10th POSTGRADUATE
Lymphoma
Conference

The new concept in R/R patient is the combination of Mab's and ADC's: Current picture and future developments (moving from right to left?)

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President:
P.L. Zinzani

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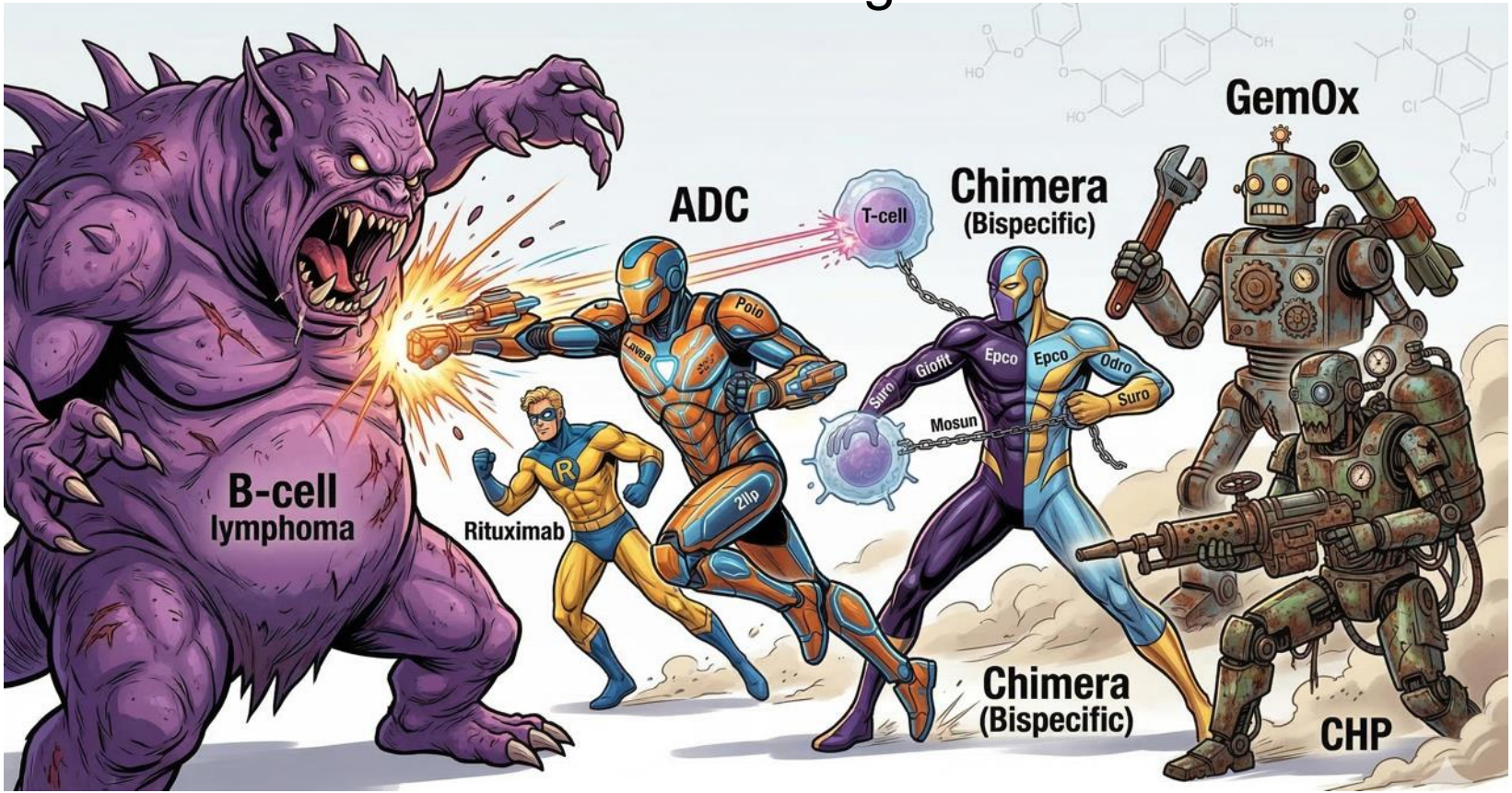
ADC and Friends: Moving from R/R to 1L




Polatuzumab
Pola-
vedotin

RR

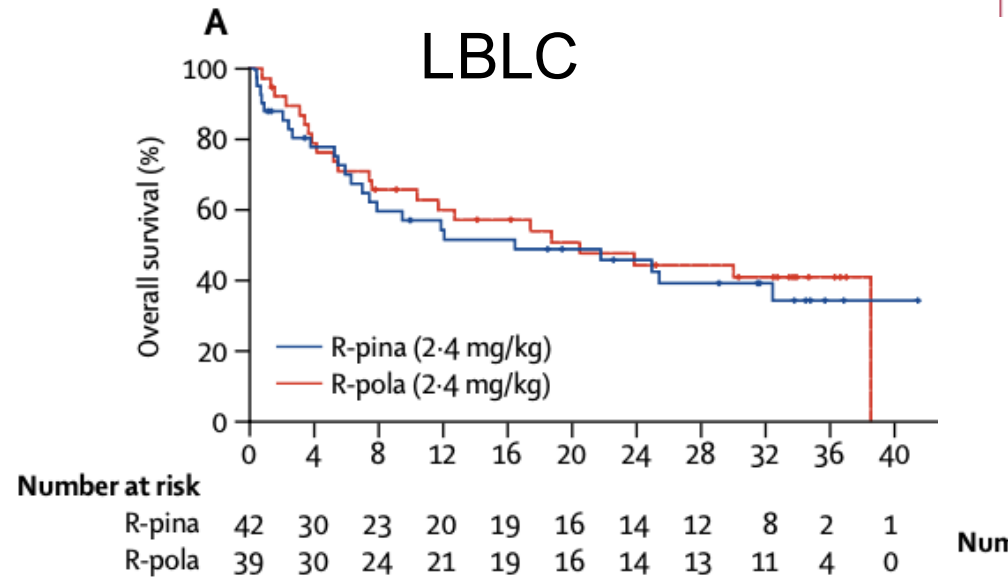
Polatuzumab vedotin or pinatuzumab vedotin plus rituximab in patients with relapsed or refractory non-Hodgkin lymphoma: final results from a phase 2 randomised study (ROMULUS)

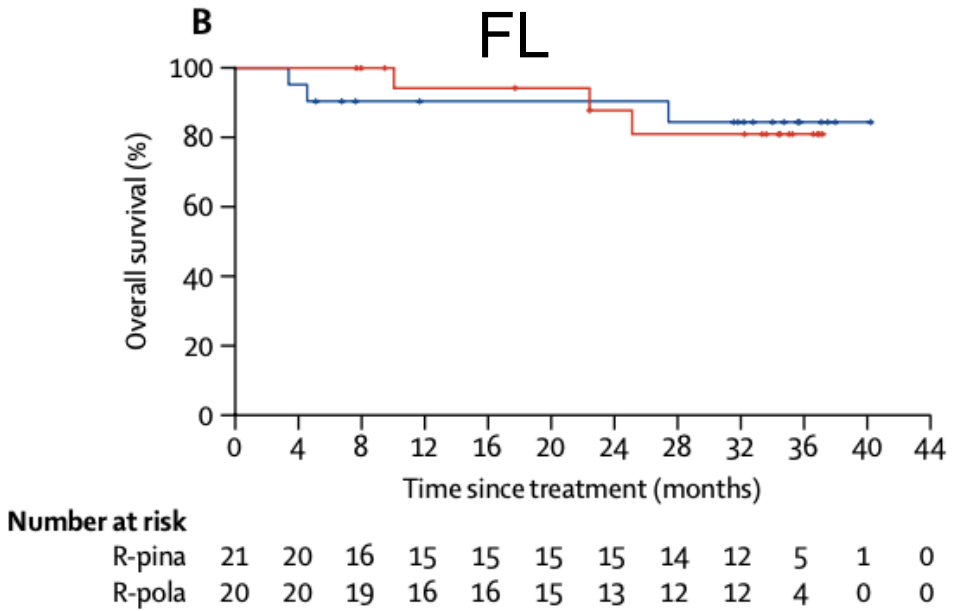
Franck Morschhauser, Ian W Flinn, Ranjana Advani, Laurie H Sehn, Catherine Diefenbach, Kathryn Kolibaba, Oliver W Press, Gilles Salles, Hervé Tilly, Andy I Chen, Sarit Assouline, Bruce D Cheson, Martin Dreyling, Anton Hagenbeek, Pier Luigi Zinzani, Surai Jones, Ji Cheng, Dan Lu, Elicia Penuel, Jamie Hirata, Michael Wenger, Yu-Waye Chu, Jeff Sharman*

Morschhauser et al, Lancet Hematology 2019

RR

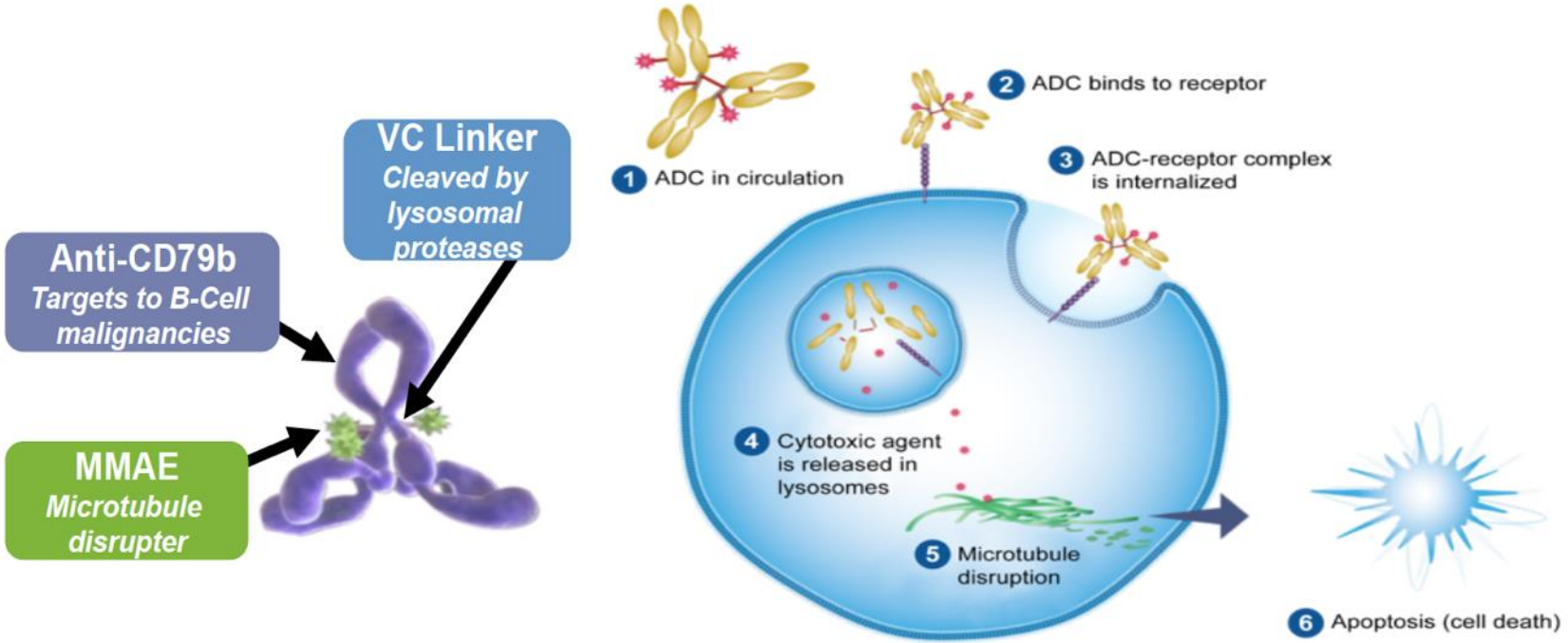
Overall Survival





Morschhauser et al, Lancet Hematology 2019

Polatuzumab Vedotin



Pola-BR vs BR

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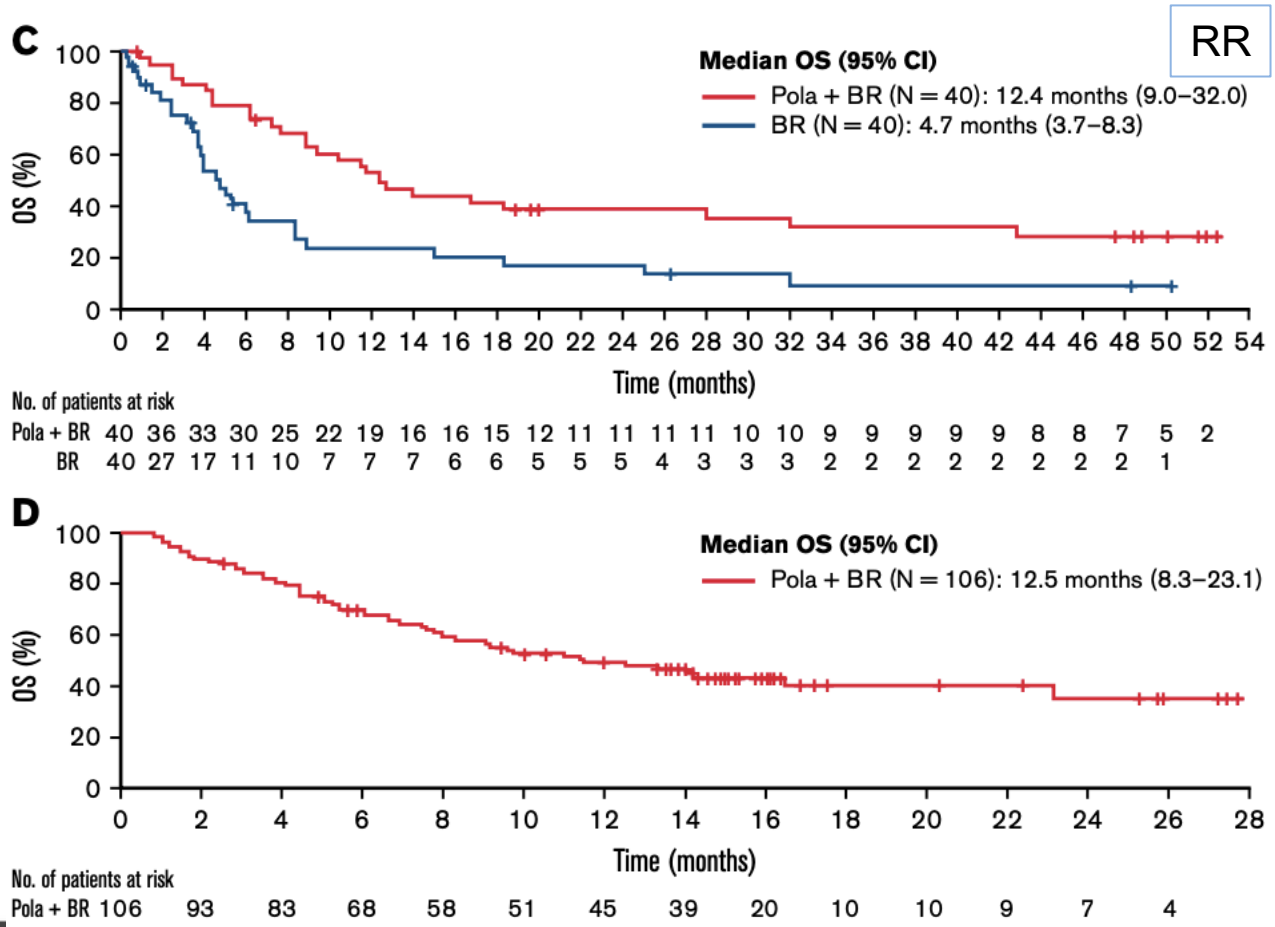
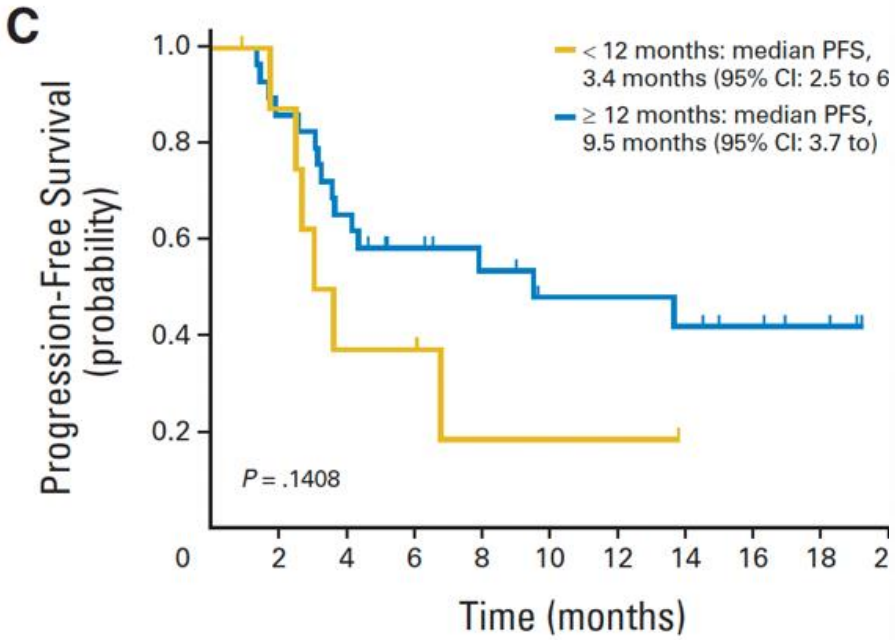


