ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI
SCIENZE MEDICHE E CHIRURGICHE

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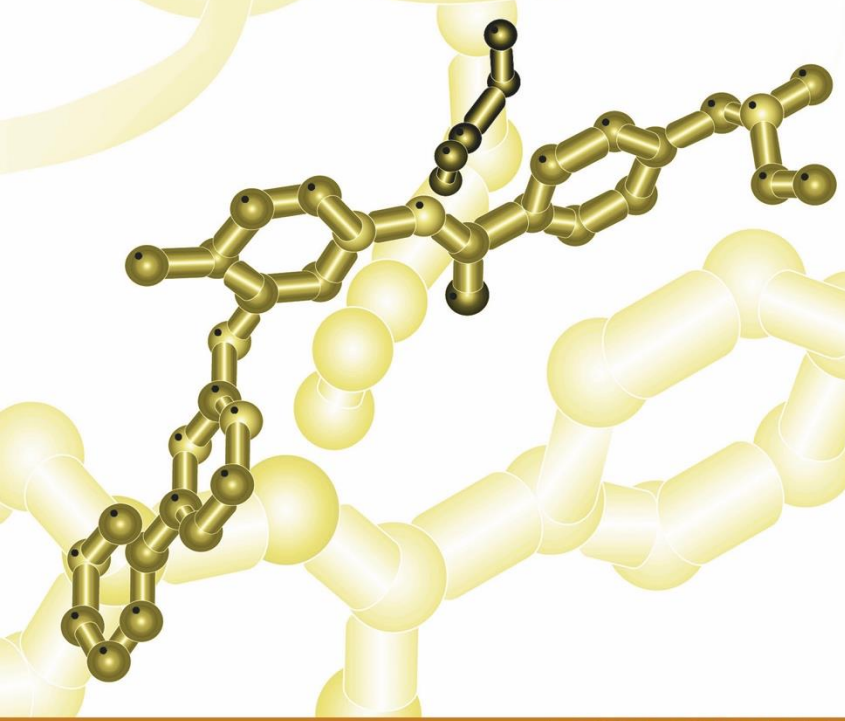


New Drugs in Hematology

President: Pier Luigi Zinzani
Co-President: Michele Cavo

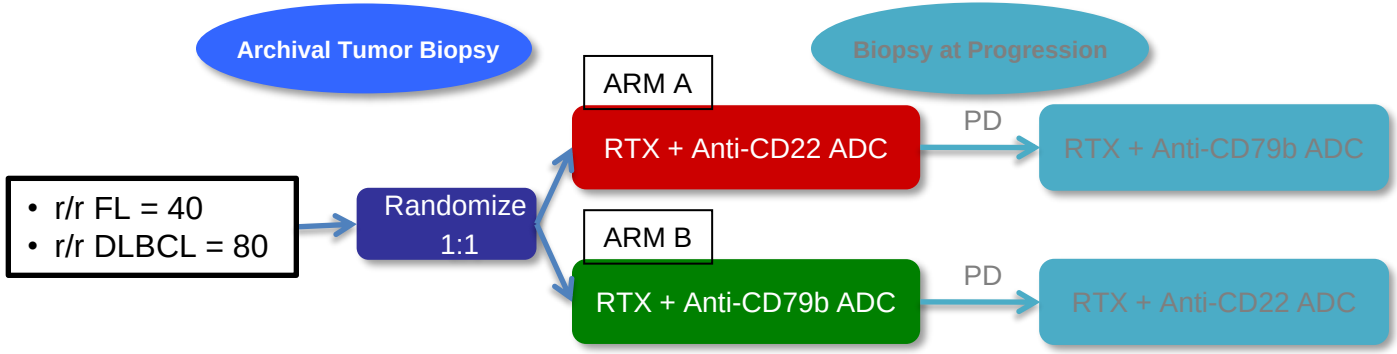
Bologna,
Royal Hotel Carlton
January 15-17, 2024

BOLOGNA BOLOGNA, ROYAL HOTEL CARLTON

Disclosures of Bruce Cheson

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Abbvie			X				
Beigene			X		X	X	
Lilly			X		X	X	
Pharmacyclics			X				
Symbio						X	
Incyte			X		X		
Morphosys			X		X		
Regeneron						X	

ROMULUS Study Design



Rituximab (375 mg/m^2) + ADC (2.4 mg/kg) administered in every-21-day cycles

Clinical Evaluations

- Anti-tumor activity was evaluated per revised IWG criteria every three months; PET scans were performed at the discretion of the investigator
- Treatment-emergent adverse events were graded per NCI CTCAE v4.0

Pharmacokinetic and Pharmacodynamic Evaluations

- PK analysis performed for total antibody, antibody-conjugated MMAE (acMMAE), and unconjugated MMAE

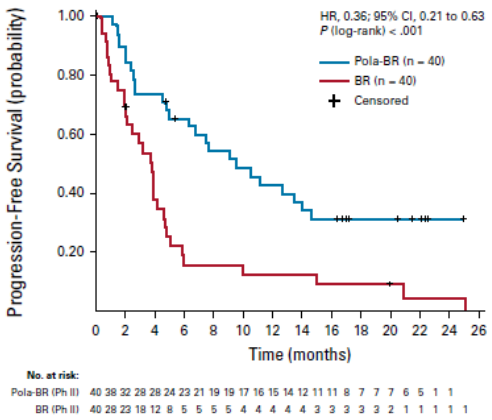
Data as of 21 February 2014; median time of follow up was 9 months (Range 7.9-9.8 months)

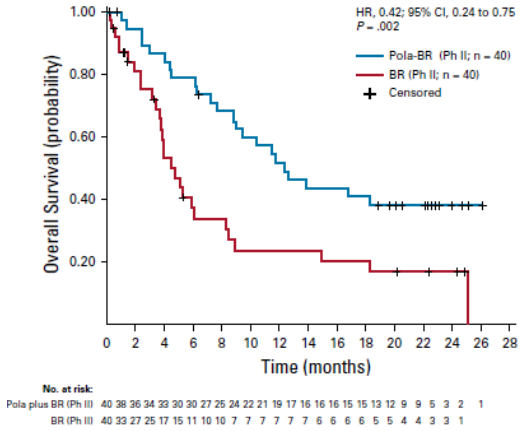
- Data from crossover patients not included in this presentation

Polatuzumab + BR vs BR: Phase 2 Trial Results

Efficacy

End of Treatment by IRC	Pola + BR (n=40)	BR (n=40)	Hazard Ratio
Overall Objective Response (ORR = CR+PR)	45.0%	17.5%	-
Complete Response	40.0%	17.5%	-
Partial Response	5.0%	0.0%	-
mDOR *(95% CI)*	12.6 (7.2, NE)	7.7 (4.0, 18.9)	0.47 (0.19, 1.14); *P* = ns
mPFS *(95% CI)*	9.5 (6.2, 13.9)	3.7 (2.1, 4.5)	0.36 (0.21, 0.63), *P* < 0.001
mOS *(95% CI)*	12.4 (9.0, NE)	4.7 (3.7, 8.3)	0.42 (0.24,0.75), *P* = 0.002





Median follow-up, 22.3 Months

Safety*	Pola + BR (n=39)	BR (n=39)
Neutropenia (Grade 3-4)	46.2%	33.3%
Thrombocytopenia (Grade 3-4)	41.0%	23.1%
Anemia (Grade 3-4)	28.2%	17.9%
Peripheral neuropathy (All grades)	43.6%	7.7%
Diarrhea (All grades)	38.5%	28.2%
Fatigue (All grades)	35.9%	35.9%
Pyrexia (All grades)	33.3%	23.1%

- Fatal AEs occurred in 9 pola-BR patients and 11 BR patients, with infection being the most common adverse event (4 pola-BR; 4 BR)

*Select AEs with >30% in all grades

Sehn et al. Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma. *J Clin Oncol.* 2020;38:155-165.

