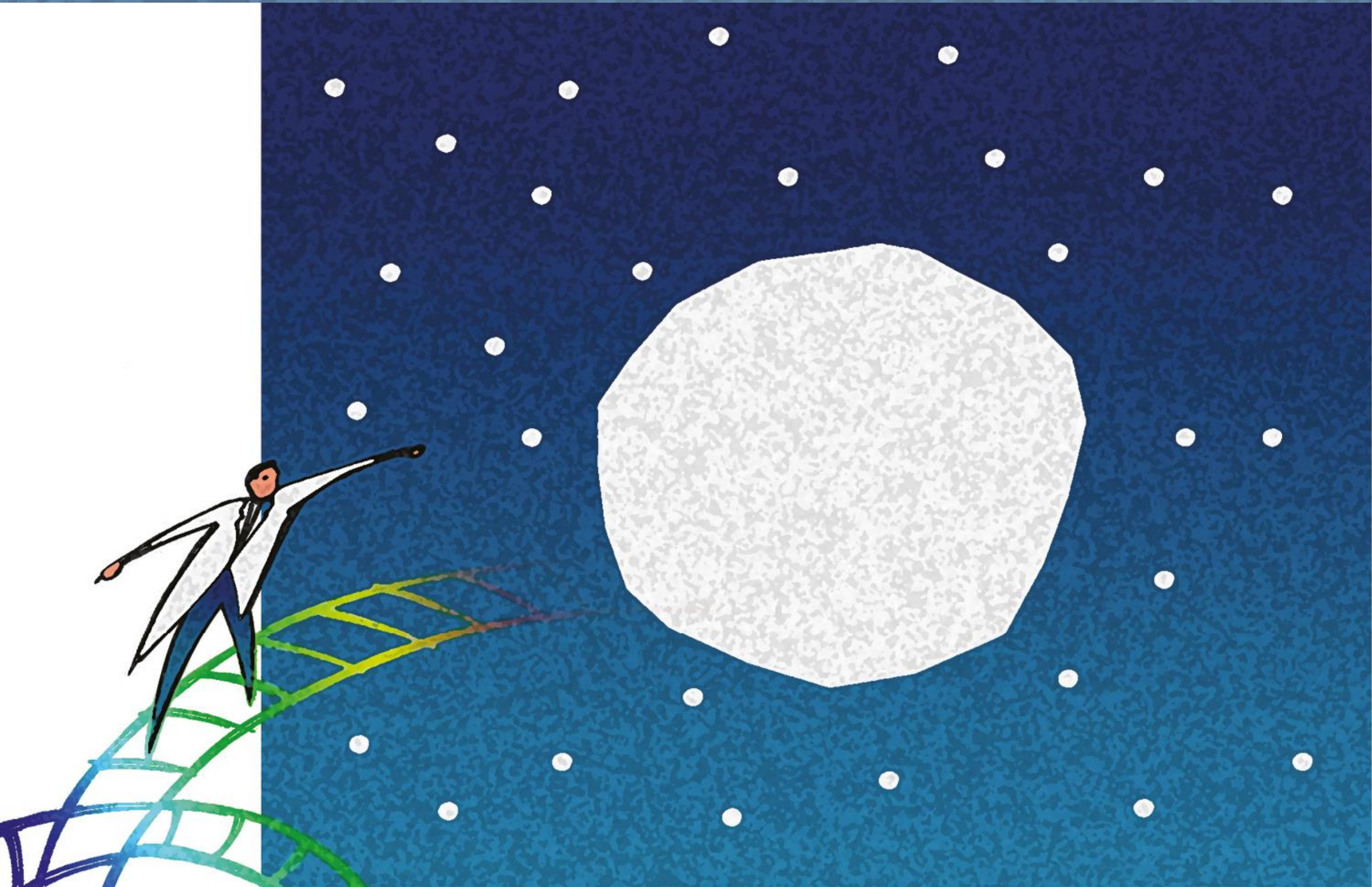




The young side of **LYMPHOMA**

gli under 40 a confronto

Reggio Emilia, Hotel Mercure Astoria
2-3 ottobre 2026

Nuove prospettive di trattamento del DLBCL dell'anziano

Dott. Bavieri Alberto

M.D Hematologist, AUSL-IRCCS Reggio Emilia

PhD student in Clinical and Experimental Medicine, UNIMORE



Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AstraZeneca					X		



AI-generated image

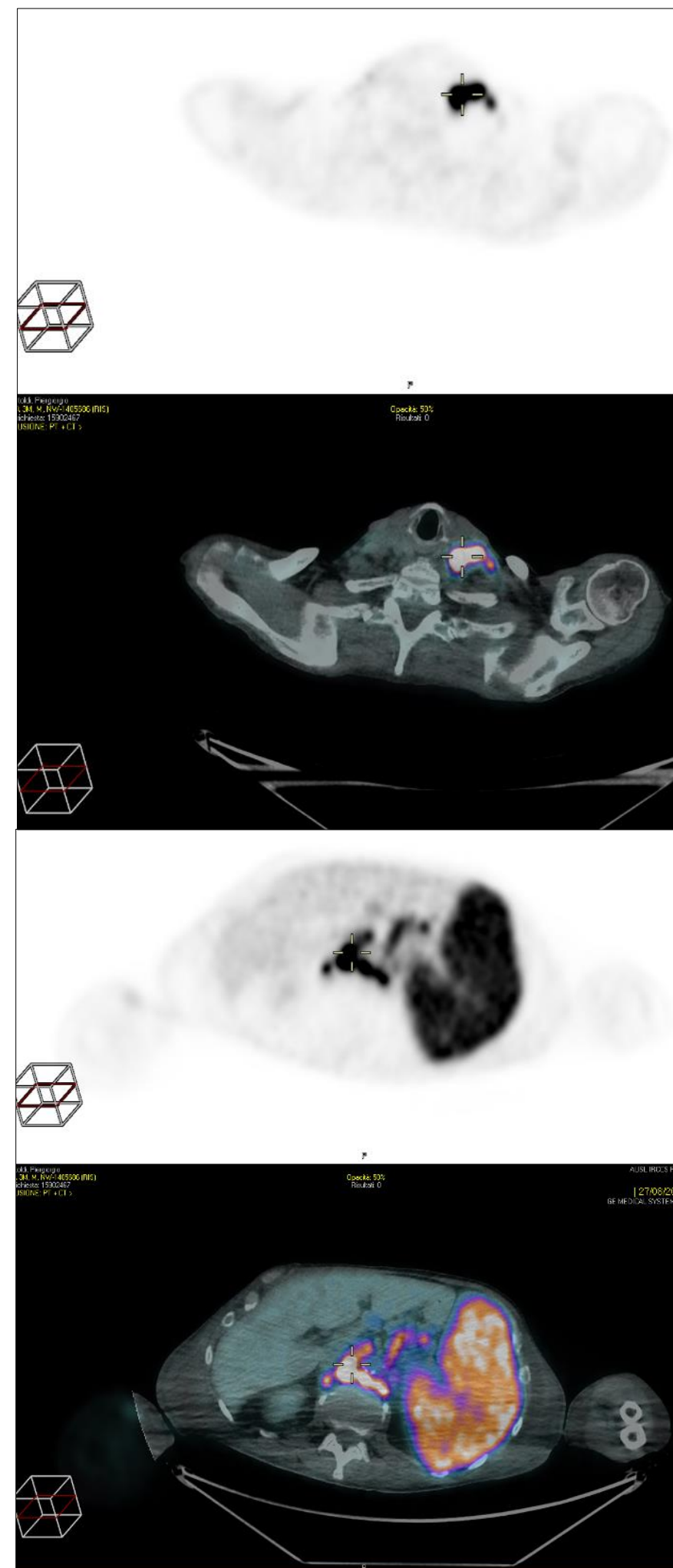
☐ F. C.

☐ Female ♀ born in 1942 in Reggio Emilia

☐ Former Italian teacher, no known allergies, never smoker

☐ Past medical history:

- Anterior rectal resection for adenocarcinoma, complicated by peritonitis (1993). No adjuvant chemotherapy or radiotherapy.
- Fibromyalgia
- Arterial hypertension, on ramipril and bisoprolol
- Ascending aortic and aortic arch aneurysm
- Bilateral cataract surgery



Diagnosis

DLBCL, non DE non DH/TH



Diagnostic procedure

Biopsy of an abdominal mass
(SUV 16)



Stage

Stage IV
(lymph nodes, spleen, bone)



Age

84 years



IPI

4
(age, stage, LDH, sites)



Cardiac history

No cardiac comorbidities
LVEF 60%

Which first-line treatment would you choose?

A

R-miniCHOP or R-miniCOMP

B

Pola-R-miniCHP
(polatuzumab + R-miniCHP)

C

Clinical trial

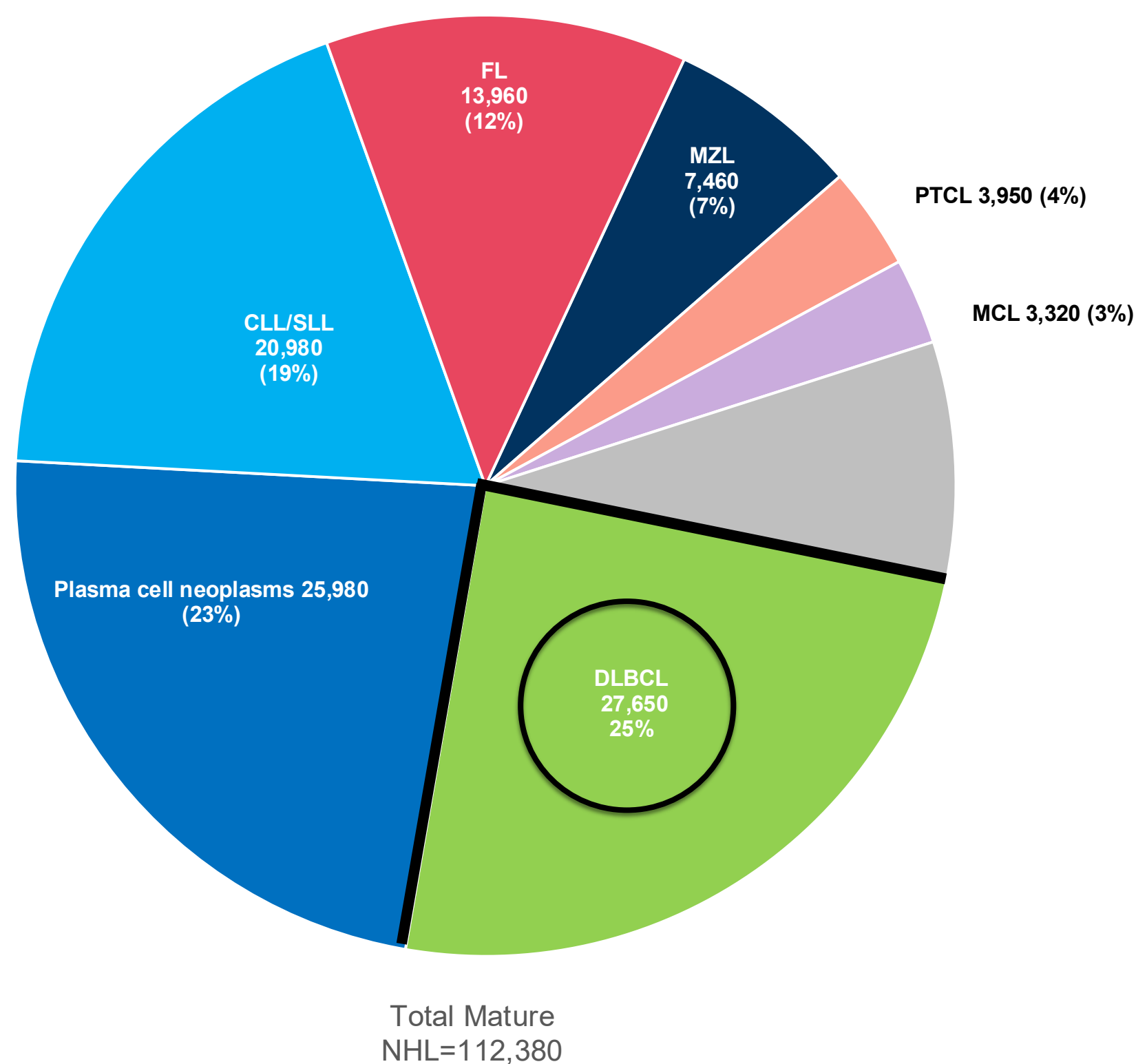
D

Palliation

E

Something is missing...

