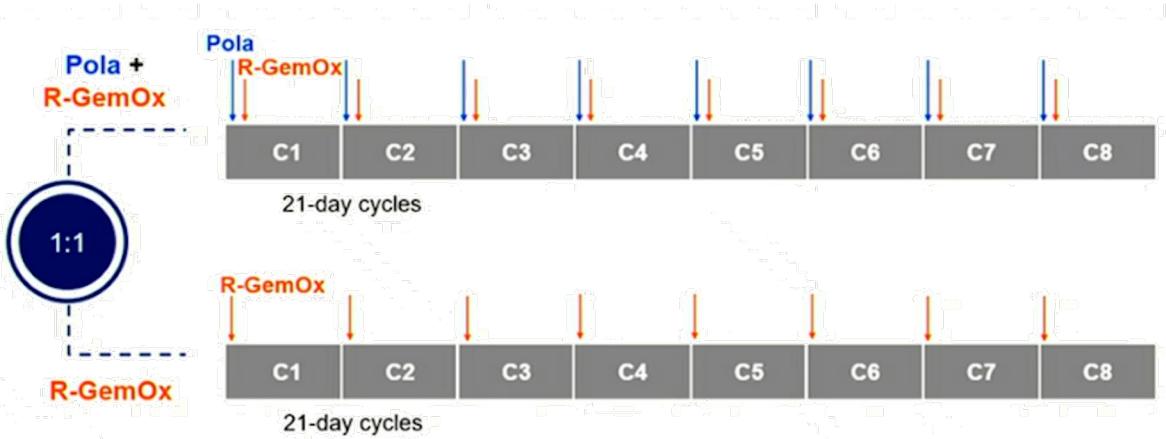
POLARGO
Pola-R-GemOx in patients with R/R DLBCL

Estimated enrolment N=270

- ✓ Histologically-confirmed DLBCL, NOS or history of transformation of indolent disease
- ✓ R/R disease
- ✓ ECOG PS 0–2
- ✓ ≥1 prior systemic therapy

Randomization stratified by:

- Number of prior lines of systemic therapy for DLBCL (1 vs ≥2)
- Outcome of last systemic therapy (relapsed vs refractory)
- Age (≤70 years vs >70 years)



Primary endpoint: OS

Secondary endpoints: PFS, CR (by IRC), and ORR (by IRC)

Matasar M, et al. EHA 2025:abstract S101

POLARGO
Pola-R-GemOx significantly improved OS

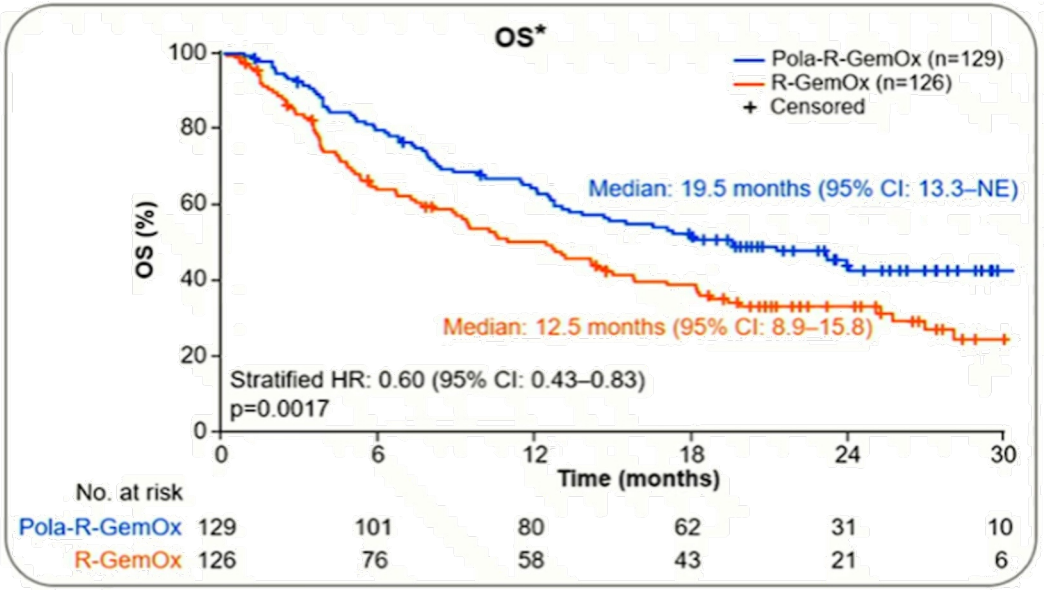
Efficacy (Pola-R-GemOx [n=129] vs R-GemOx [n=126])