Efficacy of POLA-(BR) Regimens:RWE

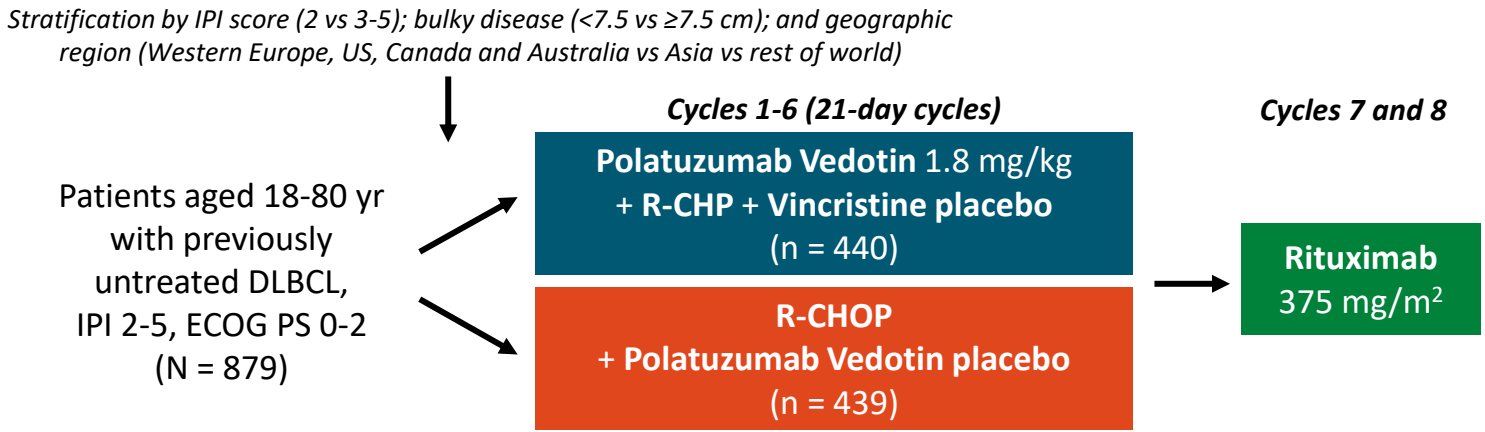
Study	Pts	Refractory (%)	OS mo	PFS mo	CR (%)	ORR (%)	mFU mo
Argnani (‘22)	55	81.8	9.0	4.9	27.3	49.1	11
Vodicka (‘22)	21	76.2	8.7	3.8	23.8	33.3	6.8
Dimou (‘21)	49	78.0	8.5	4.0	20	35	10.8
Segman (‘21)	47	23.0	8.3	5.6	40	61	6.8
Northend (‘22)	133	68.4	8.2	4.8	31.6	57	7.7
Terui (‘21)	35	66.0	NR	5.2	42.9	71.4	5.4
Dal (‘22)	71	49.3	5	NA	<32.4	47.9	5

Toxicity of POLA-(BR) Regimens

Study	Pts	Neutropenia, gr 3-4 (%)	Thrombocytopenia, gr 3-4 (%)	Neuropathy, all grades (%)
Sehn (‘20)	40	46.2	41.0	43.6
Argnani (‘22)	55	25.0	8.3	8.3
Liebers (‘21)	105	38.5	32.7	21.2
Terui (‘21)	35	31.4	20.0	19.7
Dal (‘22)	71	33.8	29.5	32.4

POLARIX: Study Design

- Multicenter, double-blind, placebo-controlled phase III trial



R-CHOP: IV rituximab 375 mg/m², cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², and vincristine 1.4 mg/m² administered on Day 1 + oral prednisone 100 mg QD Days 1-5.

- **Primary endpoint:** investigator-assessed PFS
- **Secondary endpoints:** EFS, CRR at end of treatment, DFS, OS, safety

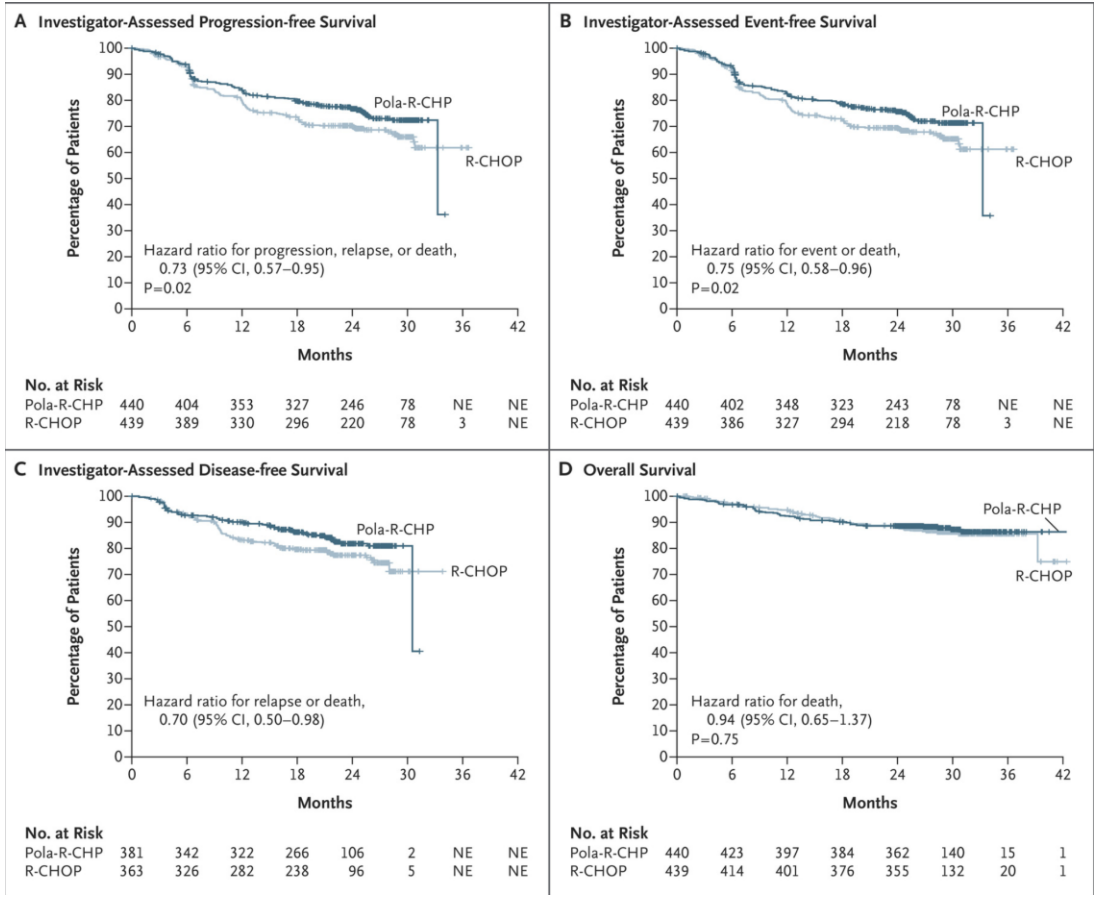
Tilly et, NEJM 386;351, 2022

POLARIX: Patient Characteristics

Characteristic	Pola-R-CHP (N=440)	R-CHOP (N=439)
Median age (range) — yr	65 (19–80)	66 (19–80)
Age category — no. (%)		
≤60 yr	140 (31.8)	131 (29.8)
>60 yr	300 (68.2)	308 (70.2)
Female sex — no. (%)	201 (45.7)	205 (46.7)
Geographic region — no. (%)†		
Western Europe, United States, Canada, and Australia	302 (68.6)	301 (68.6)
Asia	81 (18.4)	79 (18.0)
Rest of world	57 (13.0)	59 (13.4)
Ann Arbor stage — no. (%)‡		
I or II	47 (10.7)	52 (11.8)
III or IV	393 (89.3)	387 (88.2)
No. of extranodal sites — no. (%)		
0 or 1	227 (51.6)	226 (51.5)
≥2	213 (48.4)	213 (48.5)
Bulky disease — no. (%)†§	193 (43.9)	192 (43.7)

Tilly et, NEJM 386;351, 2022

POLARIX: Outcomes

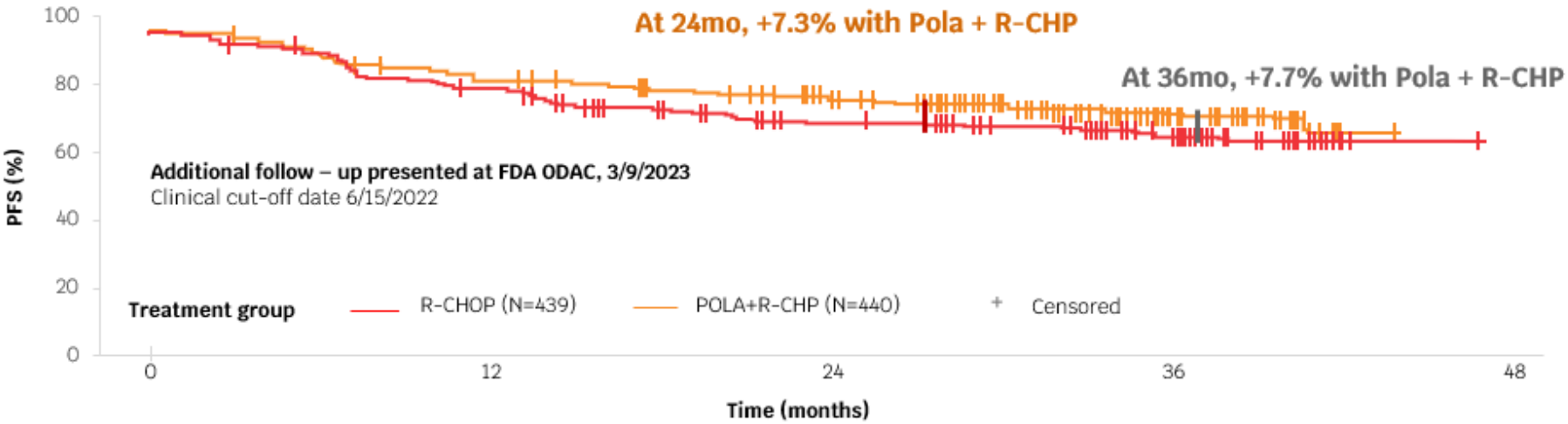


Tilly et, NEJM 386;351, 2022

POLARIX: Primary Endpoint: PFS

IDEO Hematology

Pola + R-CHP demonstrated a 27% reduction in the relative risk of disease progression, relapse or death versus R-CHOP

