POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino
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19-21 febbraio 2026

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Linfomi aggressivi di derivazione B linfocitaria

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Disclosures of Enrico Derenzini

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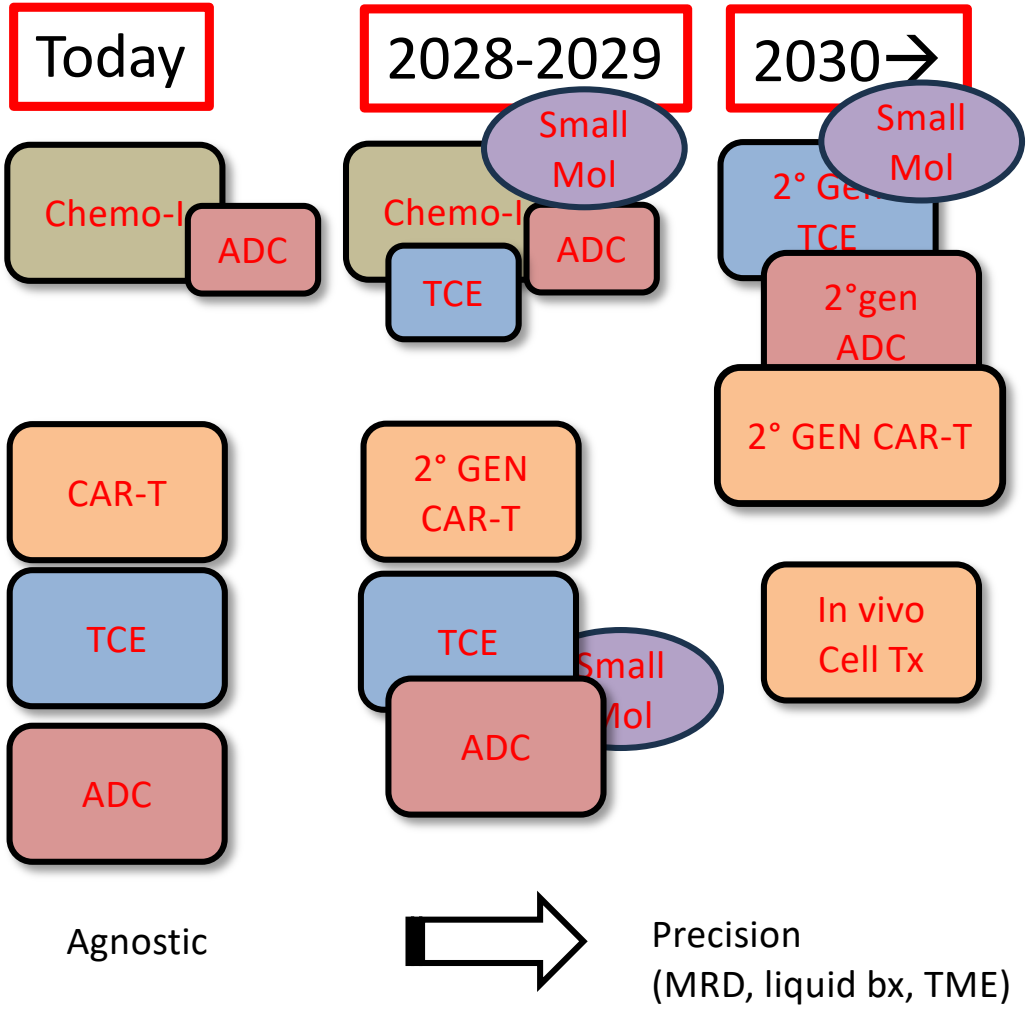
AbbVie					X	X	
Astra Zeneca						X	
Lilly						X	
Sobi					X	X	
Gilead						X	
Regeneron			X				

The evolution of therapy in DLBCL



RWE & Updates of ongoing studies
In light of sequencing strategies

1L R-CHOP+
A competitive landscape

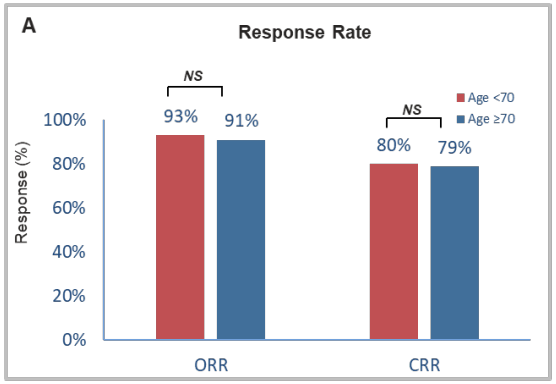
The era of novel combinations
And 1L chemofree regimens

RWE & Updates of ongoing studies
In light of sequencing strategies

Real-World Outcomes of Frontline Polatuzumab-R-CHP and Impact of Frailty in Older Adults with Diffuse Large B-Cell Lymphoma

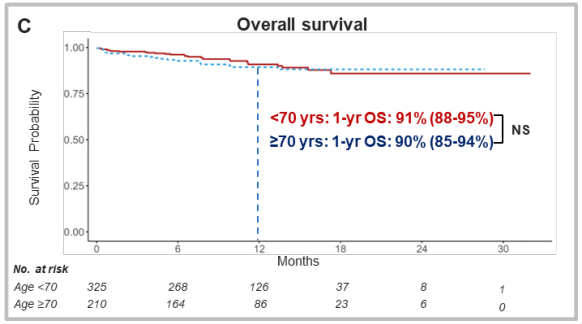
Current Combinations
1L DLBCL RWE

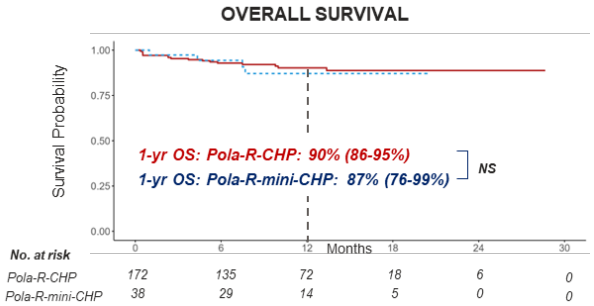
	Younger Adults Age < 70 (N = 325)	Older Adults Age ≥ 70 (N = 210)	P-value
Age	62 (53, 66)	75 (72, 77)	
Sex – no. (%)			0.6
Male	189 (58%)	128 (61%)	
ECOG Score			<0.001
0-1	274 (86%)	156 (77%)	
2+	44 (14%)	46 (23%)	
Stage			0.8
I	8 (2.5%)	5 (2.4%)	
II	31 (9.5%)	15 (7.1%)	
III	46 (14%)	37 (18%)	
IV	238 (73%)	152 (72%)	
Extranodal Dx			0.5
Yes	243 (76%)	163 (78%)	
LDH			0.7
< ULN	121 (37%)	73 (35%)	
> ULN	203 (63%)	135 (65%)	
IPI Score			<0.001
0 to 2	145 (45%)	49 (23%)	
3 to 5	180 (55%)	161 (77%)	



