Disclosures: Wonseog Kim

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Mosunetuzumab plus polatuzumab vedotin is superior to R-GemOx in transplant-ineligible patients with R/R LBCL: primary results of the Phase III SUNMO trial

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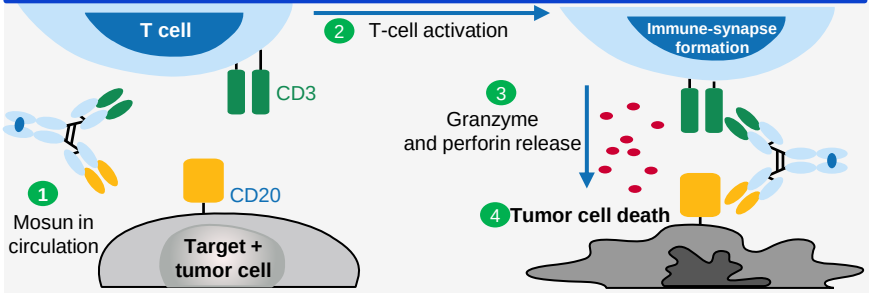
Background

- Patients with R/R LBCL unable to receive curative-intent therapies such as CAR T-cell or ASCT have a poor prognosis
  - Barriers to curative therapies may include lack of response to prior therapy, age, frailty, and/or logistical barriers
  - Toxicities of T-cell directed therapies, such as CRS, may limit access for patients and burden healthcare systems

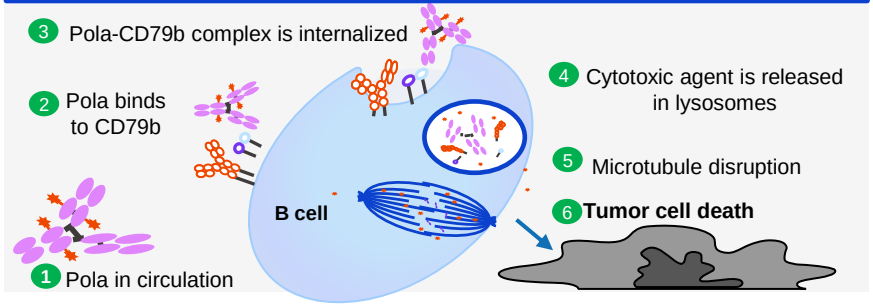
Mosunetuzumab

CD20xCD3 T-cell engaging bispecific antibody[1]



Polatuzumab vedotin

CD79b targeting antibody-drug conjugate[2]



- **Mosun-Pola** showed **highly durable responses** and a **manageable safety profile**, as an outpatient regimen, in the Phase II study[3,4]

We present the efficacy and safety of **Mosun-Pola** versus **R-GemOx** in **transplant-ineligible patients with R/R LBCL** after **≥1 prior line of therapy** from the global, randomized, Phase III **SUNMO trial** (NCT05171647)

ASCT, autologous stem cell transplant; CAR, chimeric antigen receptor; CRS, cytokine release syndrome, ICANS, immune effector-cell associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; Mosun-Pola, mosunetuzumab plus polatuzumab vedotin; R-GemOx, rituximab plus gemcitabine and oxaliplatin; R/R, relapsed/refractory.

1. Sun LL, et al. Sci Transl Med 2015;7:287ra70; 2. Dornan D, et al. Blood 2009;114:2721–9;
3. Budde LE, et al. Nat Med 2024;30:229–39;
4. Chavez JC, et al. ASH 2024; oral presentation #989.

Study design

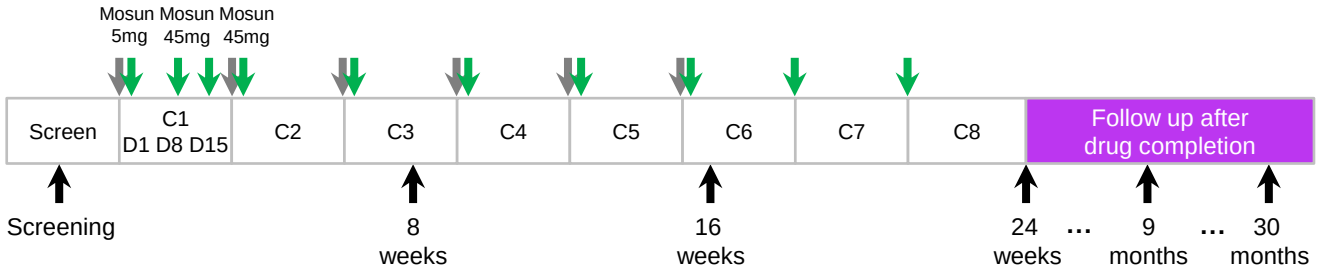
Key eligibility

R/R LBCL with ≥1 prior therapy and ASCT-ineligible:

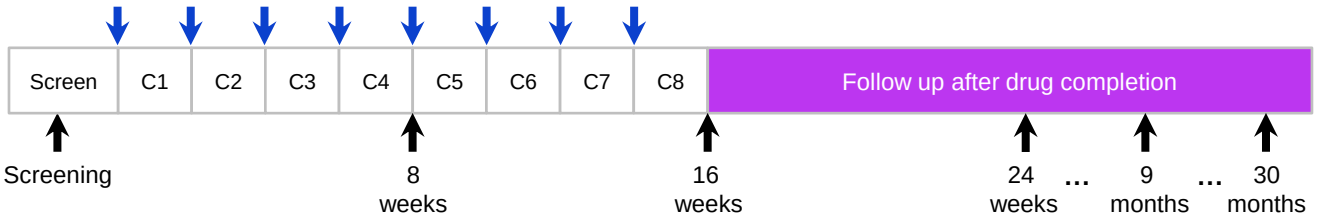
- DLBCL NOS
- Transformed FL
- HGBCL
- Grade 3B FL

