Second Opinion: Investigators Provide Perspectives on the Current and Future Use of Novel Therapies for Non-Hodgkin Lymphoma

Monday, June 1, 2026
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

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Matthew Lunning, DO
Sonali M Smith, MD

Moderator

Brad S Kahl, MD

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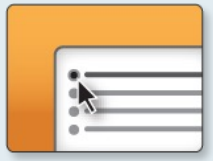

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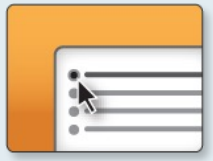

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Second Opinion

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Agenda

Module 1: Rational Incorporation of CD79b-Targeted Antibody-Drug Conjugates into the Management of Newly Diagnosed and Relapsed/ Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Flowers

Module 2: Clinical Utility of CD19-Directed Monoclonal Antibodies in the Treatment of DLBCL and Follicular Lymphoma (FL) — Dr Smith

Module 3: Optimal Use of CD19-Directed Antibody-Drug Conjugates for R/R DLBCL and FL — Dr Lunning

Module 4: Current and Future Role of Bruton Tyrosine Kinase Inhibition in Therapy for Non-Hodgkin Lymphoma — Dr Kahl

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Rational Incorporation of CD79b-Targeted Antibody-Drug Conjugates into the Management of Newly Diagnosed and R/R DLBCL

Christopher Flowers, MD, MS, FASCO

Division Head
Chair, Professor

Division of Cancer Medicine
Department of Lymphoma/Myeloma

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
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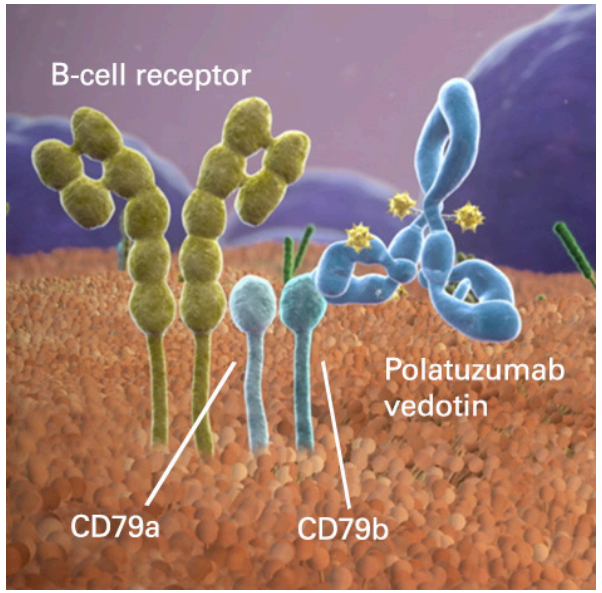
POLARIX: 1L DLBCL Phase 3



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

H. Tilly, F. Morschhauser, L.H. Sehn, J.W. Friedberg, M. Trněný, J.P. Sharman, C. Herbaux, J.M. Burke, M. Matasar, S. Rai, K. Izutsu, N. Mehta-Shah, L. Oberic, A. Chauchet, W. Jurczak, Y. Song, R. Greil, L. Mykhalska, J.M. Bergua-Burgués, M.C. Cheung, A. Pinto, H.-J. Shin, G. Hapgood, E. Munhoz, P. Abrisqueta, J.-P. Gau, J. Hirata, Y. Jiang, M. Yan, C. Lee, C.R. Flowers, and G. Salles

Patients

- Previously untreated DLBCL
- Age 18–80 years
- IPI 2–5
- ECOG PS 0–2

Stratification factors

- IPI score (2 vs 3–5)
- Bulky disease (<7.5 vs ≥7.5cm)
- Geographic region (Western Europe, US, Canada, & Australia vs Asia vs rest of world)

R 1:1

Pola-R-CHP

Polatuzumab vedotin (1.8mg/kg)* + **R-CHP + vincristine placebo**

Cycles 1–6
(1 cycle=21 days)

R-CHOP

R-CHOP† + **polatuzumab vedotin placebo**

Rituximab
375mg/m^2

Cycles 7 & 8

Primary endpoint

Progression-free survival (Investigator-assessed)

Secondary endpoints

- Event-free survival
- Complete response rate at end of treatment (PET/CT, IRC-assessed)
- Disease-free survival
- Overall survival

Safety endpoints

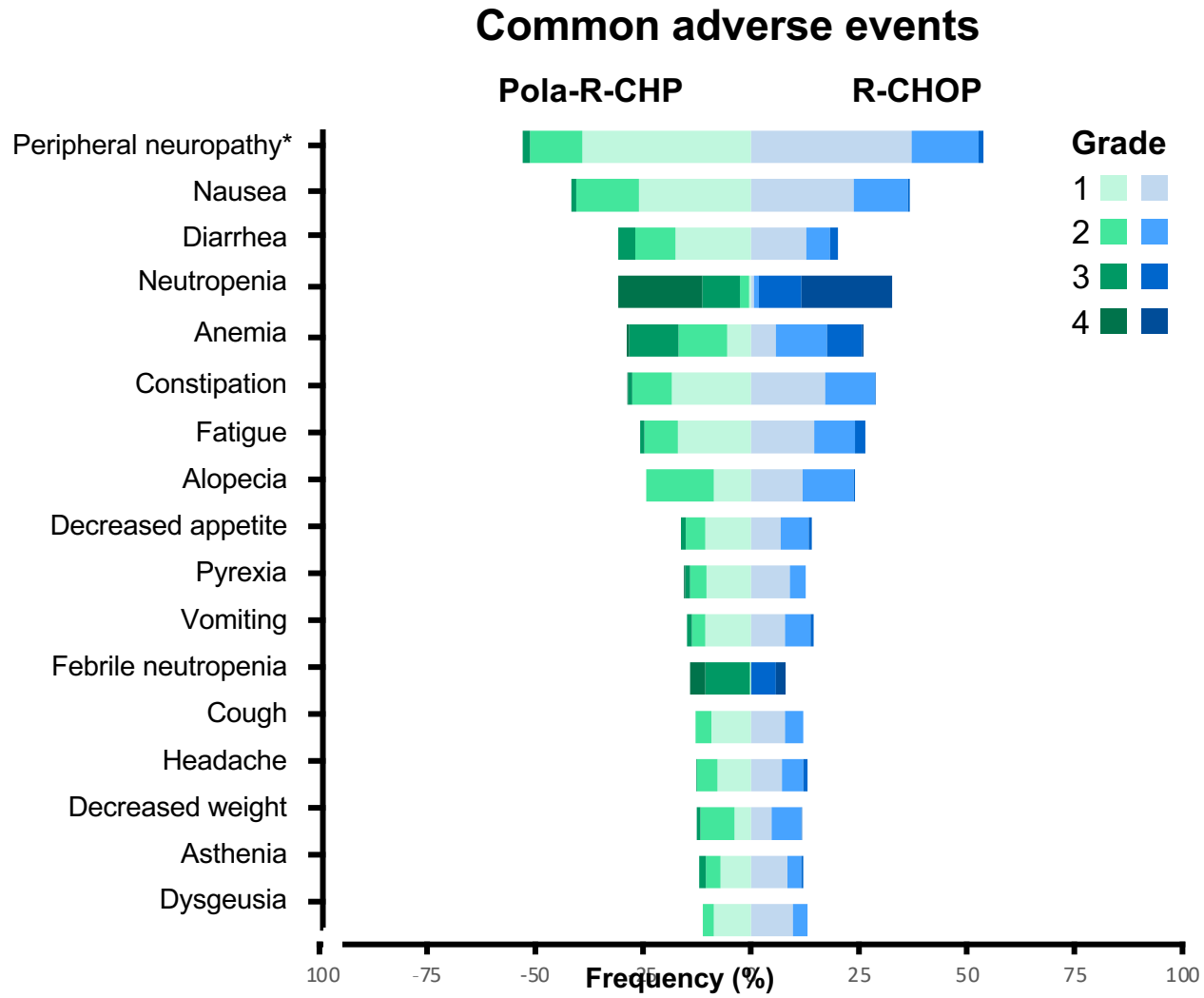
Incidence, nature, and severity of adverse events

Tilly et al. *NEJM* 2021

Safety summary

Safety profiles were similar with Pola-R-CHP and R-CHOP

n (%)	Pola-R-CHP (N=435)	R-CHOP (N=438)
Any-grade adverse events	426 (97.9)	431 (98.4)
Grade 3–4	251 (57.7)	252 (57.5)
Grade 5	13 (3.0)	10 (2.3)
Serious adverse events	148 (34.0)	134 (30.6)
Adverse events leading to:		
Discontinuation of any study drug	27 (6.2)	29 (6.6)
Polatuzumab vedotin / vincristine	19 (4.4)	22 (5.0)
Dose reduction of any study drug	40 (9.2)	57 (13.0)

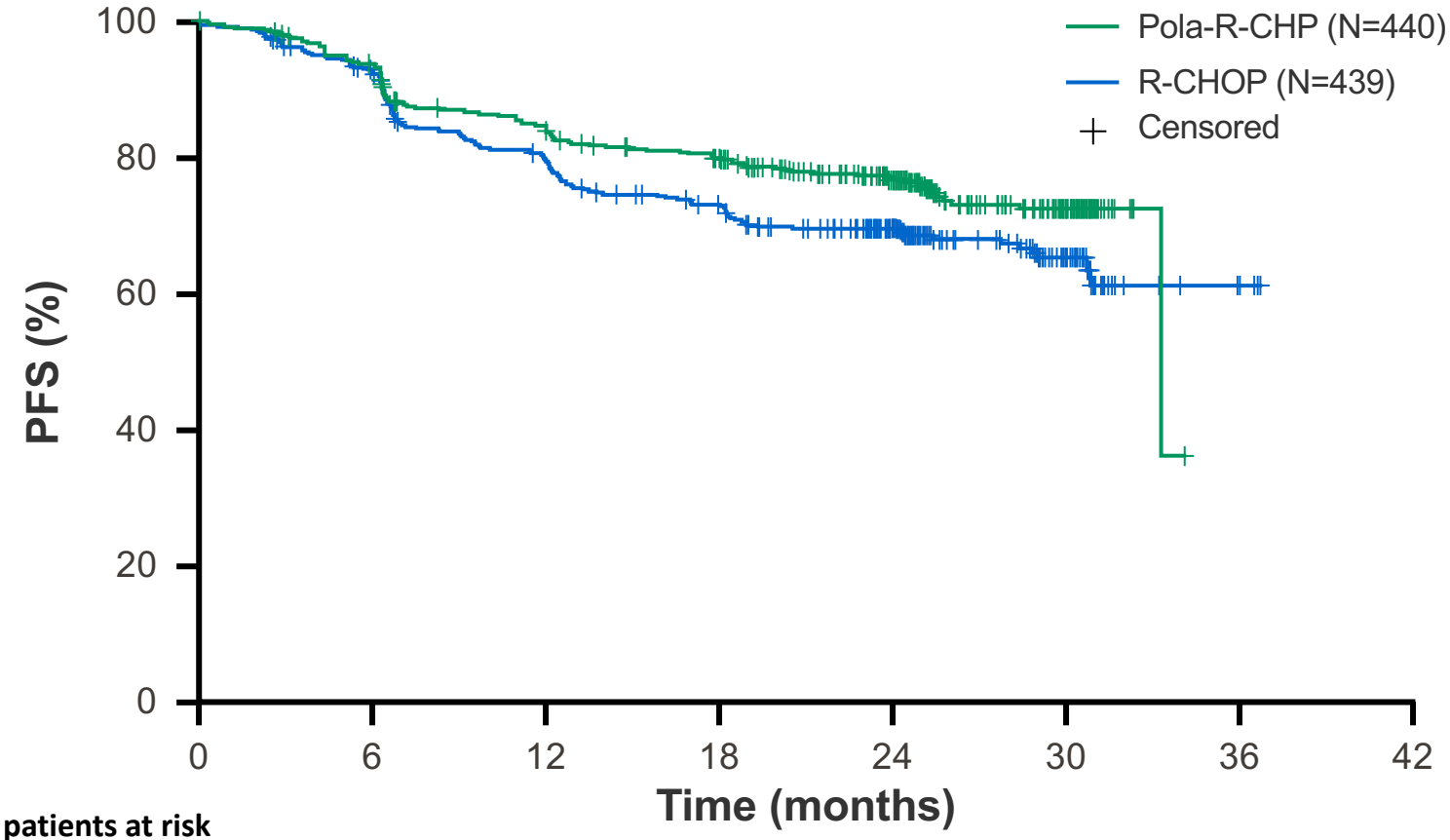


- ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
  CI, confidence interval; HR, hazard ratio; NE, not evaluable; PFS, progression-free survival.

Tilly et al. *NEJM* 2021

Primary endpoint: Progression-free survival

Pola-R-CHP significantly improved PFS vs R-CHOP



No. of patients at risk

Pola-R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

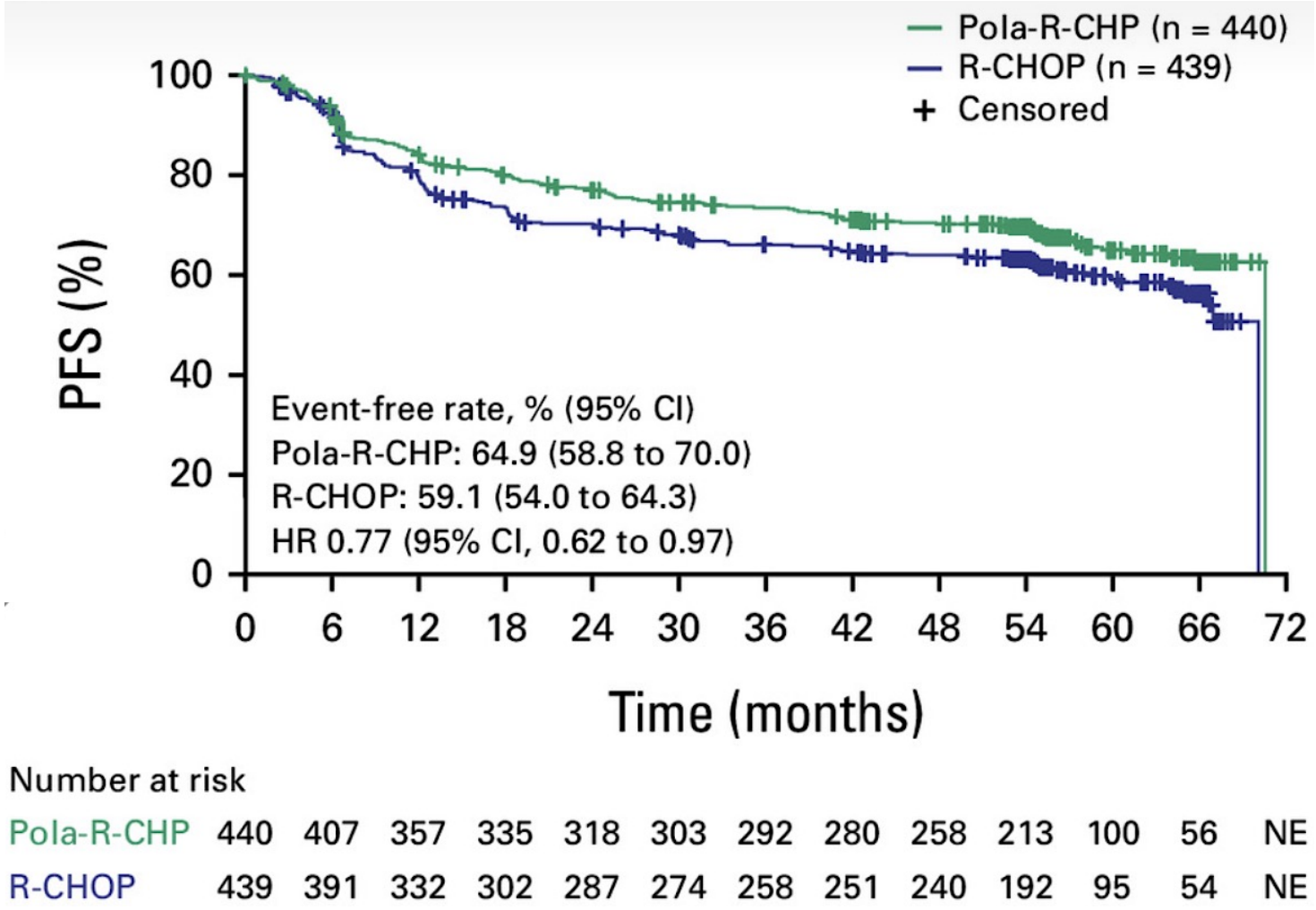
HR 0.73 **(P=0.02)**

95% CI: 0.57, 0.95

- Pola-R-CHP demonstrated a **27% reduction in the relative risk of disease progression, relapse, or death** vs R-CHOP
- **24-month PFS:** 76.7% with Pola-R-CHP vs 70.2% with R-CHOP (Δ**=6.5%**)

Tilly et al. *NEJM* 2021

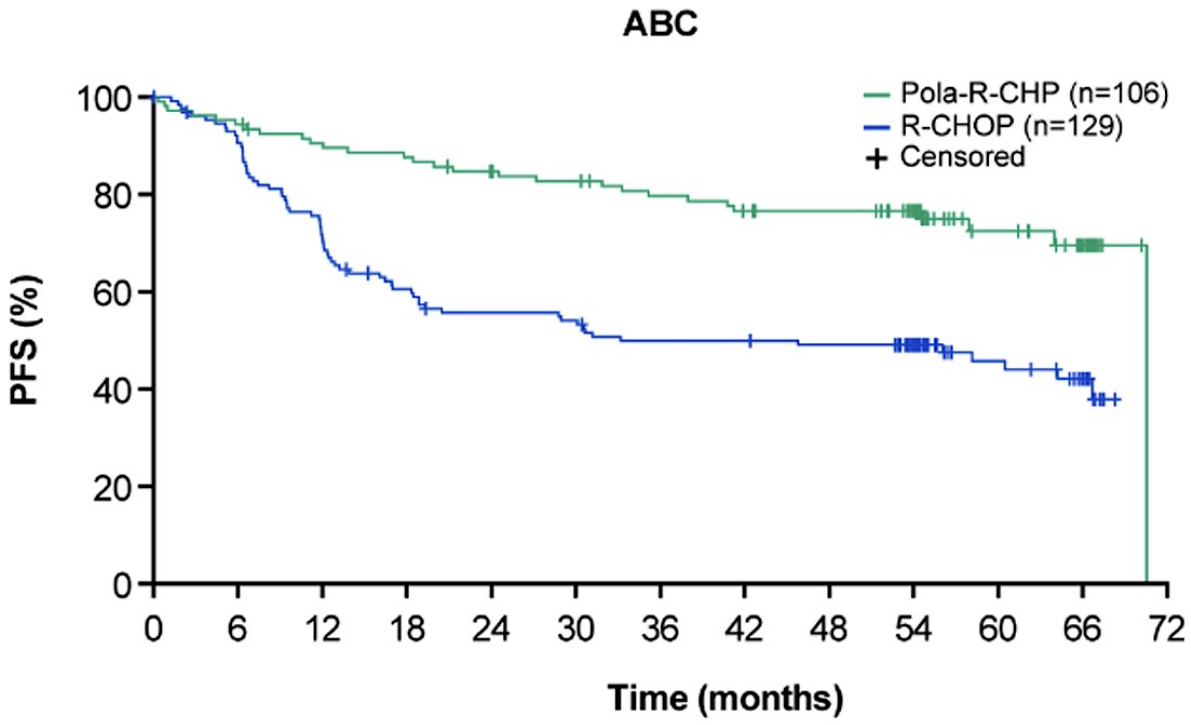
Five-year analysis of the POLARIX study in the global ITT population

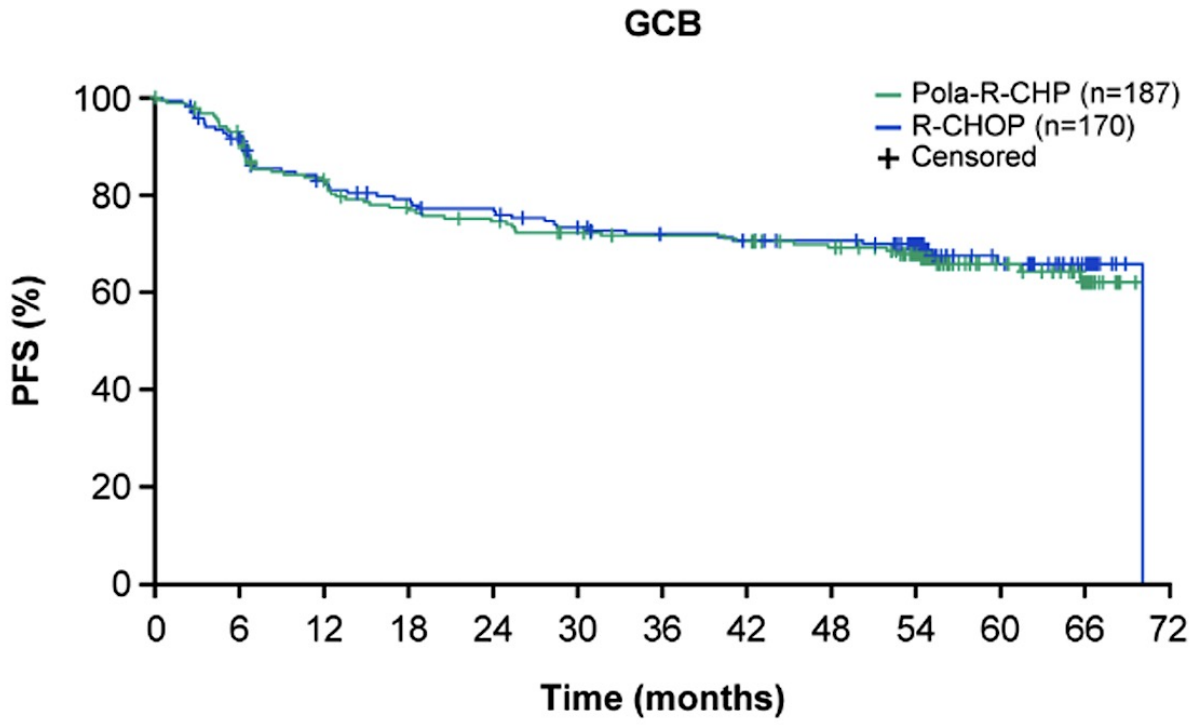


At the 5-year follow up, Pola-R-CHP had a **sustained and significant PFS benefit**, confirming results from the primary analysis of PFS at 2 years of follow up (HR 0.73).[1]

Morschhauser et al. *J Clin Oncol.* 2025

Genotype differences in treatment impact: POLARIX





Patients remaining at risk

Pola-R-CHP	106	100	94	91	86	83	78	74	70	60	28	18	NE
R-CHOP	129	115	90	75	68	66	60	60	58	46	26	17	NE

Patients remaining at risk

Pola-R-CHP	187	171	148	136	130	123	119	117	109	85	43	22	NE
R-CHOP	170	150	132	124	120	111	106	103	100	82	39	26	NE

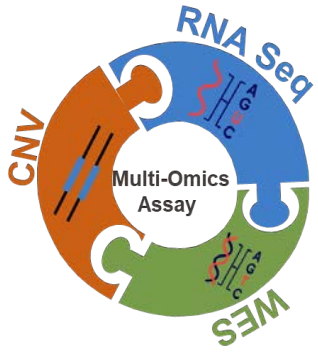
Morschhauser et al. *J Clin Oncol.* 2025

PRECISE DLBCL - Chihara

Newly Diagnosed DLBCL (n=77)

FFPE Tissue Biopsy

COO, DZ_{Sig}, LymphGen, DLBCLass LymphoMAP, LME Classification



ABC
35–40%
Unclassified
10–15%
→ **Pola-R-CHP x 5-6 cycles**

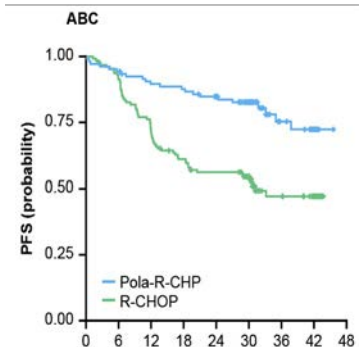
FISH DHL
Dzsig+
20–25%
→ **DA-EPOCH-R x 5-6 cycles**

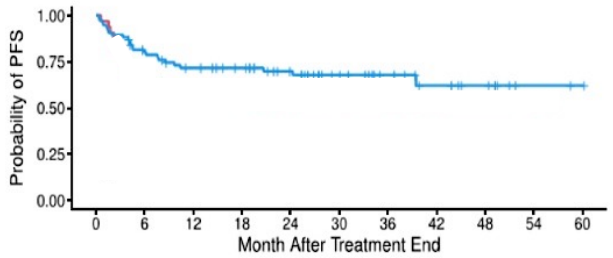
Dzsig-
GCB
25–30%
→ **R-CHOP x 5-6 cycles**

Protocol Number: 2025-1674

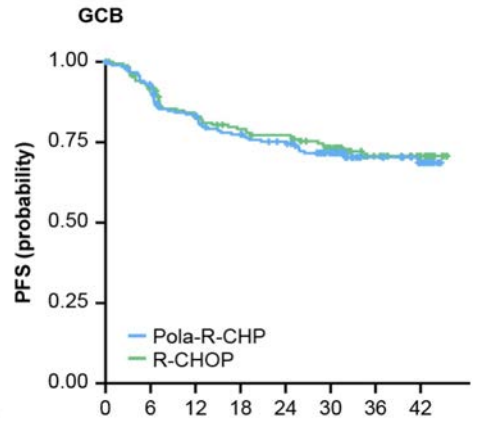
Patients may receive 1 cycle of R-CHOP while awaiting biomarker results