Median follow-up: 11.8 months

	Younger Adults Age < 70 (N = 325)	Older Adults Age ≥ 70 (N = 210)	P-value
Neutropenia, Grade 3+	88 (27%)	78 (38%)	0.017
Febrile neutropenia, Grade 3+	49 (15%)	31 (15%)	>0.9
Thrombocytopenia, Grade 3+	36 (11%)	45 (22%)	0.002
Peripheral Neuropathy – no. (%)	107 (34%)	86 (42%)	0.086
Grade 3+	3 (2.8%)	3 (3.5%)	>0.9
Cardiomyopathy	5 (1.6%)	13 (6.2%)	0.008
Infection, Grade 3+	65 (20%)	43 (21%)	0.8
Hospitalization	85 (26%)	79 (38%)	0.006
ICU Admission	16 (4.9%)	16 (7.7%)	0.3
Treatment Completion			0.2
Yes	289 (89%)	178 (85%)	
Discontinued	36 (11%)	32 (15%)	
Reason for Discontinuation			0.2
Progression	13 (36%)	6 (19%)	
Toxicity	10 (28%)	14 (44%)	
Other	13 (36%)	12 (38%)	



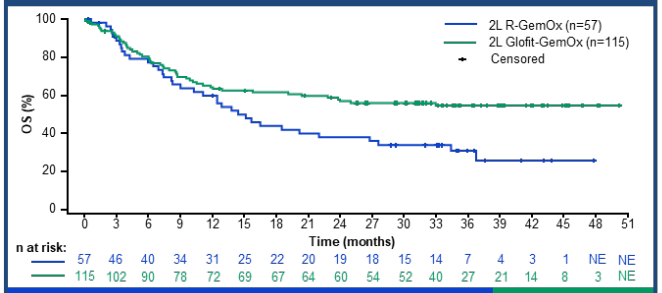


Iyengar V, et al; oral presentation ASH 2025, Blood (2024) 144 (Supplement 1): 2336.

STARGLO (NCT04408638): a randomized, global, Phase III trial

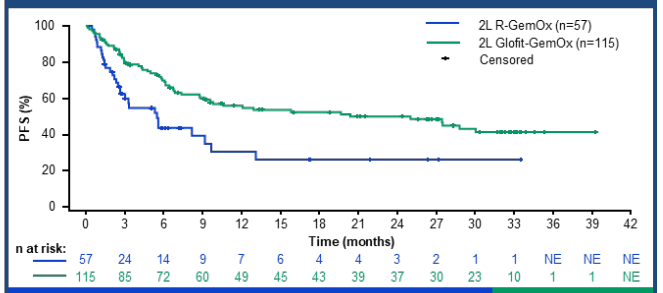
2L+ anti CD20 TCE + Chemo
Glofitamab

Overall survival

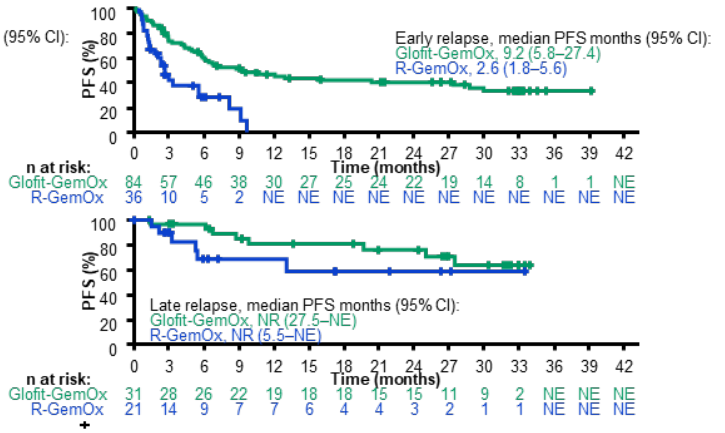


	R-GemOx 2L (n=57)	Glofit-GemOx 2L (n=115)
OS, median (95% CI); months	14.4 (10.3–26.8)	NE (22.8–NE)
36-month OS, % (95% CI)	30.8 (17.7–44.0)	54.6 (45.2–64.0)

Progression-free survival



	R-GemOx 2L (n=57)	Glofit-GemOx 2L (n=115)
PFS, median (95% CI); months	5.5 (2.6–9.7)	20.4 (9.2–NE)
30-month PFS, % (95% CI)	26.3 (10.3–42.4)	41.5 (30.8–52.2)



Outcome	Overall		2L	
	R-GemOx (n=91)	Glofit-GemOx (n=183)	R-GemOx (n=57)	Glofit-GemOx (n=115)
OS, median (95% CI); months	12.5 (7.9–16.5)	25.5 (17.0–NE)	14.4 (10.3–26.8)	NE (22.8–NE)
36-month OS, % (95% CI)	27.4 (17.3–37.5)	47.1 (39.5–54.6)	30.8 (17.7–44.0)	54.6 (45.2–64.0)
PFS, median (95% CI); months	3.3 (2.3–5.6)	14.4 (8.8–27.4)	5.5 (2.6–9.7)	20.4 (9.2–NE)
30-month PFS, % (95% CI)	15.2 (0.9–29.5)	38.1 (29.8–46.3)	26.3 (10.3–42.4)	41.5 (30.8–52.2)
ORR, n (%)	37 (40.7)	125 (68.3)	28 (49.1)	83 (72.2)
CR, n (%)	23 (25.3)	107 (58.5)	16 (28.1)	73 (63.5)
DoCR, median (95% CI); months	24.2 (6.9–NE)	NE (27.2–NE)	NE (6.5–NE)	NE (24.8–NE)

3736

Epcoritamab + GemOx Achieves Durable > 2-Year Remissions in Relapsed/Refractory 2L+ Diffuse Large B-cell Lymphoma: Long-Term Data Reinforce Clinical Potential of the Regimen Across a Diverse Patient Population

Brody J, ASH 2025, Abstr 3736, Poster Presentation

Abramson JS et al. ASH 2025 poster presentation, Blood (2025) 146 (Supplement 1): 5519.

Abdulhaq H et al. ASH 2025 poster presentation, *Blood* (2025) 146 (Supplement 1): 3743.

Poster 5514

Surovatamig (AZD0486), a CD19xCD3 T-cell Engager (TCE), Demonstrates High Rate of Minimal Residual Disease (MRD)–Negative Complete Responses in Relapsed/Refractory (R/R) Diffuse Large B-cell Lymphoma (DLBCL), Including in Patients Who Previously Progressed on CD20 TCE and CD19 CAR T-cell Therapies