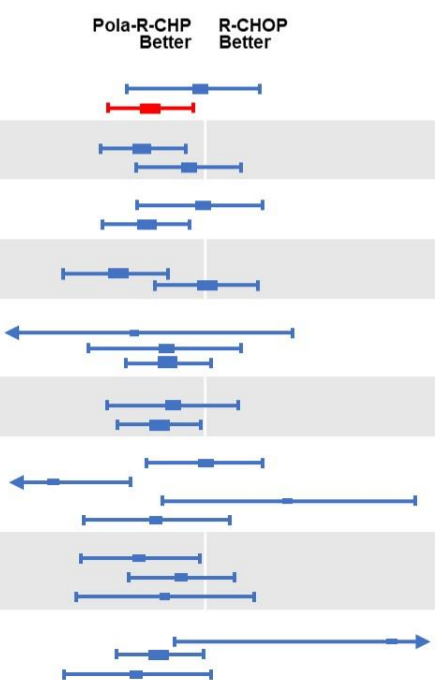


		R-CHOP N=439	Pola+R-CHP N=440
PFS	Pt with events	134 (30.5%)	107 (24.3%)
	HR [95% CI]	**0.73** [0.57, 0.95]	
	Stratified log-rank p-value	0.0177	
	2-year rate [95% CI]	70.2% [65.8%, 74.6%]	76.7% [72.7%, 80.8%]
	Difference in event free rate [95% CI]	6.5% [0.5%, 12.5%]	

FDA analysis presented at ODAC meeting 3.9.23

POLARIX: Subgroup Analysis of PFS

Baseline Risk Factors	Total N	Pola-R-CHP (N = 440) n	Pola-R-CHP (N = 440) 2-Yr Rate	R-CHOP (N = 439) n	R-CHOP (N = 439) 2-Yr Rate	HR	95% Wald CI
Age group, yr							
≤60	271	140	74.1	131	71.9	0.9	(0.6-1.5)
>60	608	300	77.9	308	69.5	0.7	(0.5-0.9)
Sex							
Male	473	239	75.9	234	65.9	0.7	(0.5-0.9)
Female	406	201	77.7	205	75.2	0.9	(0.6-1.4)
IPI score							
IPI 2	334	167	79.3	167	78.5	1.0	(0.6-1.6)
IPI 3-5	545	273	75.2	272	65.1	0.7	(0.5-0.9)
Bulky disease							
Absent	494	247	82.7	247	70.7	0.6	(0.4-0.8)
Present	385	193	69.0	192	69.7	1.0	(0.7-1.5)
Ann Arbor stage							
I-II	99	47	89.1	52	85.5	0.6	(0.2-1.8)
III	232	124	80.7	108	73.6	0.8	(0.5-1.3)
IV	548	269	72.6	279	66.1	0.8	(0.6-1.1)
Baseline LDH							
≤ ULN	300	146	78.9	154	75.6	0.8	(0.5-1.3)
> ULN	575	291	75.4	284	67.2	0.7	(0.5-1.0)
Cell of origin							
GCB	352	184	75.1	168	76.9	1.0	(0.7-1.5)
ABC	221	102	83.9	119	58.8	0.4	(0.2-0.6)
Unclassified	95	44	73.0	51	86.2	1.9	(0.8-4.5)
Unknown	211	110	73.8	101	64.3	0.7	(0.4-1.2)
Double expressor by IHC							
DEL	290	139	75.5	151	63.1	0.6	(0.4-1.0)
Non-DEL	438	223	77.7	215	75.7	0.9	(0.6-1.3)
Unknown	151	78	76.0	73	69.8	0.8	(0.4-1.5)
Double- or triple-hit lymphoma							
Yes	45	26	69.0	19	88.9	3.8	(0.8-17.6)
No	620	305	76.8	315	70.3	0.7	(0.5-1.0)
Unknown	214	109	78.5	105	66.4	0.6	(0.4-1.1)



Adapted from Tilly, NEJM, 2022;386:351

Benefits in?

- Younger ≤60 yr?
- Females?
- IPI = 2 (or 3)?
- Bulky disease (≥7.5 cm)?
- GCB subtype?
- DH/TH DLBCL?

Tilly et, NEJM 386;351, 2022

Adverse Event	Pola-R-CHP (N=435)		R-CHOP (N=438)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Peripheral neuropathy†	230 (52.9)	7 (1.6)	236 (53.9)	5 (1.1)
Nausea	181 (41.6)	5 (1.1)	161 (36.8)	2 (0.5)
Neutropenia	134 (30.8)	123 (28.3)	143 (32.6)	135 (30.8)
Diarrhea	134 (30.8)	17 (3.9)	88 (20.1)	8 (1.8)
Anemia	125 (28.7)	52 (12.0)	114 (26.0)	37 (8.4)
Constipation	125 (28.7)	5 (1.1)	127 (29.0)	1 (0.2)
Fatigue	112 (25.7)	4 (0.9)	116 (26.5)	11 (2.5)
Alopecia	106 (24.4)	0	105 (24.0)	1 (0.2)
Decreased appetite	71 (16.3)	5 (1.1)	62 (14.2)	3 (0.7)
Pyrexia	68 (15.6)	6 (1.4)	55 (12.6)	0
Vomiting	65 (14.9)	5 (1.1)	63 (14.4)	3 (0.7)
Febrile neutropenia	62 (14.3)	60 (13.8)	35 (8.0)	35 (8.0)
Headache	56 (12.9)	1 (0.2)	57 (13.0)	4 (0.9)
Cough	56 (12.9)	0	53 (12.1)	0

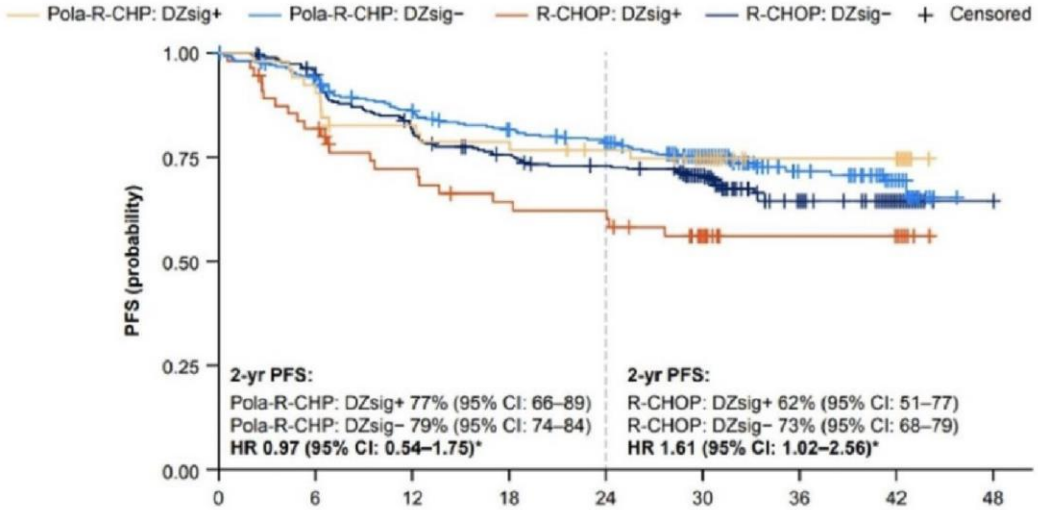
Tilly et, NEJM 386;351, 2022

Impact of Genetic Subtypes in POLARIX

Subtypes	Prevalence, n (%)		2-yr PFS, % (95% CI)	
	Pola-R-CHP n = 292	R-CHOP n = 302	Pola-R-CHP	R-CHOP
EZB	81 (28)	73 (24)	83 (76–92)	75 (65–86)
MCD	33 (11)	40 (13)	85 (73–98)	75 (63–90)
BN2	27 (9)	26 (9)	78 (63–95)	88 (77–100)
N1	1 (>1)	1 (>1)	NA	NA
ST2	17 (6)	15 (5)	76 (57–100)	86 (69–100)
Genetically composite	10 (3)	13 (4)	50 (27–93)	77 (57–100)
Other	123 (42)	134 (44)	74 (67–82)	62 (54–71)

