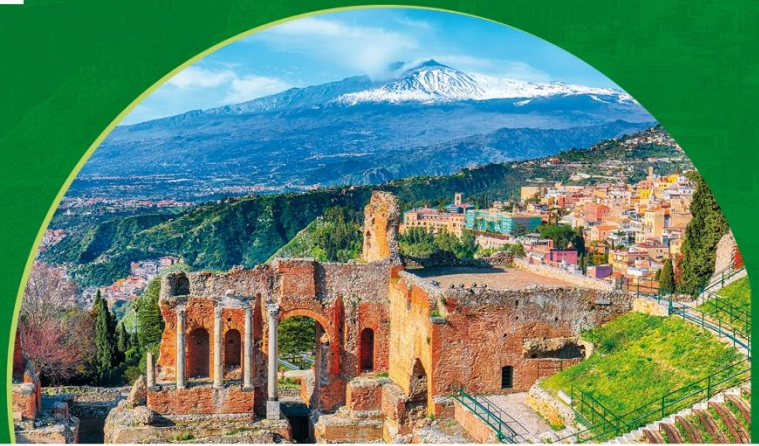
CORSO EDUCAZIONALE COMMISSIONE ANZIANI

XIII EDIZIONE

Giardini Naxos - Marriott Delta Hotels
17-18 aprile 2026



FONDAZIONE ITALIANA LINFOMI

Terapia nei linfomi aggressivi nei pazienti UNFIT/FRAIL

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SOD Ematologia
Azienda Ospedaliera Univeristaria Careggi
Firenze

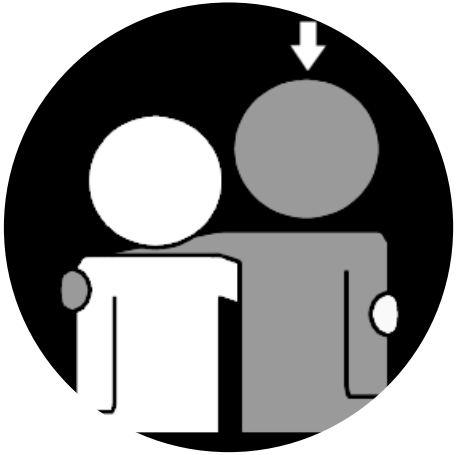
Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
ABBVIE					x	x	
INCYTE					x		
TAKEDA					x	X	
BEIGENE					x	X	
ASTRAZENECA						X	
CSL Behring						x	
ROCHE					x	x	

Terapia

Paziente

Caregiver e terapie di supporto



Quali sono gli obiettivi della terapia ?

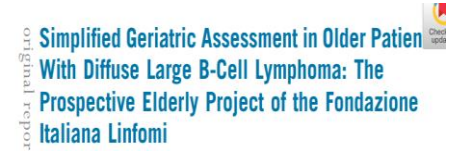
-Risposta completa e duratura (guarigione)?
-Allungamento dell'intervallo di tempo libero da malattia/terapia?
-Miglioramento dei sintomi?
-Qualità di vita?

Decision Making in Geriatric Oncology: Supported Versus Assisted Decision Making

Incorporating patient values and preferences…

«*Appropriate effort should be made to assess an older patient's capacity to make a treatment decision before deeming them to lack that capacity and be in need of a surrogate decision maker (eg. care giver)*»

DuMontier et al, Sommerlatte et al JCO Sep 2021



Criteri per valutazione geriatrica semplificata (sGA)

	FIT	UNFIT		FRAIL
ADL	**≥5***	**< 5***	**6***	**<6***
	and	*and/or*	*and*	*and/or*
IADL	**≥6***	**<6***	**8***	**<8***
	and	*and/or*	*and*	*and/or*
CIRS-G	**0 score =3-4** *and* **≤8 score =2**	**≥1 score =3-4** *and/or* **> 8 score =2**	**0 score =3-4** *and* **<5 score =2**	**≥1 score =3-4** *and/or* **≥5 score =2**
	and	*and*	*and*	*and*
Age	**<80**	**<80**	**≥80**	**≥80**
N. (1207)	**652 (54%)**	**334 (28%)**		**221 (18%)**

* Residual functions

Abbreviations: ADL, activities of daily living; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; IADL, instrumental ADL; sGA, simplified geriatric assessment.

F. Merli et al. J Clin Oncol 2021


Simplified Geriatric Assessment in Older Patien
With Diffuse Large B-Cell Lymphoma: The
Prospective Elderly Project of the Fondazione
Italiana Linfomi
original report
Simplified Geriatric Assessment in Older Patien
With Diffuse Large B-Cell Lymphoma: The
Prospective Elderly Project of the Fondazione
Italiana Linfomi
original report

EPI model parameters

Factors	HR (95% CI)	z-score	Ratio*	**Weight**	P value
FIT	1.00	-	-	**0**	-
UNFIT	1.93 (1.49 to 2.50)	4.97	2.59	**3**	<0.001
FRAIL	2.74 (2.07 to 3.62)	7.09	3.69	**4**	<0.001
IPI 1	1.00			**0**	-
IPI 2	1.55 (0.99 to 2.44)	1.92	1.00	**1**	0.055
IPI 3-5	2.90 (1.93 to 4.35)	5.14	2.68	**3**	<0.001
Hb <12 g/dL	1.28 (1.02 to 1.60)	2.13	1.11	**1**	0.033

- The EPI was the sum of the weights
- **EPI score ranging from 0 to 8**
- Good correlation with OS

FONDAZIONE ITALIANA LINFOMI

LOW 0-1

INTERMEDIATE 2-5

HIGH 6-8

F. Merli et al. J Clin Oncol 2021

Come ridurre tossicita' precoci?

Pre-fase (1-3):
Prednisone fino a 7 giorni con o senza Vincristina 1 mg

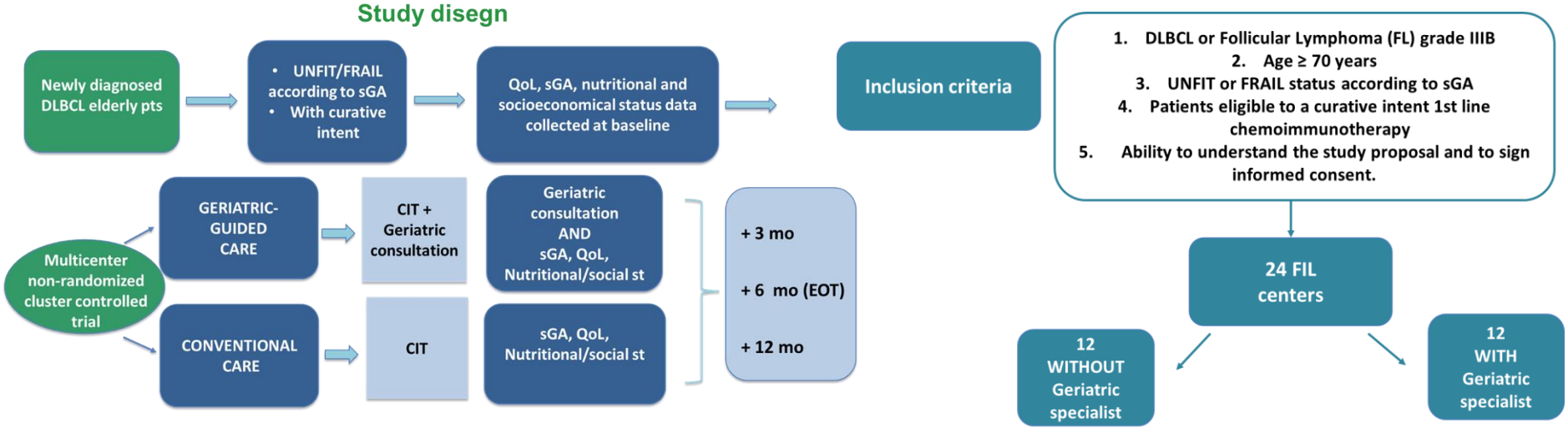
- Riduzione delle morti tossiche precoci durante il I ciclo (<2% vs 5% senza pre-fase)
- Riduzione del rischio di lisi tumorale o neutropenia febbrile
- Miglioramento del PS

G-CSF in profilassi primaria (4,5):

- Rischio di neutropenia febbrile in pz > 65 anni: 37%
- Raccomandato da linee guida ASCO
- In casistiche US 1/3 dei pz non riceveva G-CSF in profilassi primaria

1:Pfreundschuh M et al, Blood 2004; 2:Pfreundschuh M et al, Lancet Oncol 2008; 3:Peyrade F et al. Lancet Haematol 2017; 4: Smith. TJ et al, J Clin Oncol 2015; 5: Olszewski AJ et al, J Natl Compr Canc Netw 2016

Geriatric-guided care versus conventional care in elderly unfit/frail patients with Diffuse Large B-cell lymphoma in first line treatment. The Elderly Project 2.0



Benedetta Sordi
AOU Careggi, Firenze

PRIMARY ENDPOINT

EORTC QLQ-C30 score
at baseline and EOT
in geriatric guided vs conventional care group

SECONDARY ENDPOINTS

- Dynamic assessment of sGA
- Prognostic impact of sGA integrated with nutritional status parameters (BMI, albumin)
- Therapeutic choices, dose intensity, therapy completition rate
- Early mortality rate (+90 days)
- ORR and CRR
- PFS and OS
- Hospital admission rate and median duration of hospitalization
- Cost Evaluation
- Caregiver Quality of Life QoL) and Related Outcomes (CROs)

Lancet Oncol 2011; 12: 460–68
Published Online
April 8, 2011

Attenuated immunochemotherapy regimen (R-miniCHOP) in elderly patients older than 80 years with diffuse large B-cell lymphoma: a multicentre, single-arm, phase 2 trial