Expected Outcomes



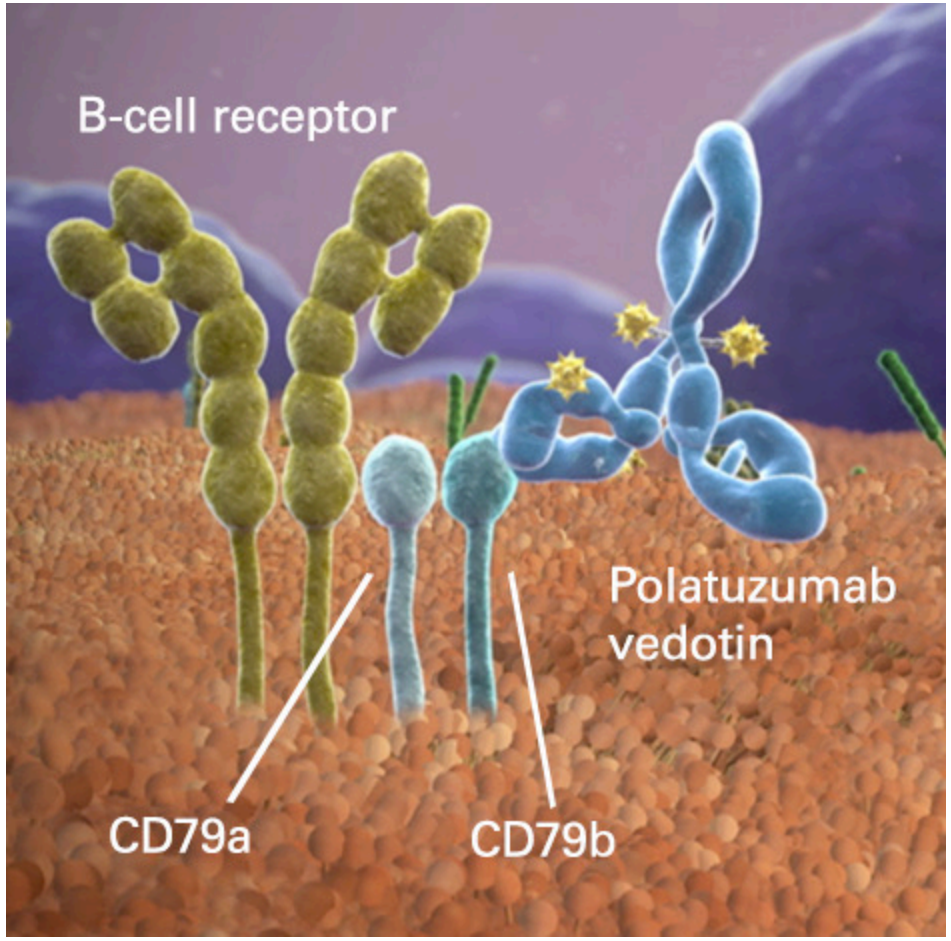


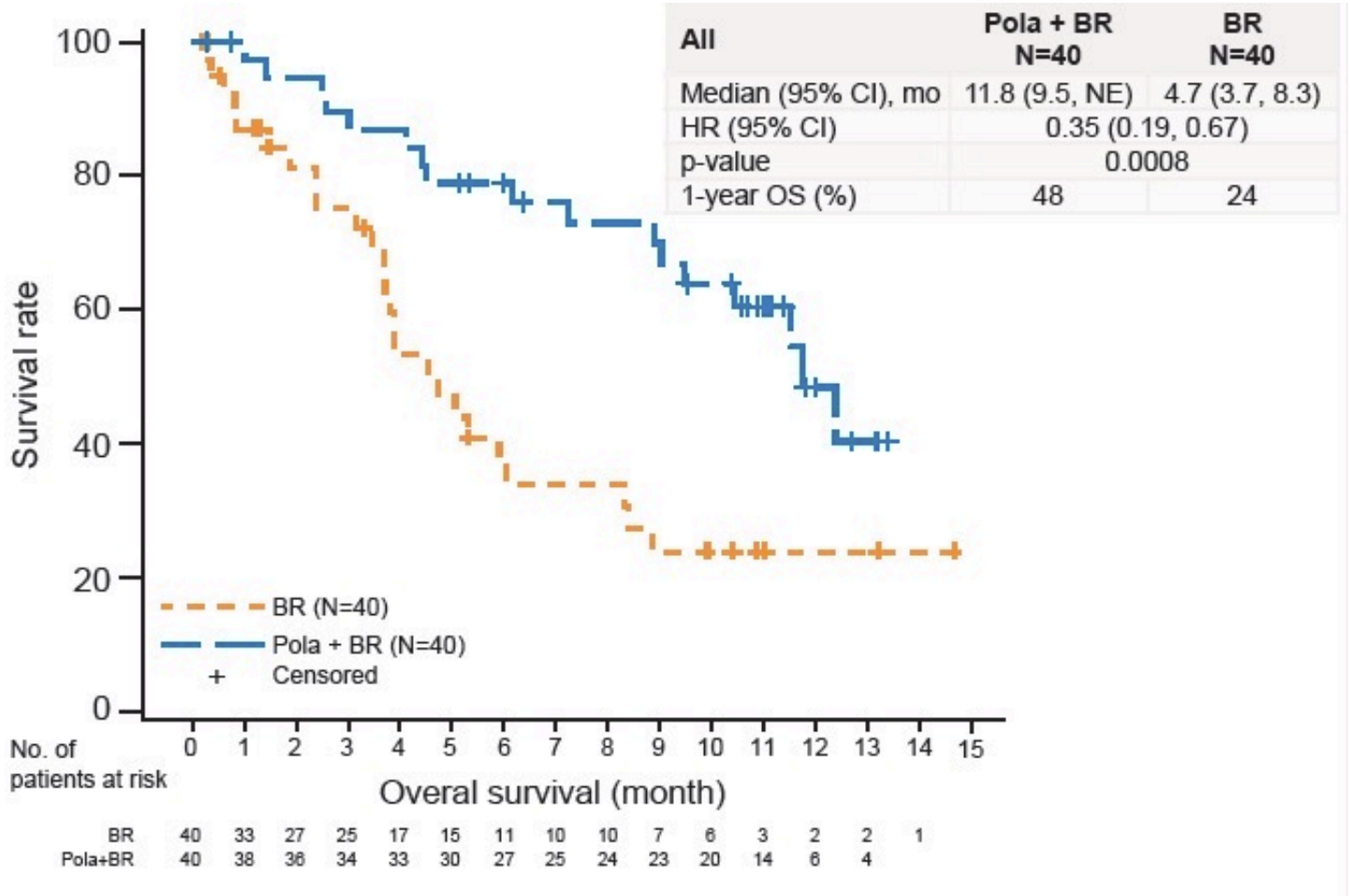
multi-center outcomes of DA-EPOCH-R
Cortese et al *Leuk Lymphoma* 2023



Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma *J Clin Oncol.* 2020

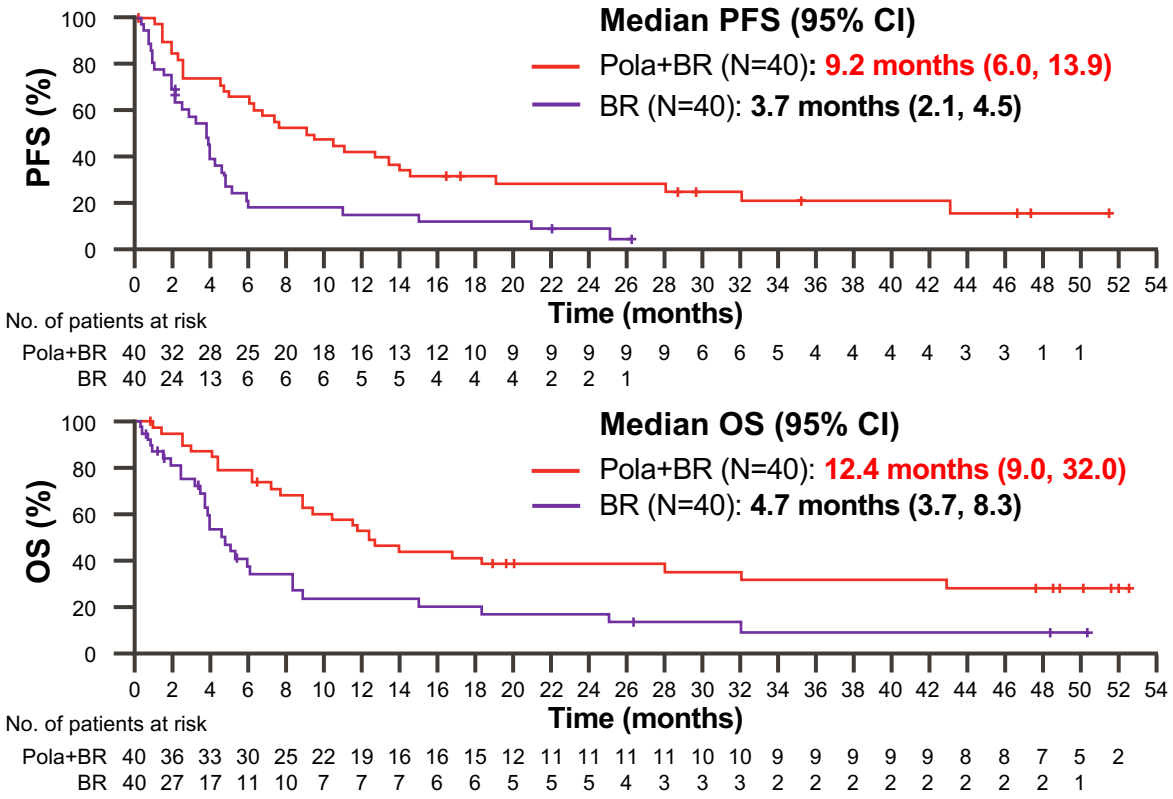
Laurie H Sehn, Alex F Herrera, Christopher R Flowers, Manali Kamdar, Andrew McMillan, Mark Hertzberg, Sarit Assouline, Tae Min Kim, Won Seog Kim, Muhit Ozcan, Jamie Hirata, Elicia Penuel, Ji Cheng, Joseph N. Paulson, Grace Ku, Matthew Matasar



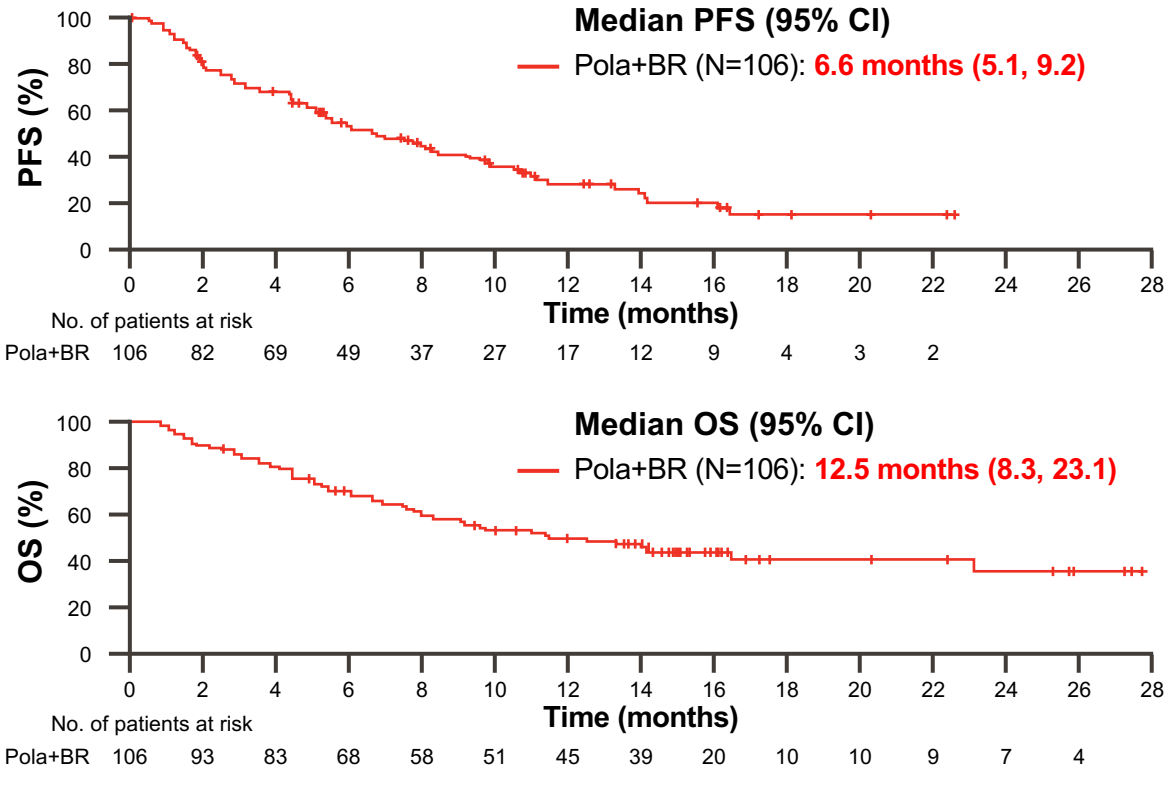


Pola-BR PFS and OS

Randomized



Extension cohort



Sehn LH et al. Blood Adv 2022

Pola BR Safety Summary

AE summary, n (%)	Randomized		Extension Cohort Pola+BR (N=106)	Pooled Pola+BR (N=151)
	BR (N=39)	Pola+BR (N=39)		
Any Grade AEs	38 (97.4)	39 (100)	105 (99.1)	150 (99.3)
Grade 3–4 AEs	28 (71.8)	34 (87.2)	83 (78.3)	122 (80.8)
SAEs	24 (61.5)	26 (66.7)	56 (52.8)	86 (57.0)
Grade 5 AEs	10 (25.6)	11 (28.2)	6 (5.7)	17 (11.3)

No new safety signals identified with longer follow-up in randomized arms + patients in the extension cohort

Common AEs, n (%)	Pooled Pola+BR (N=151)	
	Any grade	Grade 3–4
Hematological AEs		
Neutropenia	**71 (47.0)**	**49 (32.5)**
Thrombocytopenia	49 (32.5)	31 (20.5)
Anemia	49 (32.5)	19 (12.6)
Non-hematological AEs		
Infections and infestations	**74 (49.0)**	**33 (21.9)**
Diarrhea	54 (35.8)	6 (4.0)
Nausea	50 (33.1)	1 (0.7)
Pyrexia	44 (29.1)	2 (1.3)
Fatigue	40 (26.5)	3 (2.0)
Decreased appetite	39 (25.8)	4 (2.6)
AEs of special interest		
Peripheral neuropathy	**47 (31.1)**	**3 (2.0)**

Sehn LH et al. Blood Adv 2022

SUNMO Study design

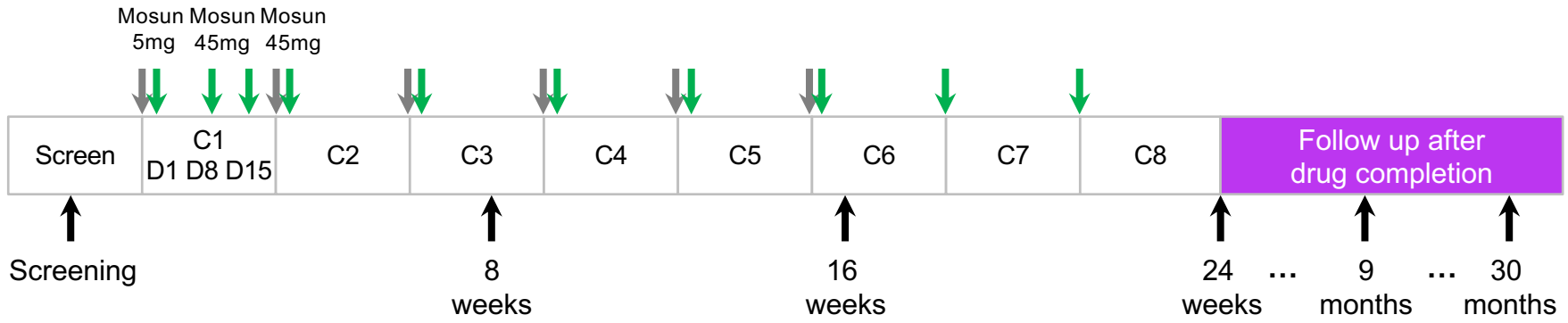
Key eligibility

R/R LBCL with ≥1 prior therapy and ASCT-ineligible:

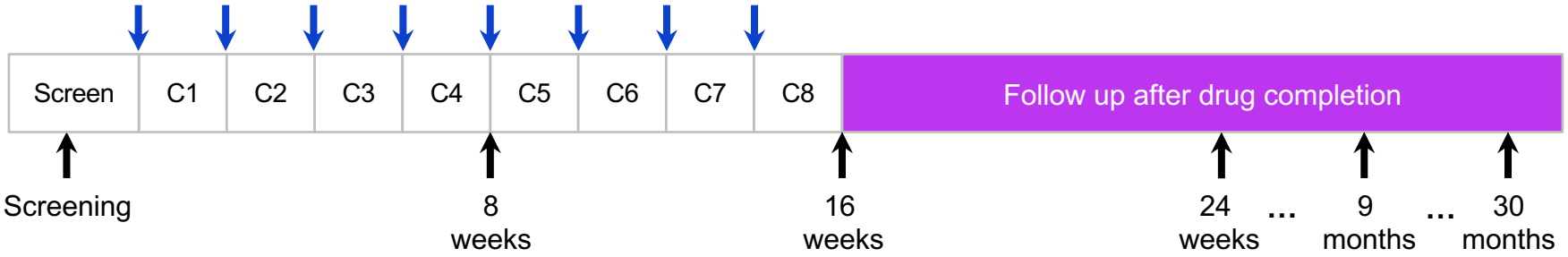
- DLBCL NOS
- Transformed FL
- HGBCL
- Grade 3B FL

2:1

Outpatient Mosun SC (8 cycles) + Pola IV (6 cycles) (21-day cycles)

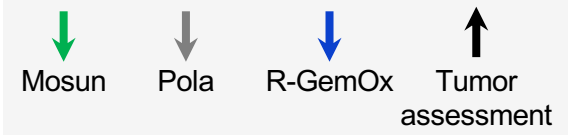


R-GemOx IV (8 x 14–21-day cycles*)



Stratification factors

- 1 vs ≥2 prior lines of systemic therapy
- Relapsed vs refractory disease

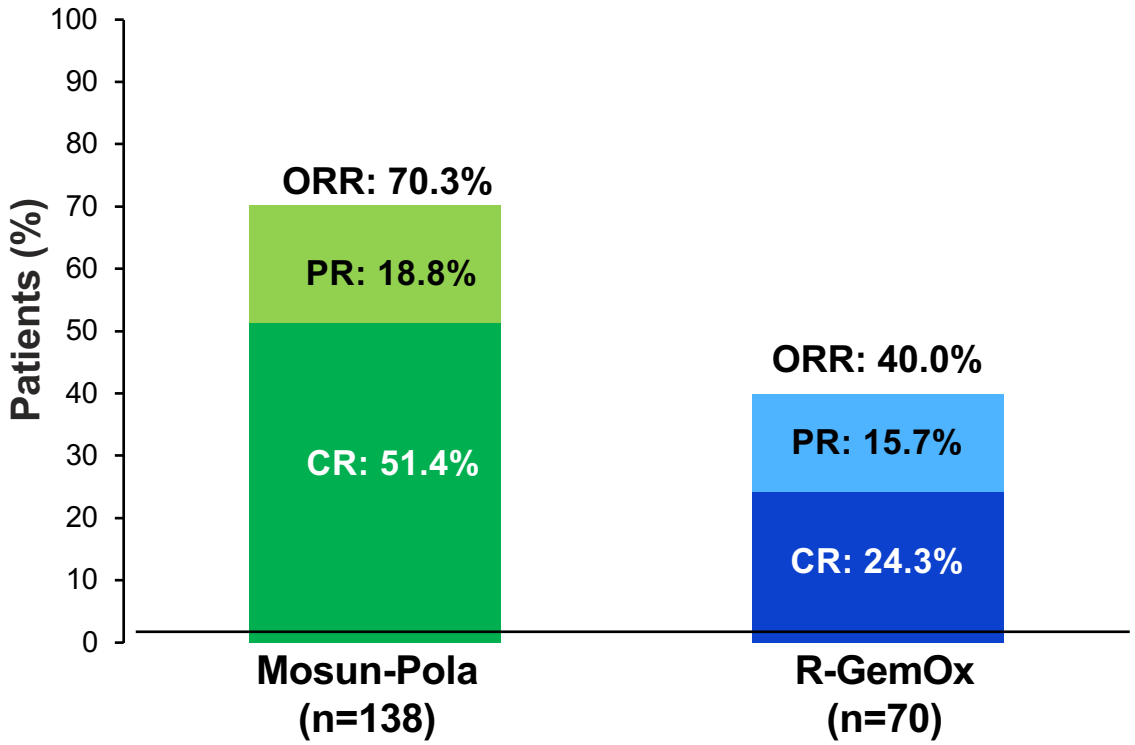


*14-day cycles unless delayed to 21-day cycles if needed in case of hematologic toxicity.
C, cycle; D, day; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IV, intravenous; NOS, not otherwise specified; SC, subcutaneous.

Presented as LBA3 by Westin et al, ICML 2025

Mosun-Pola significantly increased overall response rate versus R-GemOx

Primary Endpoint: Response rates at the primary analysis



Improvement in ORR: Mosun-Pola versus R-GemOx

ORR by IRC, % (95% CI)	Mosun-Pola	R-GemOx	ΔORR (95% CI)	P value
Interim analysis	(n=119) **69.7%** (60.7–77.8)	(n=59) **44.1%** (31.2–57.6)	25.7% (9.6–41.8)	0.0008
Primary analysis	(n=138) **70.3%** (61.9–77.8)	(n=70) **40.0%** (28.5–52.4)	30.3% (15.7–44.9)	<0.0001*

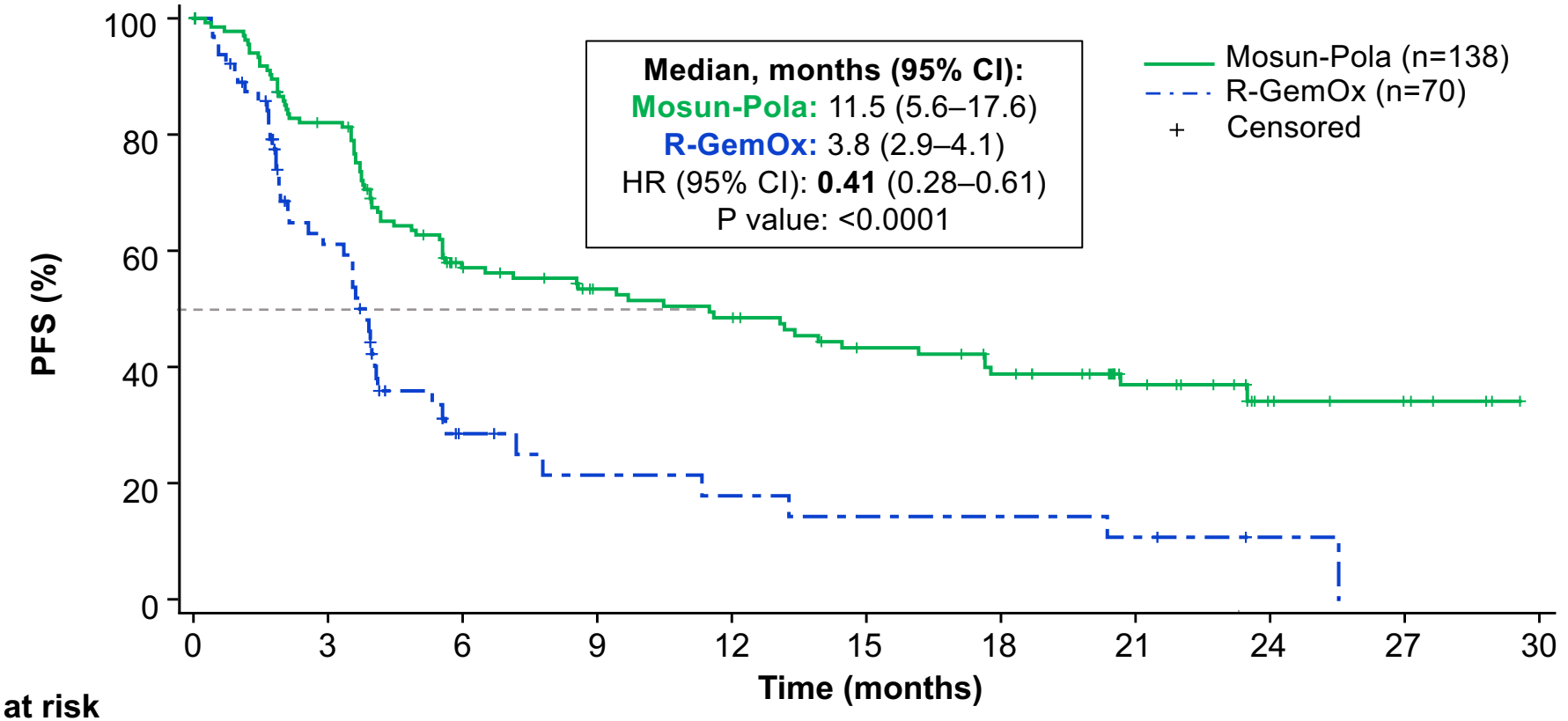
Mosun-Pola doubled the CR rate and improved the ORR by 30% compared with R-GemOx

Clinical cut-off date: 17 February, 2025.
*Descriptive P value. CR, complete response; PR, partial response.

Presented as LBA3 by Westin et al, ICML 2025

Mosun-Pola significantly prolonged progression-free survival versus R-GemOx

Primary endpoint: Progression-free survival by IRC



n at risk

Mosun-Pola	138	108	65	54	49	40	34	20	8	5	NE
R-GemOx	70	33	9	6	5	4	4	3	1	NE	NE

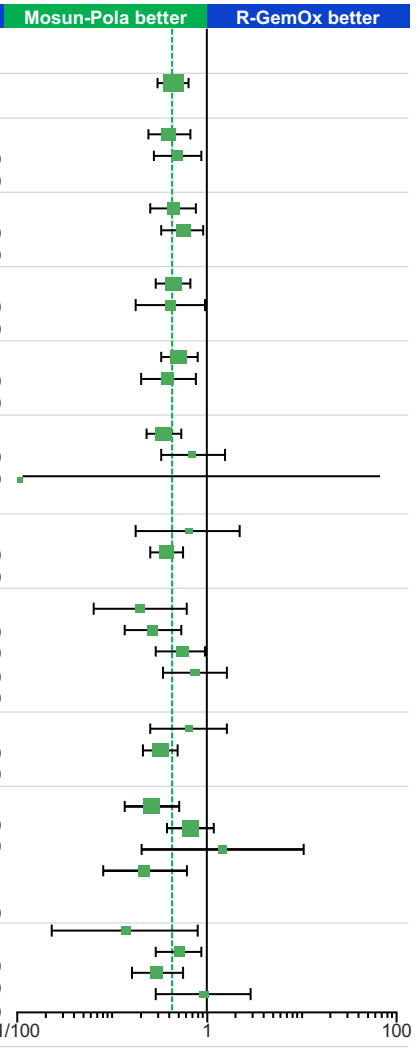
Mosun-Pola demonstrates a 59% risk reduction for progression or death compared with R-GemOx

Clinical cut-off date: 17 February, 2025. PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first.
CI, confidence interval; HR, hazard ratio; NALT, new anti-lymphoma therapy; NE, non estimable.

