Lymphoma · Leukemia & Myeloma Congress

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The Outpatient Standard: Operationalizing the 2026 R/R DLBCL Sequencing Roadmap

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Disclosures

- **Sonali M. Smith, MD, FASCO:** Advisory Board—AstraZeneca, Foresight Diagnostics, Genmab; Consultant—Roche/Genentech
- **Nilanjan Ghosh, MD, PhD, FACP:** consultant—Genentech/Roche, BMS, AbbVie, AstraZeneca, Incyte, Genmab, Merck, ADC Therapeutics, Galapagos, Pfizer; research funding—Genetech/Roche, AstraZeneca, AbbVie, Perpromene

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Learning Objectives

- Evaluate clinical evidence supporting approved and emerging therapies in R/R DLBCL, including BsAbs, ADCs, and CD19-directed agents, across lines of care and patient fitness profiles
- Apply an individualized, risk-stratified management and sequencing framework for patients with R/R DLBCL in the outpatient setting, accounting for prior therapy exposure, antigen-escape patterns, and pace of relapse
- Incorporate evidence-based outpatient monitoring protocols and step-up dosing strategies for BsAbs and targeted therapies into real-world DLBCL care delivery across diverse clinic settings

R/R = relapsed/refractory; DLBCL = diffuse large B-cell lymphoma; BsAb = bispecific antibody; ADC = antibody-drug conjugate.

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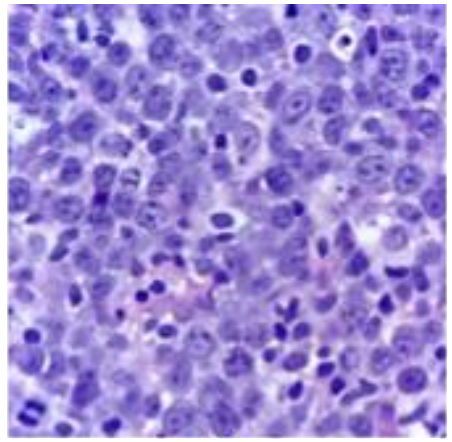
Setting the Stage: Relapsed/Refractory DLBCL

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R-CHOP (Cure Rate 50-70%) Has Been the Standard of Care for over Two Decades

R-CHOP + X	**Negative trials**: ibrutinib, bortezomib, lenalidomide*
R-CHOP → X	**Negative trials**: rituximab, enzastaurin, lenalidomide, everolimus. Autologous SCT
Infusional regimens	**Negative trials**: EPOCH-R
Response adapted R-CHOP	**Negative trials**: PET-adapted ? PET-adapted CAR-T ? ctDNA driven



- Cell-of-origin
- Genomic subtypes
- DZsig
- Clinical heterogeneity

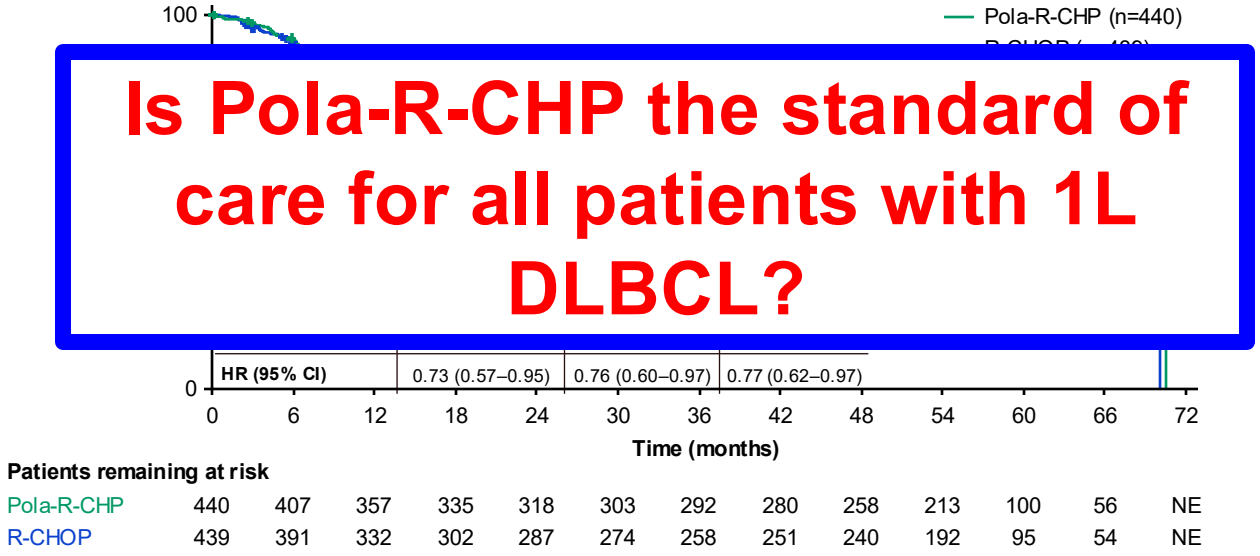
R-CHOP = rituximab, cyclophosphamide; doxorubicin, vincristine, prednisone; SCT = stem cell transplantation; EPOCH-R = etoposide, prednisone, vincristine, cyclophosphamide; doxorubicin, rituximab; PET = positron emission tomography; ctDNA = circulating tumor DNA; DZsig = dark-zone signature.
Figure adapted from Sehn LH.

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2022: First Randomized Trial to Show Improvement over R-CHOP Is POLARIX Trial (PFS Benefit Maintained at 5 Years)

No difference in overall survival

PFS in the global ITT population



Is Pola-R-CHP the standard of care for all patients with 1L DLBCL?

At the 5-year follow up, Pola-R-CHP had a **sustained and significant PFS benefit**, confirming results from the primary analysis of PFS at 2 years of follow up (HR 0.73).[1]

After 5 years of follow-up, numerically fewer deaths were observed in the Pola-R-CHP versus R-CHOP arm, with an associated HR of 0.85 (0.63–1.15).

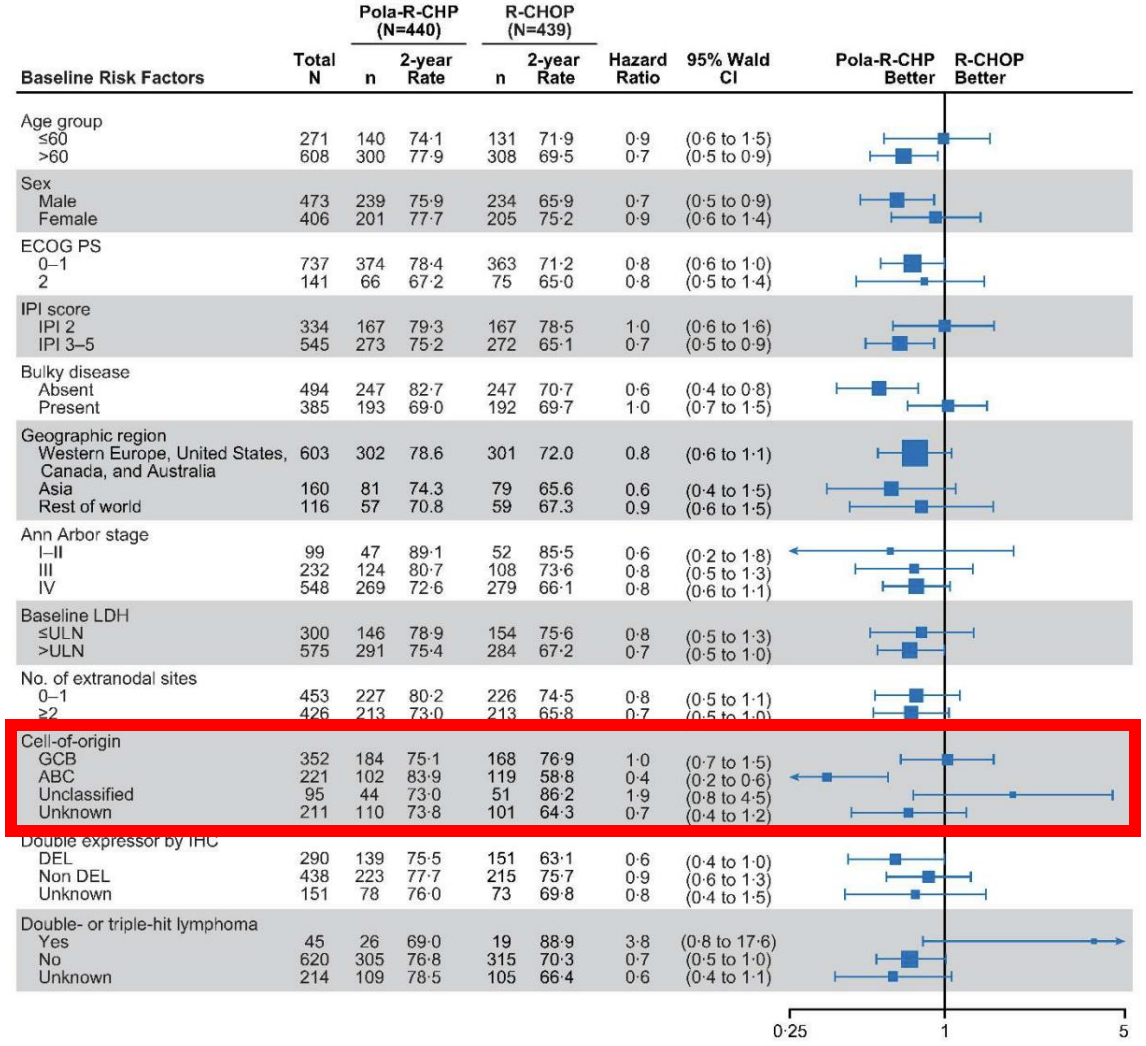
PFS = progression-free survival; ITT = intention-to-treat; pola-R-CHP = polatuzumab, rituximab, cyclophosphamide, doxorubicin, prednisolone; 1L = first-line.

Tilly H, et al. *N Engl J Med*. 2022;386(4):351-363.

POLARIX Subgroup Analysis

Pola-R-CHP better for

- Older pts
- PS 0-1
- Non-bulky disease
- ABC subtype
- No DHL/THL

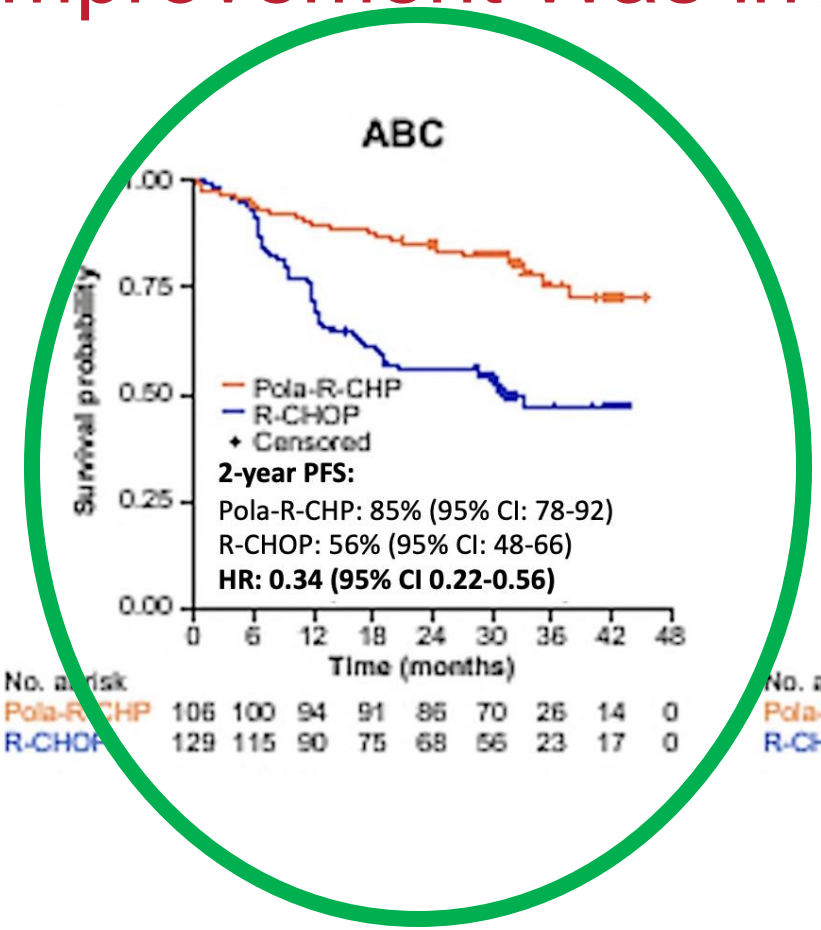


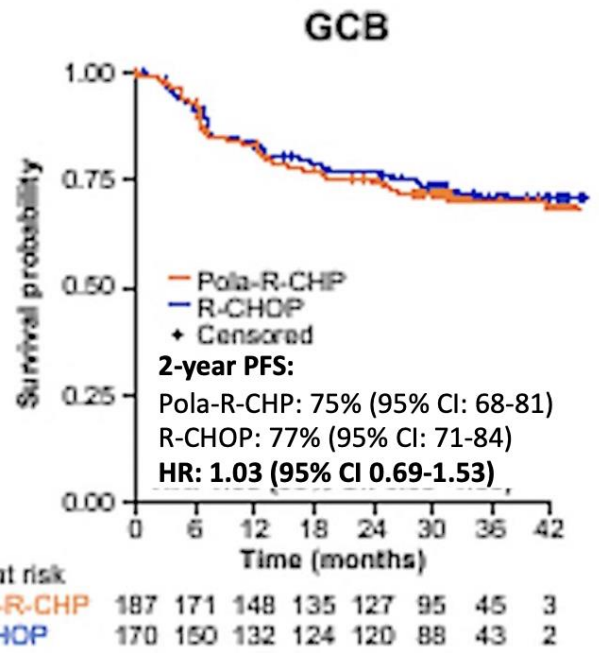
Baseline Risk Factors	Total N	Pola-R-CHP (N=440) n	Pola-R-CHP (N=440) 2-year Rate	R-CHOP (N=439) n	R-CHOP (N=439) 2-year Rate	Hazard Ratio	95% Wald CI
Age group							
≤60	271	140	74·1	131	71·9	0·9	(0·6 to 1·5)
>60	608	300	77·9	308	69·5	0·7	(0·5 to 0·9)
Sex							
Male	473	239	75·9	234	65·9	0·7	(0·5 to 0·9)
Female	406	201	77·7	205	75·2	0·9	(0·6 to 1·4)
ECOG PS							
0–1	737	374	78·4	363	71·2	0·8	(0·6 to 1·0)
2	141	66	67·2	75	65·0	0·8	(0·5 to 1·4)
IPI score							
IPI 2	334	167	79·3	167	78·5	1·0	(0·6 to 1·6)
IPI 3–5	545	273	75·2	272	65·1	0·7	(0·5 to 0·9)
Bulky disease							
Absent	494	247	82·7	247	70·7	0·6	(0·4 to 0·8)
Present	385	193	69·0	192	69·7	1·0	(0·7 to 1·5)
Geographic region							
Western Europe, United States, Canada, and Australia	603	302	78.6	301	72.0	0.8	(0·6 to 1·1)
Asia	160	81	74.3	79	65.6	0.6	(0·4 to 1·5)
Rest of world	116	57	70.8	59	67.3	0.9	(0·6 to 1·5)
Ann Arbor stage							
I–II	99	47	89·1	52	85·5	0·6	(0·2 to 1·8)
III	232	124	80·7	108	73·6	0·8	(0·5 to 1·3)
IV	548	269	72·6	279	66·1	0·8	(0·6 to 1·1)
Baseline LDH							
≤ULN	300	146	78·9	154	75·6	0·8	(0·5 to 1·3)
>ULN	575	291	75·4	284	67·2	0·7	(0·5 to 1·0)
No. of extranodal sites							
0–1	453	227	80·2	226	74·5	0·8	(0·5 to 1·1)
≥2	426	213	73·0	213	65·8	0·7	(0·5 to 1·0)
Cell-of-origin							
GCB	352	184	75·1	168	76·9	1·0	(0·7 to 1·5)
ABC	221	102	83·9	119	58·8	0·4	(0·2 to 0·6)
Unclassified	95	44	73·0	51	86·2	1·9	(0·8 to 4·5)
Unknown	211	110	73·8	101	64·3	0·7	(0·4 to 1·2)
Double expressor by IHC							
DEL	290	139	75·5	151	63·1	0·6	(0·4 to 1·0)
Non DEL	438	223	77·7	215	75·7	0·9	(0·6 to 1·3)
Unknown	151	78	76·0	73	69·8	0·8	(0·4 to 1·5)
Double- or triple-hit lymphoma							
Yes	45	26	69·0	19	88·9	3·8	(0·8 to 17·6)
No	620	305	76·8	315	70·3	0·7	(0·5 to 1·0)
Unknown	214	109	78·5	105	66·4	0·6	(0·4 to 1·1)

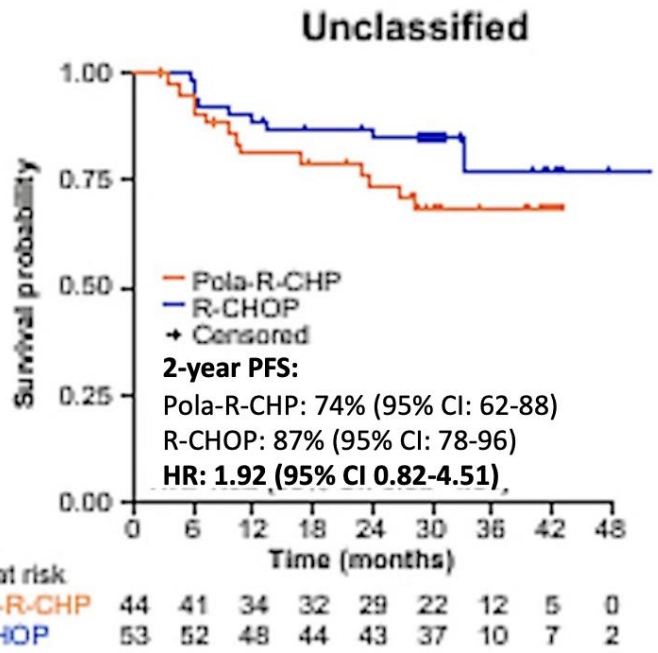
ECOG PS = Eastern Cooperative Oncology Group performance status; ABC = activated B-cell; IPI = International Prognostic Index; GCB = germinal center B-cell; DHL = double-hit lymphoma; THL = triple-hit lymphoma; LDH = lactate dehydrogenase; ULN = upper limit of normal; IHC = immunohistochemistry; DEL = double-expressor-lymphoma.

Tilly H, et al. *N Engl J Med*. 2022;386(4):351-363.

Pola-R-CHP vs R-CHOP by Cell of Origin: Most Improvement Was in ABC Subset of DLBCL

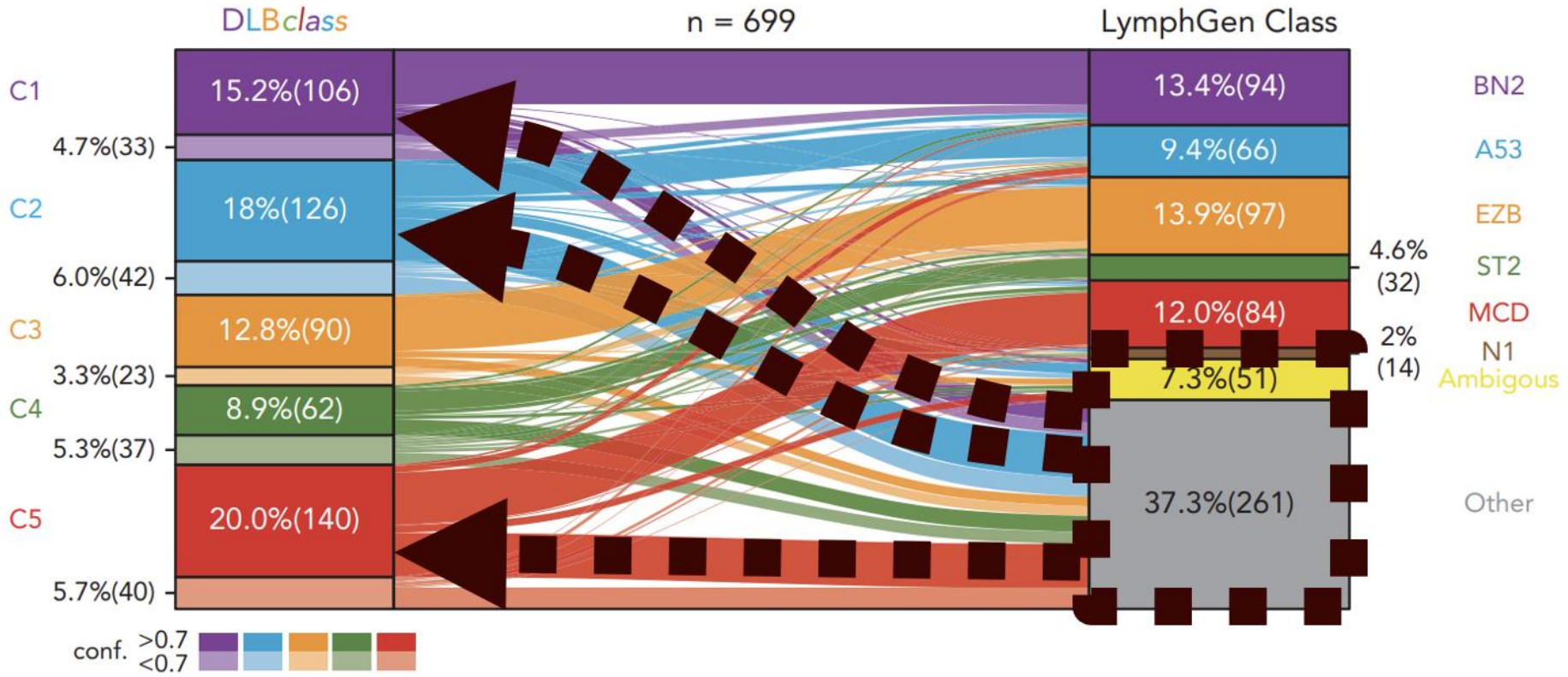






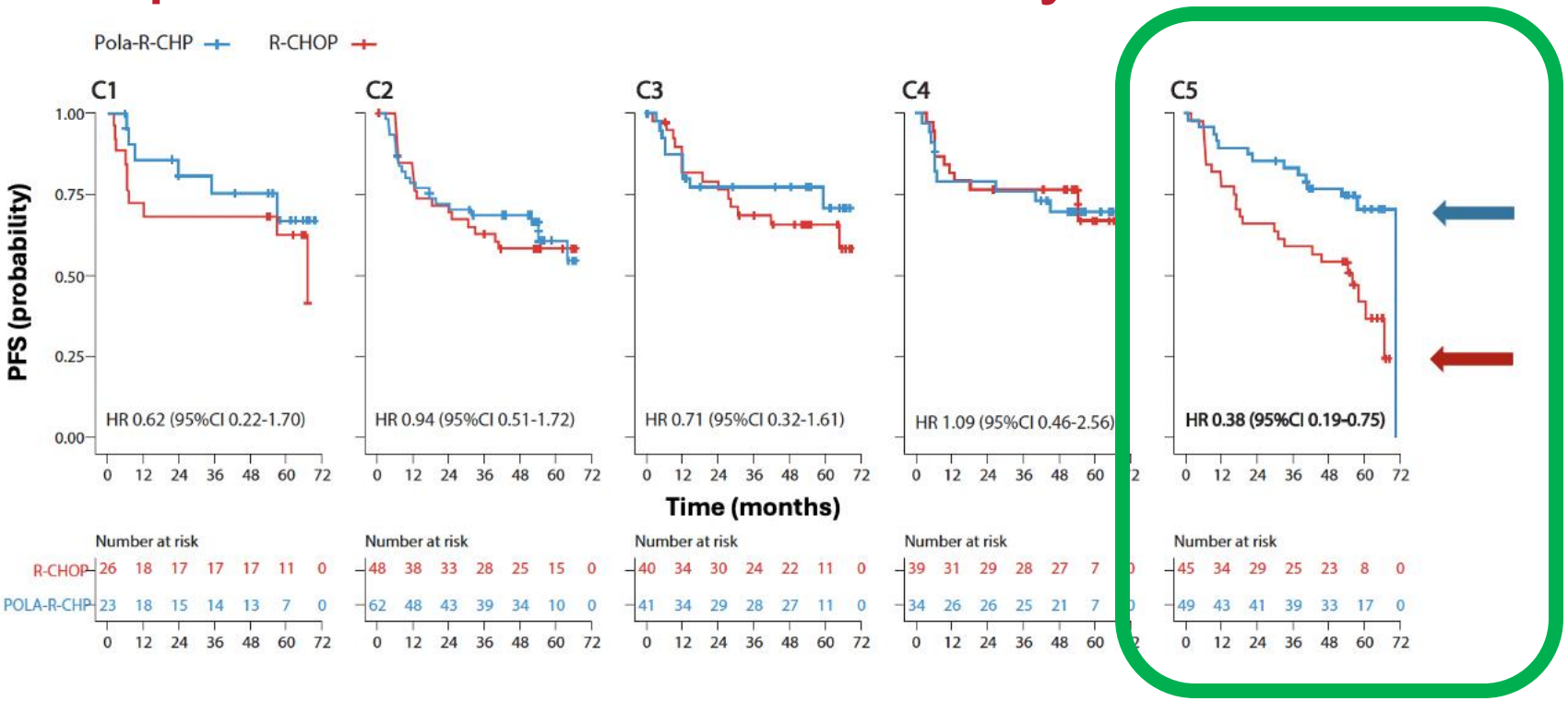
Russler-Germain DA, et al. *Blood*. 2023;142(25):2216-2219. Morchauser F, et al. *Blood*. 2023;142(Suppl 1):3000.