2:1

Outpatient Mosun SC (8 cycles) + Pola IV (6 cycles) (21-day cycles)



R-GemOx IV (8 x 14–21-day cycles*)



Stratification factors

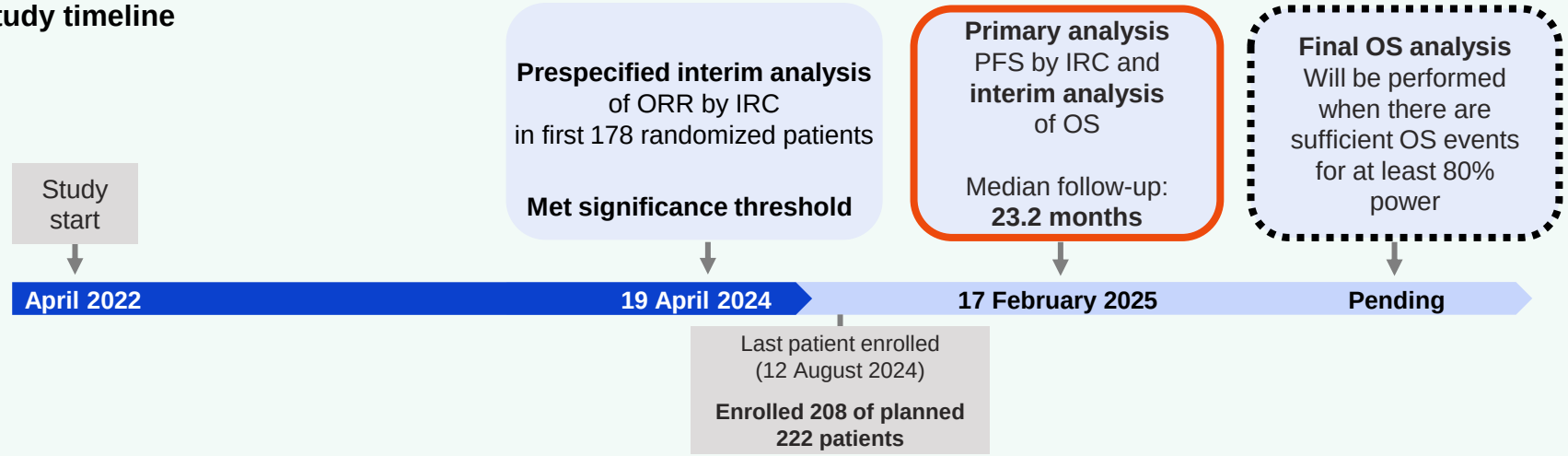
- 1 vs ≥2 prior lines of systemic therapy
- Relapsed vs refractory disease

*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.

SUNMO: Key endpoints and analysis timeline

Key endpoints	
Dual primary endpoints	Objective response rate (ORR) by IRC assessment Progression-free survival (PFS) by IRC assessment
Key secondary endpoints	Overall survival (OS)
Safety endpoints	Incidence, nature, and severity of adverse events (AEs)

Study timeline



IRC, independent review committee.

Baseline characteristics

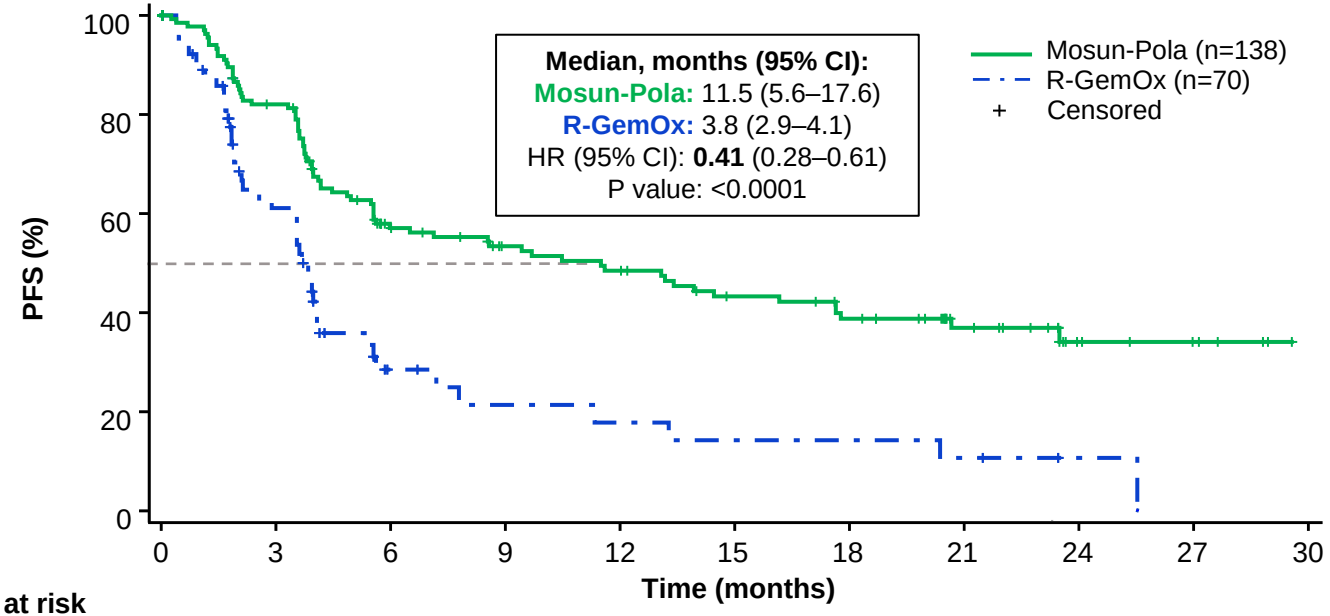
% (n), unless otherwise stated		Mosun-Pola (n=138)	R-GemOx (n=70)
Age, years	Median (range) ≥65 years	62 (23–87) 39.1% (54)	63 (29–85) 45.7% (32)
Sex	Male	55.1% (76)	64.3% (45)
Race	Asian Black or African American White Other/Unknown	40.6% (56) 2.9% (4) 44.2% (61) 12.3% (17)	37.1% (26) 1.4% (1) 54.3% (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*	*(n=135)* 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 prolonged progression-free survival versus R-GemOx