3L + Anti CD19 BsABs
Surovatamig

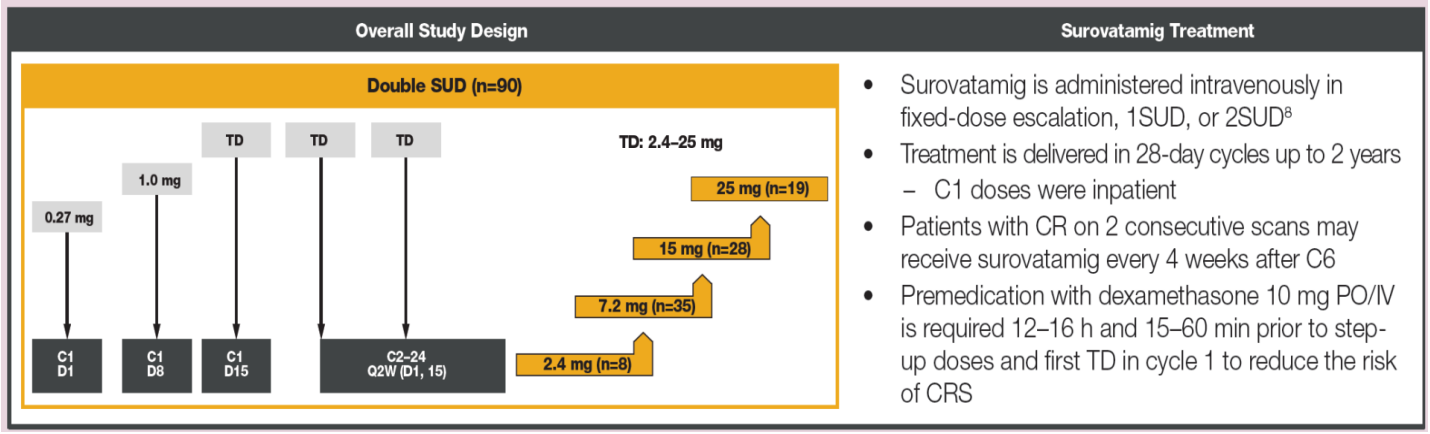
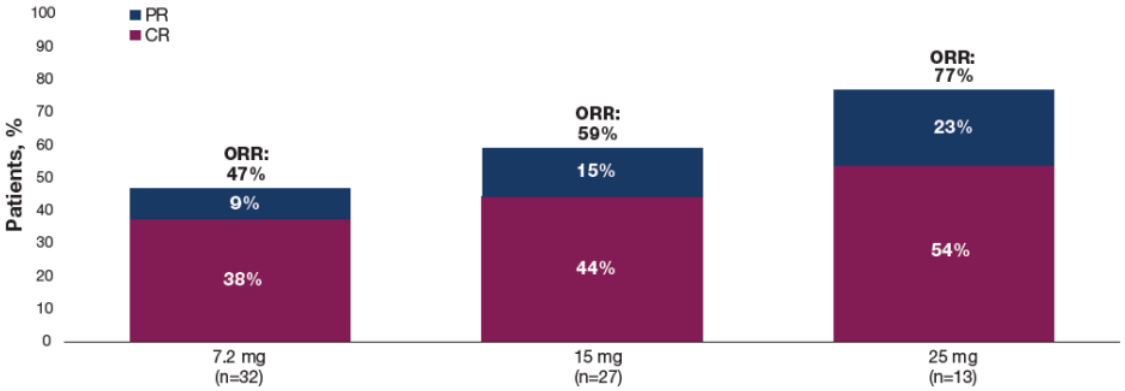
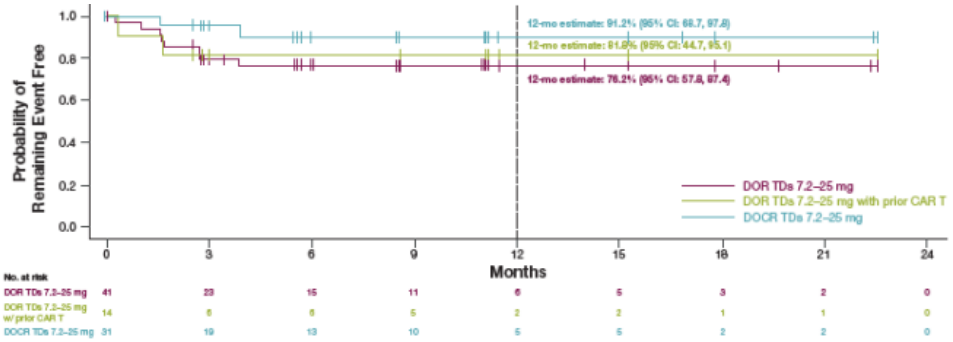


Figure 1. Response Rates by TDs of 7.2 to 25 mg in Efficacy-Evaluable Patients





Kim TM, ASH 2025, Abstr 5514, Poster Presentation

1L R-CHOP+
A competitive landscape

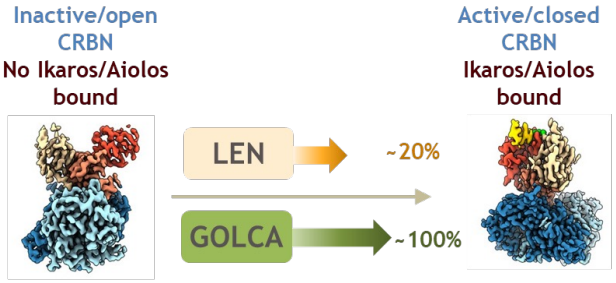
ONGOING R-CHOP+X TRIALS IN HIGH-RISK 1L DLBCL

TRIAL	TX COMPONENTS	AGNOSTIC	BIOLOGY DRIVEN	CLASS	LOW-RISK/ LIMITED STAGE
POLARIX	R-CHOP+POLATUZUMAB	X		ADC	-
waveLINE-010 study	R-CHOP+ZILOVERTAMAB	X		ADC	X IPI 1
ESCALADE	R-CHOP+ACALABRUTINIB		X (COO)	SMALL MOL (BTKi)	X IPI 1
BELIEVE-01	R-CHOP+ORELABRUTINIB		X (NGS)	SMALL MOL (BTKi)	
GOLSEEK-1	R-CHOP+GOLCADOMIDE	X		SMALL MOL (CellMOD)	X IPI 1
DEB STUDY	R-CHOP+TUCIDINOSTAT		X (IHC, MYC-BCL2)	(HDAC)	X IPI 1
GUIDANCE-002	R-CHOP+X		X (NGS)	SMALL MOL (multiple)	-
FRONT-MIND	R-CHOP+TAFA/LENA	X		SMALL MOL (IMID) + mAb	-
EPCORE DLBCL-02	R-CHOP+EPCORITAMAB	X		X IPI 2-5 (TCE)	-
SKY-GLO	R-POLA-CHP-GLOFITAMAB	X		X IPI 2-5 (TCE)	-
OLYMPIA-3	O-CHOP	X		X IPI 2-5 (TCE)	-

Golcadomide plus R-CHOP in previoulsy untreated aggressive B-cell lymphoma: 24 month efficacy results

Novel Combinations
1L DLBCL R-CHOP+
CellMODs

Allosteric regulation of CRBN[1]



- The distinct binding of golcadomide outside of the tri-TRP pocket induces the complete conversion to the active, closed conformation of cereblon vs LEN (~**100%** vs ~**20%**), leading to deeper and more rapid degradation of Ikaros/Aiolos compared with LEN
- Golcadomide deeply penetrates lymphoid tissue, an optimal feature for the treatment of lymphoma