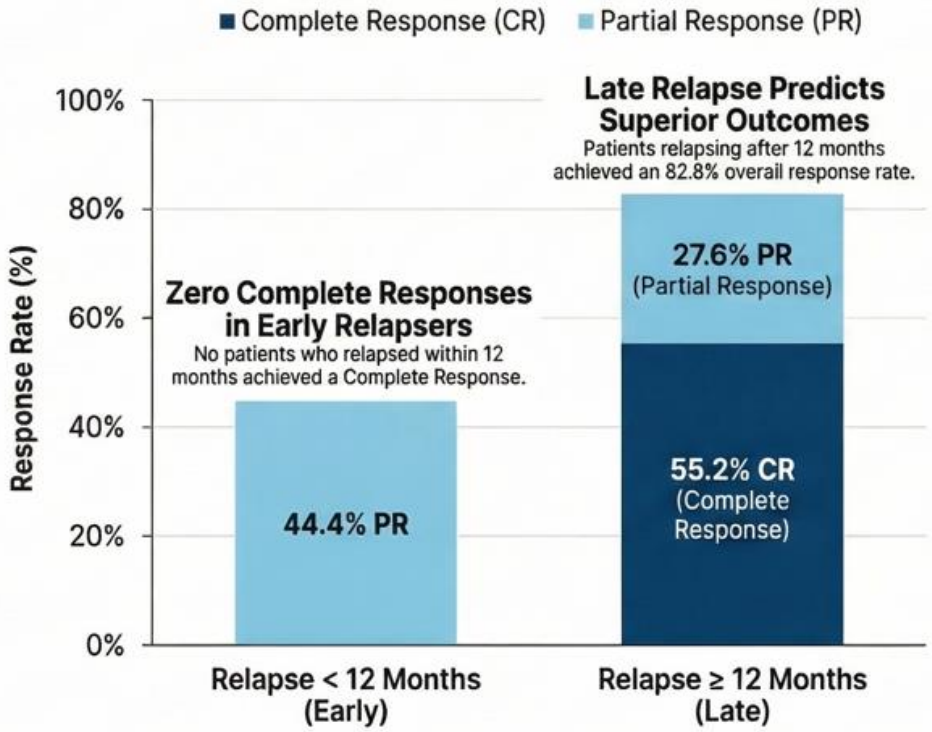
Sehn et al, Blood Advances 2022

RR

Was BR a valid control arm?

No





Ohmachi et al, JCO 2013

RR

POLARGO: randomized Phase III trial in patients with transplant-ineligible R/R DLBCL

Key eligibility criteria

- DLBCL, NOS or history of transformation of indolent disease to DLBCL
- R/R disease after ≥1 prior line of treatment
- Ineligible for transplant

Safety run-in
Enrolled n=15

→ **Pola-R-GemOx***
Q3W up to 8 cycles

→ ***Primary endpoint***
Safety and tolerability

Randomized phase
Enrolled n=255

→ R 1:1

→ **Pola-R-GemOx***
n=129
Q3W up to 8 cycles

→ **R-GemOx**
n=126
Q3W up to 8 cycles

Primary endpoint
OS

Key secondary endpoints
PFS (by INV)
CR† (by IRC)
ORR† (by IRC)

Stratification Factors
- Age (≤70 vs >70 years)
- Prior lines of therapy (1 vs ≥2)
- Relapsed vs refractory

R-GemOx (R, 375 mg/m²; Gem, 1000 mg/m²; Ox, 100 mg/m²). †PET-CT at EOT.
r, IRC, independent review committee; NOS, not otherwise specified; ORR, overall response rate;
and computed tomography; Q3W, every 3 weeks.

Matasar et al, EHA 2025

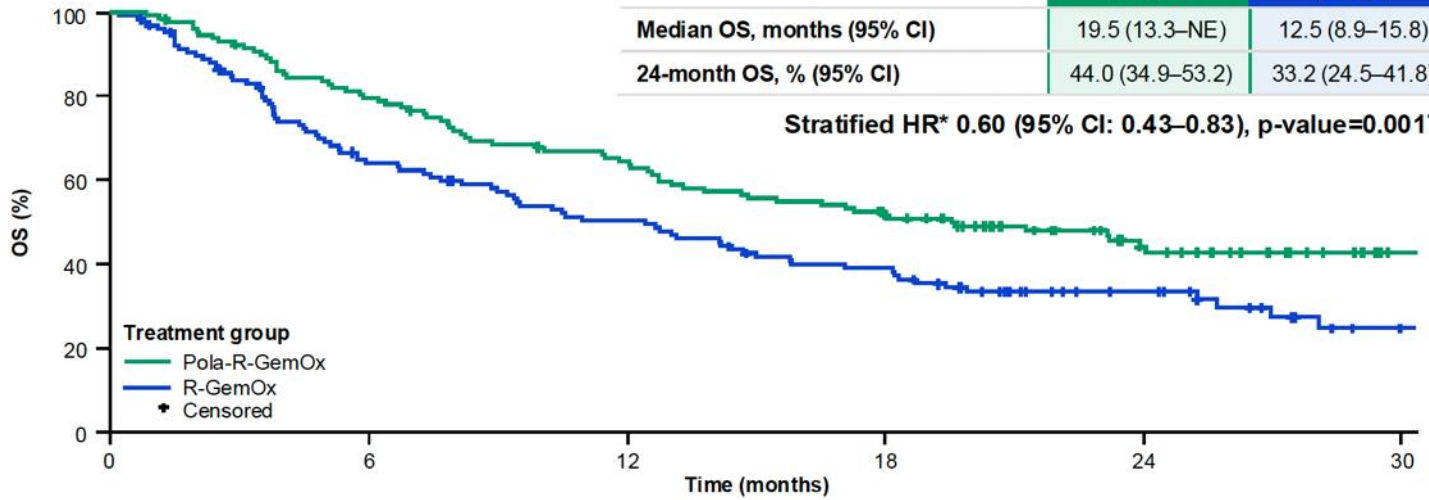
RR

Pola-R-GemOx significantly improved OS vs R-GemOx in patients with R/R DLBCL

Median OS follow-up: 24.6 months (95% CI: 23.0–26.0)

	Pola-R-GemOx (n=129)	R-GemOx (n=126)
Median OS, months (95% CI)	19.5 (13.3–NE)	12.5 (8.9–15.8)
24-month OS, % (95% CI)	44.0 (34.9–53.2)	33.2 (24.5–41.8)

Stratified HR* 0.60 (95% CI: 0.43–0.83), p-value=0.0017†

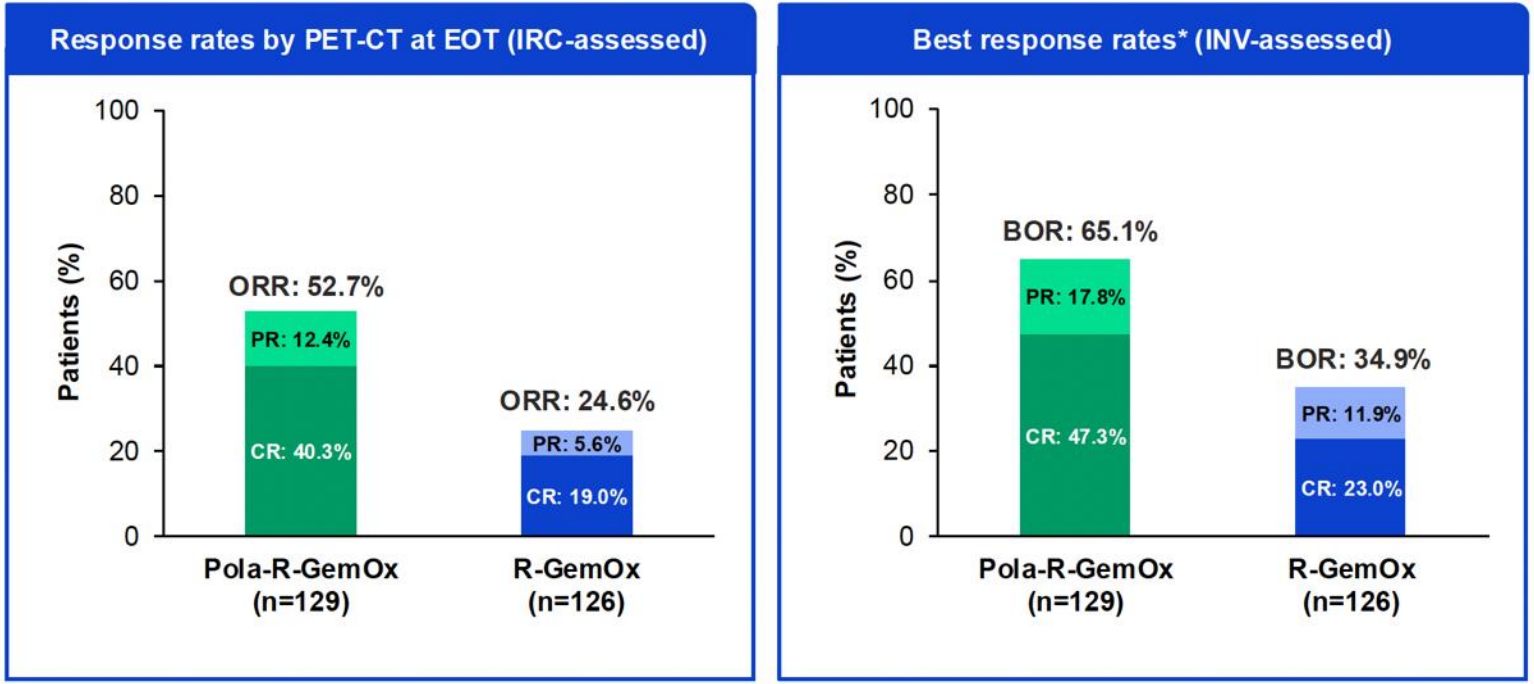


ior lines of systemic therapy (1 vs ≥2), outcome of last systemic therapy (relapsed vs refractory). †Log rank.
, NE, not estimable.

Matasar et al, EHA 2025

RR

Response rates were higher with Pola-R-GemOx vs R-GemOx

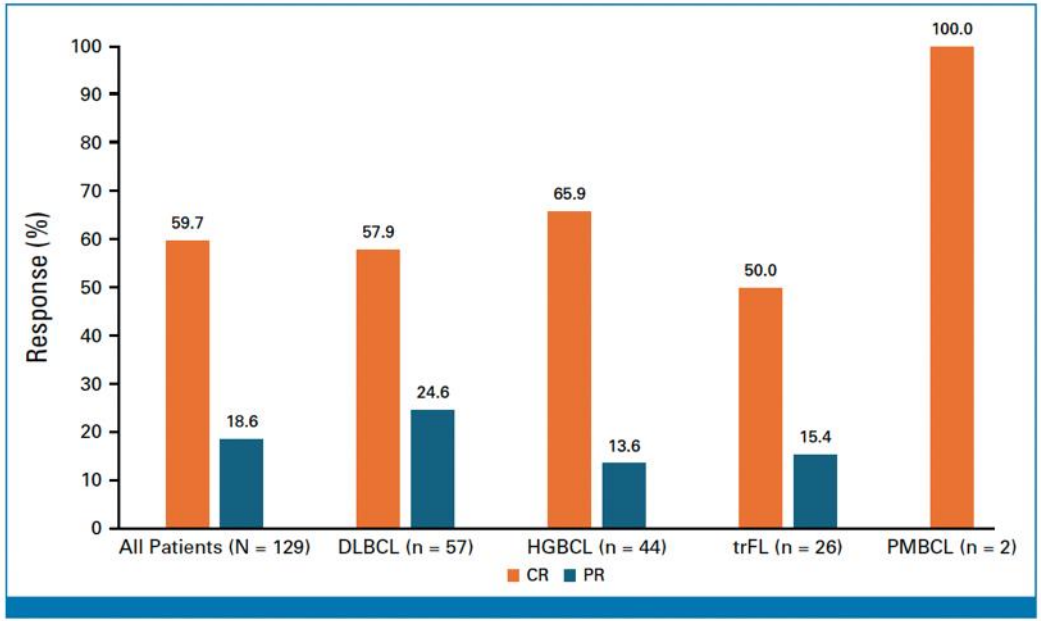


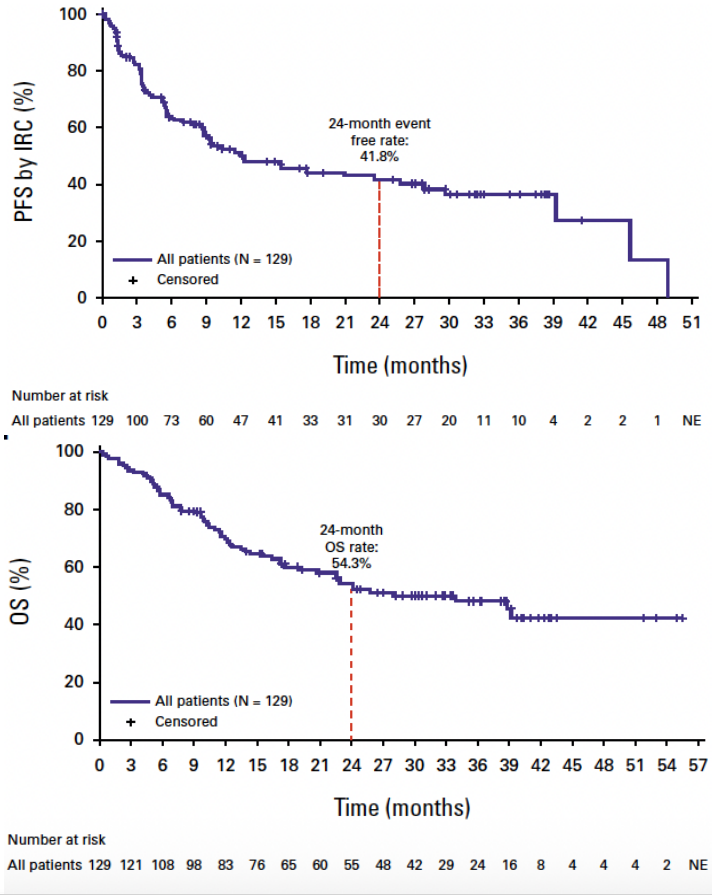
Matasar et al, EHA 2025

response.