Morschhauser, et al, ASH 2023, abstr #3000

Impact of Genetic Subtypes in POLARIX



Number at risk									
Pola-R-CHP: DZsig+	52	48	42	40	37	31	10	9	0
Pola-R-CHP: DZsig−	279	259	231	215	203	152	70	42	0
R-CHOP: DZsig+	56	45	37	32	31	18	11	10	0
R-CHOP: DZsig−	278	258	221	201	191	155	62	39	2

*HRs compare DZsig+ versus DZsig− in each treatment arm.
CI, confidence interval; DZsig, dark zone gene expression signature; HR, hazard ratio; PFS, progression-free survival; Pola-R-CHP, polatuzumab vedotin in combination with rituximab plus cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Morschhauser, et al, ASH 2023, abstr #3000

RWE Pola-R-CVP in Japan

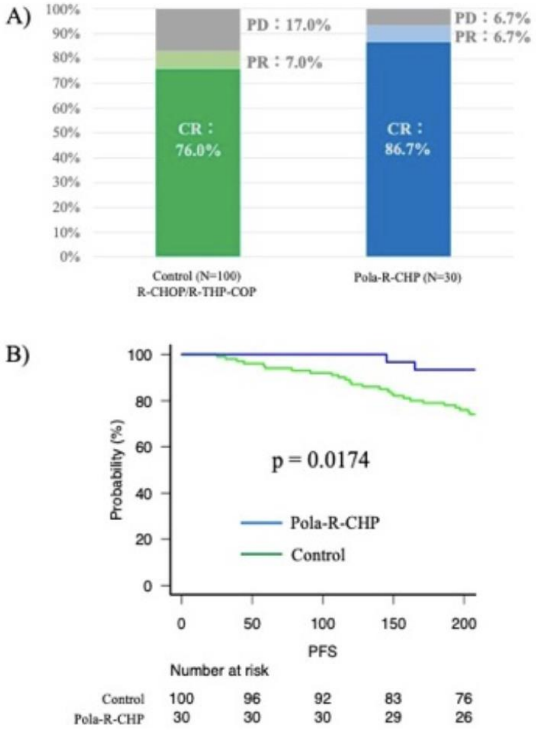


Figure 1 A) Overall response rate of all patients
B) Progression-free survival at 6 months of all patients

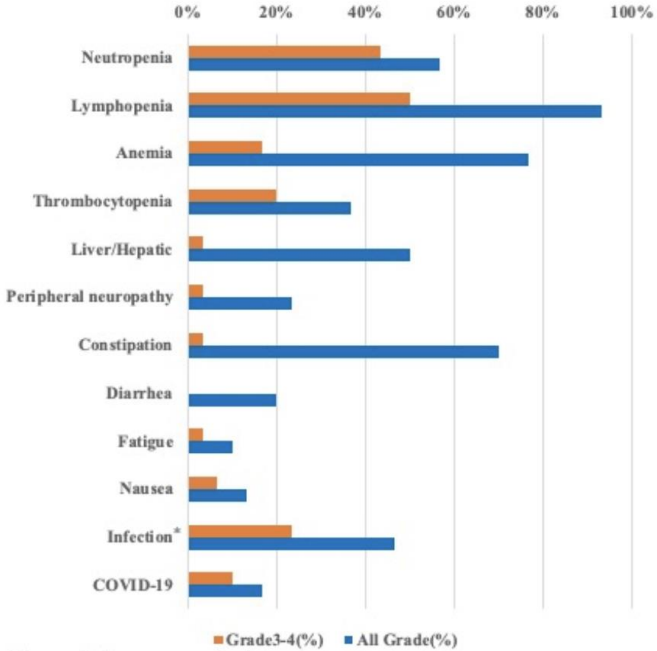


Figure 2 Summary of adverse events.
*: including COVID-19

Hotta et al, ASH 2023, abstr #3007

Score Sheet for POLARIX

Pro

- Persistent PFS advantage
- ? Higher cure rate
- Similar toxicity profile

Con

- No survival advantage
- Increased initial cost
- Distinct Subsets
  - IPS $\geq$ 2
  - Not for D-THL
  - ? COO preference
  - ? Genetic subtypes
  - ? Others
- Needs longer follow-up
- Still too much chemo!

Mosunetuzumab Plus Polatuzumab Vedotin Demonstrates a Favorable Safety Profile and Efficacy in Patients With Relapsed/Refractory LBCL: Primary Analysis of a Phase Ib/II Study

L. Elizabeth Budde,[1] Adam J. Olszewski,[2] Sarit Assouline,[3] Izidore S. Lossos,[4] Catherine Diefenbach,[5] Manali Kamdar,[6] Nilanjan Ghosh,[7] Dipenkumar Modi,[8] Waleed Sabry,[9] Seema Naik,[10] Amitkumar Mehta,[11] Shazia K. Nakhoda,[12] Stephen D. Smith,[13] Kathleen Dorritie,[14] Ting Jia,[15] Song Pham,[16] Ling-Yuh Huw,[17] Hao Wu,[17] Iris To,[17] Michael C. Wei,[17] Julio C. Chavez[18]

[1]City of Hope National Medical Center, Duarte, CA, USA; [2]Legorreta Cancer Center at Brown University, Lifespan Cancer Institute, Providence, RI, USA; [3]Jewish General Hospital, McGill University, Montreal, Quebec, Canada; [4]University of Miami/Sylvester Comprehensive Cancer Center, Miami, FL, USA; [5]Perlmutter Cancer Center at NYU Langone Health, New York, NY, USA; [6]University of Colorado, Aurora, CO, USA; [7]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [8]Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA; [9]Saskatoon Cancer Centre, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; [10]Penn State University College of Medicine, Hershey, PA, USA; [11]University of Alabama at Birmingham, Birmingham, AL, USA; [12]Fox Chase Cancer Center, Philadelphia, PA, USA; [13]Fred Hutchinson Cancer Center, University of Washington, Seattle, WA, USA; [14]UPMC Hillman Cancer Center, University of Pittsburgh, PA, USA; [15]Roche (China) Holding Ltd, Shanghai, China; [16]F. Hoffmann-La Roche Ltd, Mississauga, ON, Canada; [17]Genentech, Inc., South San Francisco, CA, USA; [18]Moffitt Cancer Center, Tampa, FL, USA

Presented at the 65th ASH Annual Meeting | December 9–12, 2023

Study overview (NCT03671018)

Key inclusion criteria

- LBCL (*de novo* DLBCL, HGBCL, trFL, or Grade 3b FL)
- ≥1 prior line of therapy, including an anti-CD20-directed therapy
- Patients who were ineligible for ASCT

Objectives

- Efficacy and safety of mosun-pola
- Primary endpoint: Best ORR[1] by independent review committee (IRC)

Mosun-pola fixed duration administration*

Mosun†

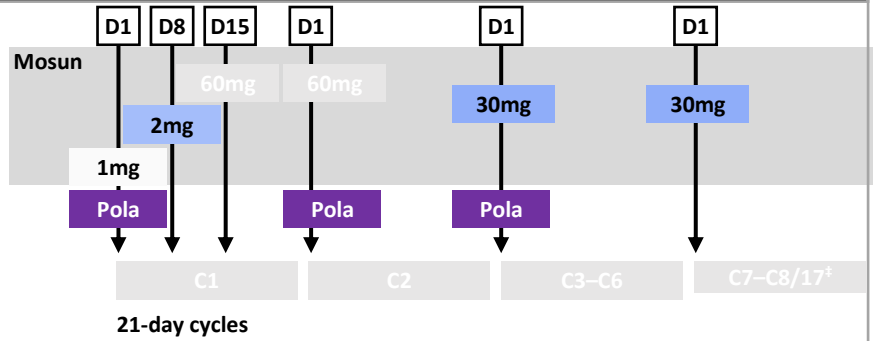
- Cycle (C) 1 step-up dosing for CRS mitigation
- Q3W intravenous infusions at RP2D (C1–8/17)‡

Pola

- Q3W intravenous infusions (1.8mg/kg) (Day [D]1, C1–6)

No mandatory hospitalization

Retreatment with mosun-pola was permitted



*Mosunetuzumab RP2D: C1D15 and C2D1 (1/2/60mg), and 30mg for subsequent cycles.
†Corticosteroid premedication was required prior to each dose in C1 and C2 and was optional for C3+.
‡Patients who achieved CR completed mosunetuzumab after C8, while patients who had PR or SD continued mosunetuzumab for a total of 17 cycles, unless progressive disease or unacceptable toxicity occurred.