DLBCL Is Biologically Complex: Genomic Classifiers Identify 5 Distinct Groups



Chapuy B, et al. *Blood*. 2025;145(18):2041-2055.

Pola-R-CHP vs R-CHOP by Molecular Classification (DLBclass): Improvement Was Primarily in C5 Subset

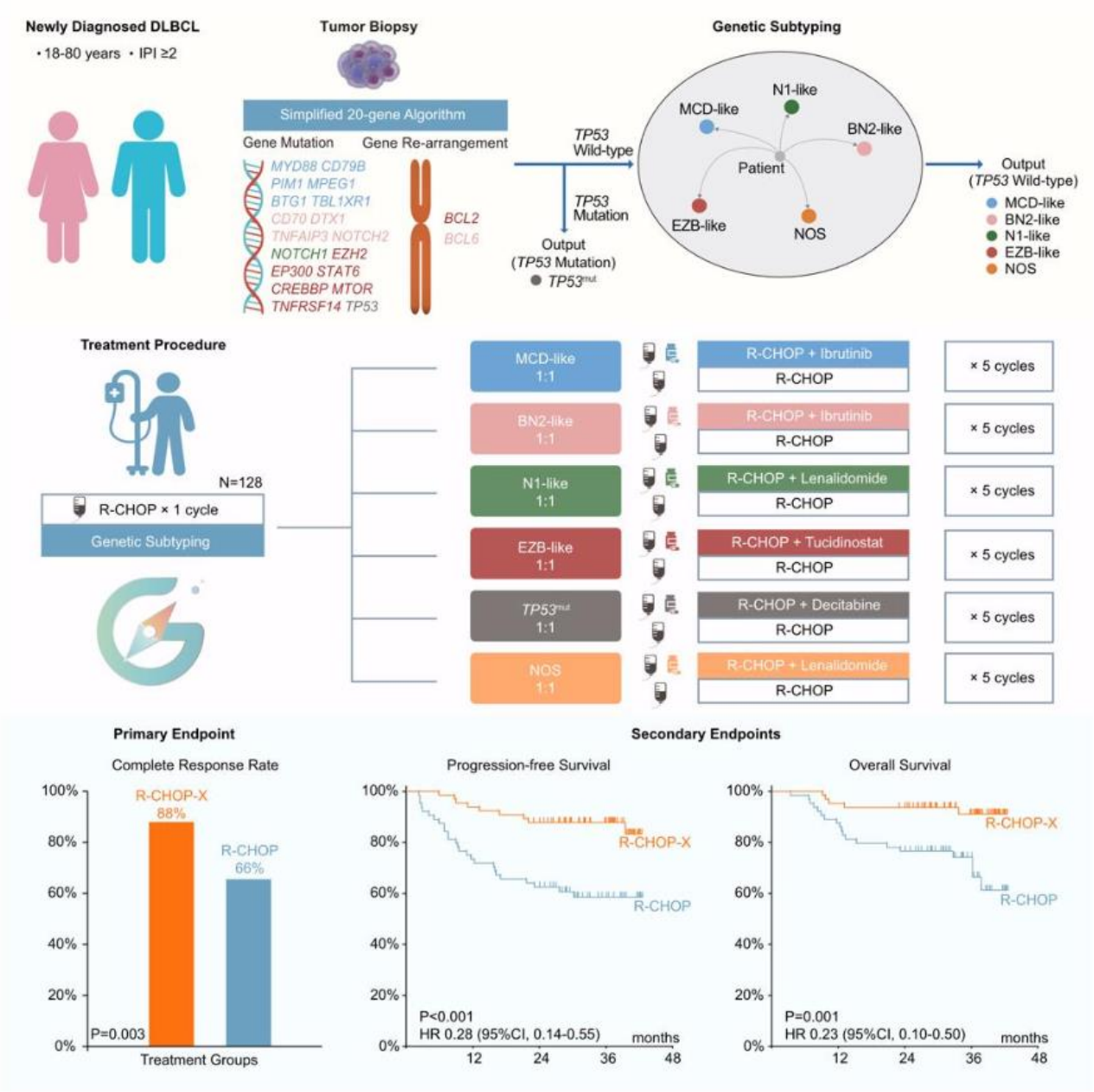


- Patients with C5 DLBCLs – 5-yr PFS higher in Pola-R-CHP versus R-CHOP treatment arm
  - Pola-R-CHP **70.4%** (95%CI 57.6-86.1)
  - R-CHOP **42.0%** (95% CI 28.0-63.0)

Calabretta E, et al. *Hematol Oncol*. 2025;43(Suppl 3):LBA1

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Guidance: R-CHOP + X

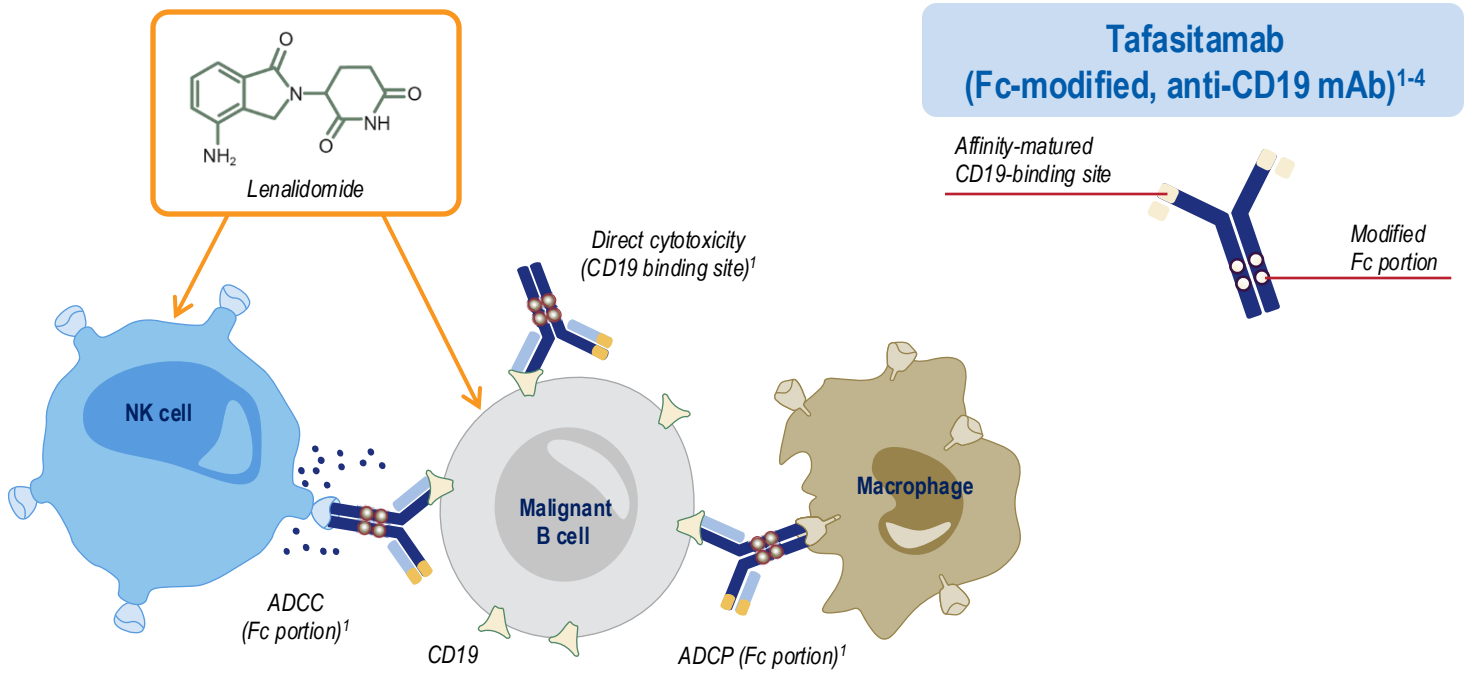


Zhang MC, et al. *Cancer Cell*. 2023;41(10):1705-1716.e5.

Background: Tafasitamab

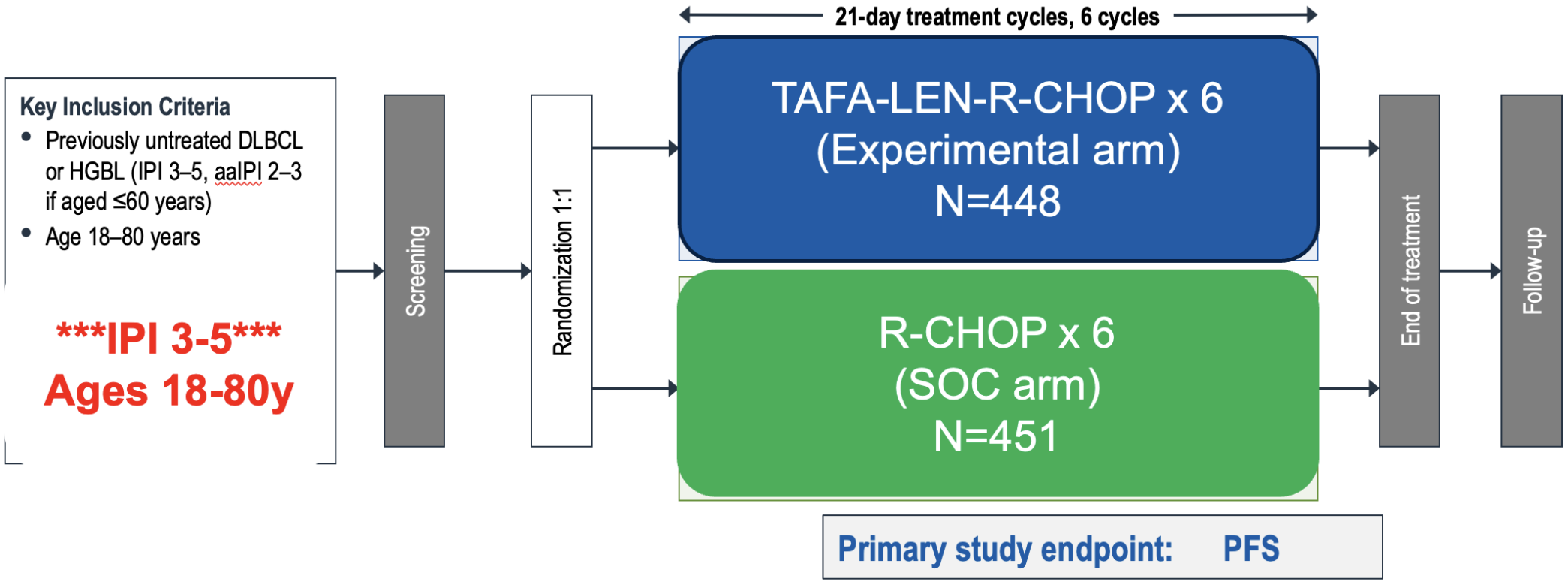
- Tafasitamab targets CD19 on malignant B cells
- The engineered Fc region increases affinity to immune effector cells
- Lenalidomide expands and activates effector cell activation and increases ADCC, ACDP, and direct cell death caused by tafasitamab

Tafasitamab + Lenalidomide Synergism in B-cell Lymphomas*



ADCC = antibody-dependent cellular cytotoxicity; ADCP = antibody-dependent cell-mediated phagocytosis; mAb = monoclonal antibody.
*Adapted from Düll J, et al. *Ther Adv Hematol*. 2021:12:20406207211027458. 1. Horton HM, et al. *Cancer Res*. 2008;68:8049-8057. 2. Awan FT, et al. *Blood*. 2010;115(6):1204-1213. 3. Woyach JA, et al. *Blood*. 2014;124(24):3553-3560. 4. Jurczak W, et al. *Ann Oncol*. 2018;29(5):1266-1272.

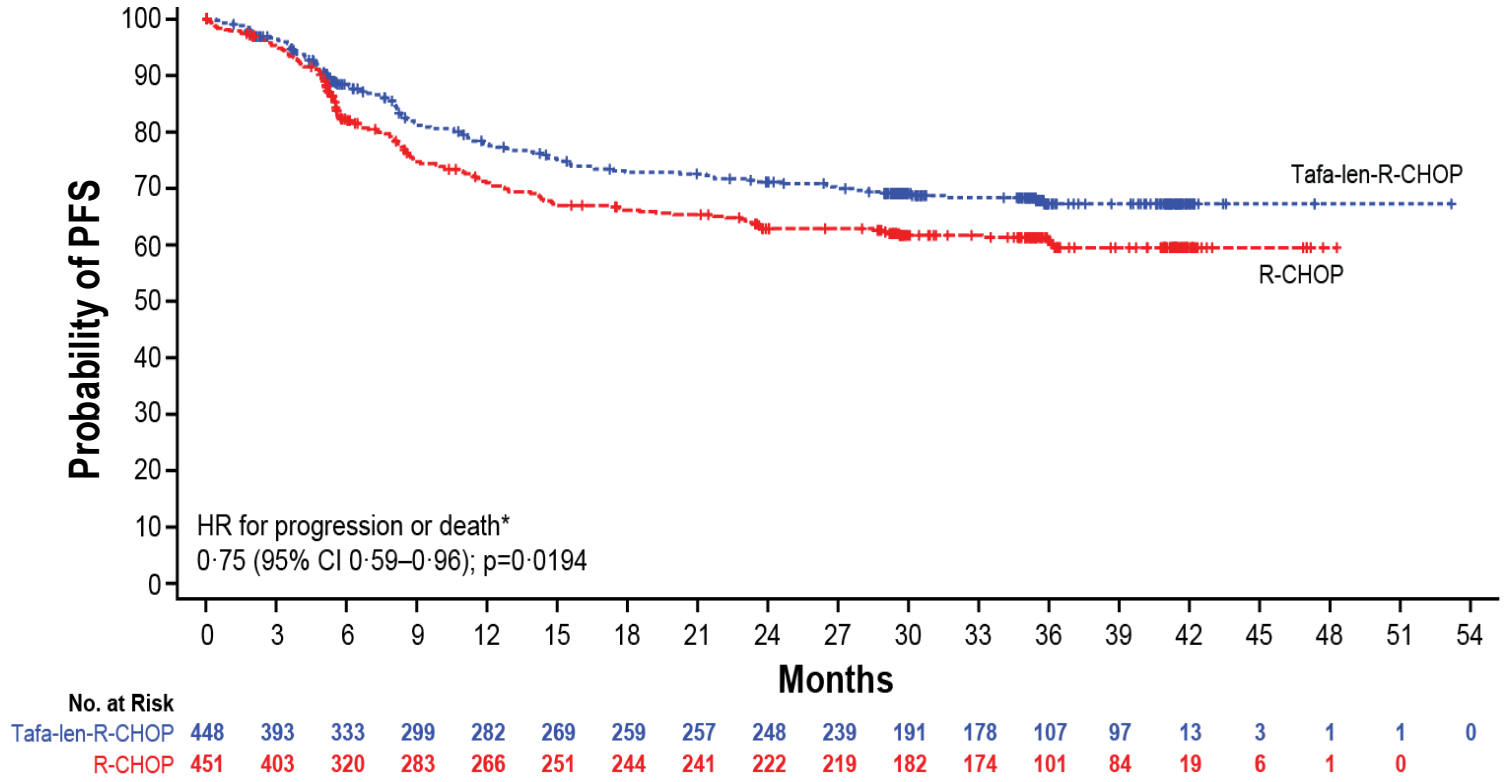
frontMIND (NCT04824092): Phase 3, Global, Multicenter, Placebo-Controlled, Double-Blind, Randomized Study



HGBL = high-grade B-cell lymphoma; aaIPI = age-adjusted IPI.
Lenz G, et al. Presented at: 67th American Society of Hematology (ASH) Annual Meeting & Exposition; 2025. Abstract 7000.

PFS by Investigator Assessment (Primary Endpoint)

Tafa-Len-R-CHOP significantly improved PFS versus R-CHOP.



Median follow-up of 35.2 months

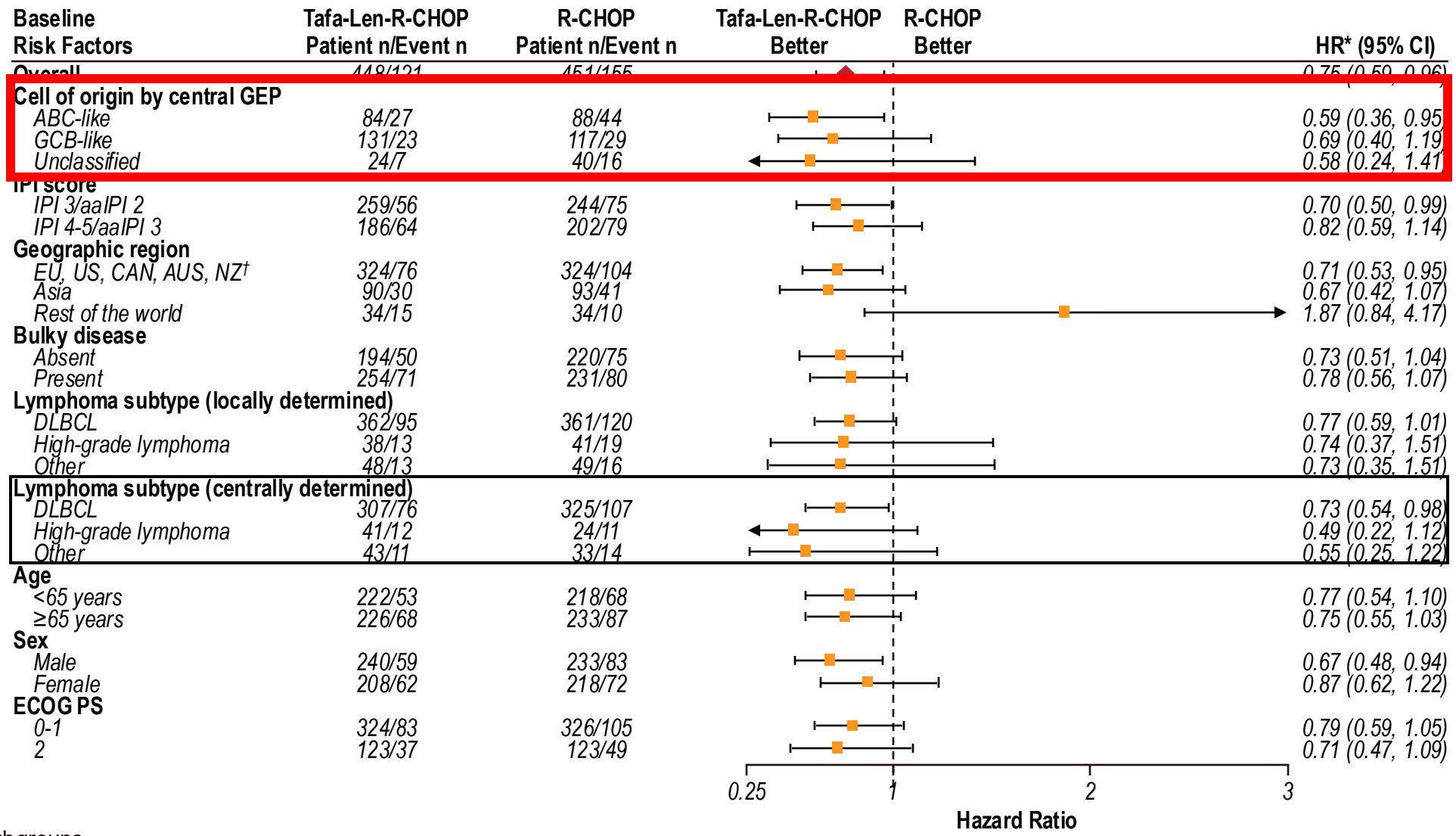
HR 0.75* (***P*=0.0194**)
95% CI 0.59-0.96

- A **25% reduction in risk of progression or death** demonstrated with Tafa-Len-R-CHOP vs R-CHOP
- **2-year PFS:**
  71.1% with Tafa-Len-R-CHOP vs 62.9% with R-CHOP (Δ**=8.2%**)
- **3-year PFS:**
  67.3% with Tafa-Len-R-CHOP vs 60.7% with R-CHOP (Δ**=6.6%**)

ITT population. *Calculated using a stratified Cox proportional hazards model.
Lenz G, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 2026. Abstract 7000.

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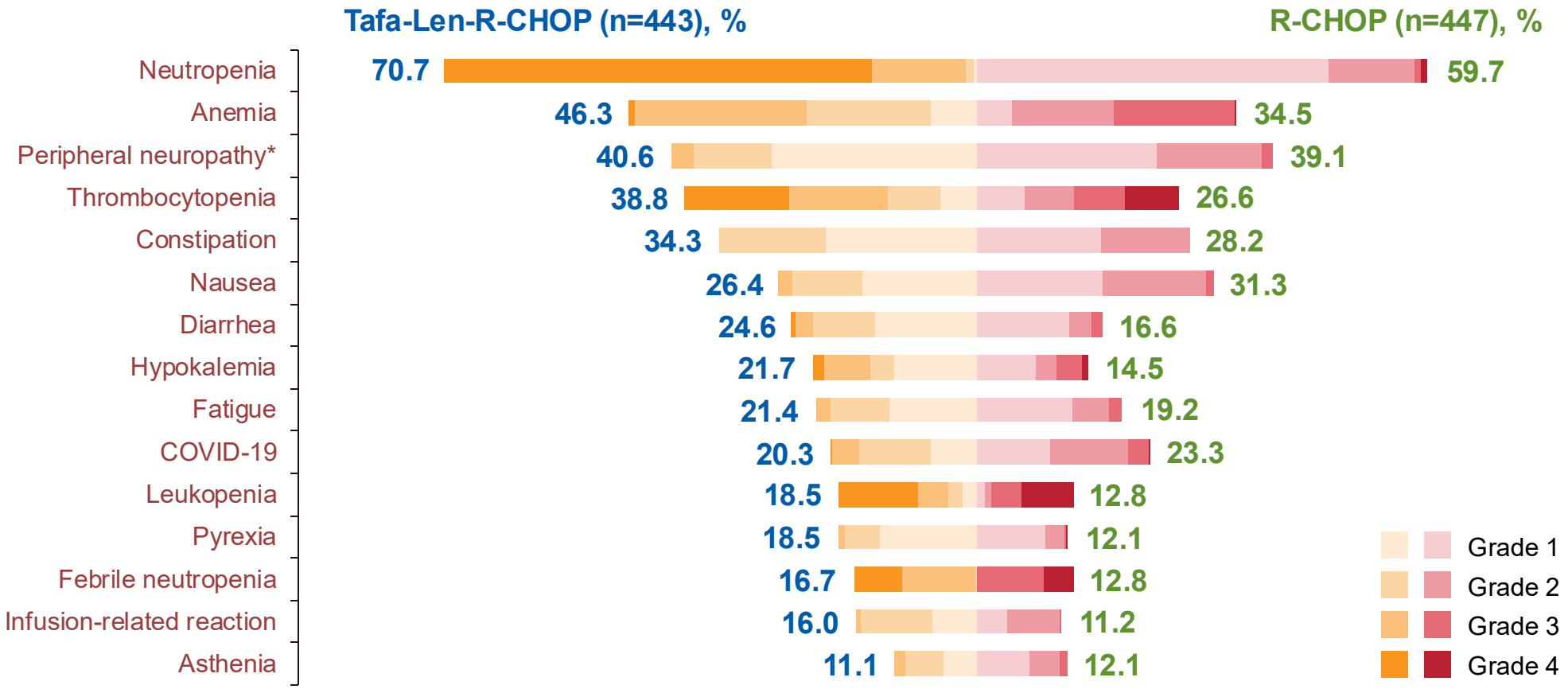
PFS by Investigator Assessment



Prespecified subgroups.
ITT population. *Calculated using a stratified Cox proportional hazards model. †Europe, USA, Canada, Australia, and New Zealand.
GEP = gene expression profiling.
Lenz G, et al. Presented at: ASCO Annual Meeting; 2026. Abstract 7000.

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DLBCL: Most Frequent TEAEs (≥12% in Any Group)



- **Most common** adverse events were **cytopenias and infectious events**
- Rate of **serious febrile neutropenia**: 13% with Tafa-Len-R-CHOP and 10% with R-CHOP

Safety population. TEAEs are Medical Dictionary for Regulatory Activities, version 27·1, Preferred Terms. *Includes standard organ class group of preferred terms.
TEAE = treatment-emergent adverse event.
Lenz G, et al. Presented at: ASCO Annual Meeting; 2026. Abstract 7000.