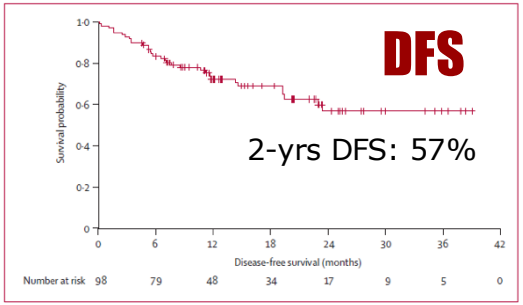
Frédéric Peyrade, Fabrice Jardin, Catherine Thieblemont, Antoine Thyss, Jean-François Emile, Sylvie Castaigne, Bertrand Coiffier, Corinne Haioun, Serge Bologna, Olivier Fitoussi, Gérard Lepeu, Christophe Fruchart, Dominique Bordessoule, Michel Blanc, Richard Delarue, Maud Janvier, Bruno Salles, Marc André, Marion Fournier, Philippe Gaulard, Hervé Tilly, for the Groupe d'Etude des Lymphomes de l'Adulte (GELA) investigators*

N=149

R miniCHOP (6 cy. every 21)

- Rituximab 375 mg/mq
- Doxorubicin 25 mg/mq
- Cyclophosphamide 400 mg/mq
- Vincristine 1 mg total
- Prednisone 40 mg/mq (oral)

6 cycles in 108 pts (median DI 97%)



Complete response	59 (40%)
Unconfirmed complete response	34 (23%)
Partial response	16 (11%)
Stable disease	2 (1%)
Progression during treatment	8 (5%)
Death	27 (18%)
Not assessed	3 (2%)

Table 5: **Response at end of treatment**

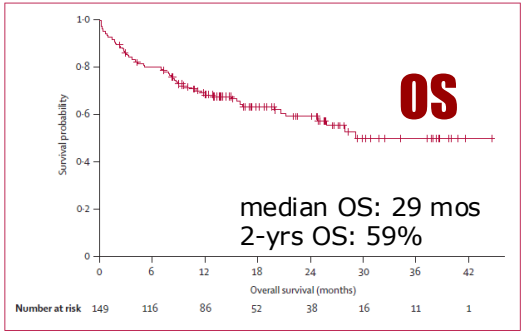


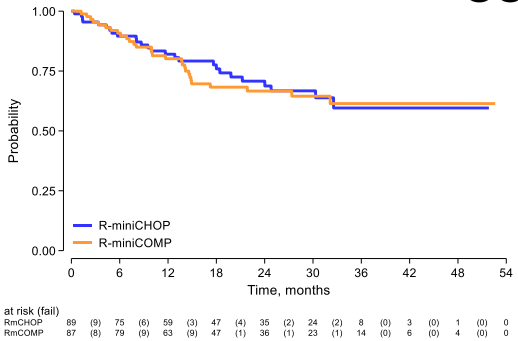
Figure 2: **Overall survival**

Comparative effectiveness of R-miniCOMP *versus* R-miniCHOP in older non-FIT patients with diffuse large B-cell lymphoma: Insights from a 'Fondazione Italiana Linfomi' cohort study

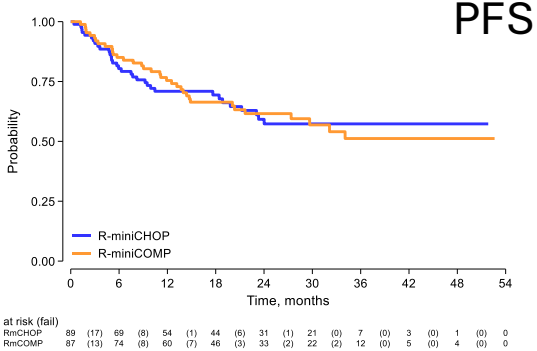
Table 1. Comparison of key clinical characteristics of non-FIT (at sGA) patients enrolled in the Elderly Project Trial

Characteristics	RminiCHOP n=89	RminiCOMP n=87	Total n=176	p
Age, median (min-max)	*82 (65-90)*	*82 (69-94)*	*82 (65-94)*	*0.849*
Age >80, n (%)	71 (80)	69 (79)	140 (80)	1.000
Gender M, n (%)	53 (60)	48 (55)	101 (57)	0.648
IPI 3-5, n (%) [n=165]	50 (60)	42 (52)	92 (56)	0.350
Hb, median (min-max)	*12.4 (6.2-16.1)*	*12.1 (6.2-16.5)*	*12.1 (6.2-16.5)*	*0.813*
Hb <12 g/dL, n (%) [n=174]	41 (47)	35 (41)	76 (44)	0.449
B-symptoms, n (%)	19 (21)	26 (30)	45 (26)	0.228
Bulky yes, n (%) [n=174]	25 (29)	31 (36)	56 (32)	0.417
EPI [n=165]				0.345
Intermediate risk	31 (37)	36 (44)	67 (41)	
High risk	53 (63)	45 (56)	98 (59)	
sGA				0.277
UNFIT	59 (66)	50 (57)	109 (62)	
FRAIL	30 (34)	37 (43)	67 (38)	
Comorbidities				
Heart >1, n (%)	22 (25)	26 (30)	48 (27)	0.500
Liver >1, n (%)	9 (10)	6 (7)	15 (9)	0.591
Hypertens >1, n (%)	36 (40)	28 (32)	64 (36)	0.276
Urogenit. >1, n (%)	10 (11)	11 (13)	21 (12)	0.819
Kidney>1, n (%)	9 (10)	7 (8)	16 (9)	0.794
Muscle >1, n (%)	2 (2)	10 (11)	12 (7)	**0.017**
CNS> 1, n (%)	4 (4)	2 (2)	6 (3)	0.682
Psychol. >1, n (%)	9 (10)	4 (5)	13 (7)	0.249
Response treat.				
CR rate [n=161]	54 (67)	45 (56)	99 (61)	0.197

OS



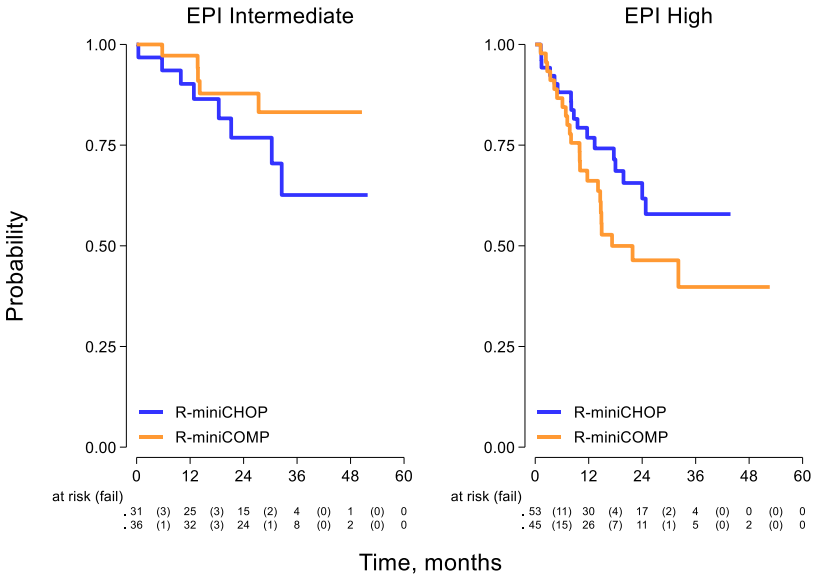
PFS



Bavieri A

Treatment by EPI
Test for interaction p=0.068

EPI intermediate	3-yr OS % (95%CI)	HR (95%CI)	p-value
R-miniCHOP	63 (36-80)	1.00	
R-miniCOMP	83 (64-93)	0.49 (0.16-1.49)	0.207
EPI High	**3-yr OS % (95%CI)**	**HR (95%CI)**	**p-value**
R-miniCHOP	58 (40-72)	1.00	
R-miniCOMP	40 (22-57)	1.60 (0.86-3.00)	0.140



R-mini COMP tended to be associated with unfavorable OS in high-risk EPI scores. A comprehensive survival analysis within vulnerable geriatric categories (unfit and frail patients) confirmed non-significant variations in predictive efficacy between R-miniCHOP and R-miniCOMP.

This study suggests that R-miniCHOP is still the preferred treatment for unfit and frail older DLBCL. The promising role of R-miniCOMP for older DLBCLs with intermediate EPI risk score warrants confirmation in bigger, randomized studies

Bavieri A et

Frontline R-mini-CHOP + X	III/1 L SWOG1918	NCT04799275	Azacitadine + mini-R-CHOP versus mini-RCHOP. Stratification by EPI
	III/1 L POLAR BEAR 80+ or 75 with frailty by CGA	NCT04332822	Mini-R-CHOP versus pola-R-mini-CHP × 6
	III/1 L ARCHED Elderly > 80 years or 61–80 years and unfit for R-CHOP	NCT05820841	Randomized trial of acalabrutinib + *R*-mini-CHOP versus R-mini-CHOP. Stratigication by age, ADL score, IPI
	II/1 L elderly ineligible for R-CHOP	NCT04663347	Epcoritamab-R-mini-RCHOP × 6 cycles +2 additional cycles of epcoritamab monotherapy
Omitting chemotherapy frontline in elderly/unfit/frail	III/1 L Elderly > 70 years, unfit/frail	NCT05179733	ZR2 versus R-mini-CHOP
	II/IL Ineligible for R-CHOP	NCT05798156	R-pola-glofit × 6 cycles, then 6 cycles consolidation
	II/1 L MorningSun; ≥ 80 years or 65–79 and ineligible for R-CHOP	NCT05207670	Subcutaneous fixed duration mosunetuzumab for up to 17 cycles (1 year)
	II/1 L EPCOR DLBCL-3 ≥ 80 years or ≥ 75 years with comorbidities	NCT05660967	Subcutaneous fixed duration epcoritamab for up to 12 cycles (1 year)
	II/1 L ACRUE ≥ 80 years or 61–79 and chemoimmunotherapy inegligible	NCT05952024	Rituximab for 8 cycles and acalabrutinib for 28 cycles

INITIAL SAFETY DATA FROM THE PHASE 3 POLAR BEAR TRIAL IN ELDERLY OR FRAIL PATIENTS WITH DIFFUSE LARGE CELL LYMPHOMA R-POLA-MINI-CHP vs. R-MINI-CHOP

Mats Jerkeman, Andres Ferreri, Peter N Brown, Julian Hamfjord, Sirpa Leppä

Presented at: European Hematology Association 2023 Hybrid Congress; June 8-11, 2023;. Abstract S227.