Primary endpoint: Progression-free survival by IRC



n at risk

Mosun-Pola	138	108	65	54	49	40	34	20	8	5	NE
R-GemOx	70	33	9	6	5	4	4	3	1	NE	NE

Mosun-Pola demonstrates a 59% risk reduction for progression or death compared with R-GemOx

Clinical cut-off date: 17 February, 2025. PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first.
CI, confidence interval; HR, hazard ratio; NALT, new anti-lymphoma therapy; NE, non estimable.

Mosun-Pola significantly prolonged progression-free survival versus R-GemOx

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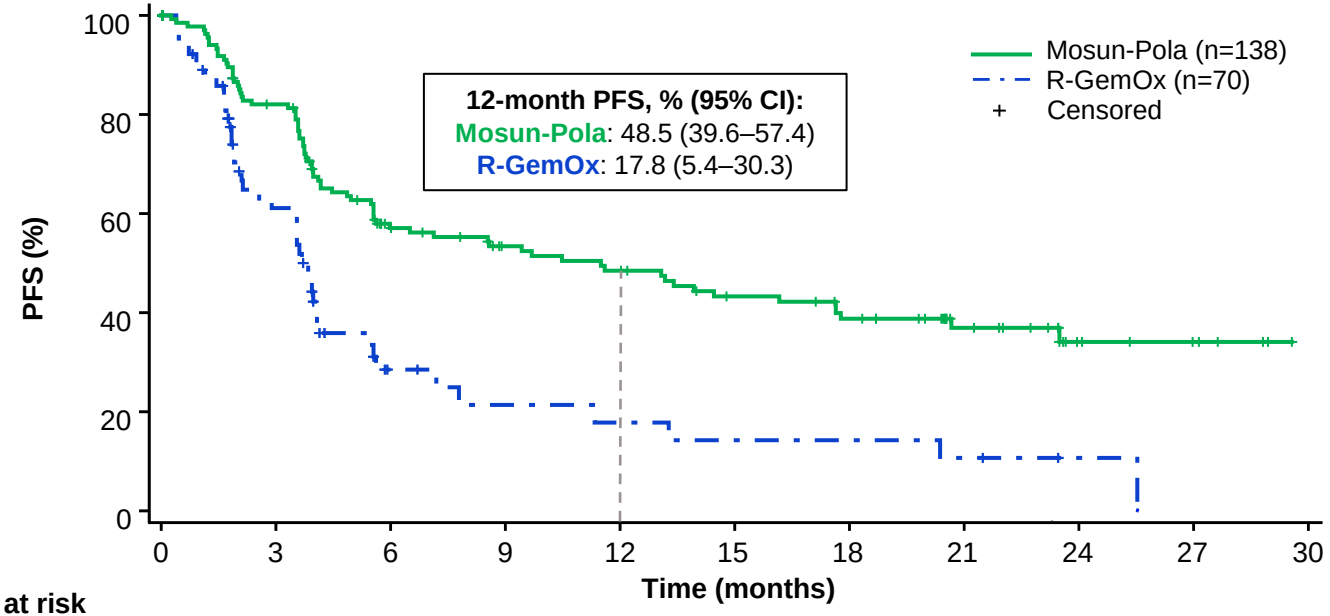

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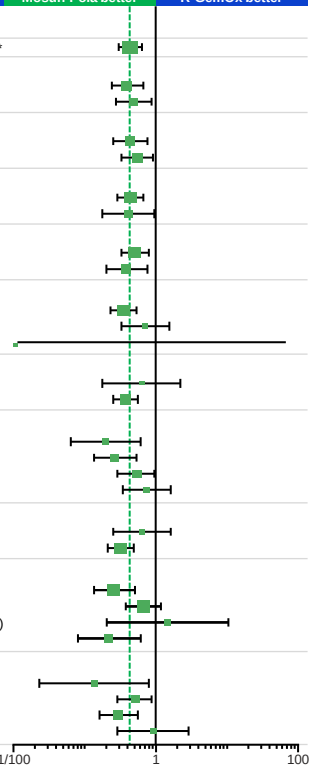
Exploratory analysis of progression-free-survival in pre-specified subgroups