RR

Glofit-Pola in R/R LBCL





Hutchings et al, JCO 2025

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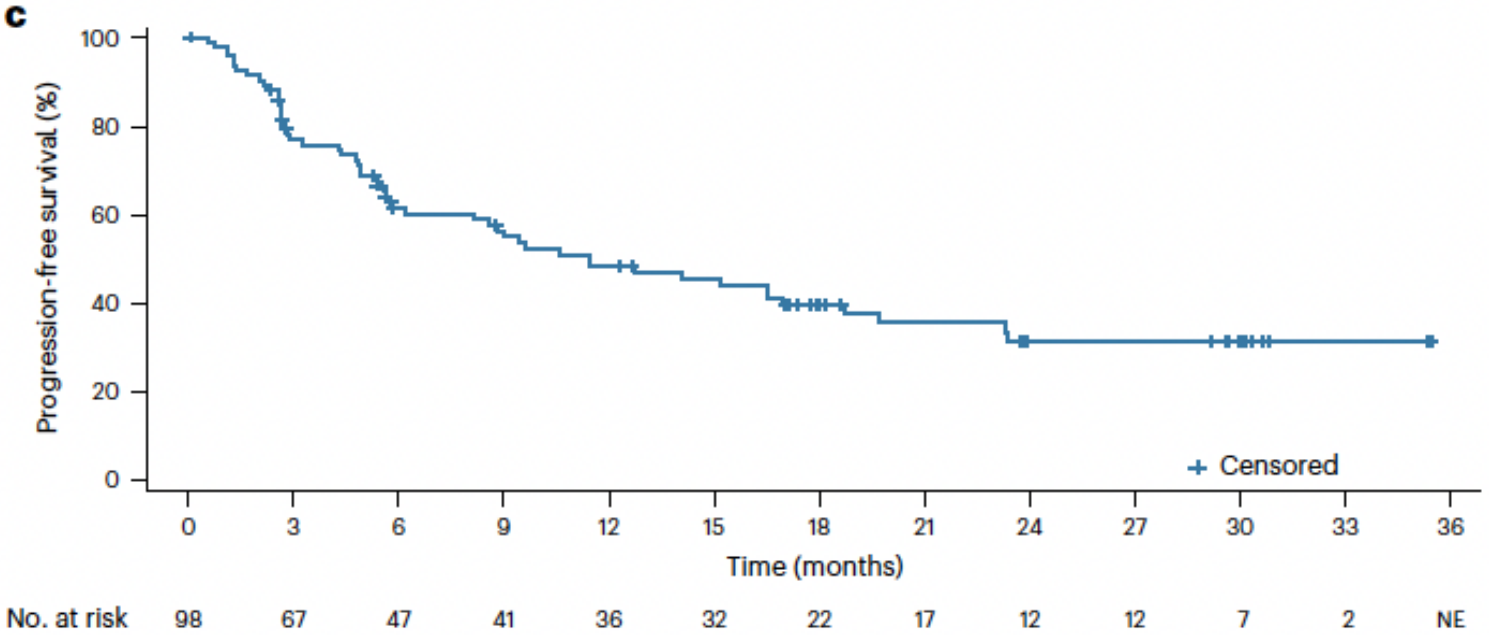
Mosun-Pola in R/R LBCL



Budde et al, Nat Med 2023

SunMo

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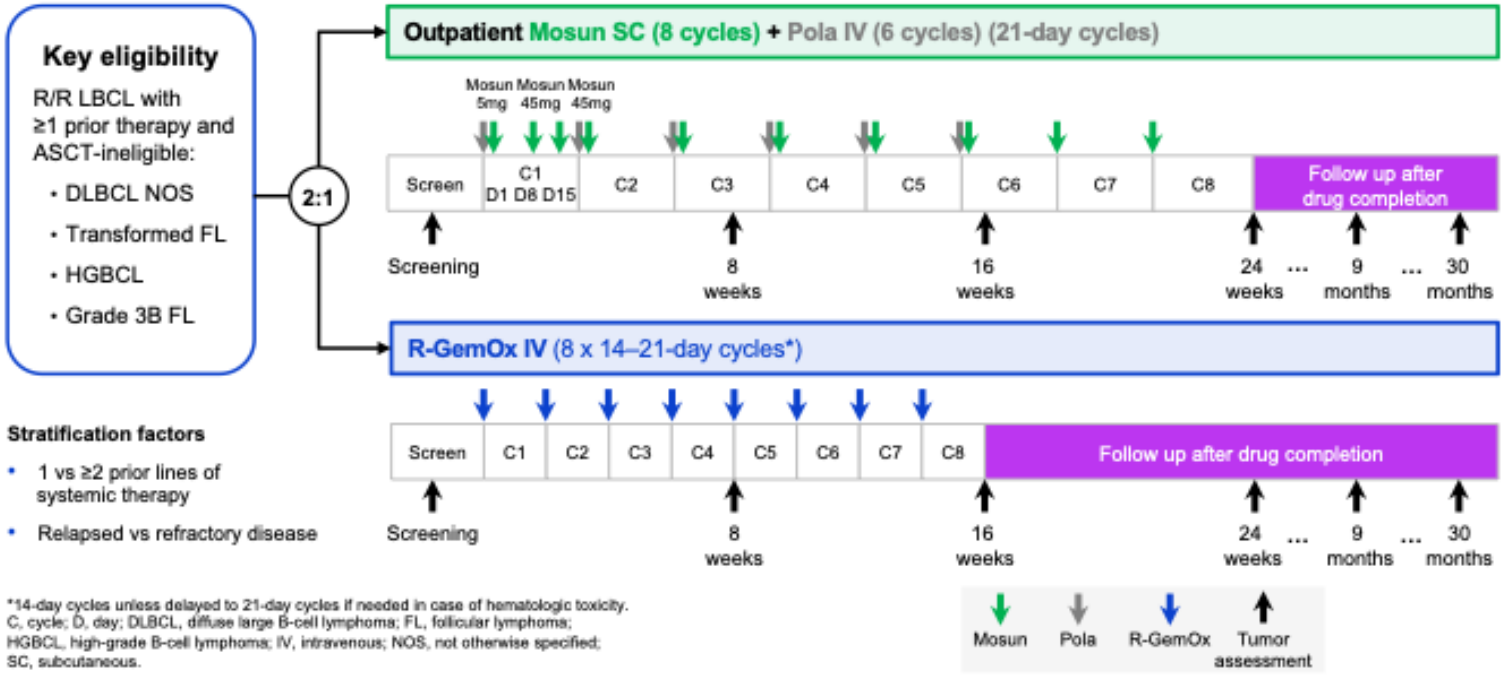
Study design



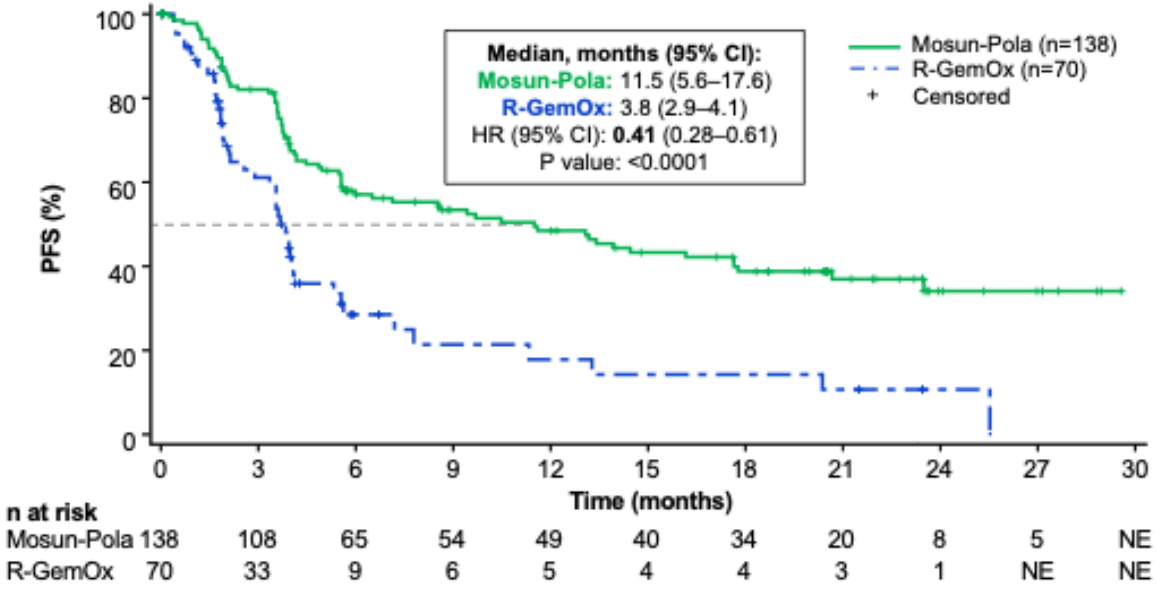
*14-day cycles unless delayed to 21-day cycles if needed in case of hematologic toxicity.
C, cycle; D, day; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IV, intravenous; NOS, not otherwise specified; SC, subcutaneous.

Presented as LBA3 by Westin et al, ICML 2025

RR

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

Primary endpoint: Progression-free survival by IRC



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

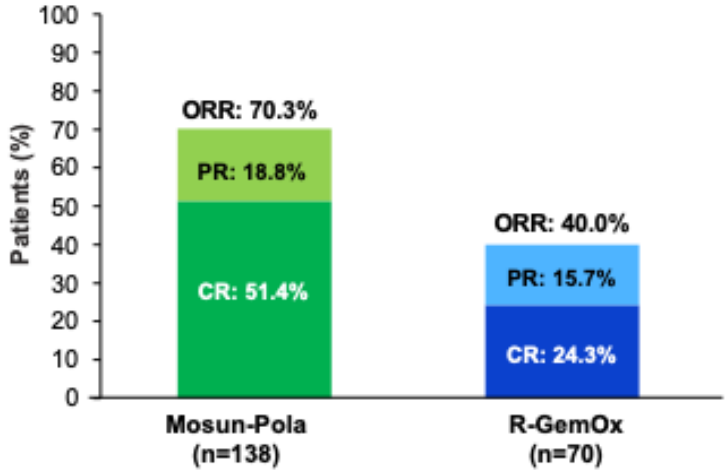
Clinical cut-off date: 17 February, 2025. PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first.
CI, confidence interval; HR, hazard ratio; NALT, new anti-lymphoma therapy; NE, non estimable.

Presented as LBA3 by Westin et al, ICML 2025

RR

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*

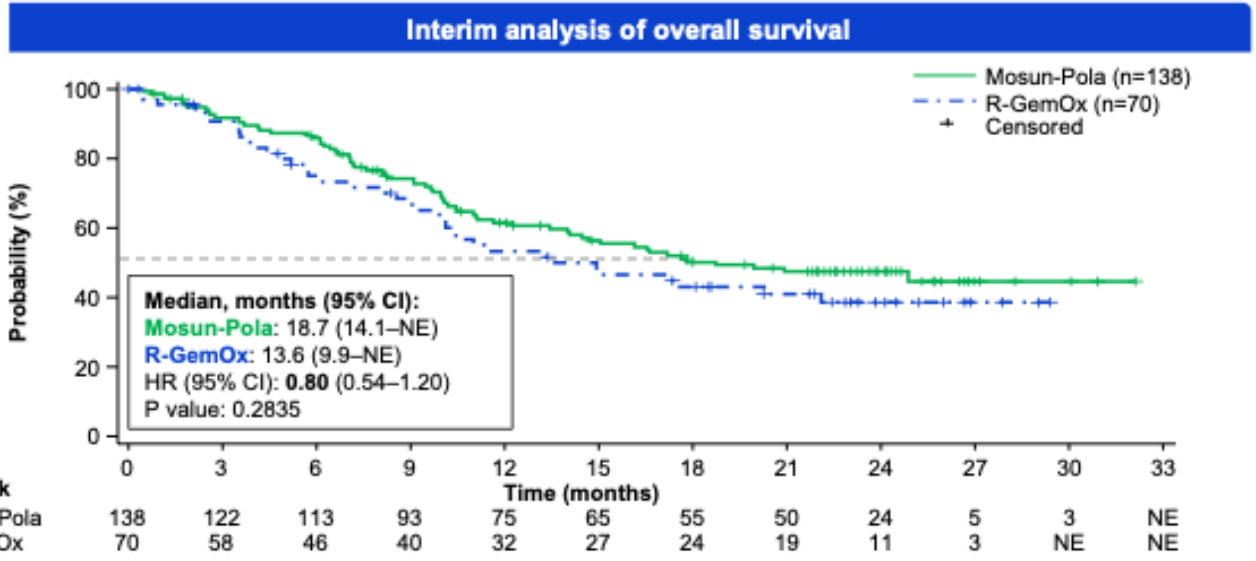
Mosun-Pola doubled the CR rate and improved the ORR by 30% compared with R-GemOx

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

Presented as LBA3 by Westin et al, ICML 2025

RR

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.