Age ≥80 years or frail 75-80 years : DLBCL, EBV+NOS, t FL, PMBCL, CBCL-LT, FL3b,TCRLBCL, HG

Frail: ADL score ≤ 5 and/or ≥3 grade 3 CIRS-G comorbiditiy and /or ≥ 1 grade 4 comorbidity Stage II-IV; PS WHO 0-3 (L)

SAE reports

- R-mini-CHOP: total 46 (65%)
  - Grade 5: death of unknown cause (2);
- R-pola-mini-CHP: total 52 (75%)
  - Grade 5: hypoxia (1), intestinal ischemia (1), pneumonia (1), SARS-CoV2 pneumonia (1)
- Most SAEs were due to infections

DSMB meeting on Sep 2022: no unexpected safety signals were found, and recommendation was to continue enrolment

Adverse events (selected)

Adverse event		R-mini-CHOP (n=71)		R-pola-mini-CHP (n=69)	
Anemia[1]	Grade 3-5	2	2.8%	10	14%
Neutropenia[1]	Grade 3-5	8	11%	9	13%
Thrombocytopenia[1]	Grade 3-5	0	0	1	1.4%
Infection	Total	32	45%	39	57%
	Grade 3-5	10	14%	11	16%
Gastrointestinal	Total	22	31%	38	55%
	Grade 3-5	12	17%	21	30%
Cardiovascular	Total	21	30%	16	23%
	Grade 3-5	6	8.5%	6	8.7%
Peripheral neuropathy	Grade 1	7	9.9%	9	13%

[1]For hematological toxicity, only grade 3-5 was recorded

RWD DLBCL 1L- Polatuzumab

- POLAROID Study: MSKCC

Aims

AIM 1 To understand the real-world efficacy and safety of Pola-RCHP in OA

Similar response rates
Similar survival outcomes
Higher rates of hematologic toxicities, cardiomyopathy and hospitalization

AIM 2 To characterize the impact of baseline fitness/frailty on outcomes with Pola-RCHP in OA.

Worse ECOG PS was associated with lower CRR and shorter PFS
Other measures of fitness (e.g., CIRS-G, ADL impairment) were not associated with response

AIM 3 **To investigate the risk-benefit profile of polatuzumab-based regimens in two subgroups:**

Patients receiving Pola-R-mini-CHP
Patients ≥80 years old

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

Results: Pola-R-mini-CHP

Baseline Characteristics

	Pola-R-CHP (N = 172)	Pola-R-mini-CHP (N = 38)	P-value
Age	74 (72, 77)	79 (75, 81)	<0.001
Age ≥80	19 (11%)	19 (50%)	
Sex – no. (%)			0.1
Male	100 (58%)	28 (74%)	
ECOG Score			0.06
0-1	131 (80%)	25 (66%)	
2+	33 (20%)	13 (34%)	
Stage			0.3
I	5 (2.9%)	0 (0%)	
II	12 (7.0%)	3 (7.9%)	
III	34 (20%)	3 (7.9%)	
IV	120 (70%)	32 (84%)	
Extranodal Dx			0.03
Yes	129 (75%)	34 (92%)	
LDH			0.8
< ULN	59 (35%)	14 (37%)	
> ULN	111 (65%)	24 (63%)	

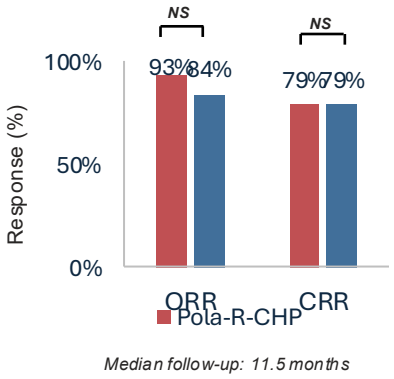
	Pola-R-CHP (N = 172)	Pola-R-mini-CHP (N = 38)	P-value
IPI Score			0.2
0 to 2	43 (25%)	6 (16%)	
3 to 5	129 (75%)	32 (84%)	
Bulky Disease	53 (31%)	11 (29%)	0.8
CNS Involvement	8 (4.7%)	2 (5.6%)	0.7
Double Expressor	49 (35%)	13 (45%)	0.3
Double Hit	5 (3.4%)	3 (11%)	0.1
Cell of Origin			>0.9
Non-GCB	108 (67%)	22 (67%)	
GCB	53 (33%)	11 (33%)	
Treatment Completion	148 (86%)	30 (79%)	0.3

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

Results: Pola-R-mini-CHP

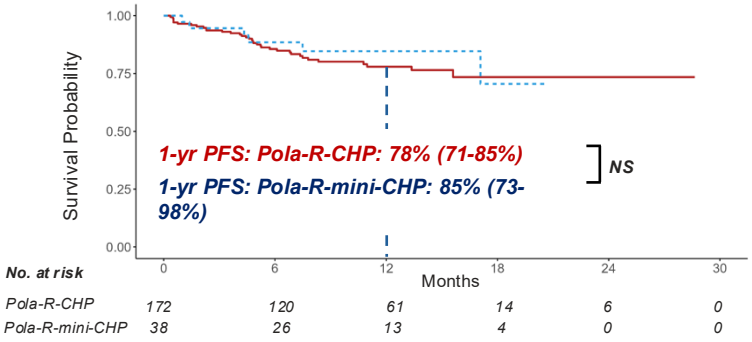
No difference in ORR, CRR, PFS, OS, or toxicity in patients treated with dose reduction

RESPONSE RATE

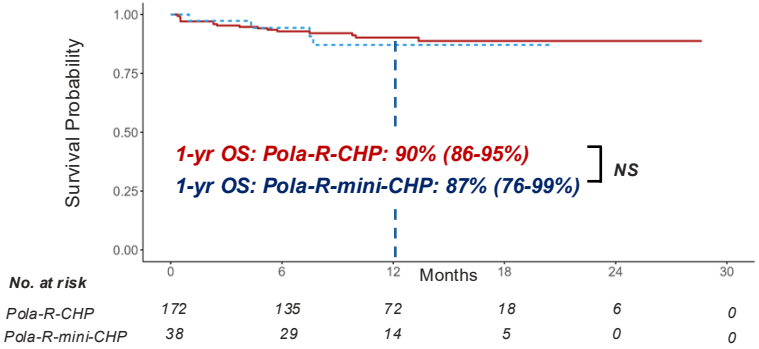


Median follow-up: 11.5 months

PROGRESSION FREE SURVIVAL



OVERALL SURVIVAL



ADVERSE EVENTS

	Pola-R-CHP (N = 172)	Pola-R-mini-CHP (N = 38)	P
Neutropenia, Grade 3+	63 (37%)	15 (41%)	0.8
Febrile neutropenia, Grade 3+	26 (15%)	5 (14%)	>0.9
Thrombocytopenia, G3+	34 (20%)	11 (30%)	0.3
Hospitalization	62 (36%)	17 (45%)	0.4
ICU Admission	13 (7.6%)	3 (7.9%)	>0.9
Peripheral Neuropathy	72 (42%)	14 (39%)	0.9
Grade 3+	2 (2.8%)	1 (7.1%)	>0.9
Cardiomyopathy	9 (5.3%)	4 (11%)	0.4
Infection, Grade 3+	34 (20%)	9 (24%)	0.7

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

Results: Pts ≥80 years

Background characteristics

	Age 70-79 (N = 178)	Age ≥ 80 (N = 32)	P-value
Age	74 (72, 76)	81 (81, 85)	
Sex – no. (%)			**0.01**
Male	102 (57%)	26 (81%)	
ECOG Score			0.9
0-1	131 (77%)	25 (78%)	
2+	39 (23%)	7 (22%)	
Stage			0.6
I	5 (2.8%)	0 (0%)	
II	11 (6.2%)	4 (13%)	
III	31 (17%)	6 (19%)	
IV	130 (73%)	22 (69%)	
Extranodal Dx			0.7
Yes	138 (78%)	25 (81%)	
LDH			0.13
< ULN	58 (33%)	15 (47%)	
> ULN	118 (67%)	17 (53%)	
IPI Score			0.8
0 to 2	41 (23%)	8 (25%)	
3 to 5	137 (77%)	24 (75%)	

	Age 70-79 (N = 178)	Age ≥ 80 (N = 32)	P-value
Bulky Disease	56 (32%)	8 (25%)	0.4
CNS Involvement	8 (4.6%)	2 (6.7%)	0.6
Double Expressor	51 (34%)	11 (48%)	0.2
Double Hit	6 (3.9%)	2 (9.1%)	0.3
Cell of Origin			**0.05**
Non-GCB	106 (64%)	24 (83%)	
GCB	59 (36%)	5 (17%)	
Pola-R-mini-CHP	19 (11%)	19 (59%)	**<0.001**
Impairments in ADLs	15 (8%)	2 (6%)	0.7
Median CIRS-G	10 [7,14]	11 [9,16]	>0.9
Geriatric Syndrome	25 (14%)	4 (13%)	>0.9
Treatment Completion	151 (85%)	27 (84%)	>0.9

