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SCIENZE MEDICHE E CHIRURGICHE

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New Drugs in Hematology

Bispecific Antibody in Combination: Mosunetuzumab

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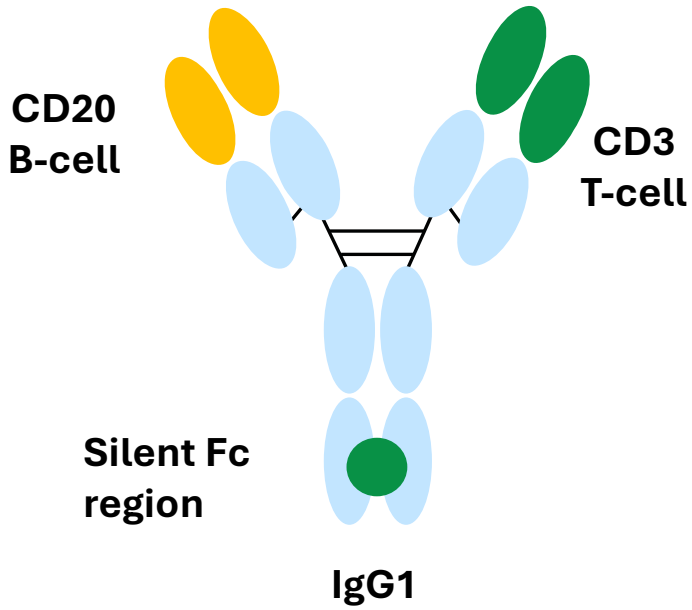
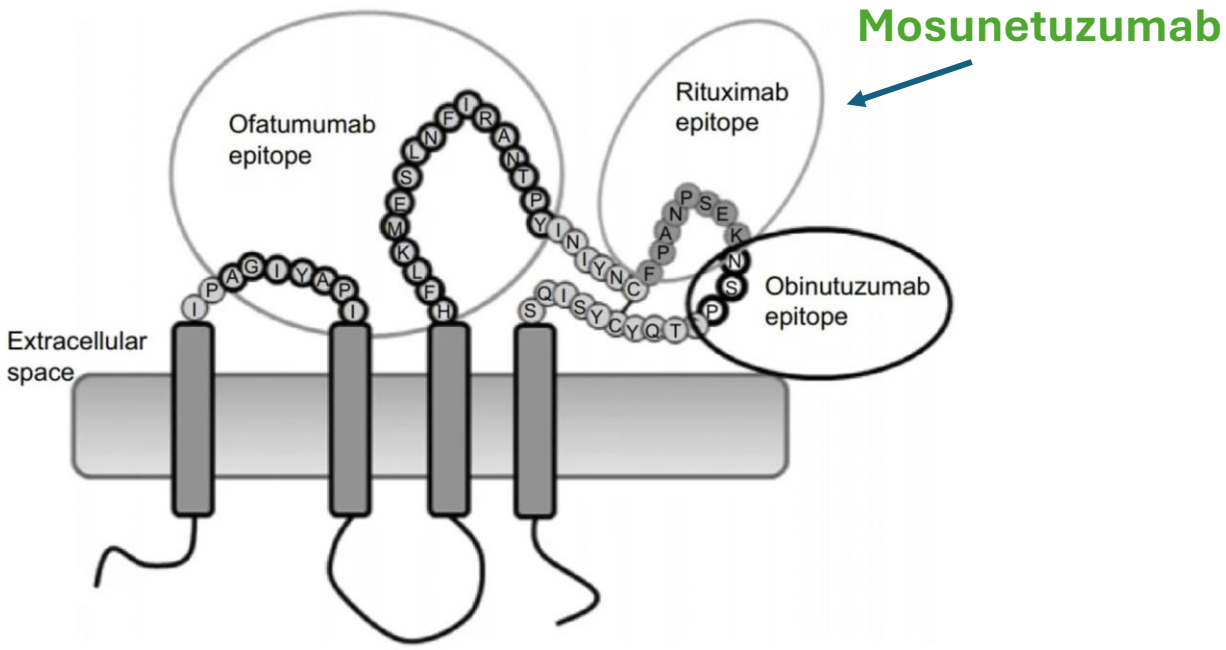
Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
ADC Therapeutics						x	
Astrazeneca	x					x	
BMS						x	
Kite Pharma						x	
Merck						x	
Genetech/Roche						x	

Mosunetuzumab: a CD20/CD3 bispecific antibody

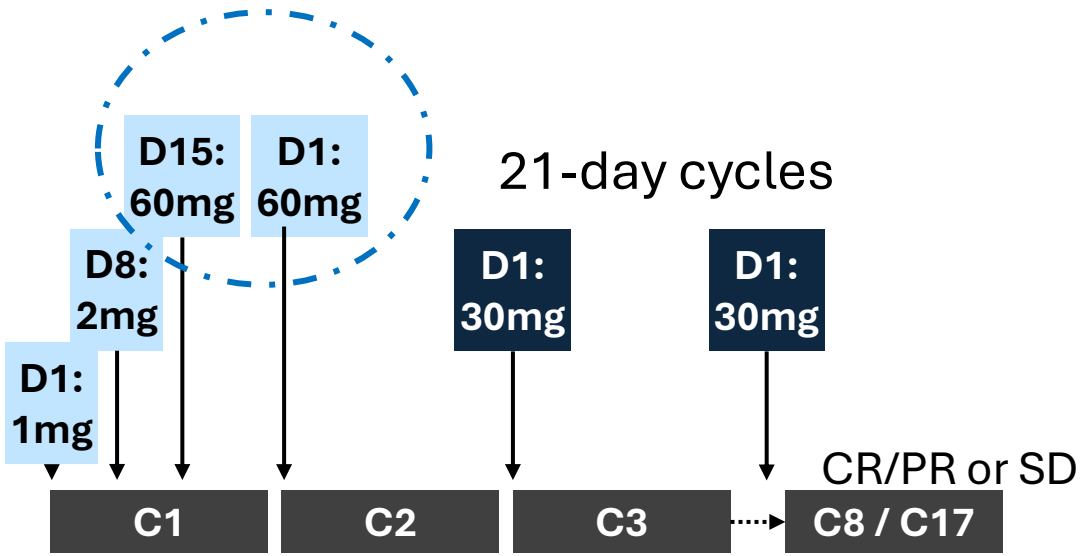


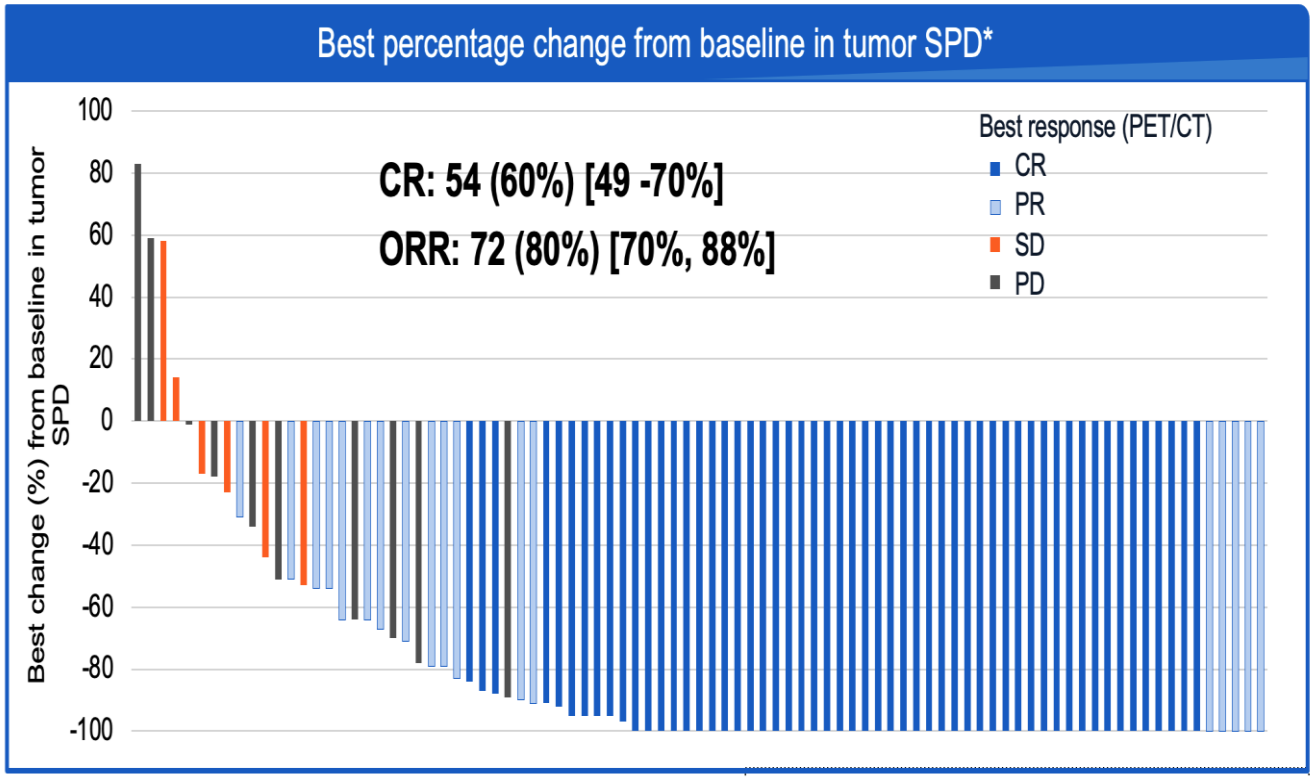


Mosunetuzumab: 1st Bispecific TCE Approved in Lymphoma

GO29781 study: phase 1/ 2, multicenter study (NCT02500407)

- Q3W **IV** administration
- C1 step-up dosing
- **Fixed-duration treatment**
- **No hospitalization**