Median PFS	ORR
7.4 vs 2.7 months	52.7% vs 24.6%

Safety (Pola-R-GemOx [n=128] vs R-GemOx [n=125])

Common AEs
- Peripheral neuropathy: 57.0% vs 28.8%
- Infections: 14.1% vs 8.0%
- Thrombocytopenia: 34.4% vs 26.4%

AEs leading to treatment discontinuation
- 23.4% vs 8.0%



Matasar M, et al. EHA 2025:abstract S101

STARGLO
Trials that may impact the 2L treatment landscape

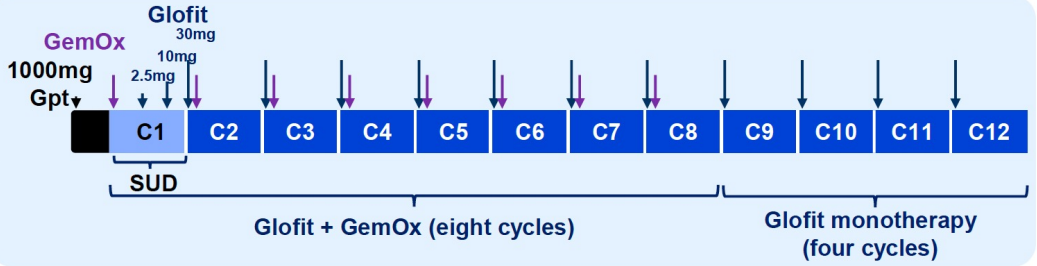
- ✓ R/R DLBCL after ≥1 prior therapy
- ✓ ECOG PS 0–2
- ✓ Ineligible for ASCT[2**]

Estimated enrolment N=270

Glofit + GemOx*

2:1

R-GemOx†



Randomization stratified by:

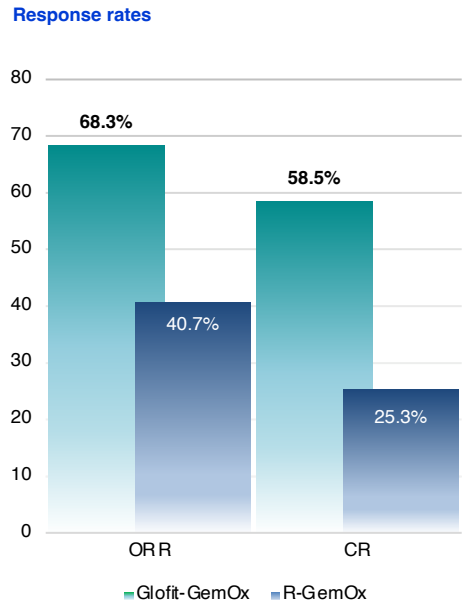
- Relapsed vs refractory disease
- 1 vs ≥2 prior lines of therapy

Primary endpoint: OS
Secondary endpoints: PFS, CR, ORR, DOR, safety, tolerability

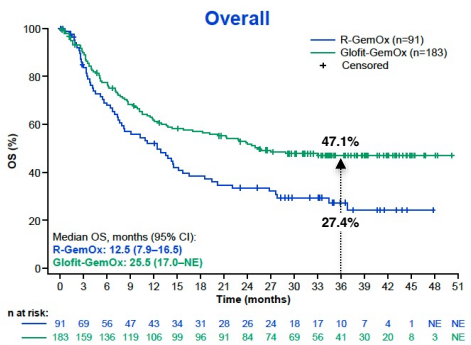
*Obinutuzumab IV pretreatment on C1D1 (1000mg); glofitamab IV on C1D8 (2.5mg), C1D15 (10mg) and C2–12D1 (30mg); gemcitabine (1000mg/m^2) and oxaliplatin (100mg/m^2) on C1D2 and C2–8D1 or D2; 21-day cycles. **Only mandated for 2L cohort
†Rituximab IV (375mg/m^2) on C1D1 and C2–8D1, gemcitabine (1000mg/m^2) and oxaliplatin (100mg/m^2) on C1D2 and C2–8D1 or D2; 21-day cycles.