DLBCL is the most common type of non-Hodgkin lymphoma (NHL)



- ☐ Median age 70 years
- ☐ More than 30% of patients being over 75 years old

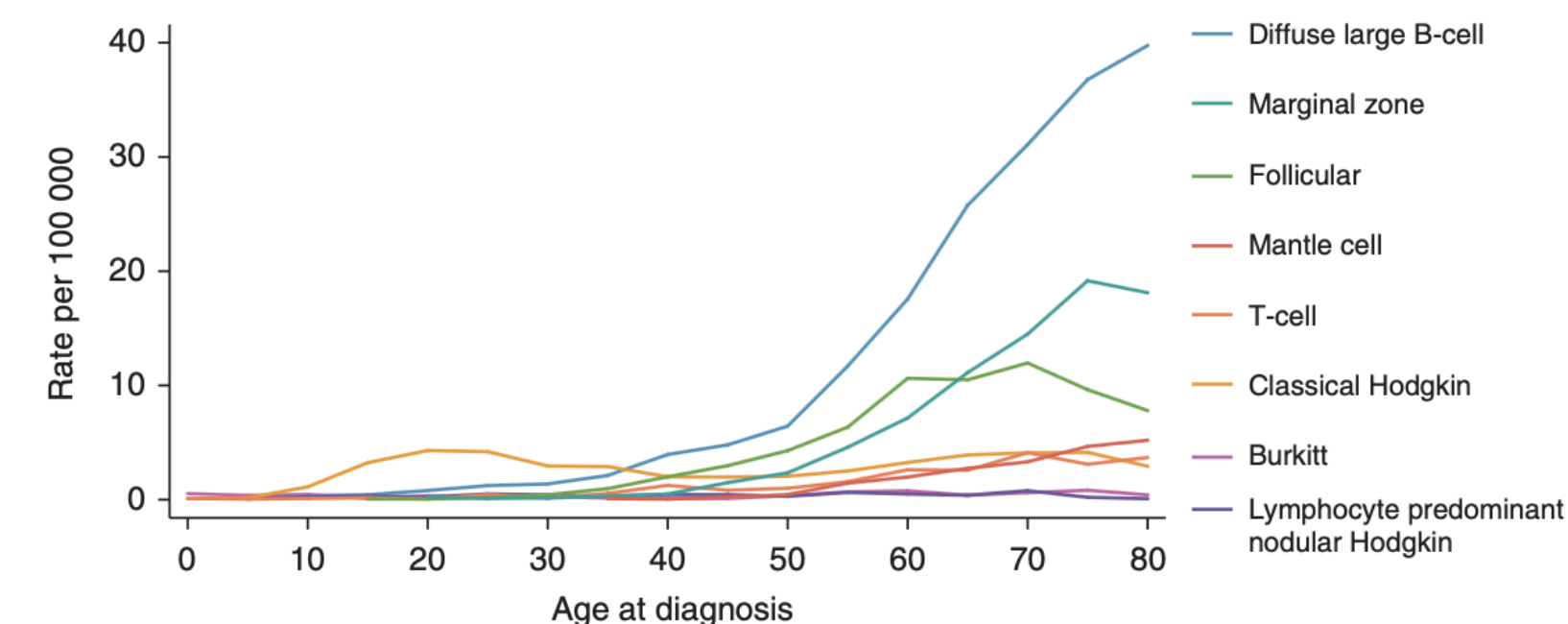
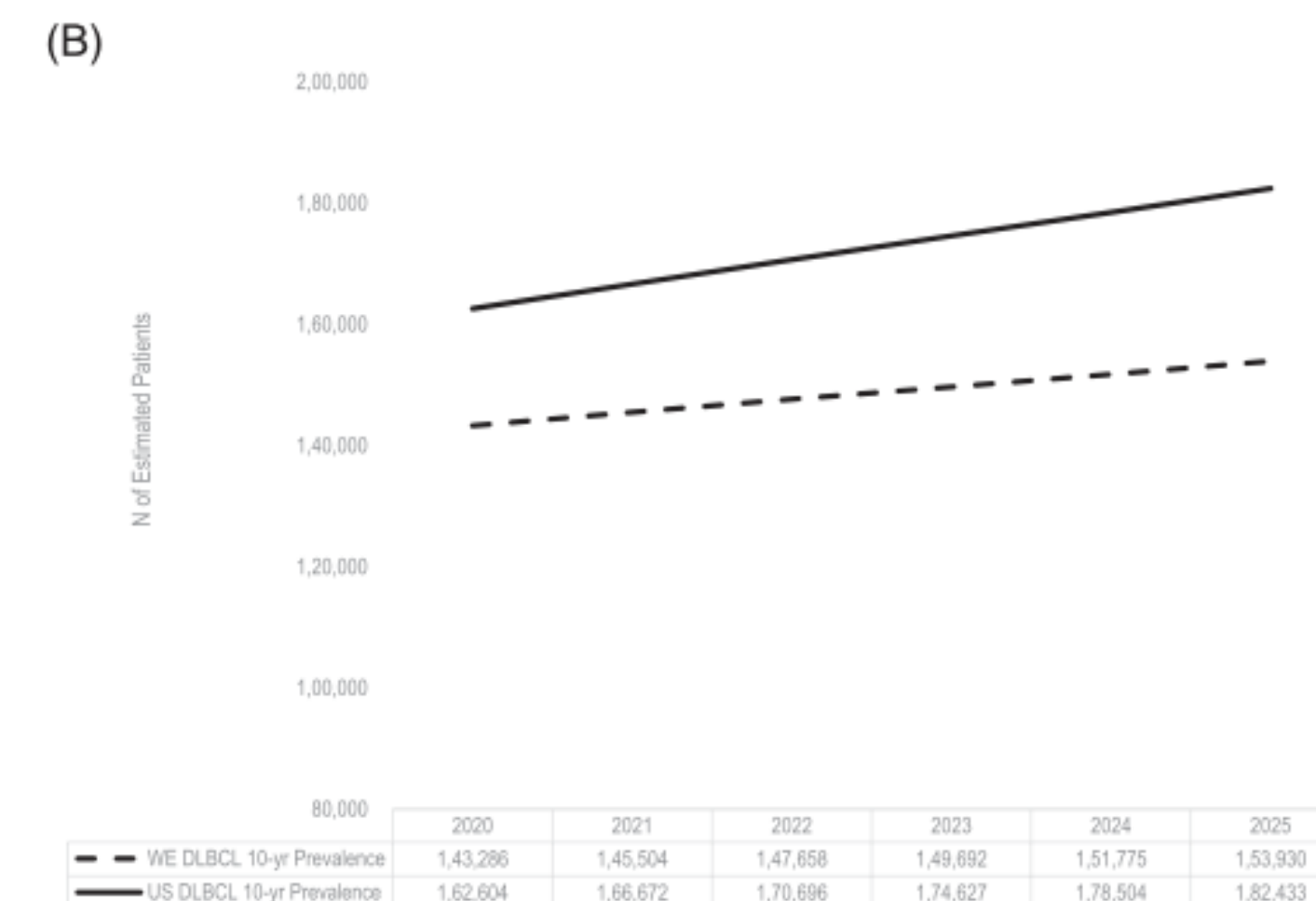
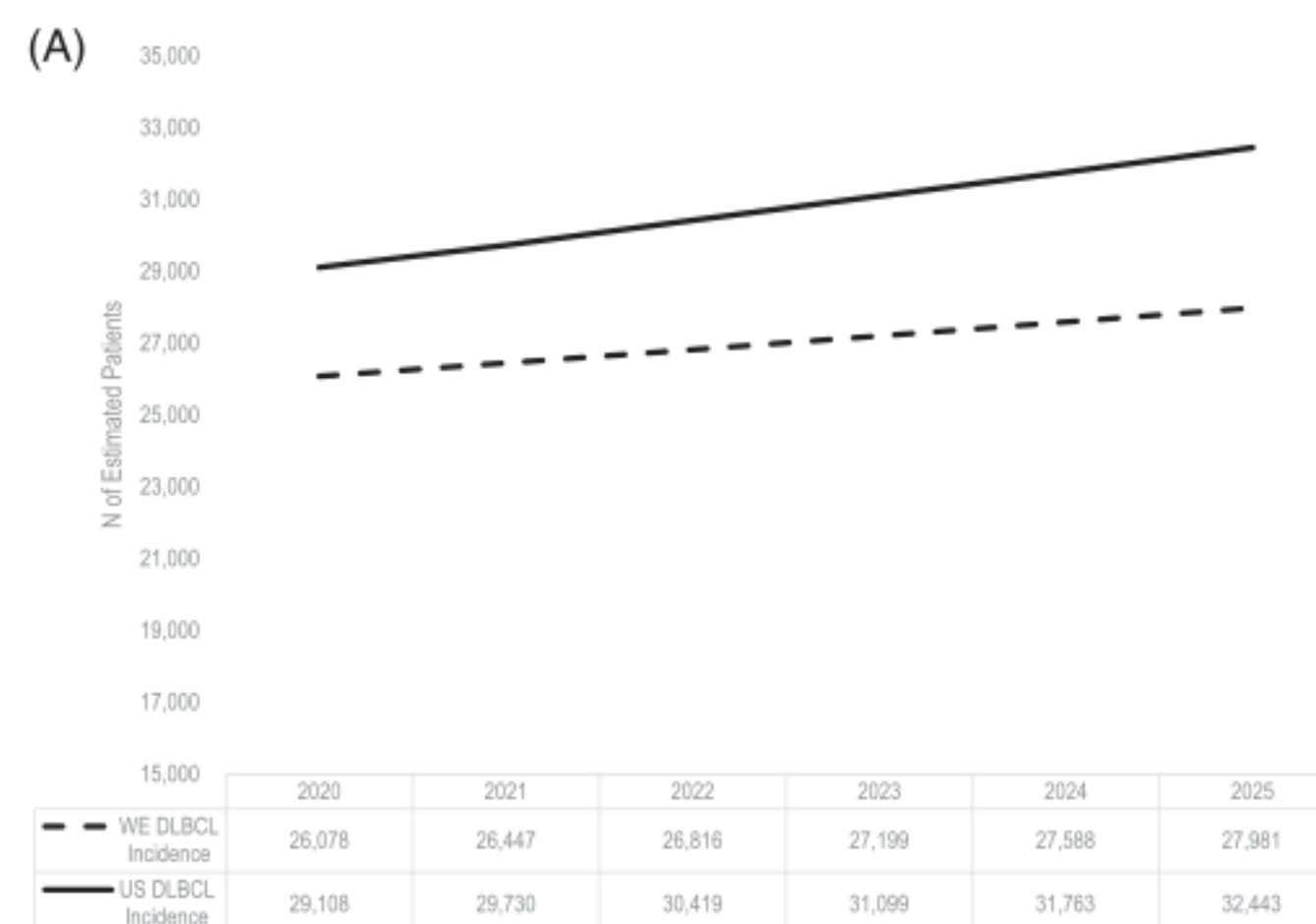


Figure 1. Age-specific rates per 100 000 by subtype: Haematological Malignancy Research Network (HMRN) 2004–2012.

As the population ages, DLBCL is expected to become more prevalent.



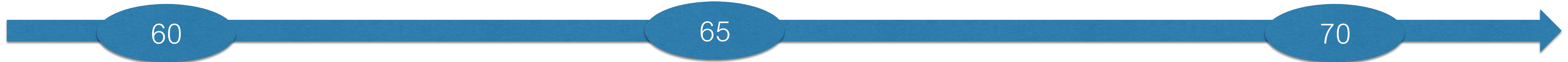
DLBCL, diffuse large B-cell lymphoma; CLL, chronic lymphocytic leukemia; FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma; PTCL, peripheral T-cell lymphoma; SLL, small lymphocytic lymphoma. Adapted from: 1. Link BK, et al. *Br J Haematol.* 2019;184(4):660-663. 2. Maurer MJ, et al. *Am J Hematol.* 2016;91(11):1096-1101. 3. Link BK, et al. *J Clin Oncol.* 2013;31(26):3272-3278. 4. Teras LR, et al. *CA Cancer J Clin.* 2016;66(6):443-459. 5. Huet S, et al. *Nat Rev Cancer.* 2018;18(4):224-239.

Kanas G, Ge W, Quek RGW, Keeven K, Nersesyan K, Jon E Arnason. Epidemiology of diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) in the United States and Western Europe: population-level projections for 2020-2025. *Leuk Lymphoma.* 2022 Jan;63(1):54-63. doi: 10.1080/10428194.2021.1975188. Epub 2021 Sep 11. PMID: 34510995.

Smith, A., Crouch, S., Lax, S. et al. Lymphoma incidence, survival and prevalence 2004–2014: sub-type analyses from the UK's Haematological Malignancy Research Network. *Br J Cancer* **112**, 1575–1584 (2015). <https://doi.org/10.1038/bjc.2015.94>

How do we define older (DLBCL) patients?

- ☐ No clear medical or biological evidence to support the chronological definition of old age



Is the disease different from DLBCL in young patients?