Presented as LBA3 by Westin et al, ICML 2025

Exploratory analysis of progression-free-survival in pre-specified subgroups

		Mosun-Pola (n=138)			R-GemOx (n=70)				
Baseline risk factors	Total n	n	Events	Median (months)	n	Events	Median (months)	HR	95% CI
All patients	208	138	76	11.5	70	45	3.8	0.41	(0.28–0.61)*
Age group									
<65	122	84	46	11.5	38	25	3.5	0.39	(0.23–0.64)
≥65	86	54	30	13.1	32	20	4.0	0.47	(0.27–0.84)
Number of prior lines of therapy									
1	91	61	32	14.5	30	22	3.6	0.38	(0.22–0.67)
≥2	117	77	44	8.6	40	23	3.9	0.49	(0.29–0.82)
Status to last prior therapy									
Refractory	145	97	63	5.5	48	36	2.6	0.39	(0.26–0.60)
Relapse	63	41	13	NE	22	9	11.3	0.37	(0.16–0.88)
Status to first prior therapy									
Refractory	121	79	54	4.2	42	31	2.6	0.46	(0.29–0.72)
Relapse	87	59	22	23.5	28	14	5.6	0.35	(0.18–0.70)
NHL subtype									
DLBCL	163	109	58	11.5	54	34	3.5	0.38	(0.24–0.59)
HGBCL	40	26	18	9.7	14	9	4.0	0.78	(0.35–1.77)
FL3b	5	3	0	NE	2	2	12.0	<0.01	(0.00–NE)
trFL									
Yes	23	17	8	13.2	6	4	11.3	0.70	(0.19–2.65)
No	185	121	68	9.4	64	41	3.6	0.41	(0.28–0.62)
IPI risk factors at study entry									
Low (0–1)	42	27	10	NE	15	7	3.9	0.21	(0.06–0.66)
Low-intermediate (2)	61	40	16	23.5	21	14	2.9	0.28	(0.14–0.59)
High-intermediate (3)	74	49	32	5.6	25	15	3.8	0.57	(0.30–1.07)
High (4–5)	31	22	18	3.5	9	9	3.5	0.81	(0.36–1.82)
Bulky disease >10cm									
Yes	33	28	22	3.6	5	5	2.6	0.71	(0.26–1.89)
No	175	110	54	16.2	65	40	3.8	0.35	(0.23–0.53)
COO category (central)									
ABC	69	42	19	17.8	27	18	4.0	0.24	(0.12–0.49)
GCB	76	56	41	5.0	20	15	3.7	0.67	(0.37–1.21)
Unclassified	20	15	8	5.6	5	1	NE	1.53	(0.19–12.43)
Missing	38	22	8	NE	16	9	3.5	0.20	(0.07–0.60)
Region at enrollment									
US and Canada	20	13	2	NE	7	3	1.9	0.13	(0.02–0.79)
Latin America	85	59	41	5.3	26	20	3.5	0.50	(0.29–0.87)
East Asia	78	53	27	17.6	25	17	3.8	0.29	(0.16–0.56)
Rest of world	25	13	6	NE	12	5	25.5	0.94	(0.28–3.07)



Mosun-Pola improved PFS in clinically relevant subgroups, including stratification factors:

- relapsed vs refractory
- 2L vs 3L+

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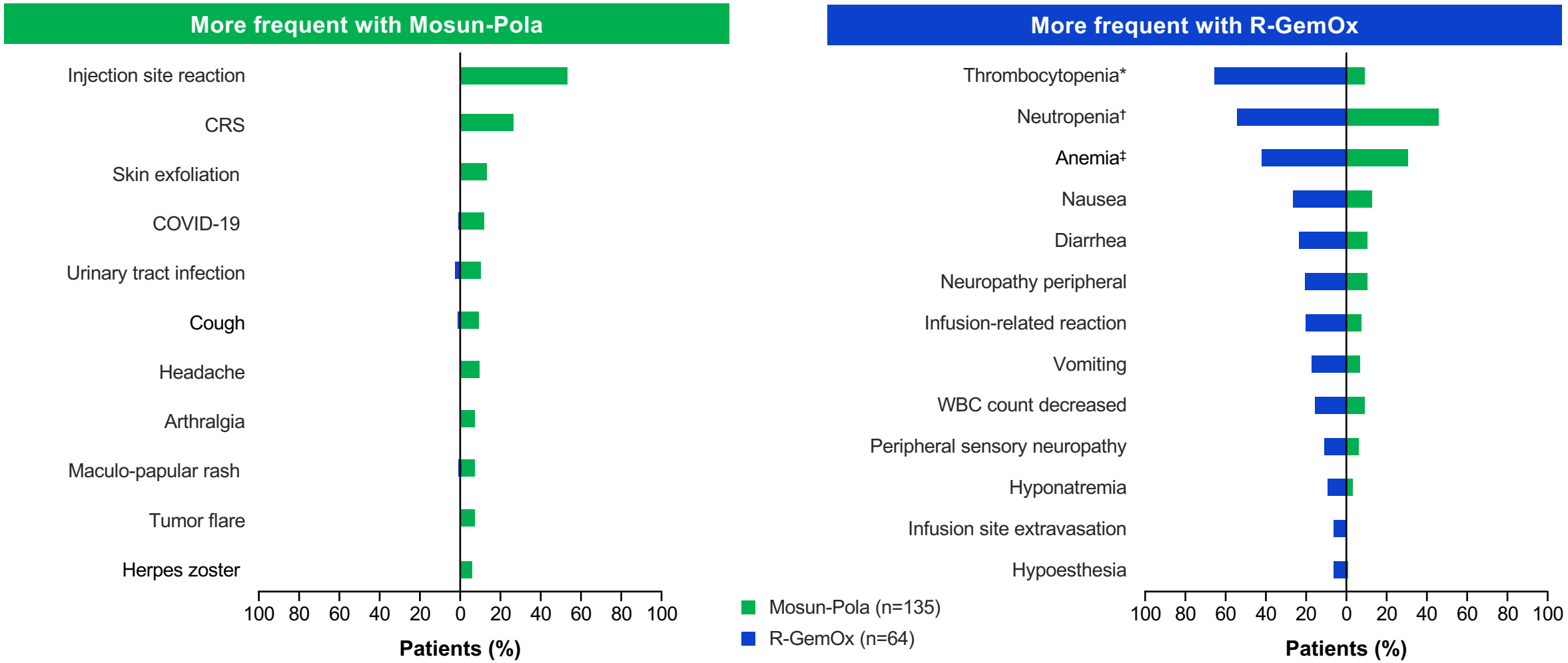
AEs with a difference of at least 5% between treatment arms



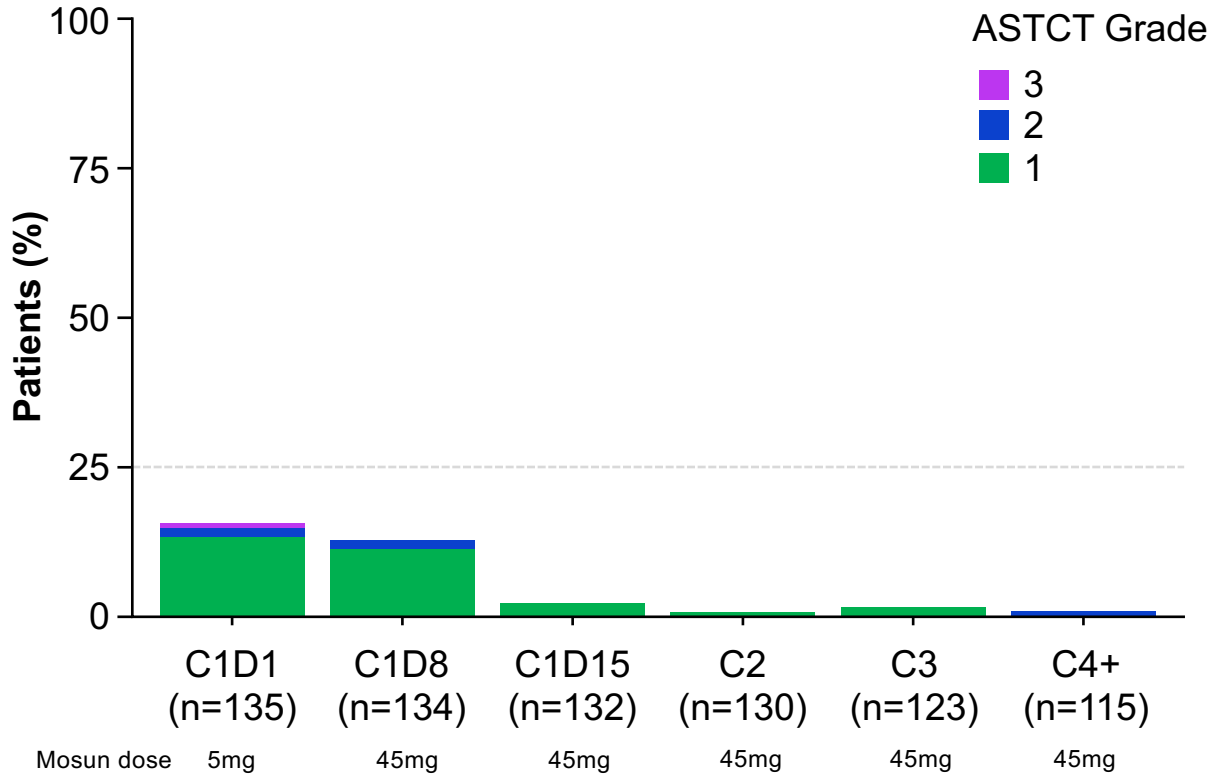
Clinical cut-off date: 17 February, 2025. *Includes thrombocytopenia and platelet count decrease. †Includes neutropenia/neutrophil count decrease. ‡Includes anemia and hemoglobin decrease.
WBC, white blood cell.

Presented as LBA3 by Westin et al, ICML 2025

CRS was infrequent, early, and 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)

CRS by cycle and grade in the Mosun-Pola arm



Mosun-Pola treatment resulted in no significant CRS (Grade 2 or higher) in 96% of patients

Presented as LBA3 by Westin et al, ICML 2025

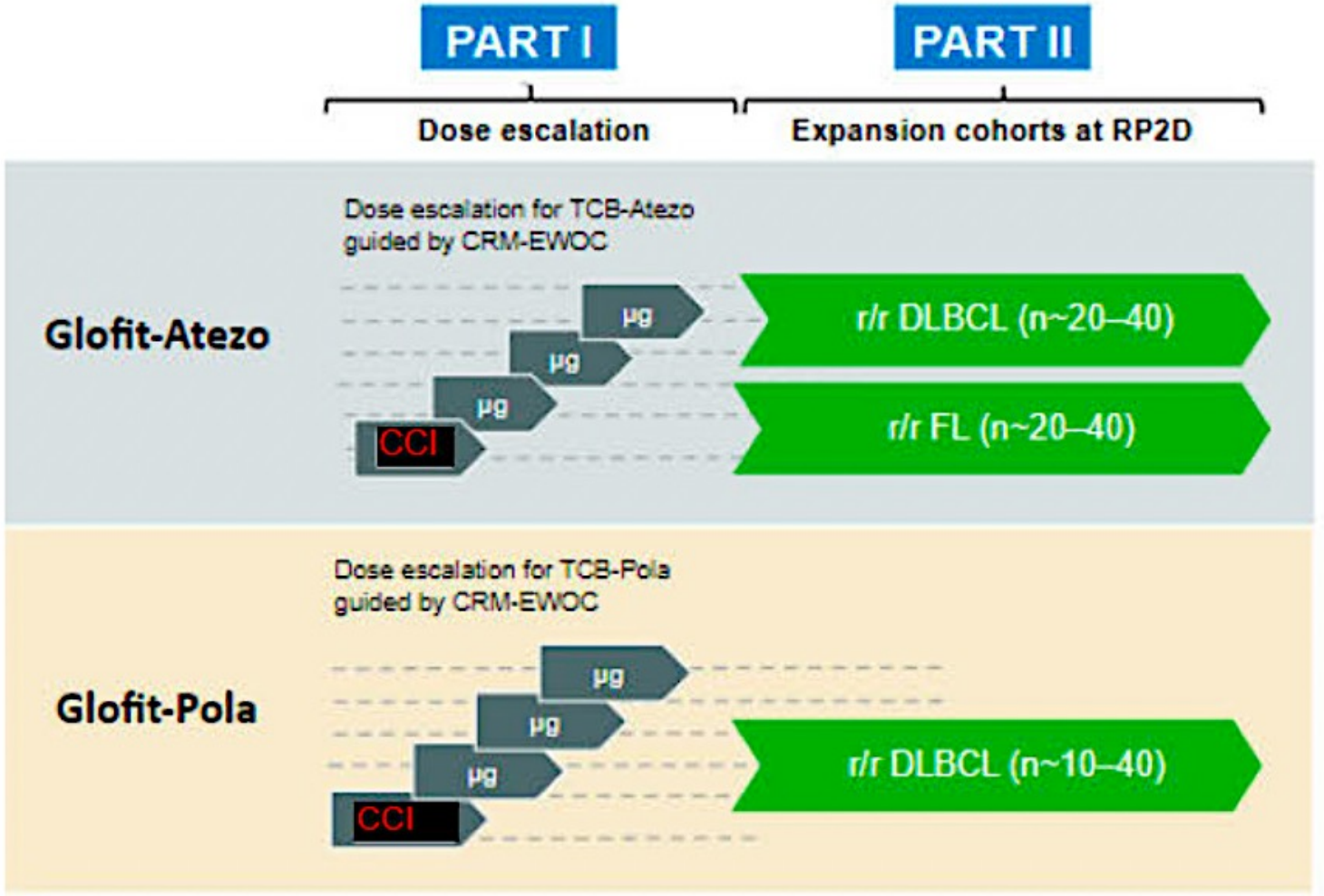
Glofitamab and Polatuzumab Vedotin: A Phase Ib/II Trial

NCT03533283

Patient Population

Part I: r/r NHL
Part II:
- r/r DLBCL (incl. r/r trFL)
- Possibly r/r FL

At least 1 prior therapy
No treatment options that are expected to prolong survival (e.g. autolog SCT)
ECOG 0-2



Hutchings M et al. *J Clin Oncol* 2025 December 20;43(36):3788-98.

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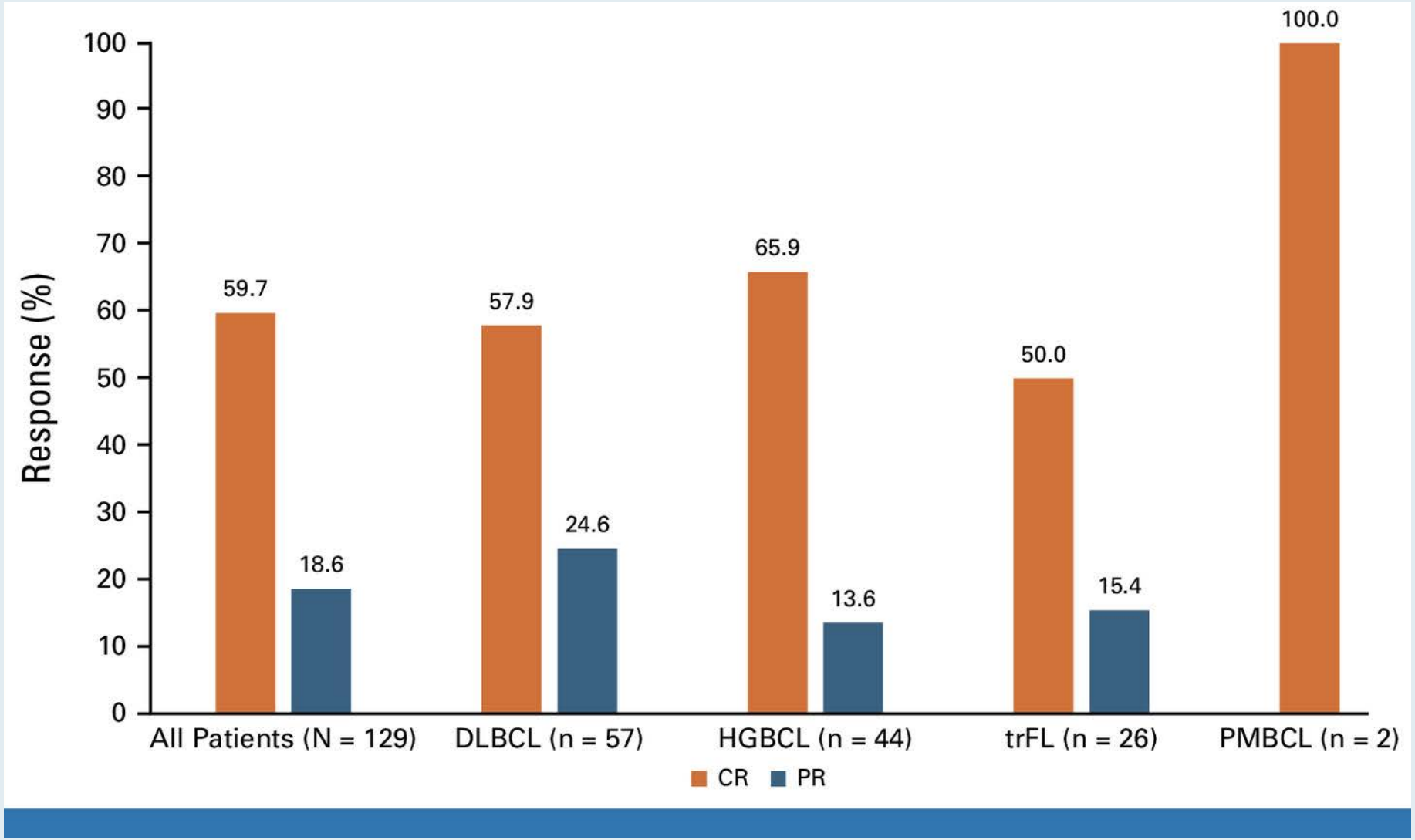
Glofitamab and Polatuzumab Vedotin: Responses



DLBCL = diffuse large B-cell lymphoma; HGBCL = high-grade B-cell lymphoma; trFL = transformed follicular lymphoma; PMBCL = primary mediastinal large B-cell lymphoma; CR = complete response; PR = partial response

Hutchings M et al. *J Clin Oncol* 2025 December 20;43(36):3788-98.

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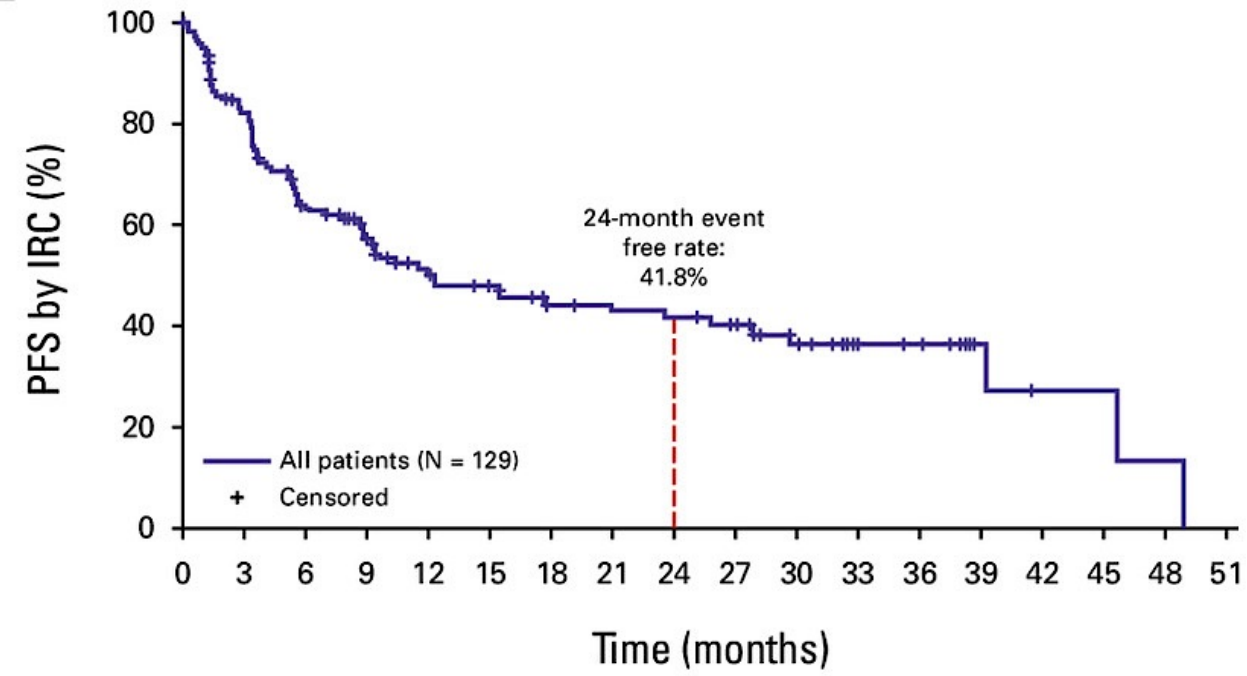
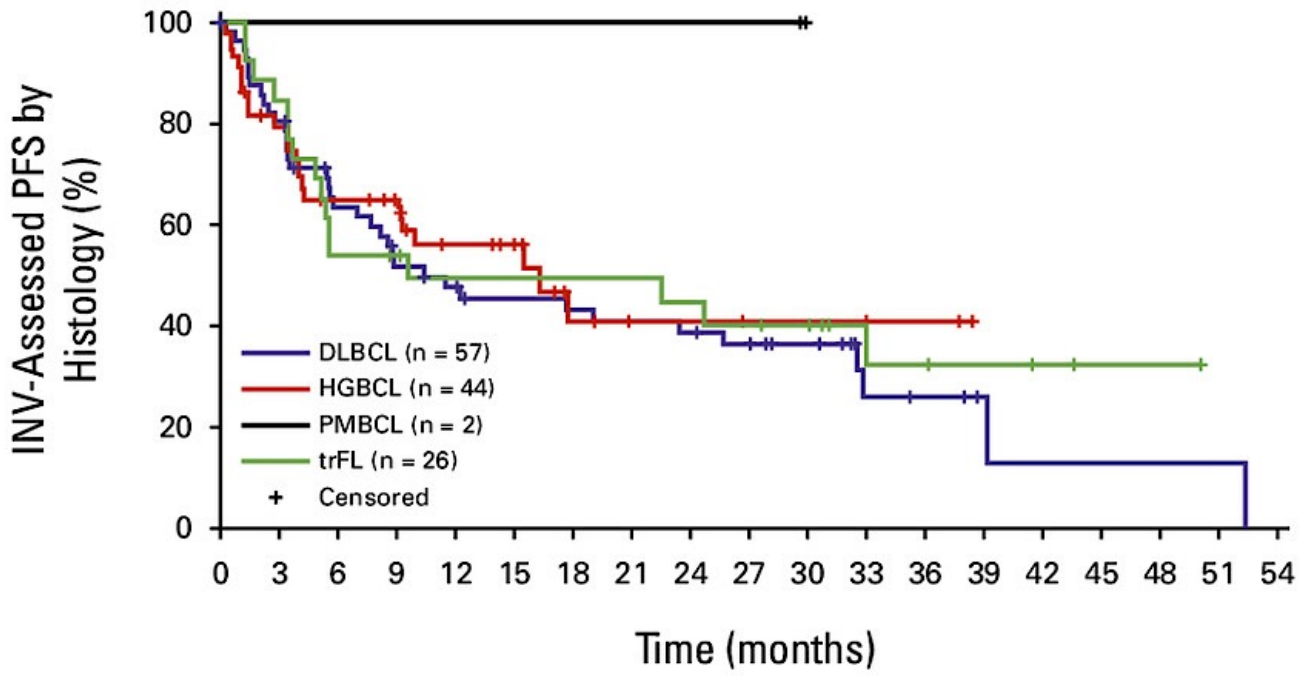
Glofitamab and Polatuzumab Vedotin: Progression-Free Survival (PFS)

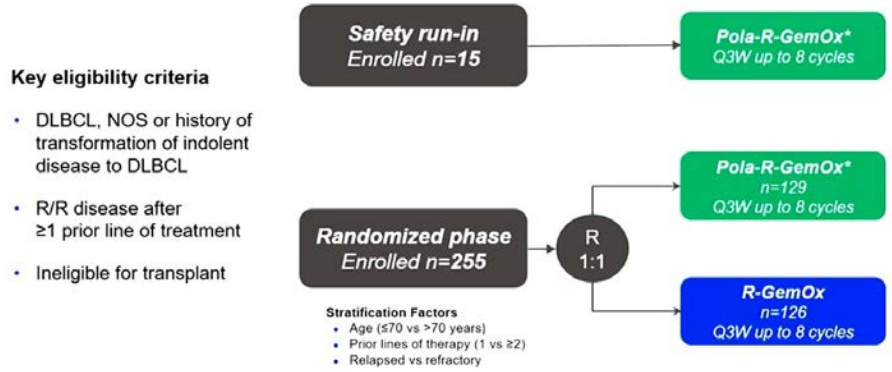




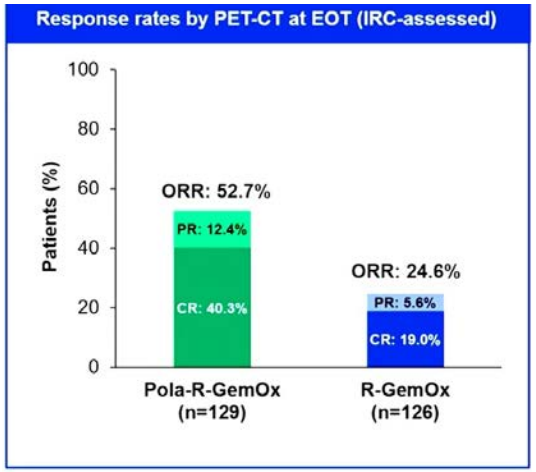
Hutchings M et al. *J Clin Oncol* 2025 December 20;43(36):3788-98.