Considerations Regarding frontMIND

- Improved PFS
- Feasible and tolerable
- Activity across biologic subgroups

- Increased cytopenias in investigational arm
- No difference in OS
- Weekly infusions for all six cycles

Qualls D, et al. *Blood.* 2025;145(2):176-189.

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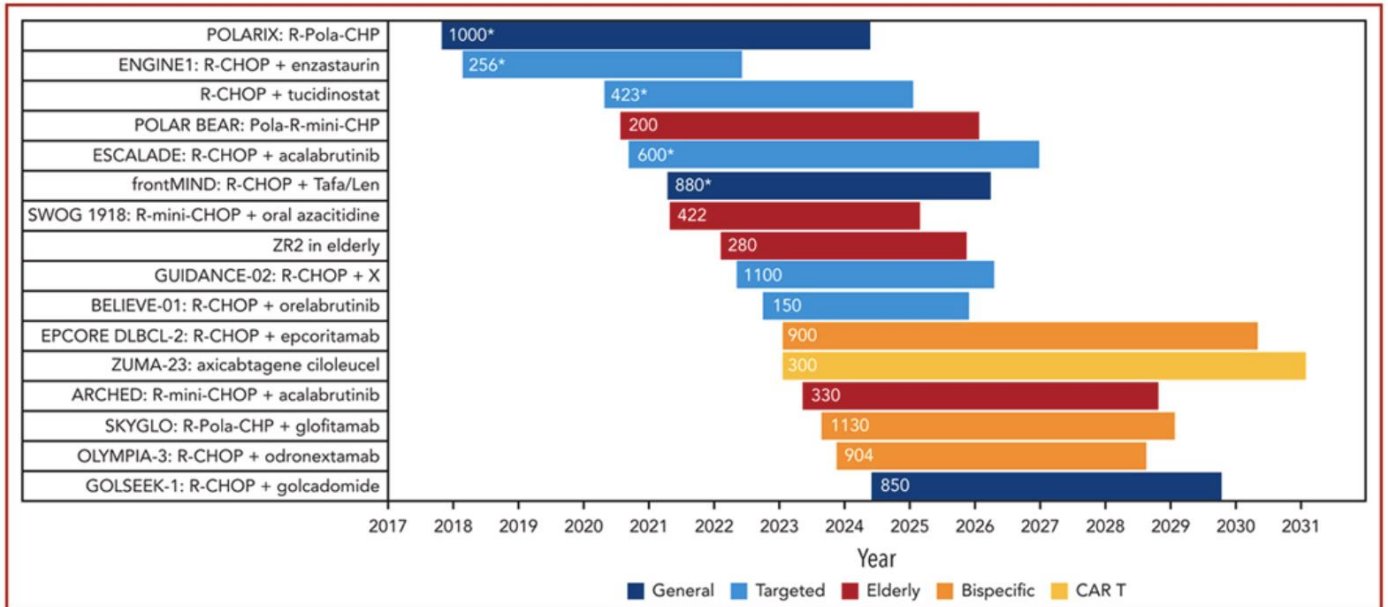
EPCORE-DLBCL-2

Epcoritamab Plus R-CHOP Improves PFS in Frontline DLBCL

- Phase 3 interim analysis
- Newly diagnosed DLBCL
- HR 0.49
- PFS vs R-CHOP, IPI 3-5 (primary population)

Medical Professionals Reference [www.empr.com]. Last updated October 5, 2026. https://www.empr.com/news/epcoritamab-r-chop-newly-diagnosed-dlbcl.

Timeline of Ongoing Frontline Trials in Large B Cell Lymphoma (LBCL)



Conclusions: **At least 15 ongoing phase 3 clinical trials may impact the frontline treatment of LBCL. Differences in inclusion criteria, interventions, primary outcomes, and generalizability may inform how these trials are implemented.**

*Qualls et al. DOI: 10.1182/**blood**.2023023789*

Visual Abstract

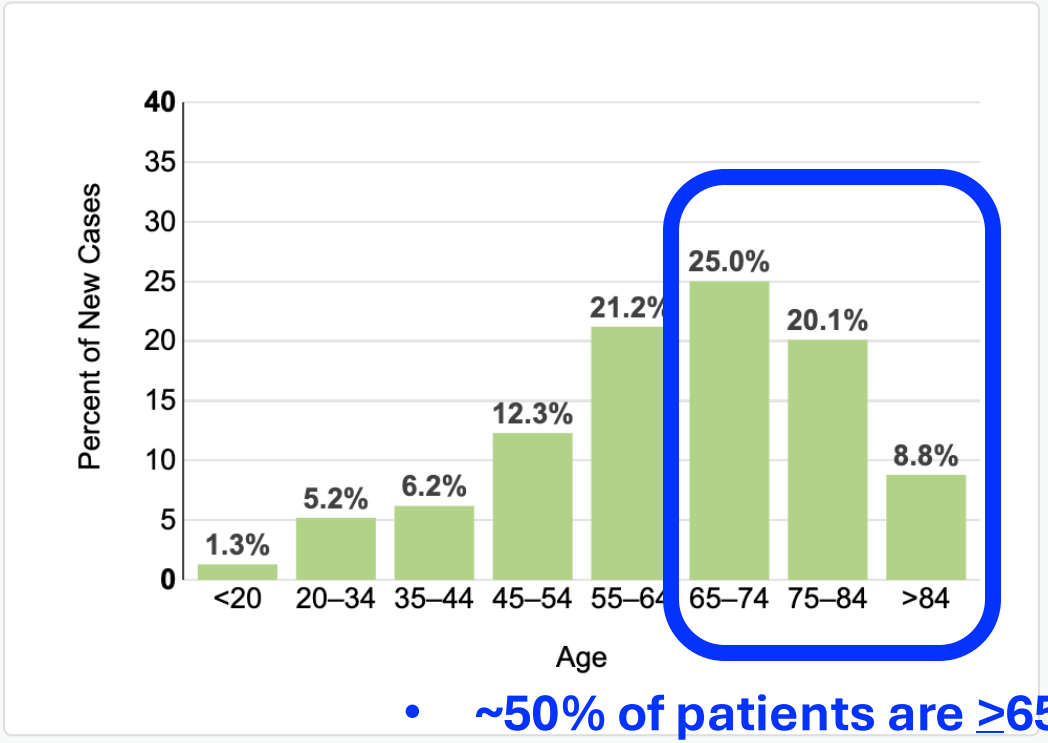
**Only a minority are designed as precision trials.*

Qualls D, et al. *Blood*. 2025;145(2):176-189.

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Most Patients with DLBCL Are Older

Percent of New Cases by Age Group: Diffuse Large B-Cell Lymphoma



Diffuse large B-cell lymphoma is most frequently diagnosed among people aged 65–74.

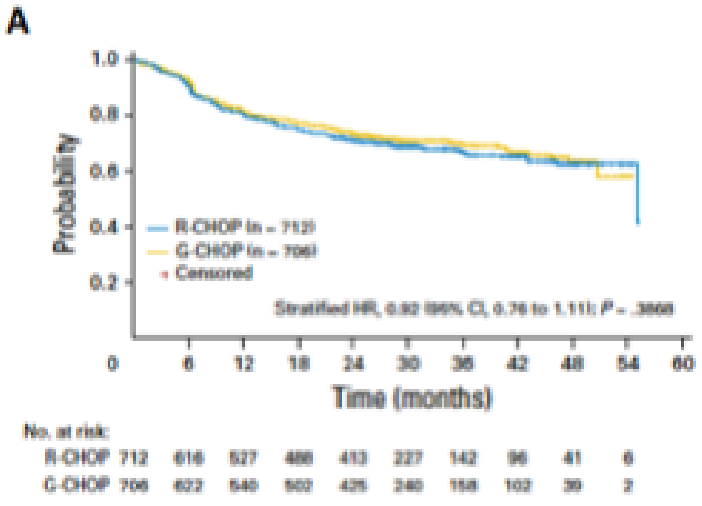
Median Age At Diagnosis
66

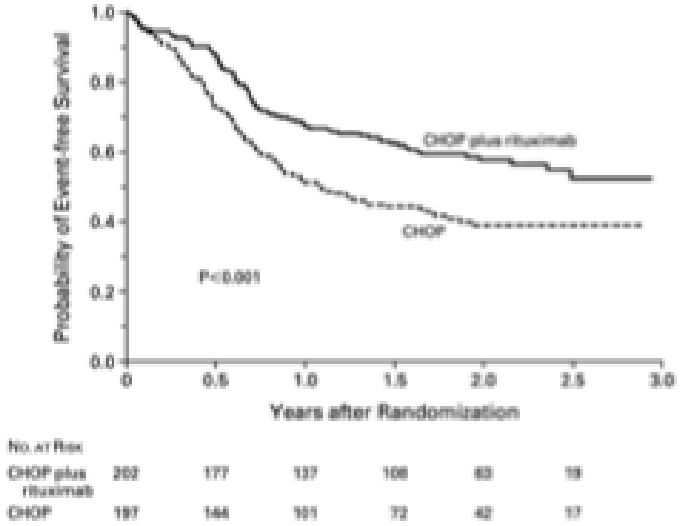
- ~50% of patients are ≥65y
- ~30% of patients are ≥75y

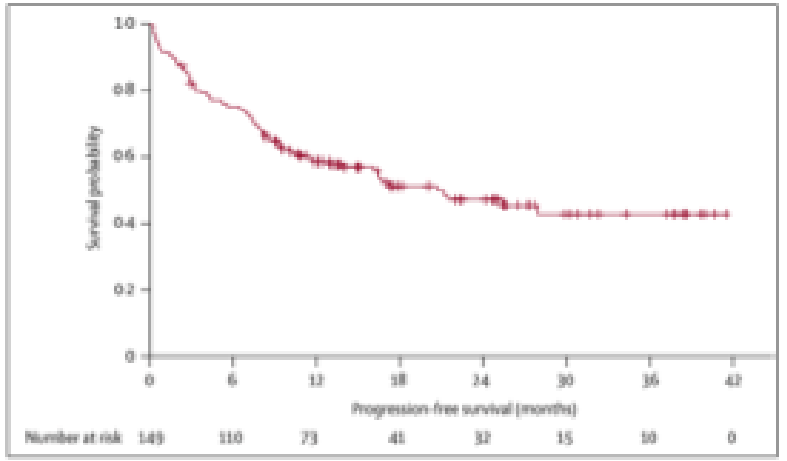
SEER 21 2013–2017, All Races, Both Sexes

National Institutes of Health (NIH) National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results Program (SEER) [seer.cancer.gov]. https://seer.cancer.gov/statfacts/html/dlbcl.html.

Relapse Risk by Age Group







GOYA trial:
Med age 62y
PFS @3y 70%

LNH98.5 trial:
Med age 69y
EFS @2y 57%

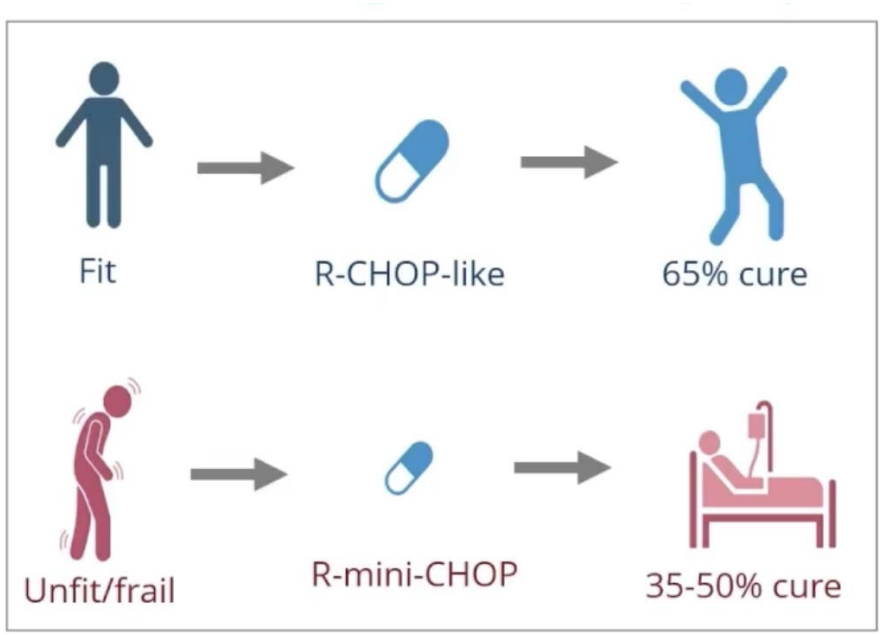
R-miniCHOP trial:
Med age 83y
EFS @2y 47%

EFS = event-free survival.

Vitolo U, et al. *J Clin Oncol*. 2017;35(31):3529-3537. Coiffier B, et al. *N Engl J Med*. 2002;346(4):235-242. Peyrade F, et al. *Lancet Oncol*. 2011;12(5):460-468

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Initial Treatment of Diffuse Large B-Cell Lymphoma in Older Adults Is Evolving



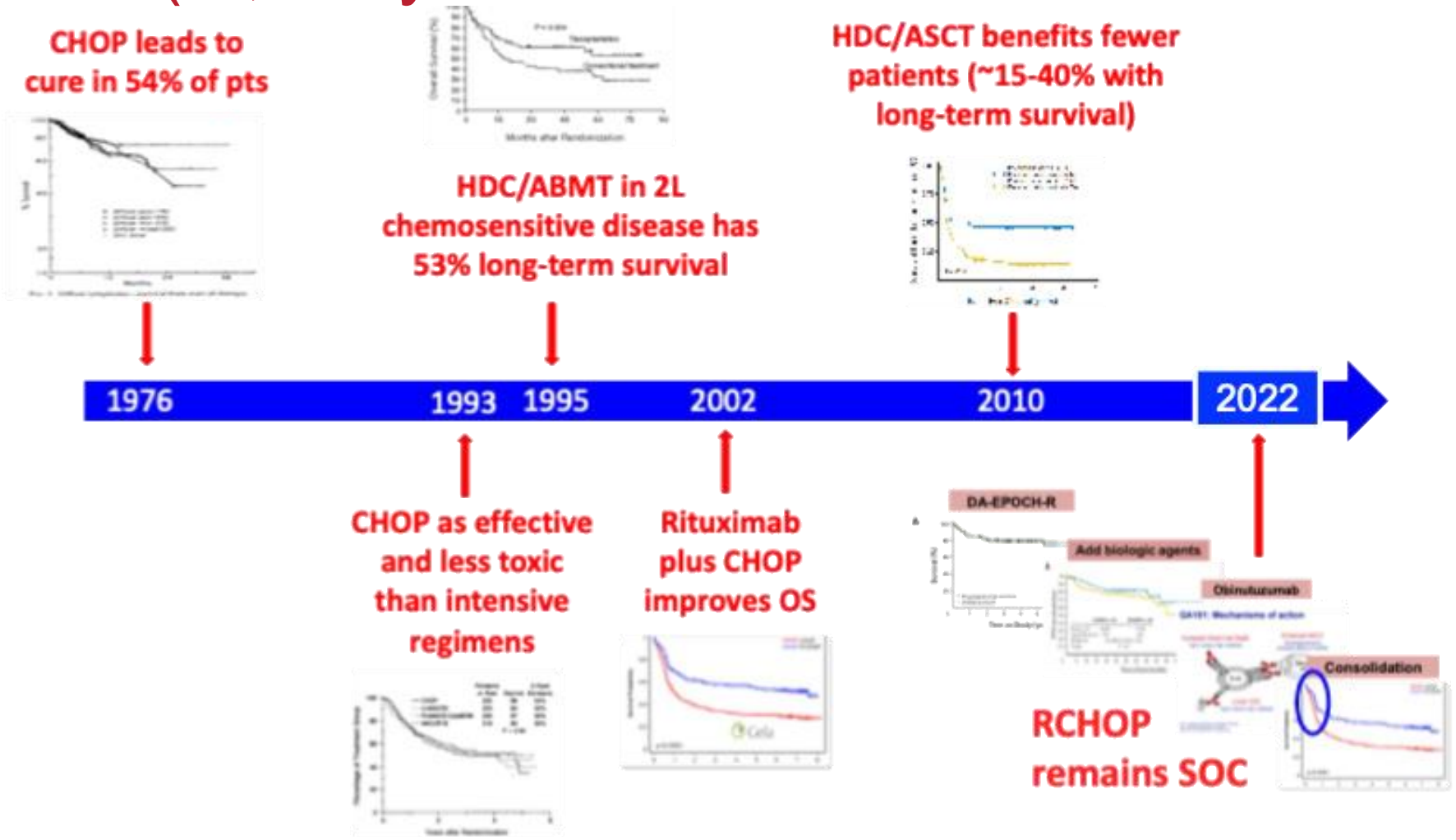
Unmet medical need

Promising new approaches from ASH 2025/EHA 2026

1) R-Pola-Glo (rituximab, polatuzumab vedotin, glofitamab)
2) Mosunetuzumab monotherapy
3) Epcoritamab monotherapy
4) Epcoritamab plus R-mini-CHOP

EHA = European Hematology Association.
Chapuy B, et al. *Blood.* 2025;146(Suppl 1):61.

The Past…(or, Why We Care about Frontline Treatment)



HDC = high-dose chemotherapy; ABMT = autologous bone marrow transplant; ASCT = autologous SCT; SOC = standard of care.

The Present…

- R-CHOP/R-mini-CHOP
- Pola-R-CHP (POLARIX trial)
- Tafa-len-R-CHOP (Frontmind trial)*
- Epco-R-CHOP (EPCORE-DLBCL-2)*

* Not FDA-approved.

The Future…

?	?	?
Clinical approaches	***Precision approaches***	***"Empiric" approaches***
IPI, stage	Transcriptomics	Bispecific agents
Age	LymphGen	CelMods
Response-adapted (PET/ctDNA/MRD)	DLBclass	Degraders
	Immune archetypes	Etc.…

MRD = measurable residual disease.

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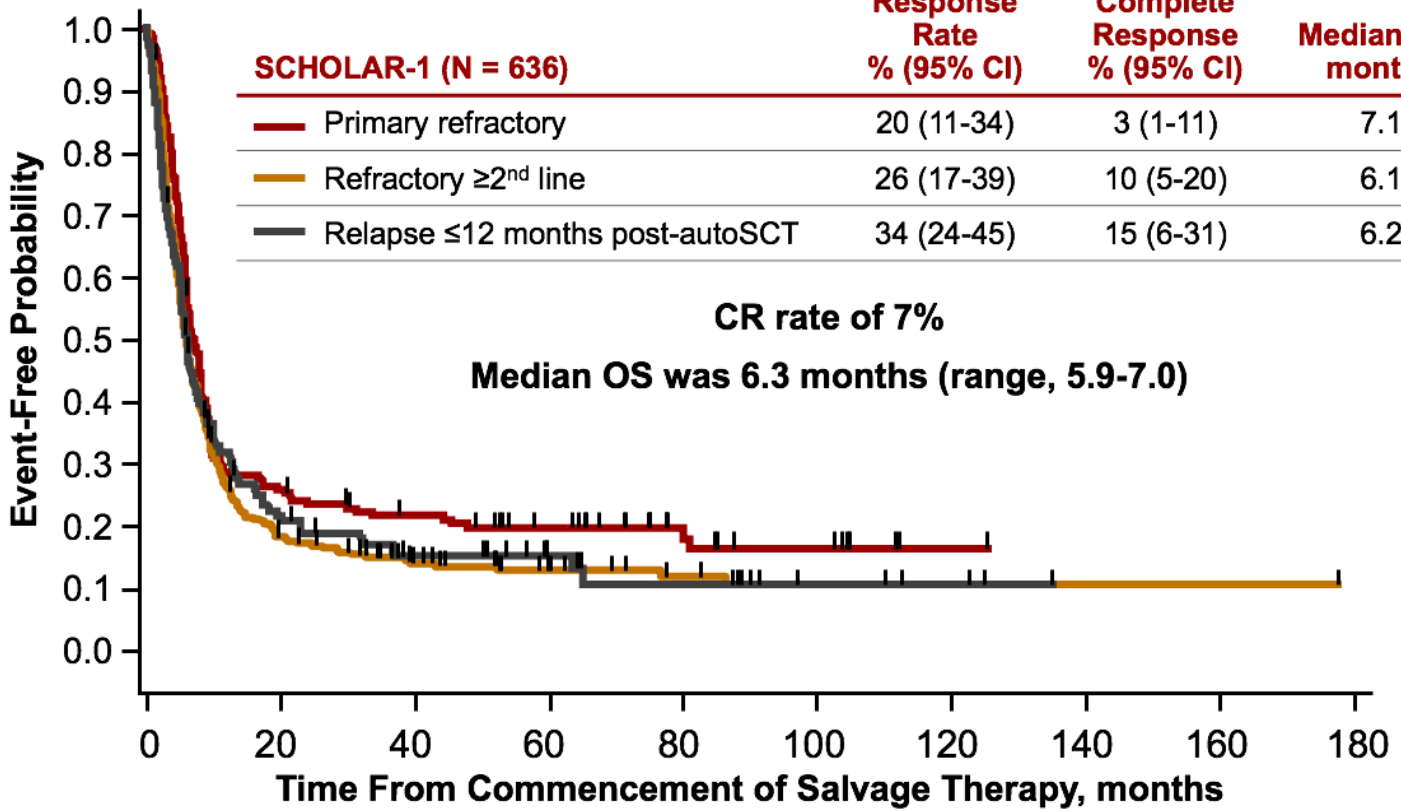
Phase 1: Strategies for Frail and Unfit Patients

A Case to Keep in Mind…

- Case study: A 78-year-old frail patient with rapidly progressing R/R DLBCL requires an individualized, outpatient treatment strategy to gain disease control
- He lives approximately 80 miles from the nearest academic center and relies for transportation on a 77-year-old spouse who will not drive on the highway

Pre-2017: Pts with R/R DLBCL Unable to Undergo Autologous Stem Cell Transplant Have Median Survivals <1 Year

SCHOLAR-1 (N = 636)	Response Rate % (95% CI)	Complete Response % (95% CI)	Median OS, months
Primary refractory	20 (11-34)	3 (1-11)	7.1
Refractory ≥2nd line	26 (17-39)	10 (5-20)	6.1
Relapse ≤12 months post-autoSCT	34 (24-45)	15 (6-31)	6.2



SCHOLAR-1 analysis was in trial-enrolled patients and does not include “real-world” patients

OS = overall survival.
Crump M, et al. *Blood*. 2017;130(16):1800-1808

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Evolving Treatment Landscape for DLBCL

Newly diagnosed advanced-stage DLBCL

↓

IPI 0-1: R-CHOP
IPI 2-5: Pola-R-CHP
IPI 3-5: Tafa-len R-CHOP*

↓

Refractory or relapse <12 m and CAR T available:
Axi-cel
Liso-cel

Refractory or relapse <12 m and CAR T not available:
Epco or glofit plus GEMOX, tafa-len, pola-BR, mosun-pola, glofit plus pola

Relapse >12 m and fit:
Chemo plus autoHCT

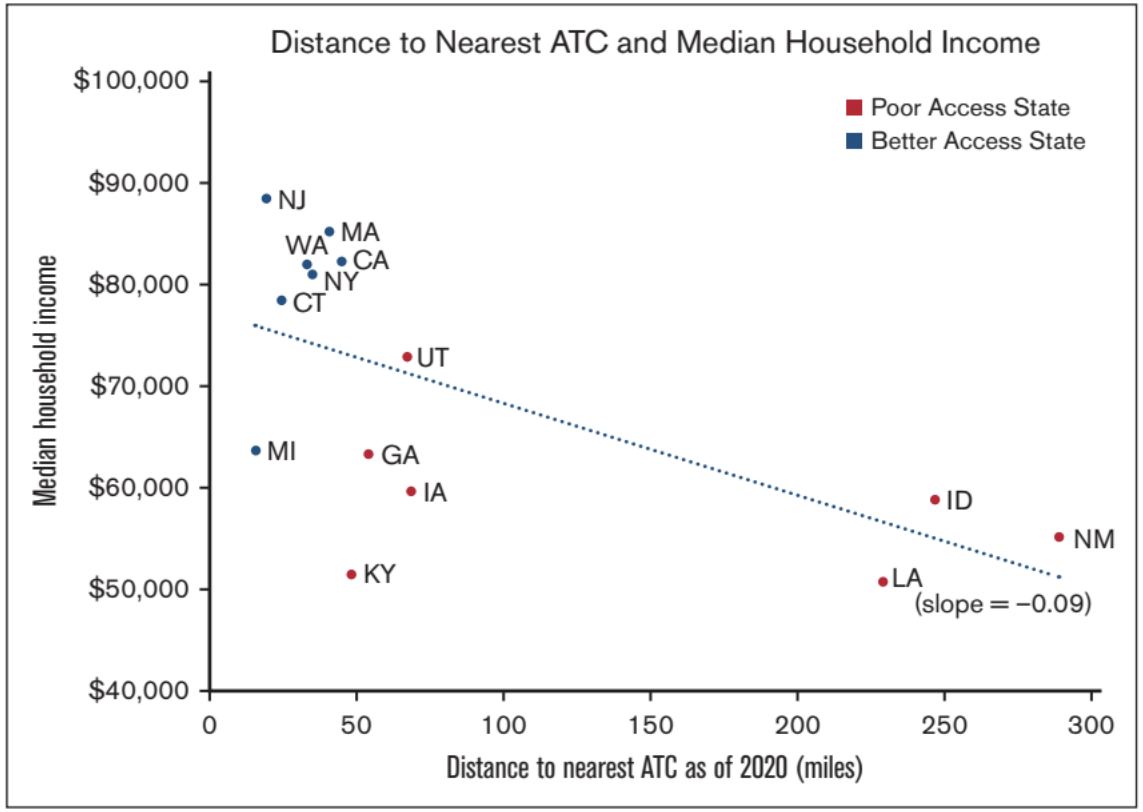
Relapse >12 m and frail:
Liso-cel
(plus all 2L options)

↓

3L+:
Axi-cel, liso-cel, tisa-cel, glofitamab or epcoritamab +/- GEMOX, tafa-len, pola-BR, lonca, BV-LenR, mosun-pola, glofit plus pola, selinexor

autoHCT = autologous hematopoietic cell transplantation; BR = bendamustine, rituximab; BV = brentuximab vedotin; 2L = second-line; 3L = third-line.