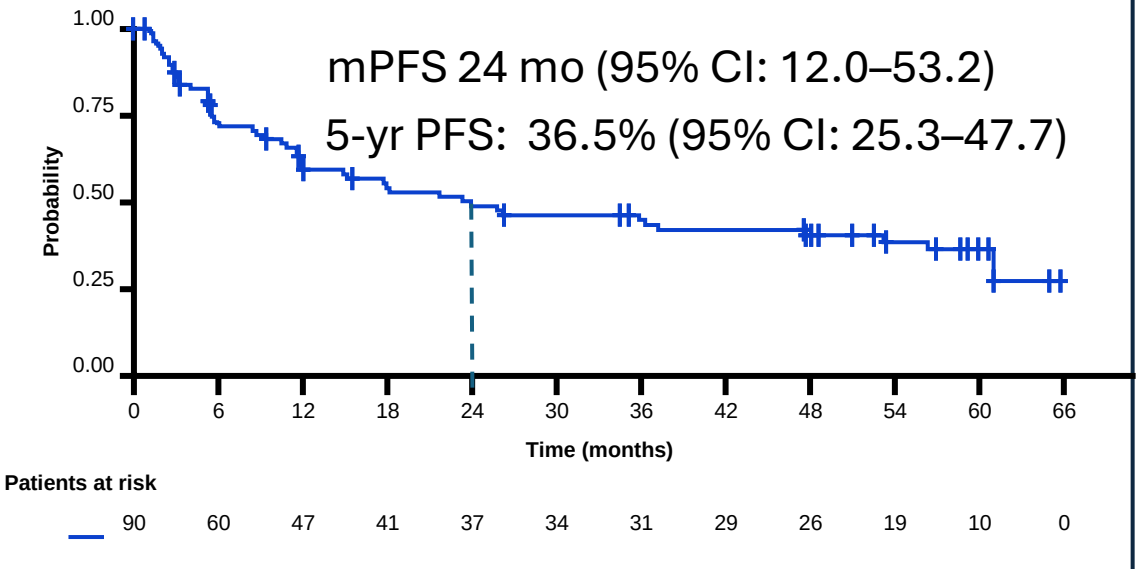


Phase 2 cohort in r/r FL
Median time to CR: 3 mo (1.2 - 18.9)
28/28 CR at EOT: uMRD

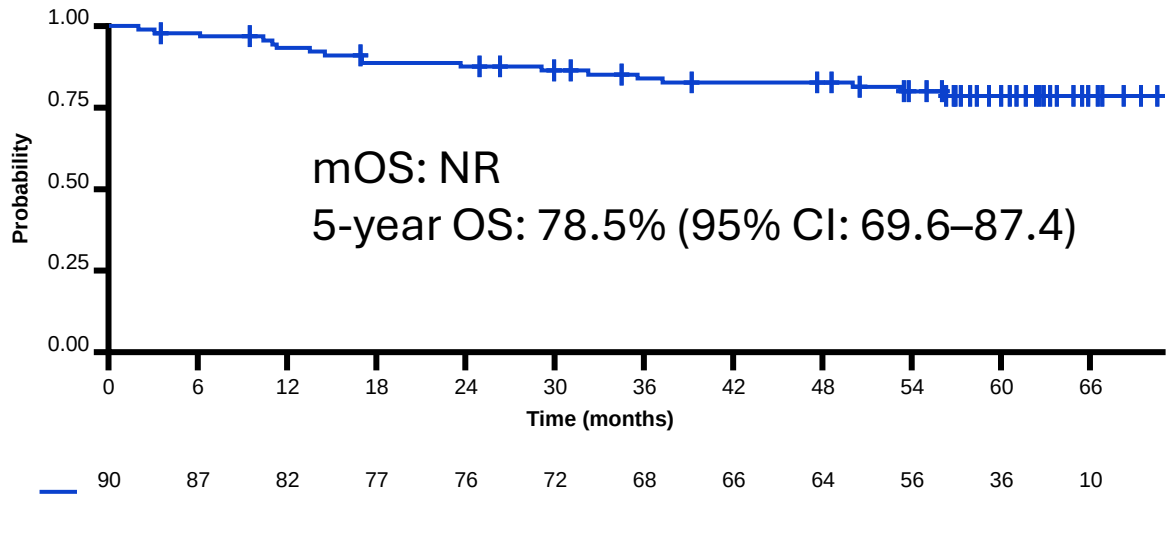
Budde et al. Lancet Oncology 2023

5-year Efficacy Outcomes

PFS in the overall population



OS in the overall population



The **median DOCR**: **NR** (95% CI: 44.1–NE)

The **5-year DOCR**: **52.1%** (95% CI: 36.2–67.9)

The **median TTNT: 64.1 months** (95% CI: 21.7–NE)

CCOD: May 1, 2025.

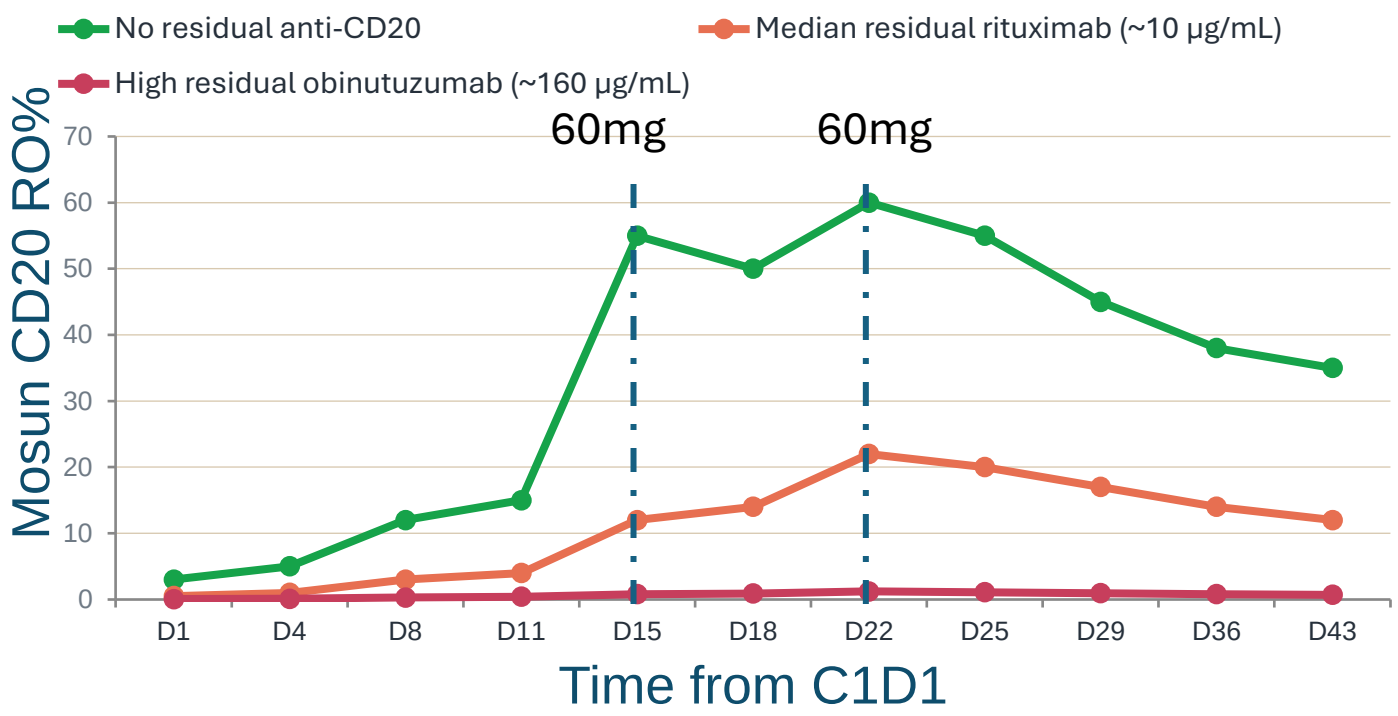
CCOD, clinical cut-off date; CI, confidence interval; NE, not estimable; TTNT, time to next treatment.

Budde et al. ASH 2025

CD20 receptor occupancy over time: the modeled story

Approved 1/2/60x2/30 mg regimen achieves near-maximal efficacy (Li et al. CPT 2025)

Modeled mosunetuzumab CD20 RO% over days 0-42



Approved IV dose schedule

C1D1: 1 mg (step-up)
C1D8: 2 mg (step-up)
C1D15: 60 mg (loading)
C2D1: 60 mg (loading)
C3D1+: 30 mg q3W maintenance

Key insights

RO% increases sharply after the C1D15 60 mg dose
this drives efficacy.
Residual rituximab/obinutuzumab can blunts RO%
Approved dose hits near-maximal efficacy: model-estimated CR 63.1%, ORR 79.1% (Li 2025).

AUC_{0-42} drives CR/ORR (Emax model; near-maximal at approved dose). ·
Maximum RO% drives Grade ≥2 CRS — step-up dosing decouples the two, creating a broad therapeutic window.

Why combine — the four-part rationale

Synergy

Distinct mechanisms hit the tumor from different angles

Depth of response

Combinations push more patients into CR. Depth correlates with durability.