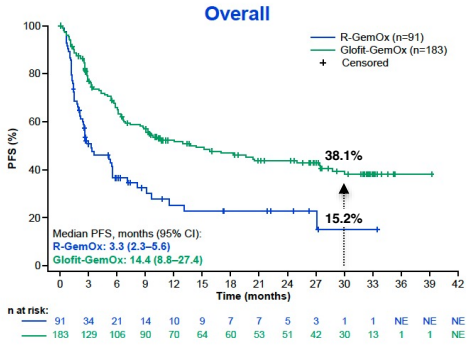
Abramson JS, et al. Lancet 2024;404:1940–54

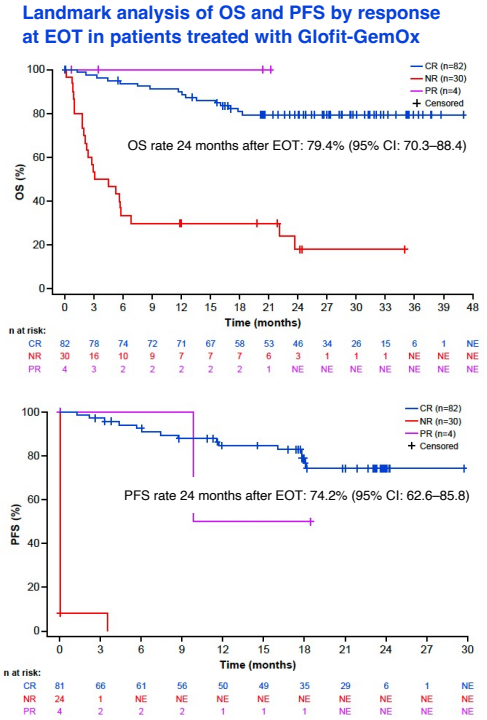
STARGLO
Enhanced survival outcomes in 2L



Median OS follow-up: 35.1 months (95% CI: 33.6–37.6)







Abramson JS, et al. Lancet 2024;404:1940–54
Abramson JS, et al. Blood 2025;146(Suppl 1):5519

STARGLO
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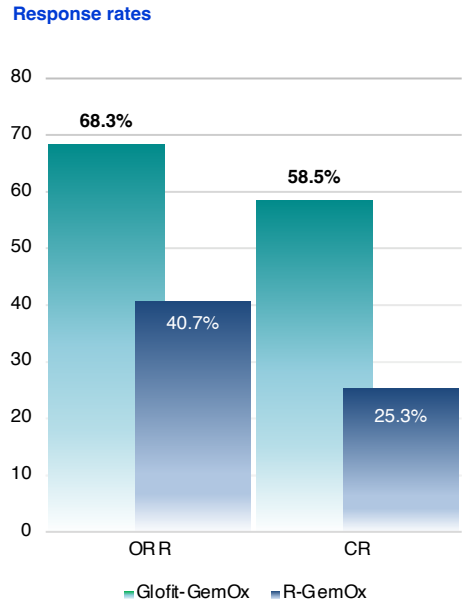

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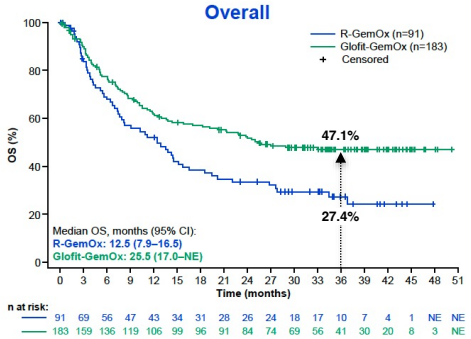
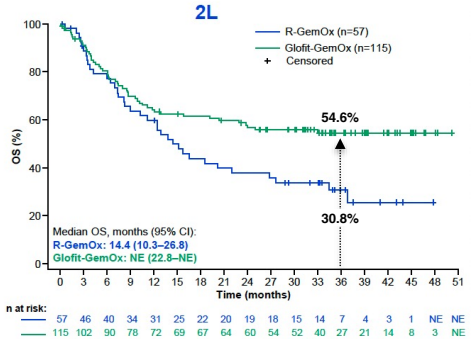
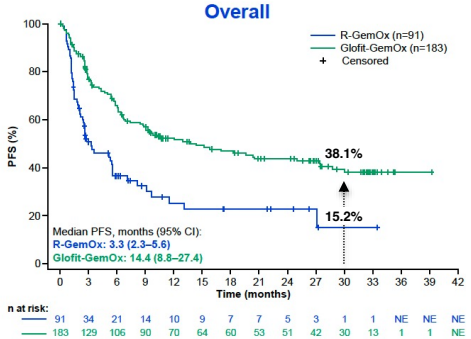
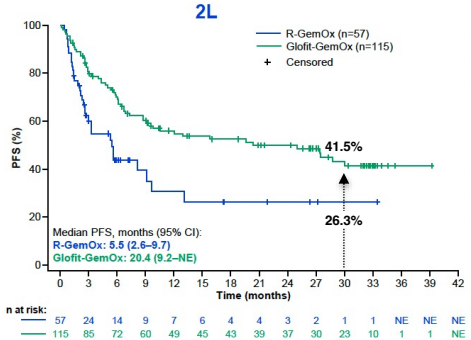