ACCESS: Impact of Geography and Median Income on CAR T Access (SEER Analysis)…The Majority of Patients Eligible for CAR T Do Not Receive CAR T



- Between 2017 and 2020, **2241** patients were treated for 3L+ DLBCL (SEER Medicare data)
- **122 (5.4%) received CAR T**
- CAR T recipients were less likely to have multiple comorbidities (odds ratio [OR], 0.904; *P*=.001) but more likely to live in higher income areas (OR, 1.176; *P*=.004)
- If distance to the nearest ATC for “poor-access” states (average distance to ATC, 104.4 miles) decreased to the average distance in “better access” states (34.2 miles), there would be a 37.6% increase in number of patients receiving CAR Ts (6.6%-9.1%; *P*<.001)

SEER = National Institutes of Health (NIH) National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results program; ATC = authorized treatment center.
Chung AP, et al. *Blood Adv*. 2025;9(18):4727-4735.

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Evolving Treatment Landscape for DLBCL

Newly diagnosed advanced-stage DLBCL

↓

IPI 0-1: R-CHOP
IPI 2-5: Pola-R-CHP
IPI 3-5: Tafa-len R-CHOP*

↓

Refractory or relapse <12 m and CAR T available:
Axi-cel
Liso-cel

Refractory or relapse <12 m and CAR T not available:
Epco or glofit plus GEMOX, tafa-len, pola-BR, mosun-pola, glofit plus pola

Relapse >12 m and fit:
Chemo plus autoHCT

Relapse >12 m and frail:
Liso-cel
(plus all 2L options)

↓

3L+:
Axi-cel, liso-cel, tisa-cel, glofitamab or epcoritamab +/- GEMOX, tafa-len, pola-BR, lonca, BV-LenR, mosun-pola, glofit plus pola, selinexor

R/R DLBCL: Non-CAR T

Anti-CD19

ADCs

BsAbs

Chemo (R-GEMOX)

R-GEMOX = rituximab, gemcitabine, oxaliplatin.

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National Comprehensive Cancer Network® (NCCN®) Guidelines Include Options for Frail/Unfit Pts (2L)

Primary refractory or relapse <12 months

No Intention to Proceed to Transplant

Preferred (in alphabetical order by category)
- CAR T-cell therapy (CD19-directed)[l] (with pre/postpheresis therapy as needed; BCEL-C 2 of 7) (if eligible)
  - Lisocabtagene maraleucel
- GEMOX + Epcoritamab-bysp[n,o]
- GEMOX + Glofitamab-gxbm[n,o]
- GEMOX[n] + Polatuzumab vedotin-piiq + Rituximab
- Lenalidomide + Tafasitamab-cxix[p]
- Polatuzumab vedotin-piiq ± Bendamustine[m] ± Rituximab
- Mosunetuzumab-axgb (IV or SC)[n,o,q] + Polatuzumab vedotin-piiq
- Glofitamab-gxbm[n,o] + Polatuzumab vedotin-piiq (category 2B)

Other recommended (in alphabetical order)
- CEOP ± Rituximab
- GDP ± Rituximab
- GEMOX ± Rituximab (if unable to receive epcoritamab-bysp, glofitamab-gxbm, or polatuzumab vedotin-piiq)
- Rituximab

Useful in certain circumstances
- Brentuximab vedotin
- Ibrutinib[n] (non-GCB DLBCL)
- Lenalidomide ± Rituximab (non-GCB DLBCL)

Relapse >12 months

No Intention to Proceed to Transplant

Preferred (in alphabetical order by category)
- CAR T-cell therapy (CD19-directed)[l] (with pre/postpheresis therapy as needed; BCEL-C 2 of 7) (if eligible)
  - Lisocabtagene maraleucel
- GEMOX + Epcoritamab-bysp[n,o]
- GEMOX + Glofitamab-gxbm[n,o]
- Lenalidomide + Tafasitamab-cxix[p]
- Polatuzumab vedotin-piiq ± Bendamustine[m] ± Rituximab
- Glofitamab-gxbm[n,o] + Polatuzumab vedotin-piiq (category 2B)

Other recommended (in alphabetical order)
- CEOP ± Rituximab
- GDP ± Rituximab
- GEMOX ± Rituximab (if unable to receive epcoritamab-bysp, glofitamab-gxbm, or polatuzumab vedotin-piiq)
- Rituximab

Useful in certain circumstances
- Brentuximab vedotin
- Ibrutinib[n] (non-GCB DLBCL)
- Lenalidomide ± Rituximab (non-GCB DLBCL)

CEOP = cyclophosphamide, etoposide, vincristine, prednisone; GDP = gemcitabine, dexamethasone, cisplatin.

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NCCN Guidelines Include Options for Frail/Unfit Pts (3L+)

THIRD-LINE AND SUBSEQUENT THERAPY

Second-line therapy regimens (BCEL-C 2 of 7 and BCEL-C 3 of 7) that were not previously given can also be used as options for third-line and subsequent therapy

Preferred	Other recommended
• T-cell mediated therapy[o] ▸ CAR T-cell therapy[l,p,r] (preferred) (in alphabetical order) ◊ Axicabtagene ciloleucel (CD19-directed) ◊ Lisocabtagene maraleucel (CD19-directed) ◊ Tisagenlecleucel (CD19-directed) ▸ Bispecific antibody therapy (including patients with disease progression after transplant or CAR T-cell therapy) (in alphabetical order) ◊ Epcoritamab-bysp[n] ◊ Glofitamab-gxbm[n]	• Lenalidomide + Brentuximab vedotin + Rituximab • Loncastuximab tesirine-lpyl[p] • Selinexor (including patients with disease progression after transplant or CAR T-cell therapy)

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Phase 2 Trial of Polatuzumab Vedotin plus BR



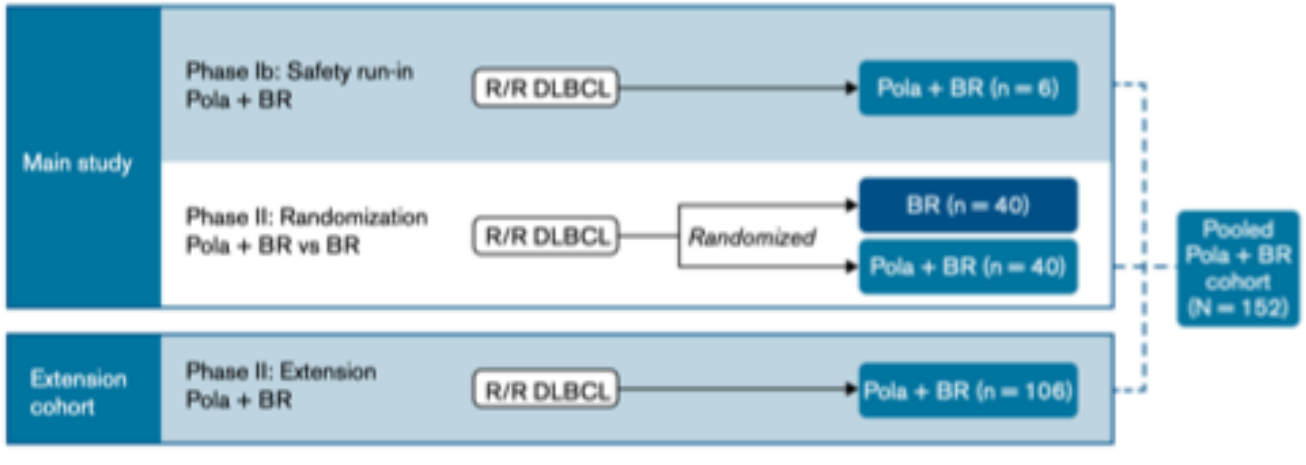
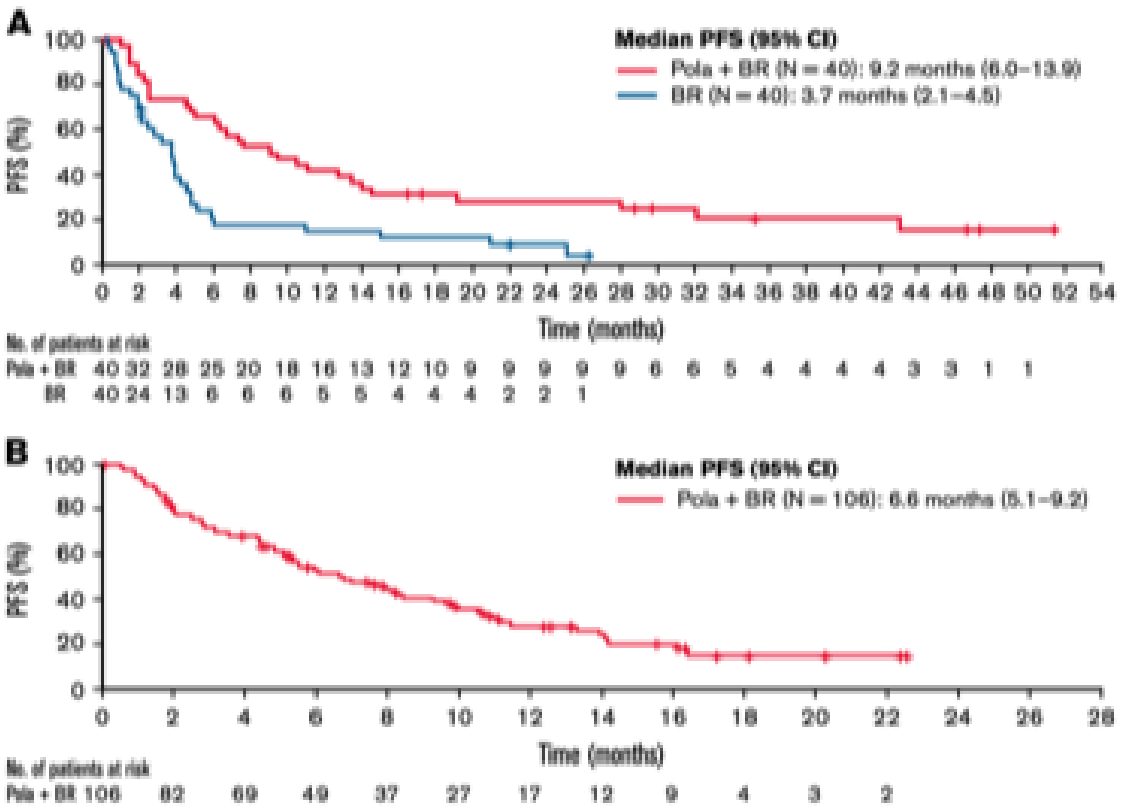


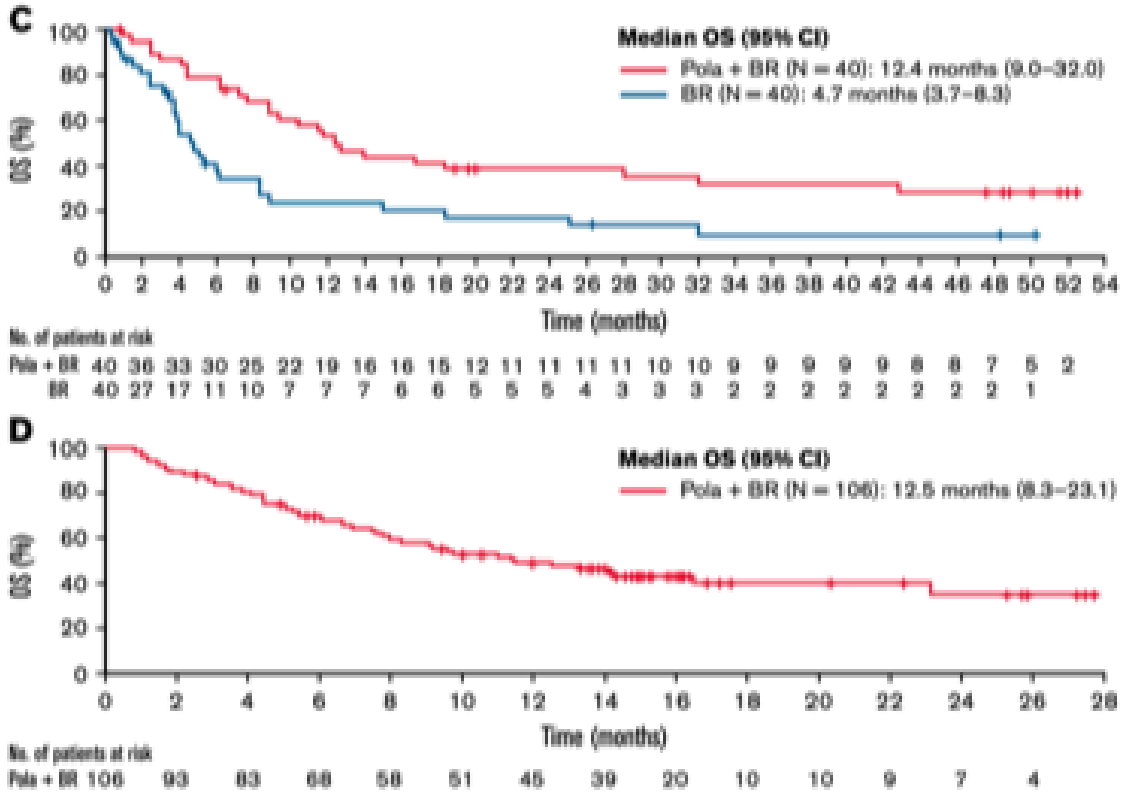
Table 1. Patient demographic and baseline clinical characteristics

ITT	Randomized		Extension cohort, pola + BR (n = 106)	Pooled, pola + BR (N = 152)
	BR (n = 40)	pola + BR (n = 40)		
Median (range) age, y	71 (30-84)	67 (33-86)	70 (24-94)	69 (24-94)
Age ≥65 y	26 (65)	23 (58)	77 (73)	103 (68)
IPI score 3-5 at enrollment	29 (73)	22 (55)	70 (66)	94 (62)
Median no. of prior therapies (range)	2 (1-5)	2 (1-7)	2 (1-7)	2 (1-7)
1 line	12 (30)	11 (28)	37 (35)	50 (33)
2 lines	9 (23)	11 (28)	27 (26)	42 (28)
≥3 lines	19 (48)	18 (45)	42 (40)	60 (39)
Primary refractory*	28 (70)	21 (53)	73 (69)	97 (64)
Refractory to last prior therapy*	33 (83)	30 (75)	81 (76)	116 (76)

Sehn LH, et al. *Blood Adv.* 2022;6(2):533-543. Sehn LH, et al. *Blood.* 2017;130(Suppl 1):2821.

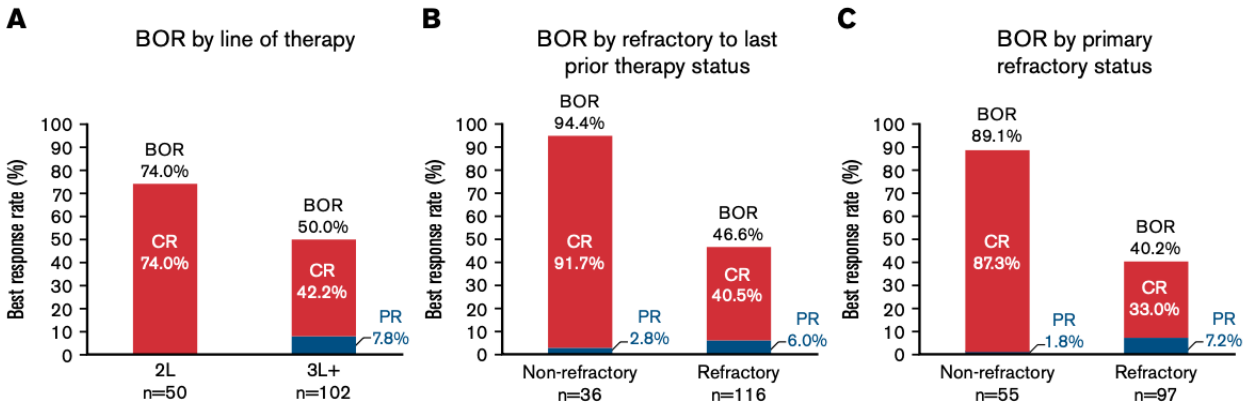
Pola-BR: Updated PFS Including Extension Cohort

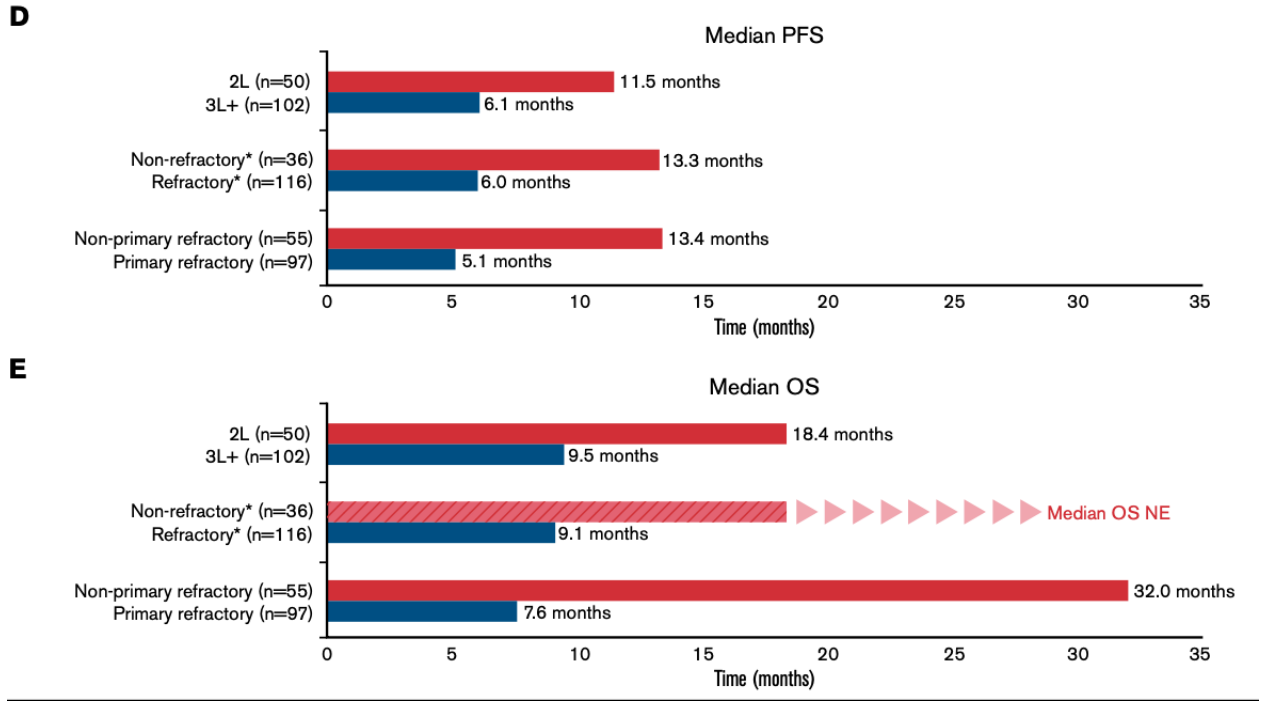




Sehn LH, et al. *Blood Adv.* 2022;6(2):533-543.

Pola-BR: Outcomes by Line of Therapy and Refractory Status





BOR = best overall response.

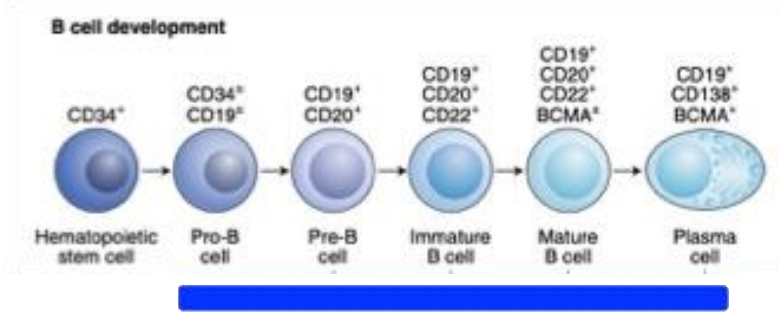
Sehn LH, et al. *Blood Adv.* 2022;6(2):533-543.

Considerations Regarding Polatuzumab Vedotin in R/R LBCL

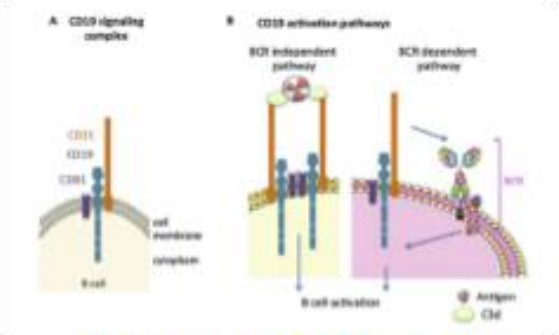
- Avoidance of bendamustine if CAR T is planned
- Peripheral neuropathy and cytopenias can be limiting
- Limited-duration approaches must be used

- Excellent partner with other regimens
- Combinations with BsAbs
  - SUNMO (polatuzumab vedotin plus mosunetuzumab)
- Combinations with chemotherapy
  - STARGLO (polatuzumab vedotin plus R-GEMOX)

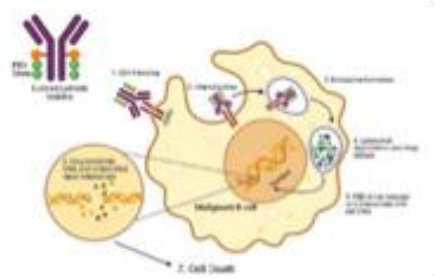
CD19 Targeting Key Principles



CD19 is a pan B-cell antigen



CD19 is part of a signaling complex with BCR dependent and independent pathways



CD19 internalizes within a lysosome

~~Naked antibodies~~

CAR T

Enhanced moAbs

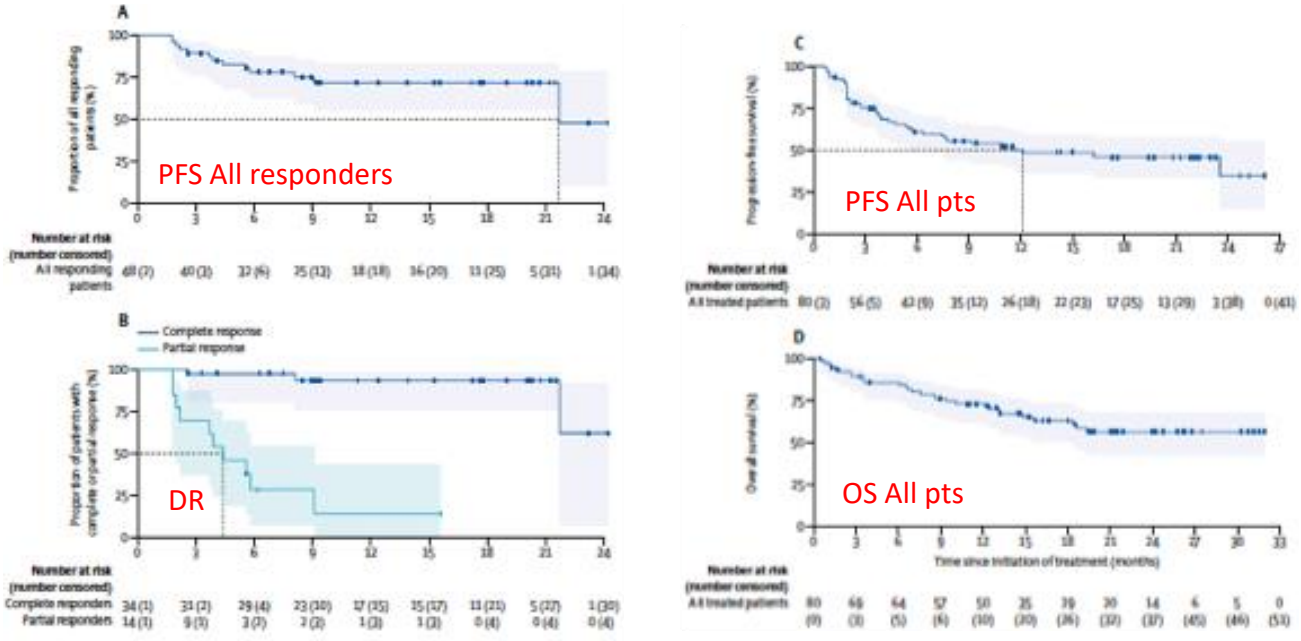
ADCs

Bispecific agents

moAb = monoclonal antibody.