		Mosun-Pola (n=138)			R-GemOx (n=70)				
Baseline risk factors	Total n	n	Events	Median (months)	n	Events	Median (months)	HR	95% CI
All patients	208	138	76	11.5	70	45	3.8	0.41	(0.28–0.61)*
Age group									
<65	122	84	46	11.5	38	25	3.5	0.39	(0.23–0.64)
≥65	86	54	30	13.1	32	20	4.0	0.47	(0.27–0.84)
Number of prior lines of therapy									
1	91	61	32	14.5	30	22	3.6	0.38	(0.22–0.67)
≥2	117	77	44	8.6	40	23	3.9	0.49	(0.29–0.82)
Status to last prior therapy									
Refractory	145	97	63	5.5	48	36	2.6	0.39	(0.26–0.60)
Relapse	63	41	13	NE	22	9	11.3	0.37	(0.16–0.88)
Status to first prior therapy									
Refractory	121	79	54	4.2	42	31	2.6	0.46	(0.29–0.72)
Relapse	87	59	22	23.5	28	14	5.6	0.35	(0.18–0.70)
NHL subtype									
DLBCL	163	109	58	11.5	54	34	3.5	0.38	(0.24–0.59)
HGBCL	40	26	18	9.7	14	9	4.0	0.78	(0.35–1.77)
FL3b	5	3	0	NE	2	2	12.0	<0.01	(0.00–NE)
trFL									
Yes	23	17	8	13.2	6	4	11.3	0.70	(0.19–2.65)
No	185	121	68	9.4	64	41	3.6	0.41	(0.28–0.62)
IPI risk factors at study entry									
Low (0–1)	42	27	10	NE	15	7	3.9	0.21	(0.06–0.66)
Low-intermediate (2)	61	40	16	23.5	21	14	2.9	0.28	(0.14–0.59)
High-intermediate (3)	74	49	32	5.6	25	15	3.8	0.57	(0.30–1.07)
High (4–5)	31	22	18	3.5	9	9	3.5	0.81	(0.36–1.82)
Bulky disease >10cm									
Yes	33	28	22	3.6	5	5	2.6	0.71	(0.26–1.89)
No	175	110	54	16.2	65	40	3.8	0.35	(0.23–0.53)
COO category (central)									
ABC	69	42	19	17.8	27	18	4.0	0.24	(0.12–0.49)
GCB	76	56	41	5.0	20	15	3.7	0.67	(0.37–1.21)
Unclassified	20	15	8	5.6	5	1	NE	1.53	(0.19–12.43)
Missing	38	22	8	NE	16	9	3.5	0.20	(0.07–0.60)
Region at enrollment									
US and Canada	20	13	2	NE	7	3	1.9	0.13	(0.02–0.79)
Latin America	85	59	41	5.3	26	20	3.5	0.50	(0.29–0.87)
East Asia	78	53	27	17.6	25	17	3.8	0.29	(0.16–0.56)
Rest of world	25	13	6	NE	12	5	25.5	0.94	(0.28–3.07)



Mosun-Pola improved PFS in clinically relevant subgroups, including stratification factors:

- relapsed vs refractory
- 2L vs 3L+

Clinical cut-off date: 17 February, 2025. *Stratified (unstratified HR, 0.43 [95% CI: 0.29–0.63]). 2L, second line; 3L+, third or later line; ABC, activated B-cell; COO, cell of origin; GCB, germinal center B-cell; IPI, International Prognostic Index; trFL, transformed lymphoma.

Exploratory analysis of progression-free-survival in pre-specified subgroups

Baseline risk factors	Total n	Mosun-Pola (n=138) n	Events	Median (months)	R-GemOx (n=70) n	Events	Median (months)	HR	95% CI
All patients	208	138	76	11.5	70	45	3.8	0.41	(0.28–0.61)*
Age group									
<65	122	84	46	11.5	38	25	3.5	0.39	(0.23–0.64)
≥65	86	54	30	13.1	32	20	4.0	0.47	(0.27–0.84)
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≥2	117	77	44	8.6	40	23	3.9	0.49	(0.29–0.82)
Status to last prior therapy									
Refractory	145	97	63	5.5	48	36	2.6	0.39	(0.26–0.60)
Relapse	63	41	13	NE	22	9	11.3	0.37	(0.16–0.88)
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Yes	33	28	22	3.6	5	5	2.6	0.71	(0.26–1.89)
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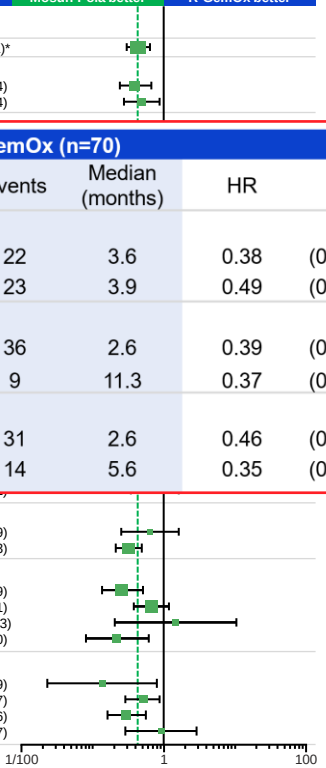
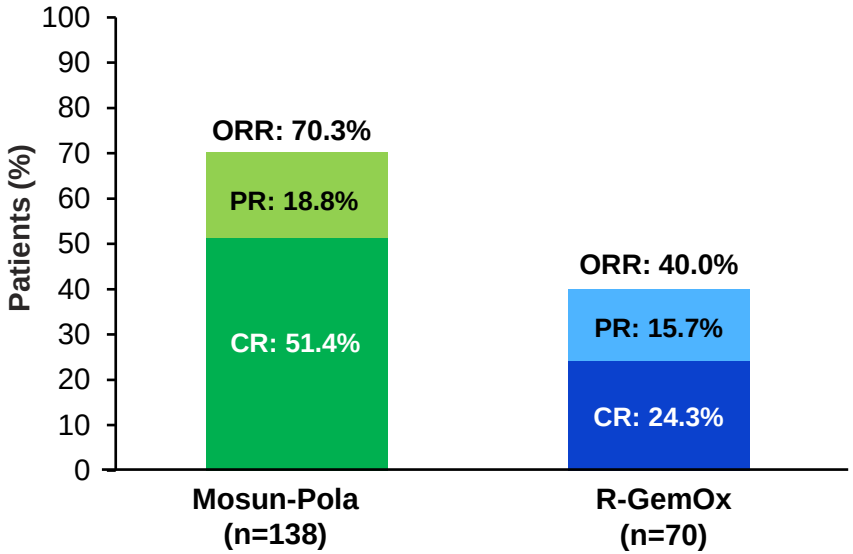


Clinical cut-off date: 17 February, 2025. *Stratified (unstratified HR, 0.43 [95% CI: 0.29–0.63]). 2L, second line; 3L+, third or later line; ABC, activated B-cell; COO, cell of origin; GCB, germinal center B-cell; IPI, International Prognostic Index; trFL, transformed lymphoma.