Presented as LBA3 by Westin et al, ICML 2025

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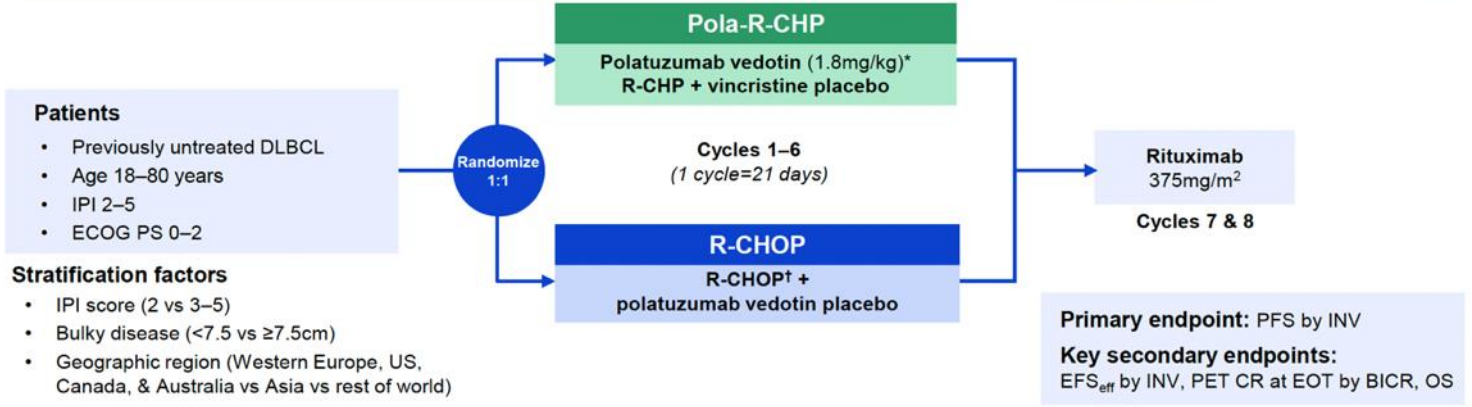
POLARIX study design



		Pola-R-CHP	R-CHOP	Total	Median PFS follow-up	Median OS follow-up
Global population	ITT‡	440	439	879	54.9 months	64.1 months
	Safety evaluable§	435¶	438#	873		

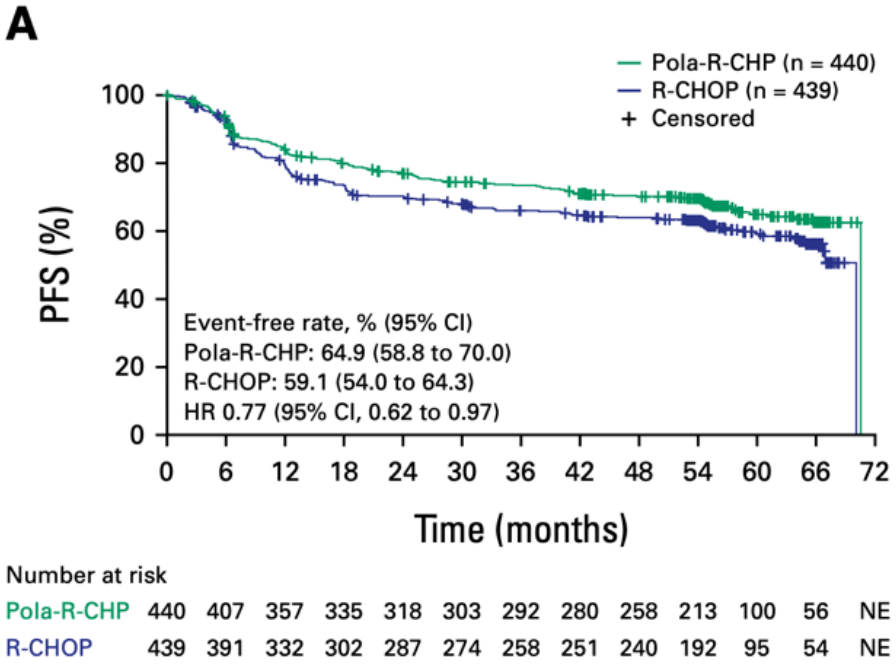
*IV on Day 1; †R-CHOP: IV rituximab 375mg/m², cyclophosphamide 750mg/m², doxorubicin 50mg/m², and vincristine 1.4mg/m² (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5; ‡As randomized population; §As treated population; ¶One patient was randomized to Pola-R-CHP but did not receive polatuzumab vedotin; #One patient was randomized to R-CHOP but did not receive vincristine.
BICR, blinded independent central review; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival (efficacy); EOT, end of treatment; INV, investigator; IPI, International Prognostic Index; OS, overall survival; PFS, progression-free survival; R, randomized; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

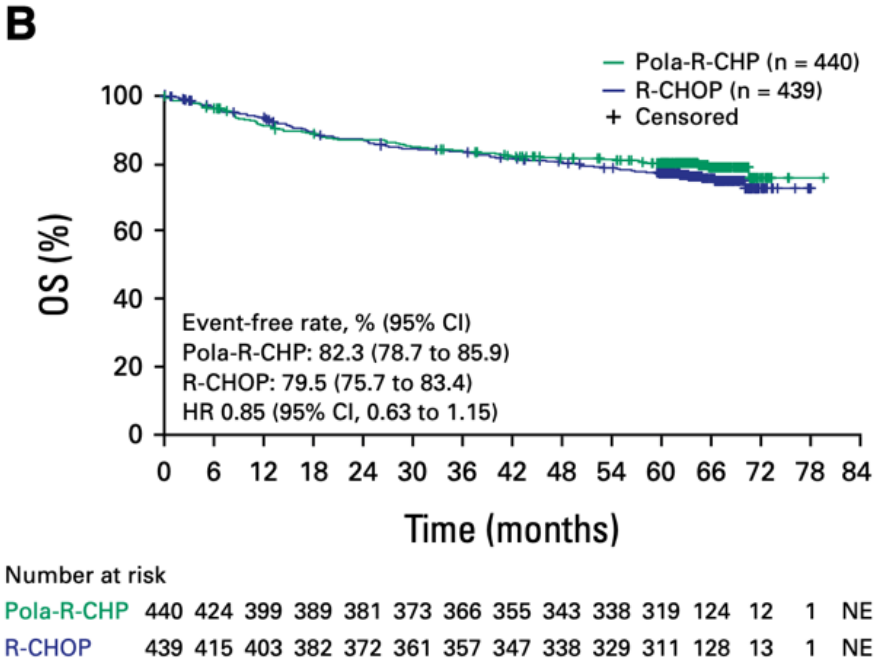
Tilly H, *et al. N Eng J Med* 2022;386:351–63.

Salles et al, ASH 2024

1L

Polarix at 5 years





Morschhauser et al, JCO 2025

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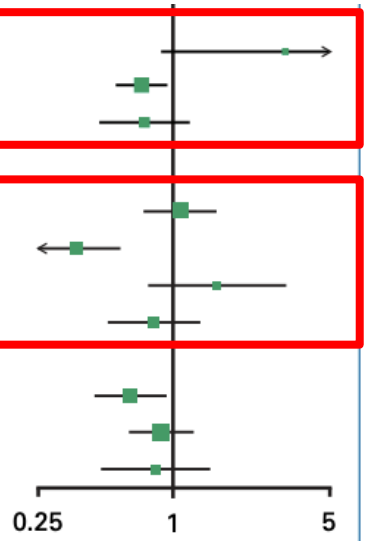
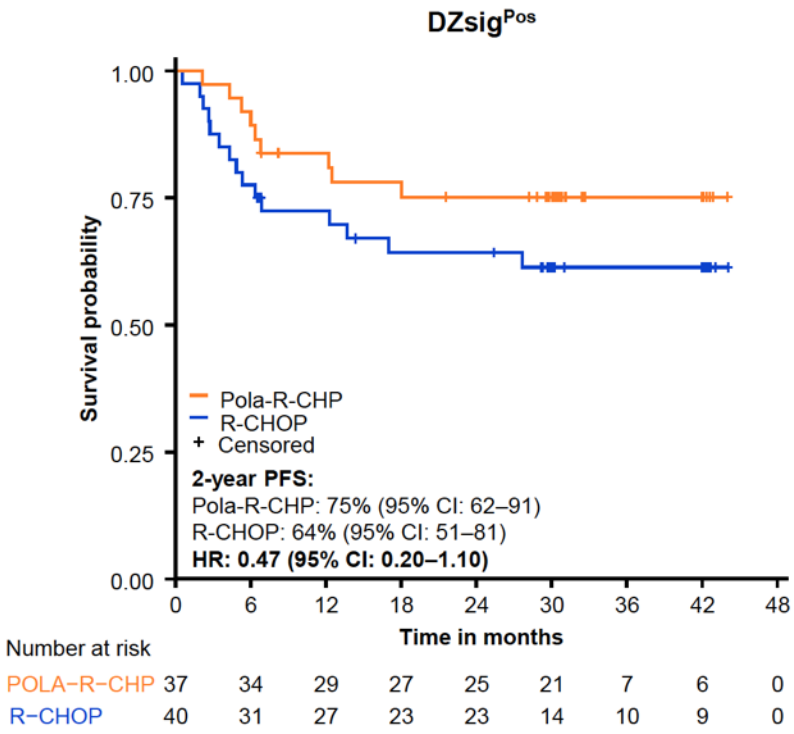
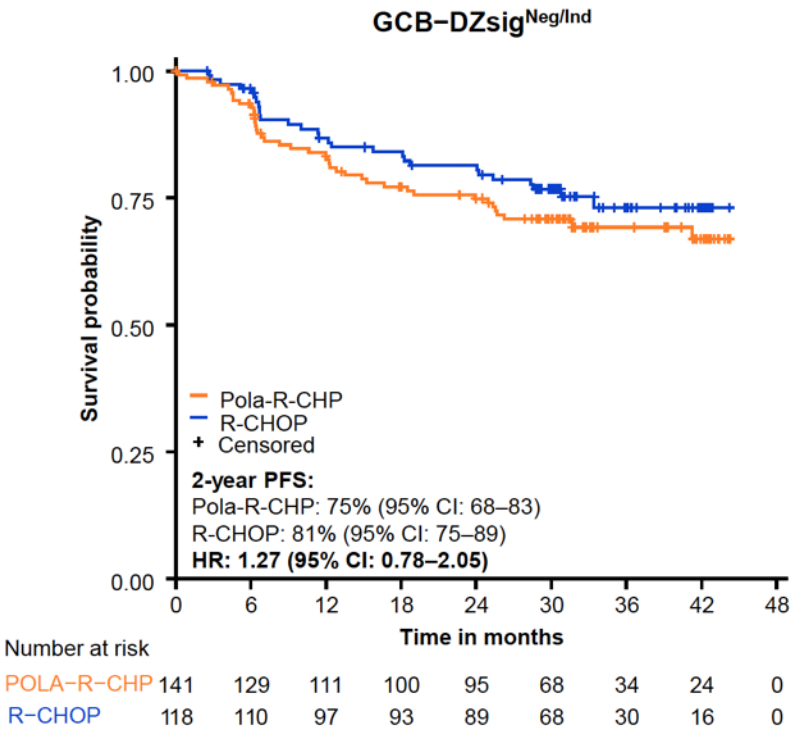
Baseline Risk Factor		PFS						
		Pola-R-CHP (n = 440)		R-CHOP (n = 439)		HR	95% Wald CI	Pola-R-CHP Better / R-CHOP Better
		No.	60-Month, %	No.	60-Month, %			
Double-/triple-hit lymphoma	DHL/THL+	26	48.8	19	83.0	**3.18**	0.89 to 11.42	
	DHL/THL–	305	65.9	315	57.6	**0.72**	0.56 to 0.94	
	Unknown	109	65.5	105	62.0	**0.75**	0.47 to 1.19	
NanoString COO	GCB	187	65.9	170	65.8	**1.07**	0.74 to 1.56	
	ABC	106	72.5	129	45.8	**0.38**	0.24 to 0.59	
	UNC	44	55.2	53	70.8	**1.60**	0.79 to 3.25	
	Unknown	103	60.2	87	59.7	**0.83**	0.51 to 1.33	
Double expressor by IHC	DEL	139	63.1	151	50.0	**0.65**	0.45 to 0.94	
	Non-DEL	223	66.6	215	64.7	**0.89**	0.64 to 1.24	
	Unknown	78	63.7	73	63.5	**0.84**	0.48 to 1.47	

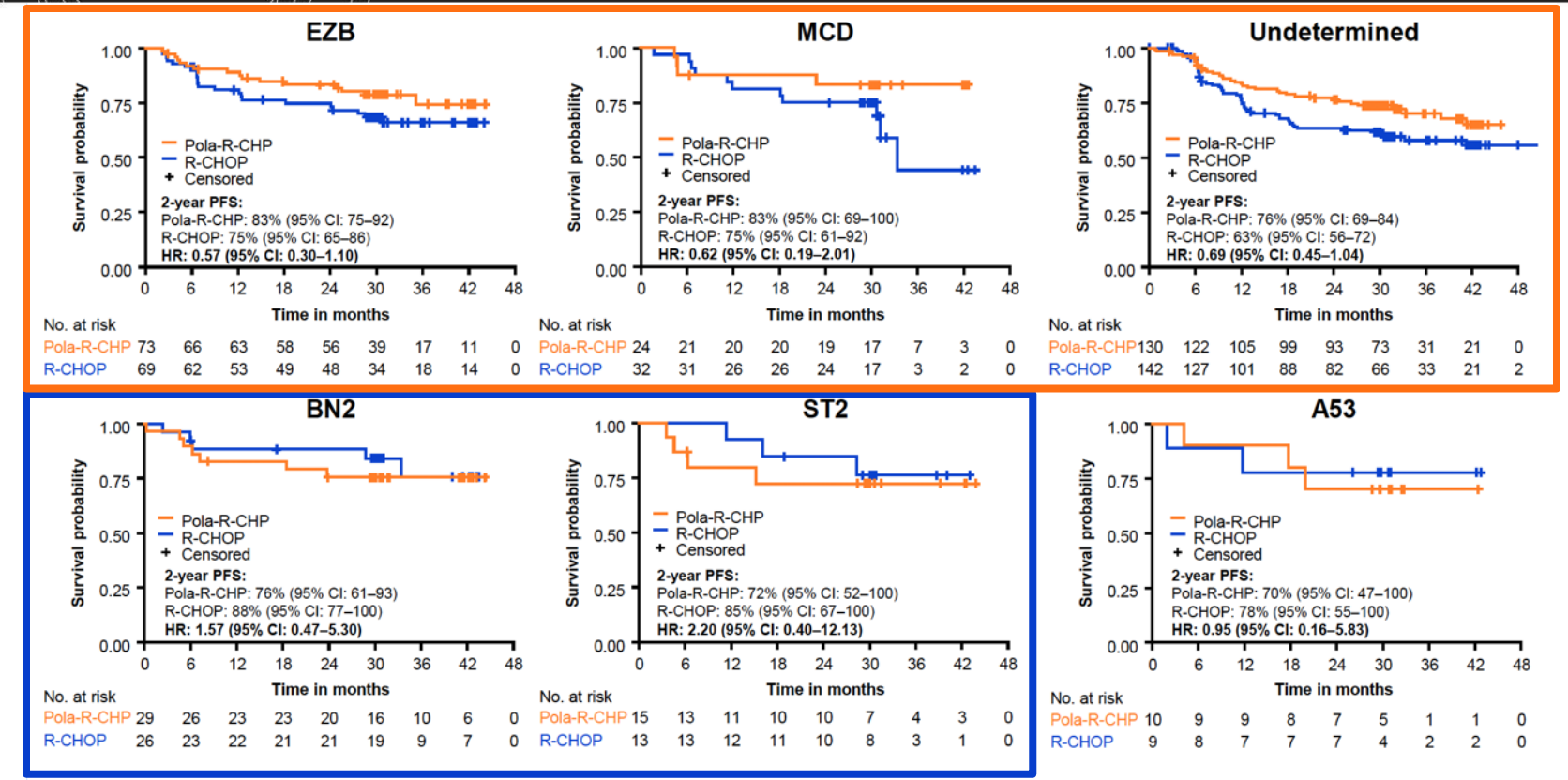


Morschhauser et al, JCO 2025





Morschhauser/Flowers et al, SOHO 2025



Morschhauser/Flowers et al, SOHO 2025

Other 1L combos

Study overview

Key inclusion criteria:

- Newly diagnosed DLBCL or HGBL
- Age 18-65
- At least one H-R feature
  - IPI ≥ 3
  - NCCN-IPI ≥ 4
  - *MYC* and *BCL2* and/or *BCL6* rearrangements
- ECOG 0-3 prior to cycle 1 or 0-1 prior to cycle 2

Key exclusion criteria:

- CNS involvement
- Prior treatment of indolent lymphoma

Study Schema:

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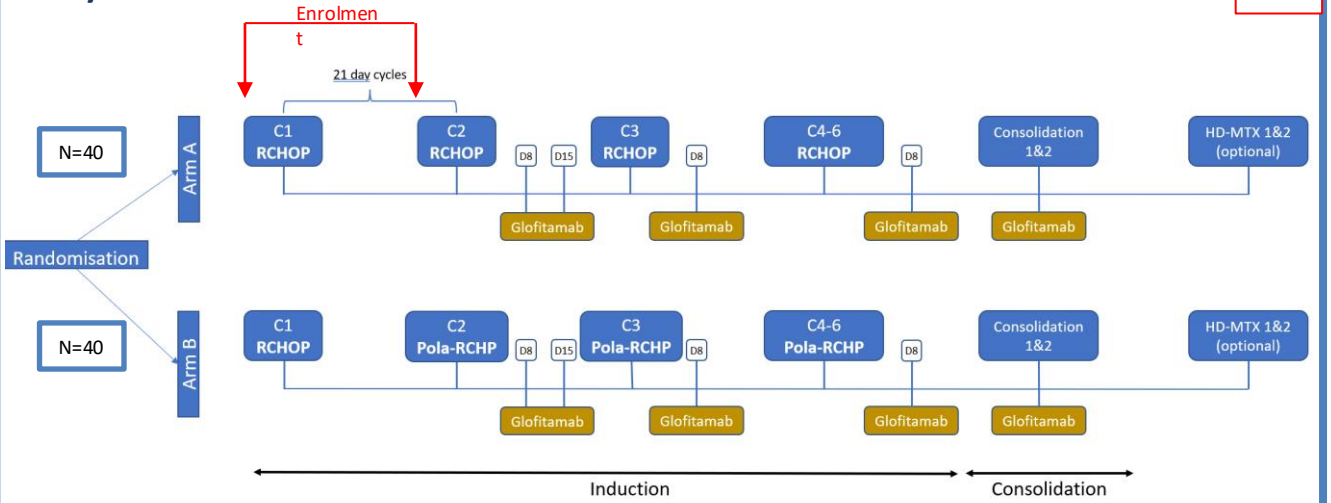


RCHOP, Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone; Pola-RCHP, polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, prednisolone; HD-MTX, high-dose methotrexate

Primary endpoints: Safety, relative dose intensity and rates of treatment discontinuation

Key secondary endpoints: Response rates by Lugano 2014, progression-free survival, overall survival, duration of response

Analysis:
All 80 patients have completed study therapy

Updated median follow up of 20.7 months

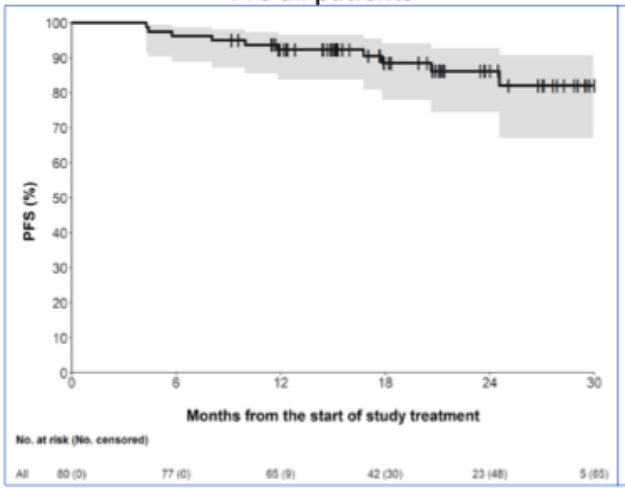
Minson et al ASH 2024

DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; H-R, high-risk; ECOG, Eastern Cooperative Oncology Group performance status; CNS, central nervous system.

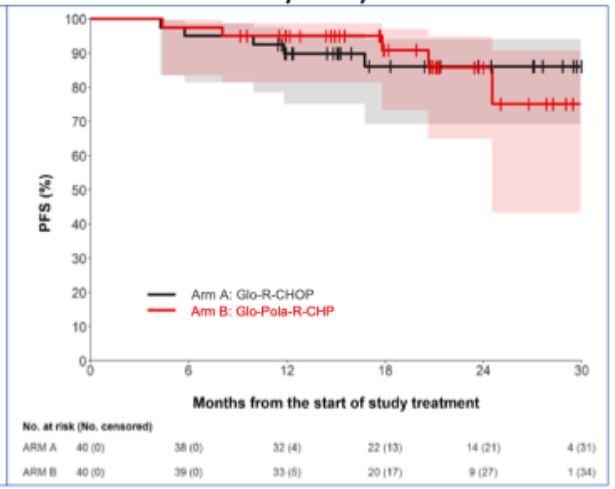
Progression free survival demonstrates durable responses

1L

PFS all patients



PFS by study arm



PFS estimate	Arm A Glo-R-CHOP (n=40)	Arm B Glo-Pola-R-CHP (n=40)	All patients (n=80)
12-month PFS, % (95% CI)	**90%** (75%-96%)	**95%** (81%-99%)	**92%** (84%-97%)
24-month PFS, % (95% CI)	**86%** (69%-94%)	**86%** (65%-95%)	**86%** (75%-93%)

PFS is highly promising in this high-risk patient population

Minson et al ASH 2024

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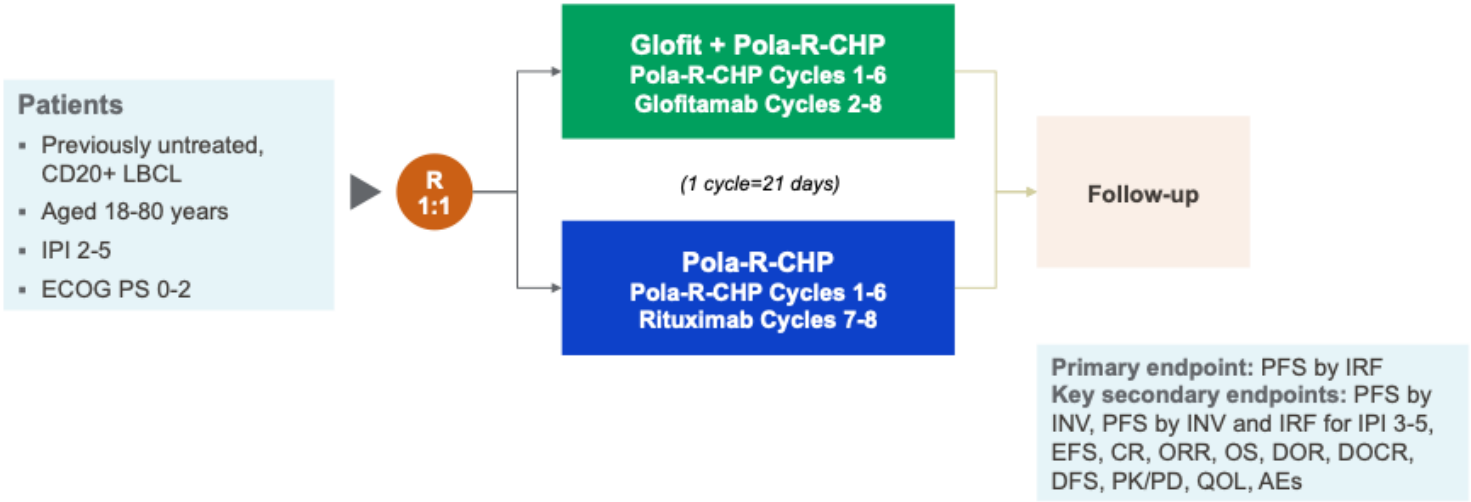
SKYGLO Global Phase 3 Multicenter, Randomized, Open-Label Study of Glofitamab + Pola-R-CHP vs Pola-R-CHP in Untreated Patients With LBCL



https://clinicaltrials.gov/study/NCT06047080. Accessed August 18, 2025.

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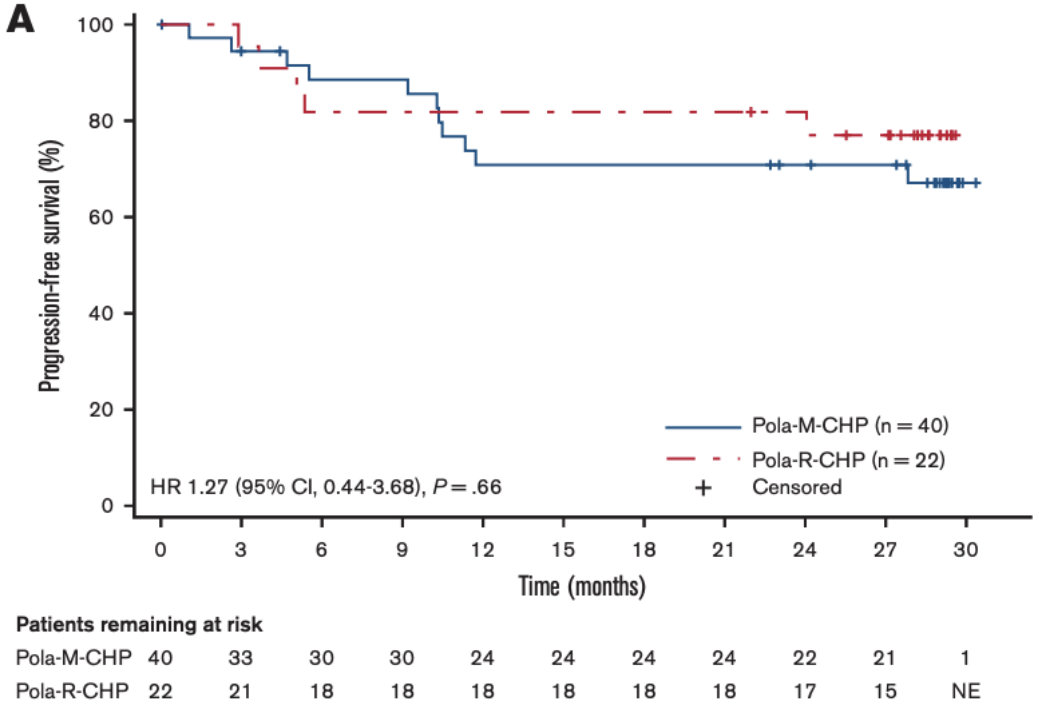
M-CHP-Pola



Westin et al, Blood Advances 2025

Mosun Pola elderly 1L
Study overview

1L

Key inclusion criteria

- Previously untreated DLBCL
- Age ≥80 years OR age 65–79 years and considered ineligible* for CIT
- ECOG PS 0–2

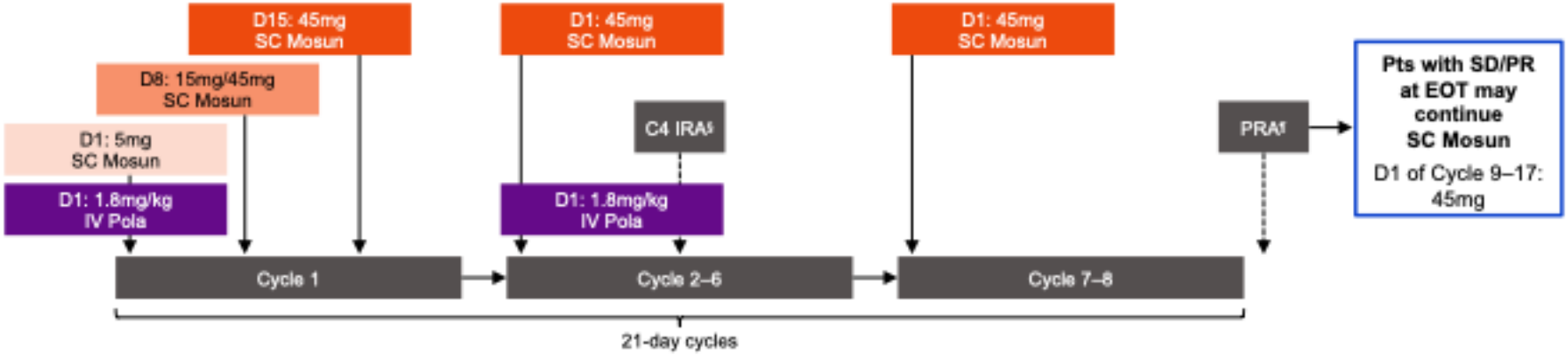
CRS mitigation strategies

- Step-up SC Mosun dosing in Cycle 1
- Pre-medication with dexamethasone in Cycle 1†
- Pre-medication with acetaminophen and diphenhydramine may also be given‡

Primary efficacy endpoint

- ORR by PET-CT at the PRA as assessed by IRC according to Lugano 2014 criteria[1]
- **Additional objectives:** Evaluation of safety, immunogenicity, pharmacokinetics, and pharmacodynamics

SC Mosun-Pola administration: Cohort C1 (N=7): 5/15/45mg; Cohort C2 + C Expansion (N=101): 5/45/45mg (target dose cohort)



*Per simplified geriatric assessment: Impairment in ≥2 ADL components and/or impairment in IADL components and/or CIRS-G score of at least one comorbidity with a severity score of 3–4 or a score of 2 in ≥6 comorbidities. †Optional from C2+. ‡Optional from C1+. §In Cycle 4 between D14 and D21. ¶6–8 weeks after Cycle 8 D1 or the final dose of study treatment for those who discontinue prematurely.

ADL, activity of daily living; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; CIT, chemoimmunotherapy; CRS, cytokine release syndrome; D, Day; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; IADL, instrumental activity of daily living; IRA, interim response assessment; IRC, independent review committee; IV, intravenous; ORR, objective response rate; PET-CT, positron emission tomography–computed tomography; PR, partial response; PRA, primary response assessment; SD, stable disease.

1. Cheson, et al. J Clin Oncol 2014;32:3059–68.

Olszewski A et al. ASH. 2023

Investigator-assessed EOT and BOR response rates

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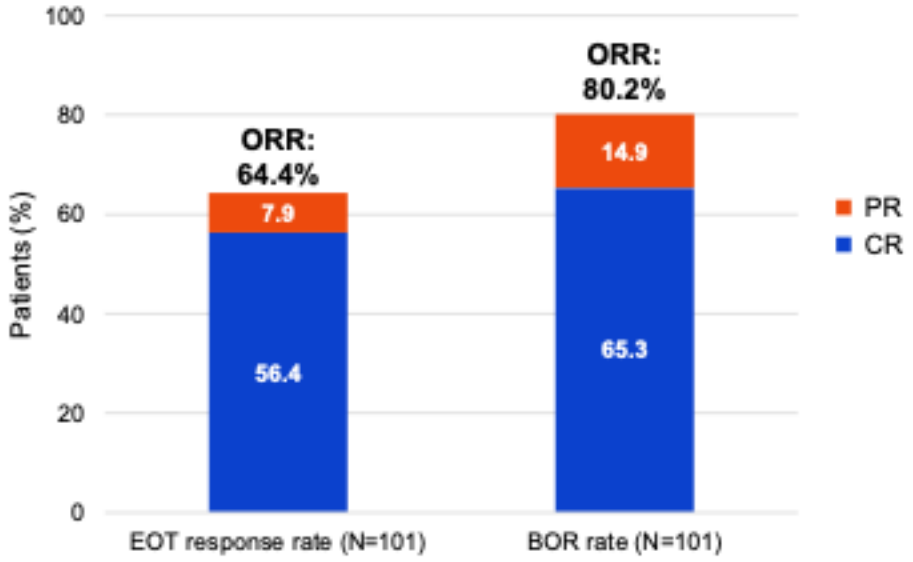
EOT response and BOR rates in Mosun-Pola target dose cohort



Response rate, n (%)	EOT N=101	BOR N=101
ORR	65 (64.4)	81 (80.2)
CR	57 (56.4)	66 (65.3)
PR	8 (7.9)	15 (14.9)
SD	4 (4.0)	4 (4.0)
PD	10 (9.9)	4 (4.0)
ND	22 (21.8)*	12 (11.9)†

- 6/8 pts with PR at EOT continued treatment beyond Cycle 8, and 3/6 pts converted from PR to CR during continuation
- The difference between BOR and EOT is attributed to 22 patients who did not reach the EOT visit due to AEs, death, and subject withdrawal, which reflects the frailty and high co-morbidity burden of the study population

Mosun-Pola induces encouraging response rates in elderly unfit or frail pts with previously untreated DLBCL

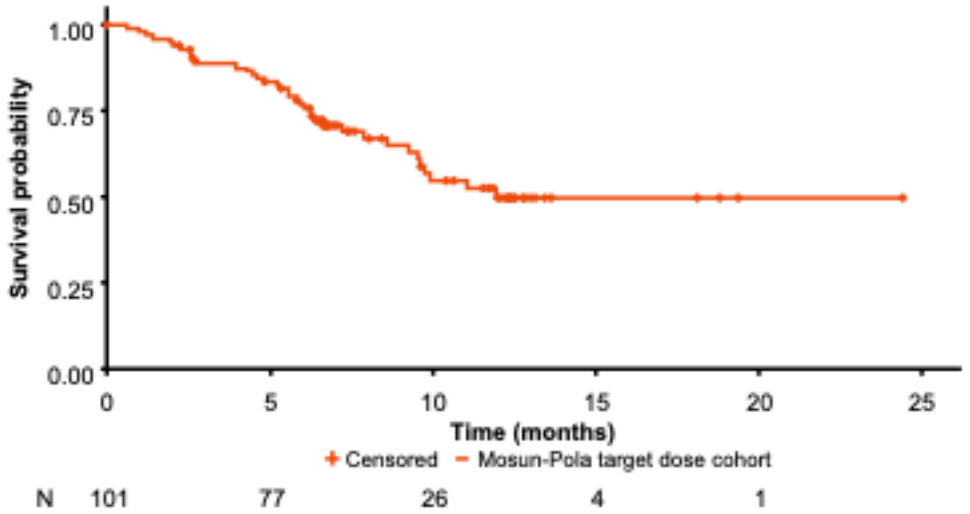
Data cut-off: August 5, 2023; *6 pts withdrew consent, 14 discontinued early due to AEs, 1 discontinued due to investigator decision, and 1 had early PD in C1; †4 pts withdrew consent, 6 discontinued early due to AEs, 1 discontinued due to PI decision, 1 had early PD in C1; BOR, best overall response; CR, complete response; ND, not done or missing; PD, progressive disease.