MIlone MC, et al. *Nat Cancer*. 2021;2(8):780-793. Jakobczyk H, et al. *Int J Pharmaceutics*. 2017;532(2):813-824. Sermer D, et al. *Blood Rev*. 2023;57:101002.

L-MIND Results: Phase 2 Trial of Tafasitamab and Lenalidomide in RR DLBCL



- **Very long response duration for CR pts**
- **ORR 60%, CR 43%**
- **Med DR 22 m but NR for CR pts**

Patient characteristics:

N=81 with med age 72 y
50% of pts 2L
42% R-ref, 44% ref

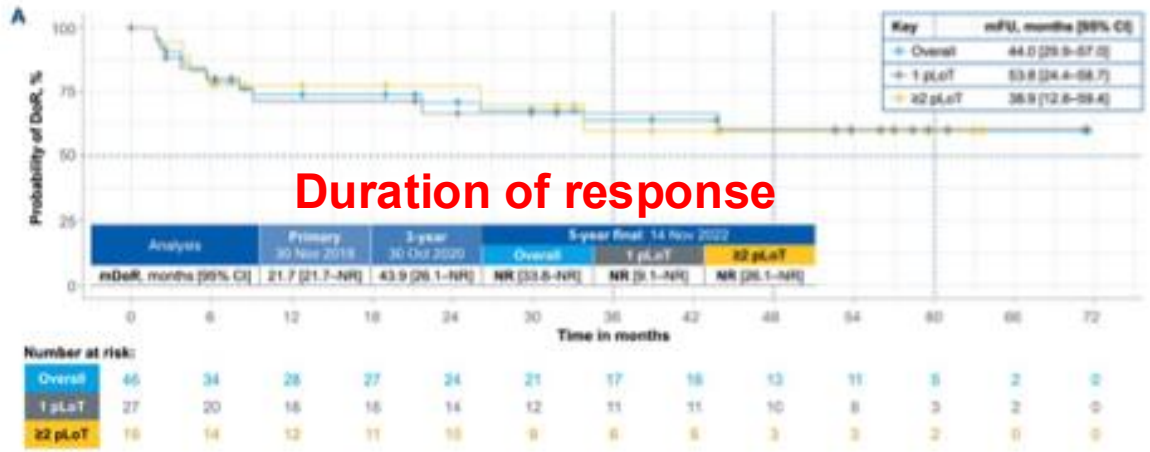
CR = complete response; DR = duration of response; ORR = objective response rate.
Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

Five-Year Follow-Up L-MIND Phase 2 Trial of Tafasitamab plus Lenalidomide in R/R DLBCL: Outcomes by Line of Treatment

Characteristics	All patients: full analysis set	1 prior line of therapy	≥2 prior lines of therapy
N	80	40	40
Age in years, median (range)	72.0 (41.0-86.0)	72.0 (53.0-86.0)	70.5 (41.0-82.0)
Age >70 years, N (%)	45 (56.3)	25 (62.5)	20 (50.0)
Prior lines, N (%)			
1	40 (50.0)	-	-
2	34 (42.5)	-	-
3	5 (6.3)	-	-
4	1 (1.3)	-	-
Primary refractory*, N (%)			
Yes	15 (18.8)	6 (15.0)	9 (22.5)
No	65 (81.3)	34 (85.0)	31 (77.5)
Refractory to previous line of therapy, N (%)			
Yes	35 (43.8)	6 (15.0)	29 (72.5)
No	45 (56.3)	34 (85.0)	11 (27.5)
Prior ASCT, N (%)			
Yes	9 (11.3)	2 (5.0)	7 (17.5)
No	71 (88.8)	38 (95.0)	33 (82.5)
Cell of origin (by IHC), N (%)			
GCB	38 (47.5)	16 (40.0)	22 (55.0)
Non-GCB	22 (27.5)	14 (35.0)	8 (20.0)
Unknown/NE	20 (25.0)	10 (25.0)	10 (25.0)

Duell J, et al. *Haematologica*. 2024;109(2):553-566.

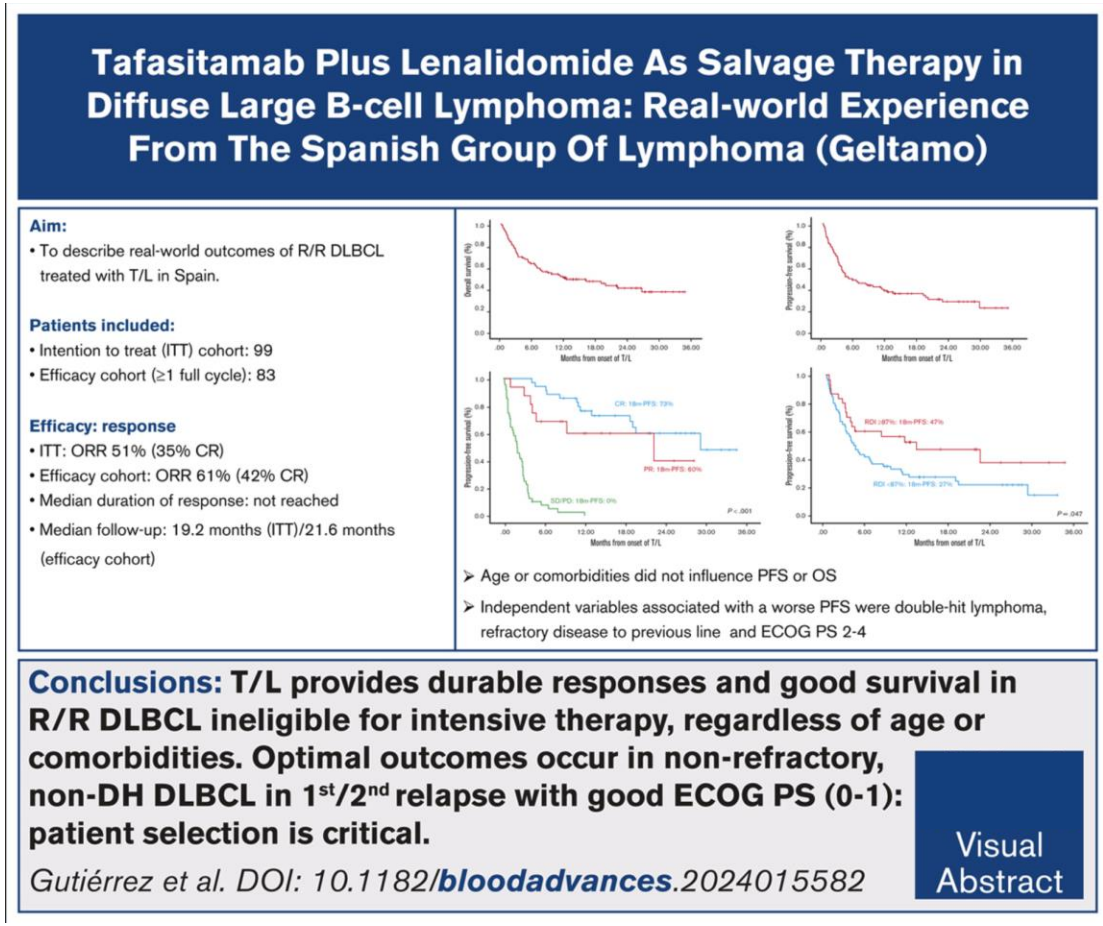
Five-Year Follow-Up L-MIND Phase 2 Trial of Tafasitamab plus Lenalidomide in R/R DLBCL: Outcomes by Line of Treatment



Duell J, et al. *Haematologica*. 2024;109(2):553-566.

Do the Clinical Trial Results Translate to the Real World?

- Zinzani PL, Rodgers T, Marino D, et al. RE-MIND: Comparing tafasitamab + lenalidomide (L-MIND) with a real-world lenalidomide monotherapy cohort in relapsed or refractory diffuse large B-cell lymphoma. Clin Cancer Res. DOI: 10.1158/1078-0432.CCR-21-1471
- Nowakowski GS, Yoon DH, Peters, et al. Improved efficacy of tafasitamab plus lenalidomide versus systemic therapies for relapsed/refractory DLBCL: RE-MIND2, an observational retrospective matched cohort study. Clin Cancer Res. 2022;28(18):4003-4017. DOI: 10.1158/1078-0432.CCR-21-3648
- Qualls DA, Lambert N, Caimi PF, et al. Tafasitamab and lenalidomide in large B-cell lymphoma: real-world outcomes in a multicenter retrospective study. Blood. 2023;142(26):2327-2331. DOI: 10.1182/blood.2023021274
- Saverno K. Real-world effectiveness of tafasitamab (Tafa) for the treatment of relapsed/refractory diffuse large B-Cell lymphoma (R/R DLBCL) in the United States. Poster Abstract #2375. Presented at: 66th American Society of Hematology Annual Meeting and Exposition; Dec 7–10, 2024; San Diego, US.
- Brem EA, Burke JM, Vukcevic M, et al. Realmind: A prospective and retrospective study to characterize real-world use of tafasitamab plus lenalidomide in US patients with relapsed/refractory diffuse large B-cell lymphoma, with a focus on patients from minority groups. Blood. 2023; 142 (Supplement 1): 6251. DOI: 10.1182/blood-2023-188482



Gutierrez A, et al. *Blood Adv*. 2025;9(19):4924-4935.

Considerations for Tafasitamab-Lenalidomide in DLBCL

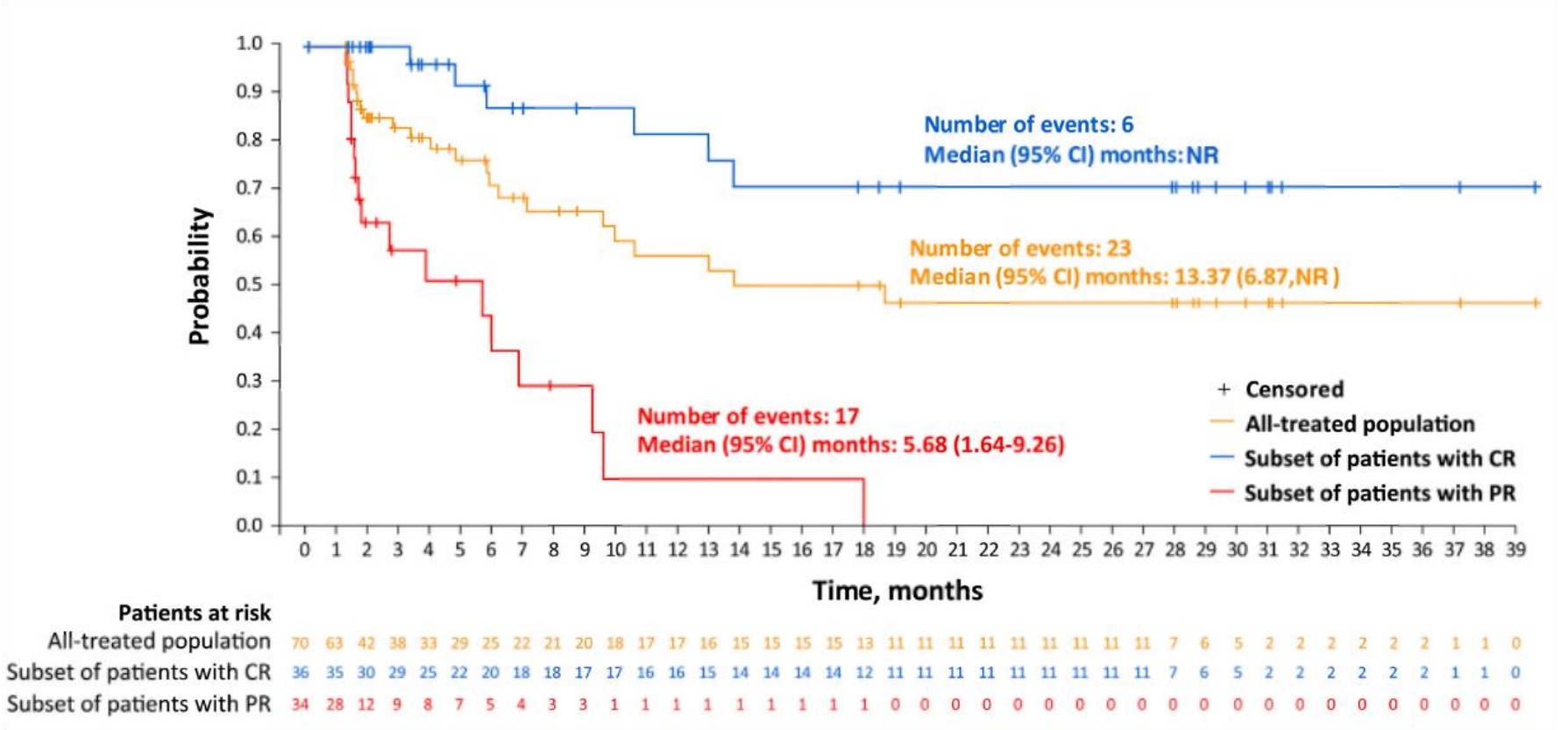
- Extended follow-up from the phase II L-MIND study supports the use of tafasitamab/lenalidomide in patients with **R/R DLBCL**
  - 2L patients have excellent outcomes
- Emerging positive findings from the phase III frontMIND trial assessing tafasitamab and lenalidomide with R-CHOP versus R-CHOP alone as **first-line therapy for DLBCL**
- Safety profile of tafasitamab; appropriate monitoring, mitigation, and management of AEs

LOTIS-2: Loncastuximab Teserine Monotherapy in R/R DLBCL (n=145)

	All-treated N=145	Best response of CR N=36	Patients with CR who were event-free ≥1 year N=16	Patients with CR who were event-free ≥2 years N=11
Sex, N (%)				
Female	60 (41.4)	22 (61.1)	13 (81.3)	9 (81.8)
Age in years, N (%)				
Median (range)	66.0 (23-94)	67.5 (45-94)	71.0 (53-84)	70.0 (53-82)
<65	65 (44.8)	13 (36.1)	3 (18.8)	3 (27.3)
≥65 to <75	59 (40.7)	15 (41.7)	7 (43.8)	5 (45.5)
≥75	21 (14.5)	8 (22.2)	6 (37.5)	3 (27.3)
Prior systemic therapies, N (%)				
Median (range)	3.0 (2-7)	3.0 (2-7)	2.0 (2-7)	2.0 (2-7)
2 prior lines	63 (43.4)	15 (41.7)	10 (62.5)	8 (72.7)
3 prior lines	34 (23.4)	5 (13.9)	2 (12.5)	1 (9.1)
>3 prior lines	48 (33.1)	16 (44.4)	4 (25.0)	2 (18.2)
Refractory, N (%)				
Primary refractory	29 (20.0)	5 (13.9)	2 (12.5)	0
Refractory to last therapy	89 (61.4)	11 (30.6)	5 (31.3)	4 (36.4)
Prior SCT, N (%)	24 (16.6)	8 (22.2)	1 (6.3)	1 (9.1)
Prior CAR T therapy, N (%)	14 (9.7)	3 (8.3)	2 (12.5)	0

Caimi PF, et al. *Haematologica*. 2024;109(4):1184-1193.

Loncastuximab teserine results: duration of response



Caimi PF, et al. *Haematologica*. 2024;109(4):1184-1193.

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Loncastuximab Teserine: Unique Adverse Effect Profile and Mitigation Strategies



- **Combinations are being evaluated**
- **Toxicity may be related to duration of therapy with lonca**

Derenzini E, et al. *Leuk Lymphoma*. 2025;66(11):1990-2002.

Tafa-Len and Lonca-T: Can Anti-CD19 Directed Treatment Be Given in the Era of CAR T?...Probably

- **Lonca-T**: (distinct epitope from commercial CAR T cell products)
  - 15 pts had subsequent CD19-directed CAR T with ORR 47% and 40% with CR
  - Median OS, PFS, and duration of response after loncastuximab were 8.2, 1.4, and 8 months, respectively
- **Tafa-len**: (same epitope from commercial CAR T cell products)
  - 3/9 patients with testing had preserved CD19 expression
  - 7/9 patients (78%) responded to CAR T
    - 4 CR
    - 3 PR

Optimal sequencing of anti-CD19 approaches?

Epperla N, et al. *Biomarker Res*. 2025;13(1):18. Caimi PF, et al. *Lancet Oncol*. 2021;22(6):790-800. Caimi PF, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(5):e335-e339.

ECHELON-3 Study Design

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

Key exclusion criteria
- **Prior BV or Len**
- Active cerebral/meningeal disease
- Grade ≥2 peripheral neuropathy

Randomization 1:1

Treatment groups

BV+Len+R (n=112)
BV 1.2 mg/kg IV Q3W + Len 20 mg PO QD + R 375 mg/m^2 IV Q3W

Placebo+Len+R (n=118)
Placebo IV Q3W + Len 20 mg PO QD + R 375 mg/m^2 IV Q3W

Primary end point
- OS in ITT population

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

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

HSCT = hematopoietic SCT; FDG = fluorodeoxyglucose; INV = investigator-assessed; DOR = duration of response.
ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated July 22, 2026. https://clinicaltrials.gov/study/NCT04404283. Bartlett NL, et al. *J Clin Oncol*. 2025;43(9):1061-1072.

ECHELON-3: Patient Demographics

	Aged ≥65 years (n=155)		Aged ≥75 years (n=86)	
	BV+Len+R (n=79)	Placebo+Len+R (n=76)	BV+Len+R (n=48)	Placebo+Len+R (n=38)
Age, median (range), years	76 (65-87)	74.5 (65-89)	79 (75-87)	78.5 (75-89)
Age ≥80 years, n (%)	23 (29.1)	15 (19.7)	23 (47.9)	15 (39.5)
GCB cell origin, n (%)[b]	**37 (46.8)**	**37 (48.7)**	**22 (45.8)**	**16 (42.1)**
CD30 status, n (%)[c]				
≥1%	**27 (34.2)**	**20 (26.3)**	**17 (35.4)**	**13 (34.2)**
<1%	52 (65.8)	56 (73.7)	31 (64.6)	25 (65.8)

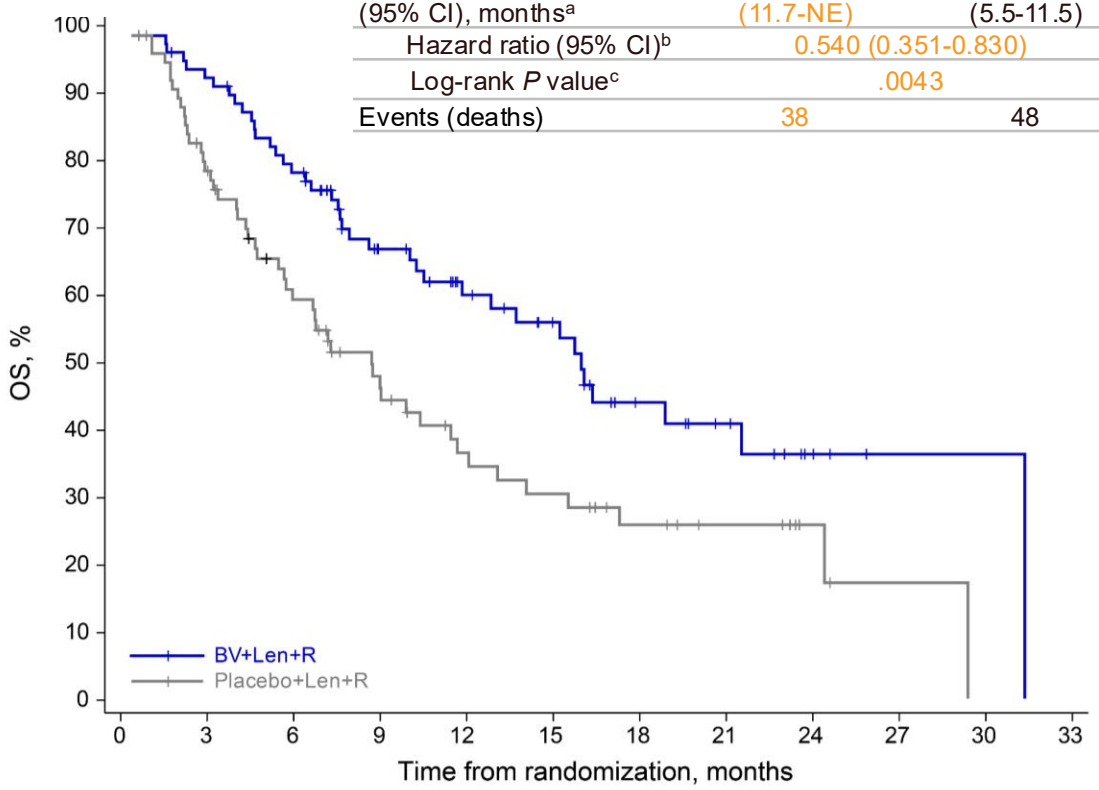
Bartlett NL, et al. *J Clin Oncol*. 2025;43(9):1061-1072.

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OS Was Improved with BV+Len+R vs Placebo+Len+R in Both Age Groups (Med F/U 16m)

Aged ≥65 years

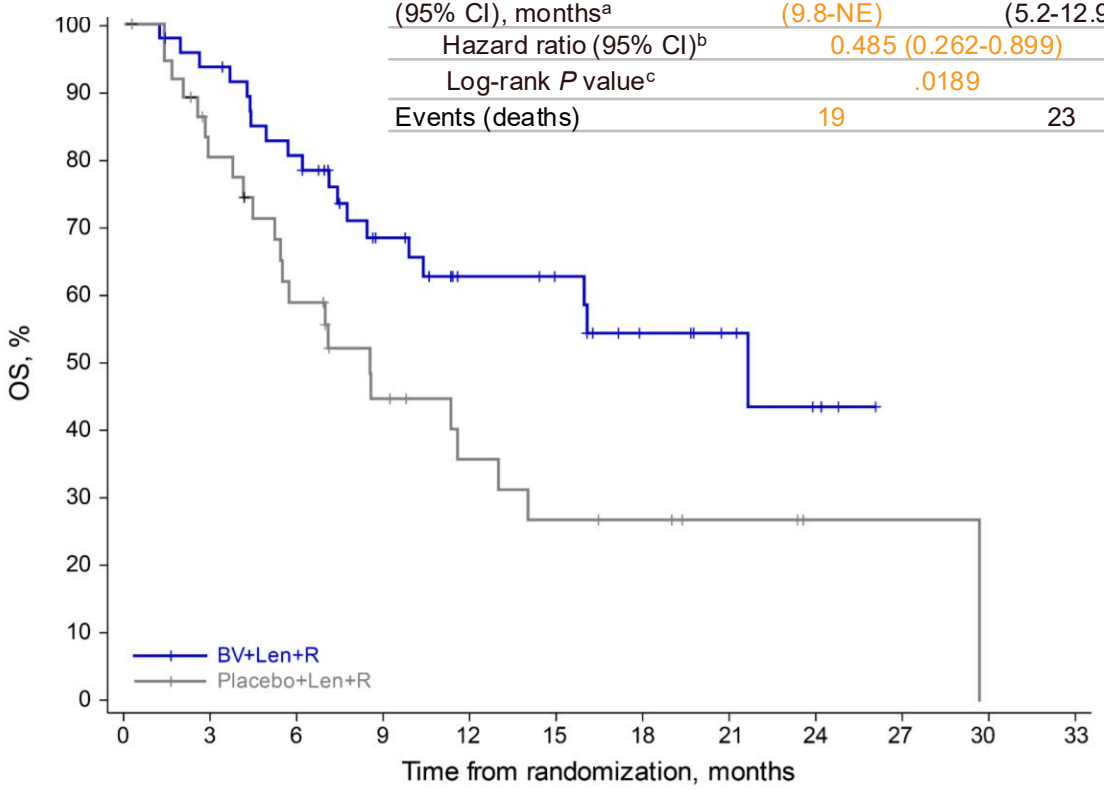
	BV+Len+R (n=79)	Placebo+Len+R (n=76)
OS, median (95% CI), months[a]	**15.9** (11.7-NE)	**8.5** (5.5-11.5)
Hazard ratio (95% CI)[b]	0.540 (0.351-0.830)	
Log-rank *P* value[c]	.0043	
Events (deaths)	38	48



No. at risk												
BV+Len+R	79	72	61	42	31	24	14	10	4	1	1	0
Placebo+Len+R	76	53	39	25	17	15	10	7	3	1	0	0

Aged ≥75 years

	BV+Len+R (n=48)	Placebo+Len+R (n=38)
OS, median (95% CI), months[a]	**21.5** (9.8-NE)	**8.5** (5.2-12.9)
Hazard ratio (95% CI)[b]	0.485 (0.262-0.899)	
Log-rank *P* value[c]	.0189	
Events (deaths)	19	23



No. at risk												
BV+Len+R	48	44	37	25	17	15	9	6	3	0	0	0
Placebo+Len+R	38	27	19	12	8	6	5	3	1	1	0	0

F/U = follow-up.