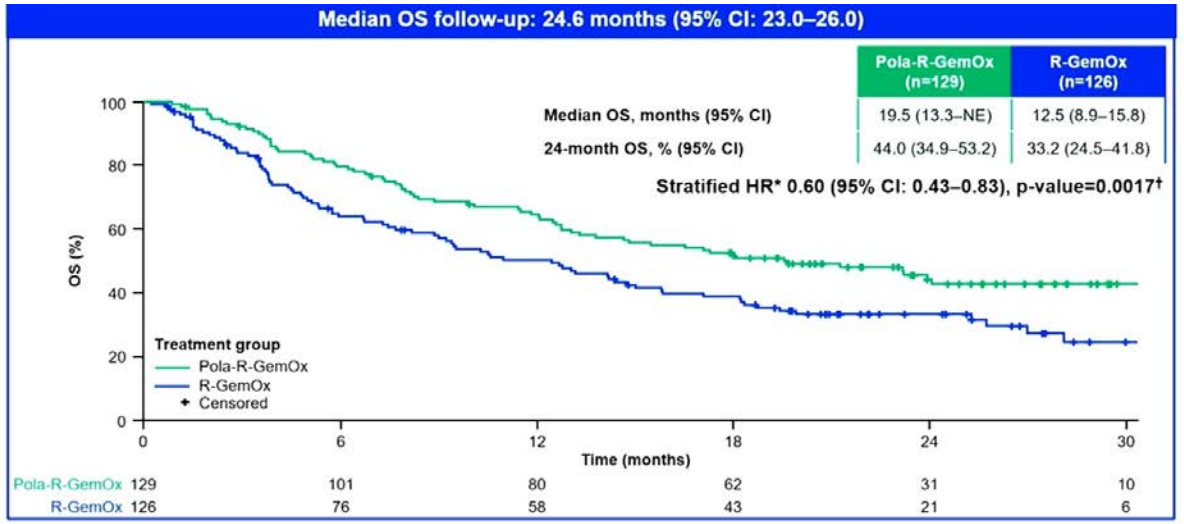
RTP RESEARCH TO PRACTICE

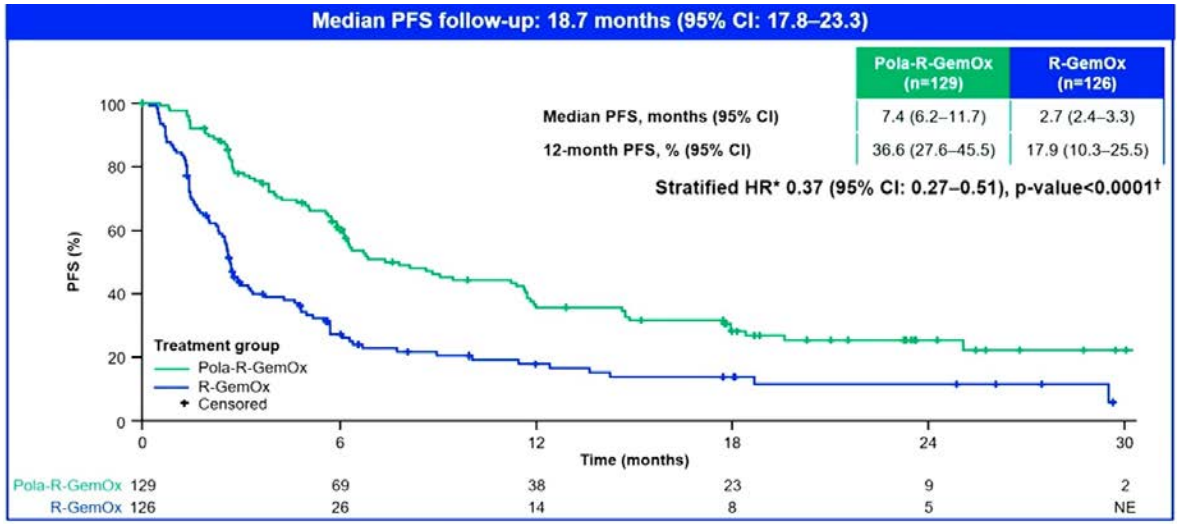
POLARGO: Phase 3 Trial of Pola-R-GemOx vs R-GemOx in Relapsed/Refractory Transplant-Ineligible DLBCL



Baseline Characteristics	R-GemOx (n=126)	Pola-R-GemOx (n=129)
Age, y, median (range)	64 (24–89)	62 (23–87)
DLBCL, n(%)	116 (92)	109 (79)
Transformed iNHL, n(%)	10 (8)	26 (19)
One prior line, n(%)	81 (64)	81 (63)
≥2 prior lines, n(%)	45 (36)	48 (37)
Primary refractory, n(%)	71 (61)	65 (56)
Refractory to last therapy, n(%)	83 (66)	85 (66)







iNHL = indolent non-Hodgkin lymphoma.

Matasar M, et al. *Hemasphere*. 2025;9(Suppl 1):3.

Second Opinion

Ann LaCasce, MD, MMSc

Neil Love, MD

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Discussion Questions

How are you selecting patients with newly diagnosed DLBCL for treatment with polatuzumab vedotin/R-CHP? Would you prefer it for any patient with an IPI of 2 or greater on the basis of the POLARIX study?

Given that POLARIX was not powered to look at cell-of-origin subsets, what do you make of those data? Do you use cell of origin to determine who should receive polatuzumab vedotin/R-CHP? Are you using gene expression profiling assays or any other type of testing to aid in this decision?

When are you employing CNS prophylaxis in DLBCL? Would you do so for this woman?

What can we do to better identify patients with DLBCL at risk for CNS relapse? Should we routinely be assessing for ctDNA in the CSF?

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Second Opinion

Gilles Salles, MD, PhD

Neil Love, MD

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Discussion Questions

What are your thoughts on recent data combining antibody-drug conjugates and bispecific antibodies in DLBCL? How enthusiastic are you about the potential use of front-line rituximab, polatuzumab vedotin and glofitamab (R-Pola-Glo) for unfit, older patients? Would you use this regimen today for any of your patients?

Given the NCCN guideline inclusion of polatuzumab vedotin in combination with mosunetuzumab, polatuzumab vedotin in combination with glofitamab and polatuzumab vedotin in combination with R-GemOx as second-line therapy for patients who are not candidates for CAR T-cell therapy, are you employing these regimens? If so, for whom?

What do you make of the early data with loncastuximab tesirine in combination with glofitamab in R/R DLBCL? What future role do you foresee for this regimen? Do you think it will eventually be moved forward into the front line, before or in lieu of chemotherapy?

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Agenda

Module 1: Rational Incorporation of CD79b-Targeted Antibody-Drug Conjugates into the Management of Newly Diagnosed and Relapsed/ Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Flowers

Module 2: Clinical Utility of CD19-Directed Monoclonal Antibodies in the Treatment of DLBCL and Follicular Lymphoma (FL) — Dr Smith

Module 3: Optimal Use of CD19-Directed Antibody-Drug Conjugates for R/R DLBCL and FL — Dr Lunning

Module 4: Current and Future Role of Bruton Tyrosine Kinase Inhibition in Therapy for Non-Hodgkin Lymphoma — Dr Kahl

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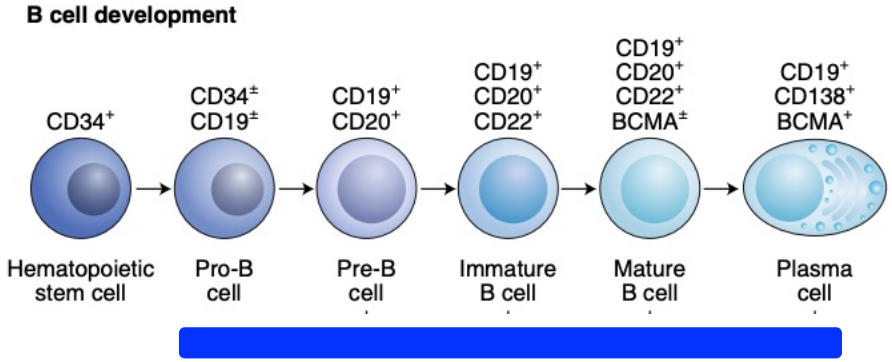
Clinical Utility of CD19-Directed Monoclonal Antibodies in DLBCL and Follicular Lymphoma (FL)

Sonali M. Smith, MD FASCO
Elwood V. Jensen Professor
Section Chief Hematology/Oncology, Department of Medicine
Co-Leader, Cancer Service LIne
The University of Chicago

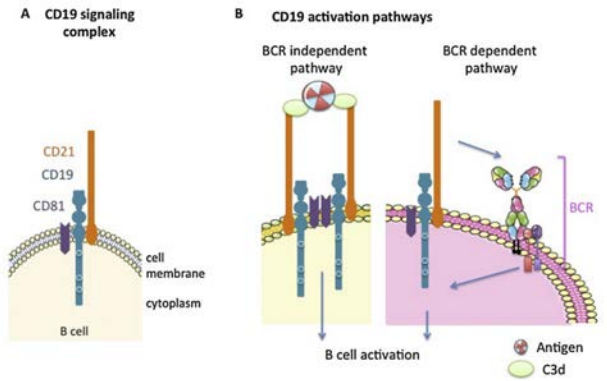
Clinical Utility of CD19-Directed Monoclonal Antibodies in DLBCL and Follicular Lymphoma (FL)

- Extended follow-up from the Phase II L-MIND study supporting the use of tafasitamab/lenalidomide in patients with R/R DLBCL
- 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
- Biologic rationale for the evaluation of tafasitamab in patients with FL
- Key efficacy and safety findings from the Phase III inMIND trial evaluating the addition of tafasitamab to lenalidomide and rituximab (R^2) in R/R FL or marginal zone lymphoma
- Safety profile of tafasitamab; appropriate monitoring, mitigation and management of AEs

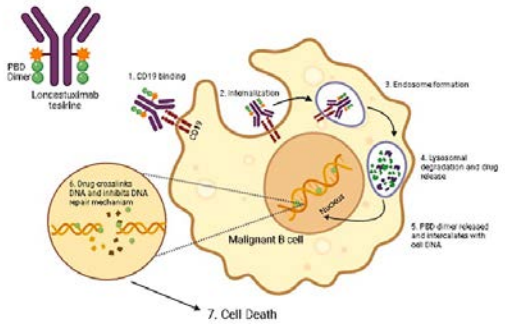
CD19 targeting key principles



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

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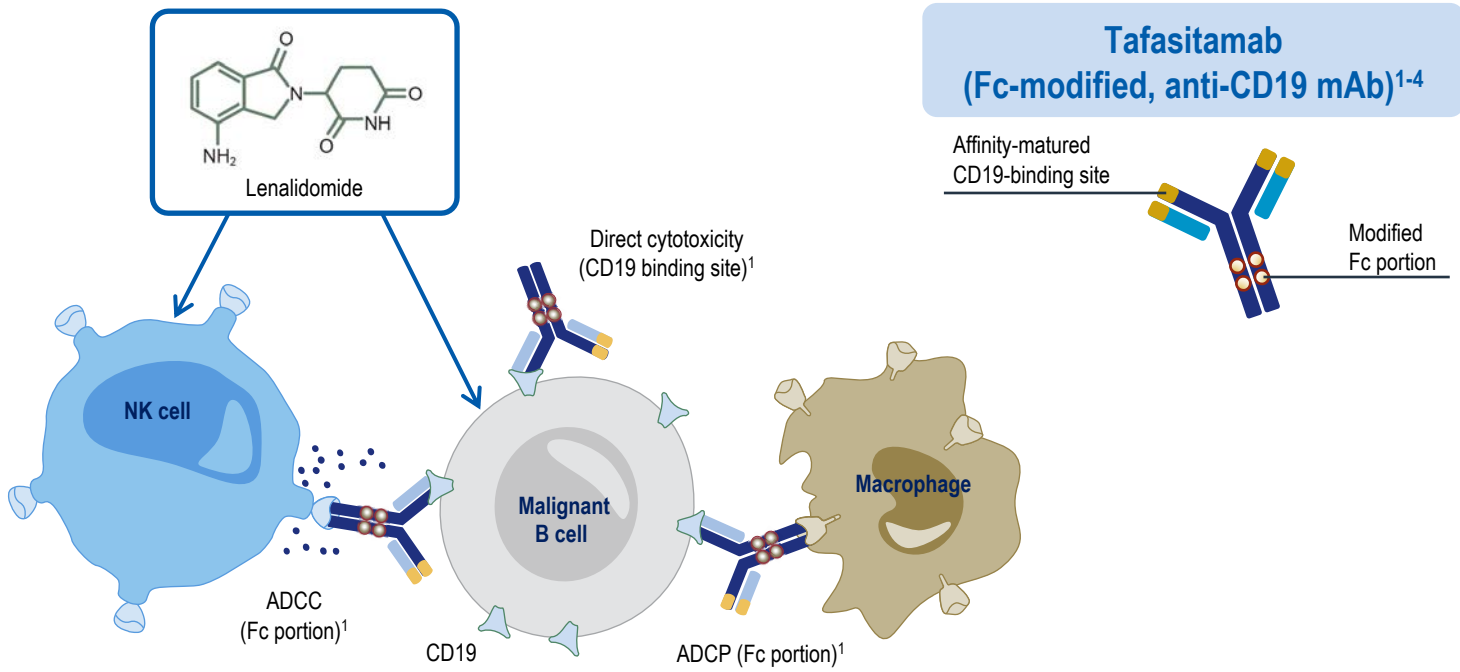
Milone Nature Cancer volume 2, pages780–793 (2021); Jacobczyk Int J of Pharmaceutics, pages: 813-824 Volume 532, Issue 2 (2017); Sermer Blood Reviews Volume 57, January 2023, 101002

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*



*Adapted from "The use of tafasitamab in diffuse large B-cell lymphoma" by Düll J, Topp M, Salles G and licensed under CC BY 4.0.

1. Horton HM, et al. *Cancer Res.* 2008;68:8049-8057. 2. Awan FT, et al. *Blood.* 2010;115:1204-1213. 3. Woyach JA, et al. *Blood*. 2014;124:3553-3560. 4. Jurczak W, et al. *Ann Oncol.* 2018;29:1266-1272.

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; Fc, fragment crystallizable; mAb, monoclonal antibody.

Five-year follow-up L-MIND phase 2 trial of tafasitamab plus lenalidomide in RR 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)

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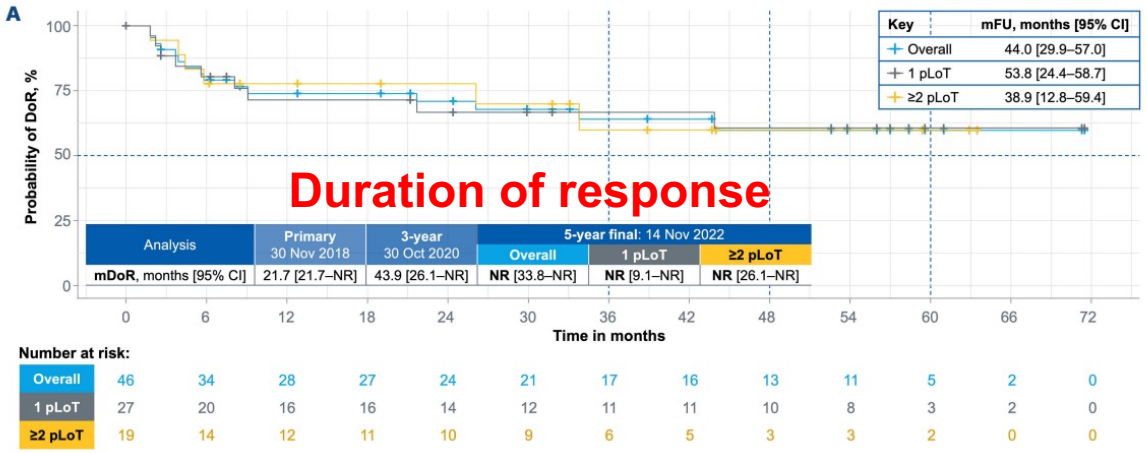
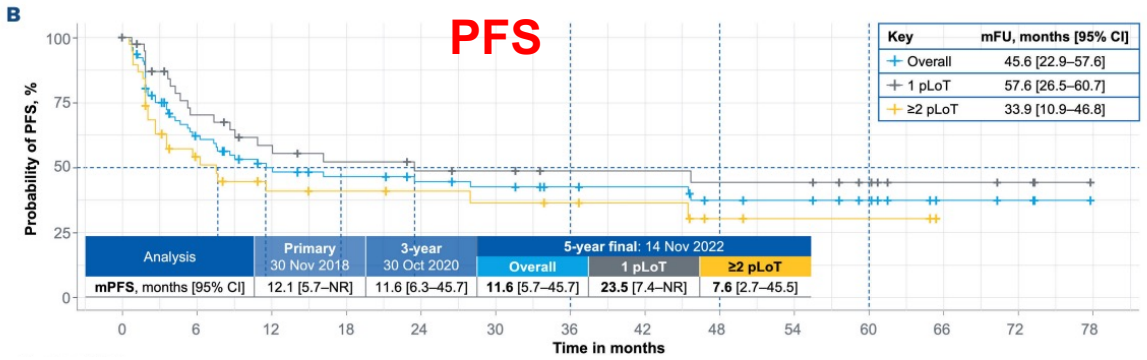
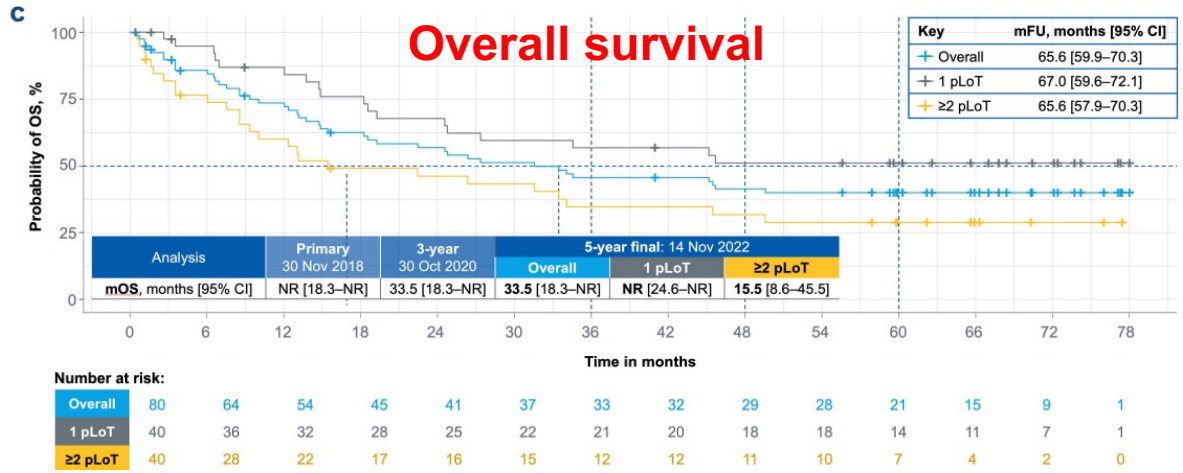
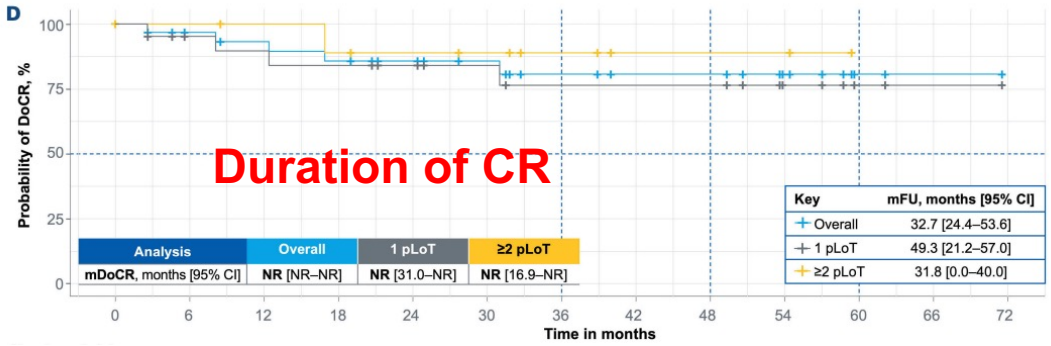
Duell Haematologica 2024 Feb 1;109(2):553-566

Five-year follow-up L-MIND phase 2 trial of tafasitamab plus lenalidomide in RR DLBCL: outcomes by line of treatment









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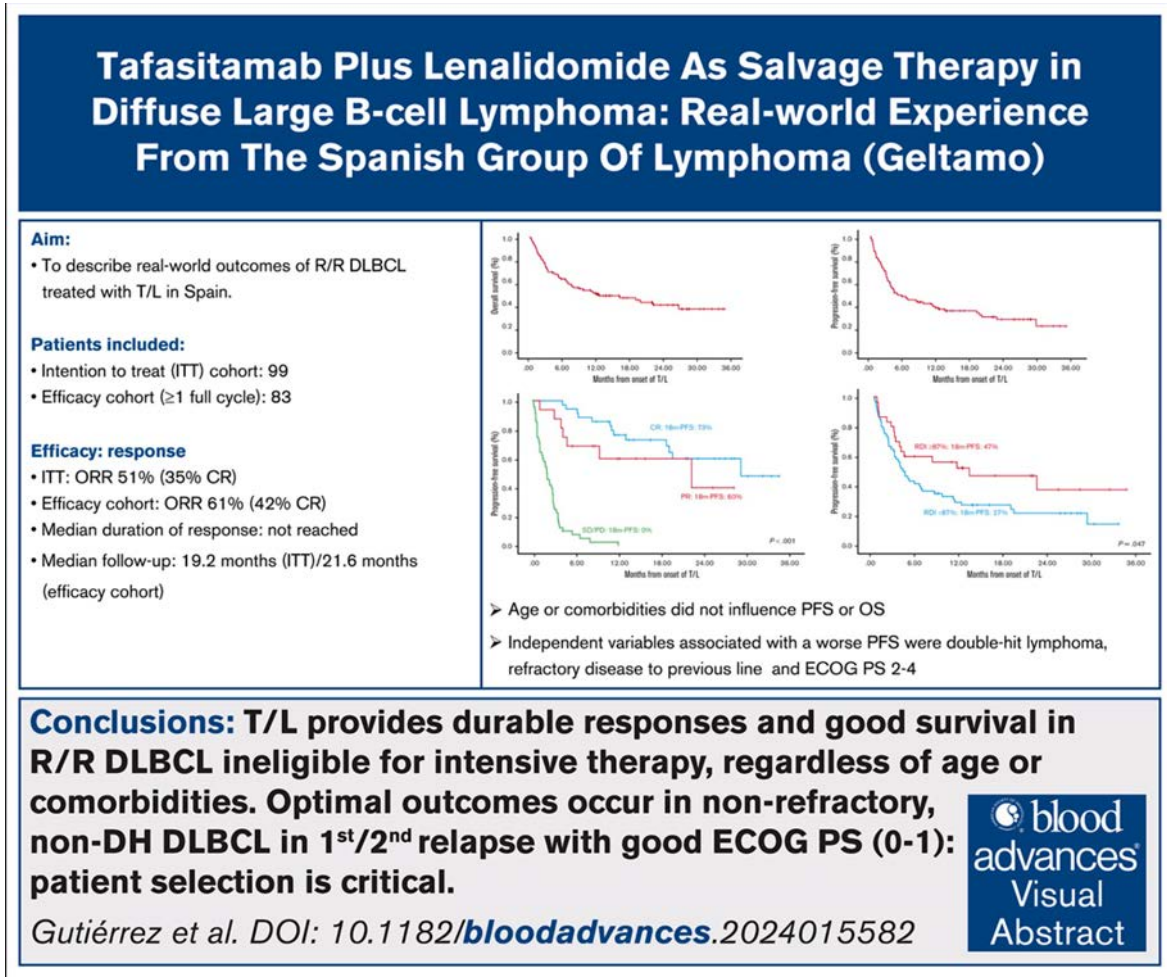
Duell Haematologica 2024 Feb 1;109(2):553-566

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



Tafasitamab Plus Lenalidomide As Salvage Therapy in Diffuse Large B-cell Lymphoma: Real-world Experience From The Spanish Group Of Lymphoma (Geltamo)

Aim:
- To describe real-world outcomes of R/R DLBCL treated with T/L in Spain.

Patients included:
- Intention to treat (ITT) cohort: 99
- Efficacy cohort (≥1 full cycle): 83

Efficacy: response
- ITT: ORR 51% (35% CR)
- Efficacy cohort: ORR 61% (42% CR)
- Median duration of response: not reached
- Median follow-up: 19.2 months (ITT)/21.6 months (efficacy cohort)

- Age or comorbidities did not influence PFS or OS
- Independent variables associated with a worse PFS were double-hit lymphoma, refractory disease to previous line and ECOG PS 2-4

Conclusions: T/L provides durable responses and good survival in R/R DLBCL ineligible for intensive therapy, regardless of age or comorbidities. Optimal outcomes occur in non-refractory, non-DH DLBCL in 1st/2nd relapse with good ECOG PS (0-1): patient selection is critical.

*Gutiérrez et al. DOI: 10.1182/**bloodadvances**.2024015582*

blood advances Visual Abstract

AT THE FOREFRONT UChicago Medicine

ASCO Annual Meeting: Abstract 7000

frontMIND: Phase 3 Study of Tafasitamab Plus Lenalidomide and R-CHOP for Patients With Newly Diagnosed Diffuse Large B-cell Lymphoma

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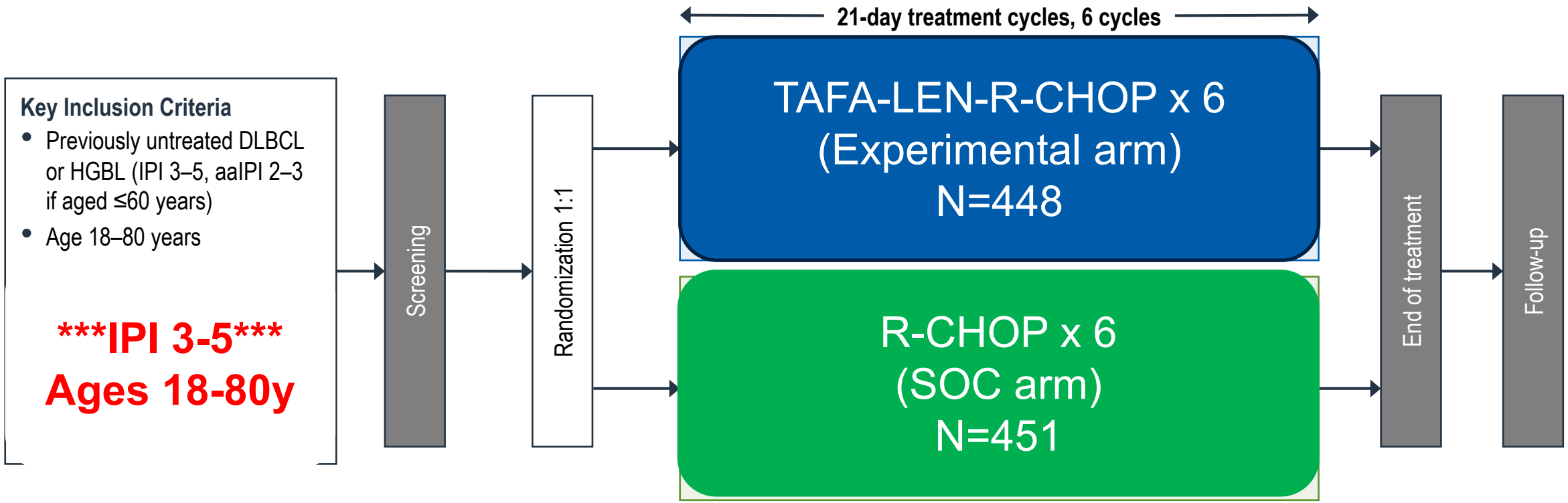
frontMIND (NCT04824092): Phase 3, Global, Multicenter, Placebo-Controlled, Double-Blind, Randomized Study



Stratification Factors

- IPI/aaIPI
- Geographic region

Study Endpoints (Investigator Assessed Unless Specified)

- **Primary study endpoint:** PFS
- **Key secondary:** EFS, OS (hierarchically tested, if statistical significance met for PFS)
- **Select other secondary:** PET-CR at EOT, ORR at EOT, PFS by cell-of-origin subtypes, HRQoL, safety
- ***Post-hoc* analysis:** PFS, EFS, OS on centrally confirmed lymphoma subtypes population

aaIPI, age-adjusted IPI; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; EOT, end of treatment; HGBL, high-grade B-cell lymphoma; HRQoL, health-related quality of life; IPI, International Prognostic Index; iv, intravenously; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; po, orally; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Demographics and Baseline Disease Characteristics