Overcome resistance

Lenalidomide, golcadomide and zanubrutinib reinvigorate exhausted T cells; Polatuzumab increases CD20 expression

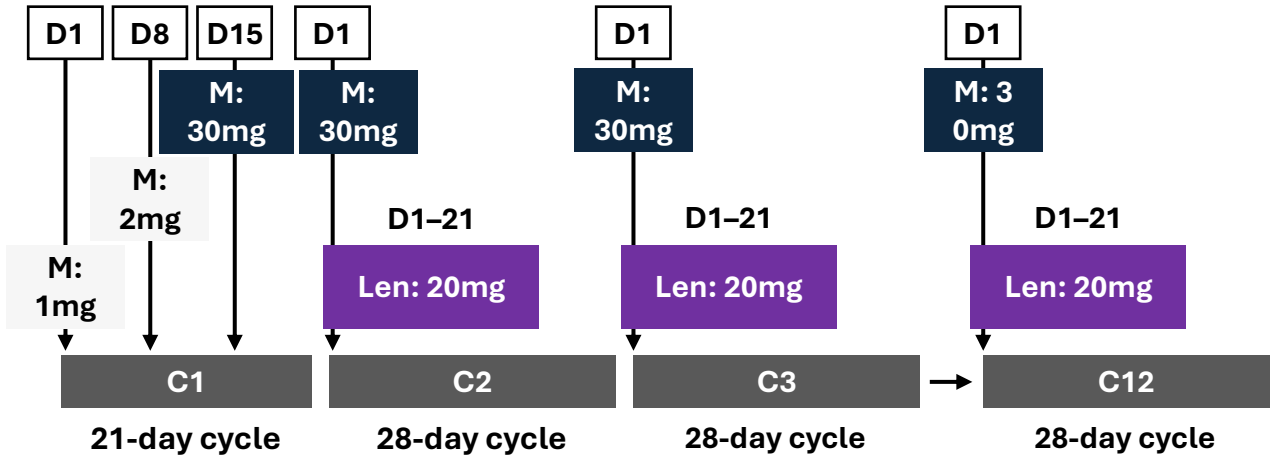
Chemo-free by design

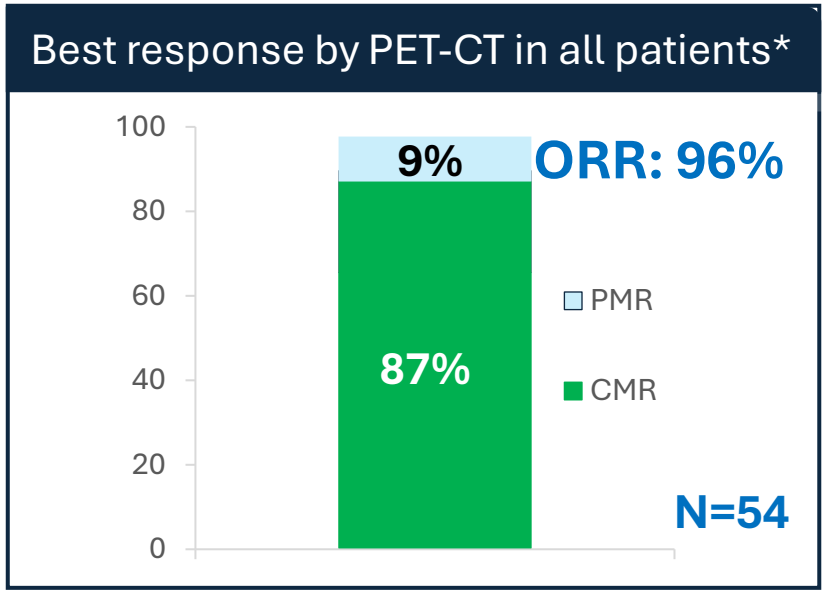
The outpatient, low-CRS, fixed-duration profile pairs well with ADCs, IMiDs/CELMoDs, and BTKi.

Mosunetuzumab moving into early lines in FL

CELESTIMO US Expansion Cohort: Mosunetuzumab+ Lenalidomide (2L+)

- CD20+ FL Grade 1–3a
- R/R to ≥1 prior chemo-immunotherapy regimen including an antiCD20 antibody; prior lenalidomide allowed
- ECOG PS 0–2





- CRS: 28% (gr1 23%, gr2 4%, gr3 1%)
- Neutropenia: 33%; febrile neutropenia: 2%
- Infection: 57%, gr 3 and above 9.4%

CELESTIMO: M-len vs R2; Phase 3

Sano et al. ASH 2025

BTKi + mosunetuzumab combinations

Rationale: BTKi reduces T-cell PD-1, increases CD8+ T-cell synapses, may mitigate T-cell exhaustion

FIL-MOZART
Phase 2 · R/R FL · Zanu

Mosunetuzumab + zanubrutinib

- **R/R FL, 1–3 prior lines (incl. anti-CD20) N=56**
- Z D-15 to D-1
  C1-12, Z+Mosun SC
  C13–C24: Z monotherapy

Safety run-in (N=10):

- no febrile neutropenia,
- no ICANS;
- only 1 G2 CRS requiring tocilizumab

MITHIC-FL2
Phase 2 · 1L HTB FL · Zanu

Mosunetuzumab + zanubrutinib

- **Previously untreated GELF+ FL g1–3A, N=54**
- Zanu started D-7 to M12 mosun SC: 8/17 cycles
- Median f/u 6.5 mo: **CR 82%, ORR 92% (Lugano)**
- CRS 61% (G1 52%, G2 9%, no G≥3); 0 ICANS, 0 TLS, 0 flare
- G3 neutropenia in only 3 pts

PROMOTE-FL
Phase 2 · R/R FL · Pirto

Mosunetuzumab + pirtobrutinib

(R/R FL g1–3A, ≥2 prior lines incl. anti-CD20

- Pirto daily started D-7; continued to 52 wk
- Mosun IV step-up: C1 1/2/60 mg → 30 mg q21D × 8/17 cycles
- trial in progress, recruiting

Ladetto ASH 2024 (design); ASH 2025 (SRI)

Falchi ASH 2025 (Abstract 463)

Di et al. ASH 2025 TiP #5394

More Mosunetuzumab combination in FL

	Regimens	Pt population	Dosing	
Phase 2 NCT05410418	Mosun + Pola	HTB, 1L	Pola-6 cycles Mosun: 8 -17 cycles	ASH2026?
Phase 2 NCT06453044	Mosun+Pola	2L+	Pola-6 cycles Mosun: 8 cycles	Ongoing
Phase 2 NCT05672251	Mosun-Lonca	HTB, 1L	Mosun 8/17 cycles Lonca: 2-4 cycles	Not yet enroll
~~Phase 2 NCT05994235~~	~~Mosunetuzumab + Tazemetostat~~	~~HTB, 1L~~	~~Mosun 8~12 cycles Taz: 12 cycles~~	

Mosunetuzumab in LBCL

	Regimens
1st line	Mosun or Mosun+pola (NCT03677154, IIT): Elderly unfit (NCT05207670) **completed** Mosun + CHOP or CHP-pola (NCT03677141): **completed**
2nd line	• **Mosun+Pola (NCT03671018, phase II); NCT05171647 (phase III) completed** • Mosun+ pola+tafasitmab+lenalidomide (NCT05615636) • Mosun+pola+lenalidomide (NCT06015880) • Mosun+ Lonca-T (NCT05672251) • Mosun-pola x 1+ CAR T + Mosun-pola (NCT05260957) • CAR T (PR+SD), randomized to Mosun, pola, M+P, or SOC (SWOG, NCT05633615) • CAR T (PR+SD+PD at day 30) followed by Mosun (NCT04889716) • Mosun+ CELMoDs (NCT05169515) • Mosun + GemOx (NCT04313608) • Mosun+platinum based chemo (DHAX or ICE) NCT05464329: Transplant eligible

Frontline: BsAb + CHOP+/- R

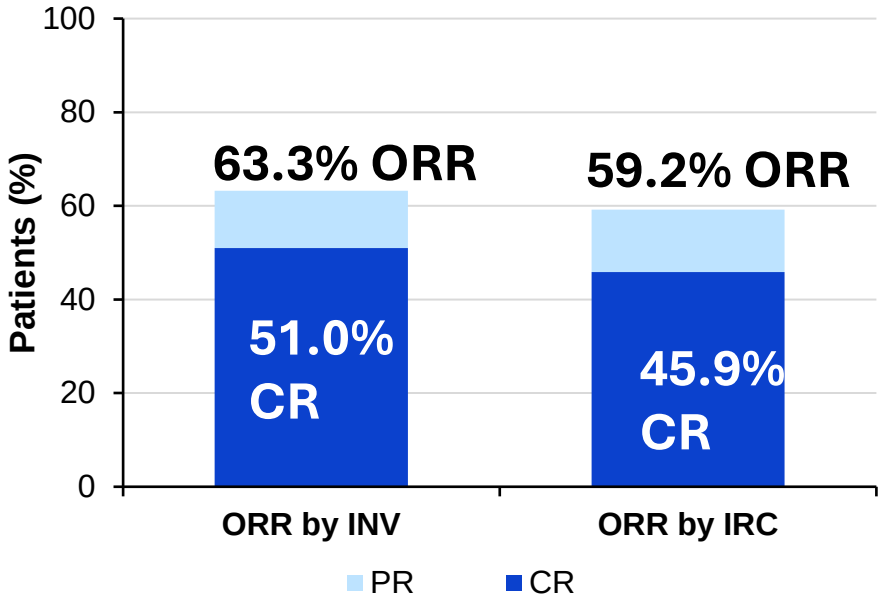
	M+CHOP[1] NCT03677141	**G+RCHOP[2]** NP40126 trial	**E+RCHOP[3]** NCT04663347
Phase, N	Phase 2, 40	Phase 1b, 58	Phase 1/2, 46
Treatment Schedule	M given C1-C6, q3w (except C1) M up to additional 11 Cycles if PR or SD	G given C2-C6, q3w (except C2) G maintenance upto 1 yr	E qw C1-4, q3w C5-6 E maintenance x 1 yy
Age (yrs)	65 (39-79)	68 (21-84)	
mIPI	52.5% ≥ 3 (all ≥ 2)	3 (1-5)	3-5
ORR; CR	95%; 90%	92.9%; 83.9%	100%, 76%
CRS	60%; 0% (gr3)	10.7%, 0% (gr3)	60%, 2% (gr3)
ICANS-like	12.5%	0	1 gr2
Gr5	1 PNA 1 PD	7% (3 COVID19 PNA, 1 IRR due to R)	1 COVID19
Neutropenia	70%; 15%	46.4%	64%
Infection	52.5%	48.2%	n/a
PFS	65.4% (CI: 49.5-81.4) (mFU 32Mo)	DOR: NR (mFU 17.1 mo)	mPFS NR (mFU 11.4Mo)

[1]Olszewski, Blood Adv, 2023; [2]Top M. et al. *Blood* (2023) 142 (Supplement 1): 3085; [3]Clausen et al. Hemasphere 2023 Aug; 7(Suppl): e55140cd