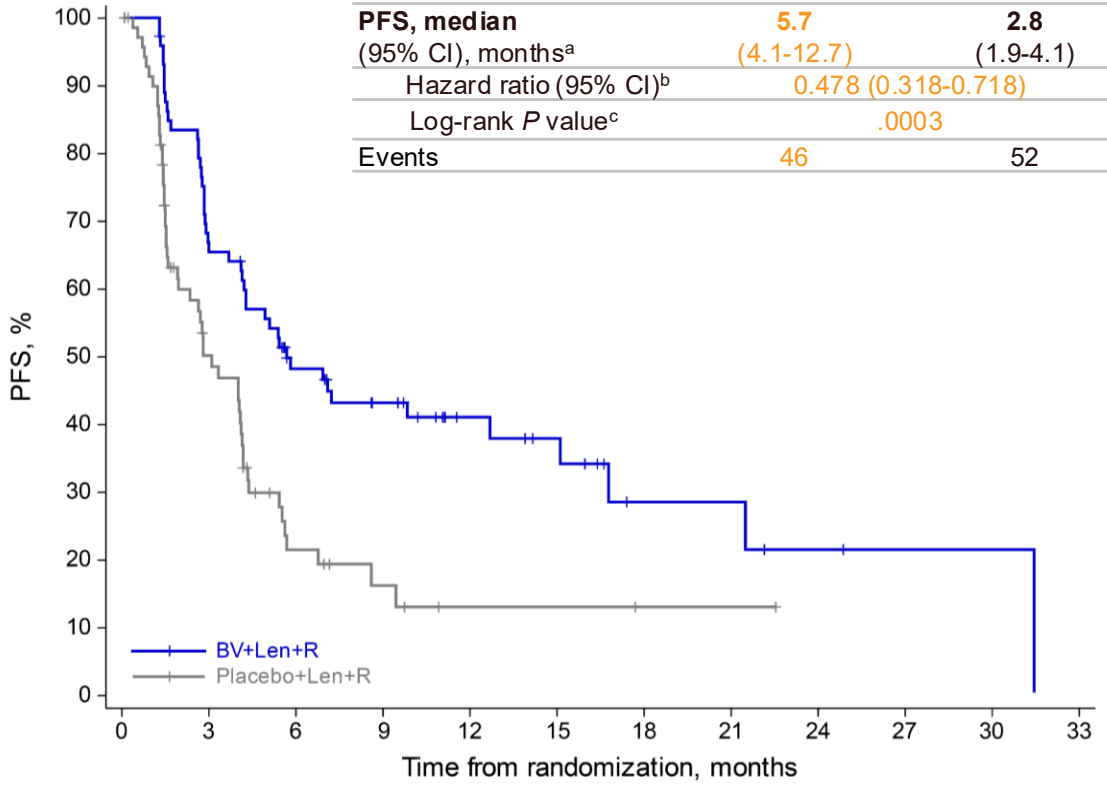
Bartlett NL, et al. *J Clin Oncol*. 2025;43(9):1061-1072.

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PFS Was Improved with BV+Len+R vs Placebo+Len+R in Both Age Groups

Aged ≥65 years

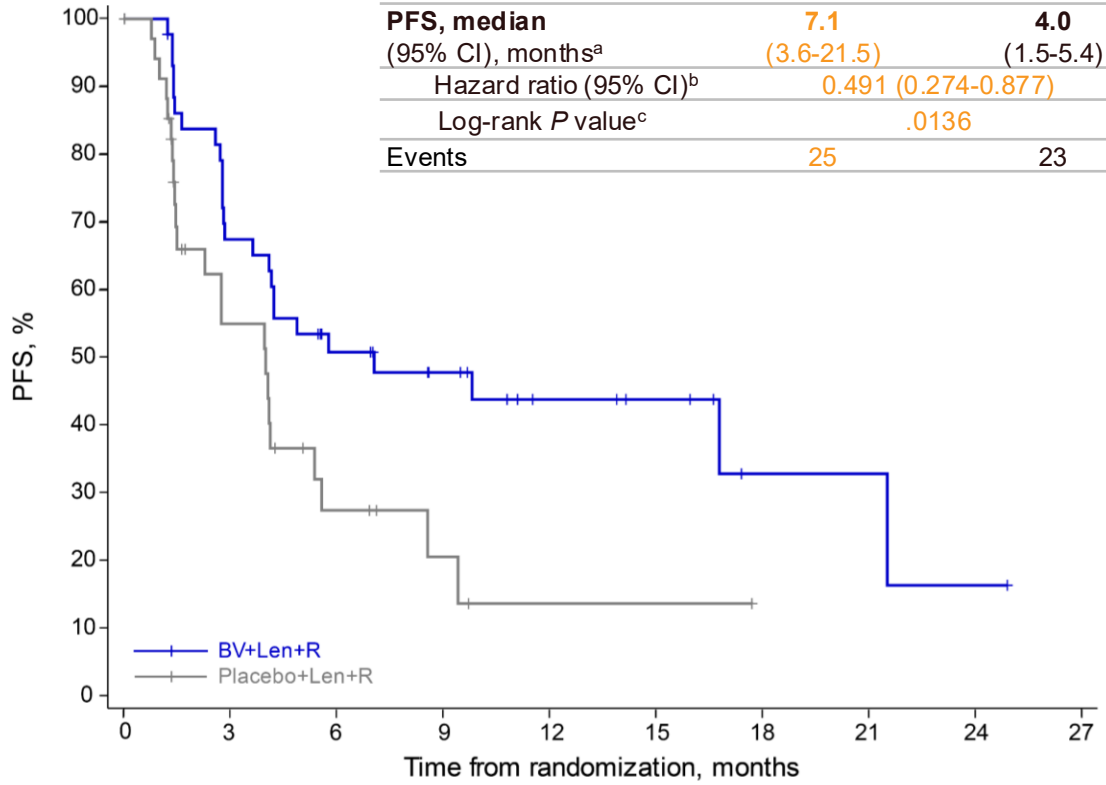
	BV+Len+R (n=79)	Placebo+Len+R (n=76)
PFS, median (95% CI), months[a]	**5.7** (4.1-12.7)	**2.8** (1.9-4.1)
Hazard ratio (95% CI)[b]	0.478 (0.318-0.718)	
Log-rank *P* value[c]	.0003	
Events	46	52



No. at risk												
BV+Len+R	79	47	30	22	13	10	4	4	2	1	1	0
Placebo+Len+R	76	30	10	5	2	2	1	1	0	0	0	0

Aged ≥75 years

	BV+Len+R (n=48)	Placebo+Len+R (n=38)
PFS, median (95% CI), months[a]	**7.1** (3.6-21.5)	**4.0** (1.5-5.4)
Hazard ratio (95% CI)[b]	0.491 (0.274-0.877)	
Log-rank *P* value[c]	.0136	
Events	25	23



No. at risk												
BV+Len+R	48	29	19	14	8	6	2	2	1	0		
Placebo+Len+R	38	15	6	3	1	1	0	0	0	0		

a PFS is the time from randomization to the earliest occurrence of progressive disease per Lugano 2014 or death. PFS is estimated using the Kaplan-Meier method. b Hazard ratio and 95% CI are based on an unstratified Cox regression model. c Two-sided *P* value from an unstratified log-rank test.

Bartlett NL, et al. *J Clin Oncol*. 2025;43(9):1061-1072.

ECHELON-3 Authors' Conclusions

- BV+Len+R demonstrated a clinically meaningful improvement in all key efficacy outcomes in patients aged ≥65 years and patients aged ≥75 years
- OS was improved with BV+Len+R vs placebo+Len+R in both age groups
  - 15.9 vs 8.5 months (*P*=.0043) in patients aged ≥65 years
  - 21.5 vs 8.5 months (*P*=.0189) in patients aged ≥75 years
- Progression-free survival (PFS) was also improved with BV+Len+R vs placebo+Len+R in both age groups
  - 5.7 vs 2.8 months (*P*=.0003) in patients aged ≥65 years
  - 7.1 vs 4.0 months (*P*=.0136) in patients aged ≥75 years
- CR rate was consistent with the overall study results (40.2% in the BV+Len+R group and 18.6% in the placebo+Len+R group regardless of age) with response typically occurring at the first assessment (6 weeks)
- No clinically meaningful safety trends in patients aged ≥65 years and patients aged ≥75 years were identified

Bartlett NL, et al. *J Clin Oncol*. 2025;43(9):1061-1072.

Back to Our Case…

- Case study: A 78-year-old frail patient with rapidly progressing R/R DLBCL requires an individualized, outpatient treatment strategy to gain disease control
- He lives approximately 80 miles from the nearest academic center and relies for transportation on a 77-year-old spouse who will not drive on the highway

Need for rapid treatment initiation without easy availability of bispecific agents or CAR T:
How would you treat??

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Sequencing Roadmap in R/R DLBCL

Nilanjan Ghosh, MD, PhD, FACP

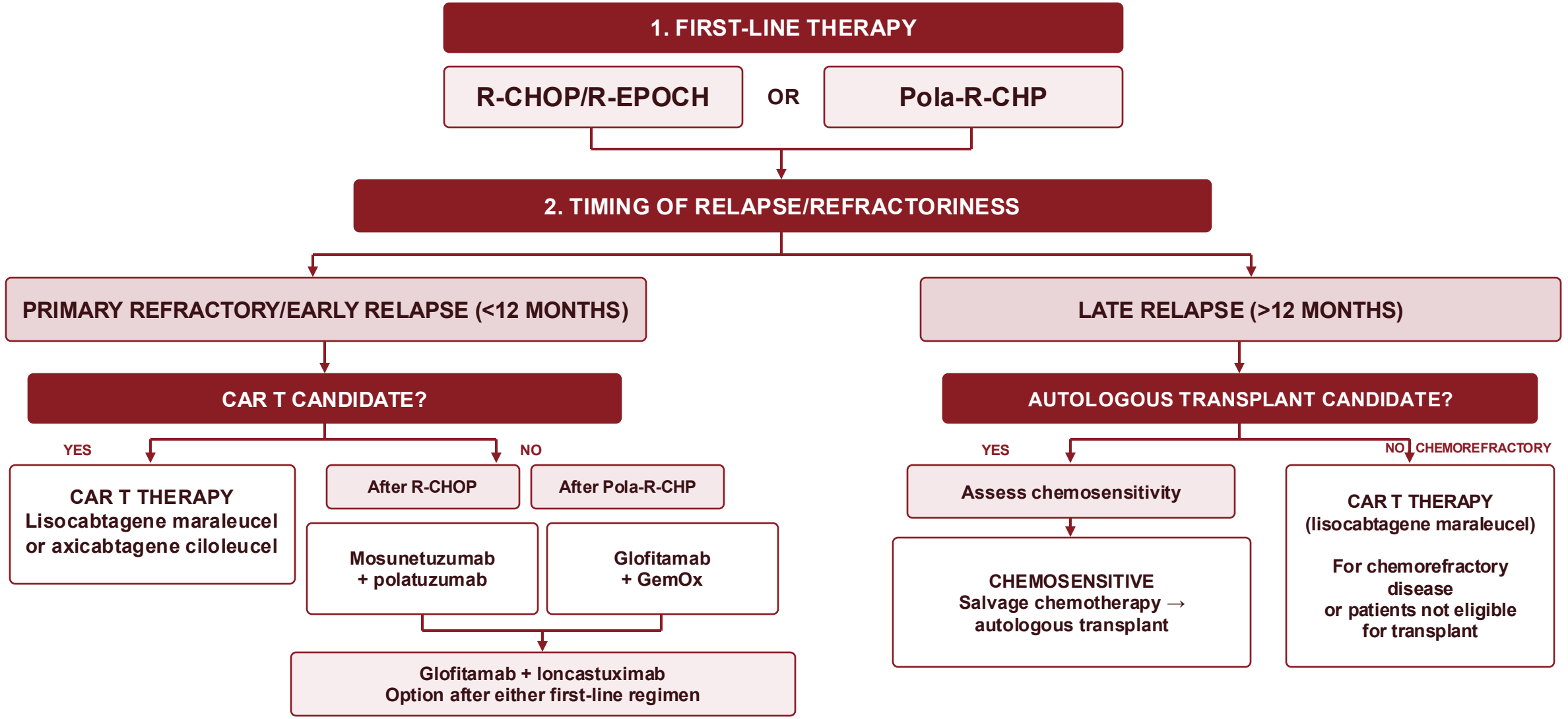
Kerry and Simone Vickar Family Foundation Endowed Chair
Professor of Cancer Medicine, Division Chief Hemato
Levine Cancer Institute, Wake Forest University School of Medicine
Charlotte, North Carolina

Agenda

- Sequencing therapies in R/R DLBCL
- Unmet need for non-CAR T-based therapies
- Bispecific antibodies and antibody drug conjugates in R/R DLBCL
- Outpatient administration of bispecific antibodies

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Sequencing Therapies in R/R DLBCL



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Poor Access to CAR T Access R/R DLBCL

US claims analysis of 8,959 patients • Komodo Health database • Jan 2021–May 2025

Retrospective cohort • ≥2 lines of therapy

Patient journey and access attrition

8,959
Eligible patients with R/R LBCL

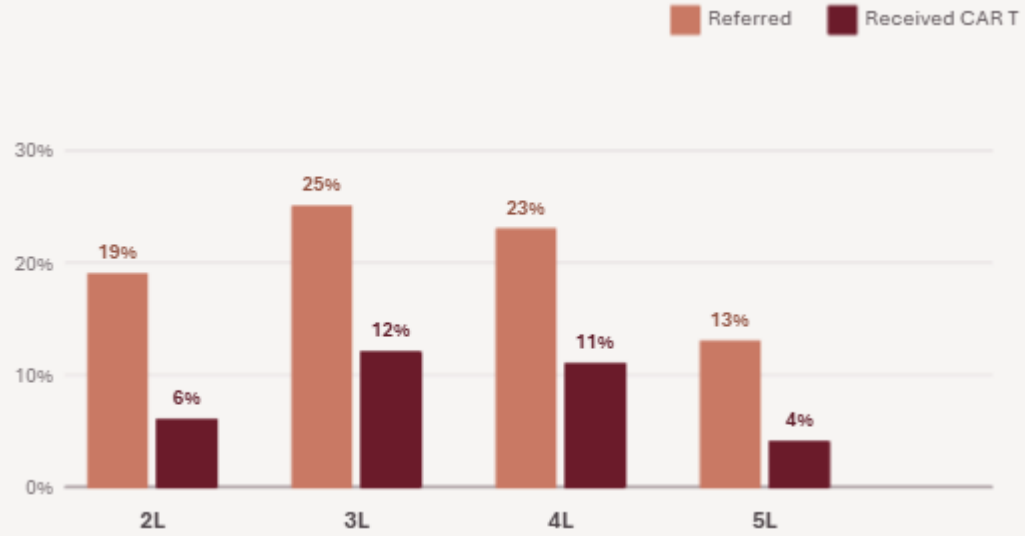
5,891 (66%)
Received care at a non–CAR T site

1,797 (31%)
Referred from a non–CAR T site

693
Referred patients who received CAR T

15%
overall received CAR T therapy (1,382/8,959)

Referral and CAR T treatment by line of therapy

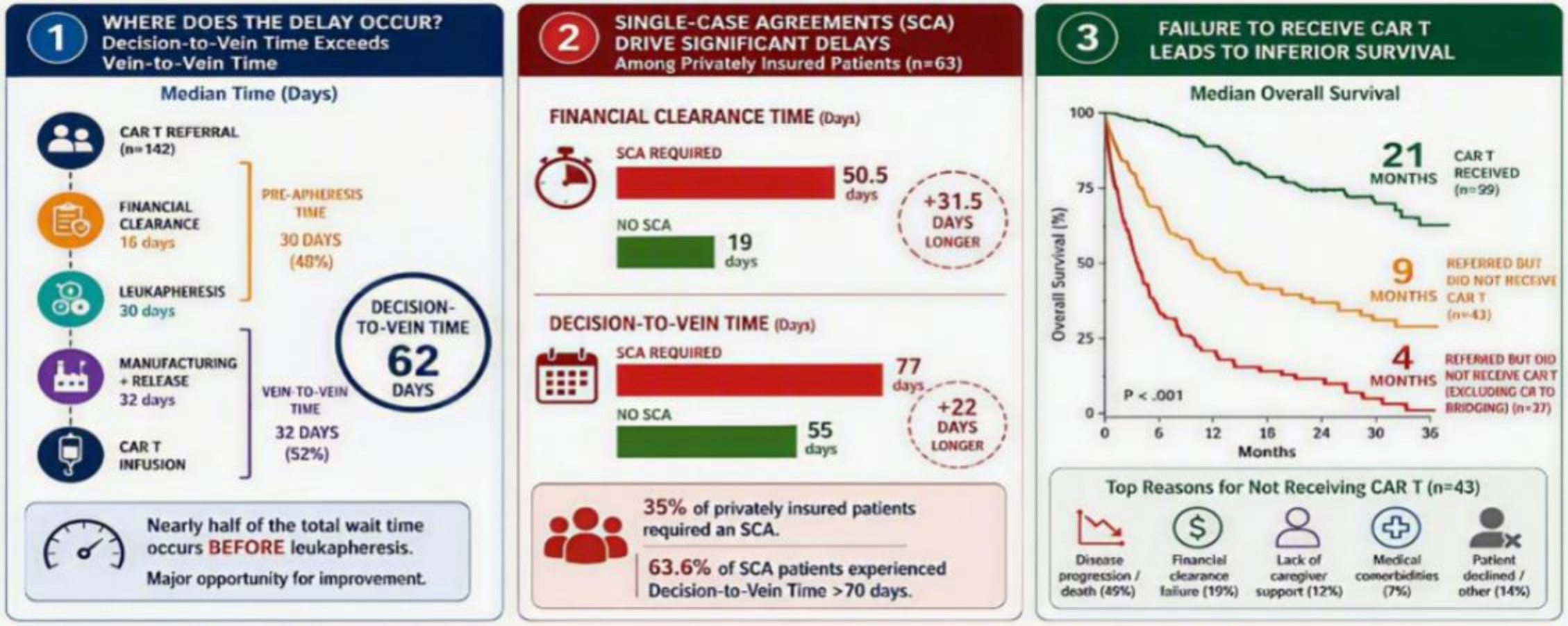


Who was less likely to be referred?

- **Older patients:** Mean age 67.3 vs 61.5 years
- **Medicare beneficiaries:** 63% vs 44%
- **Patients farther from a CAR T site:** Median 24 vs 17 miles
- **Patients in the South:** 39% vs 34%

Shadman M, et al. *Blood*. 2025;146(Suppl 1):6272.

Barriers to CAR T in R/R DLBCL



Hu B, et al. *Transplant Cell Ther*. 2024;30(11):1082.e1-1082.e10.

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Summary of Currently Approved Therapies in 3L+ DLBCL in the US

	Epcor[1,2] N=157 EPCORE NHL-1	Glofit[3–5] N=155 NCT03075696	BV + R[2 6,7] N=112 ECHELON-3	Pola + BR[8,9] N=106 (expansion) GO29365	Tafa + Len[10,11] N=80 L-MIND	Axi-cel[12,13] N=101 ZUMA-1	Liso-cel[14,15] N=270 TRANSCEND	Lonca-T[16] N=145 LOTIS-2	Lonca-T[17] N=118 Epperla, et al.
Most recent median FU, mo	37.1	37.7	15.5	48.9	65.6 (OS)	63.1	20.3	35.0	13.0
PFS, mo	4.2	4.9[c]	4.2	6.6	11.6	N/A	6.8	4.9	12.0
OS, mo	18.5	11.5[c,d]	13.8	12.5	33.5	25.8	27.5	9.5	NR
ORR, %	59	52	64	41.5	57.5	83	73	48	74
CR, %	41	40	40	39	41	58	53	25	34
DOR, mo	20.8	-	8.3	9.5	NR	11.1	23.1	13.4	7.6
DOCR, mo	36.1	29.8	18.9	-	-	62.2	-	NR	NR
Key AEs Overall (Gr 3+), %[a]	CRS: 37 (1)[b] ICANS: 6 (1 Gr5) Ser. infections: 15	CRS: 64 (4) ICANS: 5 (2) Infections: 16 (10)	Neutropenia: 46 Infections: N/A Neuropathy: 31 (6)	Neutropenia: 37 (33) Infections: 33 (22) Neuropathy: 3 (2)	Neutropenia: 49 (48) Infections: 25 (3) Anemia: 37 (7)	CRS: 93 (11) Infections: 26 (16) Neuro tox: 64 (30)	CRS: 54 (3) Infections: 34 (12) Neuro tox: 31 (10)	Neutropenia (40) Thrombocytopenia: (33)	Neutropenia, thrombocytopenia, anemia, elevated AST/ALT (grade not captured; only AEs leading to treatment interruption/ discontinuation were evaluated)
Discontinued due to AEs, %	17	9	16	20.5 (pooled data)	20	-	-	25	8

Please note this table is for illustration purposes only, and side-by-side data should be interpreted with great caution. [a]AEs reported from either prescribing information or most recent publication depending on most recent reporting of AE. [b]Dose optimization cohort. [c]Reported in primary analysis. [d]Investigator-assessed value. [e]UTIs and respiratory infections.
UTI = urinary tract infection; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome.

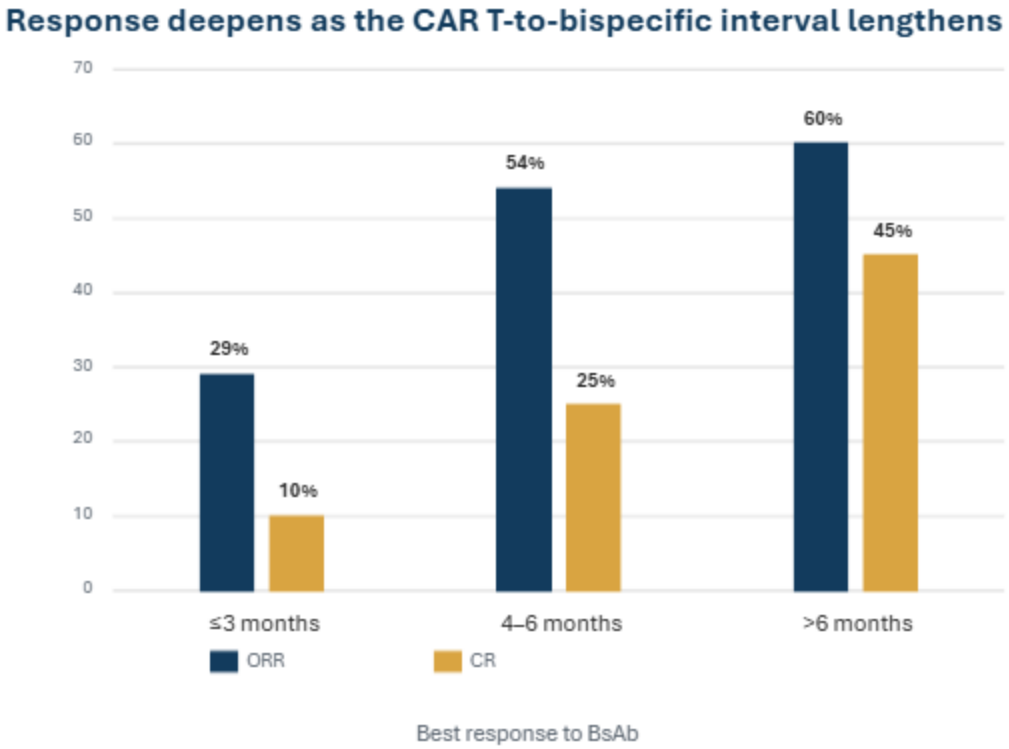
1. Cheah CY, et al. Presented at: EHA Congress; 2025. Abstract PF920. 2. Epcoritamab prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated June 17, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761324s011lbl.pdf. 3. Dickinson, MJ et al. *N Engl J Med*. 2022;387(24):2220-2231. 4. Dickinson MJ, et al. Presented at: 66th ASH Annual Meeting and Exposition; 2024. Abstract 865. 5. Glofitamab prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated June 22, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761309s007lbl.pdf. 6. Kim JA, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 2024. Abstract LBA 7005. 7. Brentuximab vedotin prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated February 11, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125388Orig1s108lbl.pdf. 8. Sehn LH, et al. *Blood*. 2022;140(Suppl 1):9464-9467. 9. Polatuzumab vedotin prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated March 18, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761121s017lbl.pdf. 10. Duell J, et al. *Haematologica*. 2024;109(2):553-566. 11. Tafasitamab prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated June 18, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761163s013lbl.pdf 12. Neelapu SS, et al. *Blood*. 2023;141(19):2307-2315. 13. US Food and Drug Administration (FDA) [www.fda.gov]. Axicabtagene ciloleucel prescribing information. Last updated August 7, 2026. https://www.fda.gov/media/193167/download?attachment. 14. Abramson JS, et al. Presented at: 66th ASH Annual Meeting and Exposition; 2024. Abstract 3125. 15. FDA [www.fda.gov]. Lisocabtagene maraleucel prescribing information. Last updated March 11, 2026. https://www.fda.gov/media/145711/download?attachment. 16. Caimi P, et al. *Haematologica*. 2024;109(4):1184-1193. 17. Epperla N, et al. *Blood Cancer J*. 2024;14(1):210.