- ☐ No major difference in histopathological features BUT different stromal gene signature (>ABC) and higher number of (EBV)-positive DLBCL

Diagnostic work-up should be as complete as for any young patient

Received: 13 March 2025 | Accepted: 6 August 2025
DOI: 10.1002/hem3.70207

HemaSphere  eha

GUIDELINES - EXPERT OPINION

Large B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up

Catherine Thieblemont^{1,2} | Maria Gomes Da Silva³ | Sirpa Leppä⁴  | Georg Lenz⁵ | Anne-Sékolène Cottereau⁶ | Christopher Fox⁷ | Armando Lopez-Guillermo⁸ | Timothy Illidge⁹ | Wojciech Jurczak¹⁰ | Hans Eich¹¹ | Igor Aurer¹² | Marek Trneny¹³ | Andreas Rosenwald¹⁴ | Andrew Davies¹⁵ | Ben (Gerben) Zwezerijnen¹⁶ | Natacha Bolanos¹⁷ | Maja Marković¹⁷ | Jean-Philippe Jais^{1,18} | Florence Broussais¹⁹  | Martin Dreyling²⁰ | Umberto Vitolo²¹ | Hervé Tilly²² | Marie José Kersten²³ 

ESMO GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

ANNALS OF ONCOLOGY DRIVING INNOVATION
IN ONCOLOGY

SPECIAL ARTICLE

Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up[☆]

T. A. Eyre¹, K. Cwynarski², F. d'Amore^{3,4}, L. de Leval⁵, M. Dreyling⁶, D. A. Eichenauer^{7,8}, A. J. M. Ferreri^{9,10}, E. Giné¹¹, M. J. Kersten¹², M. Ladetto^{13,14}, L. Specht¹⁵, C. Thieblemont¹⁶, J. Walewski^{17,18}, E. Zucca^{19,20,21} & M. Jerkeman^{22,23}, on behalf of the ESMO Guidelines Committee*

IPI	
<i>Factor</i>	
Age	≤60 or >60
Serum LDH	≤1× normal or >1
Performance status	0 or 1 versus 2–4
Stage	I or II versus III or IV
Extranodal involvement	≤1 site versus ≥2 sites
<i>IPI categories</i>	<i>All patients</i>
Low	0 or 1
Low intermediate	2
High intermediate	3
High	4 or 5
<i>Age-adjusted IPI categories</i>	<i>≤60 or >60</i>
Low	0
Low intermediate	1
High intermediate	2
High	3

CNS-IPI	
<i>Factor</i>	
Age	≤60 or >60
Serum LDH	≤1× normal or >1
Performance status	0 or 1 versus 2–4
Stage	I or II versus III or IV
Extranodal involvement	≤1 site versus ≥2 sites
Renal and/or adrenal involvement	Yes or no
<i>IPI categories</i>	<i>All patients</i>
Low	0 or 1
intermediate	2 or 3
High	4 or 5 or 6

- Assessment of the frail and elderly using the Elderly Prognostic Index can be considered [V, B].



Criteria for sGA assessment

	FIT	UNFIT		FRAIL
ADL	≥5*	< 5*	6*	<6*
	<i>and</i>	<i>and/or</i>	<i>and</i>	<i>and/or</i>
IADL	≥6*	<6*	8*	<8*
	<i>and</i>	<i>and/or</i>	<i>and</i>	<i>and/or</i>
CIRS-G	0 score =3-4 <i>and</i> ≤8 score =2	≥1 score =3-4 <i>and/or</i> > 8 score =2	0 score =3-4 <i>and</i> <5 score =2	≥1 score =3-4 <i>and/or</i> ≥5 score =2
	<i>and</i>	<i>and</i>	<i>and</i>	<i>and</i>
Age	<80	<80	≥80	≥80

* Residual functions

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

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



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

EPI model: Risk Groups Score

	N (%)	3-yr OS (95%CI)	HR (95%CI)	P value
<i>Risk groups (Score)</i>	1065	66 (62 to 69)	-	-
Low (0-1)	250 (23)	87 (81 to 91)	1.00	-
Intermediate (2-5)	510 (48)	69 (63 to 73)	2.57 (1.72 to 3.84)	<0.001
High (6-8)	305 (29)	42 (36 to 49)	6.21 (4.17 to 9.25)	<0.001
High vs Intermediate	-		2.41 (1.91 to 3.05)	<0.001

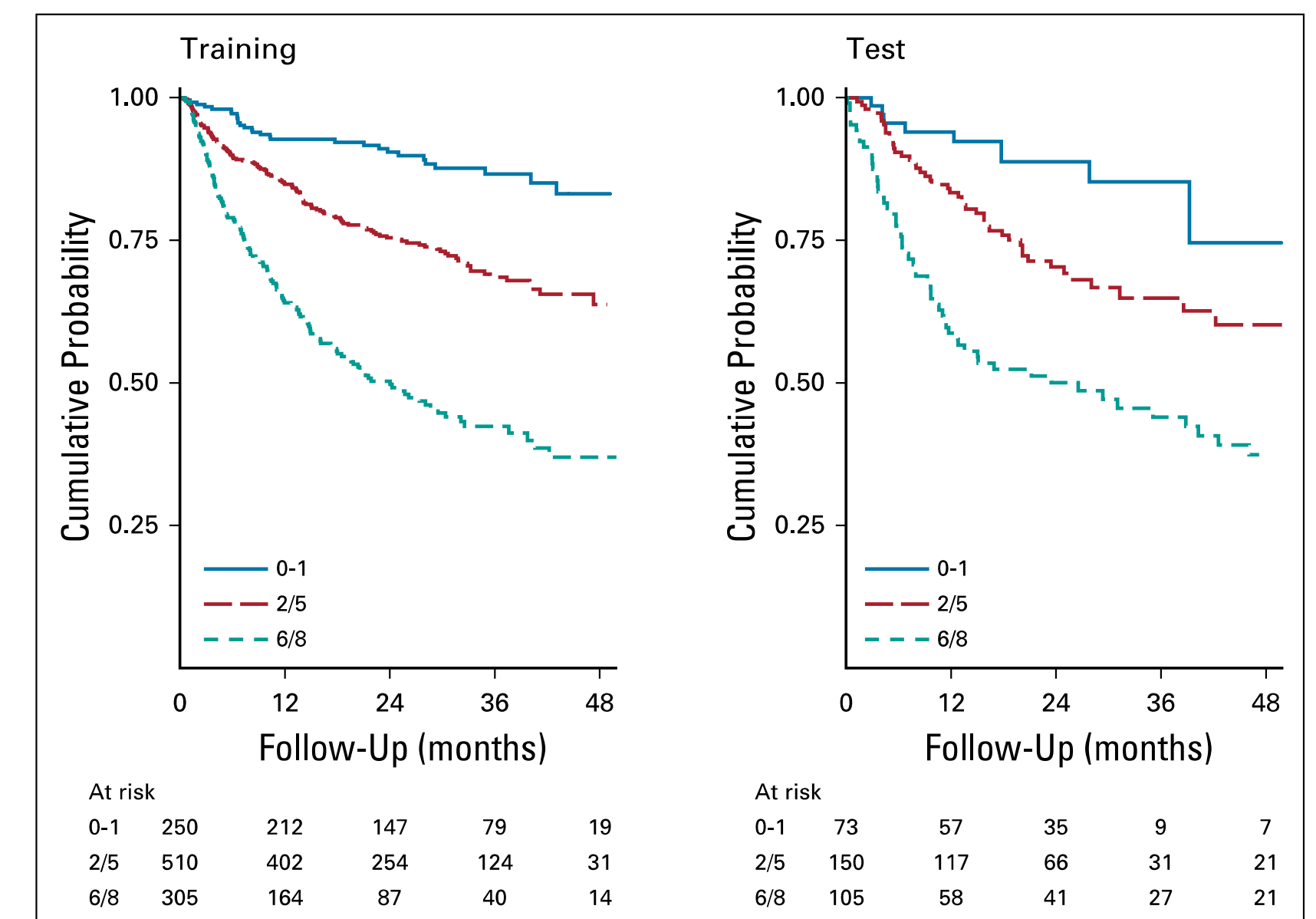
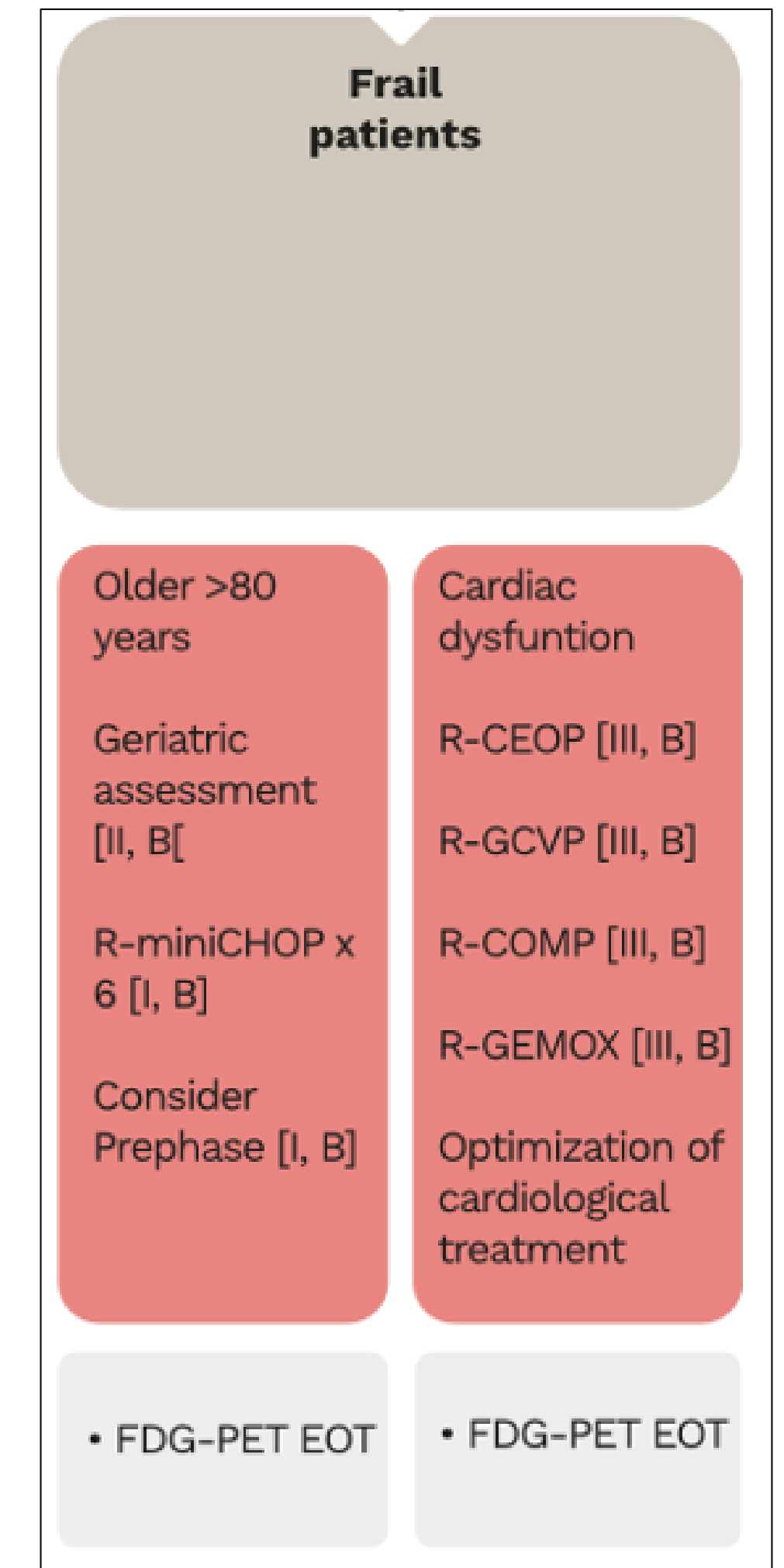
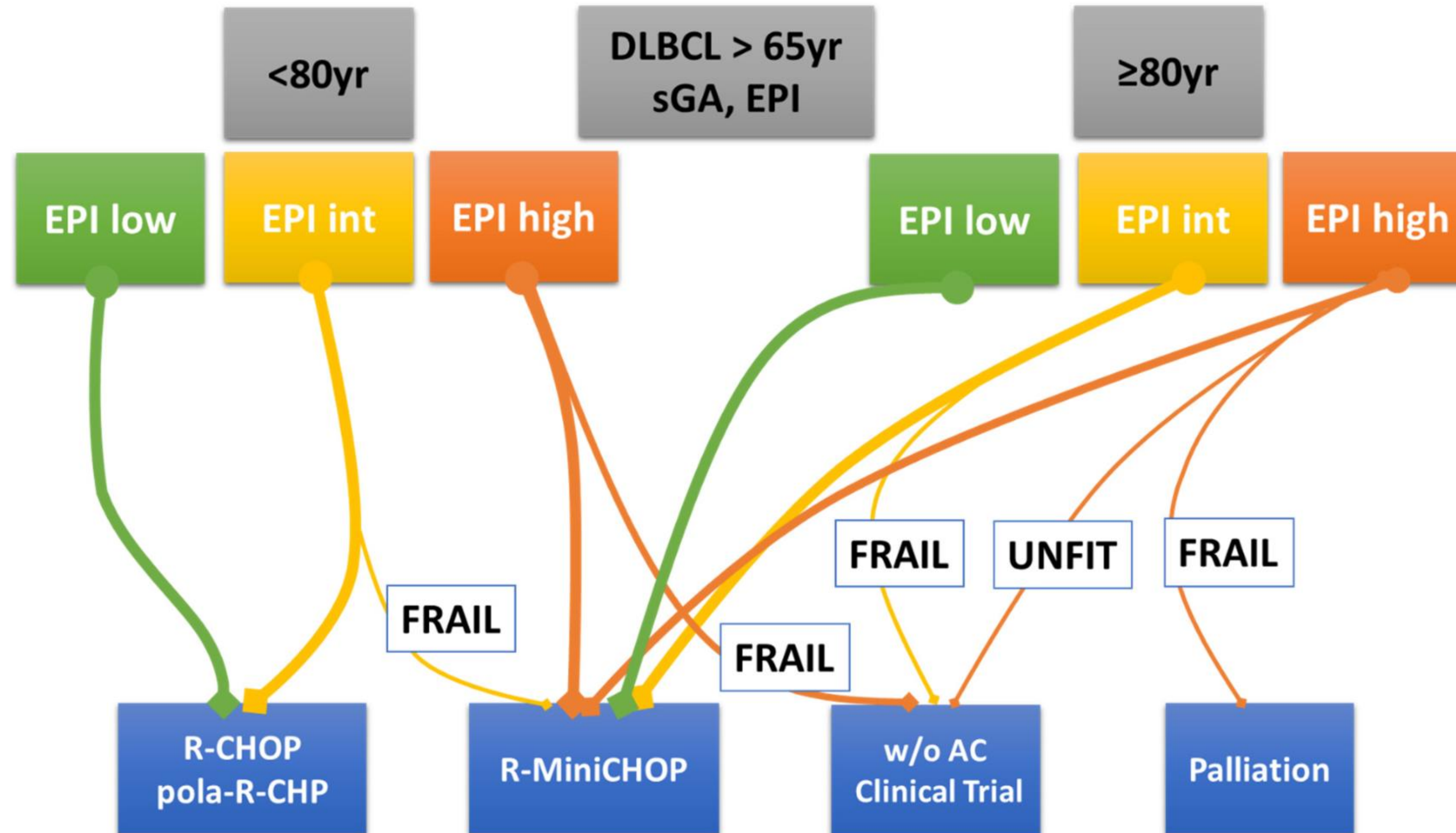
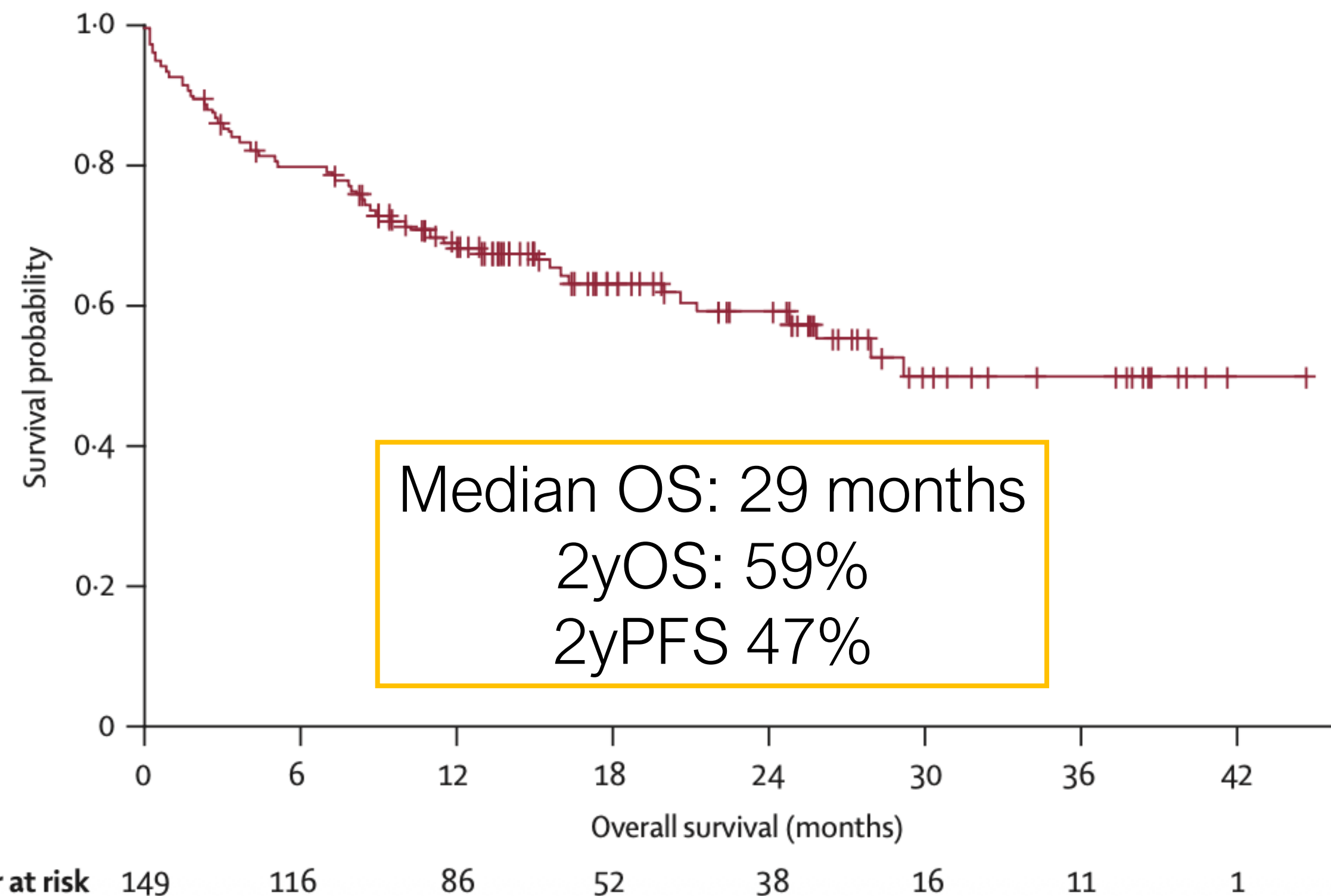