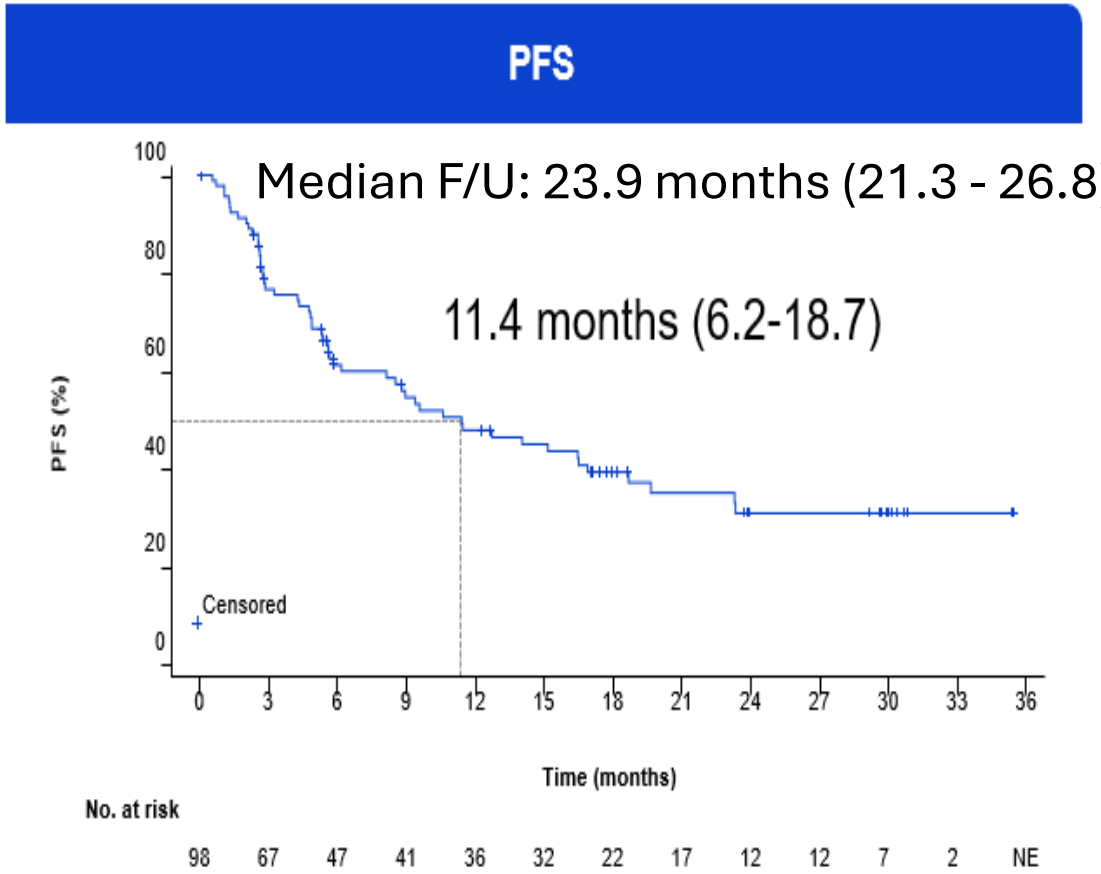
GO40516: Mosunetuzumab IV + Polatuzumab for LBCL

- r/r LBCL, n = 98
- Median age 68 (20-88)
- 2 (1-8) prior regimens

- 78% refractory
- 36% Prior CAR T
- 18.9% HGBCL



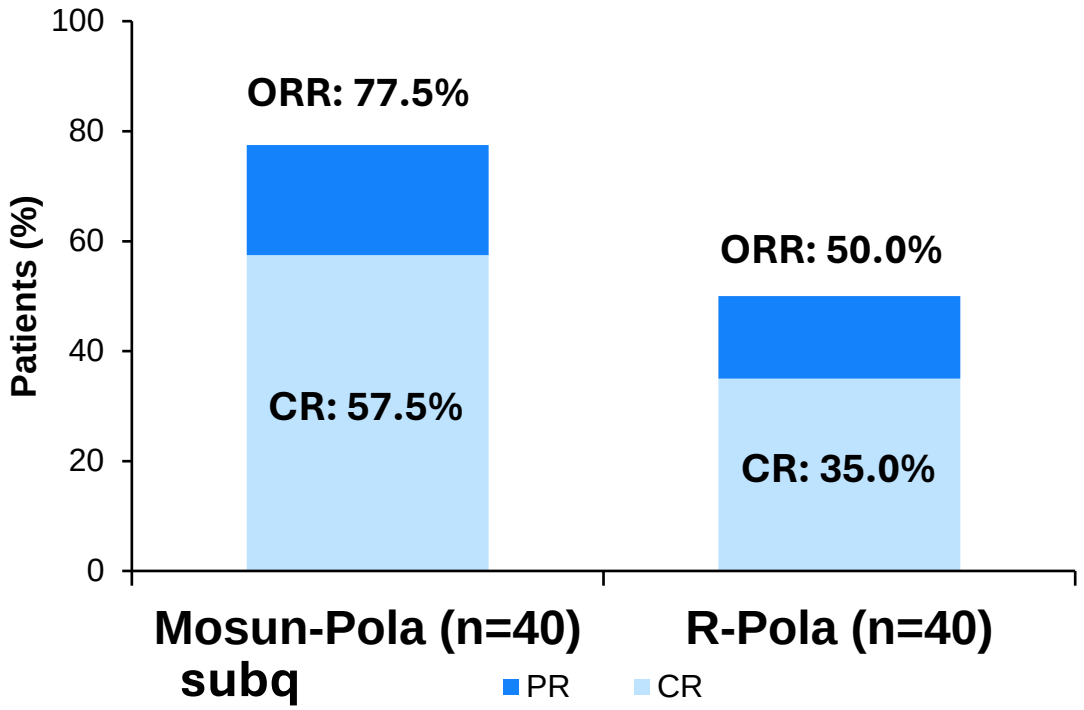
Median DoCR: NR (20.5–NR)

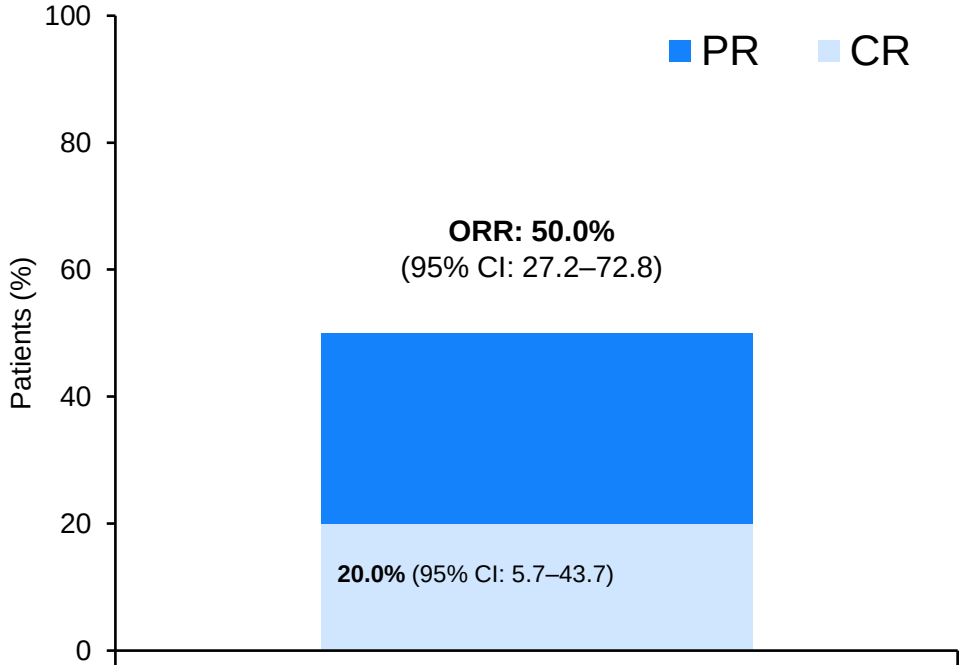


Primary efficacy endpoint of best ORR was met; p=0.0003†

Budde LE et al. Nature Medicine 2024.

GO40516: Mosun (subq)-Pola vs R-Pola





50% R-pola: crossed over to Mosun-pola

Mosun-Pola demonstrated improved efficacy versus R-Pola, with a **ΔORR of 27.5% and ΔCR of 22.5%**

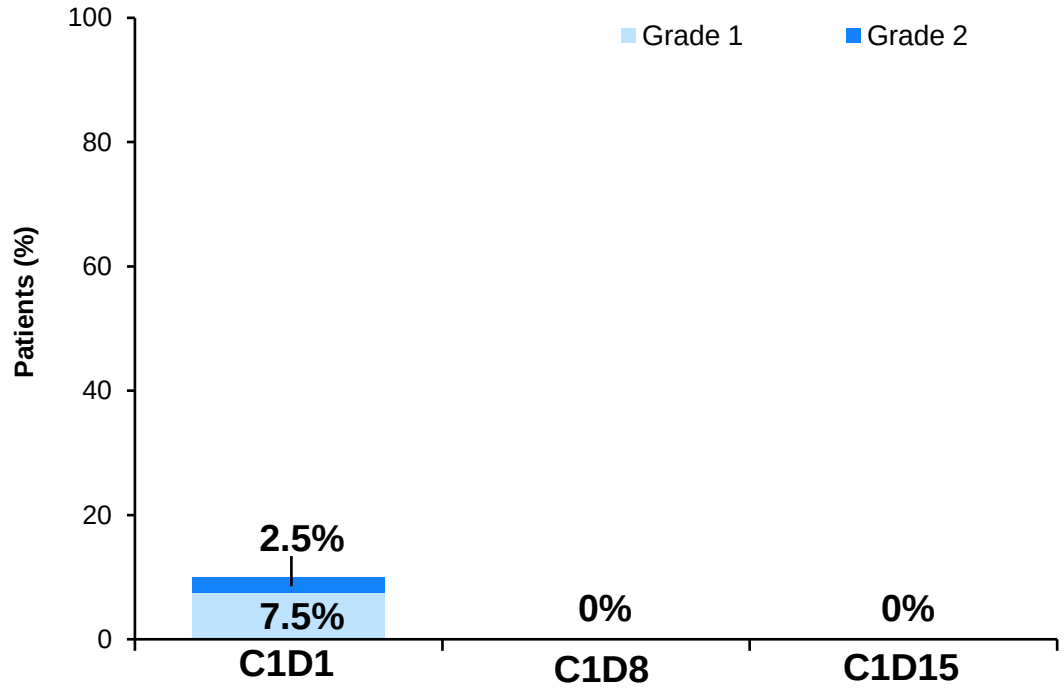
Data cut-off date: January 30, 2024.
PR, partial response.