Baseline characteristics were generally balanced between treatment arms

	Golcadomide 0.2 mg + R-CHOP[a] (n = 35)	Golcadomide 0.4 mg + R-CHOP[a] (n = 37)
Age, median (IQR), years	62.0 (52.0–69.0)	63.0 (53.0–69.0)
Female	12 (34)	20 (54)
IPI score at enrollment		
Low and low-intermediate risk (0–2)	11 (31)	11 (30)
Low-intermediate (1–2) risk with high-risk features[b]	6 (17)	5 (14)
High-intermediate risk (3)	17 (49)	16 (43)
High risk (4 or 5)	7 (20)	10 (27)
High-risk disease[c]	30 (86)	31 (84)
Hans COO[d]		
GCB	18 (51)	18 (49)
Non-GCB	12 (34)	12 (32)
Other[e]	5 (14)	7 (19)
Histology		
DLBCL NOS	27 (77)	32 (87)
Grade 3b FL	4 (11)	1 (3)
Double-hit lymphoma[f]	3 (9)	2 (5)
EBV-positive DLBCL NOS	1 (3)	0
ALK-positive LBCL	0	1 (3)
Elevated LDH	27 (77)	27 (73)
Extranodal involvement		
≤ 1 site	19 (54)	19 (51)
> 1 site	16 (46)	18 (49)

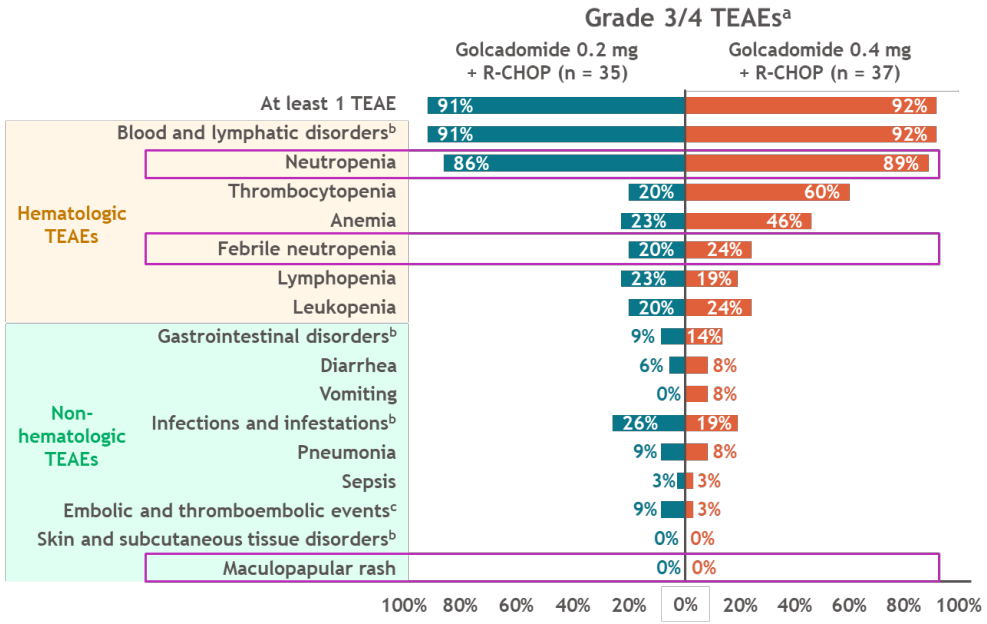
Data cutoff: May 12, 2025. Data are n (%) unless otherwise noted. [a] Includes patients who received the D1–7 schedule in dose escalation plus the RP2D in dose expansion; [b] Defined as IPI 1–2 with ≥ 1 lesion with a maximum diameter ≥ 7 cm and/or screening LDH ≥ 1.3 × ULN; [c] High-risk subgroup includes patients with IPI 3–5 disease or those with IPI 1–2 with ≥ 1 lesion with a maximum diameter ≥ 7 cm and/or screening LDH ≥ 1.3 × ULN; [d] Determined by immunohistochemistry; [e] Includes not done or unknown; [f] High-grade BCL with *MYC* and *BCL2* and/or *BCL6* rearrangements. ALK, anaplastic lymphoma kinase; BCL, B-cell lymphoma; COO, cell of origin; D, day; DLBCL, diffuse large B-cell lymphoma; EBV, Epstein-Barr virus; FL, follicular lymphoma; GCB, germinal center B cell; IPI, International Prognostic Index; IQR, interquartile range; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; NOS, not otherwise specified; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; RP2D, recommended Phase 2 dose; ULN, upper limit of normal.

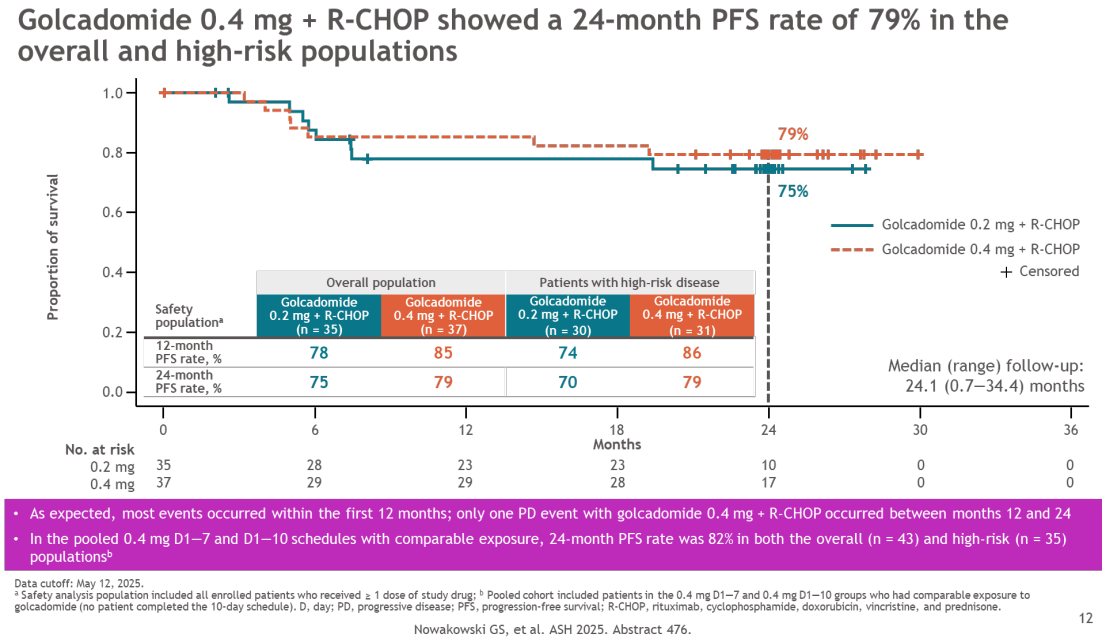
Nowakowski GS, et al. ASH 2025. Abstract 476.

Nowakowski GS, et al. ASH 2025. Abstract 476.

Golcadomide plus R-CHOP in previoulsy untreated aggressive B-cell lymphoma: 24 month efficacy results

Novel Combinations
1L DLBCL R-CHOP+
CellMODs





- As expected, most events occurred within the first 12 months; only one PD event with golcadomide 0.4 mg + R-CHOP occurred between months 12 and 24
- In the pooled 0.4 mg D1–7 and D1–10 schedules with comparable exposure, 24-month PFS rate was 82% in both the overall (n = 43) and high-risk (n = 35) populations[b]

Data cutoff: May 12, 2025.
[a] Safety analysis population included all enrolled patients who received ≥ 1 dose of study drug; [b] Pooled cohort included patients in the 0.4 mg D1–7 and 0.4 mg D1–10 groups who had comparable exposure to golcadomide (no patient completed the 10-day schedule). D, day; PD, progressive disease; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Nowakowski GS, et al. ASH 2025. Abstract 476.