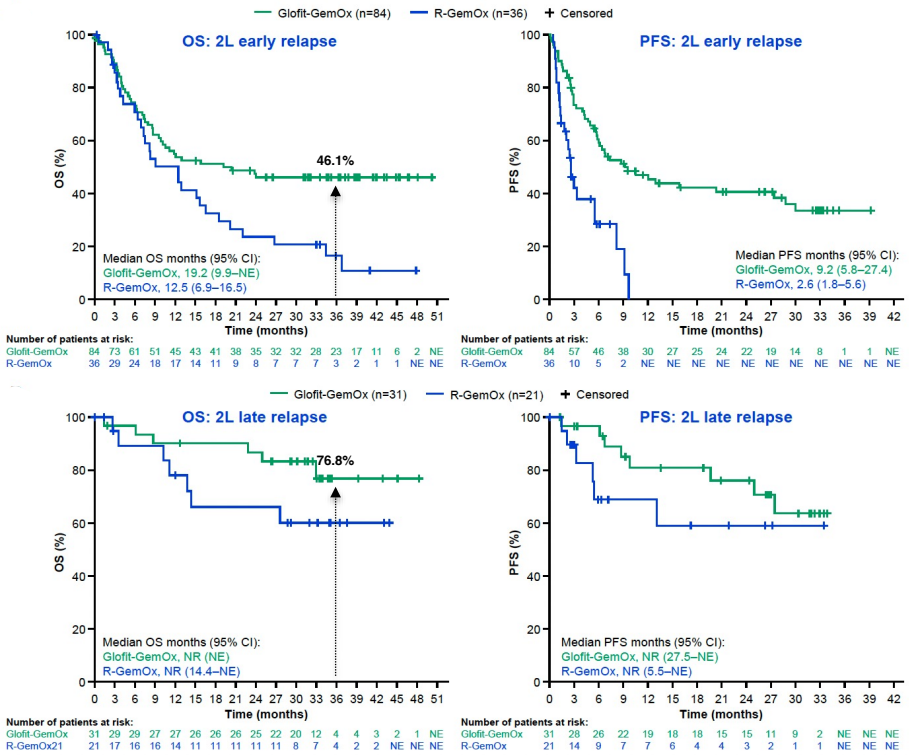


Abramson JS, et al. Lancet 2024;404:1940–54
Abramson JS, et al. Blood 2025;146(Suppl 1):5519

STARGLO
Enhanced survival outcomes across subgroups

Outcome (95% CI)	R-GemOx 2L (n=57)	Glofit-GemOx 2L (n=115)	R-GemOx 3L+ (n=34)	Glofit-GemOx 3L+ (n=68)
Median OS, mo	14.4 (10.3–26.8)	NR (22.8–NE)	6.7 (4.2–14.3)	17.0 (10.7–25.8)
36-month OS, %	30.8 (17.7–44.0)	54.6 (45.2–64.0)	21.8 (6.7–36.9)	33.2 (21.2–45.3)
Median PFS, mo	5.5 (2.6–9.7)	20.4 (9.2–NE)	1.9 (1.4–3.6)	9.2 (5.4–18.3)
CR rate, %	28.1 (17.0–41.5)	63.5 (54.0–72.3)	20.6 (8.7–37.9)	50.0 (37.6–62.4)

Median OS follow-up: 35.1 months (95% CI: 33.6–37.6)



In the 2L setting, 120 patients had primary refractory disease or early relapse (early relapse subgroup; R/R ≤12 months after treatment) and 52 patients had late relapse (relapsed >12 months after treatment).