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

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

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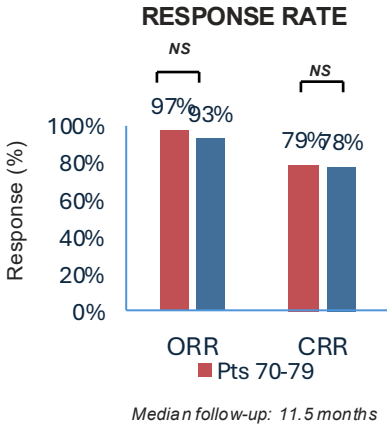
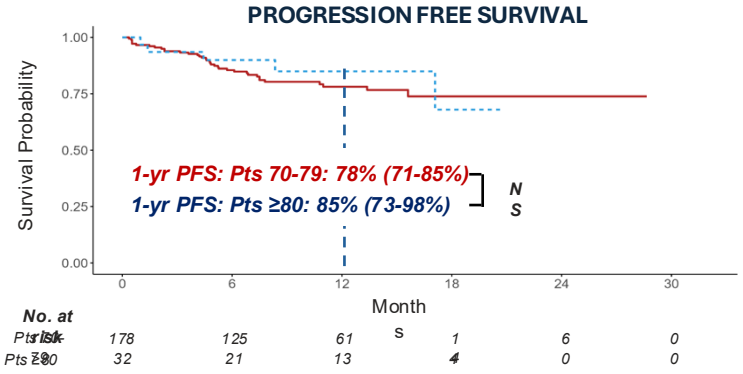
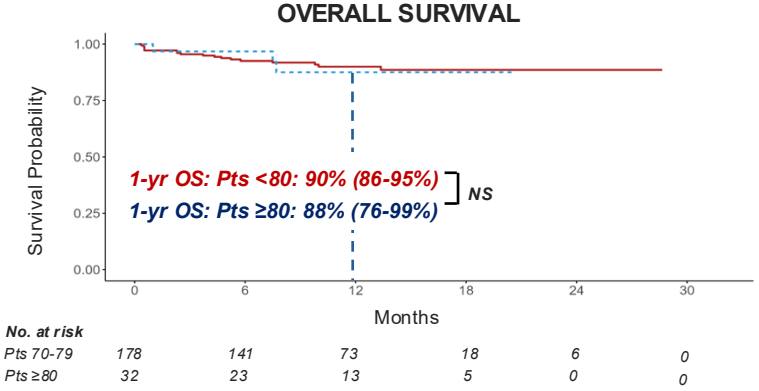
Results: Pts ≥80 years

No difference in ORR, CRR, PFS, OS, or toxicity in the oldest patients







ADVERSE EVENTS

	Age 70-79 (N = 178)	Age ≥ 80 (N = 32)	P
Neutropenia, Grade 3+	69 (39%)	9 (29%)	0.4
Febrile neutropenia, Grade 3+	30 (17%)	1 (3.2%)	0.09
Thrombocytopenia, Grade 3+	39 (22%)	6 (19%)	>0.9
Peripheral Neuropathy	79 (45%)	7 (23%)	0.05
Grade 3+	2 (2.6%)	1 (14%)	0.6
Cardiomyopathy	10 (5.6%)	3 (9.4%)	0.7
Infection, Grade 3+	38 (22%)	5 (16%)	0.6
Hospitalization	71 (40%)	8 (25%)	0.2
ICU Admission	16 (9.1%)	0 (0%)	0.2
Treatment Completion	151 (85%)	27 (84%)	>0.9

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

Conclusions

AIM 1 **Older adults (≥70 years) treated with first-line polatuzumab have similar response rates and survival outcomes compared with younger patients.**

Toxicities are manageable and do not affect rates of treatment completion.

AIM 2 **Worse baseline fitness – as measured by ECOG PS – is an independent predictor of shorter PFS.**

Other measures of fitness (e.g., CIRS-G, ADL impairment) were not associated with response

AIM 3 **Outcomes were excellent in patients receiving Pola-R-mini-CHP and those ≥80 years.**

With appropriate selection and dose modification, most patients appear to benefit from polatuzumab-based treatment.

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

Epcoritamab + R-mini-CHOP Results in 2-Year Remissions and High MRD-Negativity Rates in Elderly Patients With Newly Diagnosed DLBCL: Results From the EPCORE NHL-2 Trial

Chan Cheah,[1] Juraj Ďuraš,[2] David Belada,[3] Justin Darrah,[4] Yasmin Karimi,[5] Franck Morschhauser,[6] Gerardo Musuraca,[7] Mats Hellstrom,[8] Katerina Kopeckova,[9] Lori Leslie,[10] Anna Sureda Balari,[11] Catherine Thieblemont,[12] Umberto Vitolo,[13] Kojo Osei-Bonsu,[14] Yi Hao,[15] Monica Wielgos-Bonvallet,[15] Mina Khoshdeli,[15] Aidan Reilly,[15] Malene Risum,[16] Joost Vermaat,[17] Joshua Brody[18]

OBJECTIVE

- To evaluate efficacy and safety of epcoritamab + R-mini-CHOP in patients with 1L DLBCL ineligible to receive full-dose R-CHOP with longer median follow-up (16.8 mo)

EPCORE® NHL-2 Arm 8 Study Design

A phase 1b/2, open-label trial evaluating the efficacy and safety of fixed-duration epcoritamab + R-mini-CHOP in elderly patients with newly diagnosed DLBCL

Key inclusion criteria

- Newly diagnosed DLBCL[a]
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - HGBCL[b]
  - FL grade 3B
- ECOG PS 0–2
- Ineligible to receive full-dose R-CHOP due to:
  - ≥ 75 years of age, or
  - ≥ 65 years of age with a comorbidity[c]

	Fixed-duration treatment regimen: epcoritamab + R-mini-CHOP[d]		
	C1–2	C3–6	C7–8
Epcoritamab SC 48 mg[e]	QW	Q3W	Q4W
R-mini-CHOP: Rituximab IV 375 mg/m²	Q3W		
R-mini-CHOP: Cyclophosphamide IV 400 mg/m²	Q3W		
R-mini-CHOP: Doxorubicin IV 25 mg/m²	Q3W		
R-mini-CHOP: Vincristine IV 1 mg/m²	Q3W		
R-mini-CHOP: Prednisone IV or PO 100 mg/d[f]	D1–5 of each cycle		

Data cutoff: Sep 21, 2025
Median follow-up: 33.4 months (range, 2.8–41.1)

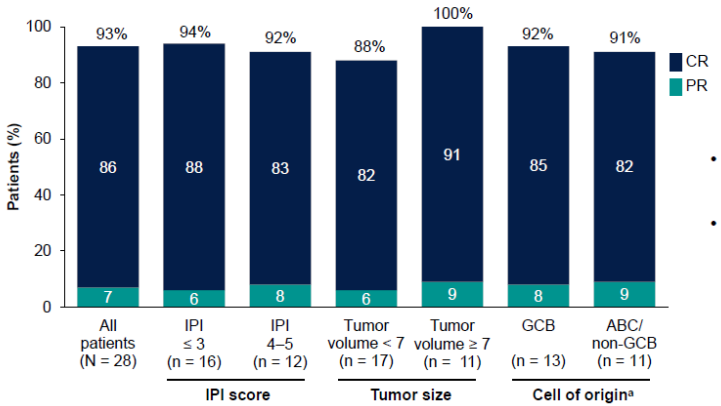
- **Primary endpoint:** ORR by investigator assessment[g]
- **Key secondary endpoints:** CR rate, DOR, DOCR, PFS, OS, MRD negativity,[h] and safety

Baseline Characteristics

	Epcoritamab + R-mini-CHOP (N = 28)
Age, median (range), years	81 (74–90)
65 to < 75 years, n (%)	1 (4)
≥ 75 years, n (%)	27 (96)
Male sex at birth, n (%)	14 (50)
Race, n (%)	
White	19 (68)
Other	1 (4)
Not reported	8 (29)
ECOG PS,[a] n (%)	
0	10 (36)
1	12 (43)
2	5 (18)
Ann Arbor staging, n (%)	
I–II	8 (29)
III	3 (11)
IV	17 (61)
Reasons not eligible for full-dose anthracycline, n (%)	
Age ≥ 75 years	27 (96)
Hypertension requiring treatment	15 (54)
Diabetes mellitus	3 (11)
History of myocardial infarction[b]	1 (4)

	Epcoritamab + R-mini-CHOP (N = 28)
DH/TH status by central FISH,[c] n (%)	
DH or TH	1 (4)
Not DH/TH	17 (61)
IPI score at screening, n (%)	
≤ 3	16 (57)
4–5	12 (43)
Cell of origin,[d] n (%)	
GCB	13 (46)
ABC/non-GCB	11 (39)
DLBCL type, n (%)	
De novo	25 (89)
Transformed[e]	3 (11)
Bulky tumor, n (%)	
< 7 cm	17 (61)
≥ 7 cm	11 (39)
LDH, n (%)	
Elevated	18 (64)
Normal	10 (36)
Time from initial diagnosis to first dose, median (range), weeks	5 (2–11)

Overall and CR Rates



- Median time to response: 1.4 months (range, 1.1–2.7)
- Median time to CR: 1.6 months (range, 1.2–8.1)

Conclusions

- Fixed-duration epcoritamab + R-mini-CHOP resulted in high response rates, rapid/sustained MRD negativity, and durable remissions in elderly patients with newly diagnosed DLBCL ineligible for full-dose R-CHOP
  - Outcomes compare favorably with historical results of R-mini-CHOP
- Safety was consistent with prior reports and the known safety profiles of epcoritamab and R-mini-CHOP