Chavez J et al. ASH 2024

Safety summary

AE summary, n (%)	Mosun-Pola (n=40)	R-Pola (n=39)
AE	40 (100.0)	39 (100.0)
Treatment-related	37 (92.5)	33 (84.6)
Grade 3/4 AE	22 (55.0)	20 (51.3)
Treatment-related	11 (27.5)	11 (28.2)
Grade 5 AE*	2 (5.0)	1 (2.6)
Treatment-related	1 (2.5)	0
AE leading to treatment discontinuation†	3 (7.5)	2 (5.1)
Treatment-related	1 (2.5)	2 (5.1)
SAE	13 (32.5)	10 (25.6)
Treatment-related	4 (10.0)	0

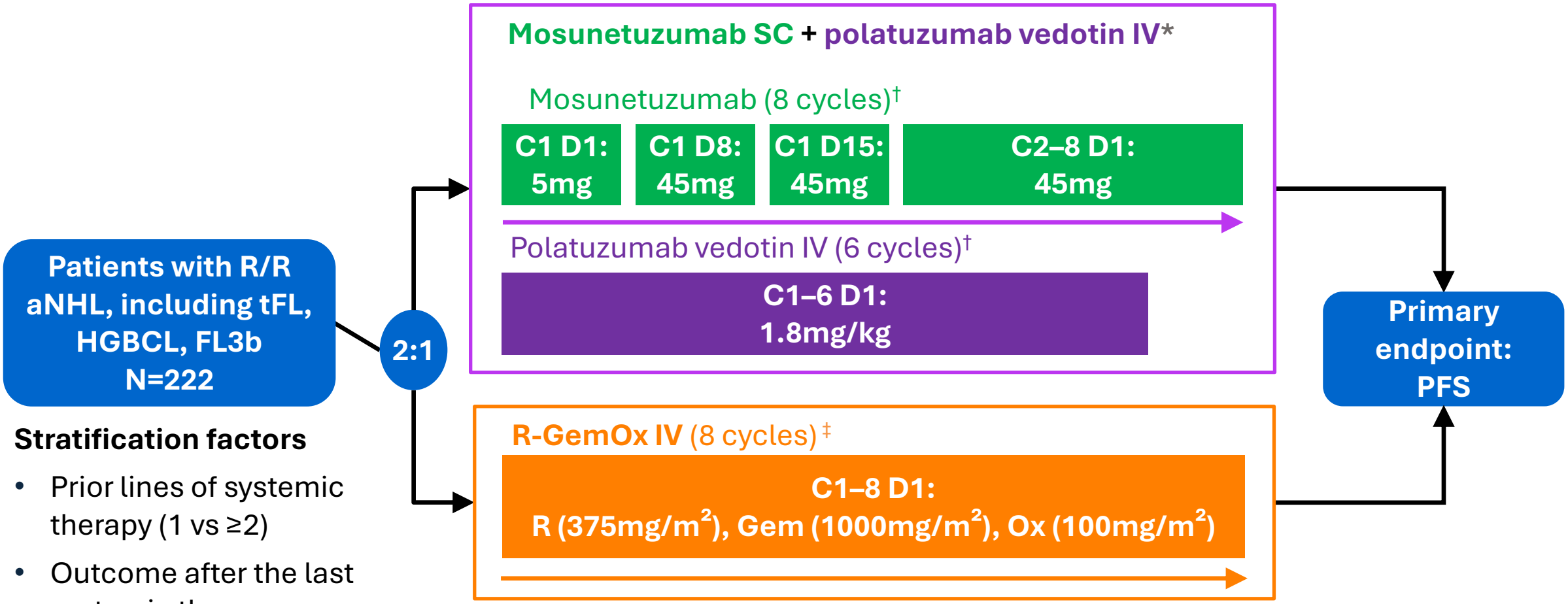
CRS by cycle and grade



CRS rates with Mosun-Pola **were infrequent, of low grade, and limited to Cycle 1**

Data cut-off date: January 30, 2024. *All events occurred during Cycle 1.
ASTCT, American Society for Transplantation and Cellular Therapy criteria.

SUNMO (NCT05171647)
a randomized, global Phase III trial in 2L+ aLBCL



Stratification factors

- Prior lines of systemic therapy (1 vs ≥2)
- Outcome after the last systemic therapy (relapsed vs refractory)

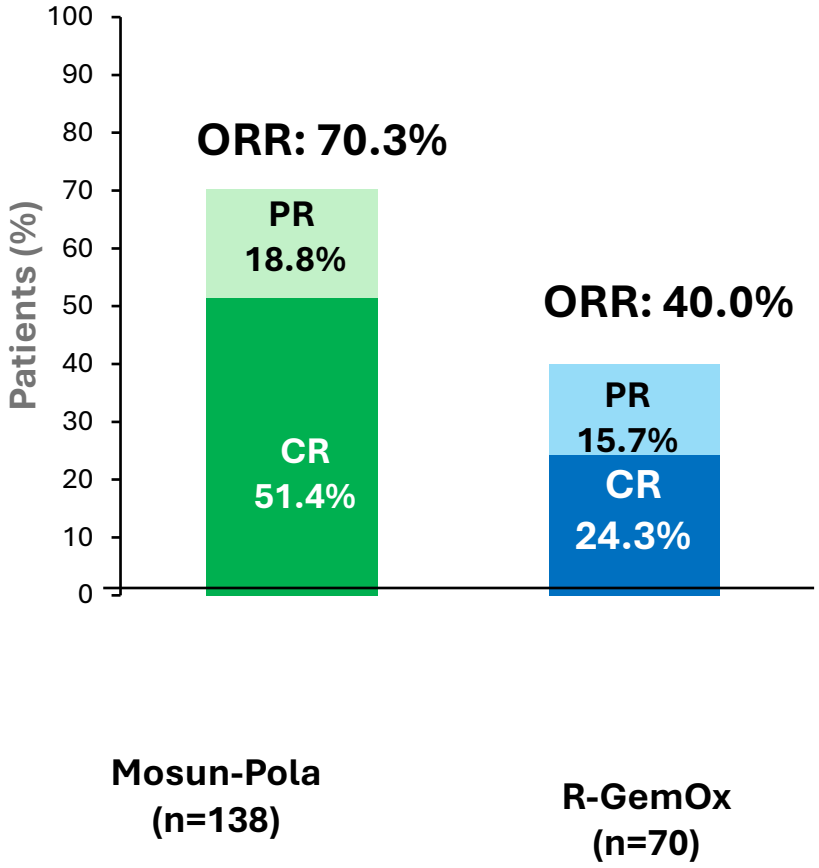
Baseline characteristics

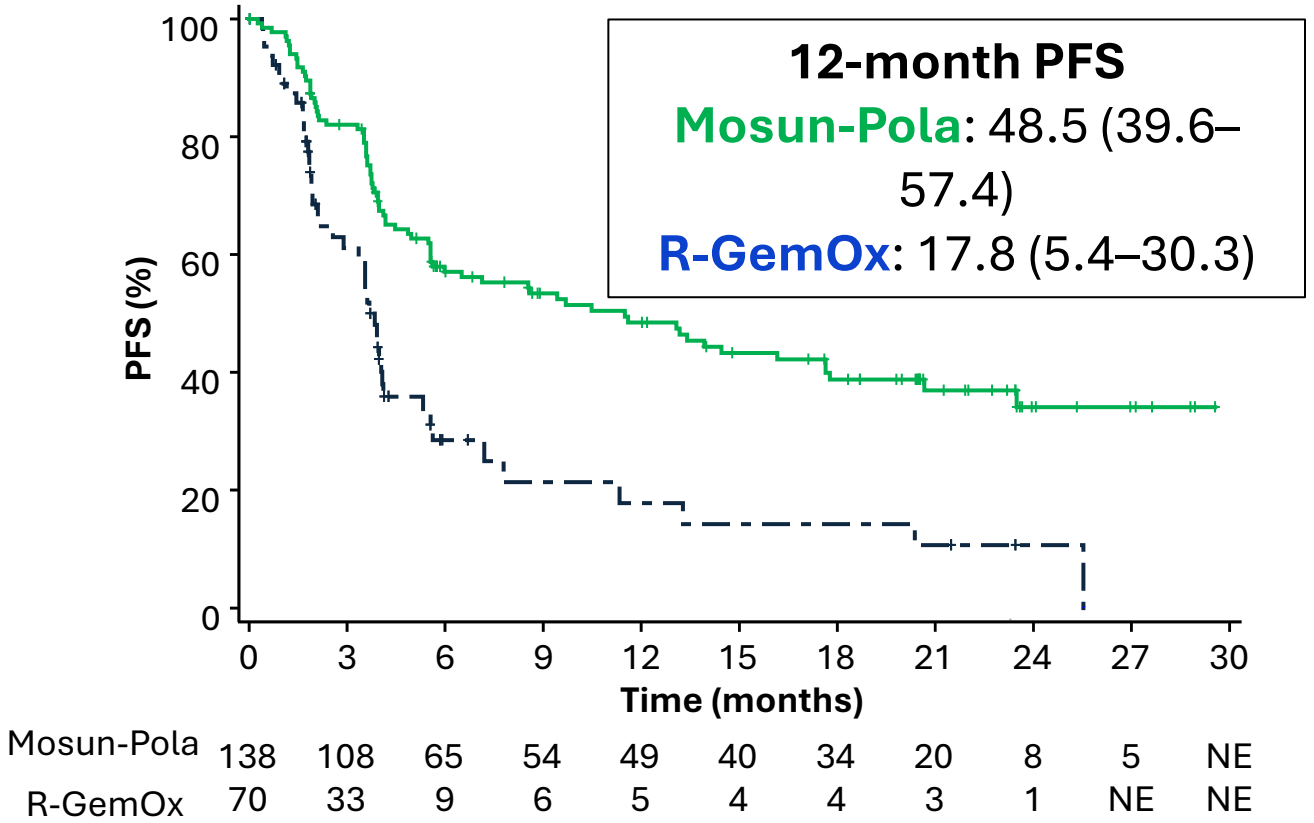
% (n), unless otherwise stated		Mosun-Pola (n=138)	R-GemOx (n=70)
Age, years	Median (range) ≥65 years	62 (23–87) 39.1% (54)	63 (29–85) 45.7% (32)
Sex	Male	55.1% (76)	64.3% (45)
Race	Asian Black or African American White Other/Unknown	40.6% (56) 2.9% (4) 44.2% (61) 12.3% (17)	37.1% (26) 1.4% (1) 54.3% (38) 7.1% (5)
ECOG PS	0 1 2	50.0% (69) 37.0% (51) 13.0% (18)	57.1% (40) 41.4% (29) 1.4% (1)
NHL subtypes	DLBCL HGBCL FL3b	79.0% (109) 18.8% (26) 2.2% (3)	77.1% (54) 20.0% (14) 2.9% (2)