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

Baseline characteristics

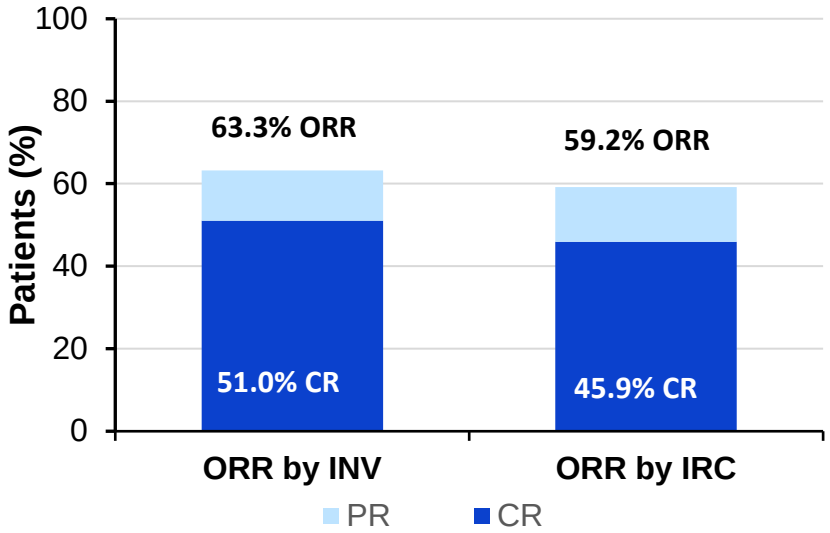
n (%), unless stated	N=98
Median age, years (range)	68 (20–88)
Male sex	70 (71.4)
ECOG PS score	
0	36 (36.7)
1	55 (56.1)
2	7 (7.1)
NHL histology	
DLBCL	68 (69.4)
HGBCL	18 (18.4)
trFL	8 (8.2)
FL Grade 3b	4 (4.1)
Cell-of-origin (n=94)*	
GCB	53 (56.4)
Non-GCB	33 (33.7)
Unknown	8 (8.5)

n (%), unless stated	N=98
Ann Arbor stage III–IV	85 (86.7)
Bulky disease, ≥6cm	33 (33.7)
Extranodal involvement	65 (66.3)
Number of prior lines of therapy	
1	35 (35.7)
≥2	63 (64.3)
Median lines of prior therapy, n (range)	2 (1–8)
Prior ASCT	11 (11.2)
Prior CAR T-cell therapy	35 (35.7)
Refractory to CAR T-cell therapy	26/35 (74.3)
Primary refractory	56 (57.1)
Refractory to†	
Last prior therapy	76 (77.6)
Any prior CD20 therapy	80 (81.6)

Clinical cut-off date: July 6, 2023.
*94 patients in the dose-expansion cohort with *de novo* LBCL, HGBCL, or trFL were evaluable for cell-of-origin assessments. GCB includes GCB derived from IHC and/or GEP. Non-germinal center B-cell like (GCB) includes non-GCB derived from immunohistochemistry (IHC), activated B cell (ABC) derived from gene expression profiling (GEP), and unclassified by GEP.
†Defined as no response to the prior therapy, or progression within 6 months of completion of the last dose of therapy.

Best response rates

Efficacy endpoint* results



Efficacy endpoint*	N=98 INV	IRC
Best ORR, n (%) [95% CI]	62 (63.3%) [52.9–72.8]	58 (59.2%) [48.8–69.0]
CR rate, n (%) [95% CI]	50 (51.0%) [40.7–61.3]	45 (45.9%) [35.8–56.3]

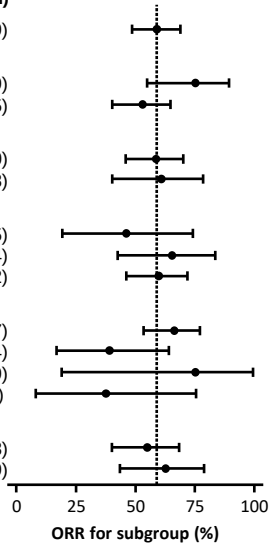
Primary efficacy endpoint of best ORR by IRC was met (59.2%; p=0.0003† vs historical control [42%]‡)

Clinical cut-off date: July 6, 2023.
*As determined by the investigator (INV) or independent review committee (IRC) using Lugano 2014 criteria.[1]
†Exact binomial test with one-sided alpha level of 2.5%. ‡Historical control based off the ROMULUS study.[2]

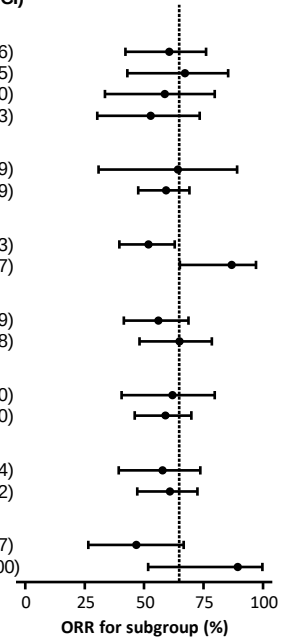
1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68;
2. Morschhauser F, et al. Lancet Haematol 2019;6:e245–65.

ORR by IRC for subgroups

Subgroups	No. of patients	ORR (95% CI)
Overall	98	59% (49–69)
Sex		
Female	28	75% (55–89)
Male	70	53% (41–65)
Age group, in years		
<75	70	59% (46–70)
≥75	28	61% (41–78)
Ann Arbor stage at study entry		
Stage I–II	13	46% (19–75)
Stage III	23	65% (43–84)
Stage IV	62	60% (46–72)
NHL subtype		
DLBCL	68	66% (54–77)
HGBCL	18	39% (17–64)
FL 3b	4	75% (19–99)
trFL	8	38% (9–76)
Cell of origin		
GCB	53	55% (40–68)
Non-GCB (by IHC and ABC by GEP)	32	63% (44–79)



Subgroups	No. of patients	ORR (95% CI)
No. of prior lines of therapy		
1	35	60% (42–76)
2	21	67% (43–85)
3	19	58% (33–80)
≥4	23	52% (31–73)
Prior ASCT		
Yes	11	64% (31–89)
No	87	59% (48–69)
Relapse or refractory to last prior therapy		
Refractory	76	51% (40–63)
Non-refractory	22	86% (65–97)
Relapse or refractory to first prior therapy		
Refractory	56	55% (41–69)
Non-refractory	42	64% (48–78)
Relapse within 12 months of first prior therapy		
Yes	26	62% (41–80)
No	72	58% (46–70)
Received prior CAR T-cell therapy		
Yes	35	57% (39–74)
No	63	60% (47–72)
Relapse or refractory to any prior CAR T-cell therapy		
Yes	26	46% (27–67)
No	9	89% (52–100)



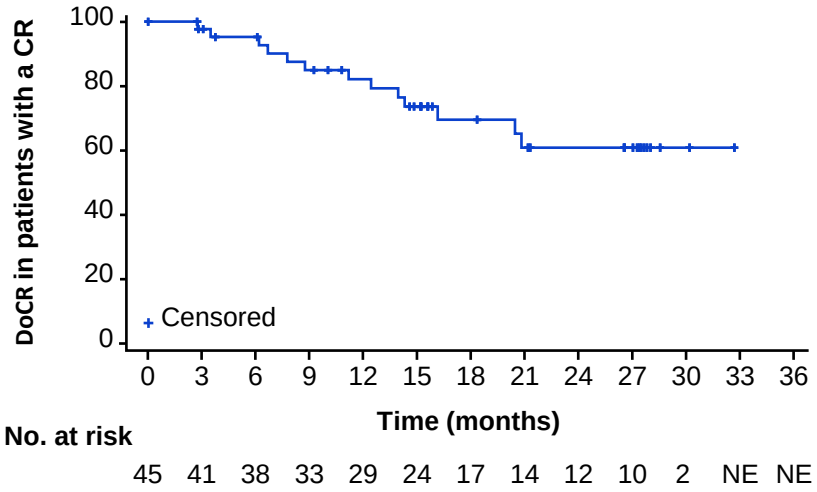
Clinically meaningful ORRs were seen across all subgroups

Clinical cut-off date: July 6, 2023.