Olszewski A et al. ASH. 2023

PFS in Mosun-Pola target dose cohort

1L

KM curve of PFS in Mosun-Pola target dose cohort



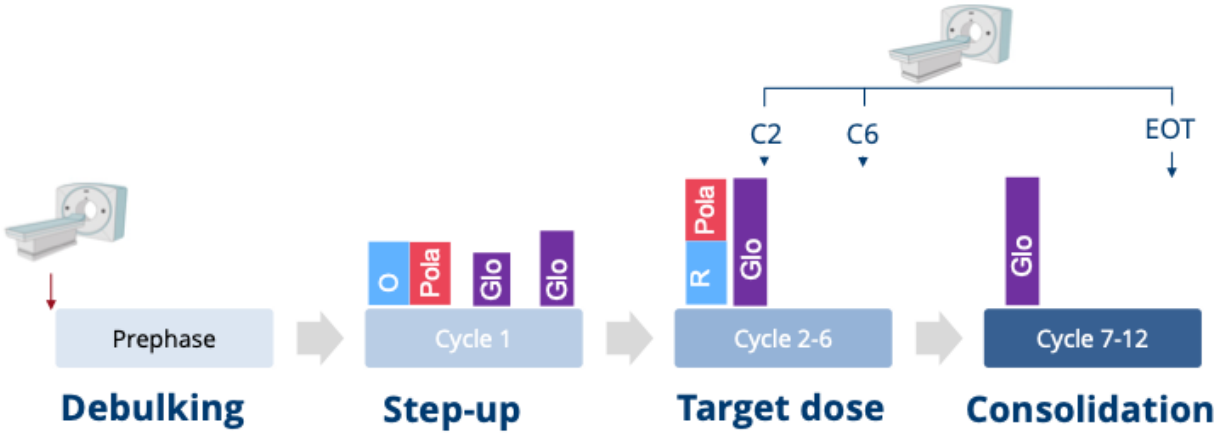
	Mosun-Pola target dose cohort N=101
Median PFS, months (95% CI)	11.9 (9.5, NE)
9-month PFS event-free rate, % (95% CI)	64.8 (54.2, 75.5)
12-month PFS event-free rate, % (95% CI)	49.7 (36.8, 62.5)
Patient disposition	
Censored/no event at CCOD	64 (63.4)
Event	37 (36.6)
Disease progression	12 (12)
Death	25 (25)

Early data show encouraging PFS with Mosun-Pola in elderly unfit or frail pts with previously untreated DLBCL

Data cut-off: August 5, 2023.

1L

R-Pola-Glo – Study Design



Indication

- **Untreated** patients >60 yo with LBCL
- Non-eligible for full dose R-CHOP

Study Design

- One-arm, multicenter phase II
- 30 centers in Germany and Austria
- **80 pts** (C1-6 mandatory inpatient)
- Mandatory prophylaxis

Endpoints

- *Primary:* **1y-PFS rate**
- *Secondary:*
  - Efficacy (OS, EFS)
  - Feasibility/Toxicity

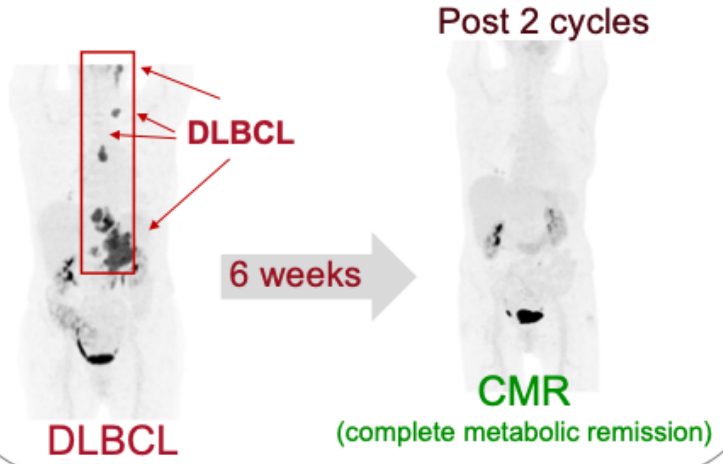
American Society of Hematology | AGMT Austrian Group • Medical • Tumor Therapy | IKF Institut für Klinische Krebsforschung | R-Pola-Glo | GLA German Lymphoma Alliance

Chapuy et al, ASH 2025

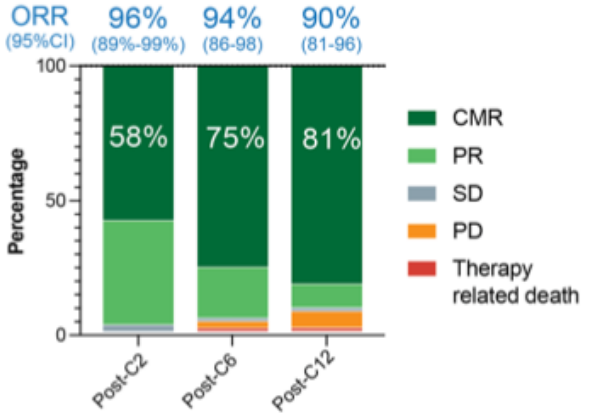
1L

R-Pola-Glo – Response

Representative Case



Response Rate (n=80)



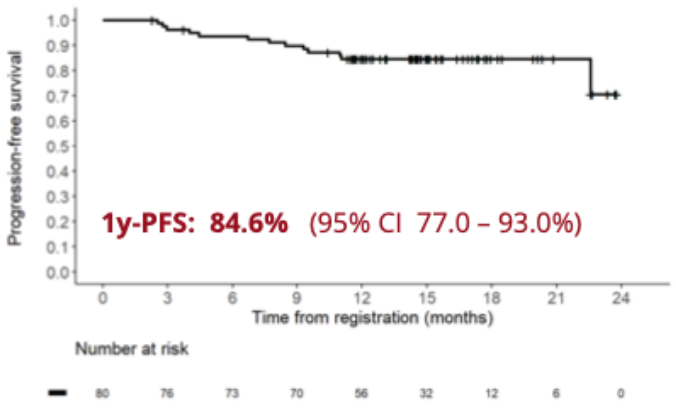
- ORR at cycles 2, 6, and EOT were 96%, 94%, and 90%; corresponding CMR rates were 58%, 75%, and 81%, respectively.
- CMR conversions were observed after C6, highlighting the role of glofitamab consolidation.

Chapuy et al, ASH 2025

1L

R-Pola-Glo – Outcome

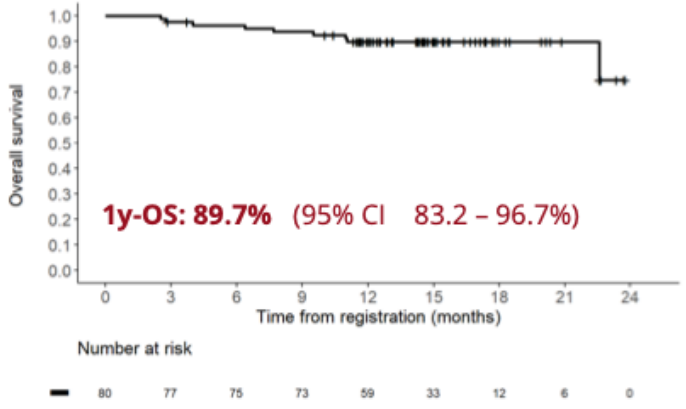
1-year Progression-free Survival (PFS)



1y-PFS: 84.6% (95% CI 77.0 – 93.0%)

Median f/u: 15 months

1-year Overall Survival (OS)



1y-OS: 89.7% (95% CI 83.2 – 96.7%)

- ➔ With a median follow-up time of 15 months, responses were durable and the 1y-PFS and 1y-OS rates were 85% and 90%, respectively.
- ➔ At time of analysis (July 2 2025), 89% (71/80) of patients were alive.

Chapuy et al, ASH 2025

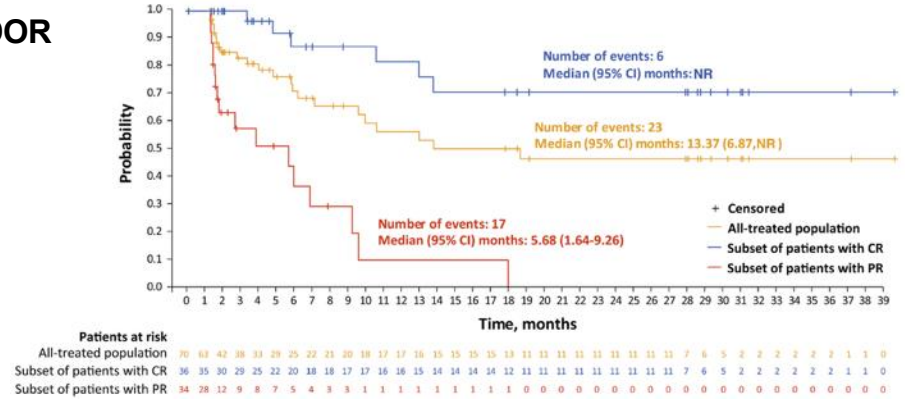

Loncastuximab
Lonca-
teserine

RR

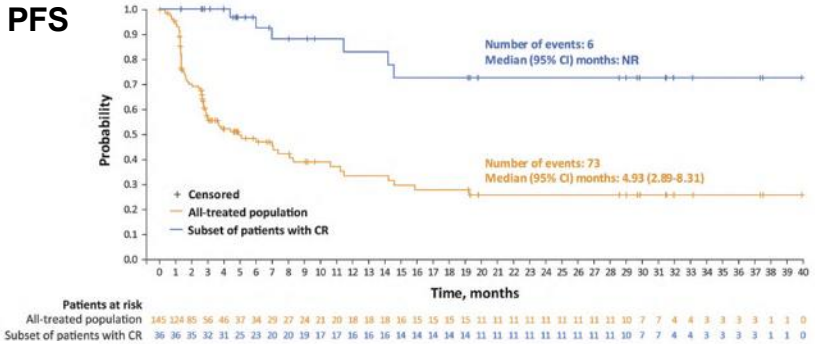
Loncastuximab teserine

Response
- ORR: 48.3% (70/145)
- CR rate: 24.8% (36/145)

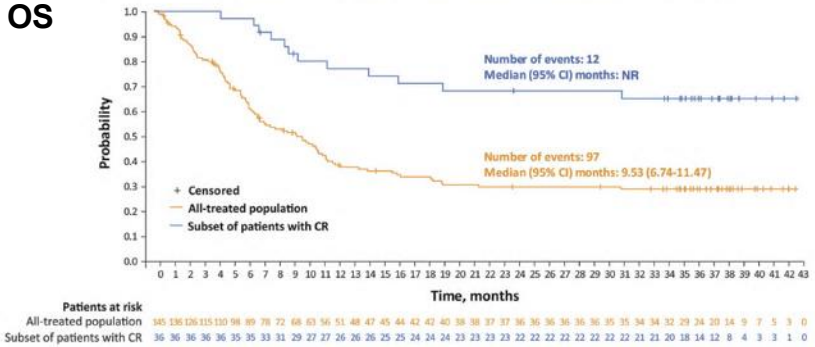
DOR



PFS



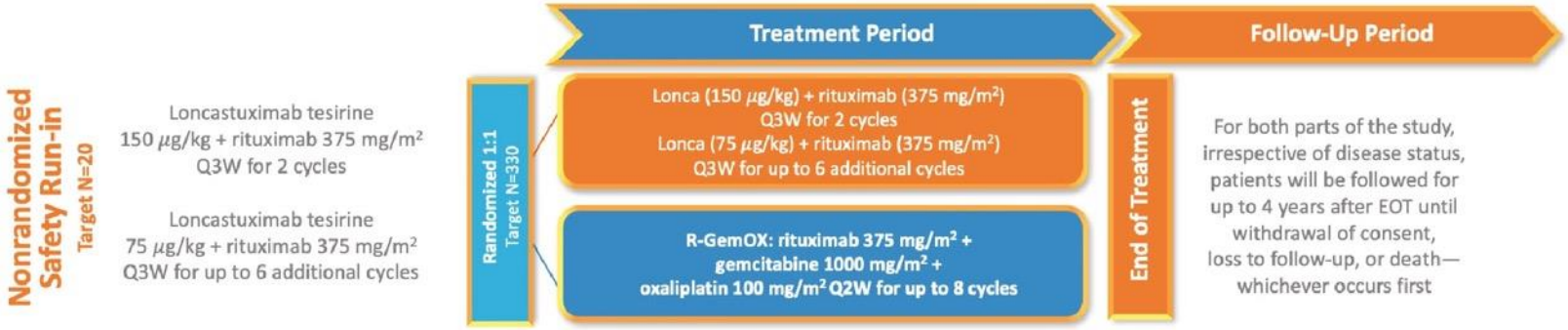
OS



Data cutoff: September 15, 2022. Median duration of follow-up: 7.8 months (range, 0.3-42.6) in the all-treated population.
Caimi PF, et al. *Haematologica*. 2024;109(4).

LOTIS-5 Lonca-T vs RGemOx in R/R DLBCL

RR



EOT, end of treatment; Q2W, every 2 weeks; Q3W, every 3 weeks; SCT, stem cell transplant.

Outcomes

- The primary endpoint is progression-free survival by independent central review.
- Key secondary endpoints include overall survival, overall response rate, safety, duration of response, pharmacokinetic parameters, and changes in patient-reported outcomes (**Table 1**).