Abramson JS, et al. Lancet 2024;404:1940–54
Abdulhaq H, et al. Blood 2025;146(Suppl 1):3743

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STARGLO
Safety profile summary

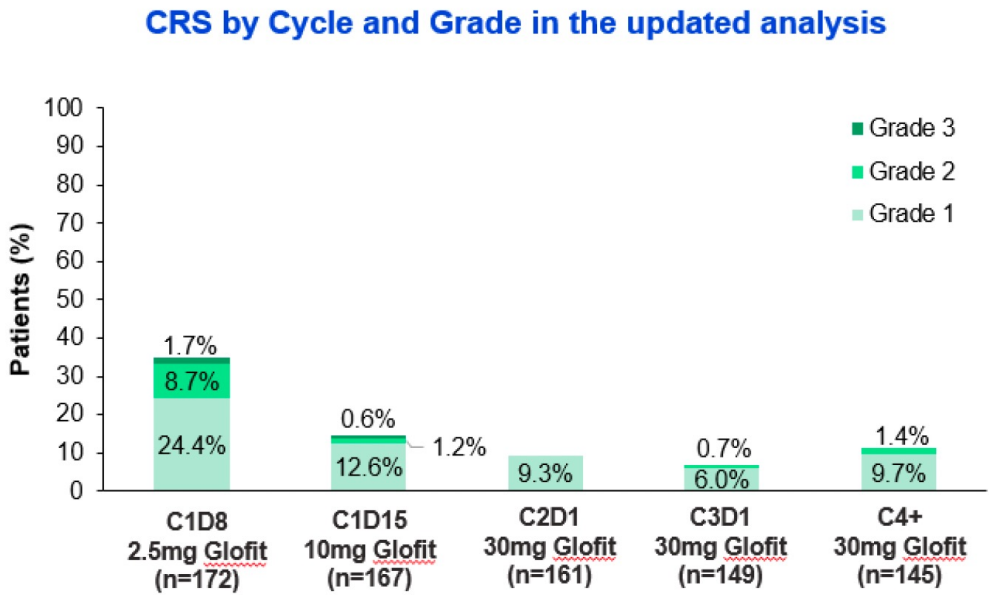
n (%), unless otherwise stated	R-GemOx n=88	Glofit-GemOx (Glofit-exposed) n=172
Number of infusions, median (range)	4 (1–8)	12 (1–14)
Serious AEs	15 (17.0)	90 (52.3)
Grade ≥3 AEs	36 (40.9)	132 (76.7)
Grade 5 AEs	4 (4.5)	12 (7.0)
AE leading to any treatment discontinuation	11 (12.5)	44 (25.6)
CRS (any grade)	NA	77 (44.8)
Grade 3–4*	NA	4 (2.3)
ICANS (any grade)	NA	4 (2.3)
Grade 3–4*	NA	1 (0.6)
Infections (any grade)	26 (29.5)	95 (55.2)
Grade 3–4	8 (9.1)	29 (16.9)
Grade 5	3 (3.4)	6 (3.5)†

CCOD: June 17, 2024. AEs, including ICANS, are graded by NCI CTCAE v5.0, CRS events are graded by ASTCT 2019.
*No grade 4 events reported.
†3 patients had COVID-19, 1 patient had a respiratory tract infection (COVID-19 associated), 1 patient had pneumonia, and 1 patient had septic shock.

Abramson JS, et al. Lancet 2024;404:1940–54

STARGLO
Cytokine Release Syndrome

n (%) of patients with ≥1 CRS AE*	Glofit-GemOx (Glofit Exposed) n=172
Any grade†	76 (44.2)
Grade 1	54 (31.4)
Grade 2	18 (10.5)
Grade 3	4 (2.3)‡
Median time to CRS onset, hours (range)	
2.5mg glofitamab (C1D8)	13.5 (4.4–134.9)
10mg glofitamab (C1D15)	32.4 (7.4–564.3)
Median CRS duration, hours (range)	
2.5mg glofitamab (C1D8)	22.7 (0.0–168.0)
10mg glofitamab (C1D15)	24.0 (0.0–248.5)
Tocilizumab for CRS management, n/n (%)	28/76 (36.8)
Corticosteroids for CRS management, n/n (%)	39/76 (51.3)



Dexamethasone premedication was mandated to prevent/mitigate CRS prior to step-up doses and at least two 30mg doses of glofitamab, until no additional CRS was observed.*Unless otherwise specified. †No Grade 4 or 5 CRS events were reported. ‡One patient had a Grade 3 CRS event confounded by a concurrent Grade 5 Septic Shock that required multiple pressors.