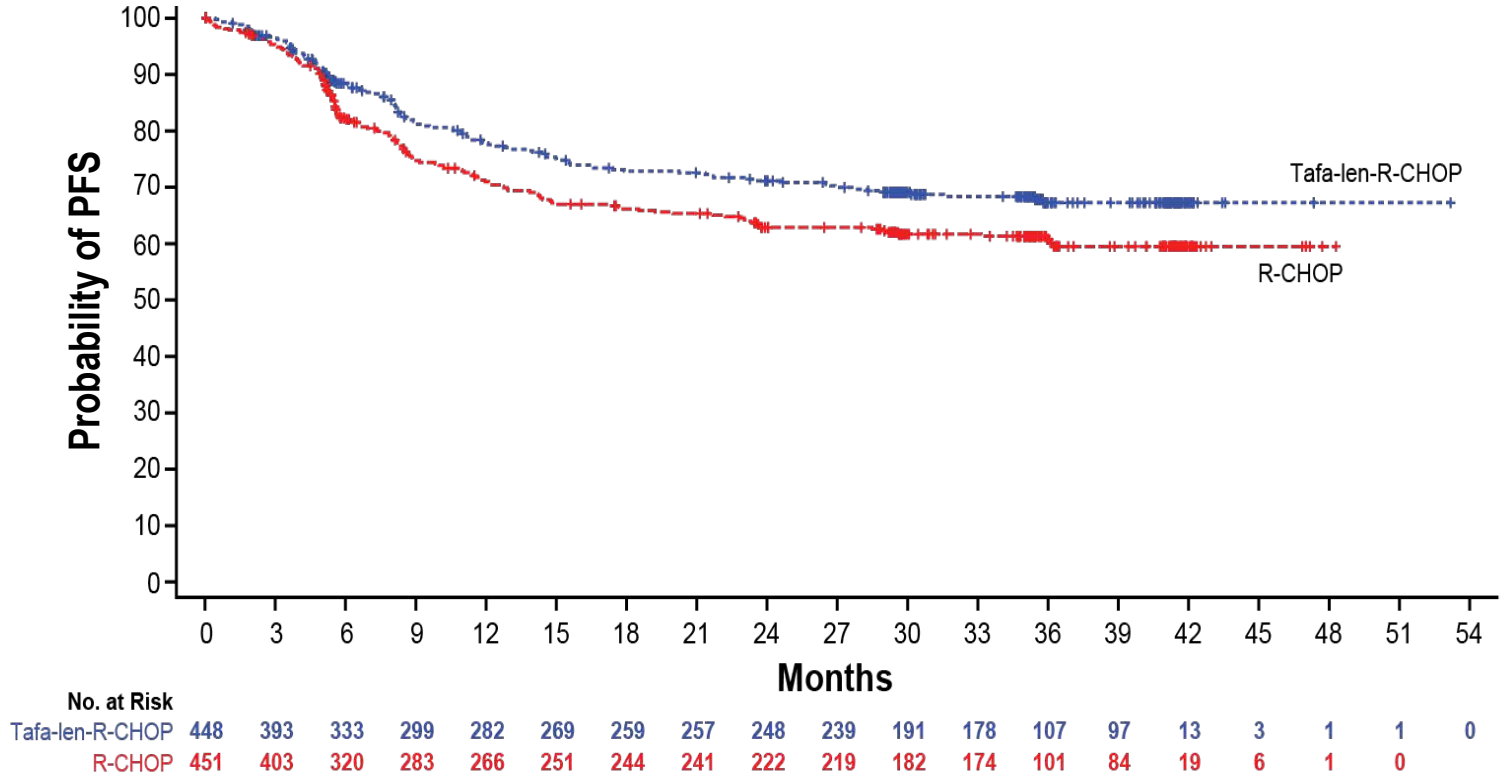
Overall ITT population

ITT Population	Tafa-Len-R-CHOP (n=448)	R-CHOP (n=451)	Total (N=899)
Median age, years (range)	65.0 (20, 80)	65.0 (18, 80)	65.0 (18, 80)
Male sex	240 (53.6)	233 (51.7)	473 (52.6)
Ann Arbor stage III or IV at enrollment	432 (96.4)	436 (96.7)	868 (96.6)
Extranodal involvement at ≥2 sites	173 (38.6)	175 (38.8)	348 (38.7)
Elevated lactate dehydrogenase level	369 (82.4)	376 (83.4)	745 (82.9)
Presence of bulky disease	254 (56.7)	231 (51.2)	485 (53.9)
ECOG PS at screening			
0-1	311 (69.4)	305 (67.6)	616 (68.5)
2	137 (30.6)	146 (32.4)	283 (31.5)
Risk group (stratification factor)			
High-intermediate risk (IPI 3/aaIPI 2)	259 (57.8)	244 (54.1)	503 (56.0)
High risk (IPI 4-5/aaIPI 3)	186 (41.5)	202 (44.8)	388 (43.2)
Median time from diagnostic biopsy to treatment initiation, days (Q1-Q3)	23.5 (17, 28)	24.0 (18, 28)	24.0 (18, 28)

Data are n (%) unless otherwise specified.
aaIPI, age-adjusted IPI; ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; ITT, intention-to-treat; Len, lenalidomide; Q, quartile; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

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%**)

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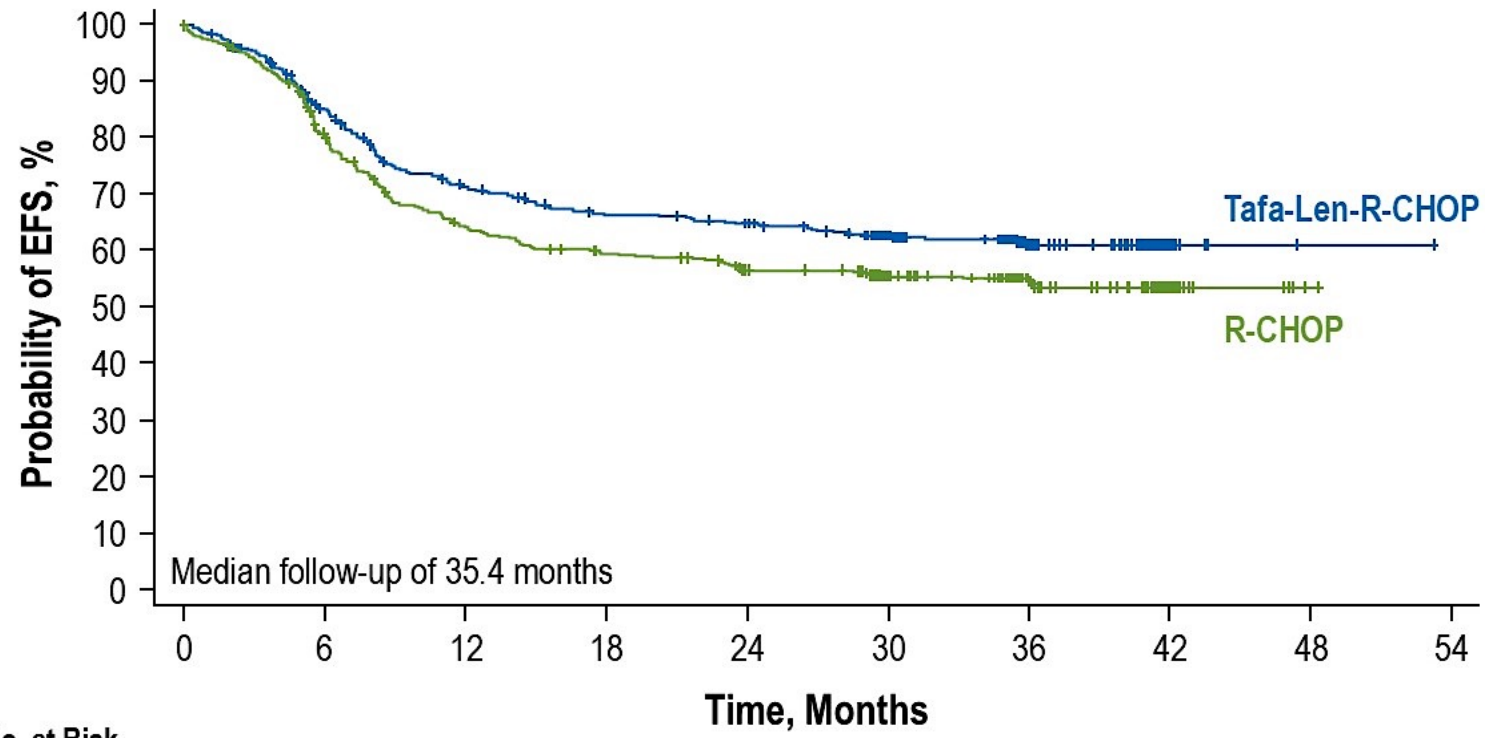
ITT population. *Calculated using a stratified Cox proportional hazards model.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Tafa-Len-R-CHOP Significantly Improved EFS vs R-CHOP

EFS by investigator assessment (key secondary)



No. at Risk										
Tafa-Len-R-CHOP	448	346	283	259	249	191	107	13	1	0
R-CHOP	451	339	267	244	222	182	101	19	1	0

HR 0.79* (*P*=0.0260)

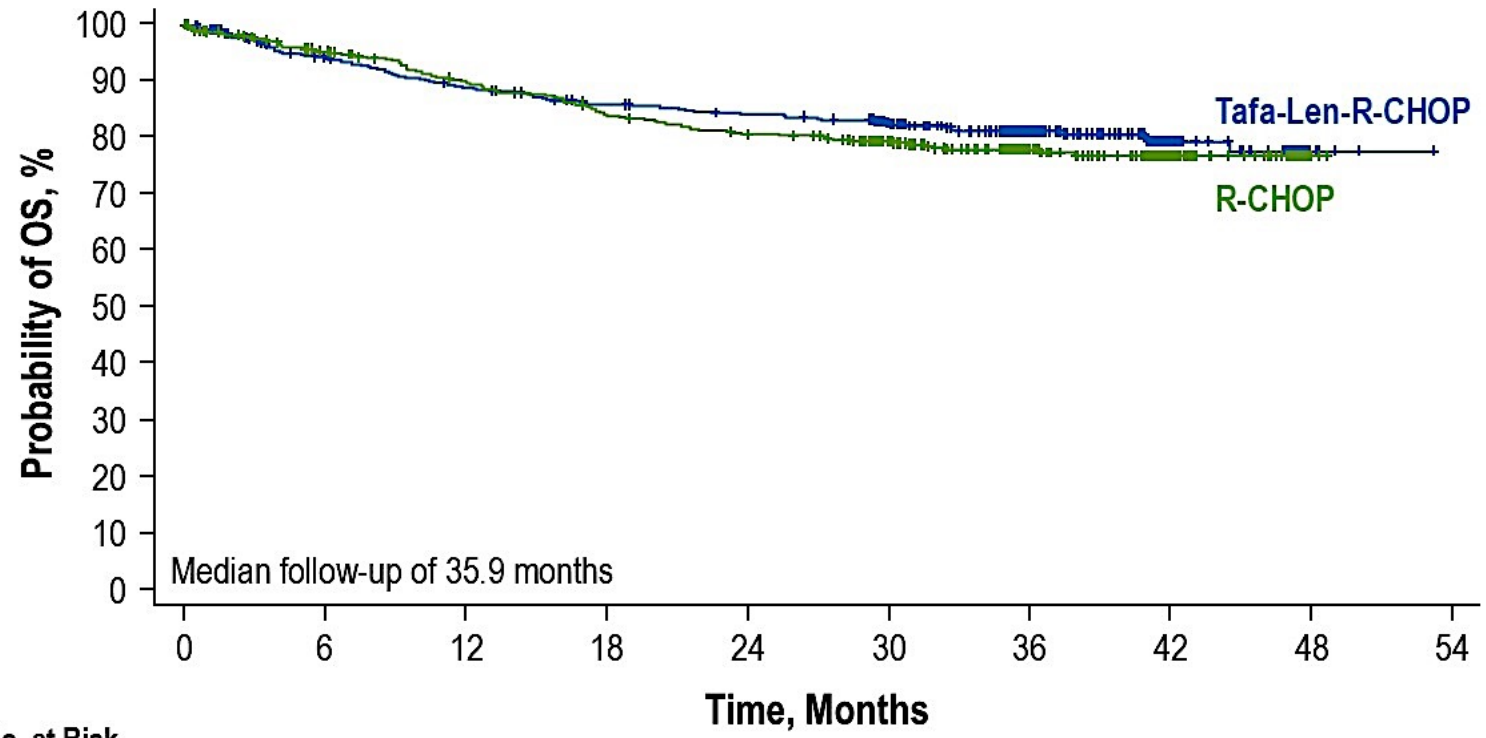
95% CI: 0.64, 0.97

- **2-year EFS:**
  65.0% with Tafa-Len-R-CHOP vs
  56.7% with R-CHOP
- **3-year EFS:**
  61.2% with Tafa-Len-R-CHOP vs
  54.8% with R-CHOP

ITT population. *Calculated using a stratified Cox proportional hazards model.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Interim Analysis of OS Demonstrated a Positive Trend

OS (key secondary)



No. at Risk										
Tafa-Len-R-CHOP	448	398	374	353	343	295	178	63	5	0
R-CHOP	451	409	379	353	336	283	167	71	2	0

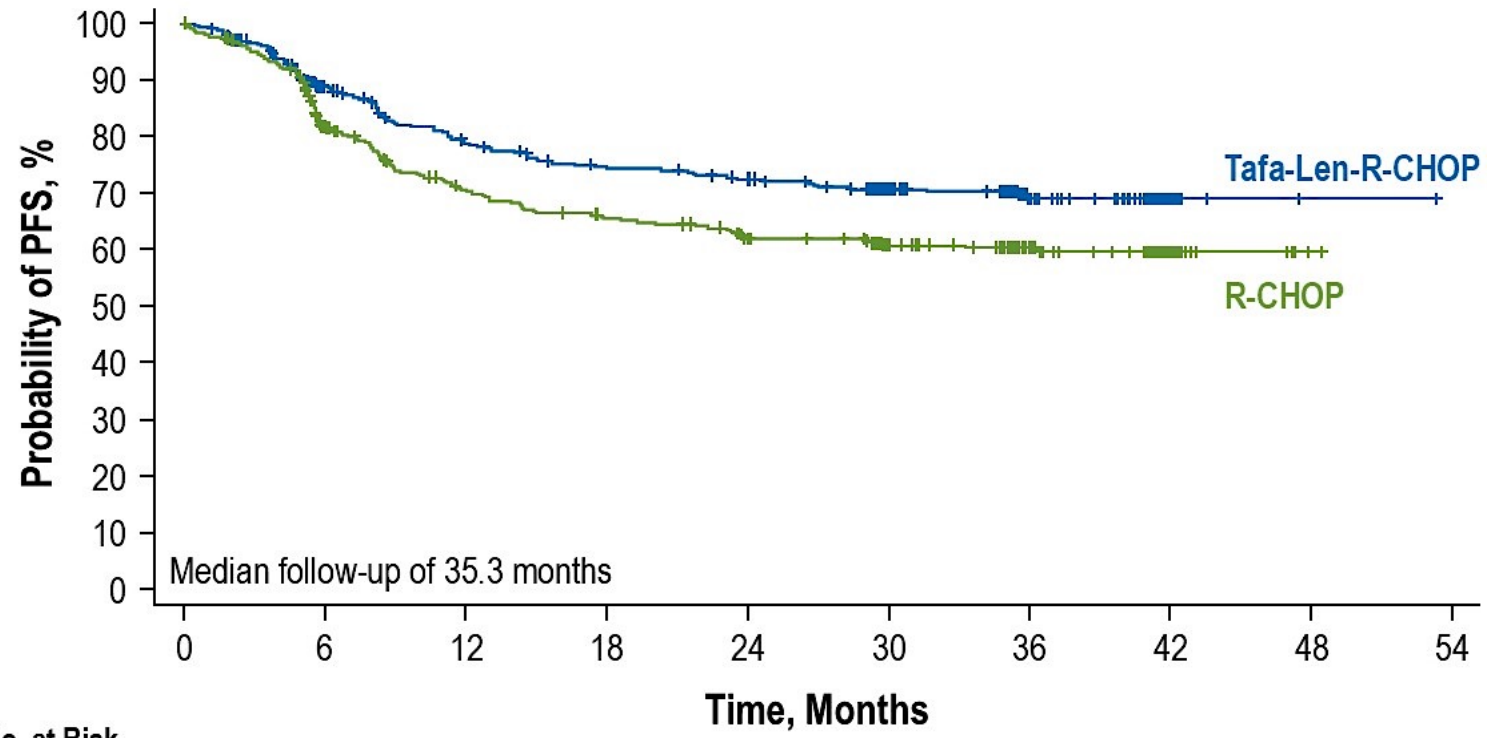
HR 0.85* (*P*=0.2703)

95% CI: 0.63, 1.14

- **2-year OS:**
  84.1% with Tafa-Len-R-CHOP vs
  80.5% with R-CHOP
- **3-year OS:**
  81.1% with Tafa-Len-R-CHOP vs
  77.8% with R-CHOP

ITT population. At the PFS primary analysis, 177 deaths had occurred. *Calculated using a stratified Cox proportional hazards model.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; OS, overall survival; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

HR for PFS Improved in Centrally Confirmed Lymphoma Subtypes (n=773)



No. at Risk										
Tafa-Len-R-CHOP	391	291	251	232	221	176	97	12	1	0
R-CHOP	382	271	224	206	186	154	85	17	1	0

HR 0.68* (*P*=0.0035)†
95% CI: 0.52, 0.88

versus

Overall ITT population:
HR 0.75 (*P*=0.0194)
95% CI: 0.59, 0.96

- **2-year PFS:**
  72.7% with Tafa-Len-R-CHOP vs
  62.2% with R-CHOP
- **Differences in 2-year PFS rates:**
  Δ=**10.5%** in centrally confirmed
  Δ=**8.2%** in the ITT

- On central review, 126 patients (14% of the ITT) did not have a confirmed lymphoma subtype either due to histology (eg, FL grade 1-3a, MCL, and BL) or inadequate sample

Post hoc analysis of PFS by Investigator; centrally confirmed lymphoma subtypes population. *Calculated using a stratified Cox proportional hazards model. †Nominal *P* value.
BL, Burkitt lymphoma; CI, confidence interval; FL, follicular lymphoma; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; MCL, mantle cell lymphoma; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Cell-of-Origin Molecular Subtypes

Central GEP assessment

ITT Population	Tafa-Len-R-CHOP (n=448)	R-CHOP (n=451)	Total (N=899)
Cell of origin (per GEP; central assessment), n	**239**	**245**	**484**
ABC-like	84 (35.1)	88 (35.9)	172 (35.5)
GCB-like	131 (54.8)	117 (47.8)	248 (51.2)
Unclassified	24 (10.0)	40 (16.3)	64 (13.2)
Cell of origin (per GEP; central assessment) results not available, n	209	206	415

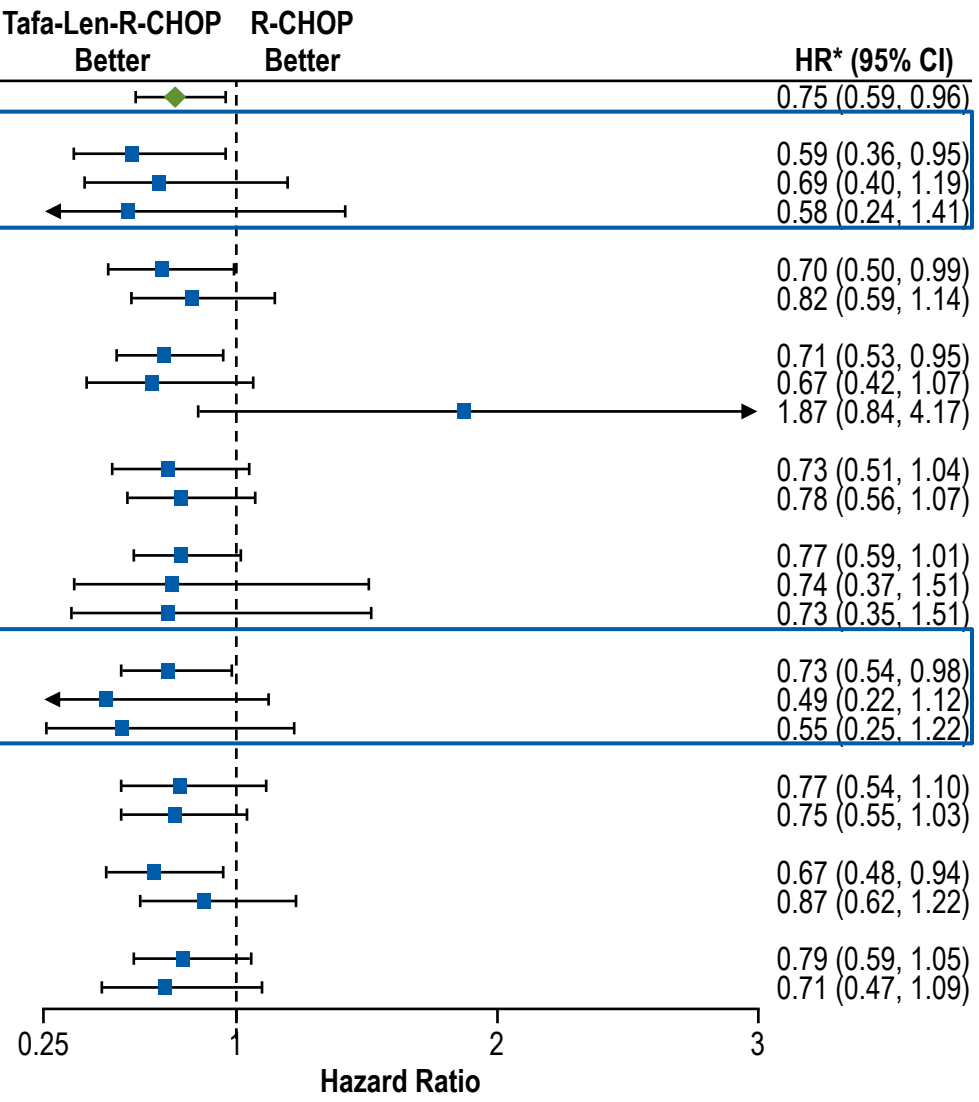
- Baseline characteristics in patients with COO subtypes determined by central GEP were very similar to the patients in the overall ITT population

Data are n (%) unless otherwise specified.
ABC, activated B cell; COO, cell of origin; GCB, germinal center B cell; GEP, gene expression profiling; ITT, intention-to-treat; Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

PFS by Investigator Assessment

Prespecified subgroups

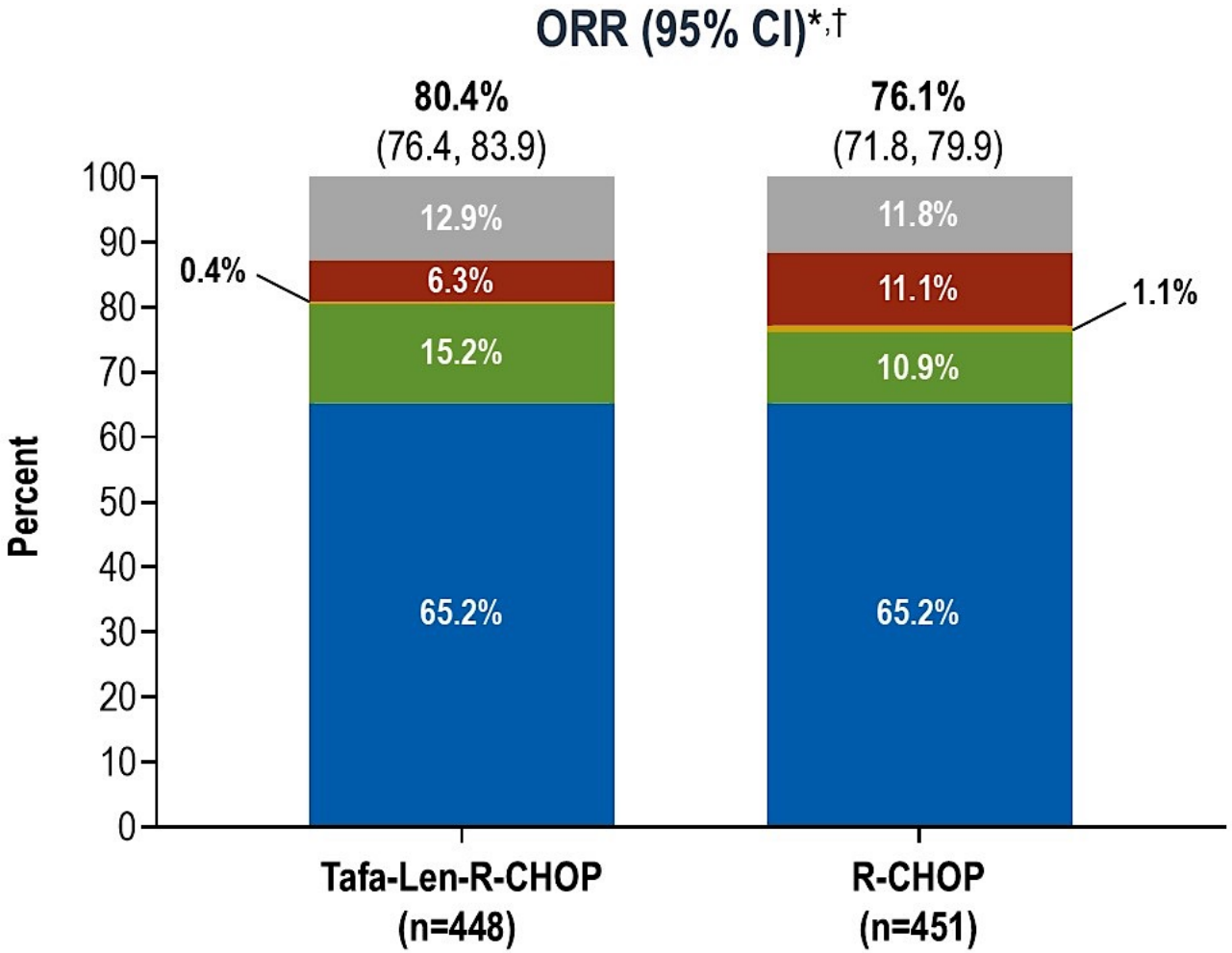
Baseline Risk Factors	Tafa-Len-R-CHOP Patient n/Event n	R-CHOP Patient n/Event n	HR* (95% CI)
Overall	448/121	451/155	0.75 (0.59, 0.96)
Cell of origin by central GEP			
ABC-like	84/27	88/44	0.59 (0.36, 0.95)
GCB-like	131/23	117/29	0.69 (0.40, 1.19)
Unclassified	24/7	40/16	0.58 (0.24, 1.41)
IPI score			
IPI 3/aaIPI 2	259/56	244/75	0.70 (0.50, 0.99)
IPI 4–5/aaIPI 3	186/64	202/79	0.82 (0.59, 1.14)
Geographic region			
EU, US, CAN, AUS, NZ†	324/76	324/104	0.71 (0.53, 0.95)
Asia	90/30	93/41	0.67 (0.42, 1.07)
Rest of the world	34/15	34/10	1.87 (0.84, 4.17)
Bulky disease			
Absent	194/50	220/75	0.73 (0.51, 1.04)
Present	254/71	231/80	0.78 (0.56, 1.07)
Lymphoma subtype (locally determined)			
DLBCL	362/95	361/120	0.77 (0.59, 1.01)
High-grade lymphoma	38/13	41/19	0.74 (0.37, 1.51)
Other	48/13	49/16	0.73 (0.35, 1.51)
Lymphoma subtype (centrally determined)			
DLBCL	307/76	325/107	0.73 (0.54, 0.98)
High-grade lymphoma	41/12	24/11	0.49 (0.22, 1.12)
Other	43/11	33/14	0.55 (0.25, 1.22)
Age			
<65 years	222/53	218/68	0.77 (0.54, 1.10)
≥65 years	226/68	233/87	0.75 (0.55, 1.03)
Sex			
Male	240/59	233/83	0.67 (0.48, 0.94)
Female	208/62	218/72	0.87 (0.62, 1.22)
ECOG PS			
0–1	324/83	326/105	0.79 (0.59, 1.05)
2	123/37	123/49	0.71 (0.47, 1.09)



ITT population. *Calculated using a stratified Cox proportional hazards model. †Europe, USA, Canada, Australia, and New Zealand.

aaIPI, age-adjusted IPI; ABC, activated B-cell; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B-cell; GEP, gene expression profiling; HR, hazard ratio; IPI, International Prognostic Index; ITT, intention-to-treat; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

ORR and CR Rate by Investigator Assessment



- **ORR** (OR 1.29 [95% CI: 0.94, 1.78]‡; *P*=0.1201§) **and PET-negative CR rate** (OR 1.00 [95% CI: 0.76, 1.31]‡, *P*=0.9873§) were **similar** between treatment arms at EOT
- **PR** rate was **numerically higher** in the Tafa-Len-R-CHOP arm

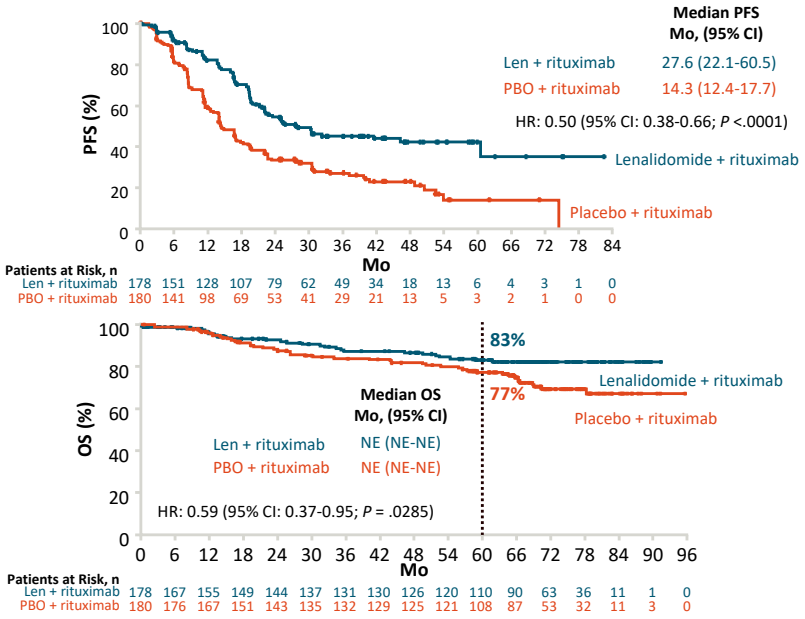
ITT population. *Objective response rate was defined as the proportion of patients who achieved a complete or partial response per Lugano 2014 criteria at EOT. †95% CI calculated using the Clopper-Pearson exact method. ‡95% CI calculated using the Wald method. §Nominal *P* value calculated using a stratified Cochran–Mantel–Haenszel test.