1955

Fixed-Duration Epcoritamab + R-CHOP in Patients With Newly Diagnosed DLBCL and High IPI Scores (3–5) Led to Sustained Remissions and Disease-Free Survival Beyond 3 Years: Results From the EPCORE NHL-2 Trial

Lorenzo Falchi,[1] Fritz Offner,[2] Sven de Vos,[3] Joshua Brody,[4] Daniel Morillo,[5] Kim Linton,[6] Sylvia Snauwaert,[7] Michael Roost Clausen,[8] Raul Cordoba,[9] Toshihiko Oki,[10] Monica Wielgos-Bonvallet,[10] Mina Khoshdeli,[10] Yi Hao,[10] Jennifer Marek,[10] Malene Risum,[11] David Belada[12]

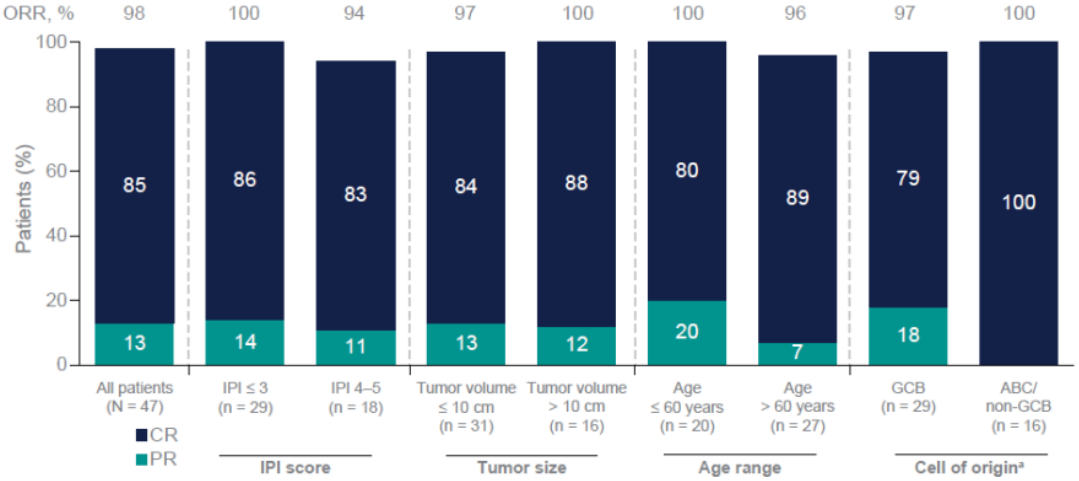
[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Department of Internal Medicine and Pediatrics, Universitair Ziekenhuis Gent, Ghent, Belgium; [3]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [4]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]Fundación Jiménez Díaz University Hospital, Madrid, Spain; [6]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK; [7]Department of Hematology, AZ Sint-Jan Hospital, Bruges, Belgium; [8]Vejle Hospital, Vejle, Denmark; [9]AbbVie, North Chicago, IL, USA; [10]Genmab, Plainsboro, NJ, USA; [11]Genmab, Copenhagen, Denmark; [12]4th Department of Internal Medicine – Hematology, Charles University, Hospital and Faculty of Medicine, Hradec Králové, Czech Republic

Key inclusion criteria

- Newly diagnosed CD20+ DLBCL[a]
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - DH/TH DLBCL[b]
  - FL grade 3B
- IPI score ≥ 3
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

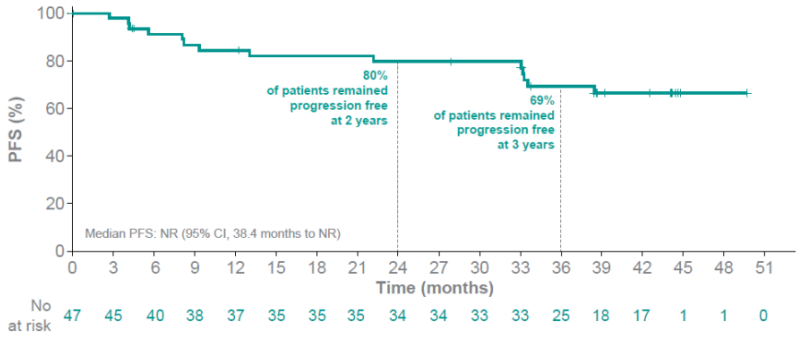
Novel Combinations
1L DLBCL R-CHOP+ TCEs

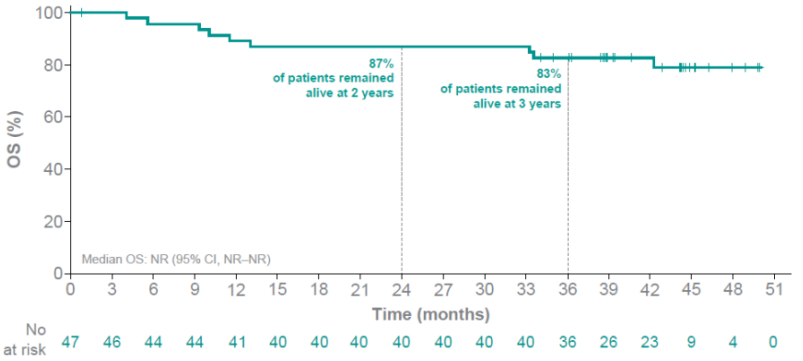
High CR Rates Across Clinically Relevant Subgroups



Data cutoff: Apr 9, 2025. Investigator assessment per Lugano criteria.[7] One patient was NE. [a]Cell of origin was unknown for 2 patients.

Sustained PFS and OS Beyond 3 Years





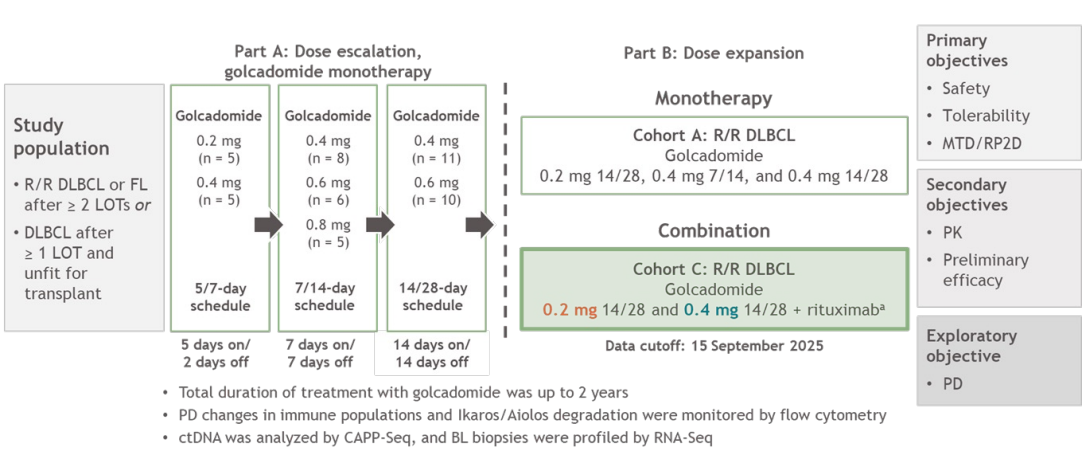
Data cutoff: Sep 21, 2025. Median follow-up for PFS: 44.1 months (95% CI, 38.6–44.2). Median follow-up for OS: 44.2 months (95% CI, 38.9–44.4).