Epcoritamab + R-mini-CHOP in elderly patients

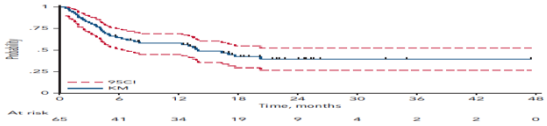
ORR: 93%; CR: 86%

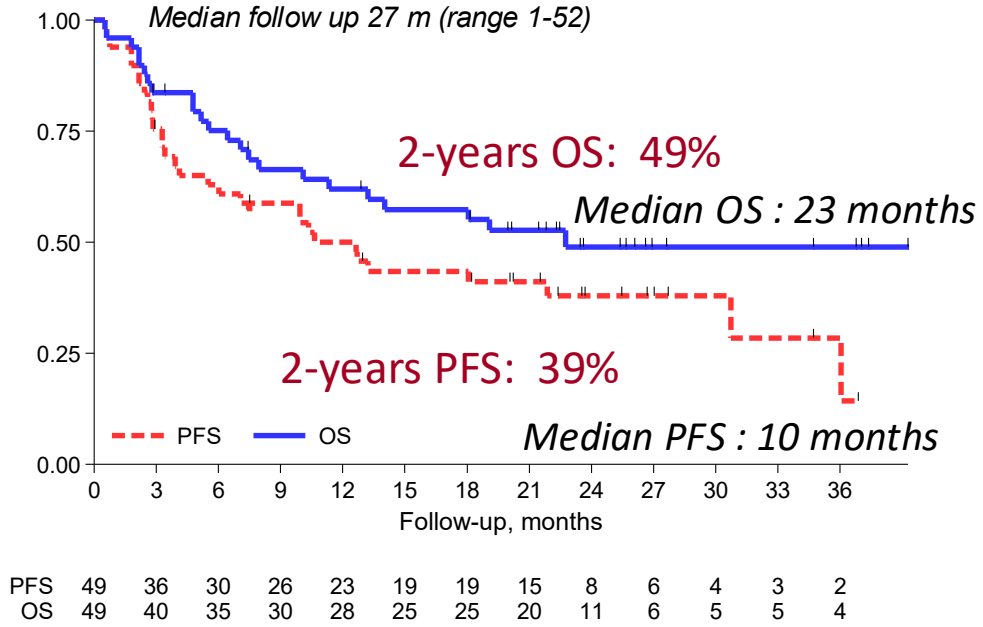
2-year PFS rate: 76%

2-year OS rate: 82%

These findings show that epcoritamab is a versatile, well-tolerated therapy across patient subgroups, including those with historically poor outcomes

Rituximab plus bendamustine as front-line treatment in frail elderly (>70 years) patients with diffuse large B-cell non-Hodgkin lymphoma: a phase II multicenter study of the Fondazione Italiana Linfomi





Rituximab: 375 mg/m² g. 1

Bendamustine: 90 mg/mq gg 2-3 ogni 28

4 cicli R-B + 2 R in stadi I-II IPI 0

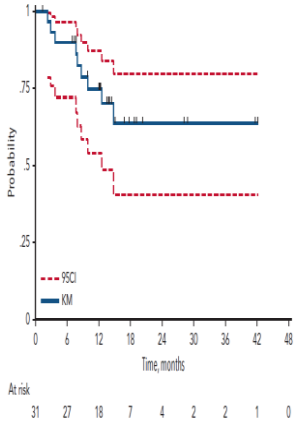
6 cicli R-B in tutti gli altri

45 Pz eleggibili
ORR 62%
CRR 53%

Chemo-free trials in elderly/unfit-frail

Storti S et al Haematologica 2018, 103(8):1345-1350

Lenalidomide plus rituximab for the initial treatment of frail older patients with DLBCL: the FIL_ReRi phase 2 study



ORR 50.8%
CR 27.7%

R 375 mg/m2 d 1 q28 x 4
Len 20 mg d 2-22 q28 x 6

CR
PR

Len 10 mg d 1-21 q 28 x 12

≥70-year-old untreated frail (sGA) patients with DLBCL
Jan17-Jun 21: 68 pts enrolled, 65 confirmed eligible and started tx
1 EP: ORR @cycle 6; gr ≥ 3 extra-hem. Toxicity
Induction treatment was completed in 37 (56.9%) patients

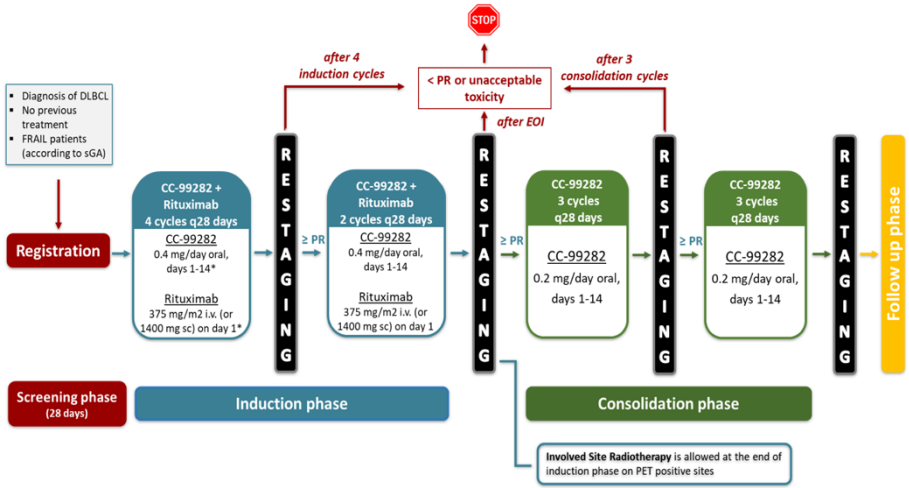


Table 2. Hematological and extrahematological grade greater than or equal to 3 AEs

	Grade 3		Grade 4		Grade 5	
	n	%	n	%	n	%
Any hematological toxicity	27		13		—	
Anemia	2	3.1	—		—	
Neutropenia	21	32.3	9	13.8	—	
Thrombocytopenia	4	6.2	2	3.1	—	
Any extrahematological toxicity	41		4		5	
Respiratory/thoracic and mediastinal disorders	5	10.0	1	2.0	1	2.0
General disorders/administration site conditions	6	12.0	1	2.0	—	
Skin and subcutaneous tissue disorders	6	12.0	1	2.0	—	
Cardiac disorders	5	10.0	—		1	2.0
Vascular disorders	3	6.0	—		3	6.0
Infections	3	6.0	1	2.0	—	
Gastrointestinal disorders	3	6.0	—		—	
Nervous system disorders	3	6.0	—		—	
Investigations	1	2.0	—		—	
Metabolism and nutrition disorders	2	4.0	—		—	
Musculoskeletal and connective tissue disorders	2	4.0	—		—	
Neoplasms benign/malignant/unspecified	1	2.0	—		—	
Psychiatric disorders	1	2.0	—		—	

mPFS 14 Mo

DOR@2Y 64%

COORDINATING INVESTIGATOR/S	Dr.ssa Alessandra Tucci (Brescia)
WRITING COMMITTEE AND SCIENTIFIC SUPPORT	Dr.ssa Annalisa Arcari (Piacenza) Dr Francesco Merli (Reggio Emilia) Dr Michele Spina (Aviano) Dr Guido Gini (Ancona) Dr Luigi Marcheselli (Modena) Dott.ssa Federica Cavallo (Torino) Dott.ssa Benedetta Puccini (Firenze) Dott.ssa Francesca Maria Quaglia (Verona) Dott. Luca Guerra (Monza) Giuseppe Gioffrè, AIL-FIL Lymphoma patient association, Roma, Italy

Gini G et al, Blood, 2023

Frontline R-mini-CHOP + X	III/1 L SWOG1918	NCT04799275	Azacitadine + mini-R-CHOP versus mini-RCHOP. Stratification by EPI
	III/1 L POLAR BEAR 80+ or 75 with frailty by CGA	NCT04332822	Mini-R-CHOP versus pola-R-mini-CHP × 6
	III/1 L ARCHED Elderly > 80 years or 61–80 years and unfit for R-CHOP	NCT05820841	Randomized trial of acalabrutinib + *R*-mini-CHOP versus R-mini-CHOP. Stratigication by age, ADL score, IPI
	II/1 L elderly ineligible for R-CHOP	NCT04663347	Epcoritamab-R-mini-RCHOP × 6 cycles +2 additional cycles of epcoritamab monotherapy
Omitting chemotherapy frontline in elderly/unfit/frail	III/1 L Elderly > 70 years, unfit/frail	NCT05179733	ZR2 versus R-mini-CHOP
	II/IL Ineligible for R-CHOP	NCT05798156	R-pola-glofit × 6 cycles, then 6 cycles consolidation
	II/1 L MorningSun; ≥ 80 years or 65–79 and ineligible for R-CHOP	NCT05207670	Subcutaneous fixed duration mosunetuzumab for up to 17 cycles (1 year)
	II/1 L EPCOR DLBCL-3 ≥ 80 years or ≥ 75 years with comorbidities	NCT05660967	Subcutaneous fixed duration epcoritamab for up to 12 cycles (1 year)
	II/1 L ACRUE ≥ 80 years or 61–79 and chemoimmunotherapy inegligible	NCT05952024	Rituximab for 8 cycles and acalabrutinib for 28 cycles