% (n), unless otherwise stated		Mosun-Pola (n=138)	R-GemOx (n=70)
Transformed FL*	Yes No	*(n=135)* 12.6% (17) 87.4% (118)	*(n=68)* 8.8% (6) 91.2% (62)
Ann Arbor Stage	I–II III–IV	24.6% (34) 75.4% (104)	20.0% (14) 80.0% (56)
Bulky disease (≥10cm)	Yes No	20.3% (28) 79.7% (110)	7.1% (5) 92.9% (65)
Number of prior lines of therapy	Median (range) 1 ≥2	2 (1–9) 44.2% (61) 55.8% (77)	2 (1–5) 42.9% (30) 57.1% (40)
Primary refractory	Yes	57.2% (79)	60.0% (42)
Refractory to last prior therapy	Yes	70.3% (97)	68.6% (48)

Clinical cut-off date: 17 February, 2025.
*Three patients in the Mosun-Pola arm and two patients in the R-GemOx arm had FL3b and were not included in the denominator for transformed FL.
3b, Grade 3b; ECOG, Eastern Cooperative Oncology Group; NHL, non-Hodgkin lymphoma; PS, performance score.

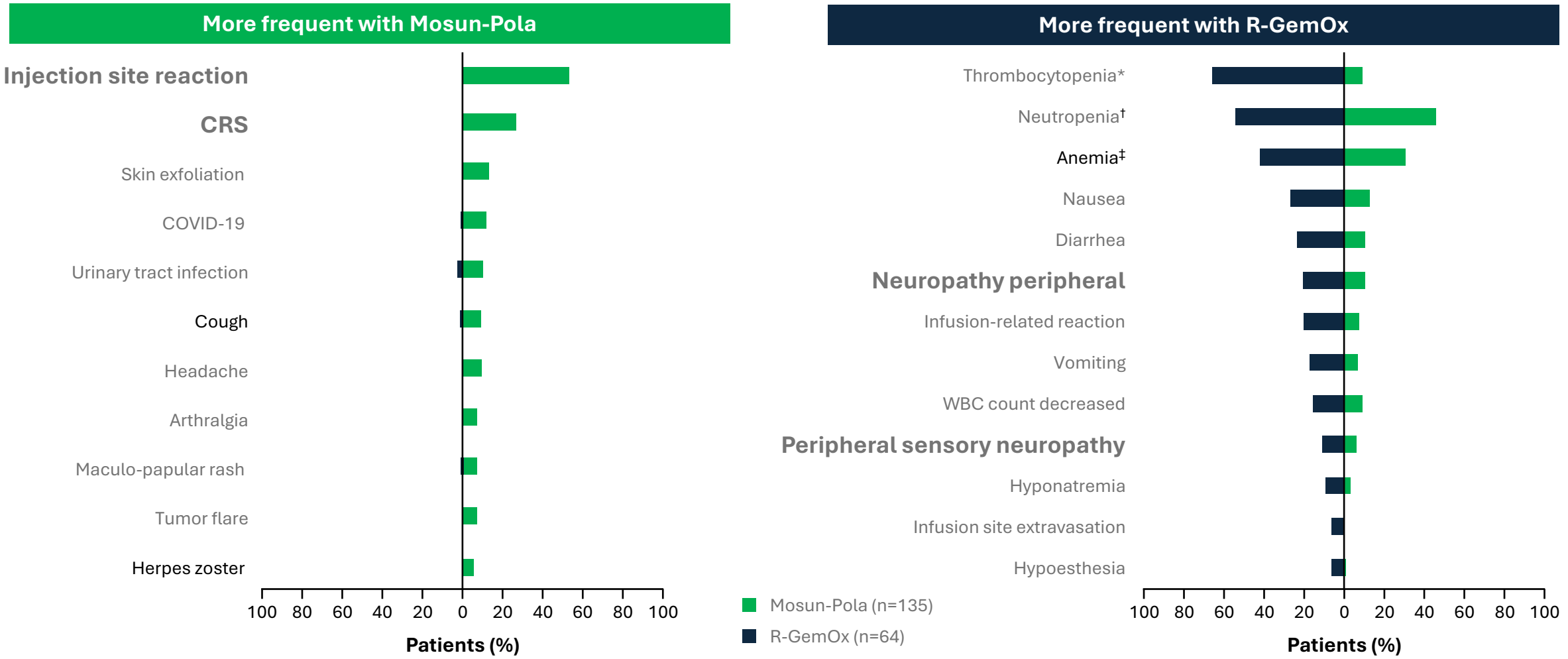
Mosun-Pola significantly increased ORR and PFS versus R-GemOx





Clinical cut-off date: 17 February, 2025.
*Descriptive P value. CR, complete response; PR, partial response.

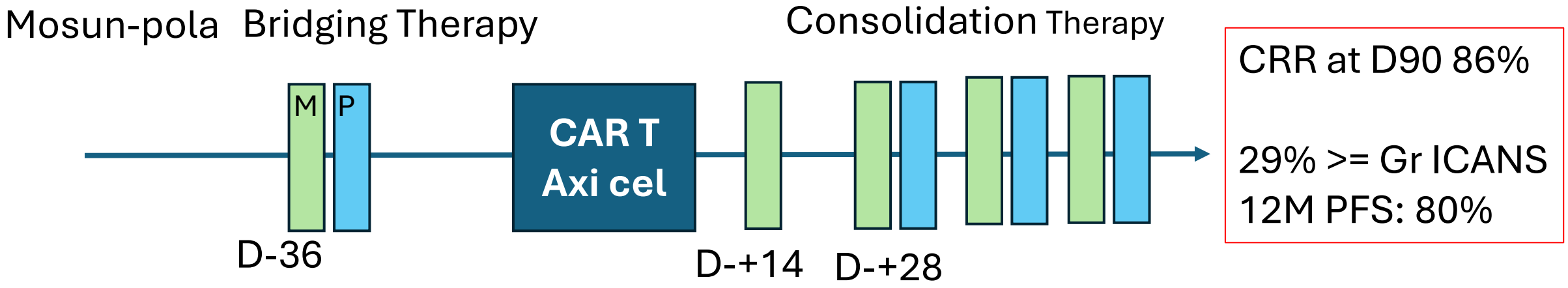
AEs with a difference of at least 5% between treatment arms



Clinical cut-off date: 17 February, 2025. *Includes thrombocytopenia and platelet count decrease. †Includes neutropenia/neutrophil count decrease. ‡Includes anemia and hemoglobin decrease.
WBC, white blood cell.

Mosunetuzumab & CAR T

NCT05260957



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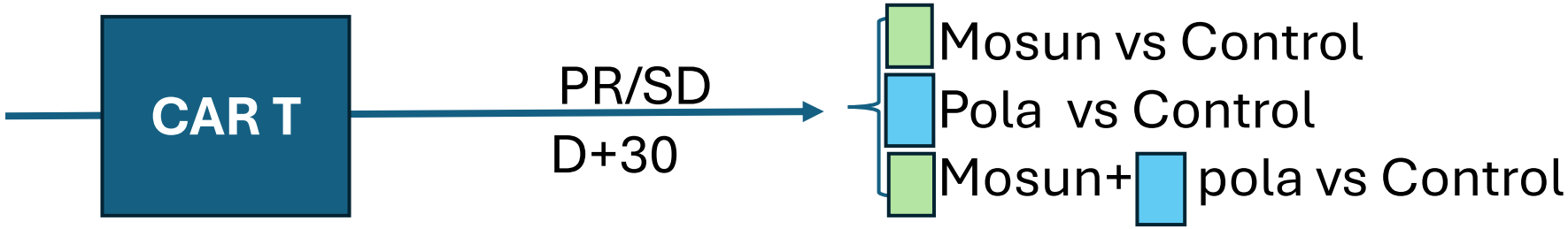

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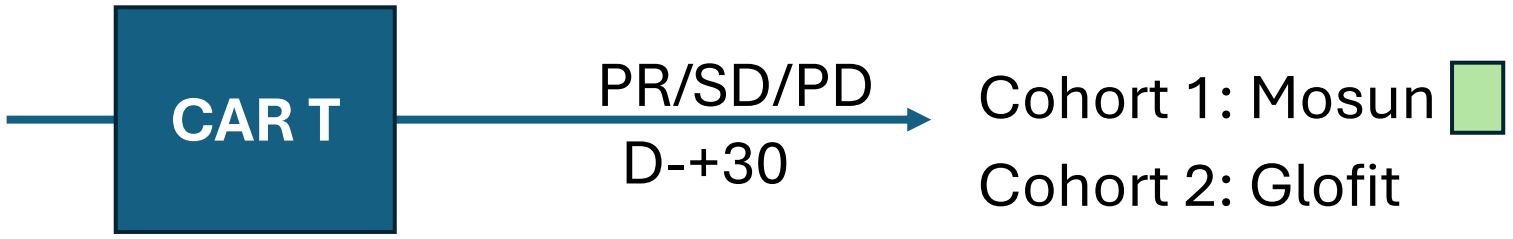


Mosun + Golcadomide — next-gen CELMoD pairing

Andreadis et al. ASH 2025 — phase 1b dose escalation, N=35 mosun arm

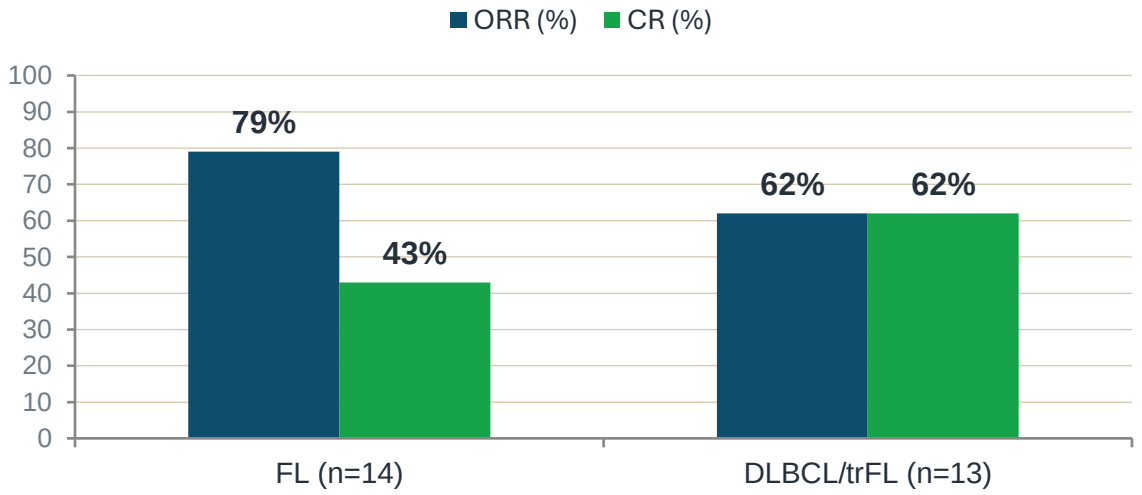
What is golcadomide?