Abramson JS, et al. Lancet 2024;404:1940–54

Redefining 2L DLBCL care

Bispecific-based combos in transplant-eligible patients

GO43693[1]

Phase Ib | ASCT/CAR T-eligible
N=41
Glofitamab + R-ICE

78%	69%
ORR	CR

Overall Response Rate

EPCORE NHL-2 Arm 4[2]

Phase Ib/II | ASCT-eligible
N=29
Epcoritamab + R-DHAX/C

76%	69%
ORR	CR

Overall Response Rate

EPCORE NHL-2 Arm 10[3]

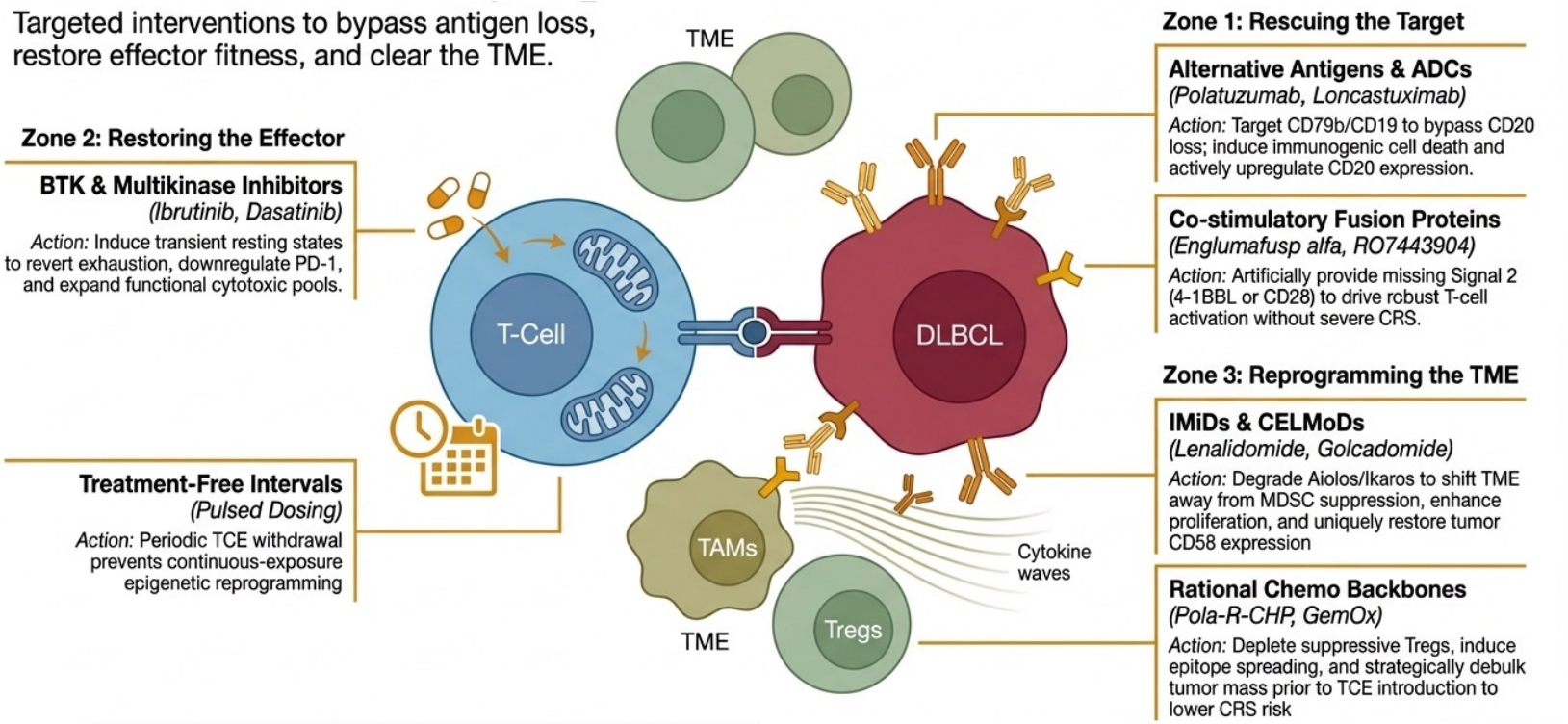
Phase Ib/II | ASCT-eligible
N=31
Epcoritamab + R-ICE