FONDAZIONE ITALIANA LINFOMI

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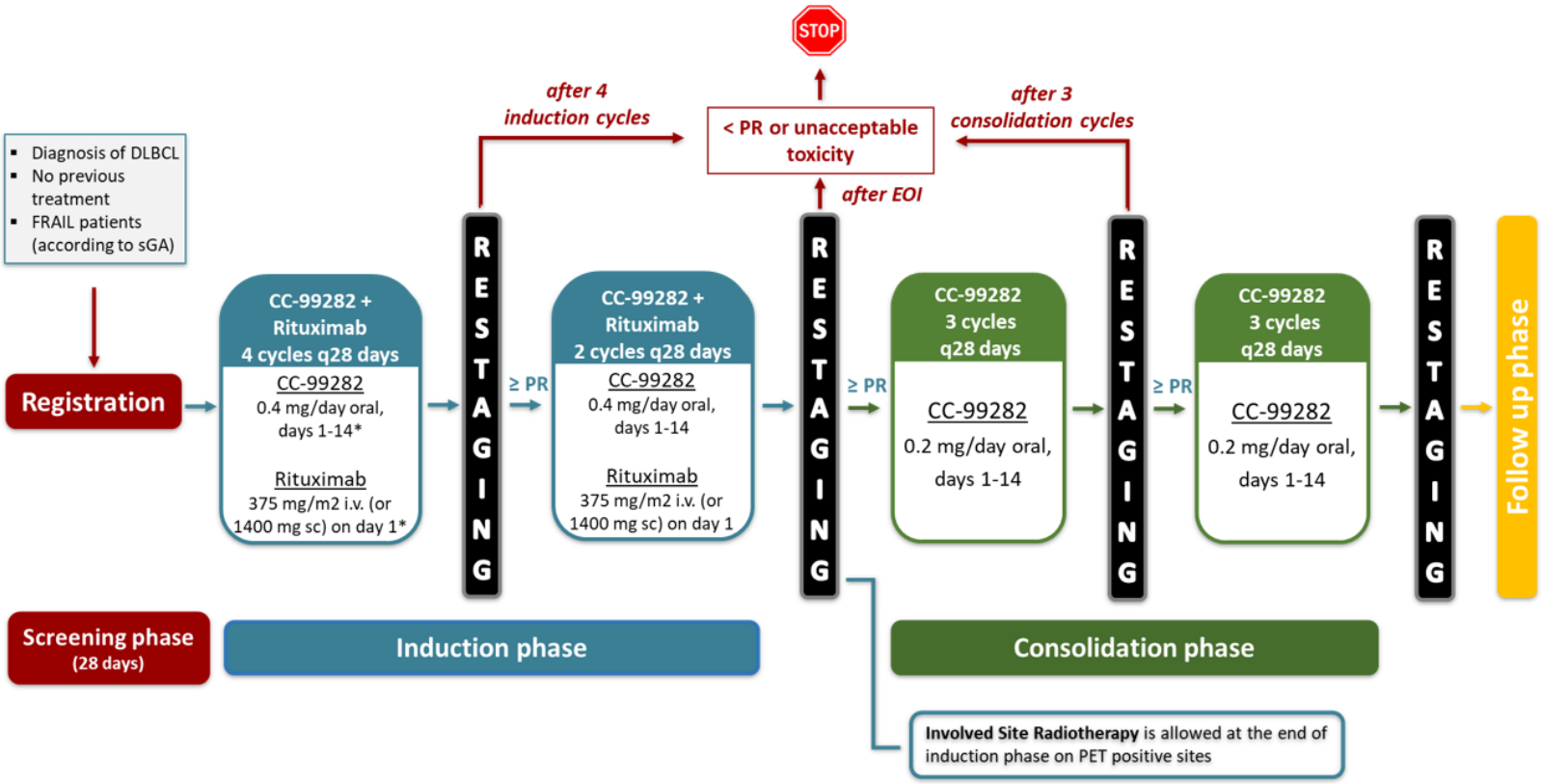
A combination of **RI**tuximab and **CC**-99282 (golcadomide) as front line therapy for **O**lder frail patients with Diffuse Large B-cells non-Hodgkin Lymphoma evaluated with a simplified Geriatric Assessment (sGA): a phase II study of the Fondazione Italiana Linfomi (FIL)

COORDINATING INVESTIGATOR/S	Dr.ssa Alessandra Tucci (Brescia)
WRITING COMMITTEE AND SCIENTIFIC SUPPORT	Dr.ssa Annalisa Arcari (Piacenza) Dr Francesco Merli (Reggio Emilia) Dr Michele Spina (Aviano) Dr Guido Gini (Ancona) Dr Luigi Marcheselli (Modena) Dott.ssa Federica Cavallo (Torino) Dott.ssa Benedetta Puccini (Firenze) Dott.ssa Francesca Maria Quaglia (Verona) Dott. Luca Guerra (Monza) Giuseppe Gioffrè, AIL-FIL Lymphoma patient association, Roma, Italy

Study design



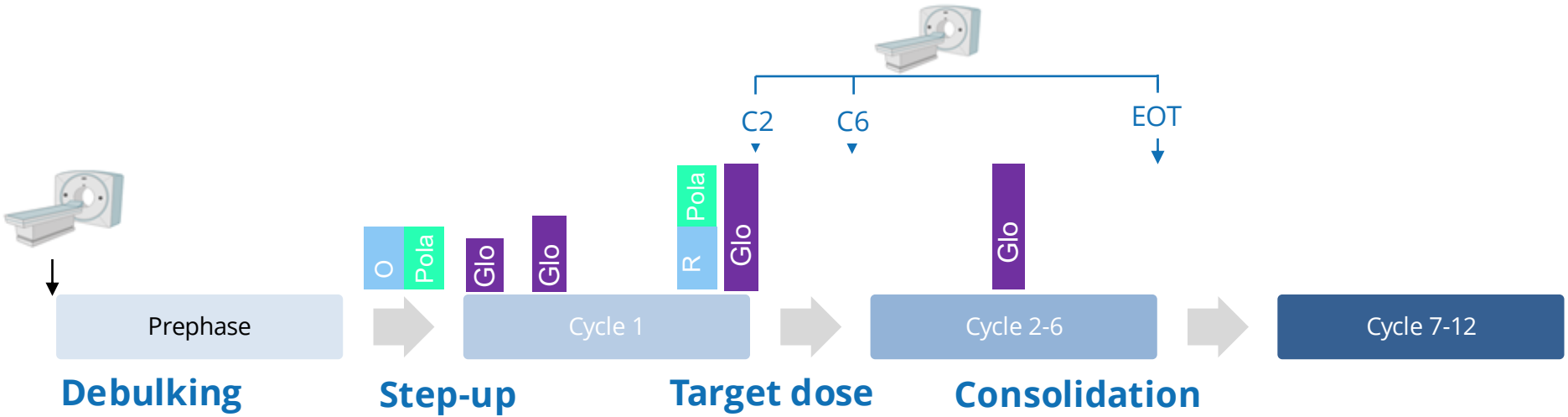
During cycle 1: CC-99282 will be administered 0,3 mg/day oral; Rituximab will be administered 375 mg/m2 on Day 1, 8, 15; Dexamethasone 5 mg p.o. on days 1, 8, 15, 22 during cycle 1

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

B. Chapuy, R. Wurm-Kuczera, R. Michael, M. Wang, P. Pichler, A. Huster, A. Kerkhoff, M. Panny, R. Schroers, A. Ossami Saidy, F. Müller, F. Damm, M. Orlinger, P. Staber, C. Schwaenen, L. Wohn, C. Schmitt, M. Hoffmann, M. Hänel, J. Düll, S. Heyn, S. Mayer, T. Weber, P. Reimer, N. Rotter, U. Schnetzke, B. von Tresckow, G. Kammerer, J. Rasvina, B. Lehner, T. Mika, D. Böckle, C. Leng, A.L. Illert, B. Altmann, B. Friedrichs, E.Willenbacher, D. Mougiakakos, C. Pott, S. Al-Batran, A. Rosenwald, D. Hellwig, S. Dietrich, B. Glass, G. Lenz, U. Keller, M. Ziepert, T. Melchardt, R. Greil

Presented at the 67th American Society of Hematology (ASH) Annual Meeting 2025 | December 6-9, 2025

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

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

R-Pola-Glo – Patients Characteristics

Baseline Parameters

Cohort (N=80)	
Median age age > 85yo	80 (66-92) 19%
Advanced Stage (III/IV)	63% (50/80)
ECOG 2	28% (22/80)
LDH, > ULN	63% (50/80)
IPI 3-5	64% (51/80)

Simplified Geriatric Assessment (sGA)

	FIT	UNFIT		FRAIL
ADL	≥5*	<5*	6*	<6*
	and	*and/or*	*and*	*and/or*
IADL	≥6*	<6*	8*	<8*
	and	*and/or*	*and*	*and/or*
CIRS-G	0 score = 3-4 and ≤8 score = 2	≥1 score = 3-4 and/or >8 score = 2	0 score = 3-4 and <5 score = 2	≥1 score = 3-4 and/or ≥5 score = 2
	and	*and*	*and*	*and*
Age	<80	<80	≥80	≥80
R-Pola-Glo (n=79)	6 (7.6)	28 (35.4)	15 (19)	30 (38)

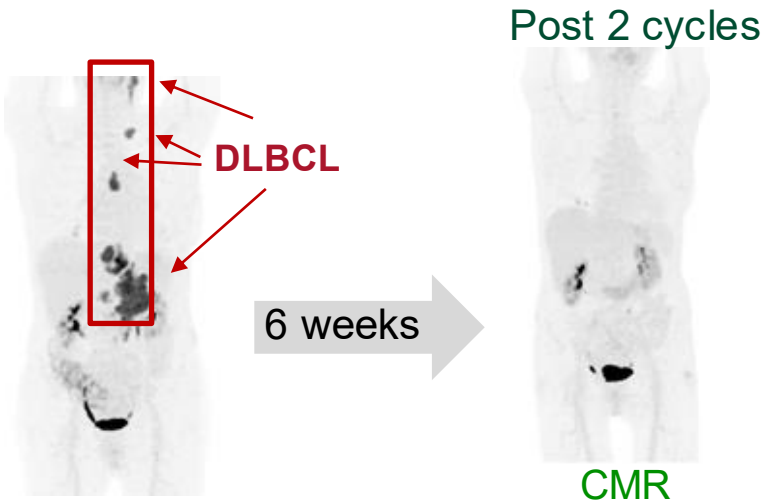
91.3% medical unfit/frail

- Representative "real world" cohort of medical unfit/frail patients with high treatment complexity.

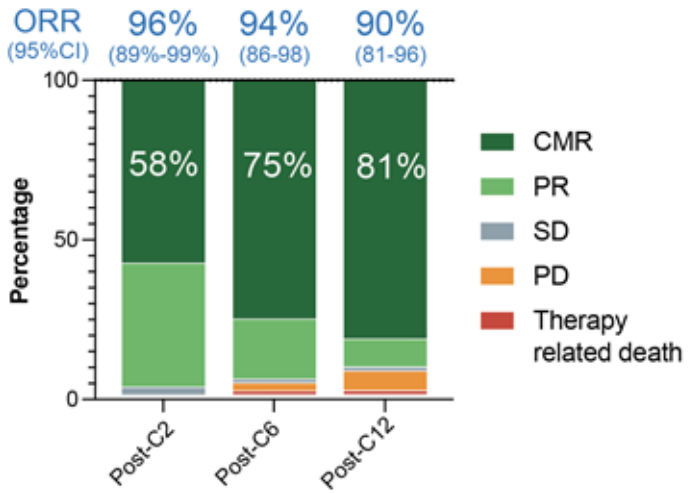
Chapuy B. et al, oral presentation ASH 2025 Blood (2025) 146 (Supplement 1): 61.