FIG 2. Overall survival stratified by the EPI in the training (A: 1,065 patients) and validation (B: 328 patients) samples. EPI, Elderly Prognostic Index.

First line treatment



How can we improve current outcomes?



Pre-phase treatment: Prednisone for 5–7 days $\pm$ vincristine 1 mg



Primary G-CSF prophylaxis



Consider liposomal doxorubicin in patients with cardiac comorbidities/ increased cardiotoxicity risk

Peyrade F, Jardin F, Thieblemont C, et al. 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. Lancet Oncol. 2011 May;12(5):460-8. doi: 10.1016/S1470-2045(11)70069-9. Epub 2011 Apr 7.

How can we improve first-line treatment in older DLBCL patients?

SWOG1918

NCT04799275

Azacitidine + mini-R-CHOP
vs mini-RCHOP
Stratification by EPI

POLAR BEAR

NCT04332822

Mini-R-CHOP vs
pola-R-mini-CHP × 6
80+ or 75 with frailty by CGA

ARCHED

NCT05820841

Acalabrutinib + R-mini-CHOP
vs R-mini-CHOP
Stratification by age, ADL score, IPI
Elderly >80 years or 61–80 unfit

NCT04663347

Epcoritamab-R-mini-RCHOP × 6
+ 2 additional cycles
in elderly ineligible for R-CHOP

NCT05179733

ZR2 vs R-mini-CHOP

Elderly >70 years, unfit/frail

NCT05798156

**R-pola-glofit × 6 cycles,
then 6 cycles consolidation**

Ineligible for R-CHOP

NCT05207670

**Subcutaneous fixed duration
mosunetuzumab (up to 17 cycles)**

≥80 years or 65–79
and ineligible for R-CHOP

NCT05660967

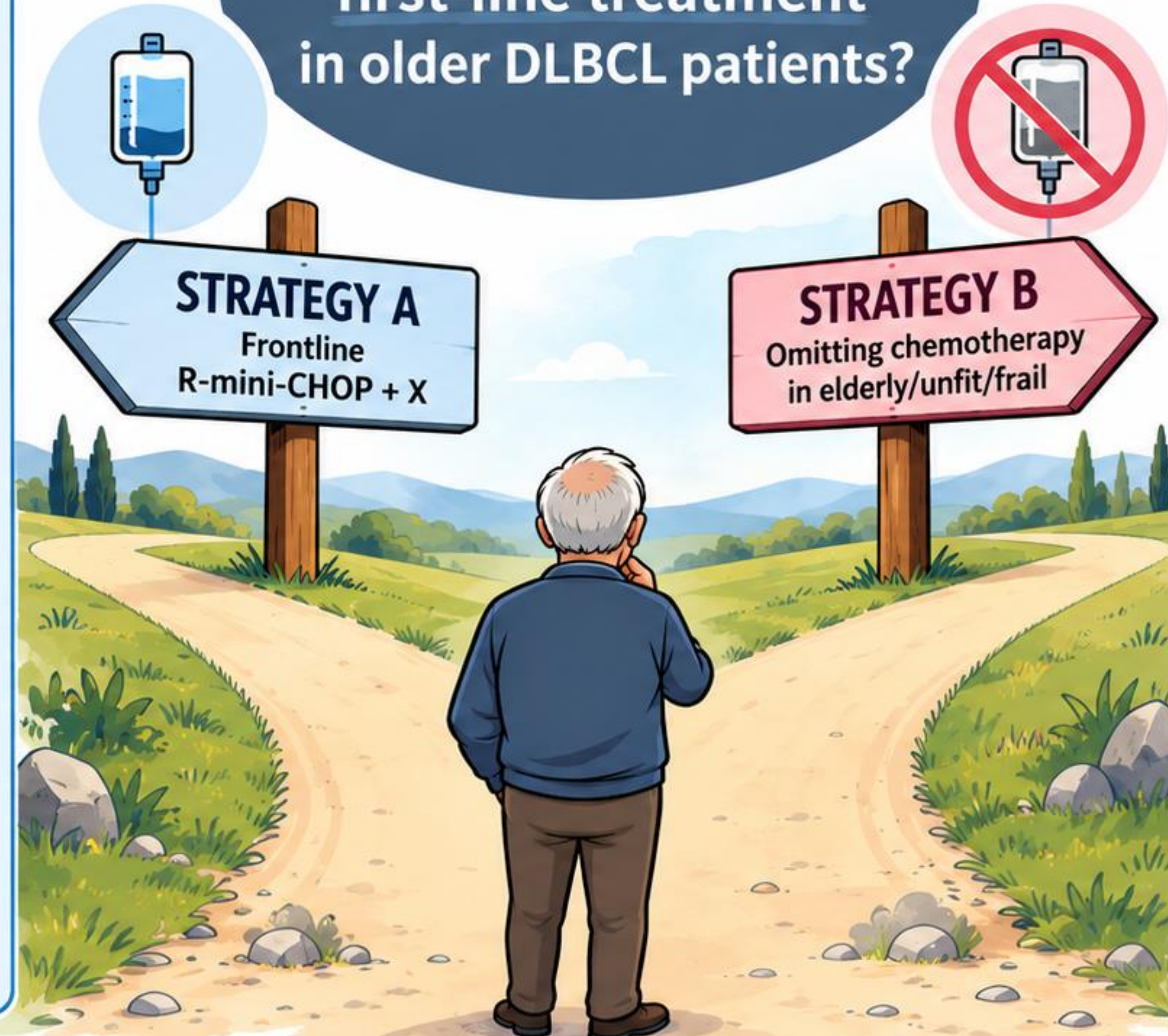
**Subcutaneous fixed duration
epcoritamab (up to 12 cycles)**

EPCOR DLBCL-3
≥80 years or ≥75 with comorbidities

NCT05952024

**Rituximab for 8 cycles
and acalabrutinib for 28 cycles**

≥80 years or 61–79
chemoimmunotherapy ineligible

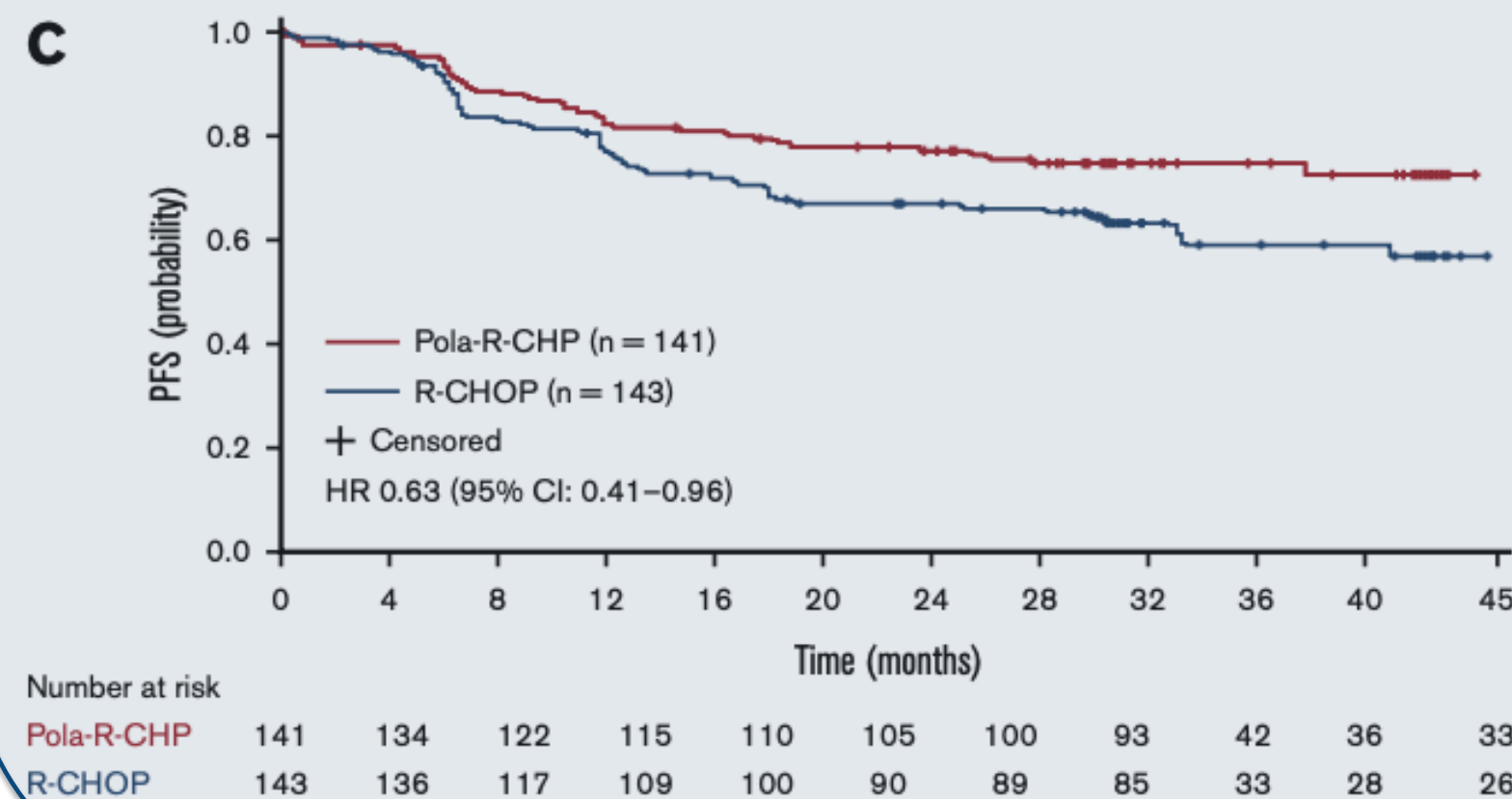


Pola-R-CHP versus R-CHOP as a Treatment for Elderly Patients with Diffuse Large B-cell Lymphoma (DLBCL): A Subgroup Analysis of the Phase 3 POLARIX Study