CI, confidence interval; CR, complete response; EOT, end of treatment; Len, lenalidomide; ITT, intention-to-treat; NE, not evaluable; OR, odds ratio; ORR, objective response rate; PD, progressive/relapsed disease; PET, positron emission tomography; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; SD, stable disease; Tafa, tafasitamab.

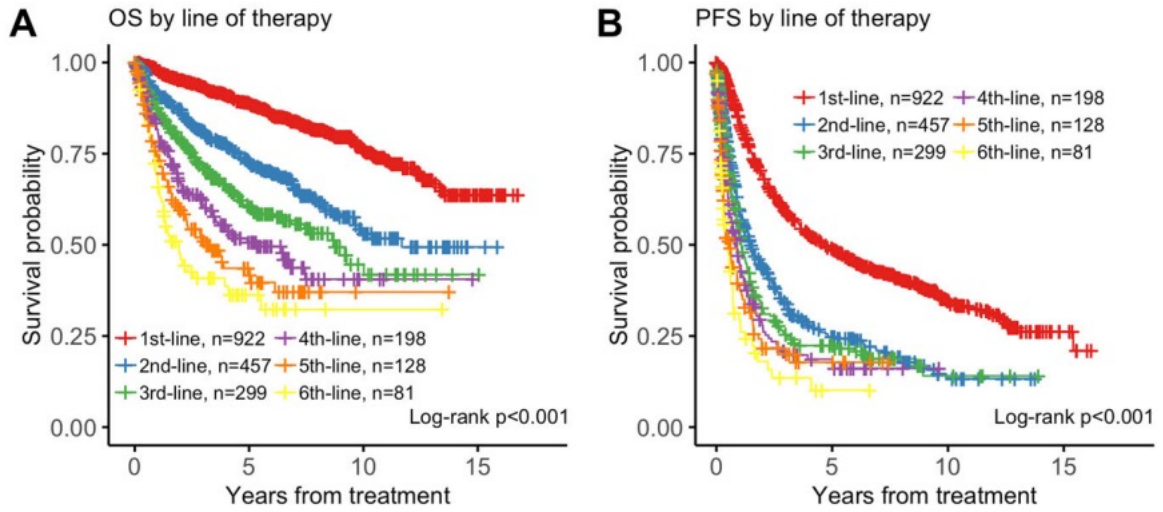
AT THE FOREFRONT
UChicago Medicine

FOLLICULAR LYMPHOMA

Follicular lymphoma: lenalidomide-rituximab is an effective regimen and backbone for further improvement



AUGMENT trial: LenR has improved PFS and OS over R monotherapy in R-sensitive disease @ 5y



PFS and OS decrease by line of treatment in the modern era

AT THE FOREFRONT
UChicago Medicine

Batlevi Blood Cancer Journal 10, Article number: 74 (2020);
Leonard JCO 2026 Apr 16:JCO2501770

Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Results From a Phase 3 Study (inMIND)

Laurie H. Sehn,[1] Stefano Luminari,[2,3] Christian W. Scholz,[4] Kai Hübel,[5] Antonio Salar,[6] Shankara Paneesha,[7,8] Björn E. Wahlin,[9] Panayiotis Panayiotidis,[10] Hui Peng Lee,[11] Ana Jimenez Ubieto,[12] Juan-Manuel Sancho,[13] Tae Min Kim,[14] Eva Domingo Domenech,[15] Takahiro Kumode,[16] Christina Poh,[17] Catherine Thieblemont,[18] Dries Deeren,[19] Edwin de Wit,[20] Michael Arbushites,[21] Marie-Laure Casadebaig[20] and Marek Trneny[22]

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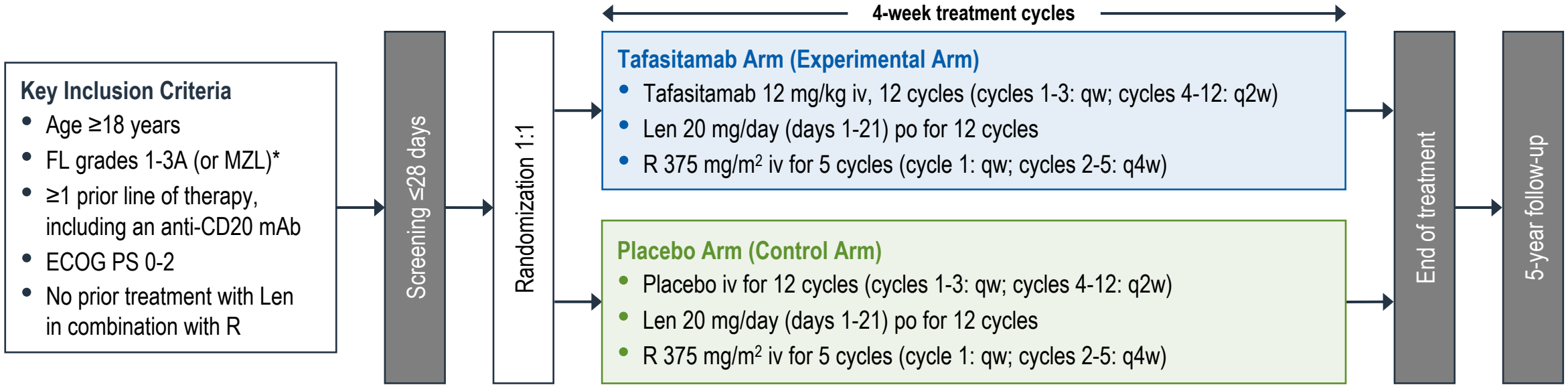
inMIND: Phase 3, Double-Blind, Placebo-Controlled, International, Multicenter Randomized Study



Stratification Factors (Patients With FL)

- POD24
- Refractoriness to prior anti-CD20 mAb therapy
- Number of prior lines of therapy (1 or ≥2)

Study Endpoints in FL Population (Investigator Assessed Unless Specified)

- **Primary study endpoint:** PFS
- **Key secondary:** PET-CR rate in the FDG-avid population, OS
- **Select other secondary:** PFS by IRC, ORR, DOR, safety, QoL, MRD
- **Exploratory:** TTNT, B-cell recovery, Ig levels, CD19 expression

- Powered to assess PFS in the FL population, triggered when 174 investigator-assessed events occurred
- OS analysis planned after 5 years of follow-up

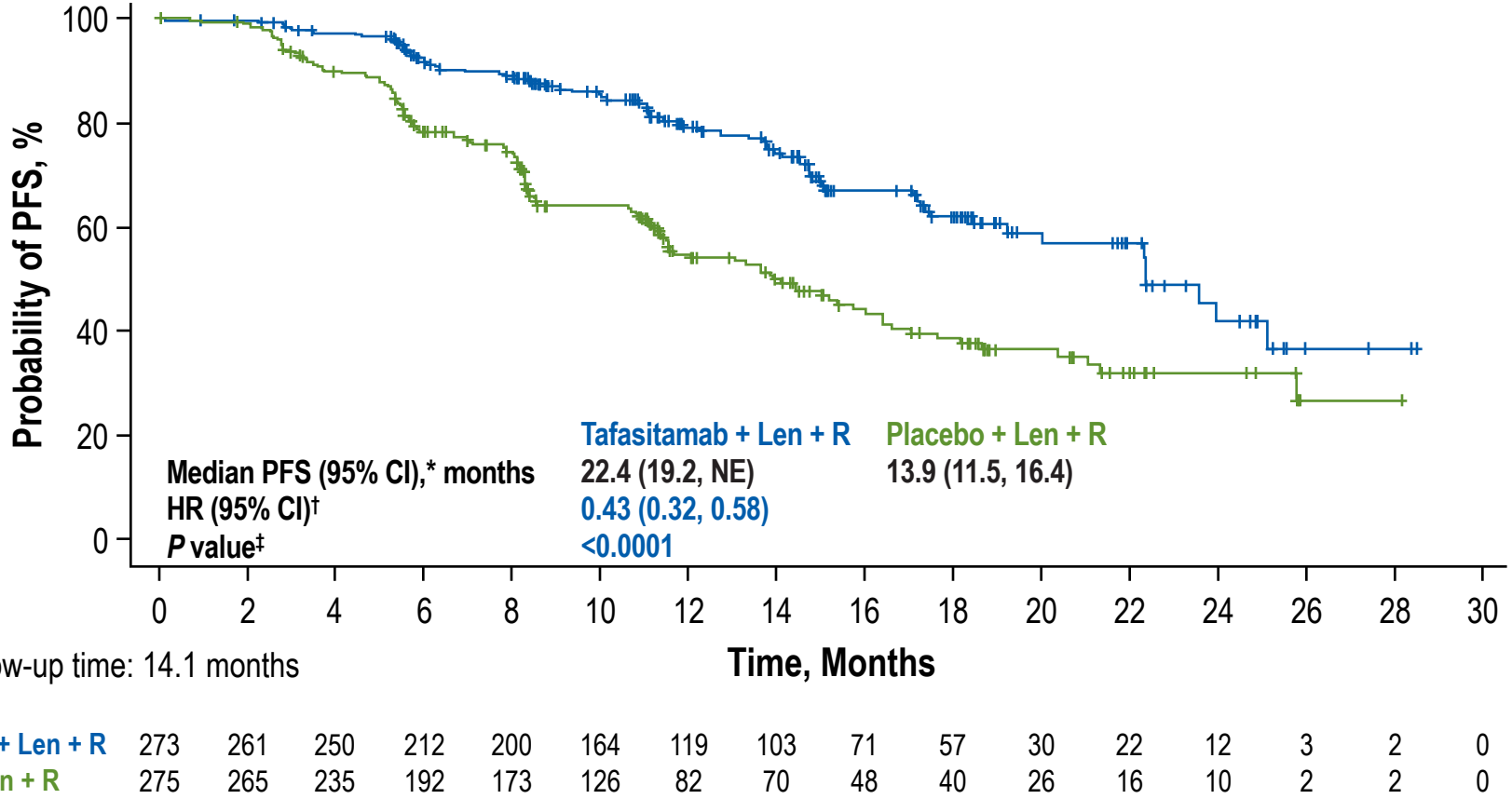
*Limited number of patients with MZL were enrolled but the study was not powered for this population; data for patients with MZL will be presented separately. DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; FL, follicular lymphoma; Ig, immunoglobulin; IRC, independent review committee; iv, intravenous; Len, lenalidomide; mAb, monoclonal antibody; MRD, minimal residual disease; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET-CR, positron emission tomography-complete response; PFS, progression-free survival; po, orally; POD24, disease progression within 24 months of initial diagnosis; QoL, quality of life; qw, weekly; q2w, every 2 weeks; q4w, every 4 weeks; R, rituximab; TTNT, time to next treatment.

Baseline Characteristics and prior treatment (n=548):

Variable	Tafasitamab + Len + R (n=273)	Placebo + Len + R (n=275)	Total (N=548)
Median age, years (range)	64.0 (36, 88)	64.0 (31, 85)	64.0 (31, 88)
≥75, n (%)	54 (19.8)	54 (19.6)	108 (19.7)
Male sex, n (%)	150 (54.9)	149 (54.2)	299 (54.6)
Median time since initial diagnosis of FL, years (range)	5.2 (0, 34)	5.5 (1, 33)	5.3 (0, 34)
FLIPI score, n (%)			
0-1	57 (20.9)	57 (20.7)	114 (20.8)
2	79 (28.9)	67 (24.4)	146 (26.6)
3-5	137 (50.2)	150 (54.5)	287 (52.4)
GELF criteria, n (%)	222 (81.3)	232 (84.4)	454 (82.8)
FL diagnosis confirmed by central pathology, n (%)	256 (93.8)	259 (90.5)	505 (92.2)
Median number of prior lines of therapy (range)	1.0 (1, 7)	1.0 (1, 10)	1.0 (1, 10)
POD24, n (%)	85 (31.1)	88 (32.0)	173 (31.6)
Relapsed/refractory status to last therapy, n (%)			
Relapsed	148 (54.2)	164 (59.6)	312 (56.9)
Refractory	112 (41.0)	97 (35.2)	209 (38.1)
Undetermined	13 (4.8)	14 (5.1)	27 (4.9)
Refractory to prior anti-CD20 therapy, n (%)	118 (43.2)	115 (41.8)	233 (42.5)

- **20% were ≥ 75y and ~80% met GELF criteria**
- **~30% had POD24**
- **~42% were refractory to prior anti-CD20 therapy**

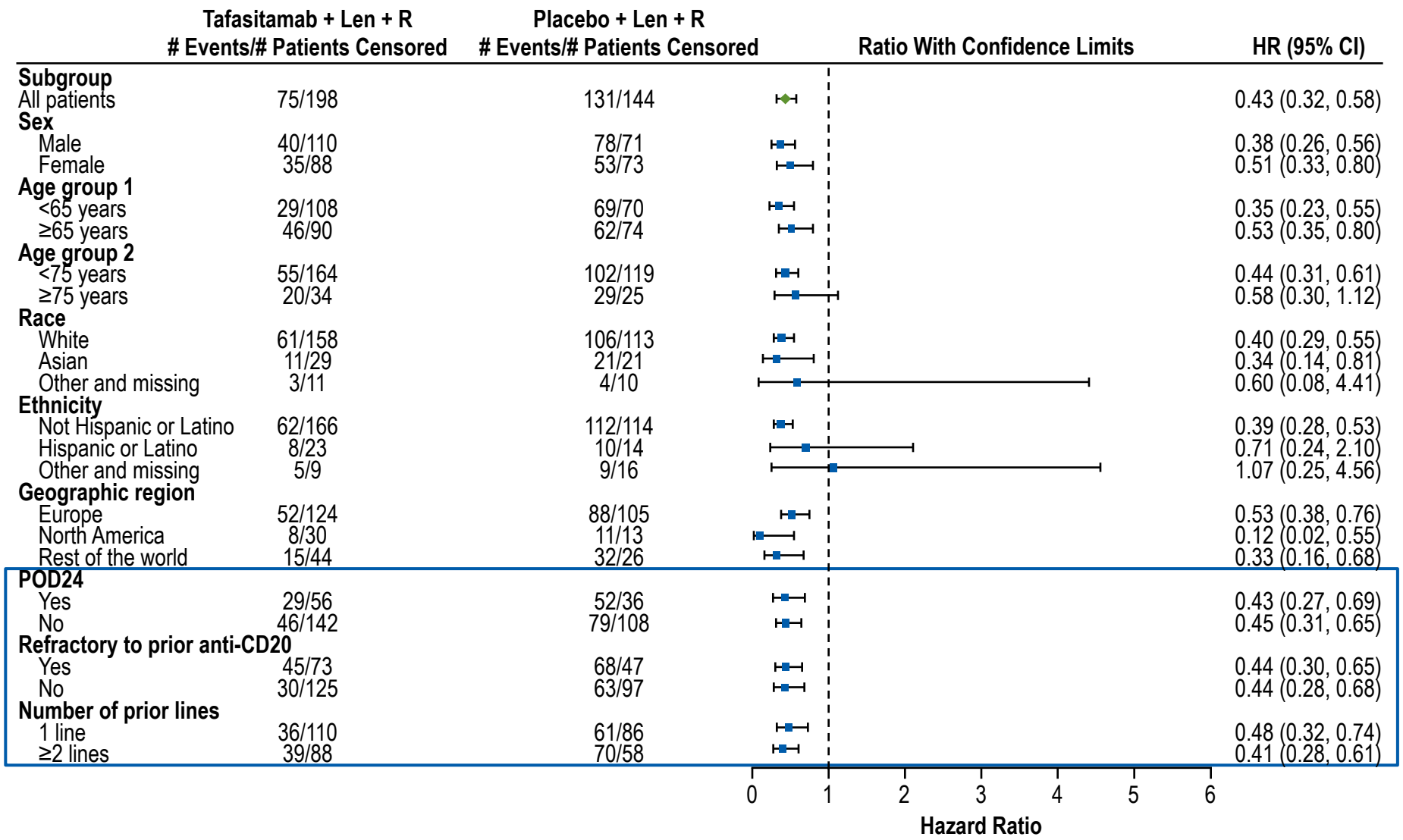
Primary Endpoint: PFS by Investigator Assessment



Significant improvement in PFS was observed with tafasitamab

ITT population. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; R, rituximab.

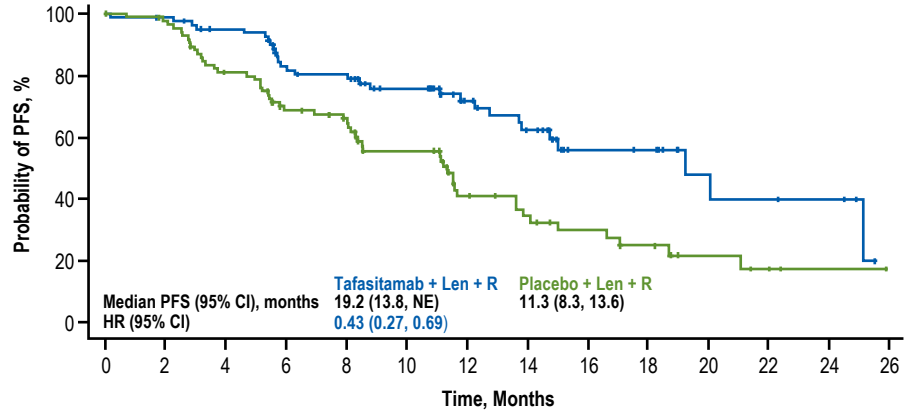
Prespecified Subgroup Analysis of PFS



ITT population. Analysis by investigator assessment. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; PFS, progression-free survival; POD24, progression of disease within 24 months; R, rituximab.

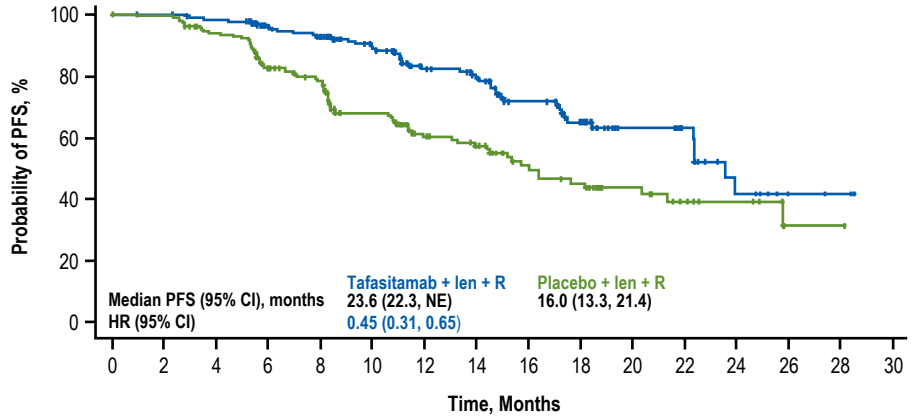
PFS by POD24 Status and Refractoriness to Anti-CD20

POD24: Yes



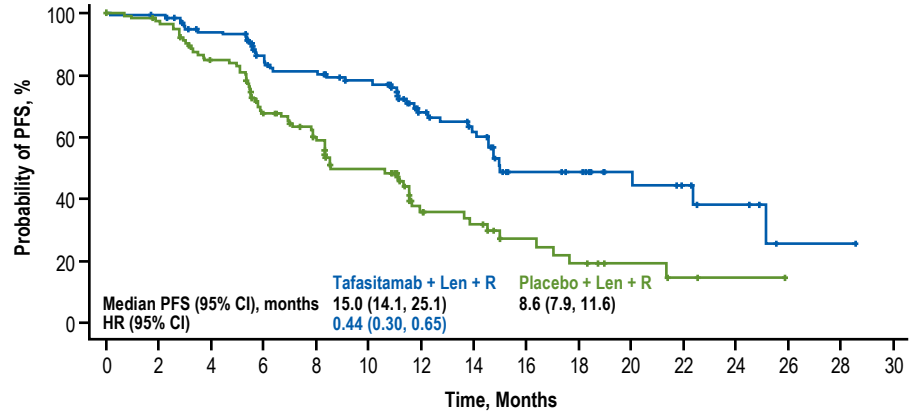
No. at Risk														
Tafasitamab + Len + R	85	81	75	60	57	46	32	25	13	12	6	5	4	0
Placebo + Len + R	88	83	67	52	46	35	21	16	12	9	5	2	1	0

POD24: No



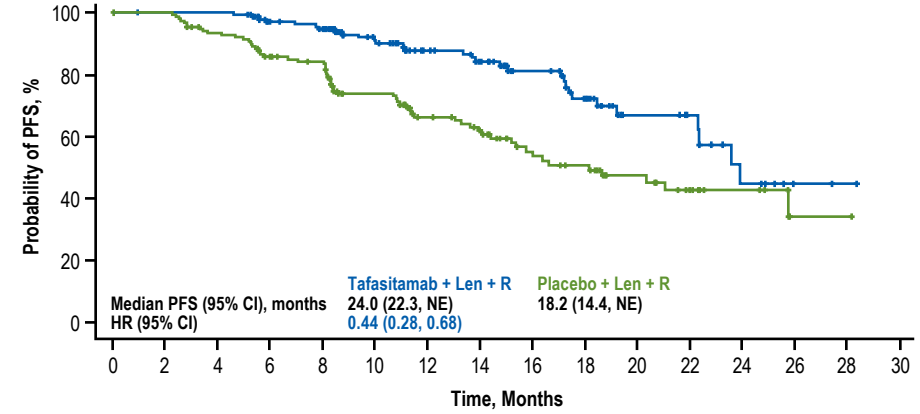
No. at Risk																
Tafasitamab + Len + R	188	180	175	152	143	118	87	78	58	45	24	17	8	3	2	0
Placebo + Len + R	187	182	168	140	127	91	61	54	36	31	21	14	9	2	2	0

Anti-CD20 Refractory: Yes



No. at Risk																
Tafasitamab + Len + R	118	113	102	86	80	71	46	38	21	19	11	8	5	1	1	0
Placebo + Len + R	115	108	91	66	54	41	20	16	10	7	4	2	1	0	0	0

Anti-CD20 Refractory: No

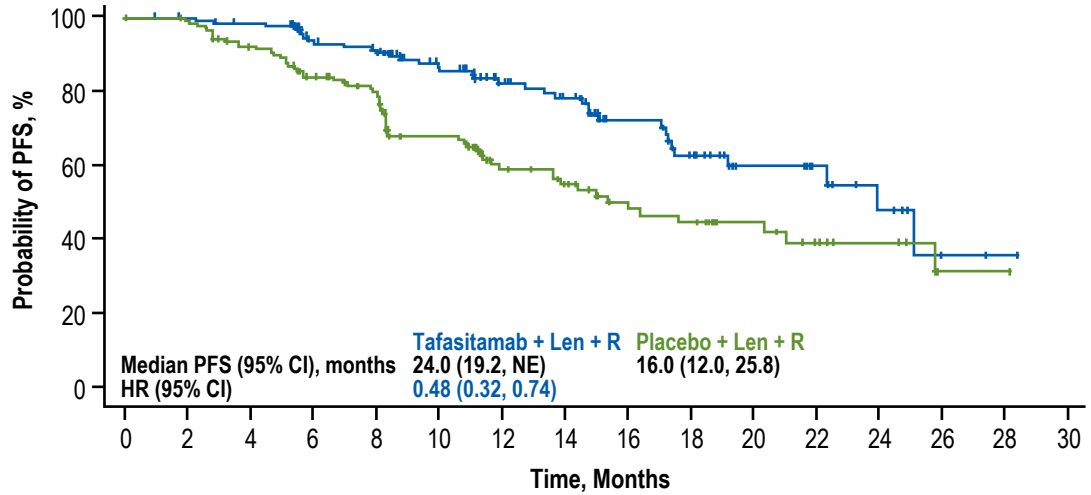


No. at Risk																
Tafasitamab + Len + R	155	148	148	126	120	93	73	65	50	38	19	14	7	2	1	0
Placebo + Len + R	160	157	144	126	119	85	62	54	38	33	22	14	9	2	2	0

ITT population. Subgroup analyses are based on stratification factor. Analysis by investigator assessment. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; POD24, progression of disease within 24 months of initial diagnosis; R, rituximab.