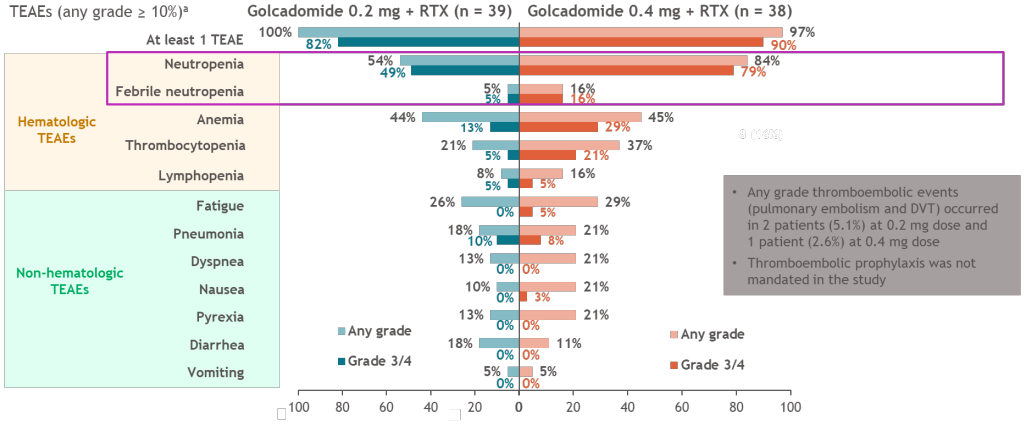
Falchi L, et al. ASH 2025. **Abstract Poster 1955.**

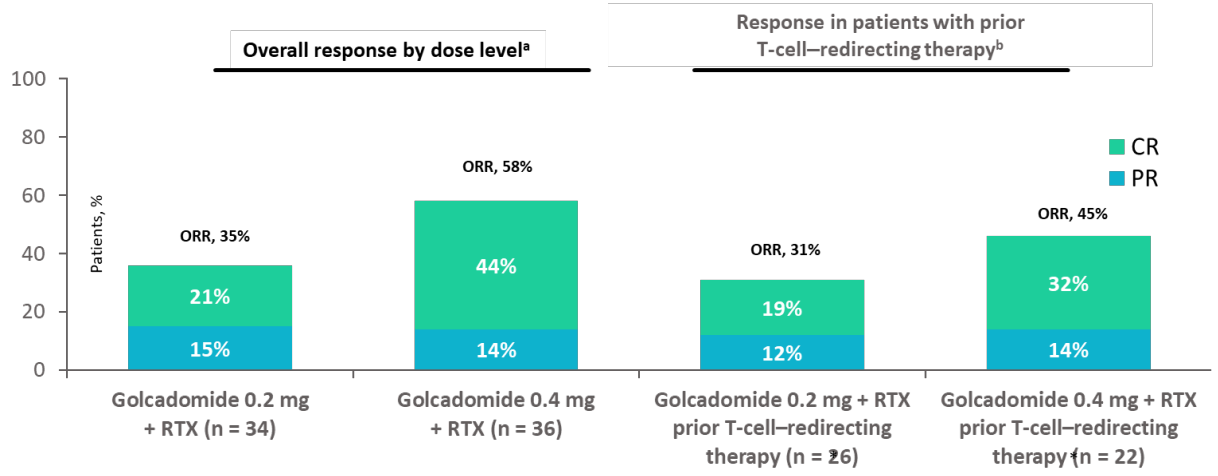
The era of novel combinations
And 1L chemofree regimens

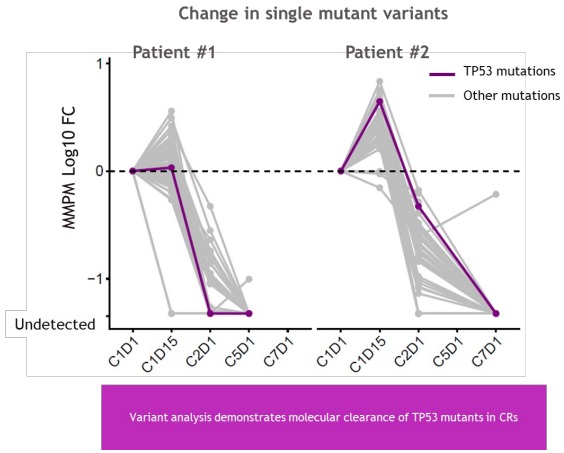
Golcadomide plus Rituximab in previoulsy treated Diffuse large B-cell lymphoma

Novel Combinations
r/r DLBCL mABs+ CellMODs









Hoffmann MS, et al. ASH 2025. Abstract 479.

Novel Combinations
r/r DLBCL
TCE+CellMODs

Mosunetuzumab (Mosun) or glofitamab (Glofit) in combination with golcadomide (Golca) demonstrates a manageable safety profile and encouraging efficacy in patients with relapsed or refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL)