Oral CELMoD (cereblon E3 ligase modulator). Degrades Ikaros/Aiolos more deeply than lenalidomide → direct B-cell kill + T-cell reinvigoration. Penetrates lymphoid tissue.

Population (N=35 mosun arm)

- R/R FL or DLBCL/trFL
- Median 3 prior lines (range 1–6)
- 29% prior CAR-T · 91% stage III/IV
- CAR-T ineligible (per protocol)

Best response by histology (pooled across 0.1/0.2/0.4 mg)



Standout findings

- 100% ORR/CR in FL at 0.4 mg golcadomide
- 5 of 8 prior-CAR-T patients achieved CR
- CRS 42.9%, 0% grade ≥3 — all resolved · Median time to response 2.6 months · No fatal AEs

Mosun+Golca, next-gen CELMoD pairing

Key inclusion criteria

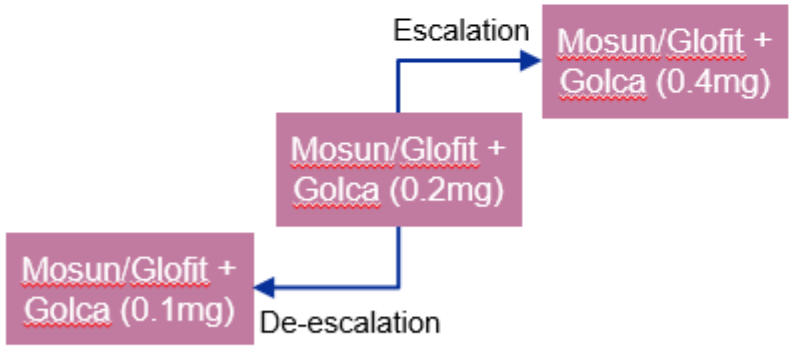
- R/R DLBCL, trFL, or FL Grade 1–3a
- ≥2 prior lines of therapy for dose escalation and ≥1 prior line of therapy for dose expansion
- CAR T-cell therapy ineligible

Endpoints

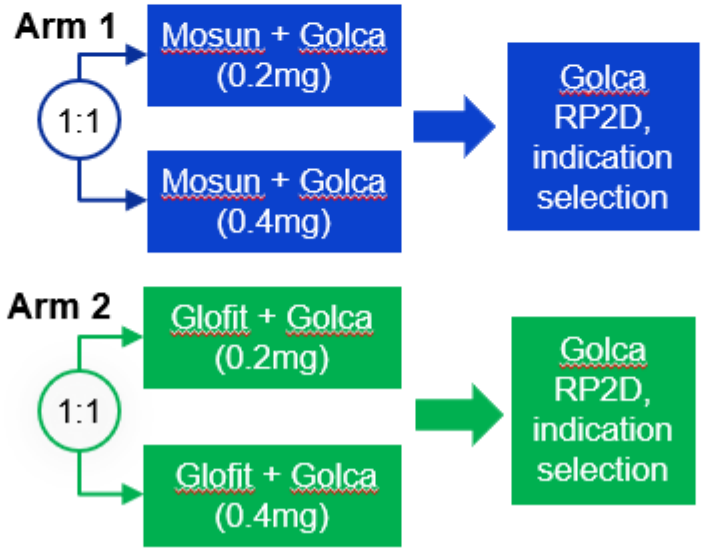
- **Primary**: Safety, DLTs, and Golca RP2D selection
- **Key secondary**: Investigator-assessed best ORR and CR rate (by Lugano 2014 criteria[1])

Study treatment administration

Dose escalation: 3L+ R/R NHL (n=3–9 in each cohort)



Dose expansion: 2L+ R/R FL, R/R DLBCL (n=20 in each cohort)



Mosun SC

- Fixed-duration treatment (5/45/45mg)*
- CRS† mitigation: C1 SUD (5mg on C1D1, 45mg on D8 and 15; 21- or 28-day cycle)
- No mandatory hospitalization

Glofit IV

- Fixed-duration treatment (2.5/10/30mg)‡
- CRS† mitigation: obinutuzumab pretreatment on C1D1 and C1 SUD (2.5mg on C1D8, 10mg on C1D15; 21-day cycle)
- Hospitalization was required 24 hours after first dose (C1D8) of Glofit

Golca oral§

- Arm 1: given daily from D1–14 in C1 or C2 onwards
- Arm 2: given daily from D1–10 in C2 or C3 onwards

Andreadis C, ASH 2025

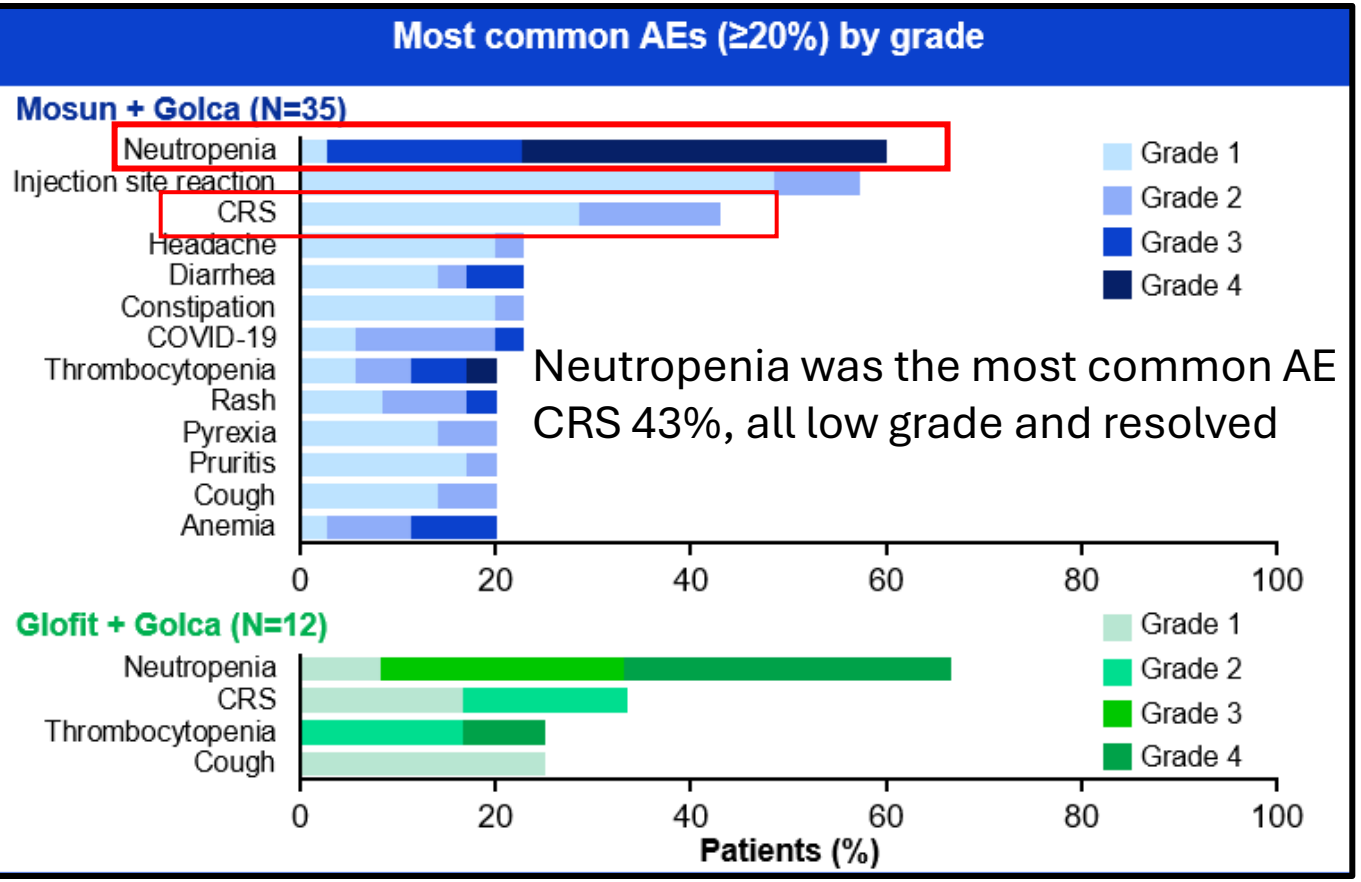
Golca + bispecific: patient characteristics

n (%) unless otherwise stated		Mosun + Golca (N=35)	Glofit + Golca (N=12)
Median age, years (range)		63.0 (30–83)	59.5 (37–76)
Male		22 (62.9)	6 (50.0)
Race	Asian	2 (5.7)	0
	Black or African American	2 (5.7)	0
	White	29 (82.9)	11 (91.7)
	Not reported or unknown	2 (5.7)	1 (8.3)
Ethnicity	Hispanic or Latino	1 (2.9)	2 (16.7)
	Not Hispanic or Latino	28 (80.0)	10 (83.3)
	Not reported or unknown	6 (17.1)	0
ECOG PS	0	19 (54.3)	8 (66.7)
	1	16 (45.7)	4 (33.3)
Ann Arbor stage III/IV		32 (91.4)	9 (75.0)
NHL histology	FL	20 (57.1)	9 (75.0)
	trFL/DLBCL	14 (40.0)	3 (25.0)
Median lines of prior therapy, n (range)		3.0 (1–6)	2.0 (1–4)
Prior therapies	CAR T-cell therapy	10 (28.6)	5 (41.7)
	Anti-CD20	34 (97.1)	12 (100)
	ASCT	2 (5.7)	1 (8.3)
	IMiDs	11 (31.4)	4 (33.3)