PFS by Line of Therapy

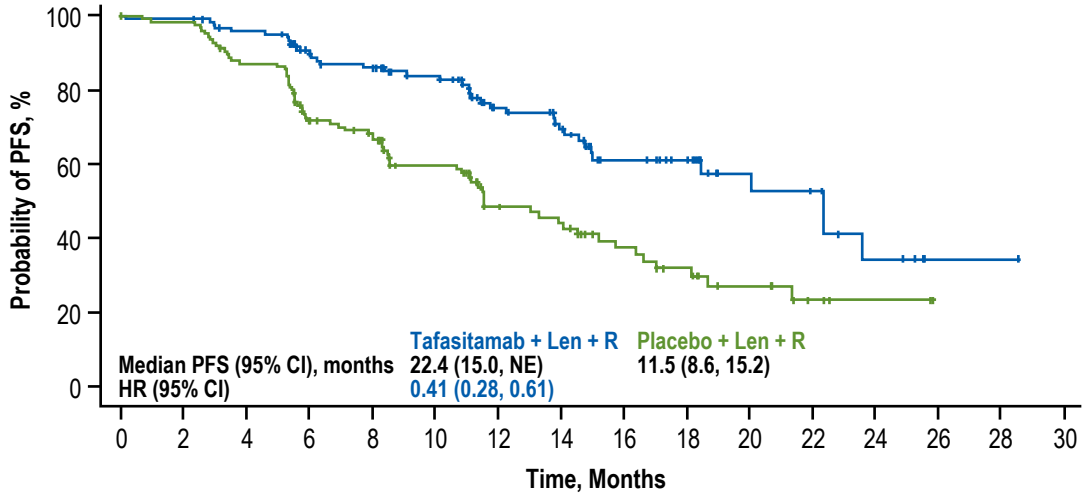
1 Prior Line (2L Treatment)



No. at Risk

Tafasitamab + Len + R	146	140	136	115	110	88	65	57	40	31	18	12	7	2	1	0
Placebo + Len + R	147	142	127	108	97	70	47	40	28	25	17	12	8	2	2	0

≥2 Prior Lines (3L+ Treatment)



No. at Risk

Tafasitamab + Len + R	127	121	114	97	90	76	54	46	31	26	12	10	5	1	1	0
Placebo + Len + R	128	123	108	84	76	56	35	30	20	15	9	4	2	0	0	0

ITT population. Subgroup analyses are based on stratification factor. Analysis by investigator assessment. 2L, second-line; 3L, third-line; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; R, rituximab.

FL Patient Population Comparison

Variable	inMIND Tafasitamab + Len + R (n=273)	inMIND Placebo + Len + R (n=275)	AUGMENT[1] R + Len (n=147)
Median age, years	64	64	62
Male, %	55	54	42
Ann Arbor stage IV at enrollment, %	55	59	30
FL grade 3A, %	25	26	12
FLIPI high risk (score 3-5) , %	50	55	37
ECOG PS 0, %	66	70	67
ECOG PS 1-2, %	34	30	33
B symptoms present, %	23	24	8
High tumor burden per GELF (yes), %	81	84	52
Refractory to last prior regimen, %	41	35	18
Refractory to anti-CD20, %	43	42	–

1, Leonard JP, et al. *J Clin Oncol.* 2019;37:1188-1899.

ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; len, lenalidomide; R, rituximab.

PET-CR and ORR

PET-CR (FDG-Avid Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients with FDG-avid disease at baseline	251	254
Patients with postbaseline PET assessments, n (%)*	201/251 (80.1)	205/254 (80.7)
Best metabolic response based on PET, n (%)†		
CMR	124 (49.4)	101 (39.8)
PMR	37 (14.7)	39 (15.4)
NMR/SD	19 (7.6)	12 (4.7)
PMD	19 (7.6)	51 (20.1)
Not done	50 (19.9)	46 (19.3)
PET-CR rate, % (95% CI)	**49.4** (43.1, 55.8)	**39.8** (33.7, 46.1)
Odds ratio (95% CI)	**1.5 (1.04, 2.13)**	
Nominal *P* value	**0.0286**	

ORR (ITT Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients, n	273	275
Best overall response, n (%)‡		
CR	142 (52.0)	112 (40.7)
PR	86 (31.5)	87 (31.6)
SD	28 (10.3)	46 (16.7)
PD	7 (2.6)	20 (7.3)
NE	2 (0.7)	0
Not done	8 (2.9)	10 (3.6)
ORR, % (95% CI)	**83.5** (78.6, 87.7)	**72.4** (66.7, 77.6)
Odds ratio (95% CI)	**2.0 (1.30, 3.02)**	
Nominal *P* value	**0.0014**	

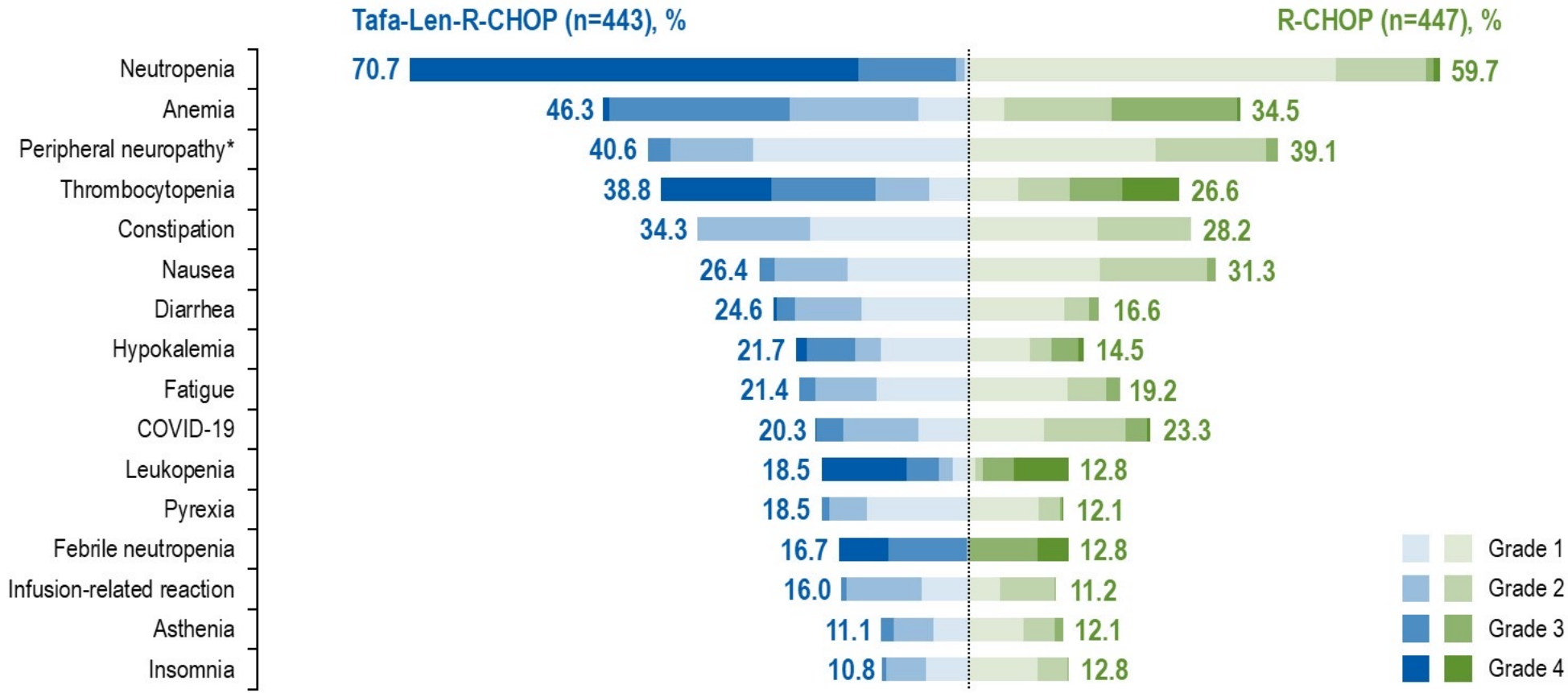
Significant improvement in PET-CR rate and ORR was observed with tafasitamab

Analysis by investigator assessment. *Calculated based on patients with a positive PET scan at baseline, defined as having a Deauville score of 4 or 5 at baseline. †Two patients (0.8%) in both arms had PET after confirmed PD or new antilymphoma treatment initiation. ‡Per Lugano 2014 classification. CI, confidence interval; CMR, complete metabolic response; CR, complete response; FDG, fluorodeoxyglucose; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; NMR, nonmetabolic response; ORR, overall response rate; PD, progressive disease; PET, positron emission tomography; PET-CR, positron emission tomography-complete response; PMD, progressive metabolic disease; PMR, partial metabolic response; PR, partial response; R, rituximab; SD, stable disease.

AT THE FOREFRONT
UChicago Medicine

SAFETY PROFILE, TOXICITY MITIGATION

Most Frequent TEAEs (≥12% in Any Group)



- **Most common** grade ≥3 adverse events were related to **cytopenias**
  - Rate of **serious febrile neutropenia:** 13.3% with Tafa-Len-R-CHOP and 9.8% 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.
Len, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab; TEAE, treatment-emergent adverse event.

FL: Most Frequent Any-Grade TEAEs (≥15% in Any Group)

Preferred Term, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Any adverse event	272 (99.3)	270 (99.3)	542 (99.3)
Neutropenia	133 (48.5)	123 (45.2)	256 (46.9)
Diarrhea	103 (37.6)	77 (28.3)	180 (33.0)
COVID-19	86 (31.4)	64 (23.5)	150 (27.5)
Constipation	80 (29.2)	67 (24.6)	147 (26.9)
Rash	60 (21.9)	58 (21.3)	118 (21.6)
Fatigue	58 (21.2)	43 (15.8)	101 (18.5)
Cough	52 (19.0)	47 (17.3)	99 (18.1)
Pyrexia	52 (19.0)	44 (16.2)	96 (17.6)
Muscle spasms	49 (17.9)	49 (18.0)	98 (17.9)
Nausea	49 (17.9)	38 (14.0)	87 (15.9)
Infusion-related reaction	43 (15.7)	41 (15.1)	84 (15.4)
Thrombocytopenia	37 (13.5)	42 (15.4)	79 (14.5)
Pruritus	44 (16.1)	28 (10.3)	72 (13.2)

Safety population. *One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. †Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). COVID-19, coronavirus disease 2019; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

FL: Grade 3 or 4 TEAEs and Dose Modifications

Most Common Grade 3 or 4 TEAEs (≥5% in Any Group)

Preferred Term, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Neutropenia	109 (39.8)	102 (37.5)	211 (38.6)
Pneumonia	23 (8.4)	14 (5.1)	37 (6.8)
Thrombocytopenia	17 (6.2)	20 (7.4)	37 (6.8)
Neutrophil count decreased	16 (5.8)	18 (6.6)	34 (6.2)
Anemia	12 (4.4)	16 (5.9)	28 (5.1)
COVID-19	16 (5.8)	6 (2.2)	22 (4.0)
COVID-19 pneumonia	13 (4.7)	3 (1.1)	16 (2.9)

- Tafasitamab and placebo dose interruptions or discontinuations due to TEAEs were similar between treatment arms, n (%):
  - Dose delay or interruption due to TEAEs: 203 (74%) vs 190 (70%)
  - Discontinued study treatment due to TEAEs: 30 (11%) vs 18 (7%)
- Len discontinuations due to TEAEs were similar between tafasitamab and placebo arms, n (%):
  - 39 (14%) vs 31 (11%)
- Len dose reductions were similar between tafasitamab and placebo arms
  - Median relative dose intensity: 86% vs 87%

Safety population. *One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. †Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). COVID-19, coronavirus disease 2019; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

Second Opinion

Ann LaCasce, MD, MMSc

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Discussion Questions

Which patients with R/R FL do you feel are optimal candidates for tafasitamab/R^2? How would you choose between this regimen, epcoritamab/R^2 and R^2 alone for individual patients, and how do patient fitness and lingering side effects from previous therapy affect this decision?

What do you make of the data indicating a potentially reduced risk of transformation after treatment with tafasitamab/R^2? Do you think this phenomenon is real, and if so, how does it affect your enthusiasm for the use of tafasitamab/R^2 vis-à-vis other available regimens?

Would you administer tafasitamab/R^2 to a patient with R/R FL who has previously experienced disease progression on R^2? Would you administer tafasitamab/R^2 and CD19-directed CAR T-cell therapy to the same patient with R/R FL in sequence? Would you assess CD19 expression before doing so?

RTP
RESEARCH
TO PRACTICE

Second Opinion

Gilles Salles, MD, PhD

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Discussion Questions

What is your take on the results of the frontMIND study? Which patients with newly diagnosed disease represent optimal candidates for first-line tafasitamab, lenalidomide and R-CHOP?

If the frontMIND regimen is approved by the FDA, how do you think you will select between that approach, polatuzumab vedotin/R-CHP and R-CHOP for patients with newly diagnosed DLBCL? Would you like to be able to use the frontMIND regimen today, if you could?

Do you have any concern that the up-front use of a CD19-based approach might impact the effectiveness of subsequent CAR T-cell therapy if it is needed down the line? Are there any data about the effectiveness of CAR T-cell therapy after tafasitamab?

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RESEARCH
TO PRACTICE

Discussion Questions

How was the frontMIND regimen tolerated compared to R-CHOP? Were there any specific toxicities that were significantly worse with the addition of tafasitamab/lenalidomide? How does the tolerability of this regimen compare to polatuzumab vedotin/ R-CHP?

For patients with DLBCL for whom you are reserving tafasitamab for the R/R setting, in which line of therapy are you typically using it?

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1: Rational Incorporation of CD79b-Targeted Antibody-Drug Conjugates into the Management of Newly Diagnosed and Relapsed/ Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Flowers

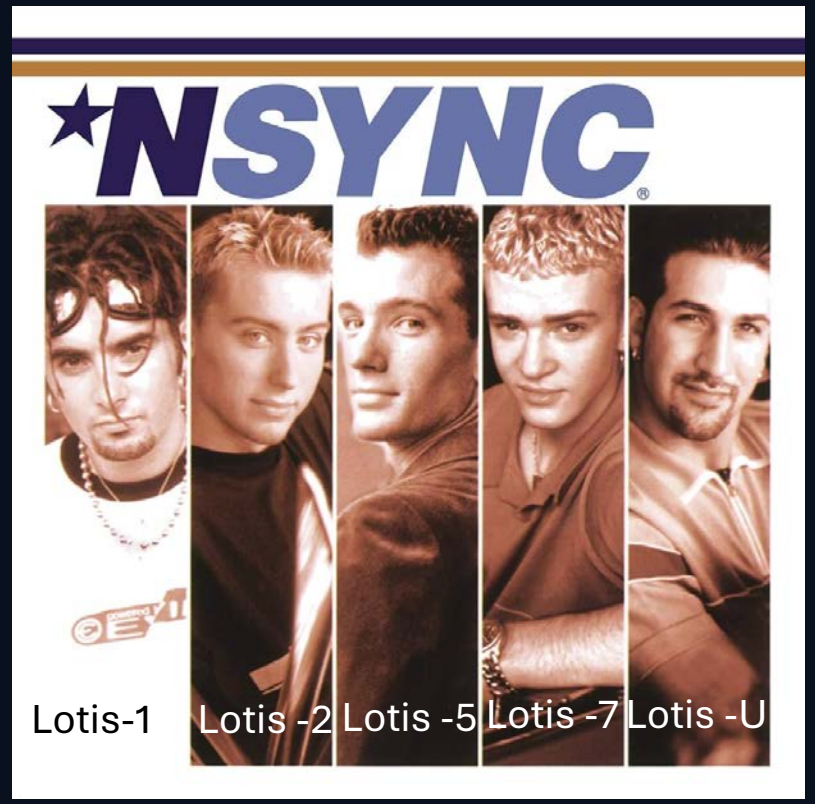
Module 2: Clinical Utility of CD19-Directed Monoclonal Antibodies in the Treatment of DLBCL and Follicular Lymphoma (FL) — Dr Smith

Module 3: Optimal Use of CD19-Directed Antibody-Drug Conjugates for R/R DLBCL and FL — Dr Lunning

Module 4: Current and Future Role of Bruton Tyrosine Kinase Inhibition in Therapy for Non-Hodgkin Lymphoma — Dr Kahl

RTP RESEARCH TO PRACTICE

Lonca-T-Dex: N'SYNCing in Rel/Ref NHL



Professor Matthew Lunning D.O., FACP
James O. Armitage, MD, Chair of Hematologic Malignancies
Interim Chief of Hematology
Medical Director, Gene & Cellular Therapy
Assistant Vice Chancellor for Clinical Research

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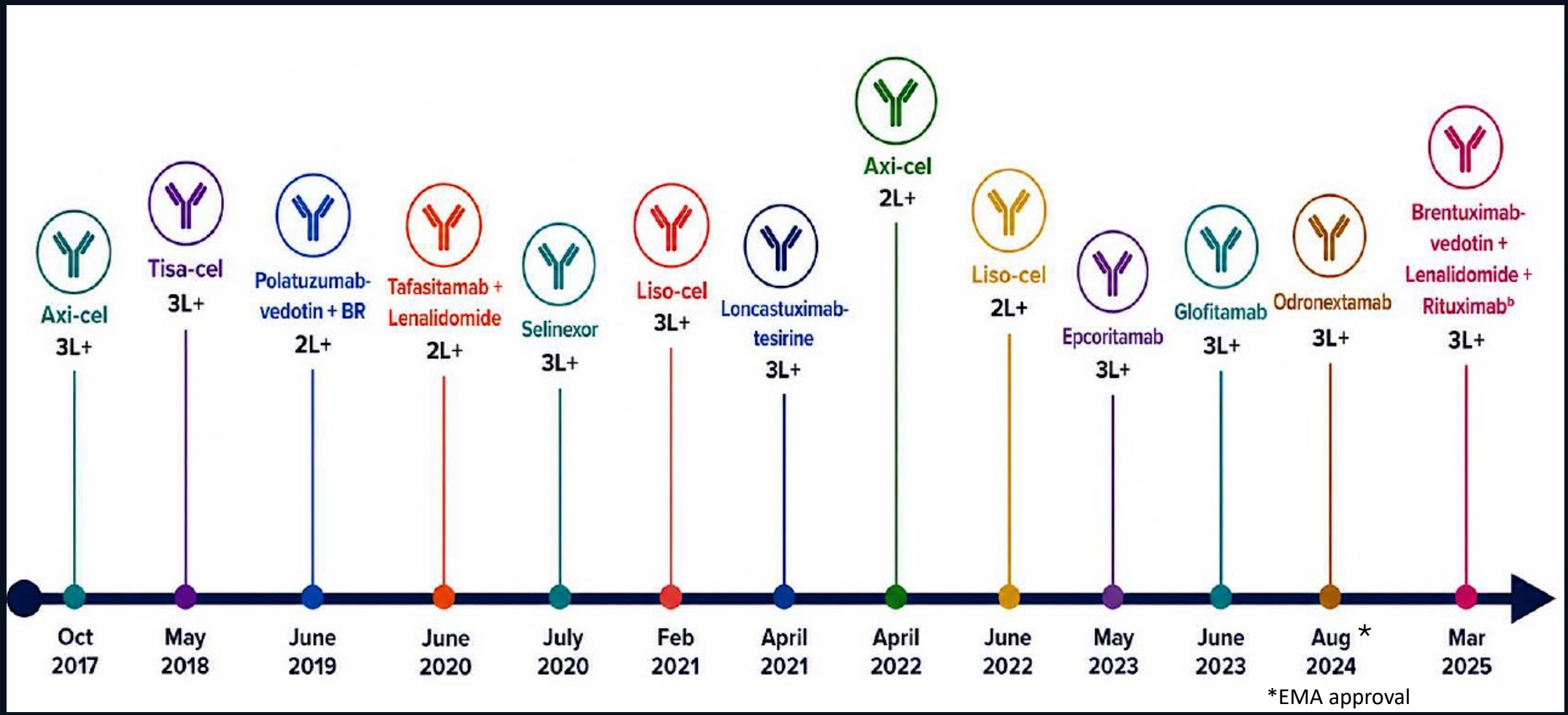
CHAOS BREEDS CONSULT



*EMA approval

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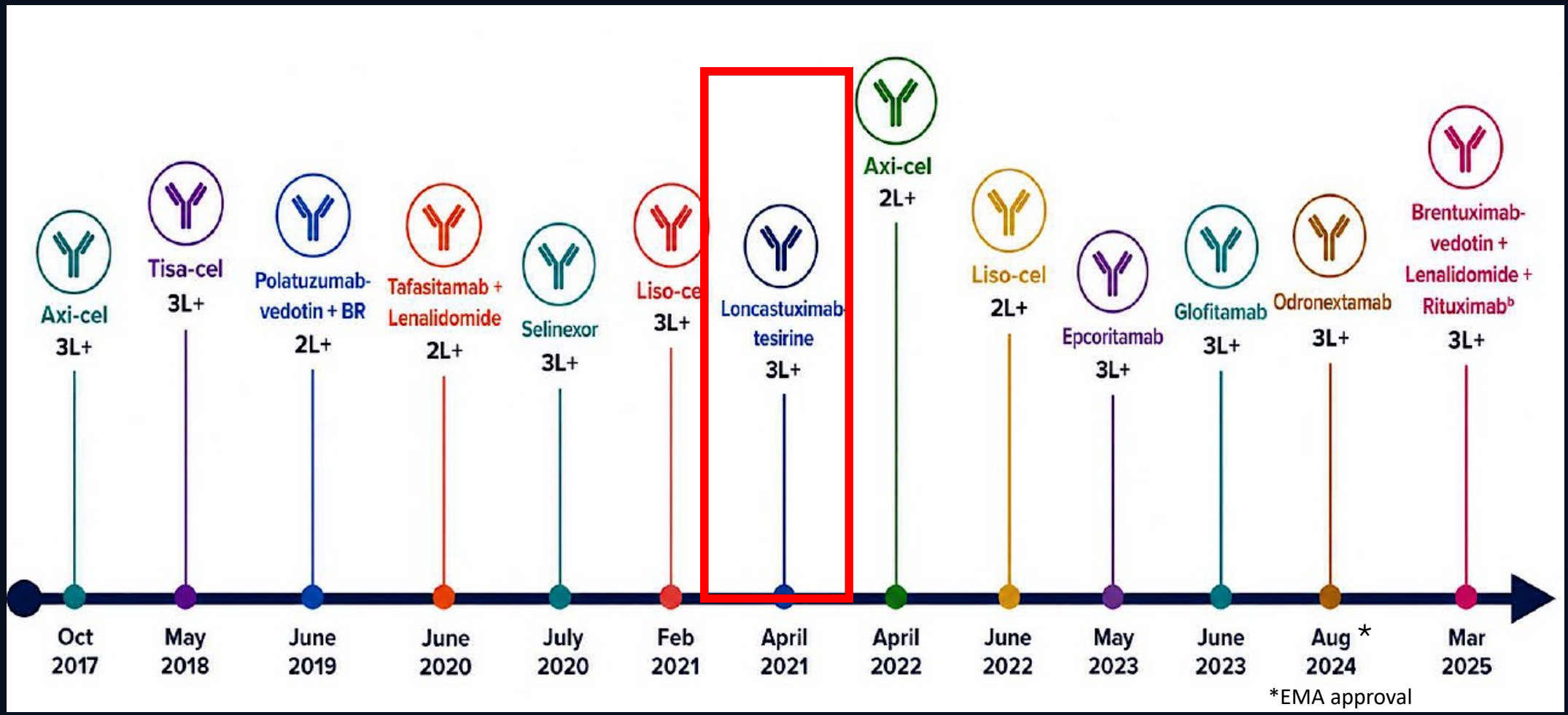

*EMA approval

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LOTIS-1:The Tryout

A Phase 1 Study of Lonca-T in Relapsed B-cell NHL

Enrolled (N=183)

↓

Safety analysis set (n=183)
DLT analysis set (n=73)
Efficacy analysis set (n=180)

↓

Discontinued treatment (N=183)

- Disease progression (n=83)
- Adverse event (n=34)
- Physician decision (n=30)
- Death (n=10)
- Withdrawal of consent (n=3)
- Non-compliance, including lost to follow-up (n=2)
- Treatment delay >21 days without sponsor approval (n=1)
- Other (n=20)

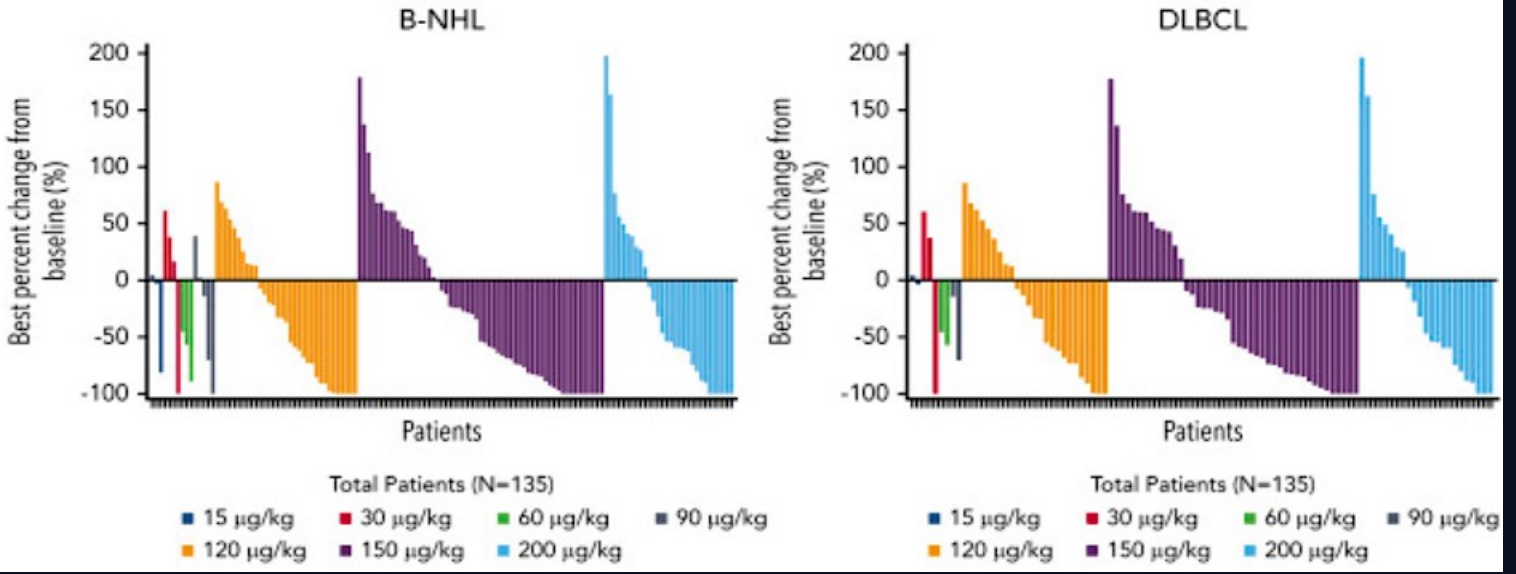
↓

Discontinued study (N=183)

- Death (n=111)
- Completed study (n=45)[a]
- Withdrawal of consent (n=7)
- Lost to follow-up (n=1)
- Other (n=19)

Dose level	Lonca (µg/kg)	
1	15	Q3W
2	30	
3	60	
4	90	
5	120	
6	150	
7	200	
8	200	Q6W

Best percent change from baseline in tumor size by dose of loncastuximab tesirine



Hamadani et al. Blood 2021

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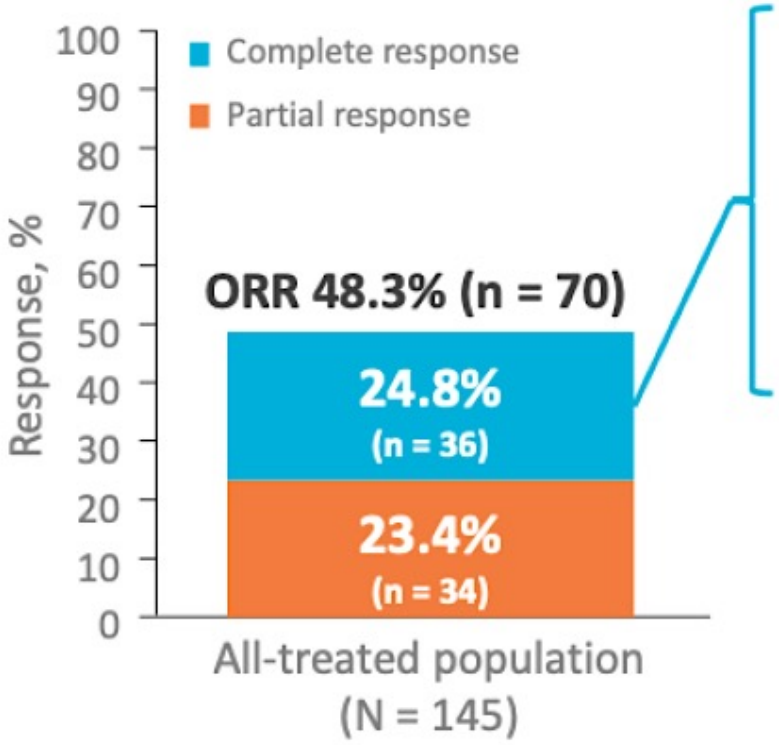
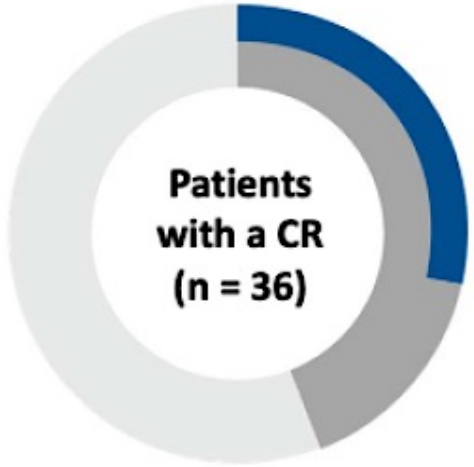
LOTIS-2: Getting to Know Each Other

A Phase 2 Study of Lonca-T in Relapsed DLBCL





Of the patients with a CR, 44% (16 of 36) were event-free for ≥1 year.