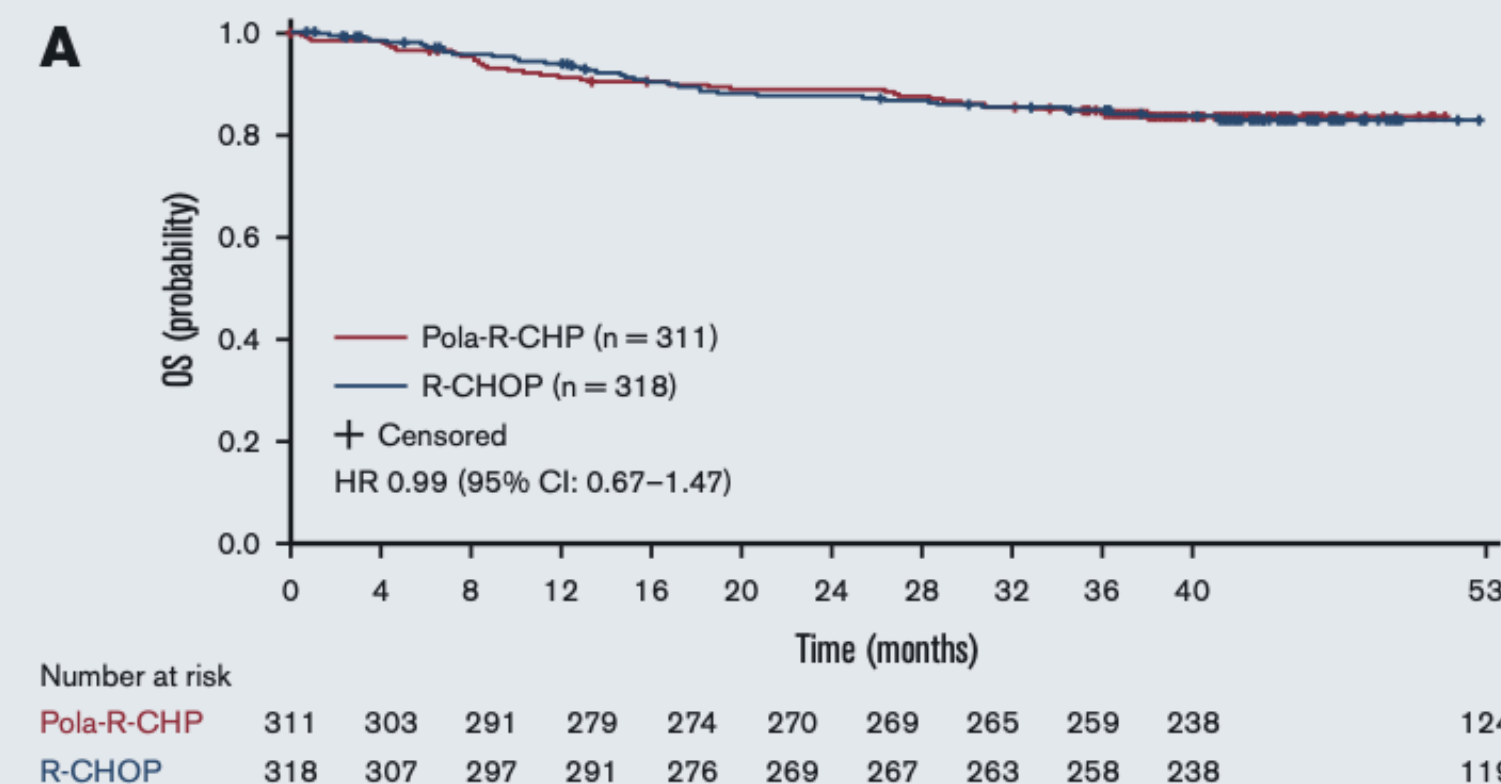
- This post hoc analysis evaluated **efficacy and safety** in **elderly patients** aged ≥ 60 , ≥ 65 , ≥ 70 , ≥ 75 years enrolled in the POLARIX study
- As of June 15, 2022, **629 patients** were included: **Pola-R-CHP**, n=311; **R-CHOP**, n=318

- Clinically meaningful improvements in PFS were observed with **Pola-R-CHP** versus **R-CHOP** across all age groups

- Among **patients ≥ 70** , the risk of disease progression, relapse or death **was reduced by 37%** with **Pola-R-CHP** versus **R-CHOP**

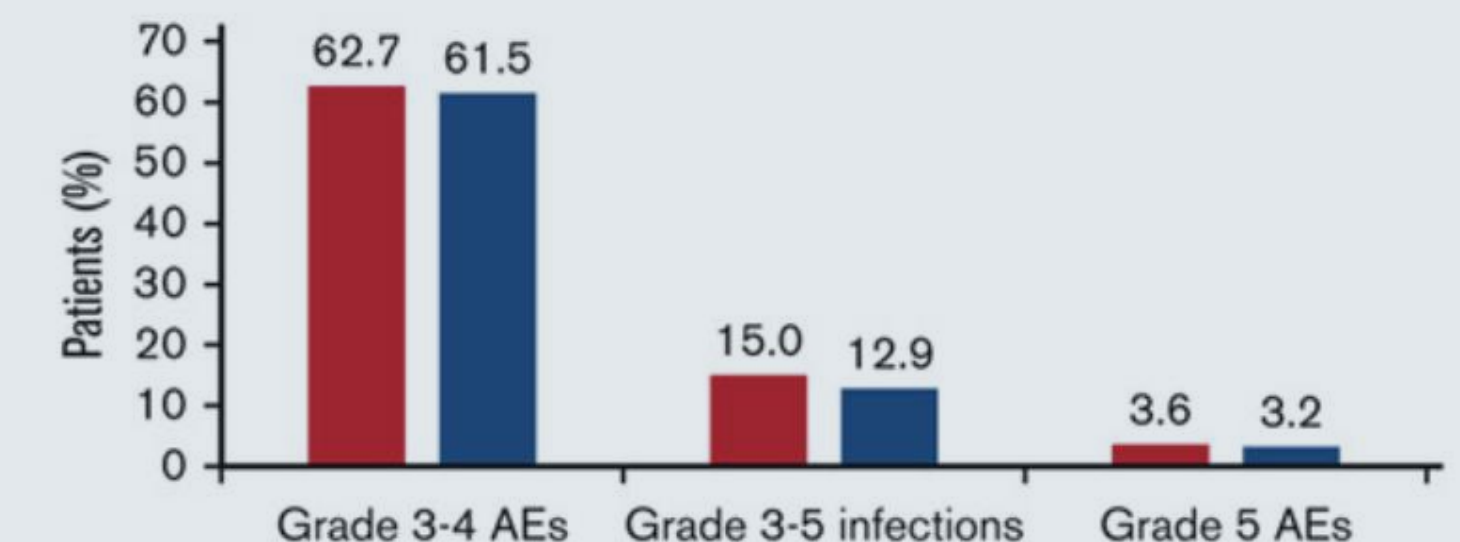


- Among **patients ≥ 60 years**, OS was similar with **Pola-R-CHP** versus **R-CHOP**



- No new toxicities were reported

- Among **patients ≥ 60 years**, safety profiles were similar with **Pola-R-CHP** versus **R-CHOP**



Hu B, Reagan PM, Sehn LH, et al.. Subgroup analysis of older patients ≥ 60 years with diffuse large B-cell lymphoma in the phase 3 POLARIX study. *Blood Adv.* 2025 May 27;9(10):2489-2499. doi: 10.1182/bloodadvances.2024014707

The benefit-risk profile favored **Pola-R-CHP** versus **R-CHOP** in elderly patients with previously untreated DLBCL, indicating that this population can achieve significant benefits from **Pola-R-CHP** treatment with manageable toxicities

POLAR BEAR: R-Pola-miniCHP vs R-miniCHOP

in elderly or frail patients with diffuse large B-cell lymphoma

Phase 3 Nordic Lymphoma Group trial – safety and initial pooled efficacy data (EHA 2026, Abstract S238)

EHA2026
Congress

June 11-14
Stockholm, Sweden

Study design



N = 300

elderly or frail patients
with previously untreated
DLBCL



55 sites

in Sweden, Norway,
Denmark, Finland,
Italy, Australia,
New Zealand



Key eligibility

- Age >80 years, or 75–80 years and frail (simplified Comprehensive Geriatric Assessment, **sCGA**)



Randomization 1:1

- R-miniCHOP** (n = 150)
- R-pola-miniCHP** (n = 150)
(polatuzumab vedotin 1.8 mg/kg, day 1, 6 cycles)



Enrollment

08/2020 – 06/2025

Patient characteristics (total population)



Median age
82 years
(range not shown)



ECOG PS 3
25 (8.3%)



<80 years
48 (16%)
frail patients



Median follow-up
14.8 months

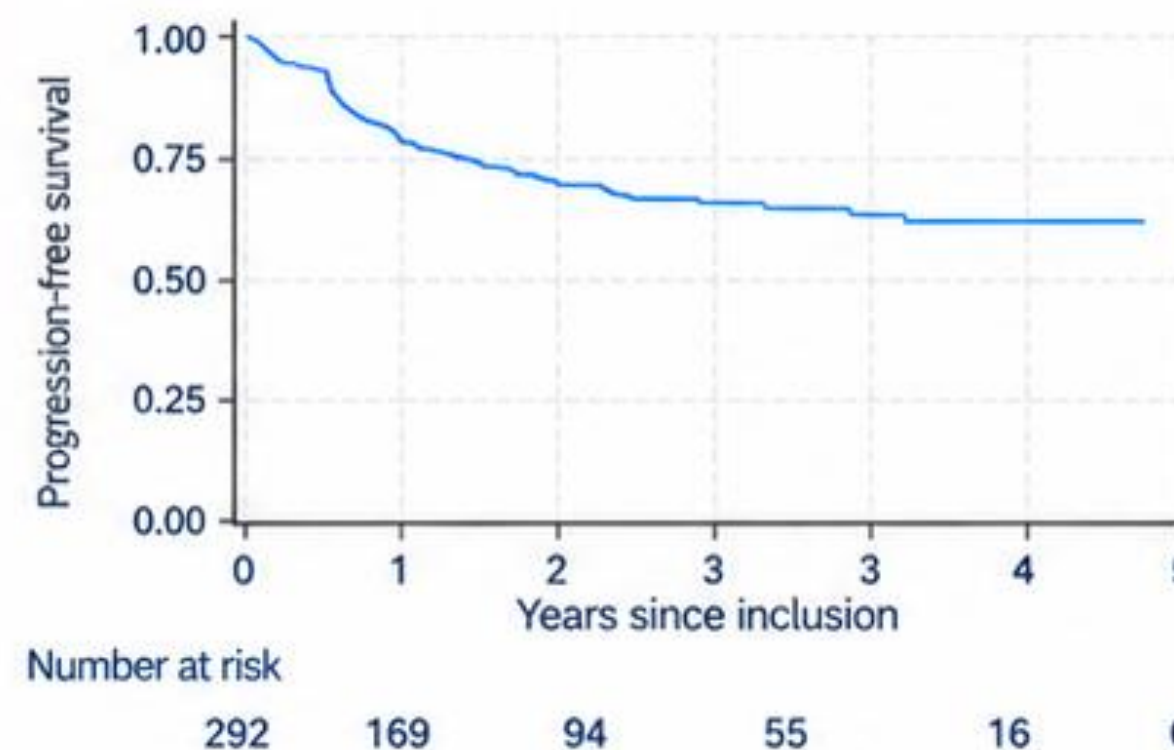
Key message



R-pola-miniCHP is feasible in elderly and frail patients with DLBCL, with encouraging 2-year outcomes and a manageable safety profile.