Mosun-Pola significantly increased overall response rate versus R-GemOx

Primary Endpoint: Response rates at the primary analysis



Improvement in ORR: Mosun-Pola versus R-GemOx

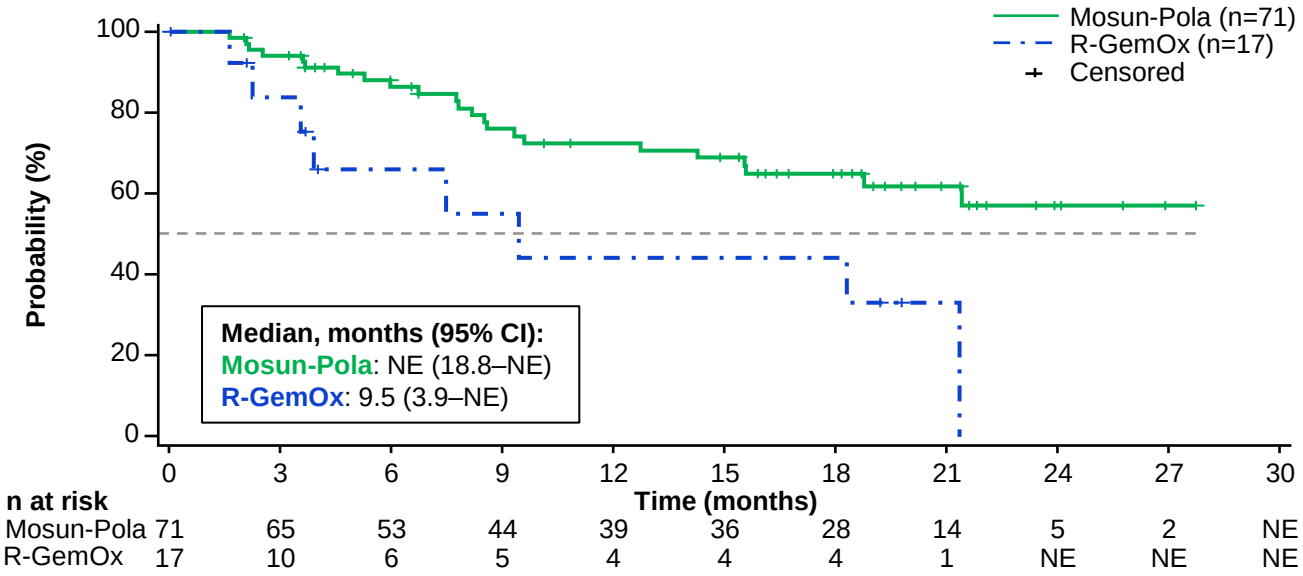
ORR by IRC, % (95% CI)	Mosun-Pola	R-GemOx	ΔORR (95% CI)	P value
Interim analysis	(n=119) **69.7%** (60.7–77.8)	(n=59) **44.1%** (31.2–57.6)	25.7% (9.6–41.8)	0.0008
Primary analysis	(n=138) **70.3%** (61.9–77.8)	(n=70) **40.0%** (28.5–52.4)	30.3% (15.7–44.9)	<0.0001*

Mosun-Pola doubled the CR rate and improved the ORR by 30% compared with R-GemOx

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

Complete responses were durable with Mosun-Pola

Duration of complete response



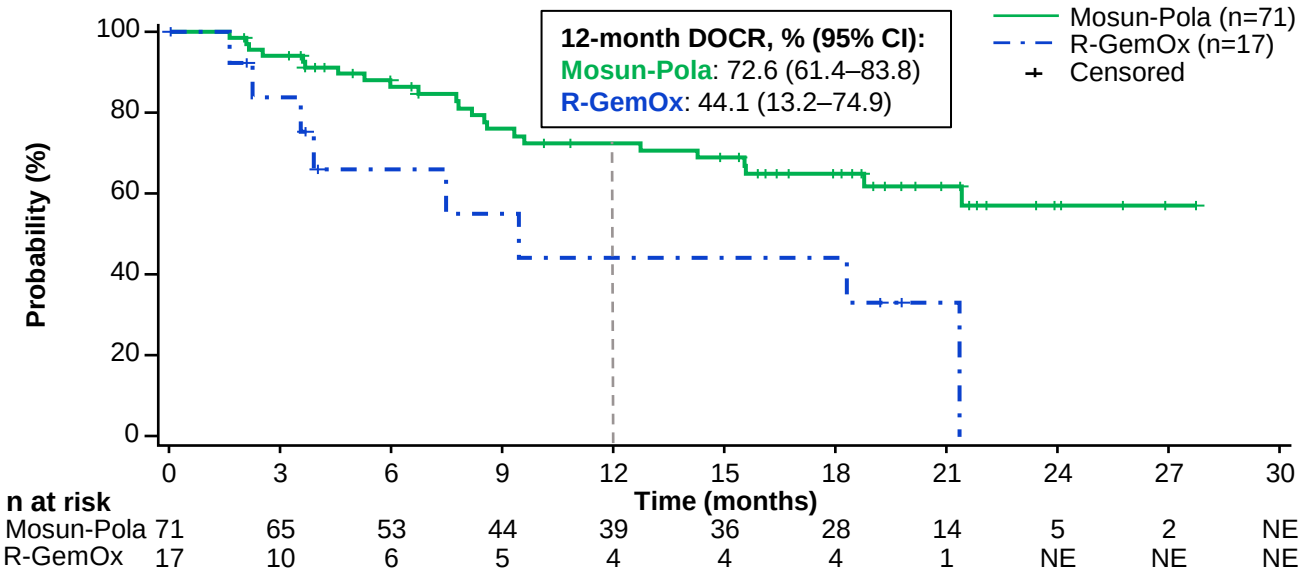
Nearly 75% of patients with a CR were still in remission with Mosun-Pola at 1 year

Mosun-Pola achieved duration remission in most patients with a complete response

Clinical cut-off date: 17 February, 2025.
Median time to first CR was 1.9 months (range 1–6) with Mosun-Pola and 3.6 months (range 2–7) with R-GemOx.
DOCR, duration of complete response.