Duration of response and complete response (DoR and DoCR)

Efficacy endpoint	IRC
Median DoR (n=58), months (95% CI)	20.8 (14.2–NR)
24-month event-free rate, % (95% CI)	49.7% (34.3–65.2)
Median DoCR (n=45), months (95% CI)	NR (20.5–NR)
24-month event-free rate, % (95% CI)	60.8% (43.2–78.4)
Median time to first CR, months (range)	2.7 (2.0–6.0)

DoCR by IRC assessment

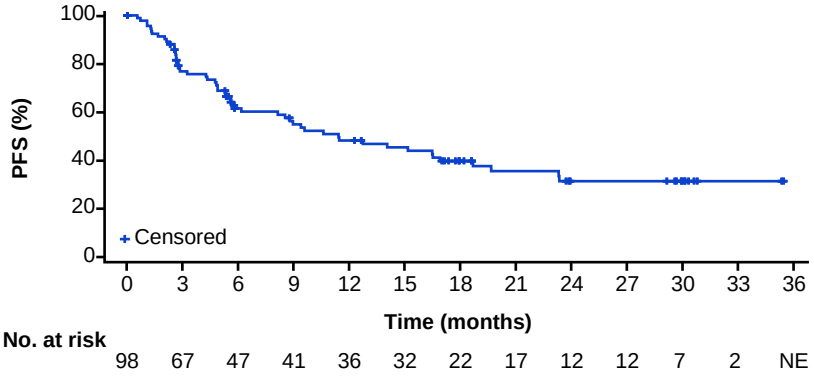


Durable CRs observed at 24 months with mosun-pola treatment

Clinical cut-off date: July 6, 2023.
NE, not estimatable; NR, not reached.

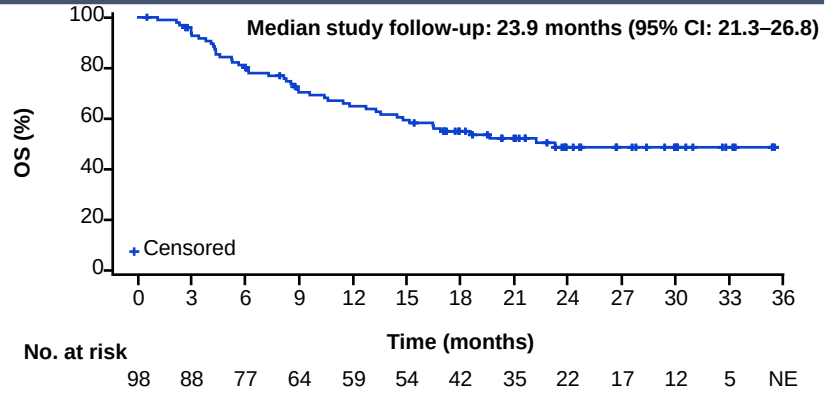
PFS and OS

PFS



	N=98
Median PFS*, months (95% CI)	11.4 (6.2–18.7)
12-month event-free rate, % (95% CI)	48.2 (37.3–59.0)
24-month event-free rate, % (95% CI)	31.3 (20.1–42.6)

OS



	N=98
Median OS, months (95% CI)	23.3 (14.8–NE)
12-month event-free rate, % (95% CI)	64.9 (55.2–74.5)
24-month event-free rate, % (95% CI)	48.6 (37.9–59.3)

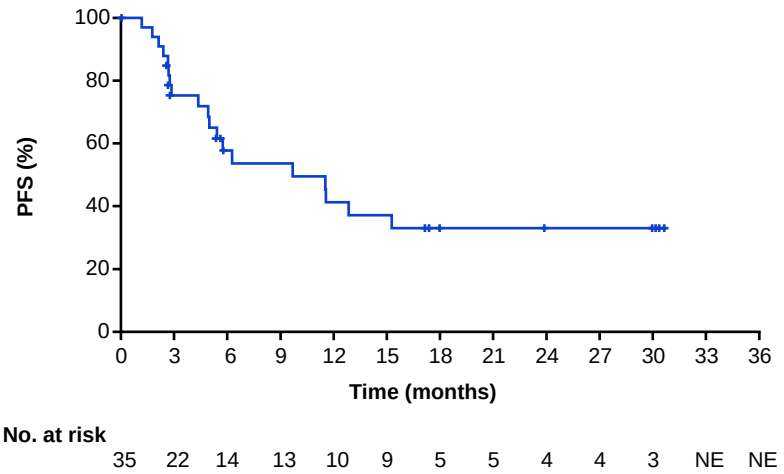
Plateauing of PFS and OS curves observed at 2 years

Clinical cut-off date: July 6, 2023.
*IRC assessed.
PFS, progression-free survival; OS, overall survival,

Efficacy in patients with prior CAR T-cell therapy

Efficacy endpoint*	n=35
Best ORR, n (%) [95% CI]	20 (57.1%) [39.4–73.7]
Median **DoR**, months (95% CI)	NR (8.8–NE)
CR rate, n (%) [95% CI]	14 (40.0%) [23.9–57.9]
Median **DoCR**, months (95% CI)	NR (12.5–NE)
Median **PFS**, months (95% CI)	9.6 (4.9–NE)
Median **OS**, months (95% CI)	15.2 (9.5–NE)

PFS in patients with prior CAR T-cell therapy



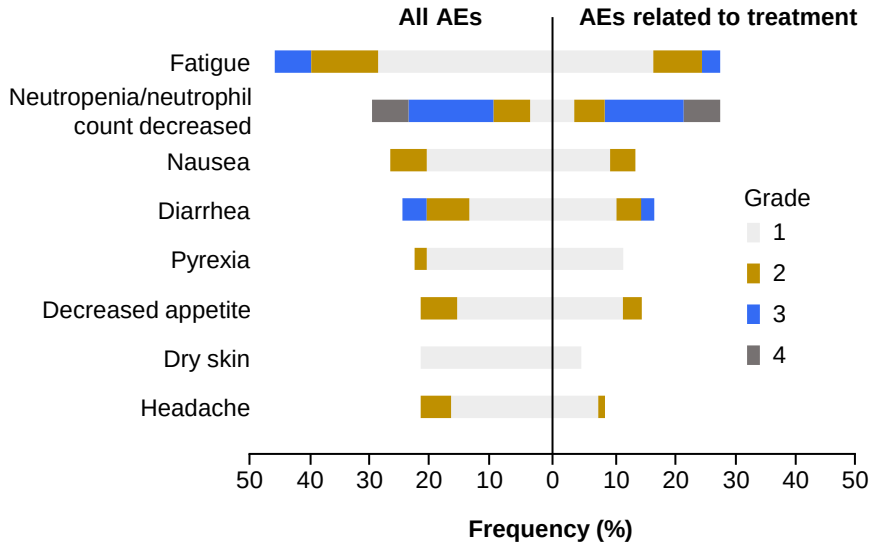
Durable responses seen in patients with prior CAR T-cell therapy

Clinical cut-off date: July 6, 2023.
*IRC-assessed.

Safety profile

AE summary, n (%)	N=98
AE	97 (99.0)
Treatment-related	88 (89.8)
Grade 3/4 AE	54 (55.1)
Treatment-related	34 (34.7)
Grade 5 AE*	3 (3.1)
Treatment-related	0
AE leading to mosun discontinuation†	4 (4.1)
Mosun-related	1 (1.0)
AE leading to pola discontinuation‡	7 (7.1)
Pola-related	4 (4.1)

AEs (≥20%) by grade

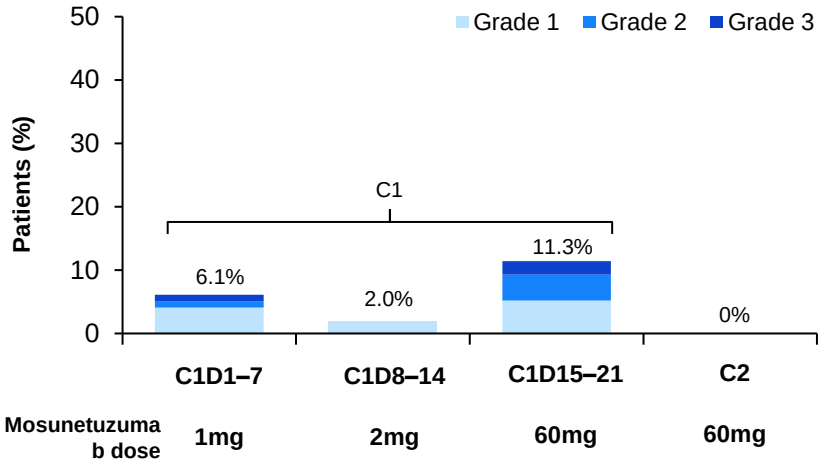


Clinical cut-off date: July 6, 2023.
*Grade 5 AEs included: two patients (2.0%) with COVID-19 pneumonia and one patient (1.0%) with pneumonia.
†Encephalopathy Grade 4 (related to mosun), pneumonia Grade 5, COVID-19 pneumonia Grade 5, and fatigue Grade 3.
‡Two cases of peripheral sensory neuropathy Grade 2 (related to pola), neuropathy peripheral Grade 2 and Grade 1 (related to pola), encephalopathy Grade 4, pneumonia Grade 5 and COVID-19 pneumonia Grade 5.