Efficacy (pooled, all patients)

Progression-free survival



2-year PFS

67%

(95% CI 60–73)

2-year OS

76%

(95% CI 70–81)

No impact on PFS

by age group (<80, 80–90, ≥90)
or comorbidity (CIRS-G <10 vs ≥10)

Safety (all patients)

	R-miniCHOP (n = 150)	R-pola-miniCHP (n = 150)
Grade ≥3 AEs	45 (30%)	54 (36%)
Grade ≥3 infections	11 (7.3%)	19 (12.7%)
GI toxicity (grade >2)	5 (3.3%)	9 (6.0%)
Peripheral neuropathy (grade ≥3)	0	2 (1.3%) Grade 1–2: 10.7% vs 17.3%
Grade 5 AEs	2 (1.3%)	8 (5.3%) (respiratory 4, infection 2, cardiovascular 1, CNS 1, GI 1)

Conclusions



- Rituximab/anthracycline-based chemotherapy remains a valid standard for elderly and frail patients with DLBCL.
- PFS at 2 years was 67% in the **entire study population**, with no significant impact of age or comorbidity.
- Toxicity profile was manageable, with no significant increase in hematologic toxicity; infectious complications and GI toxicity were generally manageable.
- Substitution of vincristine with polatuzumab vedotin did not result in a significant increase in toxicity.

EPCORE NHL-2: Epcoritamab + R-miniCHOP**2-year follow-up in elderly patients with newly diagnosed DLBCL**

Phase 1b/2 trial – safety and initial pooled efficacy data (EHA 2026, PF1007)

EHA2026
CongressJune 11-14
Stockholm, Sweden**Study design****Single-arm, phase 1b/2
N = 28**

Elderly patients with newly diagnosed (1L) DLBCL ineligible for full-dose R-CHOP

**Key eligibility**

- Age ≥ 75 years or ≥ 65 years with comorbidities (simplified CGA)
- CD20+ DLBCL

**Treatment**

Epcoritamab SC + R-miniCHOP

- Epcoritamab 48 mg (QW C1–2; Q3W C3–6; Q4W C7–8; step-up in C1)
- R-miniCHOP (Q3W, C1–6)

**Follow-up (median)****33.4 months**

(range 2.8–41.1)

Patient characteristics (N = 28)Median age
81 years
(range 74–90)GCB
46%
Non-GCB
39%Bulky disease
(≥7 cm)
39%De novo DLBCL
89%IPI 4–5
43%Completed treatment
as planned
79%
Median R-miniCHOP RDI: 94%**Key message**

Epcoritamab + R-miniCHOP shows high response rates, deep molecular responses and durable remissions in elderly patients with DLBCL, with a manageable safety profile.

Efficacy (N = 28)ORR
93%CR
86%2-year PFS
76%2-year OS
82%2-year DOR
79%2-year DOCR
79%**MRD (ctDNA, AVENIO)**MRD-negative
(at any time)**95%**
(20/21)MRD-negative
by C3D1**80%**
(16/20)

MRD-negative in high-risk subgroups

- Bulky disease (≥7 cm): **89%** (8/9)
- IPI 3–5: **93%** (14/15)

Safety (N = 28)Grade ≥3 neutropenia **43%**Grade ≥3 serious infections **32%**Grade ≥3 anemia **14%**Epcoritamab discontinuation
due to TEAEs **11%**

Most serious infections (7/9) occurred during the first 6 cycles (with R-miniCHOP).

Conclusions

- Epcoritamab + R-miniCHOP achieved high ORR (93%) and CR (86%) with durable 2-year remissions and deep MRD negativity in elderly patients with 1L DLBCL.
- Safety profile was consistent with previous reports and manageable.
- Results compare favorably with historical outcomes of R-miniCHOP, but should be interpreted with caution due to the single-arm design and small sample size.
- Randomized studies are needed to confirm the benefit of this approach.

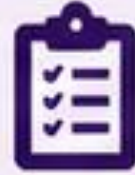
“Promising deep and durable responses — but randomized evidence is still needed.”

Bispecific antibody monotherapy in first-line elderly/unfit DLBCL

Results from two ASH 2025 oral presentations – promising efficacy with manageable safety

MorningSun: mosunetuzumab monotherapy

Fixed-duration SC mosunetuzumab in elderly/unfit patients with previously untreated DLBCL
Phase II study – ASH 2025 (Oral, Abstract #)

Study design & population	
	N = 49 (DLBCL n = 36) Community sites: 69%
	Median age 82.5 years (range 71–101)
	Key eligibility - Age ≥80 years or 65–79 years ineligible for chemoimmunotherapy - ECOG PS 1–2 (84%) - Unfit due to age/comorbidities
	Treatment Mosunetuzumab SC - Step-up dosing (C1D1, D8, D15) 45 mg Q3W, up to 17 cycles
	Median follow-up 12.5 months (range 1.4–30.8)

Efficacy (DLBCL cohort, N = 36)	
ORR 73.5%	CR rate 59.2%
12-month PFS 68.8% (95% CI 52.1–80.6)	12-month OS 77.2% (95% CI 61.1–87.3)
12-month DOR 84.6% (95% CI 66.8–93.3)	12-month DOCR 95.0% (95% CI 69.5–99.3)

Safety (N = 49)	
 Grade ≥3 AEs	65.3%
 Grade ≥3 infections	16.3%
 Serious AEs	42.9%
 Treatment discontinuation (any AE)	10.2%

EPCORE DLBCL-3: epcoritamab monotherapy

Fixed-duration SC epcoritamab in elderly patients with newly diagnosed LBCL and comorbidities
Phase II study – ASH 2025 (Oral, Abstract #)

Study design & population	
	N = 66 (stage 1 n = 44; stage 2 n = 22)
	Median age 82.5 years (range 76–95) ≥80 years: 82%
	Key eligibility - Age ≥80 years or ≥75 years with comorbidities - Ineligible for anthracycline-based therapy - All patients had ≥1 comorbidity - Renal impairment: 64% - Cardiac disorders: 41% - IPI ≥3: 64% - Bulky disease (≥7 cm): 33%
	Treatment Epcoritamab SC (fixed duration, up to 1 year) - Step-up dosing (C1D1, D8) 48 mg QW (C1–3), Q4W (C4–12)
	Median follow-up 14.9 months (95% CI 11.8–16.7)

Efficacy (overall population, N = 66)	
ORR 70%	CR rate 58%
Median PFS 13.0 months (95% CI 5.4–NR)	Median OS NR (95% CI 13.0–NR)
12-month PFS (estimated) 54%	12-month OS (estimated) 65%

MRD negativity (ctDNA, AVENIO)	
MRD-negative at any time 88% (23/26)	Early MRD negativity by C3D1 and sustained in a majority through C12D1. MRD negativity associated with longer PFS.

Safety (N = 66)	
 Any grade AEs	94%
 Grade ≥3 AEs	61%
 Grade ≥3 infections	18%
 CRS (any grade)	70%
 ICANS (any grade)	18%
 Treatment discontinuation (any AE)	14%

Most common: CRS (70%), diarrhea (23%), fatigue (21%)	
Infections (any grade): 59%	
G1: 38%; G2: 27%; G3: 5% (94% in C1; 97% resolved)	
G1: 8%; G2: 8%; G3: 3%	
Two additional G5 AEs (pneumonia, death)	



Single-agent bispecific antibodies show meaningful activity and durable responses in elderly/unfit patients with newly diagnosed LBCL, with manageable safety.

Longer follow-up and comparative studies are needed to define their role versus standard chemoimmunotherapy approaches.

Chemo-free and chemo-light strategies in first-line elderly/unfit DLBCL

Two emerging anthracycline-free strategies in older/unfit DLBCL

ZR²: zanubrutinib + rituximab + lenalidomide

Phase II study in elderly patients with ip previously untreated DLBCL
ASH 2025 (Visual abstract)

Study design & population

-  **N = 40**
De novo DLBCL
Age ≥75 years
-  **Median age 78 years**
-  **Key eligibility**
 - Age ≥75 years
 - Unfit/frail by CGA: 85%
 - No requirement for chemotherapy
-  **Treatment**
Zanubrutinib + rituximab + lenalidomide
 - Lenalidomide maintenance in responders
 - RT in selected patients
-  **Median follow-up 24 months**

Efficacy (N = 40)

ORR 75%	CR rate 65%
2-year PFS 67.1% (95% CI 50.1–79.4)	2-year OS 82.4% (95% CI 66.5–91.2)

Safety (N = 40)

 Grade ≥3 neutropenia	35%
 Grade ≥3 transaminase increase	12.5%
 Grade ≥3 pulmonary infection	12.5%
 Atrial fibrillation (any grade)	0%

R-Pola-Glo: rituximab + polatuzumab + glofitamab

Phase II frontline study in elderly and medically unfit/frail patients with aggressive B-cell lymphoma
ASH 2025 (Oral Presentation)

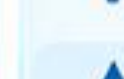
Study design & population

-  **N = 80**
Aggressive B-cell lymphoma (mostly DLBCL)
Age ≥75 years or unfit/frail
-  **Median age 80 years**
>85 years: 19%
-  **Key eligibility**
 - Unfit/frail by sGA: 91%
 - Ineligible for full-dose R-CHOP
 - No requirement for chemotherapy
-  **Treatment**
Rituximab + polatuzumab + glofitamab
 - 6 cycles induction
 - 6 cycles glofitamab consolidation
-  **Median follow-up 15 months**

Efficacy (N = 80)

CMR at EOT 81%	1-year PFS 85%
1-year EFS 82%	1-year OS 90%

Safety (N = 80)

 Grade ≥3 infections	22%
 CRS (any grade)	31% Grade ≥3: 1%
 ICANS (any grade)	4%
 Treatment discontinuation (due to AEs)	~20% (80% completed)



Targeted/immunologic combinations can achieve high response rates in older/unfit patients without standard chemotherapy, with manageable safety profiles.

Randomized comparisons with R-miniCHOP are needed to define their role in clinical practice.

What about FIL?

FIL-RICCO



Rituximab + golcadomide (CC-99282)



Population

Older unfit/frail patients (sGA), untreated DLBCL
Ineligible for anthracycline-based therapy



Treatment

Rituximab + golcadomide
6 induction cycles + 6 consolidation cycles
± involved-site radiotherapy



Design

Phase 2, single arm
N = 47



Status



Open, recruiting
EU CT: 2023-506206-38-00

OLEANDER



Odronextamab ± lenalidomide



Population

Older unfit/frail patients (sGA), untreated DLBCL



Treatment

Induction: odronextamab ± lenalidomide
Response-adapted: odronextamab alone or +
miniCHOP



Design

Phase 2, two phases
N = 75 (50 + 25)

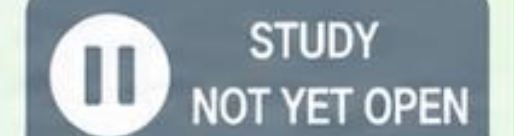


Status

Not yet open

Expected start: May 2027

R-EPCORITAMAB



Fixed-duration epcoritamab +
rituximab



Population

Older unfit/frail patients (sGA), untreated LBCL
Ineligible for anthracycline-based therapy



Treatment

Arm A: epcoritamab + rituximab × 12 cycles
Arm B: R-CVP × 8 cycles



Design

Phase 2, randomized 1:1
N = 150
Primary endpoint: 1-year PFS



Status

In development

Which first-line treatment would you choose?

A R-miniCHOP or R-miniCOMP

B Pola-R-miniCHP
(polatuzumab + R-miniCHP)

C Clinical trial

D Palliation

E EPI SCORE



2030

Which first-line treatment would you choose for F.C. in 2030?