87%	65%
ORR	CR

Overall Response Rate

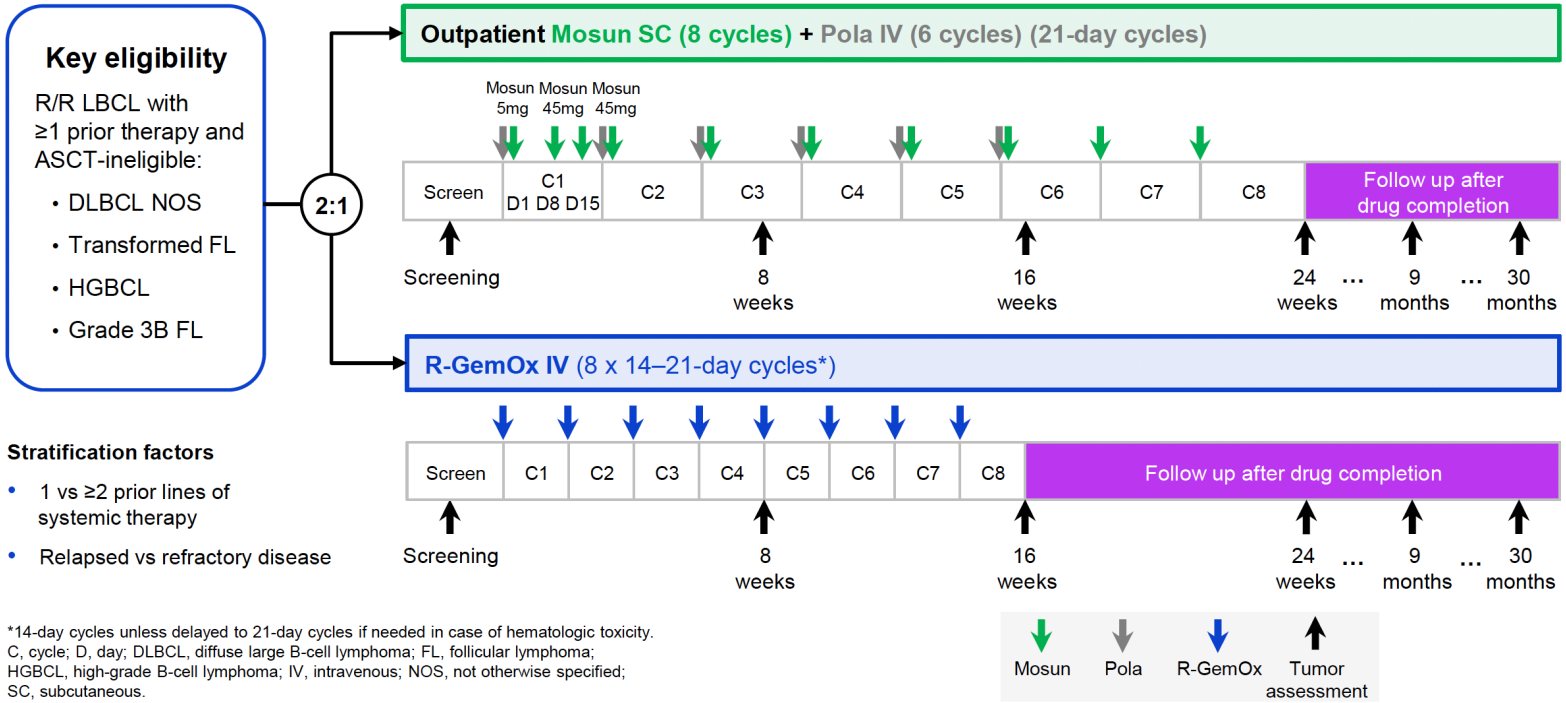
1. Diefenbach CS, et al. Blood 2024;144(Suppl 1):987
2. Karimi Y, et al. J Clin Oncol 2024;42(16_Suppl):7032
3. de Vos S, et al. Hematol Oncol 2025;43(S3):e322

The new light
Overcoming mechanisms of resistance



Adapted from Harrop S, et al. Br J Haematol 2026;208:13–24

SUNMO: Study design



*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.