Complete responses were durable with Mosun-Pola

Duration of complete response



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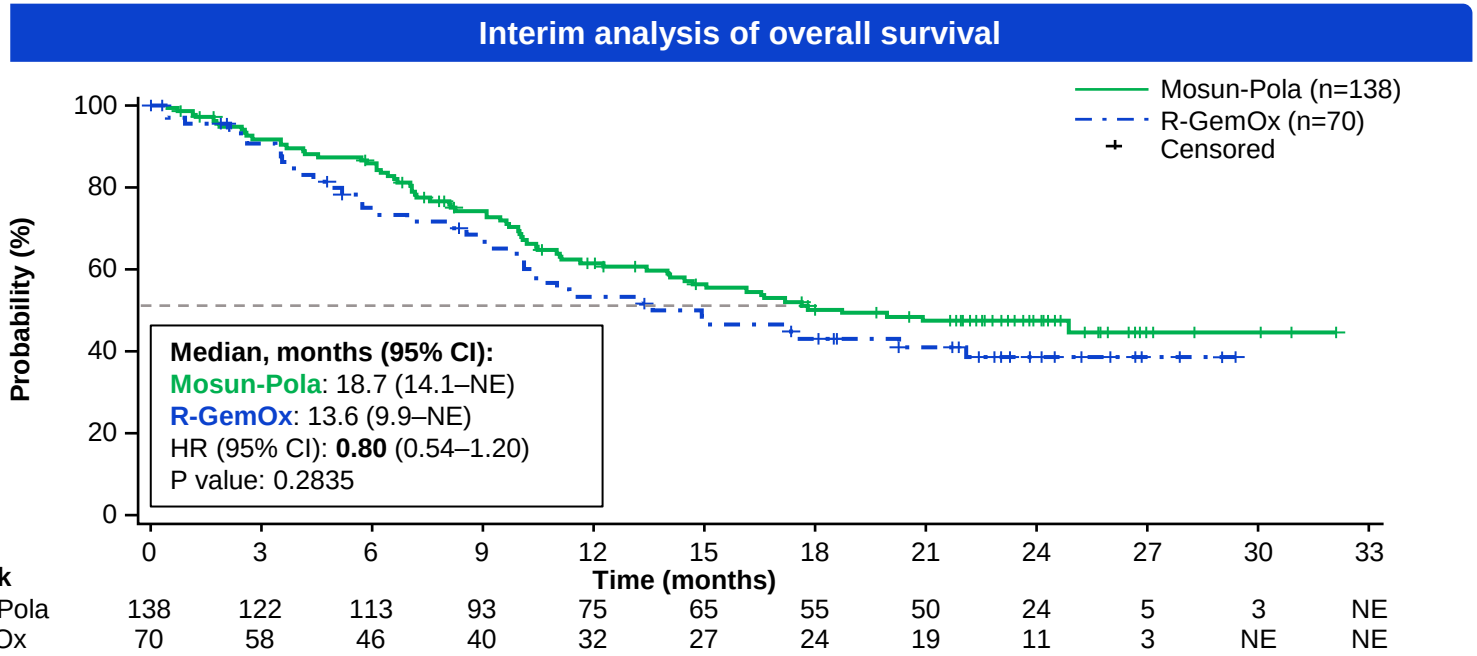
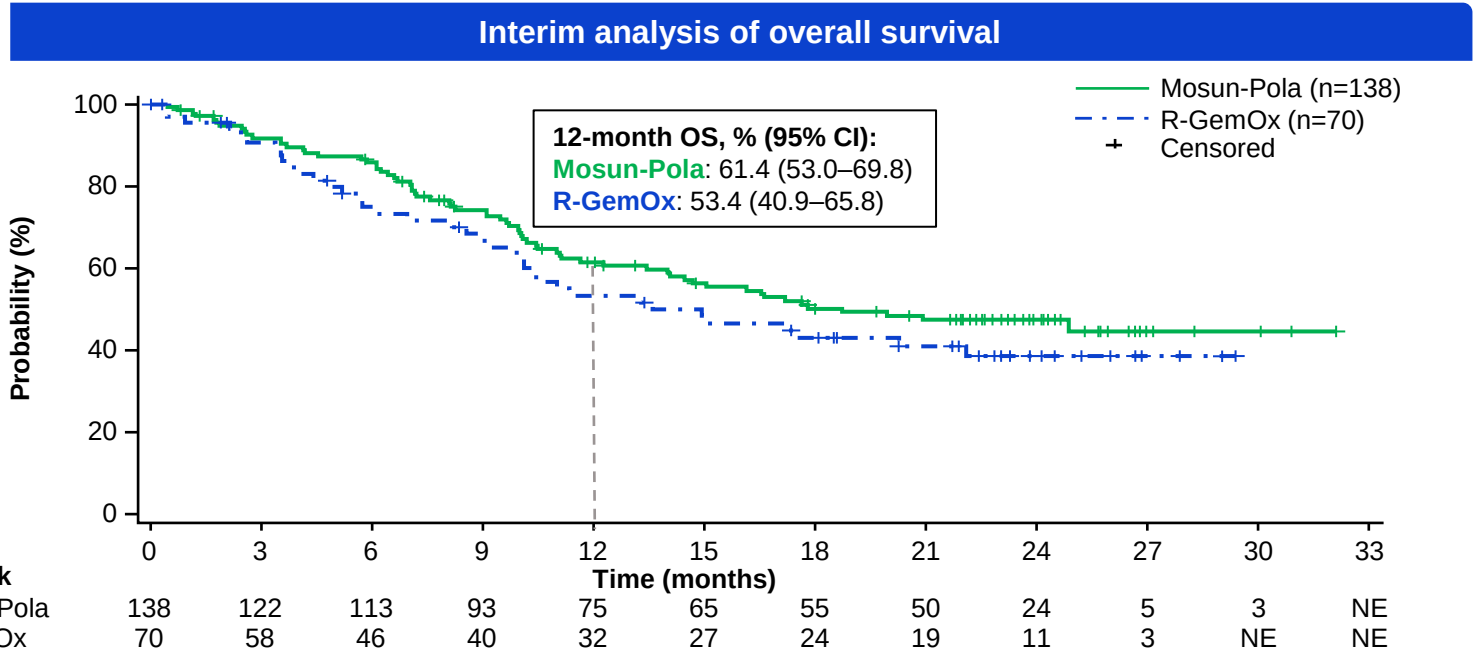
Interim analysis showed overall survival was prolonged with Mosun-Pola versus R-GemOx