R-Pola-Glo – Response

Representative Case



Response Rate (n=80)

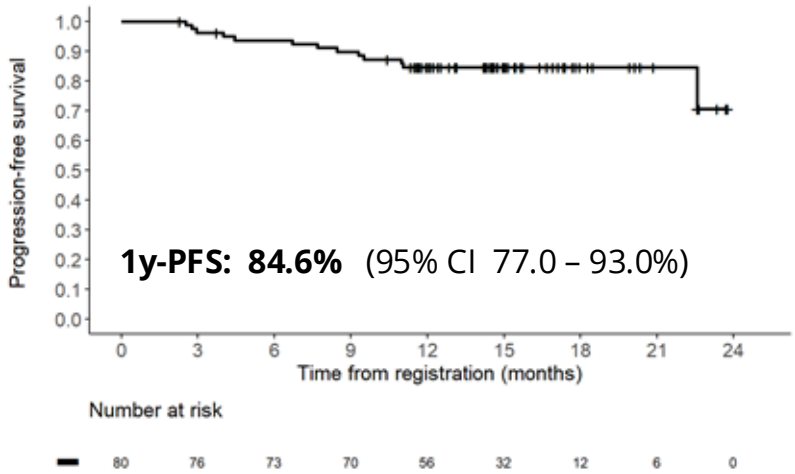


- ORR at cycles 2, 6, and EOT were 96%, 94%, and 90%; corresponding CMR rates were 58%, 75%, and 81%, respectively.
- CMR conversions were observed after C6, highlighting the role of glofitamab consolidation.

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

R-Pola-Glo – Outcome

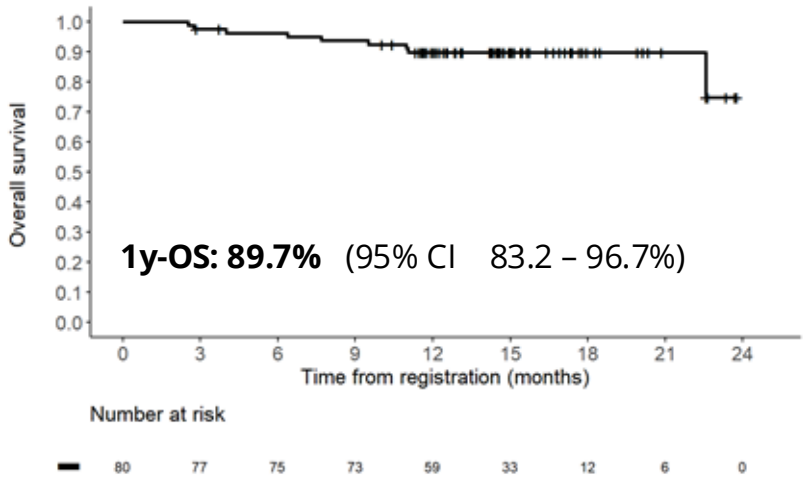
1-year Progression-free Survival (PFS)



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

Conclusions

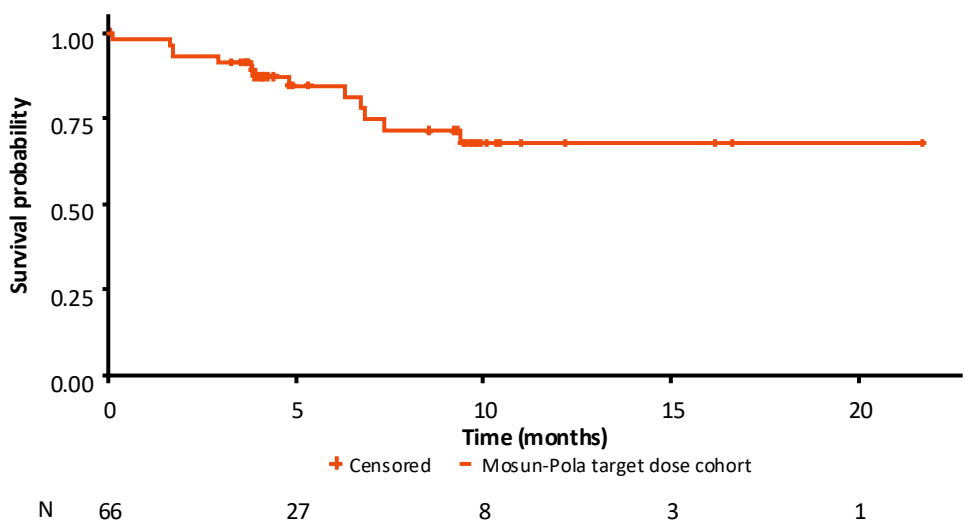
- R-Pola-Glo achieved high and durable CMR rates with a manageable safety profile.
- Responses translated into a high 1-year survival rate in elderly/frail and medically unfit patients with aggressive B-cell lymphoma.
- Our results demonstrates that an anthracycline-free regimen can induce durable remissions in a population considered to be ineligible for standard approaches.

R-Pola-Glo demonstrate higher response rates and improved survival outcomes at 1 year compared with regimes considered as SOC, supporting its further clinical evaluation as a frontline option for this vulnerable patient population.

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

Mosunetuzumab and Polatuzumab Vedotin Demonstrates Preliminary Efficacy in Elderly Unfit/Frail Patients with Previously Untreated Diffuse Large B-Cell Lymphoma

KM curve of DOCR in the Mosun-Pola target dose cohort



	Mosun-Pola target dose cohort N=101
Complete responders, n (%)	66 (65.3)
Median follow up time, months (range)	12.6 (1–25)

	Mosun-Pola target dose cohort N=66
Median DOCR, months (range)	NE
9-month DOCR event-free rate, % (95% CI)	71.4 (56.8, 85.9)
Patient disposition	
Censored/no event at CCOD	53 (80.3)
Event	13 (19.7)
Disease progression	2 (3)
Death after CR	11 (17)

Mosun-Pola induces durable CRs in elderly unfit or frail pts with previously untreated DLBCL

Data cut-off: August 5, 2023. DOCR, duration of complete response; KM, Kaplan-Meier.

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

Conclusions

- Fixed-duration epcoritamab monotherapy induced early, deep, and durable responses in elderly patients with newly diagnosed LBCL and comorbidities
- Safety outcomes, including the occurrence of CRS and ICANS, were consistent with expected rates in this elderly population
- Epcoritamab offers a compelling, single-agent, chemotherapy-free alternative for patients ineligible for anthracycline-based regimens, demonstrating strong efficacy with a favorable benefit-risk profile

Fixed-duration epcoritamab monotherapy in elderly patients

ORR: 73%; CR: 62%
1-year PFS rate: 54%
1-year OS rate: 65%

These findings, together with those from other trials (EPCORE NHL-2; NCT04663347) suggest that epcoritamab, as monotherapy or in combination with SOC, can be a favorable option for elderly patients with newly diagnosed DLBCL, a population with significant unmet need and poor outcomes

Zanubrutinib with Rituximab and Lenalidomide in *de novo* Diffuse Large B Cell Lymphoma

Context of Research

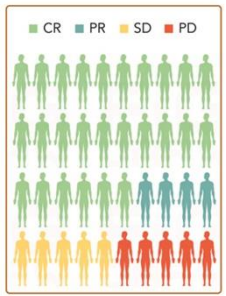
Older patients with diffuse large B cell lymphoma (DLBCL) may have more unfavorable tumor microenvironmental features, which could lead to worse clinical outcomes

Aim of This Study

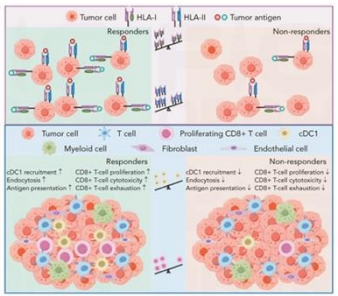
To assess the efficacy and safety of zanubrutinib in combination with rituximab and lenalidomide (ZR2) in patients with *de novo* DLBCL aged ≥75 years (NCT04460248)