CRS summary

CRS by ASTCT criteria[1]	N=98
Any grade, n (%)	18 (18.4)
Grade 1	10 (10.2)
Grade 2	5 (5.1)
Grade 3	3 (3.1)
Median time to first CRS onset relative to last dose, days (range)	1.0 (0–2)
Median CRS duration, days (range)	2 (1–5)
CRS management, n (%)	
Corticosteroids	6 (6.1)
Tocilizumab	3 (3.1)
Single vasopressors	2 (2.0)
Events resolved, n (%)	18/18 (100)

CRS by cycle and grade



CRS mostly low grade and confined to C1

Clinical cut-off date: July 6, 2023.
ASTCT, American Society for Transplantation and Cellular Therapy criteria.

1. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

Other adverse events of interest

AE summary, n (%)	N=98
ICANS*	
Any grade	5 (5.1)
Grade 3–4†	2 (2.0)
Peripheral neuropathy	
Grade 1	16 (16.3)
Grade 2	12 (12.2)
Neutropenia	
Any grade	29 (29.6)
Grade 3–4	20 (20.4)

AE summary, n (%)	N=98
Serious infections	
Any grade	13 (13.3)
Grade 3–4	9 (9.1)
Grade 5‡	3 (3.1)
Tumor flare	
Grade 1	3 (3.1)

Mosun-pola had a manageable safety profile in patients with R/R LBCL

*Mosunetuzumab-related neurological AEs potentially consistent with ICANS.
†One patient had Grade 4 encephalopathy on study D12 in the context of baseline mild dementia made worse from hospitalization and acute congestive heart failure leading to hypoxia. Another patient had Grade 3 confusional state and Grade 3 dysarthria in the setting of concurrent Grade 2 CRS and Grade 3 pneumonia (all starting on study D23), and the patient ultimately succumbed to pneumonia.
‡Two patients (2.0%) with COVID-19 pneumonia and one patient (1.0%) with pneumonia. There were no events of febrile neutropenia.

Pola-Mosun In Untreated Elderly Frail LBCL

- 108 pts; median age 81 yr; 66% advanced stage
- 59% unfit, 40% frail, 81% ECOG 0-1
- Fatal AEs 14%.
- Median f/u 7.5 m
- BORR 80%, CR 61%; EOT 55%, 45%

Olszewski et al, ASH 2023, abstr #855

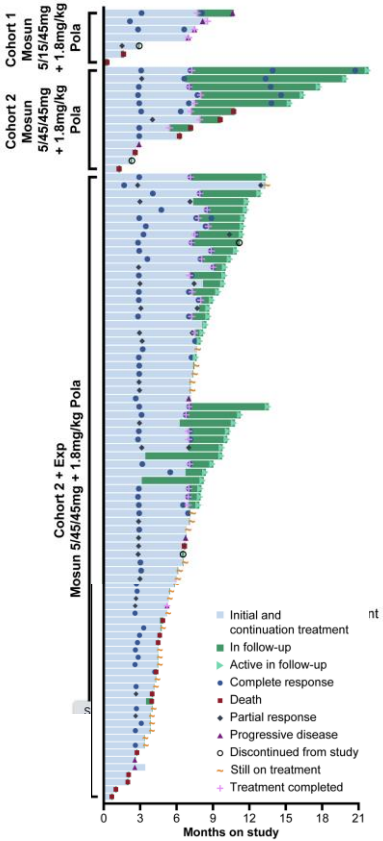
Mosun-Pola in uElderly Frail LBCL

Table: Baseline and disease characteristics

Characteristics, n (%)	M-Pola Cohort (N=108)
Median age (range), years	81.0 (66–94)
Age ≥80	66 (61.1)
sGA*	
Fit	1 (0.9)
Unfit	64 (59.3)
<80 years	41 (38.0)
≥80 years	23 (21.3)
Frail	43 (39.8)
Gender	
Female	56 (51.9)
ECOG PS	
0–1	87 (80.6)
2	21 (19.4)
Ann Arbor stage	
III–IV	71 (65.7)
aa-IPI	
0	21 (19.4)
1	32 (29.6)
2	41 (38.0)
3	14 (13.0)
Extranodal involvement	77 (71.3)
Elevated LDH	59 (54.6)
Bulky disease (≥7.5cm)	30 (27.8)
HGBCL†,‡	
Double hit	8 (7.4)
Triple hit	2 (1.9)
Cell of origin‡	
GCB	49 (45.4)
Non-GCB	56 (51.9)
Unknown	3 (2.8)

*Eligible patients were ≥80 years or per sGA (Merli et al. J Clin Oncol 2021): 65–79 years and ineligible for chemoimmunotherapy with at least: ≥2 ADL and/or IADL impairments, and/or a CIRS-G score of ≥1 comorbidity with a severity score of 3–4, or score of 2 in ≥8 comorbidities (unfit) or ≥80 years with ≥1 ADL and/or ≥1 IADL

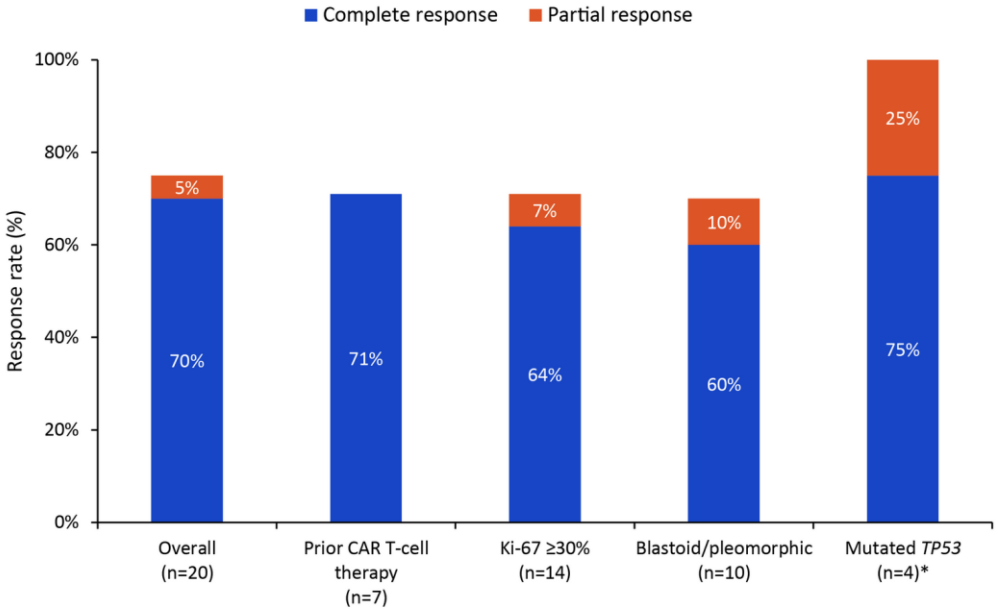
Figure: Response and time on M-Pola treatment



Olszewski et al, ASH 2023, abstr #855

Pola-Mosun in MCL (n=20)

Figure: Best overall response rates in high-risk MCL subgroups



*The *TP53* status of 10 patients was unknown or not done, therefore these patients were not included in this analysis.