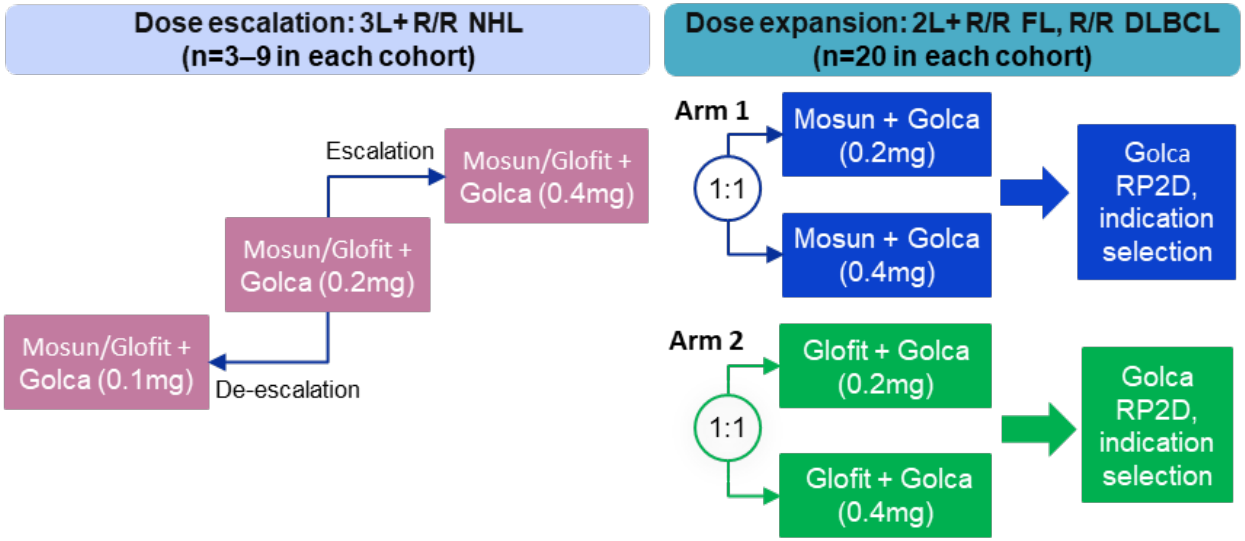
Key inclusion criteria

- 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



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§

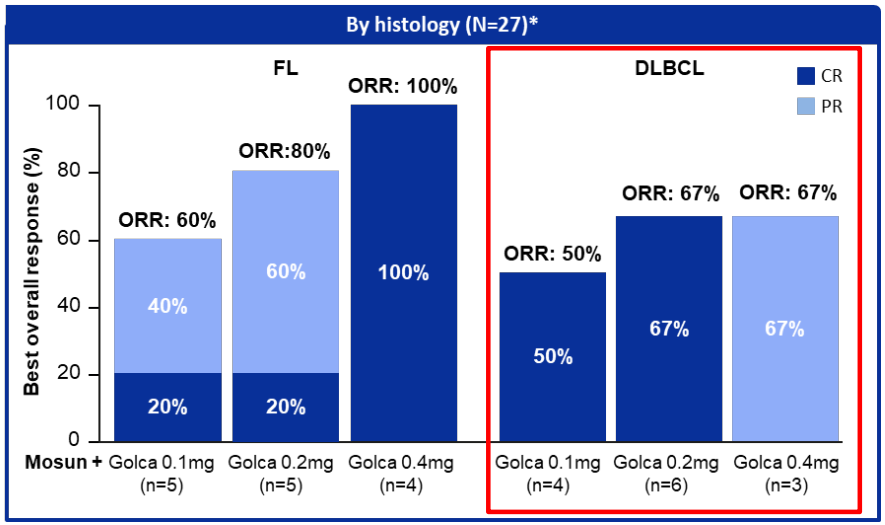
- Arm 1: given daily from D1–14 in C1 or C2 onwards
- Arm 2: given daily from D1–10 in C2 or C3 onwards

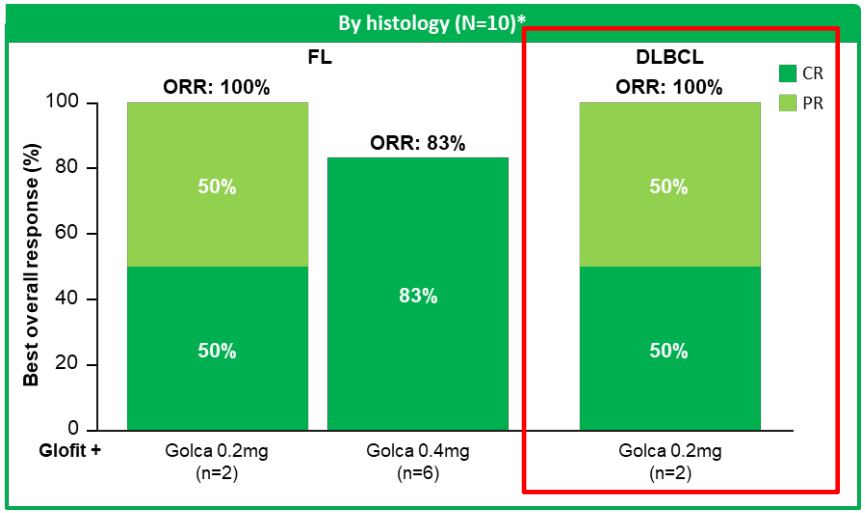
Andreadis C et al, oral presentation ASH 2025, Blood(2025) 146 (Supplement 1): 66.

Novel Combinations
r/r DLBCL
TCE+CellMODs

Baseline characteristics & Results

n (%) unless otherwise stated		Mosun + Golca (N=35)	Glofit + Golca (N=12)
Median age, years (range)		63.0 (30–83)	59.5 (37–76)
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 et al, oral presentation ASH 2025, Blood(2025) 146 (Supplement 1): 66.

Novel chemofree Regimens
1L DLBCL

Fixed-Duration Epcoritamab Monotherapy Induces High Response and MRD-Negativity Rates in Elderly Patients With Newly Diagnosed Large B-Cell Lymphoma and Comorbidities: Results from EPCORE DLBCL-3

EPCORE® DLBCL-3 Study Design

A 2-stage, open-label, phase 2 trial of fixed-duration epcoritamab in elderly patients with newly diagnosed LBCL and comorbidities

Key inclusion criteria

- Newly diagnosed CD20+ LBCL
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - Double-hit or triple-hit DLBCL
  - FL grade 3B
- ICE score ≥ 8[a]
- ECOG PS 0–2
- Ineligible for anthracycline-based therapy/cytotoxic chemotherapy due to:
  - ≥ 80 years of age, or
  - ≥ 75 years of age with a comorbid condition[b]
- Measurable disease by CT or MRI

1:1 RANDOMIZATION

Stage 1	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W

Stage 2 (expansion)	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W

	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W
Lenalidomide PO 10–20 mg[d]	QD D1–21	

Epcoritamab + lenalidomide not selected for stage 2

Data cutoff: Sep 21, 2025

Median follow-up: 18.1 months

- **Primary endpoint:** CR rate per Lugano criteria[1]
- **Key secondary endpoints:** ORR, time to response, DOR, DOCR, PFS, OS, MRD negativity,[e] and safety

36% age ≥85 y

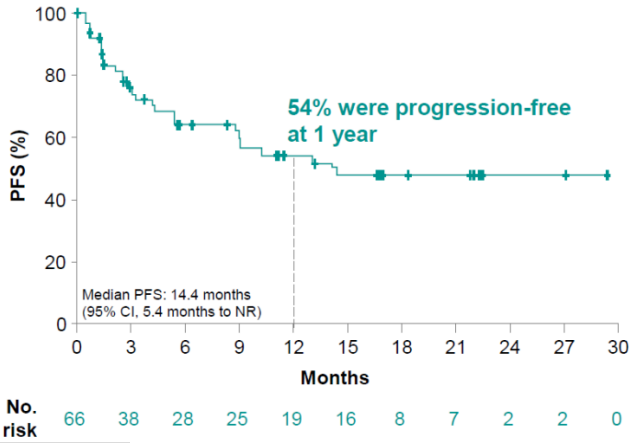
64% IPI 3-5

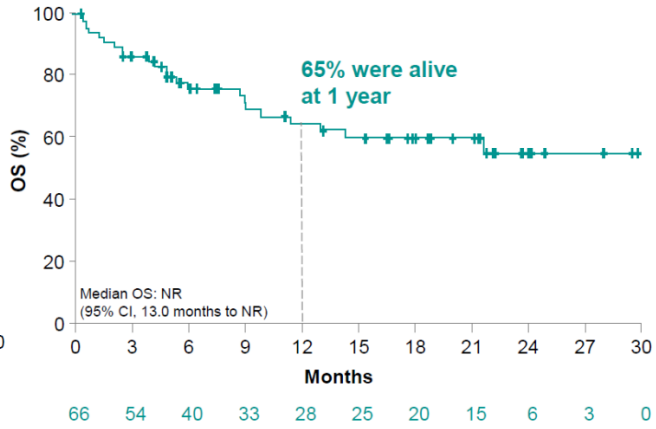
Vitolo U, et al. ASH 2025. Abstract 63.