OS numerically favoured Mosun-Pola versus R-GemOx (HR: 0.80) at the interim OS analysis

Clinical cut-off date: 17 February, 2025.

Interim analysis showed overall survival was prolonged with Mosun-Pola versus R-GemOx



OS numerically favoured Mosun-Pola versus R-GemOx (HR: 0.80) at the interim OS analysis

Clinical cut-off date: 17 February, 2025.

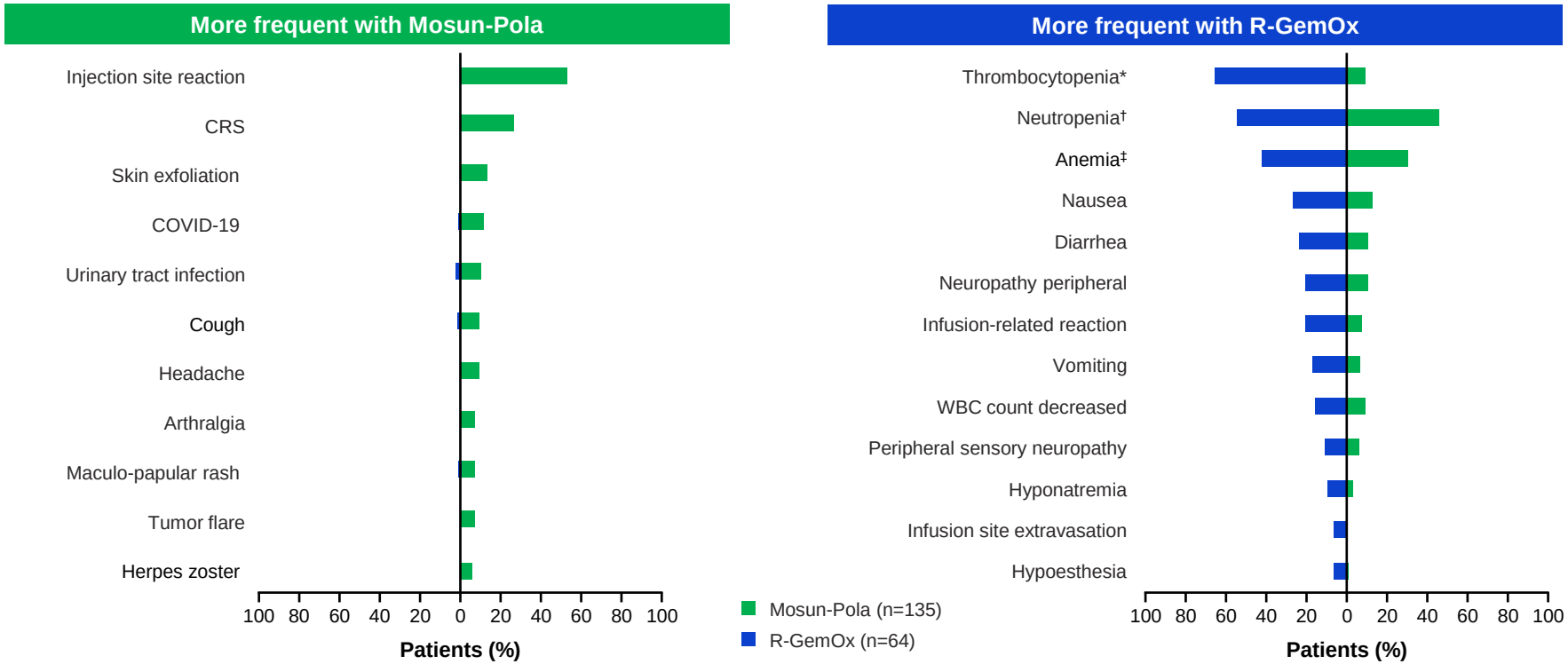
Safety summary

% (n), unless otherwise stated	Mosun-Pola n=135	R-GemOx n=64
Number of cycles, median (range)	8.0 (1–8)	5.0 (1–8)
Any AE	97.0% (131)	95.3% (61)
Treatment-related AE	93.3% (126)	89.1% (57)
SAEs	33.3% (45)	25.0% (16)
Treatment-related SAE	24.4% (33)	20.3% (13)
Grade 3–4 AE	58.5% (79)	57.8% (37)
Treatment-related Grade 3–4 AE	52.6% (71)	51.6% (33)
Grade 5 AE	5.2% (7)	6.3% (4)
Treatment-related Grade 5 AE*	1.5% (2)	3.1% (2)
AE leading to any study drug discontinuation†	2.2% (3)	4.7% (3)

AE rates are comparable between Mosun-Pola and R-GemOx, with fewer AEs leading to treatment discontinuation in the Mosun-Pola arm

Clinical cut-off date: 17 February, 2025. *Mosun-Pola: COVID-19 and COVID-19 pneumonia (n=1 each); R-GemOx: COVID-19 pneumonia and pneumonia (n=1 each). †Mosun-Pola: pneumonitis, infusion-related reaction, and cytomegalovirus infection reactivation (n=1 each); R-GemOx: delirium, embolism, and respiratory syncytial virus infection (n=1 each).
COVID-19, coronavirus disease-19; SAE, serious adverse event.