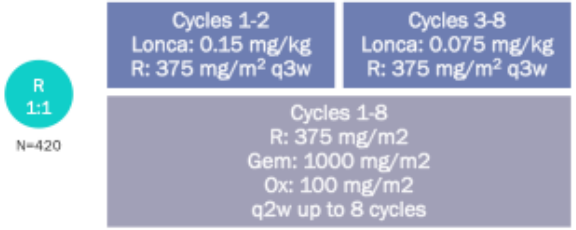
Hamadani et al, ASCO 2022

Safety Run-in Results of Phase 3 LOTIS-5 Trial of Lonca-R in R/R DLBCL

RR

Key Eligibility Criteria

- R/R DLBCL after ≥1 prior line of treatment
- Ineligible for SCT



Primary endpoints: PFS (by ICR)
Key secondary endpoints: OS, ORR, CR, DOR, safety, PK parameters, Lonca ADAs, PROs

Efficacy outcomes	
Safety run-in population (N=20)	
ORR (95 % CI), %	80.0 (56.3-94.3)
CRR (95 % CI), %	50.0 (27.2-72.8)
Median PFS (95 % CI), months	8.3 (4.5-NE)
Responders (n=16)	
Median DOR (95 % CI), months	8.02 (3.19-NE)
Events, n (%)	5 (31.3)
Complete Responders (n=10)	
Median DOR, months (95% CI)	NE (3.19-NE)
Events, n (%)	3 (30.0)

- Median DOR: 37.2 mo
- Prior SCT: 1 (5%)
- ECOG 1: 10 (50%)
- Median prior LOT: 1 (1-7)
  - 8 (40) had ≥2 prior LOT

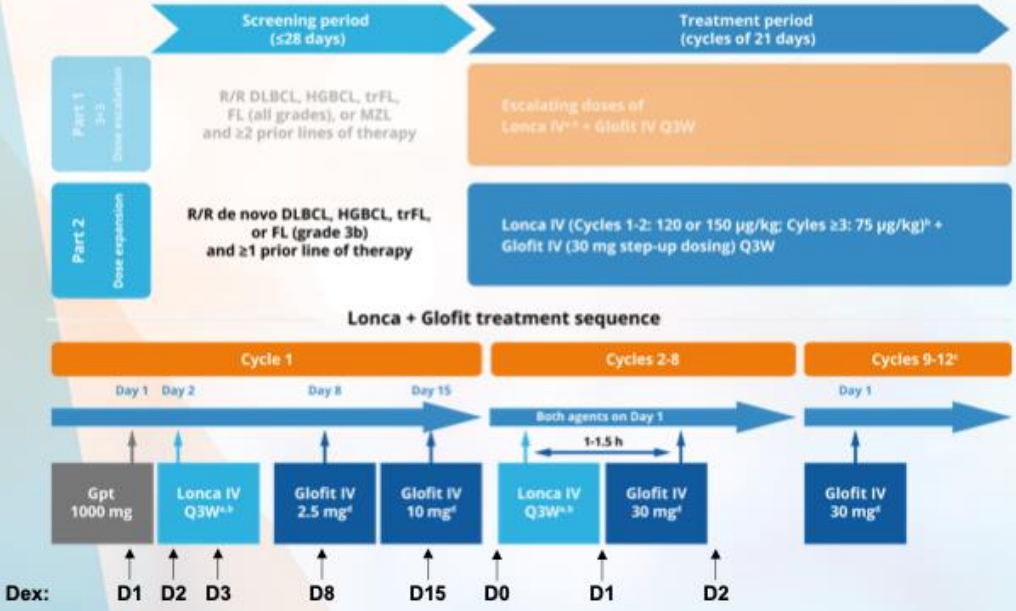
Safety outcomes, n (%)	N=20
All grade TEAE	20 (100)
Grade ≥3 TEAE (>10%)	11 (55)
GGT increased	5 (25)
Neutropenia	4 (20)
COVID-19	3 (15)
Serious AEs	6 (30)
TEAEs leading to withdrawal	8 (40)

- Serious AEs included infection [6 (30%)] and the following in 1 (5%) patients each: hyponatremia, anaphylactic reaction, pleural effusion, malaise, and neurological decompression
- 9 (45%) died due to PD [15 (25%)], COVID-19 [2 (10%)], pancreatic neoplasia [1 (5%)], liver failure [1 (5%)]

Carlo-Sella C, et al. EHA 2025. Abstract PS1957.

LOTIS-7 Lonca-T + Glofit Phase 1

STUDY DESIGN & PATIENT POPULATION



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

2L+, second line or later; 3L+, third line or later; B-NHL, B-cell non-Hodgkin lymphoma; CAR-T, chimeric antigen receptor T cell; CR, complete response; CRS, cytokine release syndrome; D, day; Dex, dexamethasone; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FL, follicular lymphoma; Glofit, glofitamab; Gpt, obinutuzumab; HGBCL, high-grade B-cell lymphoma; IV, intravenous; Lonca, loncastuximab tesirine; MTD, maximum tolerated dose; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, every 3 weeks; RDE, recommended dose for expansion; RFS, relapse-free survival; R/R, relapsed or refractory; SCT, stem cell transplant; trFL, transformed follicular lymphoma.
[a]...kg; and dose level 3, 150 µg/kg. [b]If the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3 per label. [c]Participants may continue Glofit up ...cles (or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurs first). The follow-up period is for ≤2 years from the end of treatment. [d]The first ...r mandatory hospitalization; subsequent doses require hospitalization if grade ≥2 CRS occurs.

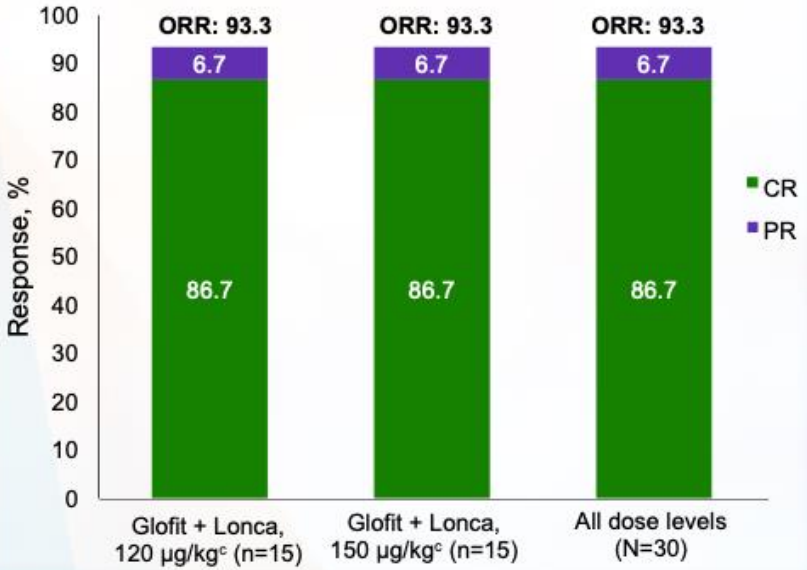
Aldaruccio et al, ICML 2025

LOTIS-7 Lonca-T + Glofit Phase 1: Preliminary Results

BEST OVERALL RESPONSE & DURATION OF RESPONSE

EFFICACY EVALUABLE POPULATION (N=30)[a]

Best overall response[b]



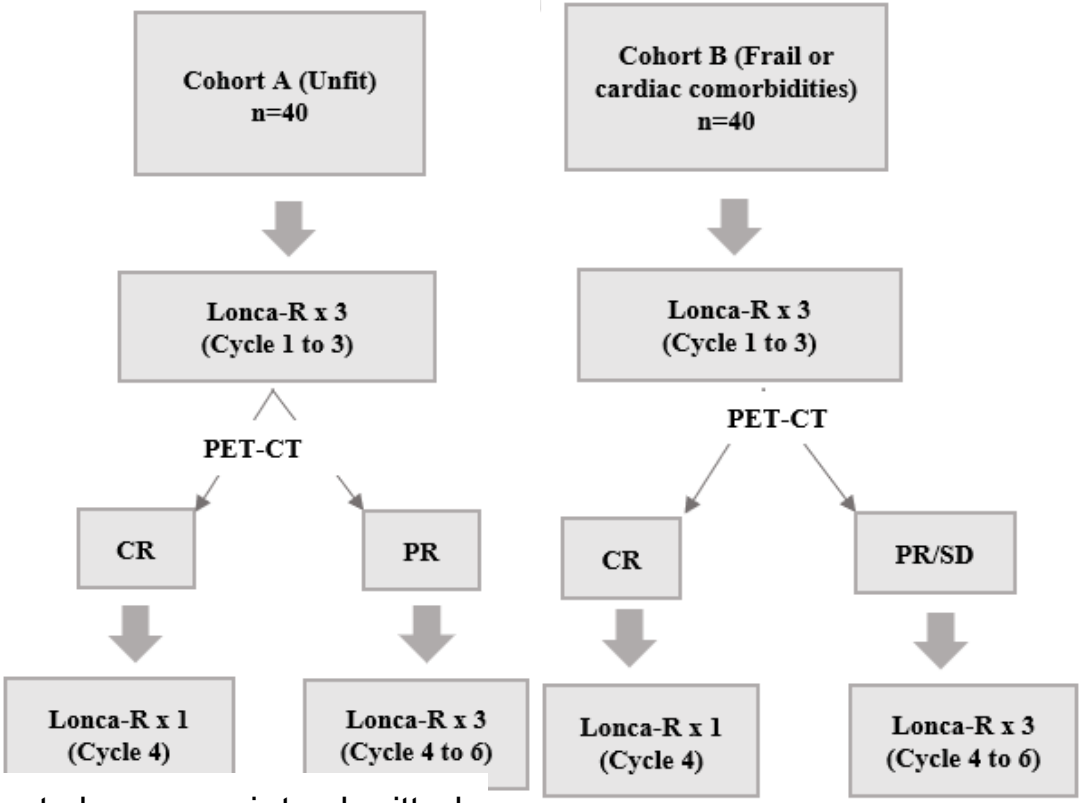
Duration of response

Characteristic, n (%)	Glofit + Lonca, 120 µg/kg[c] (n=15)	Glofit + Lonca, 150 µg/kg[c] (n=15)	All dose levels (N=30)
DOR[d] Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5

Data cutoff: April 14, 2025.
CR, complete response; DOR, duration of response; Glofit, glofitamab; Lonca, loncastuximab tesirine; NE, not estimable; ORR, overall response rate; PR, partial response.
[a]The efficacy evaluable population (N=30) included all patients who received ≥1 dose of the study drug with a valid baseline and ≥1 valid postbaseline disease assessment. Patients who did not have a postbaseline assessment owing to early clinical progression or death to rounding. [c]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3. [d]In the efficacy evaluable population, the DOR and probability of maintaining an event-ng all patients who had a best response of CR or PR.

Aldaruccio et al, ICML 2025

LOTIS-9 Lonca-T+R in elderly/unfit 1L LBCL



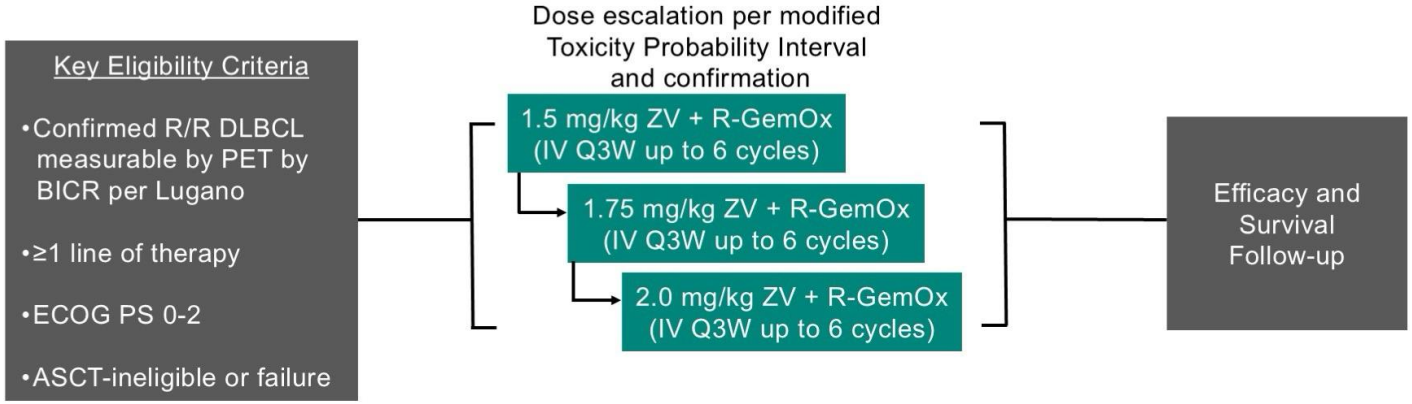
Closed due to grade 5 events that were considered unrelated to study treatment

Nair & Westin et al, manuscript submitted


Zilovertamab
Zilo-
vedotin

waveLINE-003 Phase 2 Study Design (NCT05139017)

Phase 2/3, open label study of zilovertamab vedotin in combination with R-GemOx in DLBCL



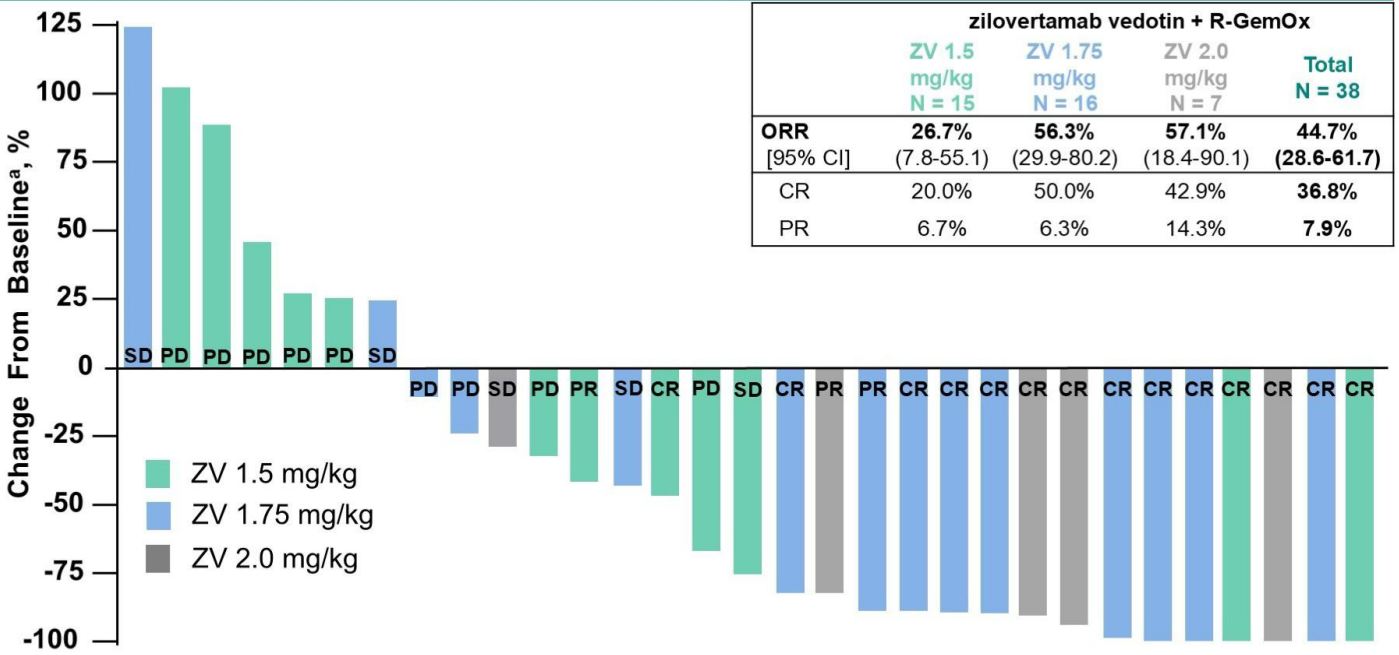
Endpoints:
- Primary: Safety and RP2D
- Tertiary/Exploratory: Objective response and duration of response per Lugano criteria by BICR, and overall survival

Blinded Independent Central Review; ECOG PS, Eastern Cooperative Oncology Group Performance Score; IV, intravenous; PET, Positron Emission Tomography; Q3W, every 3 weeks; RP2D, recommended Phase 2 dose.