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Bispecific Antibodies and ADCs in R/R DLBCL

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Timing after CAR T-Cell Failure Strongly Predicts Bispecific Outcomes



EARLY	INTERMEDIATE	LATE
2.17 mo	3.73 mo	10.47 mo
median PFS	median PFS	median PFS

EARLY	INTERMEDIATE	LATE
4.17 mo	9.07 mo	Not reached
median OS	median OS	median OS

Clinical interpretation

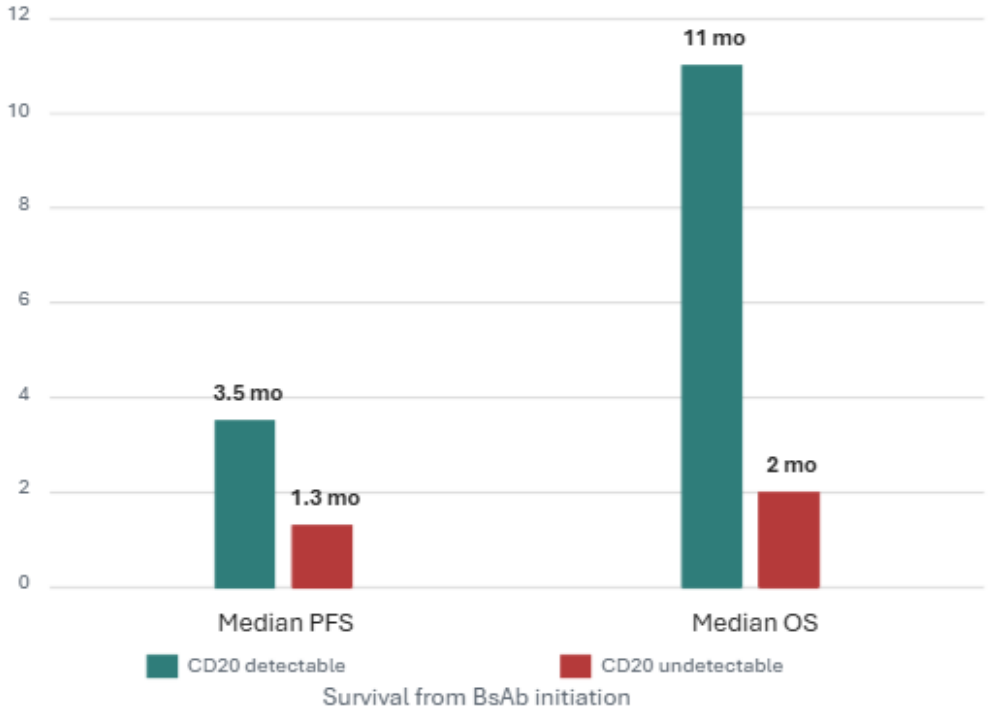
In this post-CAR T cohort, relapse timing strongly stratified outcomes. Early failure (≤3 months) identified poor response and survival, whereas late failure (>6 months) was associated with the greatest benefit. For relapse beyond 3 months, BsAb as first salvage outperformed later use after intervening therapy.

Takeaway: early CAR T failure reflects aggressive biology and limited benefit from BsAb monotherapy.

Shumilov E, et al. *Blood Adv*. 2025;9(15):3955-3966.

CD20 Status Strongly Predicts Bispecific Outcomes

Markedly inferior survival when CD20 is undetectable before treatment



CD20 loss after bispecific failure



Paired biopsies

89.5% lost detectable CD20

17 of 19 paired samples

At post-BsAb biopsy: 30/35 (86%) were CD20–

Clinical implications

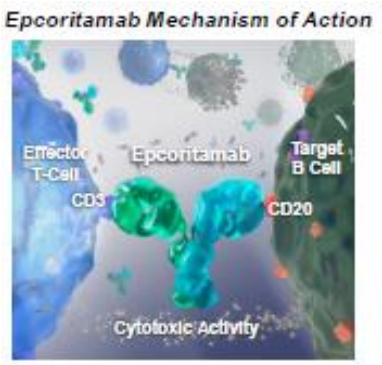
- Confirm CD20 expression when feasible before a CD20-directed bispecific.
- Consider re-biopsy after progression to identify target loss and guide subsequent therapy.

Brooks TR, et al. *Blood*. 2025;146(18):2177-2188.

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Epcoritamab in R/R DLBCL: 2026 FDA Label Update

Step-up dosing is unchanged; monitoring after the first full dose is now individualized



Cycle 1 step-up schedule for DLBCL/high-grade B-cell lymphoma

Day 1	Day 8	Day 15	Day 22
0.16 mg	**0.8 mg**	**48 mg**	**48 mg**
Step-up 1	Step-up 2	First full dose	Full dose

After cycle 1: 48 mg weekly in cycles 2-3; every 2 weeks in cycles 4-9; every 4 weeks from cycle 10 onward.

WHAT CHANGED

Cycle 1 Day 15, 48 mg

FDA label now directs clinicians to assess whether hospitalization or outpatient monitoring is appropriate.

Routine hospitalization is no longer the default label recommendation.

Continue monitoring for CRS and ICANS and administer recommended premedications, post-medications, and prophylaxis.

Practice implication: Use a clinic-specific risk and monitoring pathway rather than automatic admission for every patient.

Epcoritamab prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated June 17, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761324s011lbl.pdf.

Epcoritamab in R/R DLBCL

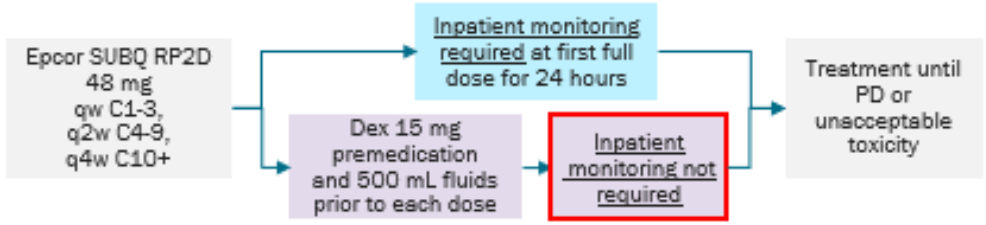
Study Design (Phase 1/2)[1-3]

Key Eligibility Criteria

- R/R CD20+ mature B-cell neoplasm
  - C1 optimization: DLBCL NOS (de novo or transformed from FL)
- ECOG PS 0-2
- ≥2 prior lines of systemic antineoplastic therapy
- Prior CAR T-cell therapy allowed

- **Primary endpoint:** ORR (expansion) and CRS (C1 optimization)
- **Secondary endpoints:** MRD, DOR, TTR, PFS, OS, CR, safety/tolerability

Expansion (N=157)[2]



C1 Optimization (N=81)[3]

Patient Demographics[1]	N=157
Median age, years	62
Disease, n (%) – DLBCL | Gr3B FL | HGBCL | PMBCL	139 (89) | 5 (3) | 9 (6) | 4(3)
Median prior LOT (range), n	3 (2-11)
Primary refractory, n (%)	95 (61)
Prior CAR T-cell therapy, n (%)	61 (39)

Long-Term Efficacy[1]

Response, %	LBCL (N=157)	Patients in CR at 2 Years (n=32)
mDOR, mo (95% CI)	20.8	-
mDOCR	36.1	NR
mPFS, mo (95% CI)	4.2 (2.8-5.5)	NR
mOS, mo (95% CI)	18.5 (11.7-27.7)	NR

Safety[2,3]

C1 Optimization Impact on CRS Rates/Severity	Expansion (N=157)	C1 Optimization (n=81)
CRS, n (%)	80 (51)	30 (37)
Grade 1	50 (32)	21 (26)
Grade 2	25 (16)	8 (10)
Grade 3	5 (3)	1 (1)
Treated with tocilizumab, n/n (%)	23/80 (29)	13/30 (43)
Treated with corticosteroid, n/n (%)	17/80 (21)	6/30 (20)
Led to discontinuation, n (%)	1 (1)	0
CRS resolution, n/n (%)	78/80 (98)	30/30 (100)
Median resolution time, days (range)	2 (1-27)	2 (1-15)

TTR = time to response; HGBCL = high-grade B-cell lymphoma; PMBCL = primary mediastinal B-cell lymphoma; m = median; LOT = line of therapy.

1. Cheah CY, et al. Presented at: EHA Congress; 2025. Abstract PF920. 2. Karimi Y, et al. Presented at: ASCO Annual Meeting; 2024. Abstract 7039. 3. Thieblemont C, et al. Presented at: EHA Cognress; 2024. Abstract P1151.

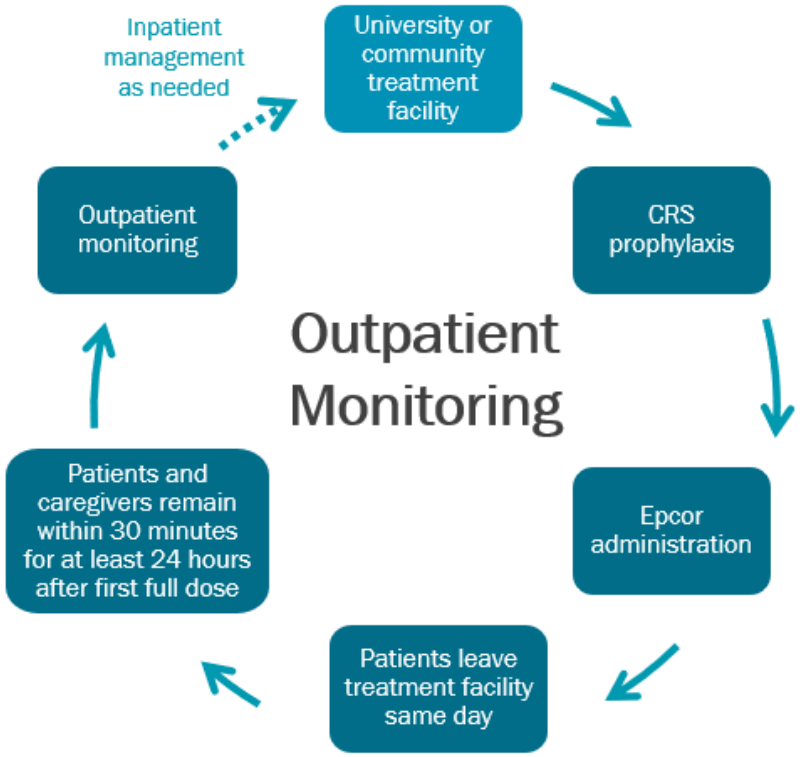
Epcoritamab in R/R DLBCL: EPCORE NHL-6

Key Eligibility Criteria
- R/R DLBCL
- ≥1 prior LOT
- Failed prior ASCT or ineligible for ASCT

Objective
- To assess whether Epcor can be safely **monitored in the outpatient setting, with reactive instead of prophylactic hospitalization** for patients with R/R DLBCL or R/R FL across US university and community sites

Epcor: 28-d cycles; C1 SUD: 0.16 mg, 0.8 mg, 48 mg; C2-3: qw; C4-9: q2w; C10+: q4w

Patients received safety education, including early identification and reporting of symptoms of CRS and ICANS, and were required to stay within 30 minutes of the site of care for 24 hours after the first full dose in C1



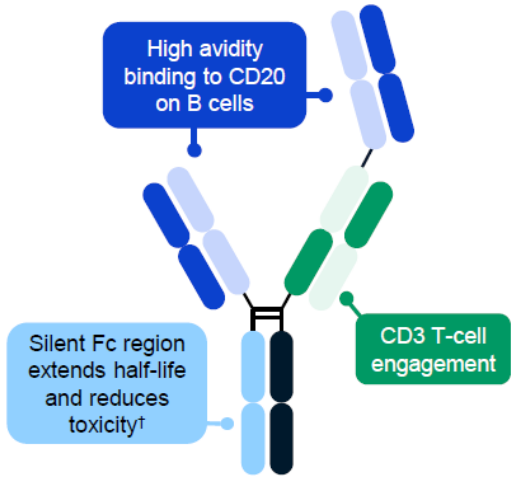
Patient Characteristics	DLBCL (N=92)
Median age, years	69
Ann Arbor stage III-IV, n (%)	76 (83)
Baseline IPI ≥3, n (%)	47 (51)
Bulky disease ≥7 cm, n (%)	22 (24)
Prior CAR T-cell therapy, n (%)	22 (24)
Line of therapy, n (%) 2L 3L+	 42 (46) 50 (54)
Ongoing treatment at data cutoff, n (%)	46 (50)

Median follow-up of 7.6 months.

SUD = step-up dose.

Vaidya R, et al. *Clin Lymphoma Myeloma Leuk*. 2025;25(Suppl 1):S790-S791.

Glofitamab: 2:1 CD20×CD3 Design, Fixed-Duration Therapy



Two CD20-binding arms create high-avidity B-cell binding; one CD3 arm recruits T cells. A silent Fc region supports half-life while limiting Fc-mediated activity.

Obinutuzumab pretreatment + cycle 1 step-up dosing

C1D1	C1D8	C1D15	C2–12 D1
Obinutuzumab **1,000 mg**	Glofitamab **2.5 mg**	Glofitamab **10 mg**	Glofitamab **30 mg Q3W**

Fixed duration: 12 cycles (approximately 8.5 months)

52%	40%	29.8 mo	56.4%
ORR	CR	Median DoCR	24-mo DoCR

Prior CAR T (33%), refractory to CAR T (30%)
3-year follow-up: 56.4% of patients achieving CR remained in remission at 24 months.

Dickinson MJ, et al. *Blood*. 2024;144(Suppl 1):865.

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Glofitamab: Adverse Events, CRS Profile and Monitoring Implications

CRS in the 3-year pivotal analysis



64.3% any-grade CRS

Grade 1 48.1% | Grade 2 12.3% | Grade 3 2.6% | Grade 4 1.3%

High-grade CRS was uncommon, but the risk is concentrated around step-up and initial target dosing.

Current US-label monitoring

2.5 mg dose
Hospitalize during and for 24 h after infusion

10 mg dose
Hospitalize if CRS occurred with 2.5 mg; otherwise monitor per label

30 mg target dose
Hospitalize if CRS occurred with 10 mg; otherwise monitor per label

All doses
Treat where CRS can be recognized and managed

AE leading to treatment discontinuation: 14 (9%); AE leading to glofitamab dose modification/interruption: 30 (20%)
B-cell recovery was observed starting from 12-18 months after EOT

Dickinson MJ, et al. *Blood*. 2024;144(Suppl 1):865. Glofitamab prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated June 22, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761309s007lbl.pdf.

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STARGLO: Durable Remissions after Fixed-Duration Glofit-GemOx

Phase 3 randomized trial in ASCT-ineligible R/R DLBCL | Glofit-GemOx n=183 vs R-GemOx n=91 | Median OS follow-up 35.1 months

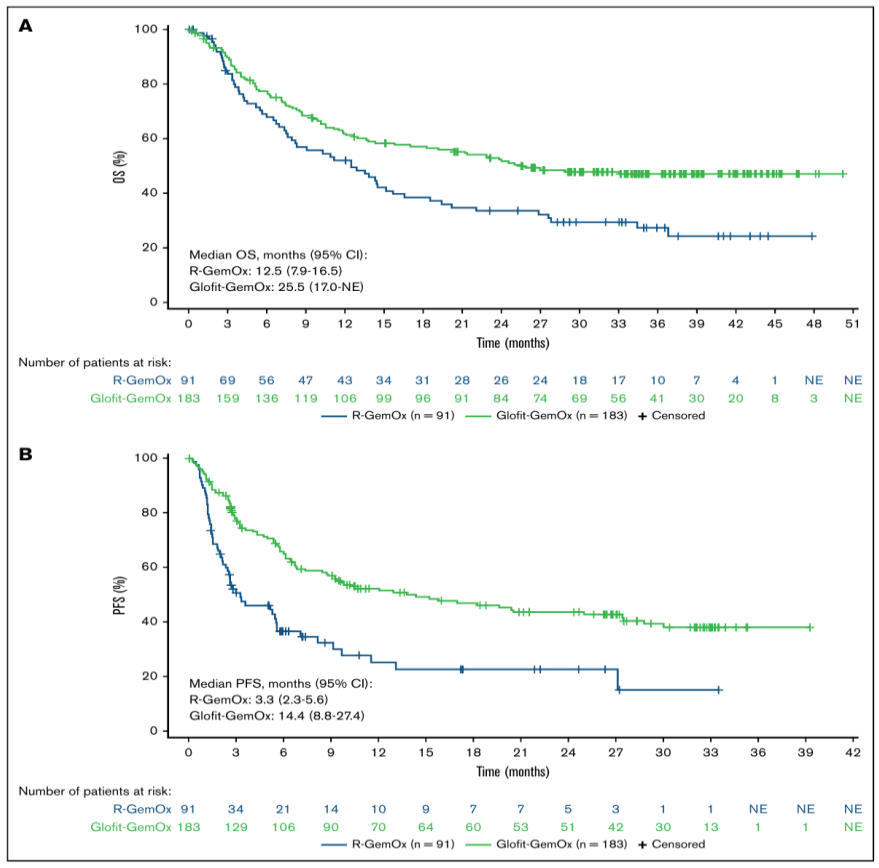


Figure 2. Efficacy in the intention-to-treat population. Kaplan-Meier (KM) estimates of OS (A) and IRC-assessed PFS (B).

25.5 mo
Median OS
vs 12.5 mo; HR 0.60

47.1%
3-year OS
vs 27.4%

14.4 mo
Median PFS
vs 3.3 mo; HR 0.41

38.1%
30-month PFS
vs 15.2%

FIXED-DURATION THERAPY

Glofitamab through cycle 12
GemOx through cycle 8

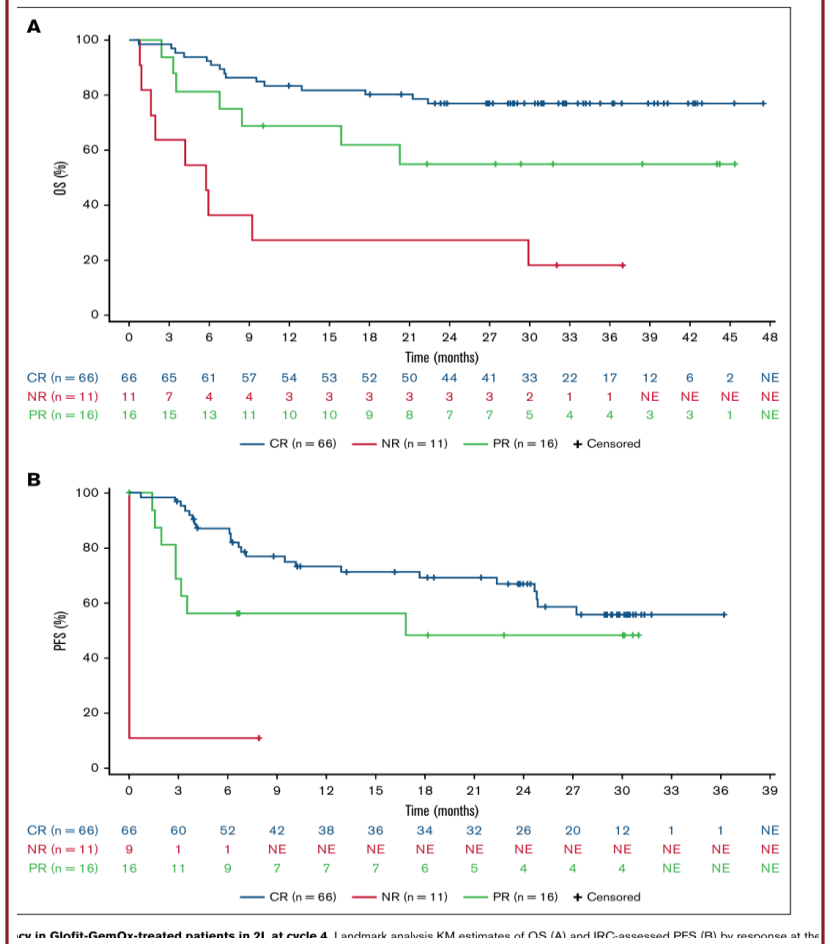
Key message: survival benefit persists well beyond completion of therapy.

Figure 2. Data cutoff May 1, 2025.
Abramson JS, et al. *Blood Adv*. 2026;10(15):5367-5377.

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Early Complete Response Identifies the Long-Term Remission

Second-line Glofit-GemOx landmark analysis at first tumor assessment, cycle 4



CR curves remain high and flatten through prolonged follow-up

85%
CRs by cycle 4
91/107 overall CRs

77.0%
30-month OS
2L patients with cycle-4 CR

55.7%
30-month PFS
2L patients with cycle-4 CR

NR
Median OS & PFS
2L patients with cycle-4 CR

REMISSION AFTER TREATMENT ENDS

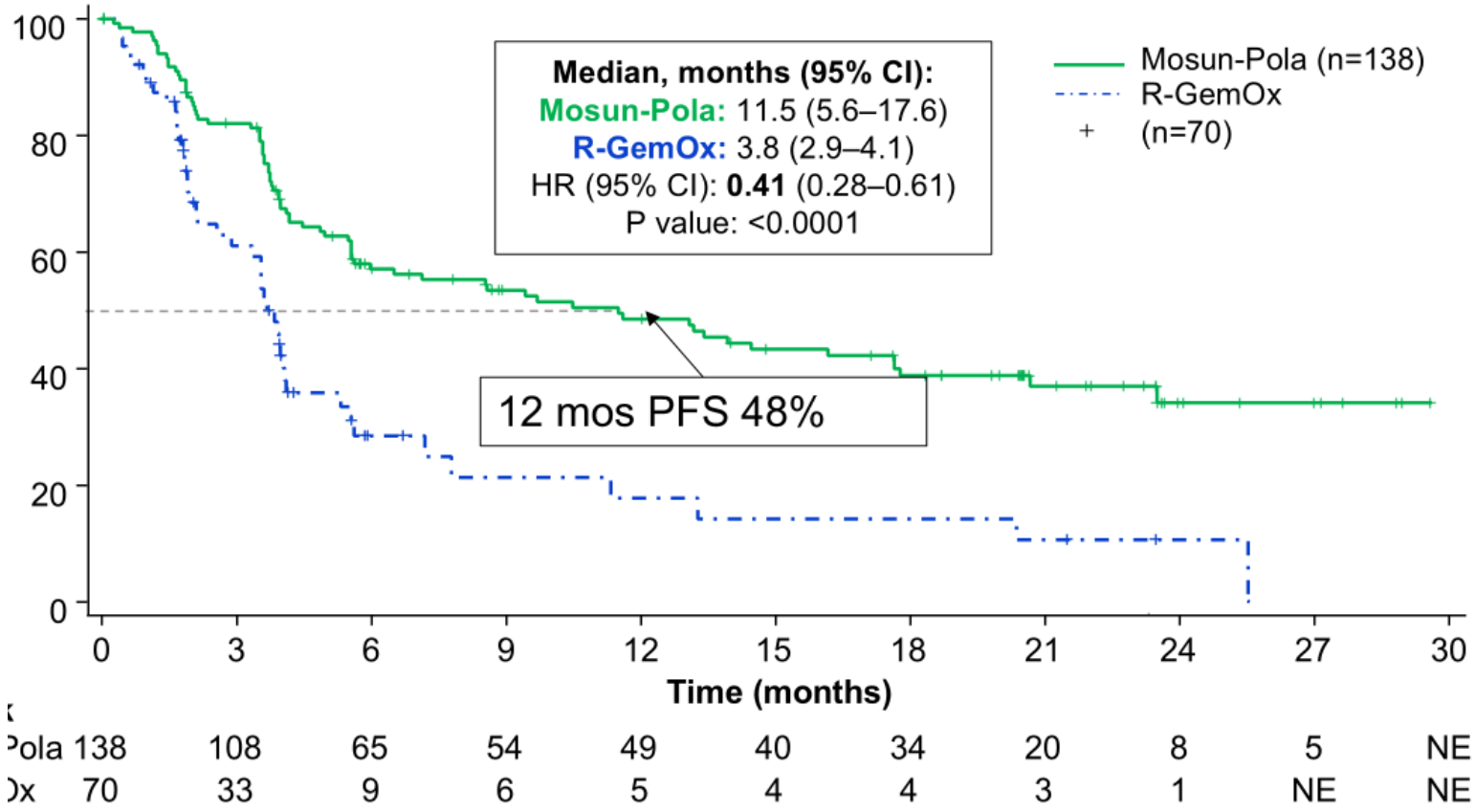
Among patients in CR at end of treatment:
24-month post-EOT OS 79.4% | PFS 74.2%

The durable tail is concentrated in patients achieving an early, deep complete response.