A Epcoritamab + R-miniCHP



B R-pola-miniCHP



C Clinical trial



D Palliation



E Bispecific antibody single agent
(e.g. epcoritamab or mosunetuzumab)



F Chemo-free combination
(e.g. ZR2 or R-polaGLO, R-golcadomide)



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R/R LBCL

Stratification of the patients by time to failure

2L

Biopsy recommended

Primary refractory or R<12 months

R>12 months

CAR-T eligible

No intention to proceed to CAR-T

Axi-cel [I, A] or liso-cel [I, A]

Glofitamab-GemOx [I, A],
Clinical trial, 2L therapy*
or best supportive care

Transplant eligible

No intention to proceed to transplant

Immunochemotherapy** followed
by HDT/ASCT if CR/PR [I, A]

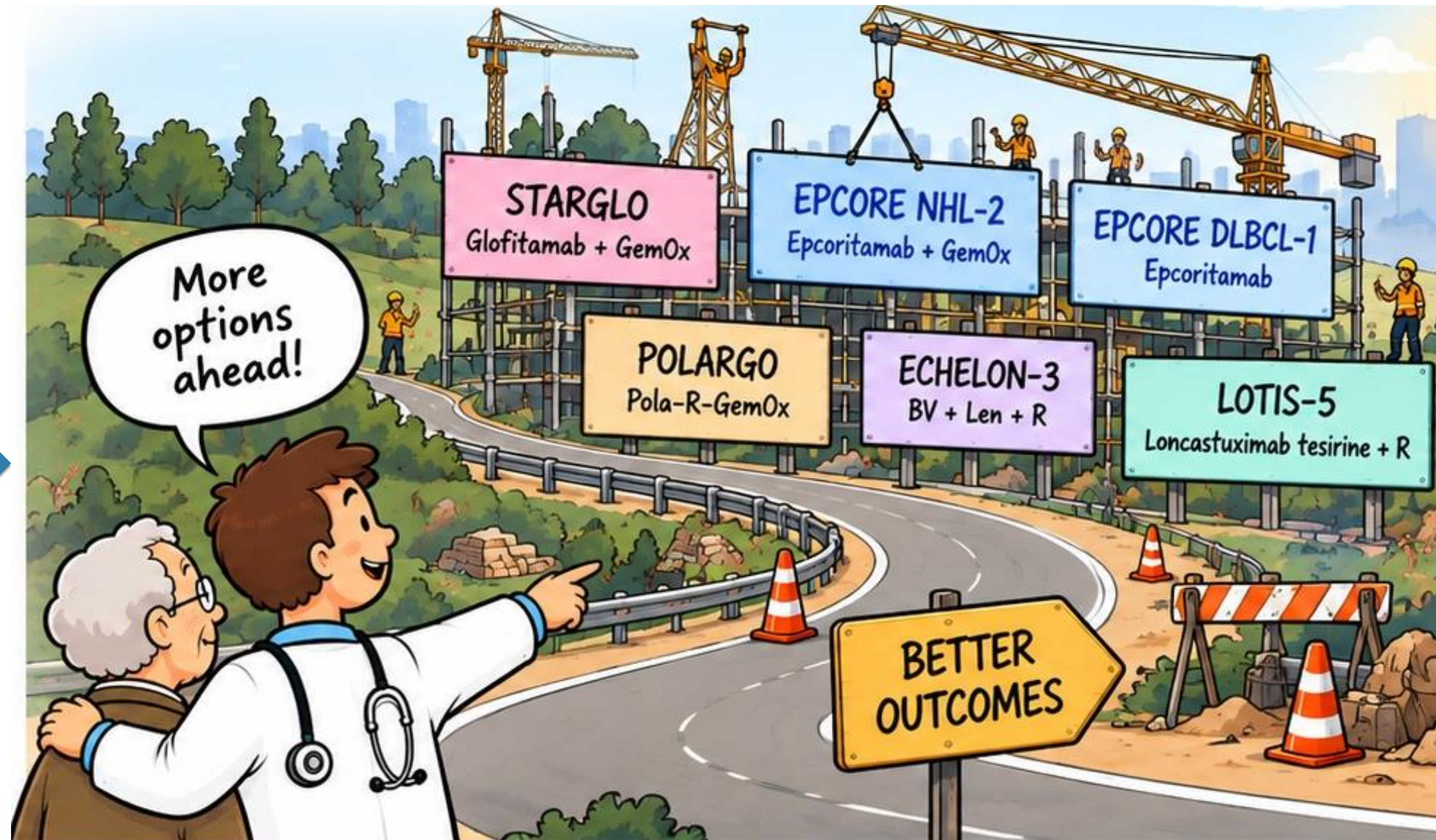
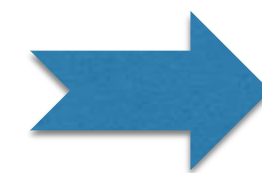
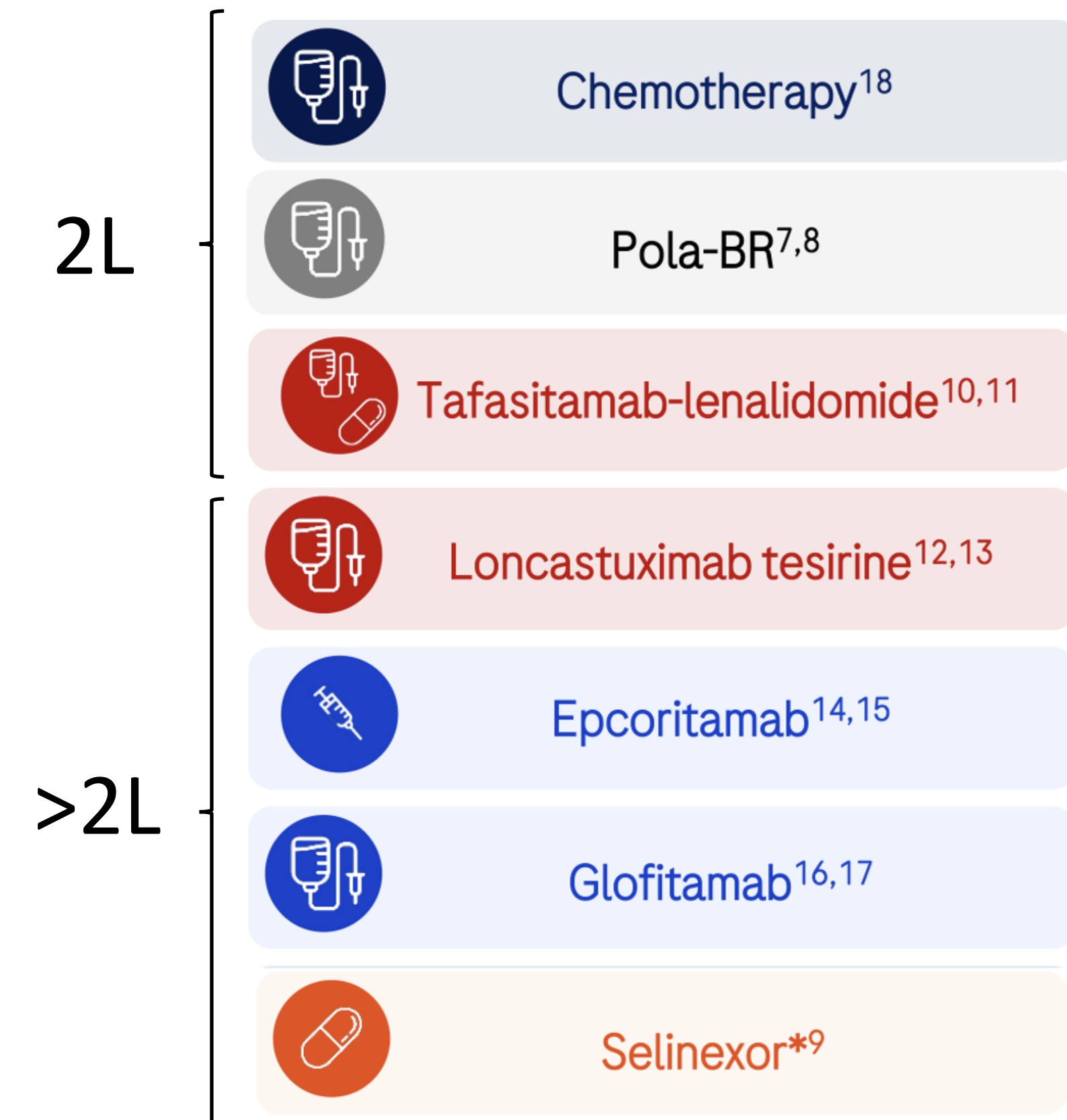
Glofitamab-GemOx [I, A],
Clinical trial, 2L therapy*
or best supportive care

*2L therapy: epcoritamab+ Gemox [III, C] when available; tafasitamab-LEN [III, C] in non refractory patients; R-chemotherapy [I, B]: R-GemOx or Pola-BR [III, B]

**2L immunochemotherapy before HDT/ASCT: R-DHAX (P or C), R-ICE, R-GDP, R-ESHAP; in case of CMR, proceed to HDT/ASCT [I, A]

FOCUS ON FITNESS AND COMORBIDITIES, NOT ON AGE

For the CAR-T–ineligible patient, the landscape has changed



* Product/indication not approved. Experimental use.

1. YESCARTA SmPC; 2. YESCARTA USPI; 3. BREYANZI SmPC; 4. BREYANZI USPI; 5. KYMRIAH SmPC; 6. KYMRIAH USPI; 7. POLIVY USPI; 8. POLIVY SmPC; 9. XPOVIO USPI; 10. MINJUVI SmPC; 11. MONJUVI USPI; 12. ZYNLONTA USPI; 13. ZYNLONTA SmPC; 14. EPKINLY USPI; 15. EPKINLY SmPC; 16. COLUMVI USPI; 17. COLUMVI SmPC

18. Tilly H, et al. Ann Oncol 2015;26:116–25; 19. Sehn LH. Blood Cancers Today 2023. Available at: <https://bloodcancerstoday.com/post/how-to-choose-the-right-treatment-when-there-are-so-many-options-in-dlbcl>; 20. Westin & Sehn. Blood 2022;139:2737–46; 21. Sehn LH & Salles G. N Engl J Med 2021;384:842–58; 22. Duarte C, et al. ASCO Educational Book 2023;43:1–9.

The young side of LYMPHOMA

gli under 40 a confronto

Focus on older patients

Trial (phase)	Regimen (experimental vs control)	Population (older patients)	Median age (range)	Efficacy (experimental vs control)				Key safety (experimental)	Take-home message
				ORR	CRR	PFS	OS		
STARGLO (III) 	Glofitamab + GemOx vs R-GemOx	R/R DLBCL transplant-ineligible (after 1L) 63% ≥ 65 years	68 (18–94)	68.3% vs 40.7%	58.5% vs 25.3%	13.8 m vs 3.6 m	25.5 m vs 12.9 m	CRS 44% (G1 31.4%) ICANS 2.3%	Significant survival benefit with manageable toxicity in an older population.
EPCORE NHL-2 (Ib/II) 	Epcoritamab + GemOx (Arm 5)	R/R DLBCL transplant-ineligible (median 2 prior lines) 35% ≥ 75 years	72 (41–86)	85.4%	61.2%	68.5% at 12 m	21.6 m	CRS 52% (G3 1%) ICANS 2.9% (G3+ 1%)	High response rates and durable remissions with epcoritamab + GemOx in an elderly, transplant- ineligible population.
EPCORE DLBCL-1 (III) 	Epcoritamab vs R-GemOx or BR	R/R CD20+ DLBCL (after ≥1L) Transplant-ineligible or relapsed after ASCT ~ 60% ≥ 65 years	71 (28–89)	51% vs 48%	38% vs 26%	30% vs 13% (at 24 m)	38% vs 33% (at 24 m)	CRS 53% (G3 3%) ICANS 4% (G3–4 1%) Infections 30% (G3–4)	First phase III showing PFS and higher CRR with bispecific monotherapy vs chemotherapy.
POLARGO (III) 	Pola-R-GemOx vs R-GemOx	R/R DLBCL transplant-ineligible (after 1L) 35% ≥ 70 years	65 (20–85)	52.7% vs 24.6%	40.3% vs 19.0%	7.4 m vs 2.7 m	19.5 m vs 12.5 m	G3–4 AEs 57% Thrombocytopenia 34% Infections 14% Peripheral neuropathy 57%	Antibody–drug conjugate– based chemoimmunotherapy improves outcomes, with predictable hematologic and neurologic toxicity.
ECHELON-3 (III) 	BV + lenalidomide + R vs Placebo + R	R/R DLBCL transplant- and CAR-T ineligible (after ≥2L) Subgroup ≥ 65 years	75 (≥ 65 years)	64.3% vs 41.5%	40.2% vs 18.6%	4.2 m vs 2.6 m	13.8 m vs 8.5 m	Neutropenia 46% Diarrhea 31%	Chemotherapy-free approach with OS benefit also in patients ≥ 65 years.
LOTIS-5 (III) 	Loncastuximab tesirine + R vs R-GemOx	R/R DLBCL transplant-ineligible (after 1L) ~ 38–41% ≥ 75 years	72–73 (22–90)	~58%* vs ~44%*	~40%* vs ~27%*	HR 0.73 (PFS)	No OS benefit in ≥ 75 years (HR 1.38)	Higher G5 in ≥ 75 years (zbraccio lonca-R) Hematologic toxicity and infections	PFS benefit with relevant activity; caution in ≥ 75 years due to safety and OS data.

Reggio Emilia, 2-3 ottobre 2026

EPCORE DLBCL-1 EHA-2409 (Oral presentation)

Epcoritamab vs investigator's choice chemoimmunotherapy in R/R LBCL

EHA2026
Congress

June 11-14
Stockholm, Sweden

Study design and population



Population

CD20+ R/R LBCL, ASCT-ineligible or relapsed after ASCT
≥ 1 prior line (1 capped at 25%)



Design

Randomized phase 3, open-label
N = 483 (epcor 241 | CIT 242)
Median age 71 years (range 28–89)
73% ≥ 2 prior lines | 15% prior SCT | 11% prior CAR-T



Treatment (28-day cycles)

Epcoritamab

SC, 2 step-up doses → 48 mg
QW (C1–3), Q2W (C4–9), Q4W (C10+)
until PD or unacceptable toxicity

Investigator's choice CIT

R-GemOx (Q2W × 4) or
BR (Q3W × 6)



Endpoints

Dual primary endpoints: PFS (IRC) and OS
Key secondary: ORR, CRR, DOR, TTNT, safety

Key results



PFS (IRC)

24-month PFS
HR 0.74 (95% CI 0.60–0.92)
P = 0.0059

Epcor
30%

CIT
13%



Complete response rate

CRR: 38% vs 26%
P = 0.0032

Epcor
38%

CIT
26%



Duration of response

Median DOR: 37 vs 6 months
DOCR: NR vs 11 months

Epcor
37 mo

CIT
6 mo



Time to next treatment

Median TTNT: 7 vs 4 months
P < 0.0001

Epcor
7 mo

CIT
4 mo



Overall response rate

ORR: 51% vs 48%

Epcor
51%

CIT
48%



Epcoritamab significantly improved PFS and CRR vs investigator's choice CIT in R/R LBCL, with deep and durable responses and less frequent use of subsequent therapies. Safety was consistent with the known profile, with higher infection rates in the epcor arm.