CAR, chimeric antigen receptor; Ki, kinase inhibitor; MCL, mantle cell lymphoma; *TP53*, tumor protein 53

Wang et al, ASH 2023, abstr 734

Combinations with Polatuzumab:Glofitamab

- Pola – C1, D2 then D1 C2-6; Glofit SUD, 10/30 mg x 12
- 111 pts LBCL; 71.2% refractory to prior regimen
- Median 2 prior regimens; 24.3% prior CAR-T
- ORR (eval pts) – 78%, CMR 56%
  - NOS – ORR 85.7%, CMR 65.7%
  - HGBCL – ORR 60%, CMR 44%
  - Prior CAR-T – ORR 77.8%, CMR 44%
- Median OS NR at 15.2 mo

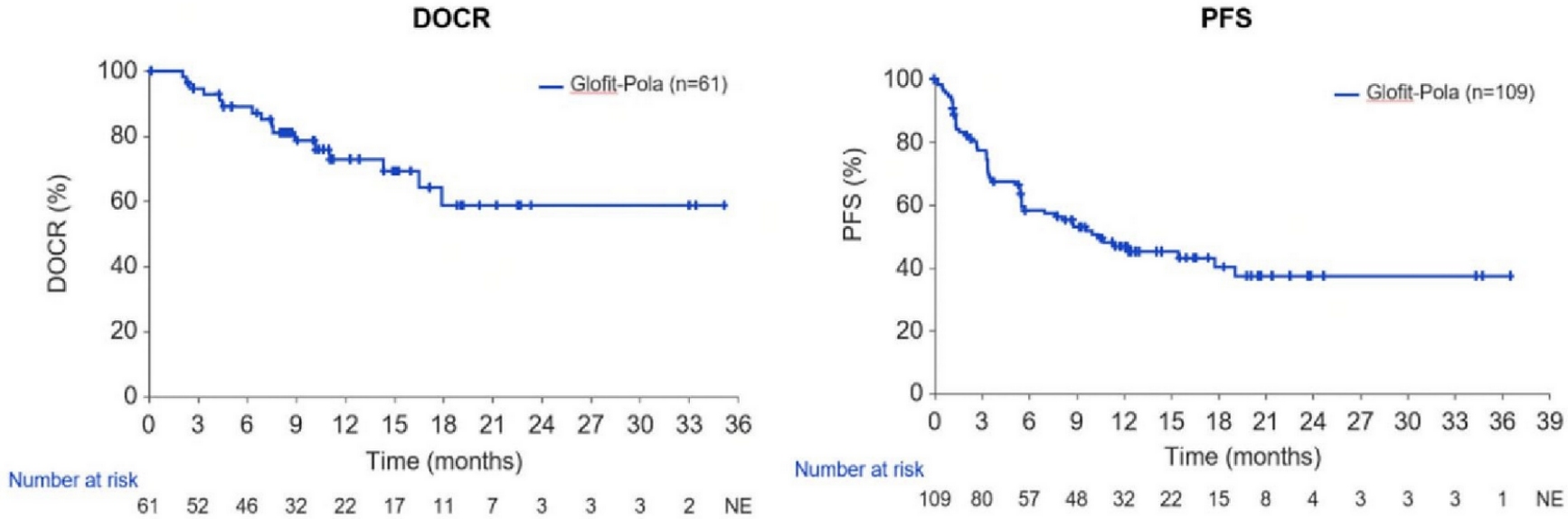
Hutchings et al, ASH 2023, abstr #4460

Pola-Glofit: DOCR

	6 mo	12 mo
• DLBCL NOS (34)	84.2%	59.2%
• trFL (14)	92.9%	85.7%
• HGBCL (11)	100%	100%

Hutchings et al, ASH 2023, abstr #4460

Figure: DOCR and PFS with Glofit+Pola



DOCR, duration of complete response; Glofit+Pola, glofitamab in combination with polatuzumab vedotin; NE, not estimable; PFS, progression-free survival.

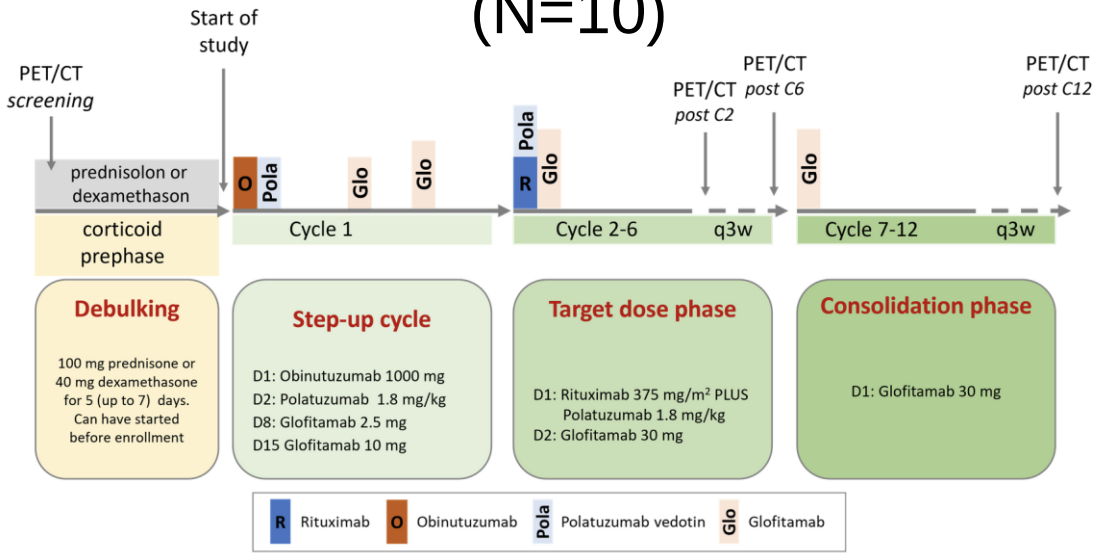
Hutchings et al, ASH 2023, abstr #4460

Pola-Glofit: Toxicities

- PN – 24.3% (all gr 1/2; 8/24 resolved)
- ICANS – 3 pts (gr 1/2)
- Gr 3-4 AEs in 61.3% – neutropenia 29.7%
- SAEs in 58.6%; gr 5 in 6.3% (5/7 due to COVID)
- 9.9% D/C therapy due to an AE

Hutchings et al, ASH 2023, abstr #4460

R-Pola Glofit: >60y, R-CHOP ineligible (N=10)



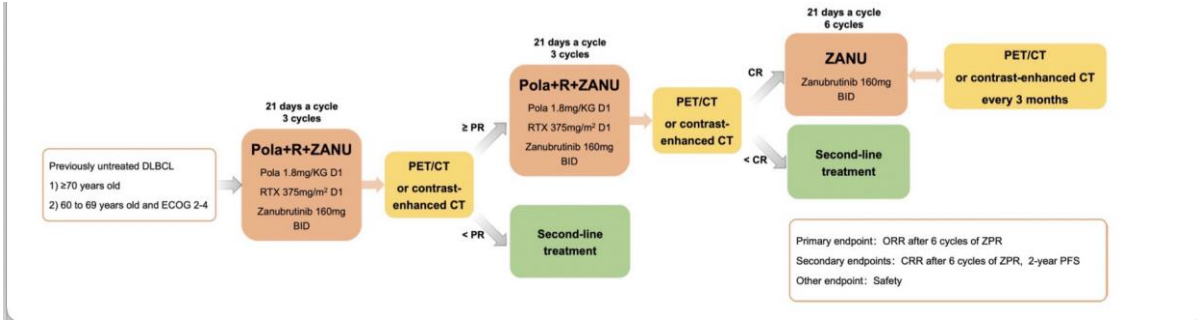
Age – 79y; 70% advanced stage

NO GR 4/5 AE; 3 gr 1 CRS

NO ICANS, polyneuropathy

Melchardt et al, ASH 2023, abstr # 1734

1747 Polatuzumab Vedotin, Zanubrutinib and Rituximab Achieved Rapid and Deep Response in Previously Untreated Frail and Elderly Diffuse Large B-Cell Lymphoma Patients



Ren et al, ASH, 2023, abstr #1747

439 Early Results Indicate Acceptable Safety and Promising Efficacy of Venetoclax in Combination with Pola-R-CHP for Untreated High-Risk BCL-2-Positive -Cell Lymphoma Including Double/Triple Hit Lymphoma

Zelenetz et al, ASH 2023, abstr #439

Pola-R-CHP-Ven

- Median age 64y; 90% advanced stage
- 75% IPI $\geq$ 3; 25% D/THL
- 5 dose cohorts, 10 pts each
- 4 enrolled thus far
- ORR (30 pts); ORR/CMR 86.7% (100% in D/THL)

Zelenetz et al, ASH 2023, abstr #439

Conclusions

- Polatuzumab is an effective and well tolerated ADC, primarily for LBCL
- Pola-R-CHP as initial treatment can be considered *a* new standard in IPI >2
- Considering cost-effectiveness, the most appropriate subsets need to be identified (e.g., not DHL; ?ABC)
- Combination strategies with novel agents appear to be effective and tolerable
- Potential to replace CIT in select untreated patients