Andreadis C, ASH 2025

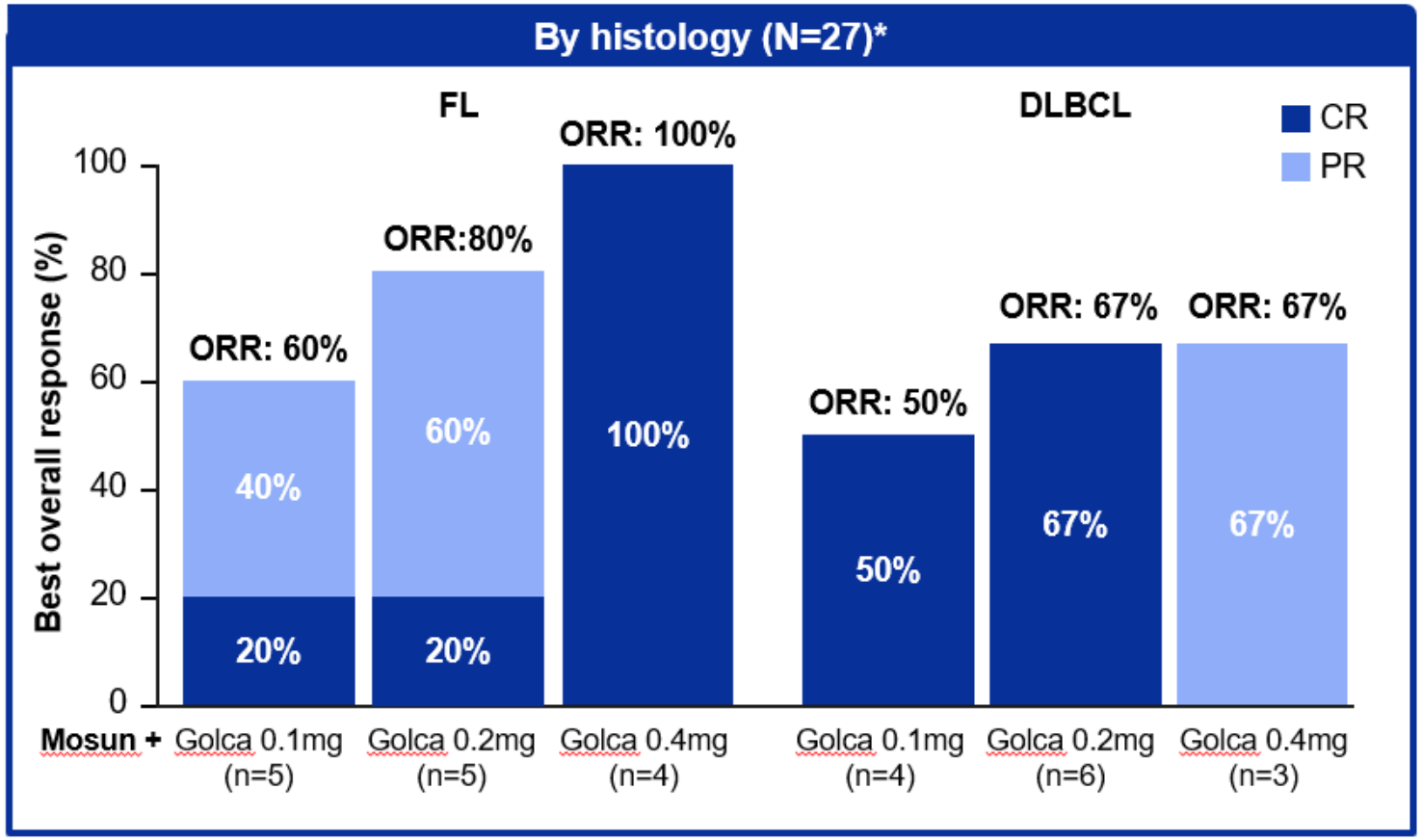
Golca + bispecific: manageable toxicity

n (%) unless otherwise stated	Mosun + Golca (N=35)	Glofit + Golca (N=12)
AE	35 (100)	12 (100)
Grade 3/4 AE	26 (74.3)	8 (66.7)
Serious AE	23 (65.7)	6 (50.0)
AESI*	13 (37.1)	4 (33.3)
Grade 5 (fatal) AE	0	0
AE leading to treatment discontinuation	6 (17.1)†	0
AE leading to dose modification/ interruption	19 (54.3)‡	6 (50.0)§



Andreadis C, ASH 2025

Golca + mosun: efficacy

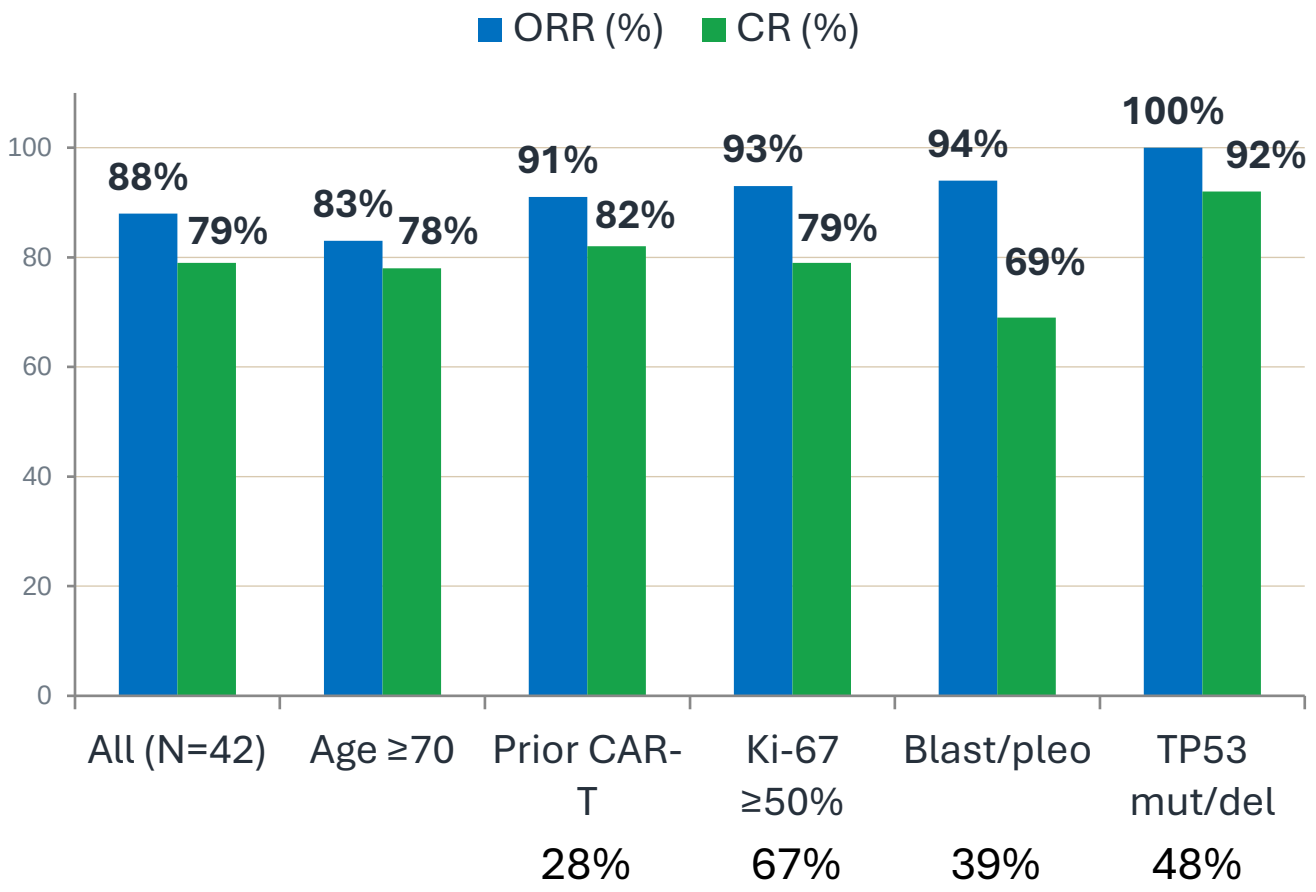


- Median time to first response for all patients (N=27)*: 2.6 months (range: 2–4)
- Response in patients who received prior CAR T-cell therapy (n=8):
  - Overall, 5 patients achieved a CR
    - Two patients had FL and one achieved CR
    - Six patients had DLBCL and four achieved a CR

High response rates were observed in patients with FL and DLBCL including those who received prior CAR T-cell therapy

Andreadis C, ASH 2025

Mosun + Pola in R/R post-BTKi MCL: Phase 2 expansion, N=42



- 71% patients had at least 3 high risk features.
- Median LOT: 3 (2-9)
- Median age: 68 (48-82)

18.6 mo
Median PFS

20.7 mo
Median OS

75%
12-mo PFS

83%
12-mo OS

Safety highlights

CRS 43% — all G1–2, no G≥3, all resolved in C1
ICANS: 1 G2 event (resolved)
G3-4 neutropenia 41%
G5 infections 12%

Budde et al. ICML 2025 · Wang et al. SOHO 2025; Budde et al. Blood, 2026 ·

Conclusions

- Mosunetuzumab is moving up in clinical development in B cell lymphomas.
- Its high benefit-risk ratio, outpatient use, and q 3w dosing & fixed duration schedule make it an attractive bispecific antibody to be an excellent partner in a chemo free/chemo-lyte combination regimen.
- Questions remain

    Will SUNMO be approved in the second line LBCL use?

    Who are the best partners?

    How to optimally sequence with other regimens?