Figures 3 and 5; landmark analyses.
Abramson JS, et al. *Blood Adv*. 2026;10(15):5367-5377.

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Mosun-Pola Significantly Prolonged PFS Versus R-GemOx



PFS BENEFIT

11.5 mo
Median PFS with Mosun-Pola
vs 3.8 mo with R-GemOx

0.41
Hazard ratio
95% CI 0.28-0.61; *P*<0.0001

48%
12-month PFS
Mosun-Pola

59%
Reduction in risk
of progression or death

Clinically meaningful PFS improvement

Clinical cutoff: 17 February 2025. PFS censored at earliest NALT or ≥2 missing tumor assessments.
Budde LE, et al. *J Clin Oncol*. 2025;43(36):3799-3811.

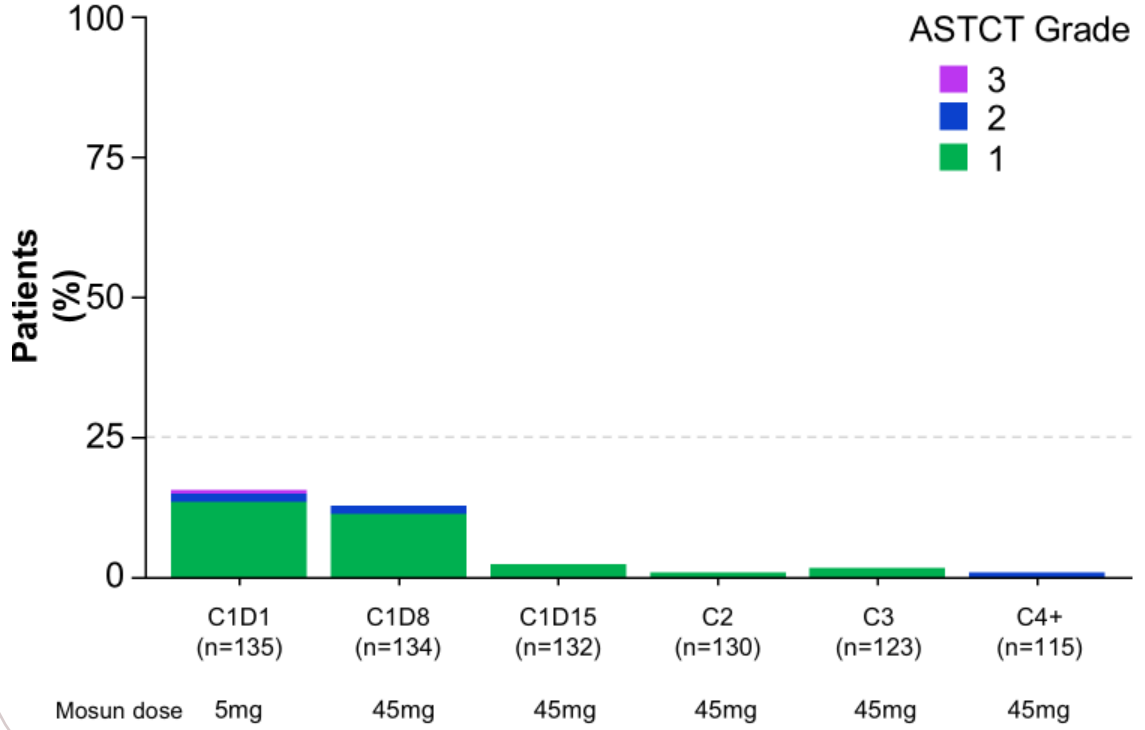
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Mosun-Pola CRS Was Infrequent, Early, and Predominantly Low-Grade

Patients with ≥1 CRS AE, % (n)	Mosun-Pola n=135
Any grade	25.9% (35)
Grade 1	21.5% (29)
Grade 2	3.7% (5)
Grade 3	0.7% (1)
Any serious event of CRS*	5.2% (7)
Median onset to first CRS, days (range)	3 (1–6)
Median duration, days (range)	3 (1–11)
Tocilizumab for CRS management	4.4% (6)
Corticosteroids for CRS management	3.7% (5)

Overall CRS: 25.9% | Grade 3: 0.7% | No grade 4-5 CRS shown

CRS by cycle and grade in the Mosun-Pola arm



CRS was most frequent at C1D1 and C1D8, then declined sharply

96% of patients had no significant CRS (grade 2 or higher)

Clinical cutoff: 17 February 2025. Serious CRS events required new or prolonged hospitalization. ASTCT grading.
ASTCT = American Society for Transplantation and Cellular Therapy.
Budde LE, et al. *J Clin Oncol*. 2025;43(36):3799-3811.

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LOTIS-7: Dual Targeting with Loncastuximab Tesirine + Glofitamab

Phase 1b, open-label, multinational trial in 2L+ relapsed/refractory LBCL | ICML 2025 | Data cutoff: April 14, 2025

LONCASTUXIMAB TESIRINE

CD19-directed ADC

PBD payload → DNA damage/apoptosis

+

GLOFITAMAB

CD20×CD3 T-cell engager

T-cell recruitment → B-cell cytotoxicity

Rationale

Complementary CD19 and CD20 targeting
Distinct mechanisms with limited expected toxicity overlap

C1D1	C1D2	C1D8	C1D15	Cycles 2–8	Cycles ≥3
Obinutuzumab 1,000 mg	Lonca IV 120 or 150 µg/kg	Glofitamab 2.5 mg	Glofitamab 10 mg	Glofitamab 30 mg Q3W + Lonca Q3W	Lonca reduced to 75 µg/kg

ANALYSIS POPULATION

41	30	71 y	2	51%	20%
treated LBCL patients	efficacy evaluable	median age	median prior lines	primary refractory	prior CAR T

PBD = pyrrolobenzodiazepine.

Alderuccio JP, et al. Presented at: International Conference on Malignant Lymphoma (ICML); 2025. Abstract 078.

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LOTIS-7: High Early Response Rate with Manageable CRS/ICANS

Efficacy-evaluable population N=30; safety population N=41

EFFICACY

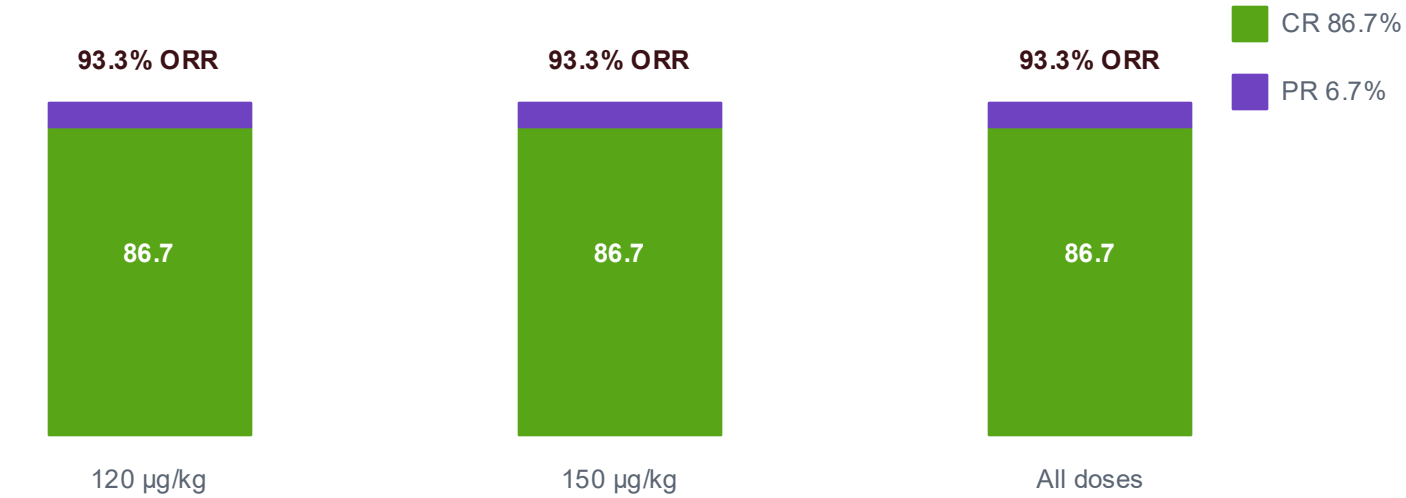
93.3%
ORR
28/30

86.7%
CR
26/30

42 days
Median time to response
CR or PR

NE
Median DOR
28 responders

BEST OVERALL RESPONSE



SAFETY HIGHLIGHTS

56.1%	Grade 3/4 TEAEs
24.4%	Grade 3/4 neutropenia
39.0%	Any-grade CRS
2.4%	Grade 3 CRS
7.3%	Any-grade ICANS
0	Grade ≥3 ICANS/grade 5 TEAEs

Dose-selection signal

150 µg/kg start: lower any-grade CRS (23.8% vs 55.0%) and shorter median time to CR (42 vs 80 days). Expansion proceeded at 150 µg/kg.

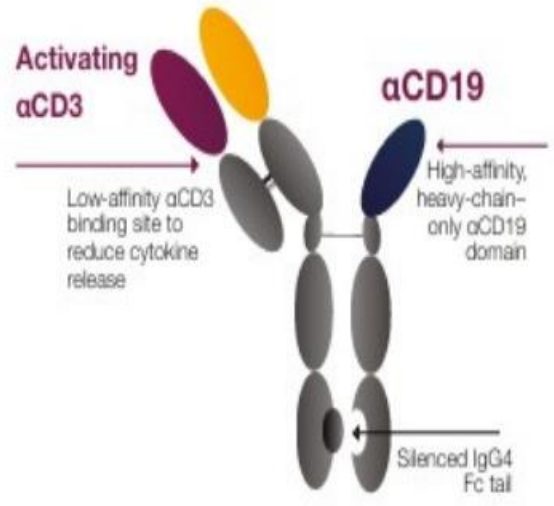
Clinical takeaway: Promising phase 1b activity for an ADC-bispecific combination; interpretation remains limited by small sample size and immature durability data.

Alderuccio JP, et al. Presented at: ICML; 2025. Abstract 078.

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Surovatamig (AZD0486): CD19xCD3 Design and Activity in R/R DLBCL

Fully human IgG4 CD19×CD3 T-cell engager | attenuated/low-affinity CD3 binding designed to reduce cytokine release



Low-affinity CD3 binding → lower cytokine release potential

DOSE-DEPENDENT EFFICACY

7.2 mg		15 mg		25 mg	
47%	38%	59%	44%	77%	54%
ORR	CR	ORR	CR	ORR	CR

ACTIVITY AFTER PRIOR THERAPY

45%	CR after CD20 TCE	5/11
35%	CR after CD19 CAR T	11/31
90%	MRD-negative CRs	26/29

12-month: DOR 76% | DoCR 91% | PFS 44%

LOW-GRADE CRS WITH DOUBLE STEP-UP DOSING

49% — **Any-grade CRS**
All events low grade

27% — **Any-grade ICANS**
Grade 3: 8%

29% — **Grade ≥3 neutropenia**
Anemia 15% | pneumonia 9%

35 h — **Median grade 3 ICANS duration**
Reversible with corticosteroids

No high-grade CRS in the double step-up cohort

Clinical takeaway: attenuated CD3 engagement may help limit CRS while maintaining dose-dependent antitumor activity and responses after CD20 TCE or CAR T failure.

Data cutoff May 19, 2025.

Kim TM, et al. Blood. 2025;146(Suppl 1):5514.

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Outpatient Administration of Bispecific Antibodies

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LCI Hospital-at-Home Monitoring Model

Four-layer monitoring pathway supporting outpatient detection and escalation of CRS and ICANS

1 PATIENT SELF-MONITORING

Wearable strap (heart rate, respiratory rate), pulse oximeter, blood pressure cuff, and thermometer. Vital signs entered every 4 hours via tablet.

2 24/7 REMOTE NURSE MONITORING

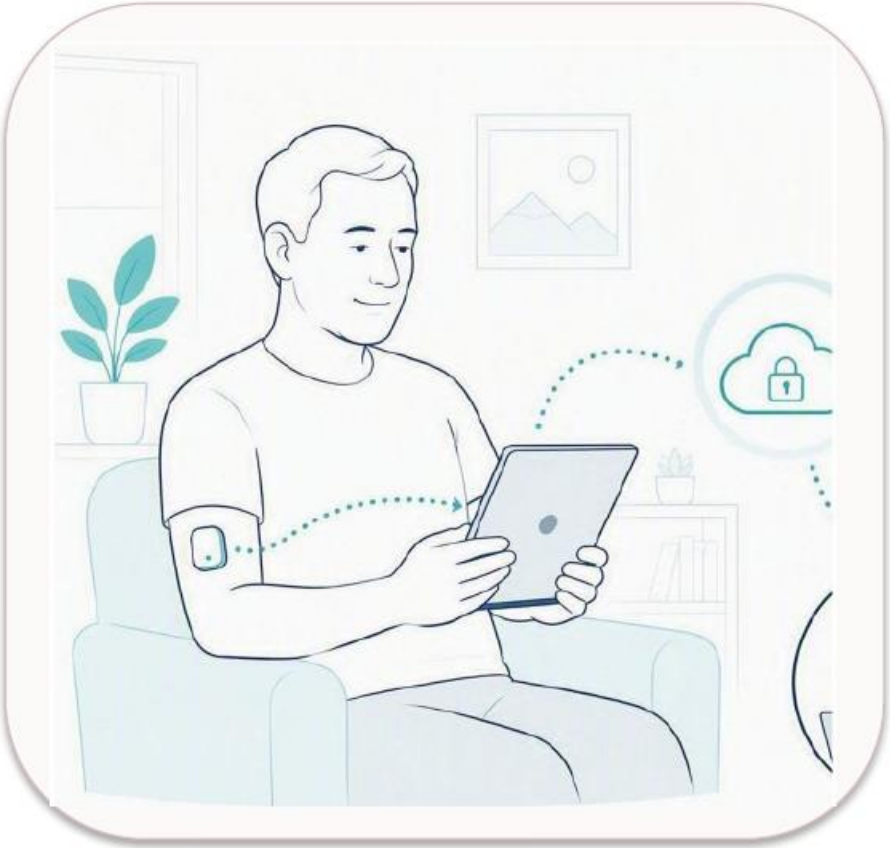
Continuous nurse coverage monitors vital signs on a live dashboard. Nurses filter calls and escalate only when criteria are met, which is uncommon.

3 DAILY EMS HOME VISIT

In-person vital signs and a daily ICE (Immune Effector Cell-associated Encephalopathy) score performed by the emergency medical services team in the patient's home.

4 DAILY VIRTUAL INTERNIST

Video check-in with the Hospital-at-Home internist for clinical assessment and care coordination.



CAREGIVER IS PART OF THE SYSTEM

Educated on signs of CRS and ICANS before discharge, with teach-back and a direct line to the monitoring nurse. Nurses filter calls that do not need a physician; escalations are uncommon.

Monitoring combines patient-entered vital signs, continuous nursing oversight, daily in-home assessment, and virtual physician review.

LCI = Levine Cancer Institute.

Varga C, et al. Presented at: 22nd Annual International Myeloma Society (IMS) Meeting & Exposition; 2025. Abstract PA-097.

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The Minimum Viable Program

You do not need a Hospital-at-Home service to start. You do need every one of these.

01 TOCILIZUMAB ON SITE

Stocked and releasable at the infusion center, not ordered from a central pharmacy at 6 pm.

02 A NAMED ESCALATION PHYSICIAN

Available 24/7.

03 A DEFINED RECEIVING FACILITY

One hospital that has agreed in advance to accept these patients, with a warm handoff pathway.

04 A WRITTEN CRS/ICANS SOP

Institutionally approved, in the hands of the monitoring team, the ED and the admitting service.

05 STRUCTURED SYMPTOM MONITORING

At minimum: scheduled temperature checks and a documented escalation trigger.

06 AN EDUCATED CAREGIVER

Taught to take a temperature, recognize confusion, and call.

Minimum infrastructure: immediate treatment access, clear ownership, a receiving pathway, a shared SOP, structured monitoring, and an informed caregiver.

SOP = standard operating procedure; ED = emergency department.

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SOP: The Patient Has a Fever

Fever is the first and usually the only sign. Every person in the pathway should know these four steps cold.

1

ACT, DON'T WAIT

At the first fever the patient or caregiver needs to act. Assess temperature trend and associated symptoms.

2

RULE OUT INFECTION

Always. Neutropenia and infection are far more dangerous than grade 1 CRS, and they look identical at the door.

3

TREAT AT HOME IF POSSIBLE

Acetaminophen +/- dexamethasone per protocol. Most grade 1 CRS resolves here. Keep the monitoring interval tight.

4

ESCALATE ON CRITERIA

Persistent fever → tocilizumab pathway (outpatient infusion center if possible). Grade 2 or higher CRS, or any ICANS → ED and admission at the receiving facility.

ONE PEARL: Fever outside the step-up window is unlikely to be CRS, with the exception of the first full dose.

Recognize early, exclude infection, treat promptly, and escalate using predefined criteria.

Atrium Health bispecific antibody CRS and neurotoxicity management guideline.

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SOP: The Patient Is Confused

Recognize subtle neurotoxicity early and act promptly when ICANS is suspected.

RECOGNIZE IT

- ICE (immune effector cell-associated encephalopathy) score daily, and with any change
- Earliest signs are subtle: word-finding difficulty, lethargy, handwriting change, inattention
- **The caregiver is usually the first to notice. Teach them what to look for.**
- Differential: infection/sepsis, CNS infection, medication, CVA, CNS involvement by malignancy

ACT ON IT

Dexamethasone in the pocket. Patients go home from infusion with dexamethasone in pocket and explicit instructions on when to take it, so the first dose is given at home.

- Any grade ICANS → present for evaluation and admit
- Steroids are the backbone. Tocilizumab does not treat ICANS; use it only for concurrent CRS.
- Hold the bispecific and involve neurology per protocol

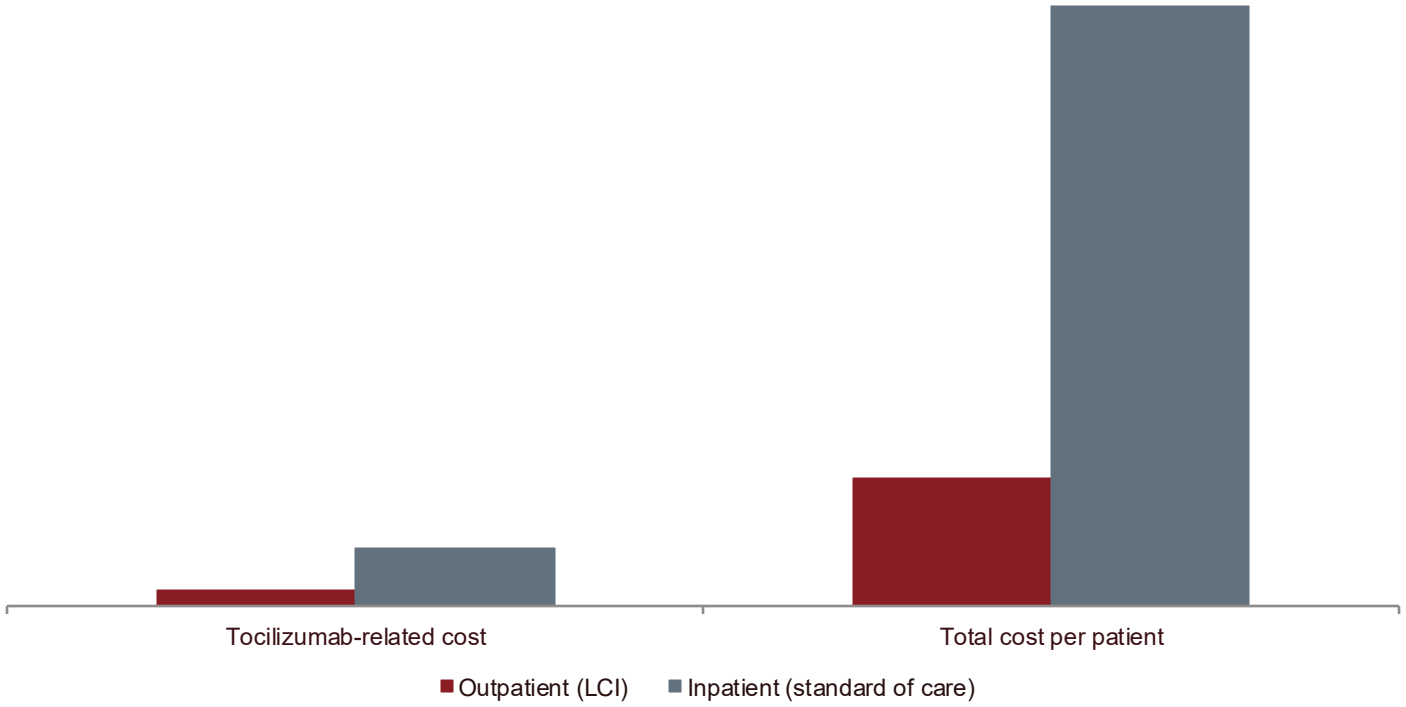
Caregiver recognition, immediate evaluation, and early corticosteroids are central to the ICANS pathway.

Tocilizumab max 800 mg per dose, up to 3 doses in 24 h and 4 doses total. Refractory CRS: persistent despite 3 toci doses and steroids.
CVA = cerebrovascular accident

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What It Saves

Retrospective comparison of outpatient step-up dosing with prophylactic dexamethasone at LCI (N = 32) versus standard 48-hour inpatient monitoring at Wake Forest (N=24).



78%

reduction in total cost per patient with outpatient step-up dosing

- All ICANS events were grade 1
- No treatment-related deaths in either arm
- Inpatient bed days freed for patients who need them
- Savings are amplified where dex prophylaxis reduces toci use

Outpatient step-up dosing reduced total cost per patient while preserving a favorable safety profile in this retrospective comparison.

Varga C, et al. Presented at: 22nd Annual IMS Meeting & Exposition; 2025. Abstract PA-097.

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Taking It to the Regional Sites

The hub does not have to do the dosing. It has to provide the education.

1 DOSE LOCALLY

The patient receives step-up dosing at their own community infusion center, close to home, in a familiar clinic.

2 MONITOR CENTRALLY?

The patient is registered with the central remote monitoring service (HaH)?, which covers them through the entire step-up window.

3 ESCALATE TO ONE PLACE

If intervention is needed, tocilizumab or admission, the patient goes to the designated main campus. The pathway is agreed upon in advance.

4 SUPPORT THE SITE

Hub attending available during business hours; on-call attending after hours. The monitoring nurses filter calls, so escalations are few.

BEFORE THE FIRST PATIENT AT A NEW SITE, CONFIRM:

- ☐ Infusion center can stock and release tocilizumab
- ☐ The SOP is physically in the hands of the monitoring team
- ☐ Receiving facility has agreed to the admission pathway
- ☐ Site team has been visited by MDs, APPs, RNs, pharmacists, clinic and nurse managers
- ☐ After-hours escalation contact is documented and tested
- ☐ Local ED has been briefed

TIMING MATTERS: As bispecifics move into earlier lines of therapy, volume will outgrow academic centers. Build the pathway before the wave, not during it.

HAH = hospital-at-home.
Levine Cancer Institute satellite rollout experience.

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Key Learning Points

1	**Sequence by disease course**	Start with relapse timing, prior first-line regimen, fitness, and candidacy for CAR T or autologous transplant.
2	**Preserve access to curative-intent therapy**	For primary refractory or early-relapse disease, prioritize timely CAR T referral while minimizing access and bridging delays.
3	**Match target to biology and prior exposure**	Biopsy at relapse and reassess CD20/CD19; timing after CAR T may help identify higher-risk biology.
4	**Use non-CAR T options strategically**	Bispecific antibodies and ADC-based combinations provide active alternatives; fixed-duration regimens can produce durable remissions, especially after an early CR. Bispecific antibody combinations may be curative for a proportion of patients
5	**Build delivery pathways, not just drug lists**	Risk-adapted outpatient step-up dosing can expand regional access when supported by a standardized SOP, trained caregivers, remote monitoring, and a clear escalation plan.

Bottom line: The optimal R/R DLBCL strategy integrates biology, timing, treatment goals, and a delivery model that brings effective therapy closer to the patient.

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Q&A Session