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

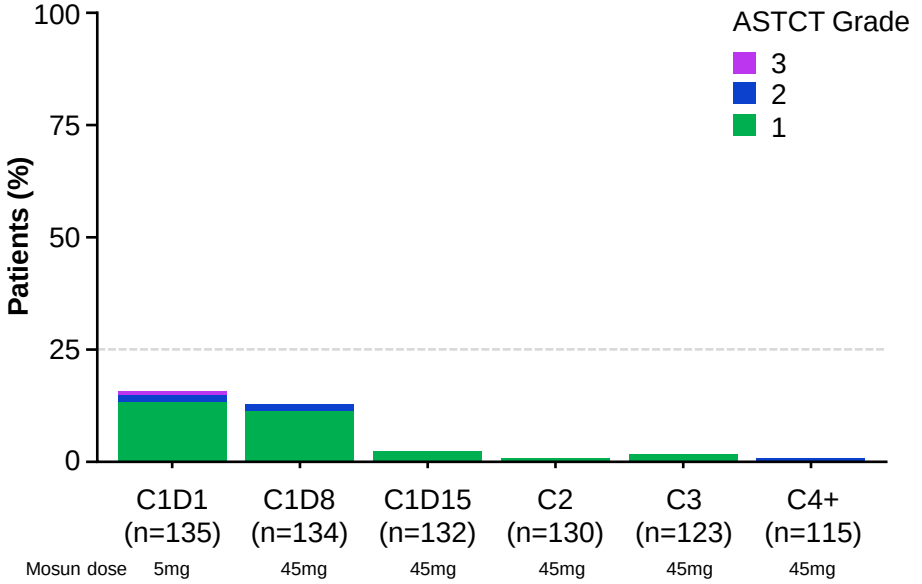


Clinical cut-off date: 17 February, 2025. *Includes thrombocytopenia and platelet count decrease. †Includes neutropenia/neutrophil count decrease. ‡Includes anemia and hemoglobin decrease.
WBC, white blood cell.

CRS was infrequent, early, and low grade

Patients with ≥1 CRS AE, % (n)	Mosun-Pola n=135
Any grade	25.9% (35)
Grade 1	21.5% (29)
Grade 2	3.7% (5)
Grade 3	0.7% (1)
Any serious event of CRS*	5.2% (7)
Median onset to first CRS, days (range)	3 (1–6)
Median duration, days (range)	3 (1–11)
Tocilizumab for CRS management	4.4% (6)
Corticosteroids for CRS management	3.7% (5)

CRS by cycle and grade in the Mosun-Pola arm



Mosun-Pola treatment resulted in no significant CRS (Grade 2 or higher) in 96% of patients

Clinical cut-off date: 17 February, 2025. *Events which required new or prolonged hospitalisation.
ASTCT, American Society for Transplantation and Cellular Therapy.

Other AEs of interest

% (n)	Mosun-Pola n=135	R-GemOx n=64
Injection site reaction	52.6% (71)	N/A
Grade ≥3	0	N/A
ICANS	0	N/A
Peripheral neuropathy	24.4% (33)	42.2% (27)
Grade ≥3	0	0
Tumor flare	6.7% (9)	0
Grade ≥3	1.5% (2)	0
Pneumonitis/interstitial lung disease	5.2% (7)	0
Grade ≥3	2.2% (3)	0
HLH	0	0

% (n)	Mosun-Pola n=135	R-GemOx n=64
Tumor lysis syndrome	0.7% (1)	0
Grade ≥3	0.7% (1)	0
Infections	51.1% (69)	31.3% (20)
Grade ≥3*	15.6% (21)	14.1% (9)
Serious infections	16.3% (22)	14.1% (9)
Neutropenia	45.9% (62)	54.7% (35)
Grade ≥3	33.3% (45)	31.3% (20)
Febrile neutropenia	2.2% (3)	3.1% (2)

The safety profile of Mosun-Pola is consistent with the known risk of the individual study drugs

Clinical cut-off date: 17 February, 2025. *3.7% (n=5) of patients in the Mosun-Pola arm and 6.3% (n=4) of patients in the R-GemOx arm had a Grade 5 event.
N/A, not applicable; HLH, hemophagocytic lymphohistiocytosis.

Conclusions

SUNMO is the first positive Phase III trial without conventional chemotherapy

- Mosun-Pola reduced the risk of death or progression by 59%
  - Tripled the median PFS
  - Doubled the CR rate

Mosun-Pola has the **lowest CRS incidence and severity among T-cell directed therapies** to date

- With 96% of patients not having significant CRS, **Mosun-Pola** may expand patient access to a highly effective therapy and allow for broad outpatient usage at more treatment centers

Mosun-Pola is a fixed duration outpatient regimen that combines a bispecific antibody with an ADC, which provided **clinically meaningful and statistically significant improvements in PFS and response** in patients with transplant-ineligible R/R LBCL

ADC, antibody-drug conjugate.

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