Novel chemofree Regimens 1L DLBCL

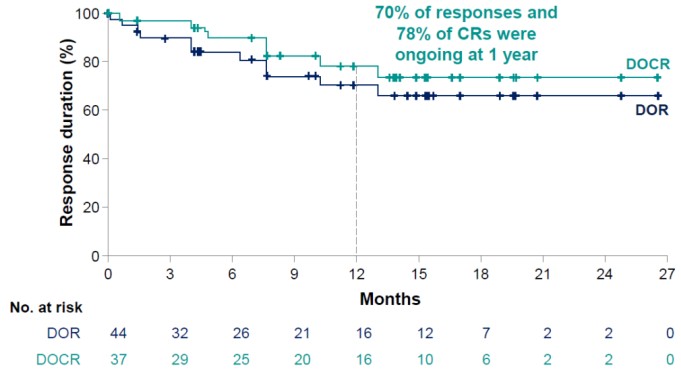
Best Response	Response-Evaluable Population (n = 60)
ORR, n (%)	44 (73)
CR	37 (62)
PR	7 (12)
SD	5 (8)
PD	7 (12)
NA	4 (7)

PFS and OS Sustained > 1 Year

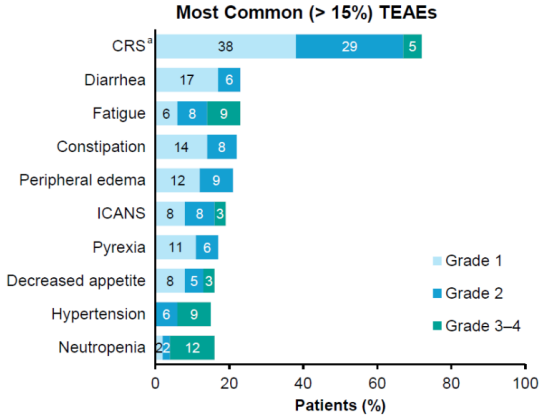




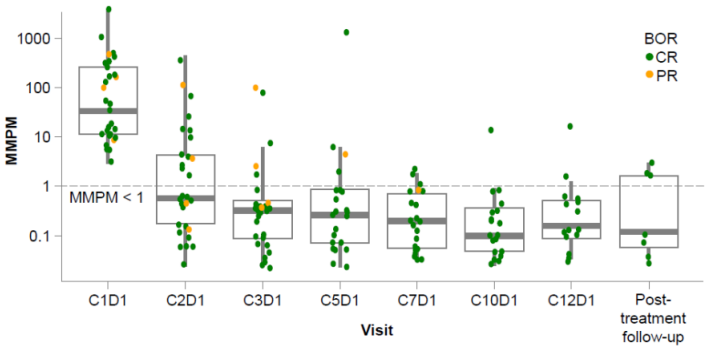
Responses Were Durable and Sustained Over Time



Safety Profile



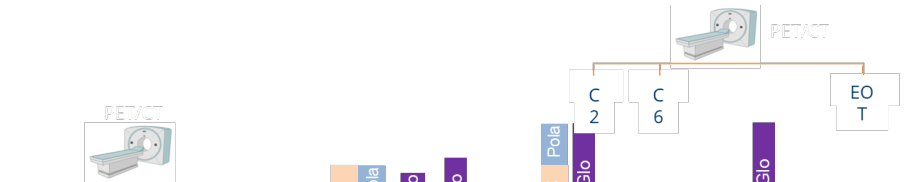
High rates of MRD negativity



Vitolo U, et al. ASH 2025. Abstract 63.

Novel chemofree Regimens
1L DLBCL

Phase II Frontline Chemolight R-Pola-Glo Trial Induces High and Durable Response Rates in Elderly and Medically Unfit/Frail Patients With Aggressive B-Cell Lymphoma



Indication

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

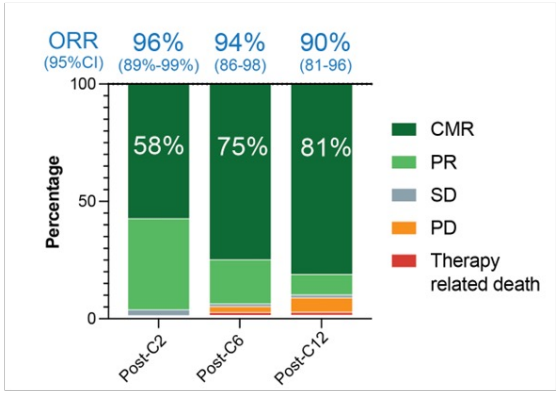
Study Design

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

Endpoints

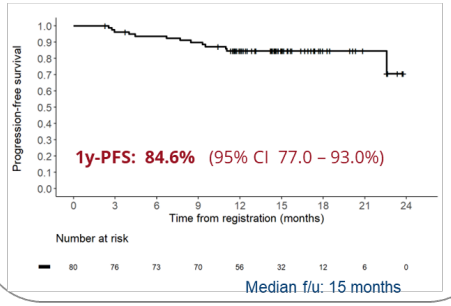
- *Primary:* **1y-PFS rate**
- *Secondary:*
  - Efficacy (OS, EFS)
  - Feasibility/Toxicity

Response Rate (n=80)

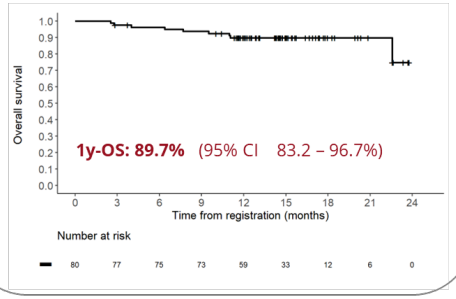


19% age ≥85 y

1-year Progression-free Survival (PFS)



1-year Overall Survival (OS)



Infections

Infections	66% (n=53)
Grade 3	19% (n=15)
Grade 4	3% (n=2)
Grade 5, all COVID COVID+RSV Unknown	4% (n=3) 1 1 1

64% IPI 3-5

Chapuy B. et al, oral presentation ASH 2025 Blood (2025) 146 (Supplement 1): 61.

Conclusions

RWE confirms the efficacy of ADCs in combination with systemic chemoimmunotherapy in 1L DLBCL

Anti CD20-CD3 TCEs in combination with chemoimmunotherapy will soon represent a valuable treatment option in 2L r/r DLBCL not eligible for ASCT/CAR-T including early relapses.

Anti CD19-CD3 TCEs show high activity in 3L+ including patients previously exposed to t-cell redirecting therapies.

Novel combinations of R-CHOP and TCE / small molecules will likely improve outcomes in 1L DLBCL

TCE-based regimens will be the basis of novel 1L chemofree treatment strategies