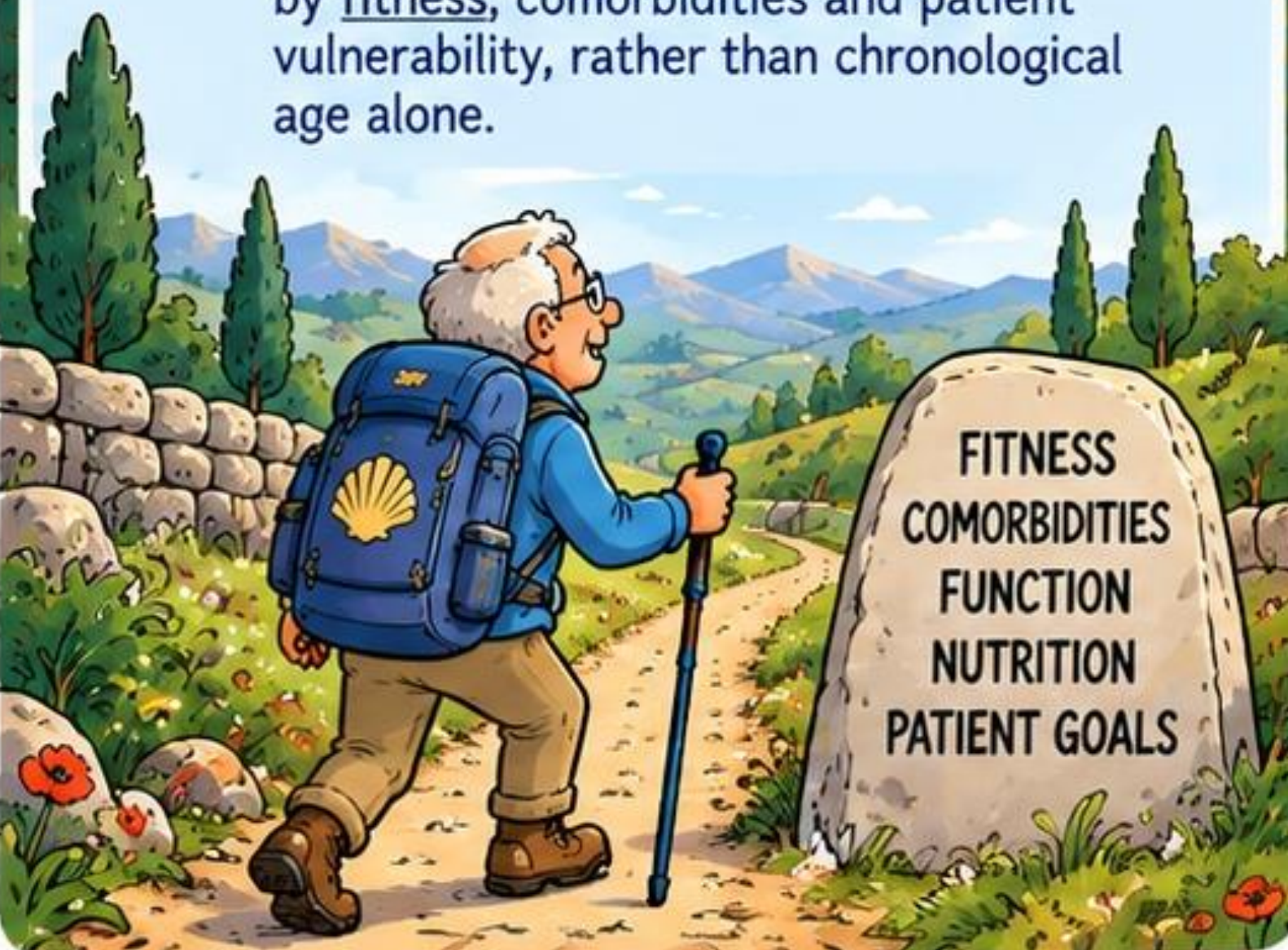
EHA 2026
Abstract S235

Older patients, new horizons in DLBCL

Different paths, one goal: better outcomes for older patients with DLBCL.

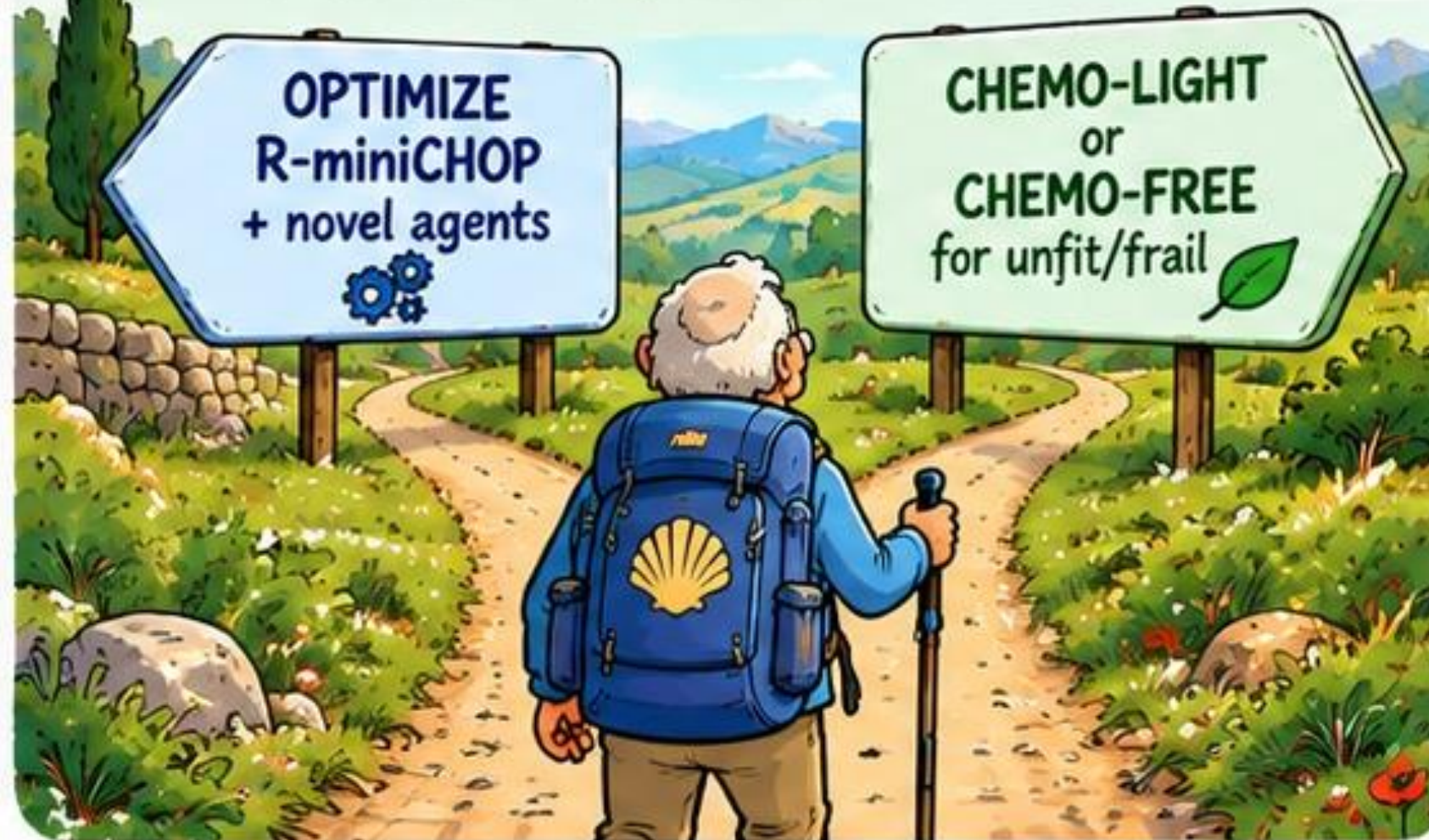
1 AGE ≠ FITNESS

Treatment decisions should be driven by fitness, comorbidities and patient vulnerability, rather than chronological age alone.



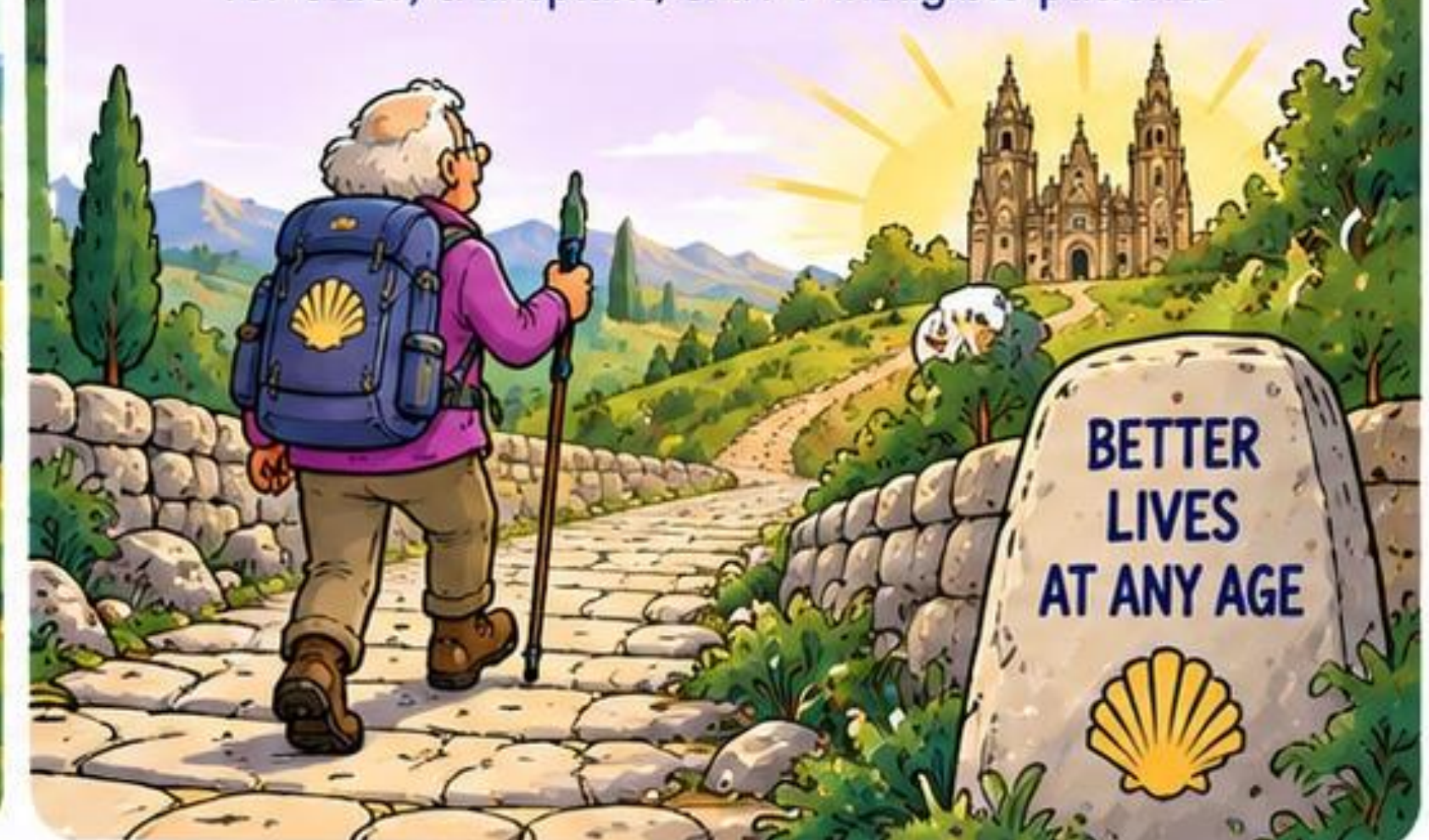
2 FIRST LINE: FROM DOSE ATTENUATION TO TREATMENT INNOVATION

The future lies in both optimizing R-miniCHOP and developing chemo-light/chemo-free strategies for unfit and frail patients.



3 R/R DLBCL: MORE OPTIONS, MORE PERSONALIZATION

Bispecific antibodies, ADC-based combinations and novel targeted approaches are reshaping treatment for older, transplant/CAR-T-ineligible patients.



*Different paths, one goal:
better outcomes for older patients with DLBCL.*



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NOT AI-generated image



**And
thank you
for the
attention!**

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