Budde LE, et al. J Clin Oncol 2025;43:3799–811
Westin J, et al. Hematol Oncol 2025;43(S3):LBA3

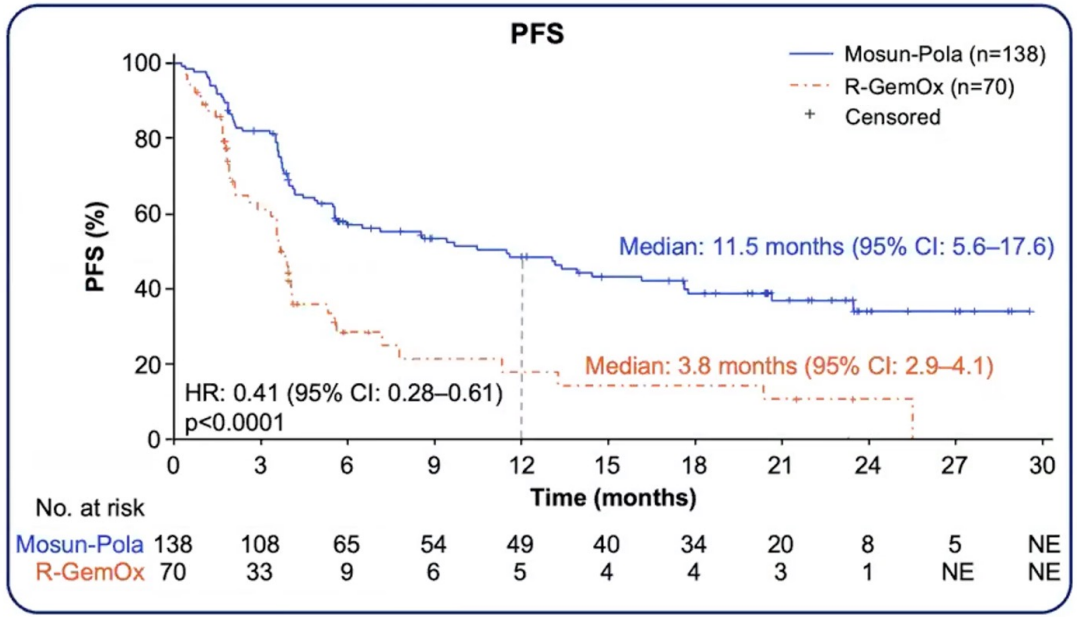
SUNMO
Mosun-Pola significantly prolonged PFS

Efficacy (Mosun-Pola [n=138] vs R-GemOx [n=70])

ORR	CRR
70.3% vs 40.0%	51.4% vs 24.3%

Safety (Mosun-Pola [n=135] vs R-GemOx [n=64])

- CRS (Mosun-Pola only): Grade 1, 21.5%; Grade 2, 3.7%; Grade 3, 0.7%
- No ICANS reported
- Peripheral neuropathy: 24.4% vs 42.2%
- Thrombocytopenia: 8.9% vs 65.6%



Median follow-up: 23.2 months

18-months PFS event-free rate, % (95% CI): Mosun-Pola 39 (30–48) vs R-GemOx 14 (2.5–26)

Budde LE, et al. J Clin Oncol 2025;43:3799–811
Westin J, et al. Hematol Oncol 2025;43(S3):LBA3

Take-home messages

R/R DLBCL in LATAM: a large unmet need

Limited access to diagnostics, novel agents, and CAR-T — yet patients mirror international profiles

CAR-T is transformative but not the answer for most

Cost, manufacturing, infrastructure, and availability limit CAR-T to a minority — especially in LATAM

CD20 × CD3 BsAbs: the accessible alternative

Off-the-shelf, outpatient, manageable CRS, active in heavily pretreated patients

Combinations and earlier lines will expand BsAbs

2L combinations (STARGLO), and next-gen strategies overcoming resistance are already here

Acknowledgments

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All patients and their families

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