Armand et al, ASCO 2025

Overall Response Rate

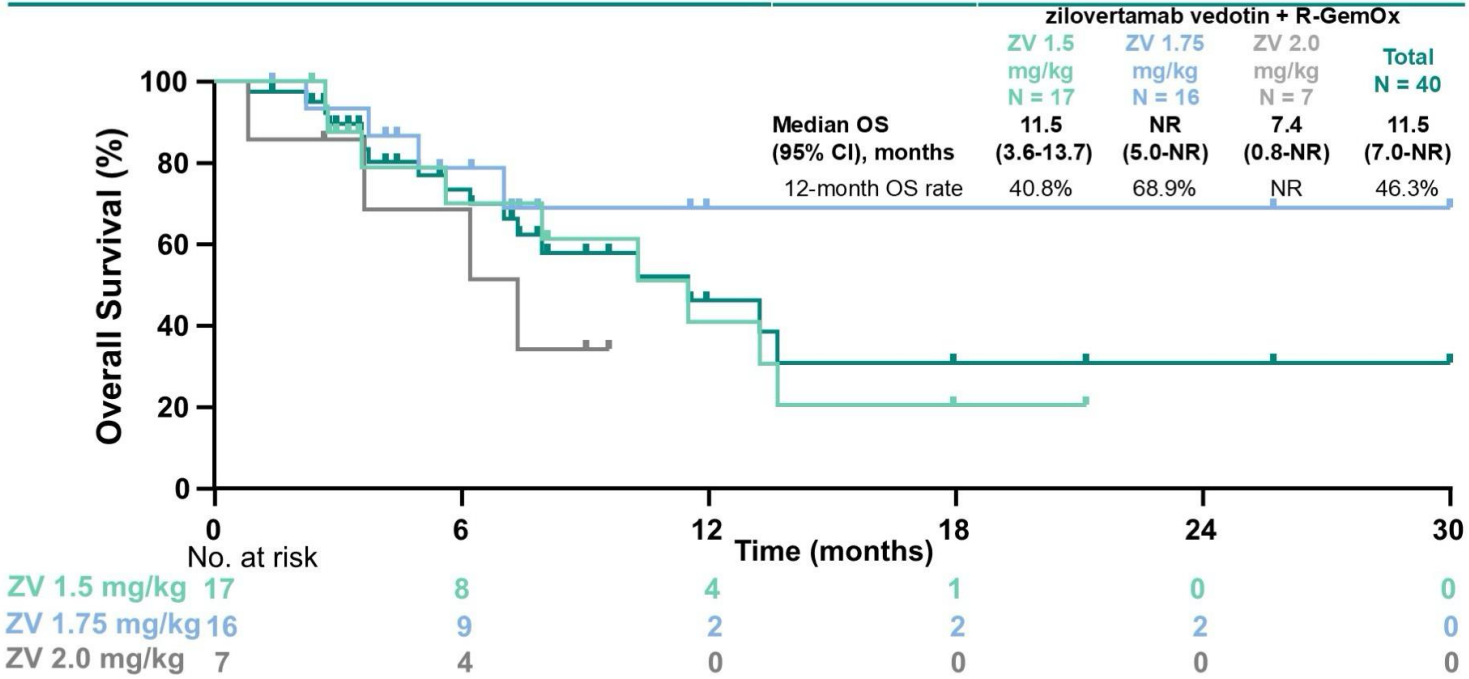
	zilovertamab vedotin + R-GemOx			
	ZV 1.5 mg/kg N = 15	ZV 1.75 mg/kg N = 16	ZV 2.0 mg/kg N = 7	Total N = 38
ORR [95% CI]	**26.7%** (7.8-55.1)	**56.3%** (29.9-80.2)	**57.1%** (18.4-90.1)	**44.7%** **(28.6-61.7)**
CR	20.0%	50.0%	42.9%	**36.8%**
PR	6.7%	6.3%	14.3%	**7.9%**



Data cutoff: 1August2024. aBest percentage change from baseline SPD

Armand et al, ASCO 2025

Overall Survival

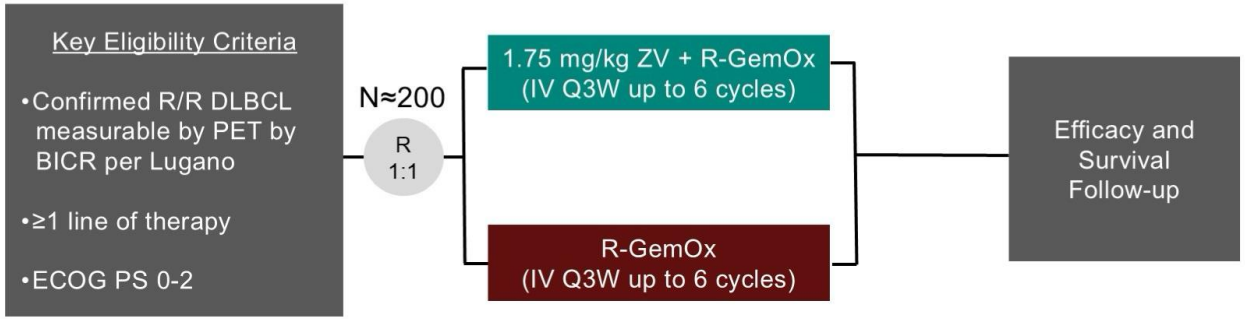


Data cutoff: 1August2024. Tick marks represent data censored at the time of last imaging assessment.

Armand et al, ASCO 2025

waveLINE-003 Phase 3 Study Design (NCT05139017)

Zilovertamab vedotin in combination with R-GemOx versus R-GemOx in R/R DLBCL



Endpoints:
- Primary: Progression-free survival per Lugano criteria by BICR, and overall survival
- Secondary: Objective response and duration of response per Lugano criteria by BICR

Armand et al, ASCO 2025


Brentuximab
Brentux-vedotin

ECHELON-3 trial design

Phase 3 in Relapsed/Refractory Diffuse Large B-Cell Lymphoma

Key inclusion criteria

- R/R DLBCL with eligible subtypes[a]
- Age ≥18 years
- **≥2 prior lines of therapy**
- **Ineligibility for or disease relapse following HSCT or CAR T-cell therapy**
- ECOG PS 0-2
- FDG-avid, measurable disease

Key exclusion criteria

- Prior BV or Len
- Active cerebral/meningeal disease
- Grade ≥2 peripheral neuropathy

Randomization 1:1

BV+Len+R (n=112)

BV 1.2 mg/kg IV Q3W + Len 20 mg PO QD + R 375 mg/m^2 IV Q3W[b]

Treatment groups[c]

Placebo+Len+R (n=118)

Placebo IV Q3W + Len 20 mg PO QD + R 375 mg/m^2 IV Q3W[b]

Primary endpoint

- OS in ITT population

Secondary endpoints

- PFS_{INV} and ORR_{INV} using the response criteria per Lugano 2014 in ITT population
- $CR\ rate_{INV}$
- DOR_{INV}
- OS in CD30-positive population
- Safety and tolerability

Stratification

- CD30 status (≥1% vs <1%)
- Cell of origin (GCB or non-GCB)
- Prior treatment with CAR-T therapy (received or not)
- Prior treatment with SCT (received or not)

- Per protocol, G-CSF prophylaxis was required

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; GCB, germinal center B cell; HSCT, hematopoietic stem cell transplant; INV, investigator; ITT, intention to treat; IV, intravenous; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, oral; Q3W, every 3 weeks; QD, once daily; R, rituximab; R/R, relapsed or refractory; SCT, stem cell transplant.

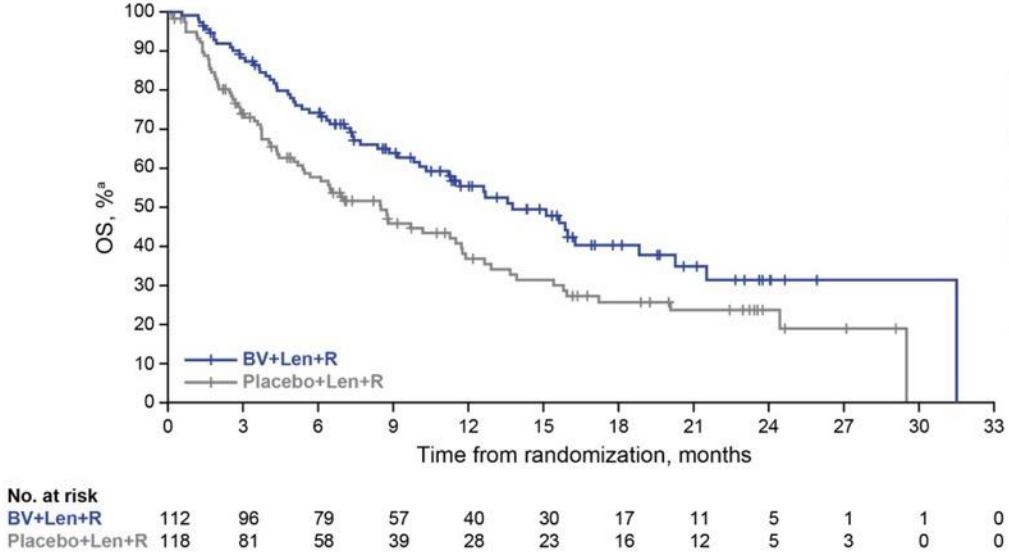
[a] Eligible subtypes include but are not limited to transformed DLCBL, high-grade double-/triple-hit lymphoma, and not otherwise specified.

[b] Starting with cycle 2, R can be administered intravenously or subcutaneously (1400 mg subcutaneously Q3W).

[c] Treatment was allowed to continue until disease progression or unacceptable toxicity.

Primary endpoint met with significant improvement in Overall Survival

BV+Len+R reduced risk of death by 37% compared with placebo+Len+R



	BV+Len+R (n=112)	Placebo+Len+R (n=118)
OS, median (95% CI), months	**13.8** (10.3-18.8)	**8.5** (5.4-11.7)
Hazard ratio (95% CI)[b]	0.629 (0.445-0.891)	
Log-rank *P* value[c]	.0085	
Events (deaths)	58	76
Follow-up, median (95% CI), months	15.5 (12.2-18.1)	18.9 (12.2-23.2)

- BV+Len+R prolonged median OS by 5.3 months compared with placebo+Len+R
- Prespecified O'Brien-Fleming efficacy boundary was crossed at this interim analysis

BV, brentuximab vedotin; CD, cluster of differentiation; GCB, germinal center B cell; Len, lenalidomide; OS, overall survival; R, rituximab.

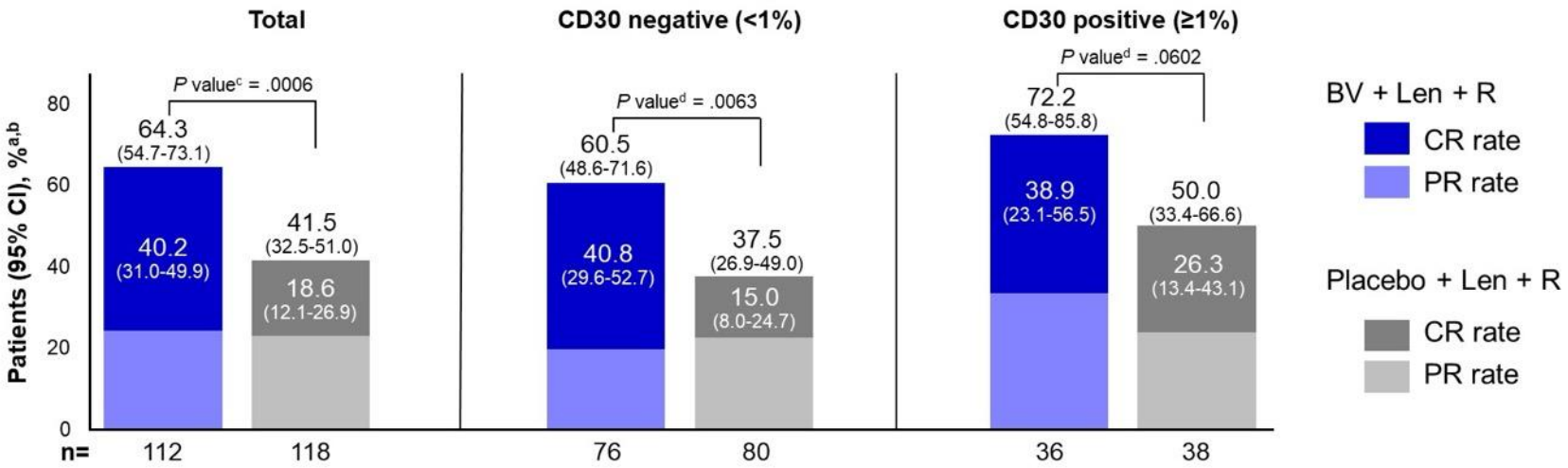
[a] OS is time from randomization to death due to any cause. OS is estimated using Kaplan-Meier method.

[b] Hazard ratio and 95% CI are based on a stratified Cox regression model with stratification factors (GCB or non-GCB) and CD30 status (≥1% or <1%) at randomization. Hazard ratio of <1 favors BV+Len+R. Nonbinding futility boundary hazard ratio is 1.1.

[c] Two-sided *P* value from a stratified log-rank test with stratification factors of cell origin and CD30 status at randomization. O'Brien-Fleming efficacy boundary 2-sided *P* value is .0232.

Overall Response Rate was significantly higher with BV+Len+R

40% CR rate with BV+Len+R and ORR improvement regardless of CD30 expression



- In the total population, the median DOR (95% CI) was longer with BV+Len+R: 8.3 months (4.2-15.3 months) vs 3.0 months (2.8-5.4 months)
  - In patients who had a CR, the median DOR (95% CI) was 18.9 months (11.1 months-NR) with BV+Len+R and NR (2.8 months-NR) with placebo+Len+R
  - The median time to CR onset (range) was 1.58 months (1.2-7.3 months) with BV+Len+R and 1.61 months (0.7-4.6 months) with placebo+Len+R

BV, brentuximab vedotin; CD, cluster of differentiation; CR, complete response; DOR, duration of response; GCB, germinal center B cell; Len, lenalidomide; NR, not reached; ORR, objective response rate; PR, partial response; R, rituximab.
[a] Exact 95% CI computed using the Clopper-Pearson method (Clopper 1934).
[b] Best response per Lugano 2014 by investigator assessment. Includes metabolic and nonmetabolic response. Response assessments after progressive disease or start of new anticancer therapy are excluded.
[c] Two-sided *P* value based on Cochran-Mantel-Haenszel test controlling for stratification factors cell of origin (GCB or non-GCB) and CD30 status (≥1% or <1%) at randomization.
[d] Two-sided *P* value based on Fisher exact test.

Phase III R/R DLBCL Trial Outcomes Comparison

Trial Name	Complete Response (CR)	Median PFS (mo)	Median OS (mo)
POLARGO	**40.3%** (vs 19.0%)	**7.4** (vs 2.7)	**19.5** (vs 12.5)
SUNMO	**51.4%** (vs 24.3%)	**11.5** (vs 3.8)	**18.7** (vs 13.6)*
ECHELON-3	**40.0%** (vs 19.0%)	**4.2** (vs 2.6)	**13.8** (vs 8.5)
LOTIS-5	*pending*	*pending*	*pending*

*Values in parentheses denote control arm outcomes.

* OS is interim analysis

Conclusions: Moving from right to left

ADC plus friends is changing management for LBCL

Unmet needs:

- Is vedotin after vedotin effective?
- Biomarkers +/- helpful in Pola-vedotin – same for other ADC?
- Optimal combination partner?

Grazie Mille