Findings

The CR rate with ZR2 was 65%



Microenvironmental features related to ZR2 efficacy



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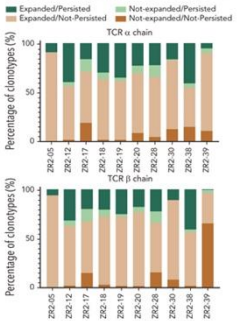
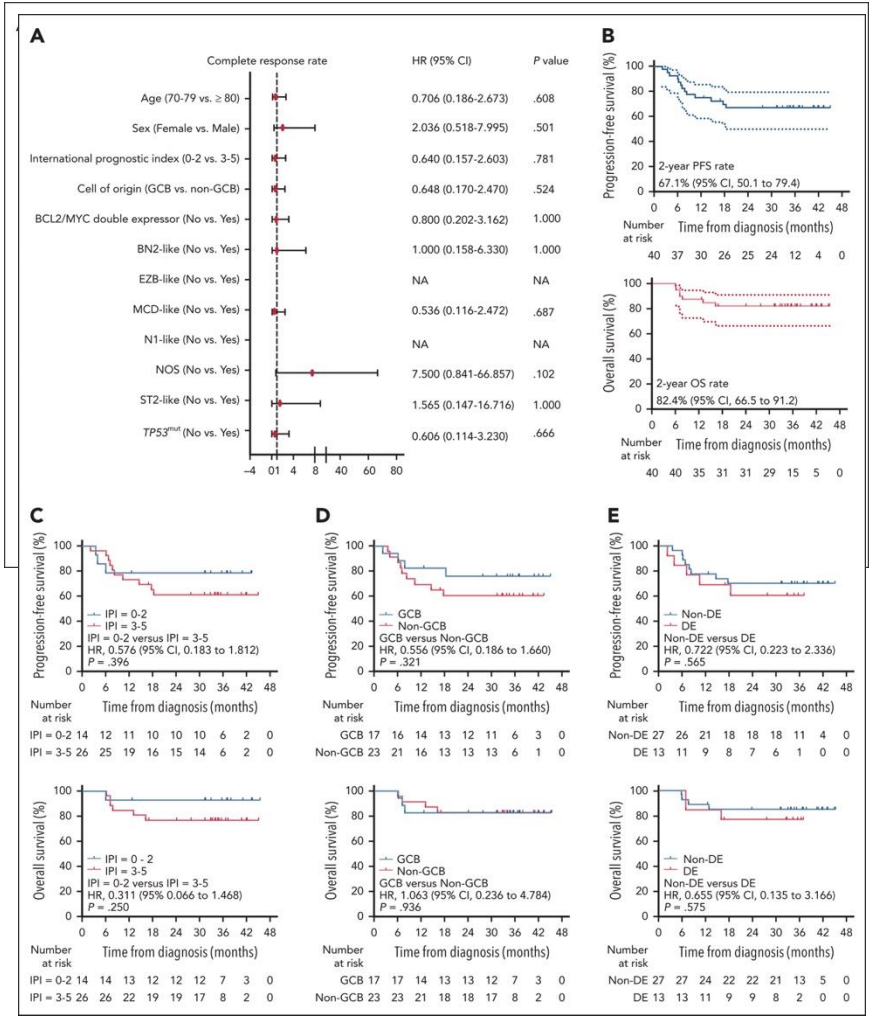
TCR sequencing of PBMCs from patients with durable remission



Conclusions: ZR2 yielded a CRR of 65.0% in older patients with *de novo* DLBCL, and its efficacy was associated with HLA up-regulation of lymphoma cells and cDC1 activation. TCR sequencing of the peripheral blood mononuclear cells from patients with durable remission detected the expanded T cell clones at 3 years post-treatment.

*Xu et al. DOI: 10.1182/**blood**.2025028649*

blood Visual Abstract



How I treat older patients with relapsed/refractory diffuse large B-cell lymphoma

Danielle S. Wallace, Kah Poh Loh, and Carla Casulo

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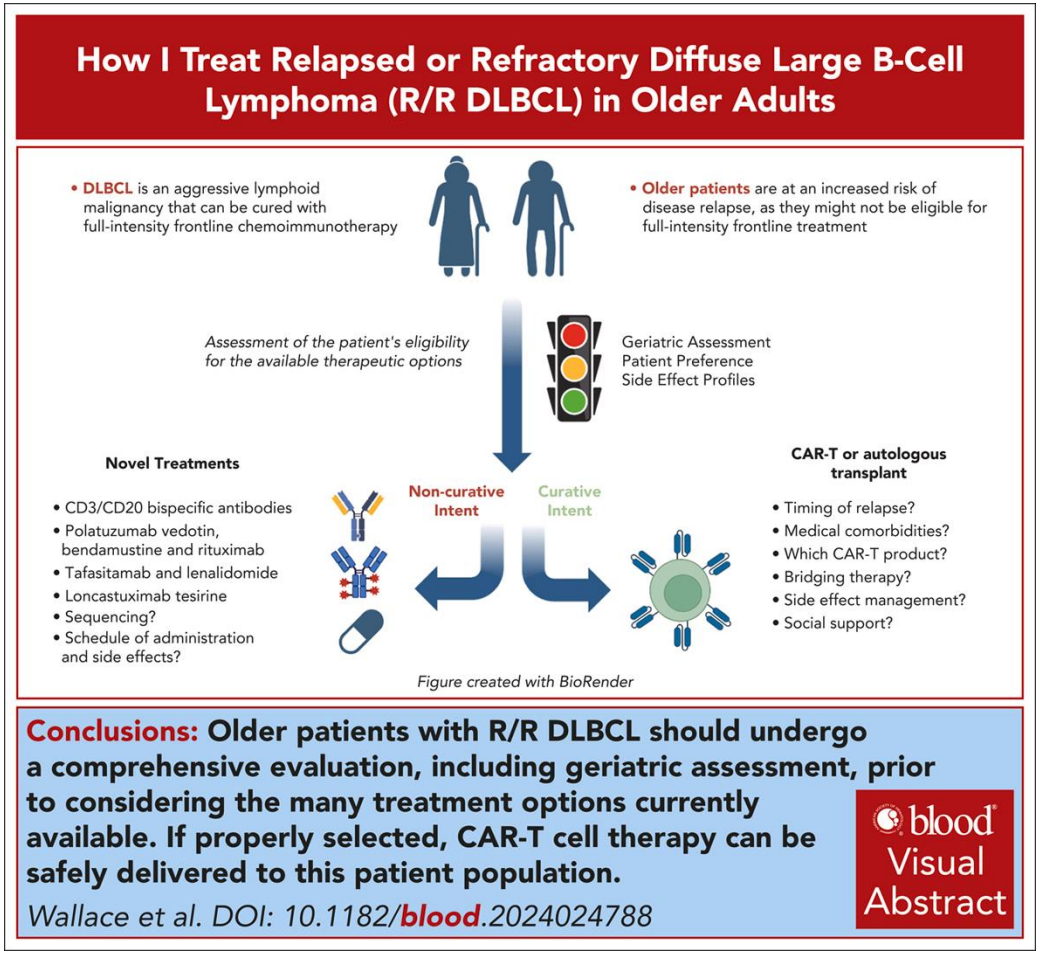
How do we sequence these agents in older patients?



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Whenever possible, we prioritize clinical trials.

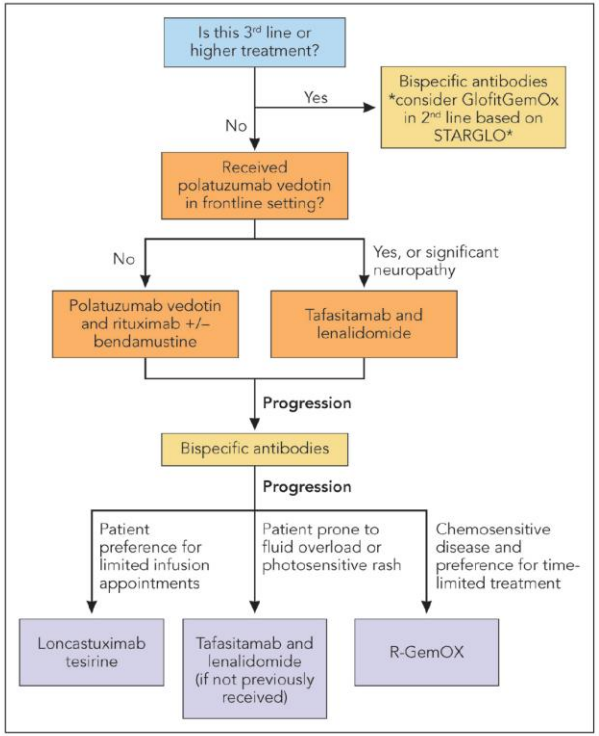

Figure 2. Our approach to the older patient with R/R DLBCL after CAR T-cell therapy or who is ineligible for or uninterested in CAR T-cell therapy in the absence of a clinical trial. Glofit, glofitamab. Professional illustration by Patrick Lane, ScEYEnce Studios.

Table 6.

Novel treatments for R/R DLBCL

BR, bendamustine-rituximab; CRR, complete response rate; DOR, duration of respons

Novel agent	Median age	Median lines of previous therapies	Primary refractory patients (%)	ORR/CRR (%)	DOR, median (mo)	PFS, median (mo)	OS, median (mo)	Notable toxicities
Glofitamab[73]	66	3	58	52/40	18.4	4.9	8.9	CRS, neutropenia
Epcoritamab[74]	64	3	61	63/39	12.0	4.4	Not reached	CRS, neutropenia
Polatuzumab vedotin + BR[75]	70	2	64	57/53	9.5	6.6	12.5	Peripheral neuropathy, neutropenia
Tafasitamab and lenalidomide[76]	72	2	19	58/41	Not reached	24	Not reached	Diarrhea, rash, neutropenia
Lonca-t[77]	66	3	20	48/25	13.4	4.9	9.5	Neutropenia, peripheral edema, rash
Selinexor[72]	67	2	Not provided	28/12	9.3	2.6	9.1	Nausea, fatigue, anorexia

Conclusioni

- ✓ Nel pz anziano non-FIT la scelta del miglior programma terapeutico deve partire da una valutazione accurata dello stato di fitness attraverso la valutazione geriatrica multidimensionale (ADL, IADL, CIRS)
- ✓ Nei pz UNFIT, l'obiettivo del trattamento puo' essere la cura, utilizzando regimi di CT a dosi ridotte o in casi selezionati utilizzando antraciclina liposomiale, uso pre-fase e della profilassi con G-CSF
- ✓ Nei pz FRAIL l'obiettivo del trattamento era per lo piu' la palliazione dei sintomi e il mantenimento di una discreta qualità di vita (QoL)
- ✓ Ipotizzabile un cambio di paradigma nella prima linea utilizzando i nuovi anticorpi bispecifici e/o nuove molecole riducendo/omettendo la CT
- ✓ La Qualità della vita (QoL) valutata al basale e in corso di terapia in associazione ad un percorso geriatrico potrebbero svolgere un ruolo importante nella gestione del paziente UNFIT/FRAIL con DLBCL per un trattamento individualizzato
- ✓ La terapia di seconda linea nel pz recidivato/refrattario non-FIT, non candidabile CAR-T , è ancora un unmet clinical need

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