Of the patients with a CR, 31% (11 of 36) were event-free for ≥2 years.

Median (range) number of treatment cycles	
All-treated population	3.0 (1-26)
Pts with a CR	8.0 (1-26)
Pts with a CR, event-free ≥1 year[a]	12.5 (1-26)
Pts with a CR, event-free ≥2 years[a]	13.0 (1-22)

Caimi et al ICML 2023

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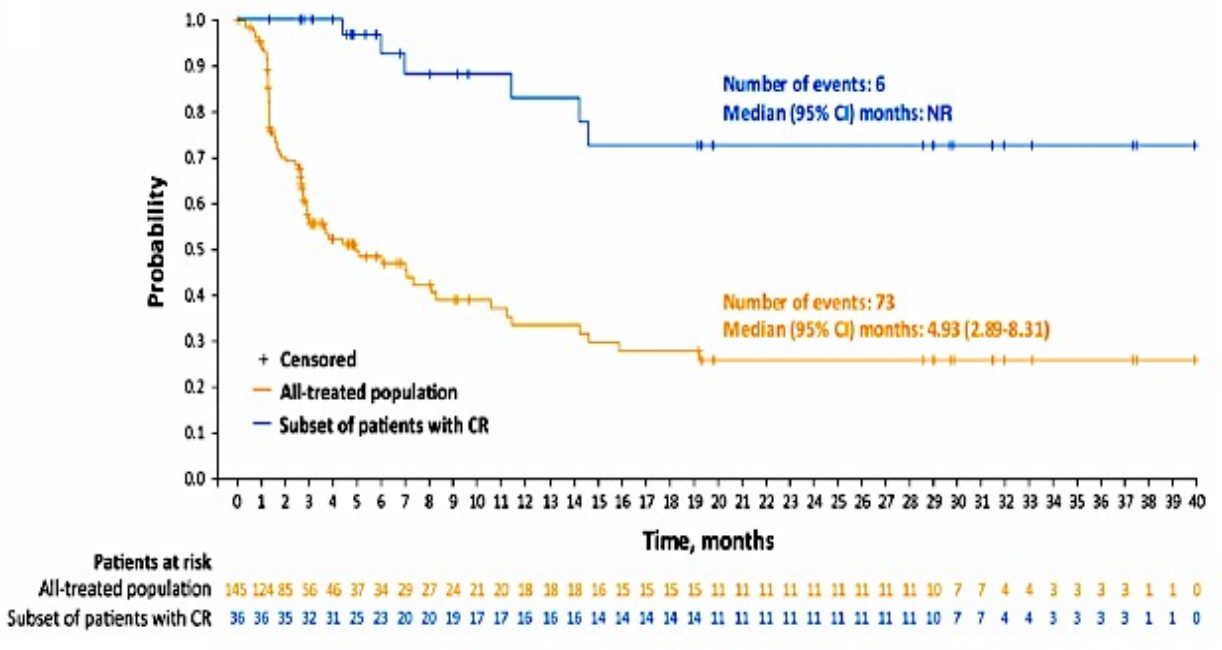
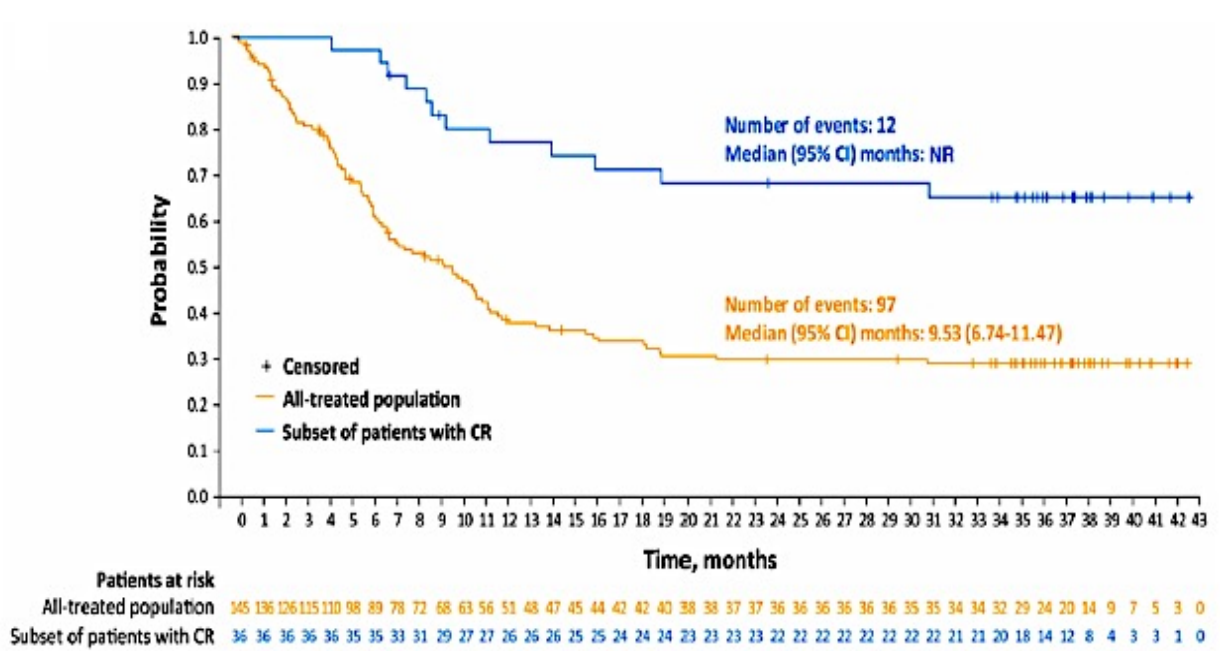
LOTIS-2: Getting to Know Each Other

Progression Free Survival



Overall Survival



Caimi et al. Haematologica 2024

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LOTIS-2: Getting to Know Each Other

TEAEs, any grade in ≥30% of patients	All-treated population, N = 145	Patients with a CR, n = 36
Patients with any TEAE	98.6%	100%
Increased GGT	42%	50%
Neutropenia	40%	42%
Thrombocytopenia	33%	36%
Anemia	26%	36%
Peripheral edema	20%	33%
Nausea	23%	31%

TEAEs, grade ≥3 in ≥10% of patients	All-treated population, N = 145	Patients with a CR, n = 36
Patients with any TEAE	73.8%	75%
Neutropenia	26%	28%
Thrombocytopenia	18%	19%
Increased GGT	17%	19%
Anemia	10%	8.3%
Leukopenia	9%	14%
Hypophosphatemia	6%	11%

Caimi et al ICML 2023

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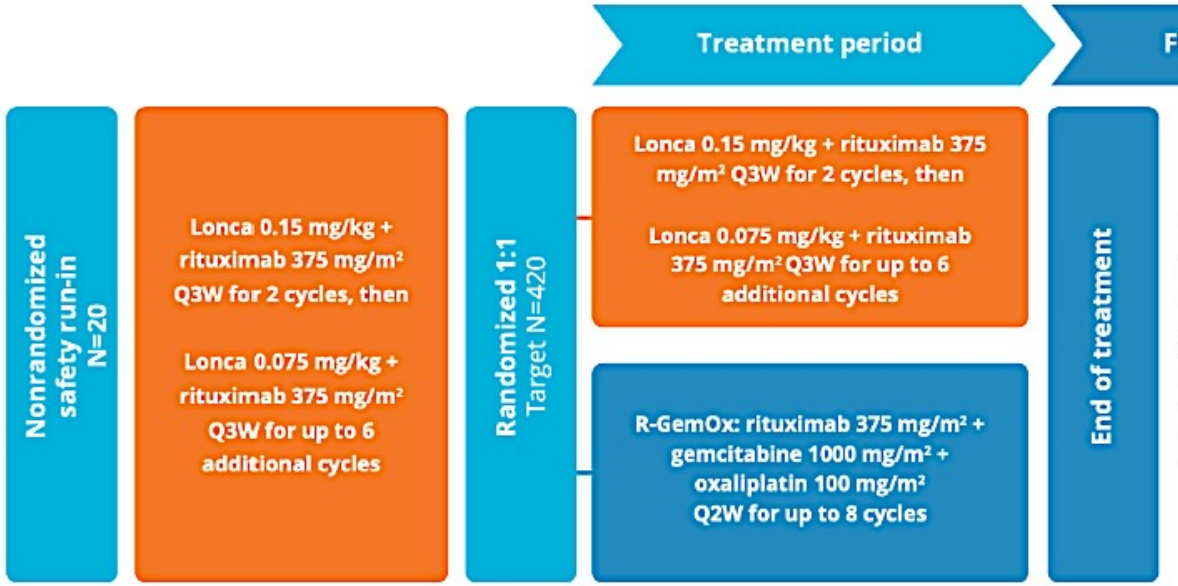
LOTIS-5: Harmonizing

Phase 3 Trial of Lonca-T with R Versus R-GemOx in Relapsed DLBCL



For both parts of the study, irrespective of disease status, patients will be followed for up to 4 years after EOT until withdrawal of consent, loss to follow-up, or death—whichever occurs first

Study Endpoints

Primary endpoint: PFS

Secondary endpoints: OS, ORR, CR rate, DOR, safety, PK parameters, Lonca ADAs, and PROs

Exploratory endpoints: Correlations between clinical activity and Lonca exposure and tumor and/or blood biomarkers

Eligibility Criteria

- Main inclusion criteria include
  - Adults with a pathologic diagnosis of R/R DLBCL (including DLBCL transformed from indolent lymphoma) or HGBCL, following ≥1 multi-agent systemic treatment regimen
  - Measurable disease (2014 Lugano Classification[7])
  - Not a candidate for SCT
  - Eastern Cooperative Oncology Group performance status score of 0-2

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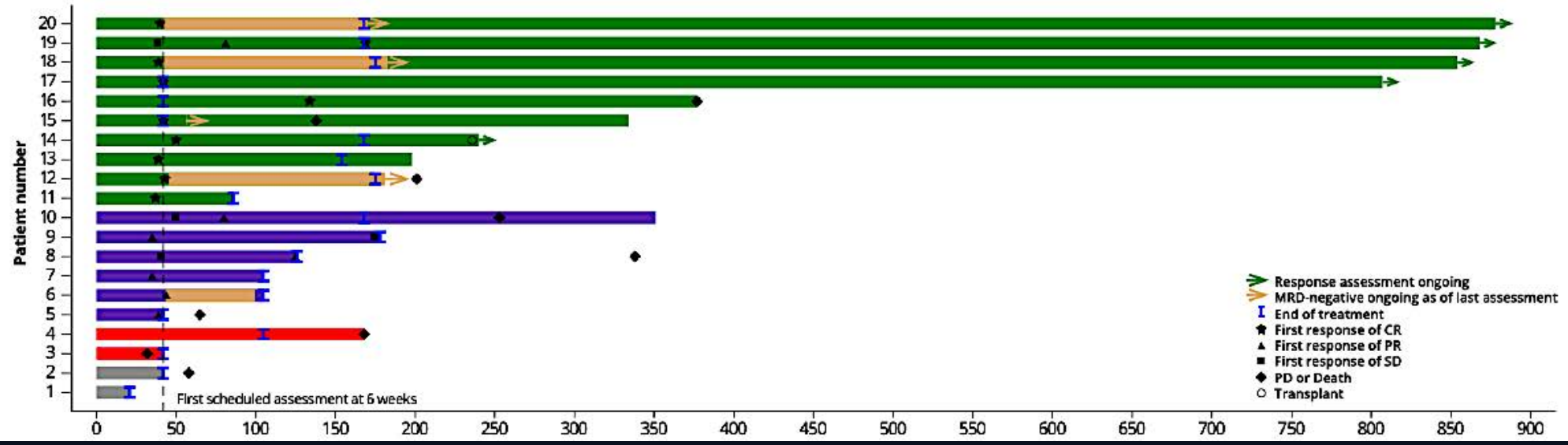
LOTIS-5: Harmonizing

Efficacy outcomes in safety run-in population (N=20)	
ORR (95% CI), %	80.0 (56.3-94.3)
CRR (95% CI), %	50.0 (27.2-72.8)
Median PFS (95% CI), months	8.3 (4.5-NE)
Efficacy outcomes in responders (n=16)	
Median DOR (95% CI), months	8.02 (3.19-NE)
Events, n (%)	5 (31.3)



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LOTIS-5: Harmonizing

Safety endpoint, n (%)	
All grade TEAE	20 (100)
Grade ≥3 TEAE	11 (55)
GGT increased	5 (25)
Neutropenia	4 (20)
COVID-19/COVID-19 pneumonia	3 (15)
Alanine aminotransferase increased	1 (5)
Anemia	1 (5)
Aspartate aminotransferase increased	1 (5)
Blood alkaline phosphatase increased	1 (5)
Cataract	1 (5)
Cellulitis gangrenous	1 (5)
Cytomegalovirus infection reactivation	1 (5)
Hyponatremia	1 (5)

Safety endpoint, n (%)	
Malaise	1 (5)
Neurological decompensation	1 (5)
Photosensitivity reaction	1 (5)
Pleural effusion	1 (5)
Tumor lysis syndrome	1 (5)
Urinary tract infection	1 (5)
Serious adverse events	9 (45)
Infection	6 (30)
Hyponatremia	1 (5)
Anaphylactic reaction	1 (5)
Pleural effusion	1 (5)
Malaise	1 (5)
Neurological decompensation	1 (5)
TEAEs leading to any study drug withdrawal	8 (40)

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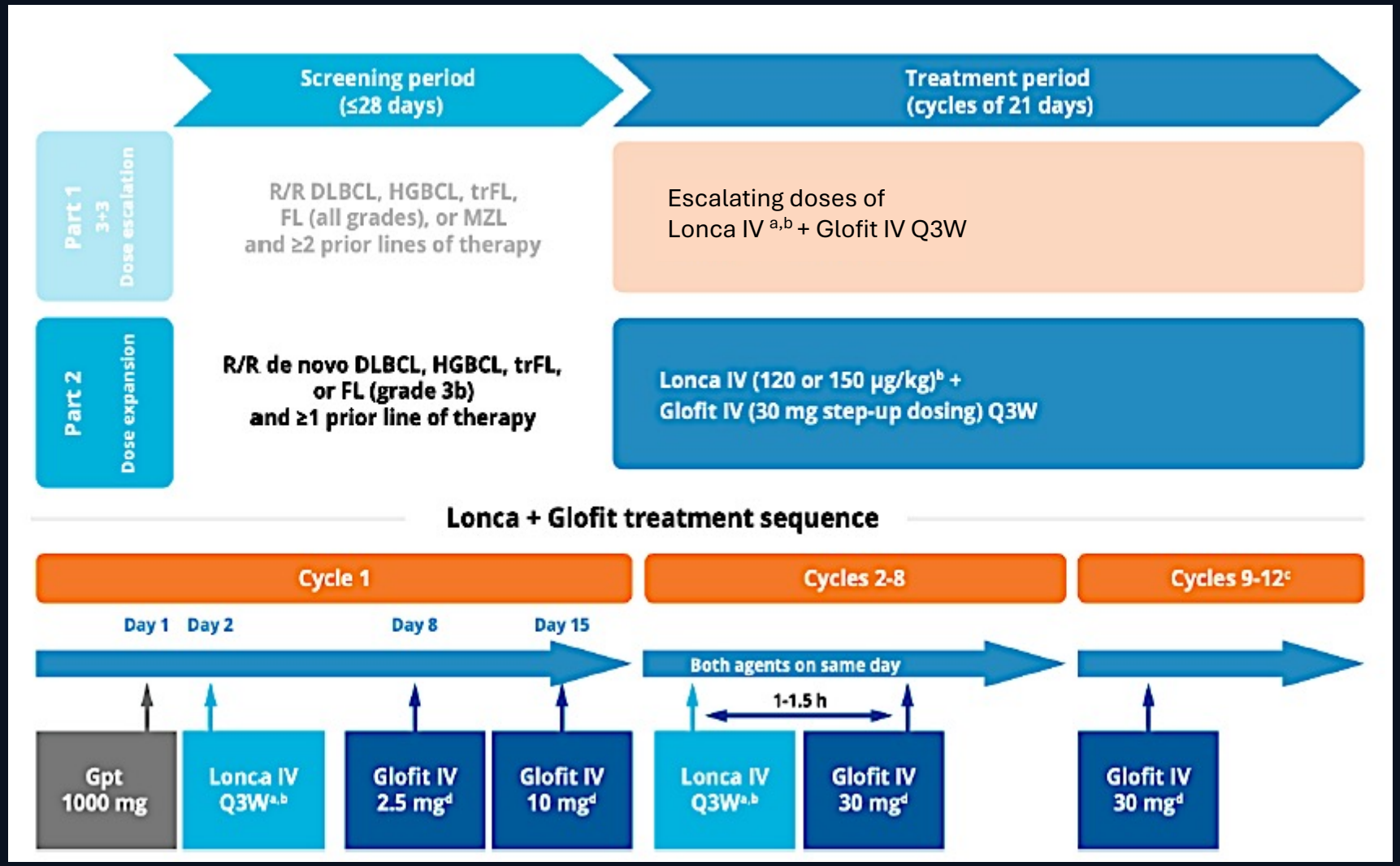
LOTIS-7: Guest Artists

Phase 1b Trial of Lonca-T with Glofitamab in Relapsed DLBCL



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LOTIS-7: Guest Artists

Efficacy measures	Glofit + Lonca 120 µg/kg	Glofit + Lonca 150 µg/kg	Total
Best overall response	(n=15)	(n=15)	(N=30)
ORR (CR+PR), n (%) [95% CI]	14 (93.3) [68.1-99.8]	14 (93.3) [68.1-99.8]	28 (93.3) [77.9-99.2]
CR, n (%) [95% CI]	13 (86.7) [59.5-98.3]	13 (86.7) [59.5-98.3]	26 (86.7) [69.3-96.2]
PR, n (%)	1 (6.7)	1 (6.7)	2 (6.7)
SD, n (%)	1 (6.7)	0	1 (3.3)
PD, n (%)	0	1 (6.7)	1 (3.3)
DOR	(n=14)	(n=14)	(n=28)
Event, n (%)	0	1 (7.1)	1 (3.6)
Median	NE	NE	NE
Probability to remain event-free for 6 months (95% CI)	100 (100-100)	90.9 (50.8-98.7)	95.2 (70.7-99.3)
Time to first response (CR or PR)	(n=14)	(n=14)	(n=28)
Median, days	42.0	42.0	42.0
Time to first CR	(n=13)	(n=13)	(n=26)
Median, days	80.0	42.0	70.5

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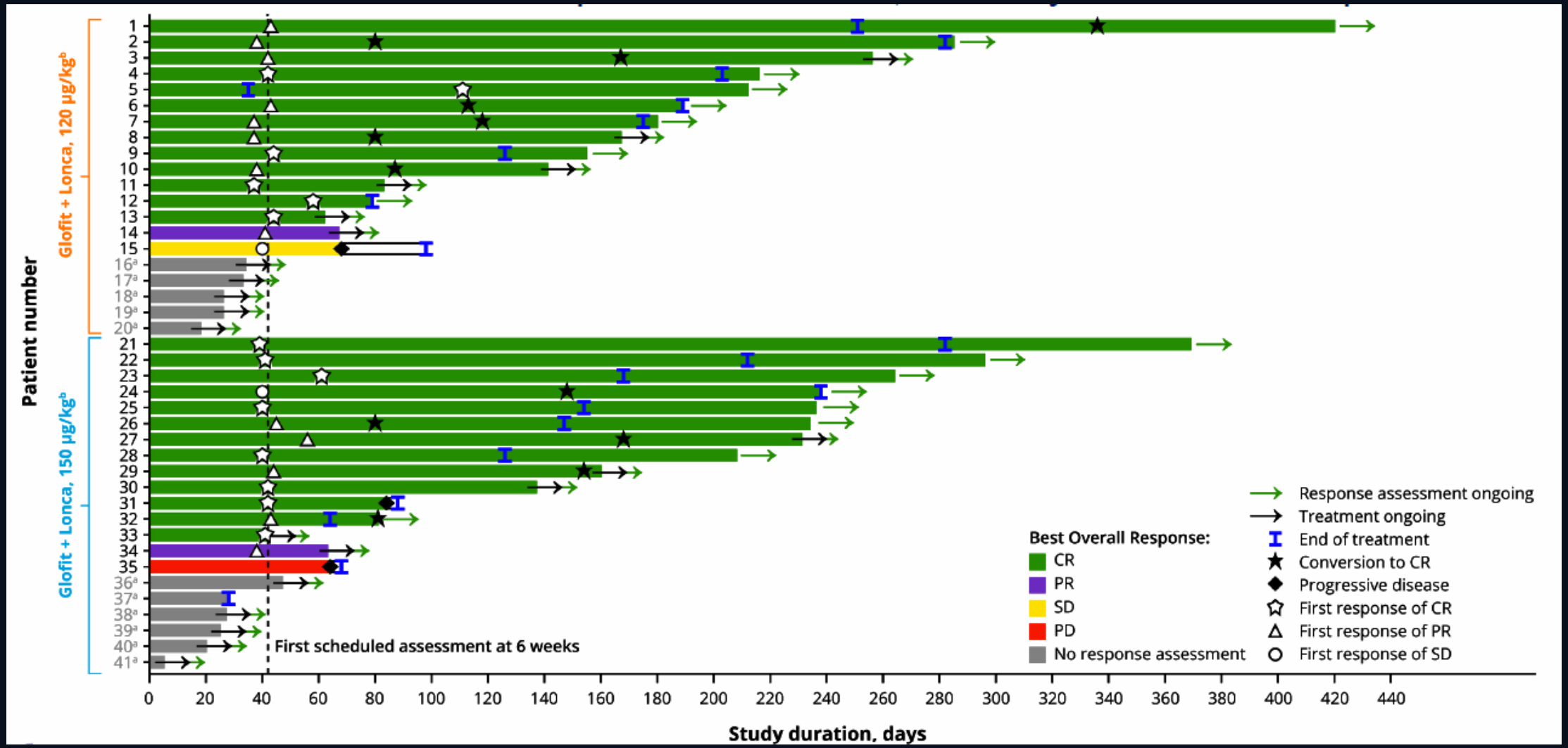
LOTIS-7: Guest Artists



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LOTIS-7: Guest Artists

Characteristic, n (%)	Glofit + Lonca, 120 µg/kg (n=20)	Glofit + Lonca, 150 µg/kg (n=21)	All dose levels (N=41)
Any-grade TEAEs	20 (100)	18 (85.7)	38 (92.7)
Grade ≥3 TEAEs	11 (55.0)	12 (57.1)	23 (56.1)
Grade ≥3 TEAEs occurring in >5% of patients			
Neutropenia	4 (20.0)	6 (28.6)	10 (24.4)
Anemia	1 (5.0)	3 (14.3)	4 (9.8)
Aspartate aminotransferase increased	2 (10.0)	1 (4.8)	3 (7.3)
Gamma-glutamyltransferase increased	1 (5.0)	2 (9.5)	3 (7.3)
Thrombocytopenia	2 (10.0)	1 (4.8)	3 (7.3)
Grade ≥3 treatment-related TEAEs	9 (45.0)	11 (52.4)	20 (48.8)
Grade ≥3 treatment-related TEAEs occurring in >5% of patients			
Neutropenia	4 (20.0)	6 (28.6)	10 (24.4)
Anemia	0	3 (14.3)	3 (7.3)
Aspartate aminotransferase increased	2 (10.0)	1 (4.8)	3 (7.3)
Thrombocytopenia	2 (10.0)	1 (4.8)	3 (7.3)
Rates of CRS and ICANS			
CRS, grade 1	7 (35.0)	5 (23.8)	12 (29.3)
CRS, grade 2	3 (15.0)	0	3 (7.3)
CRS, grade 3	1 (5.0)	0	1 (2.4)
CRS, grade ≥4	0	0	0
ICANS, grade 1	1 (5.0)	0	1 (2.4)
ICANS, grade 2	1 (5.0)	1 (4.8)	2 (4.9)
ICANS, grade ≥3	0	0	0
TEAEs leading to study drug discontinuation			
TEAEs leading to Lonca discontinuation only	1 (5.0)	2 (9.5)	3 (7.3)
TEAEs leading to Glofit discontinuation only	0	3 (14.3)	3 (7.3)

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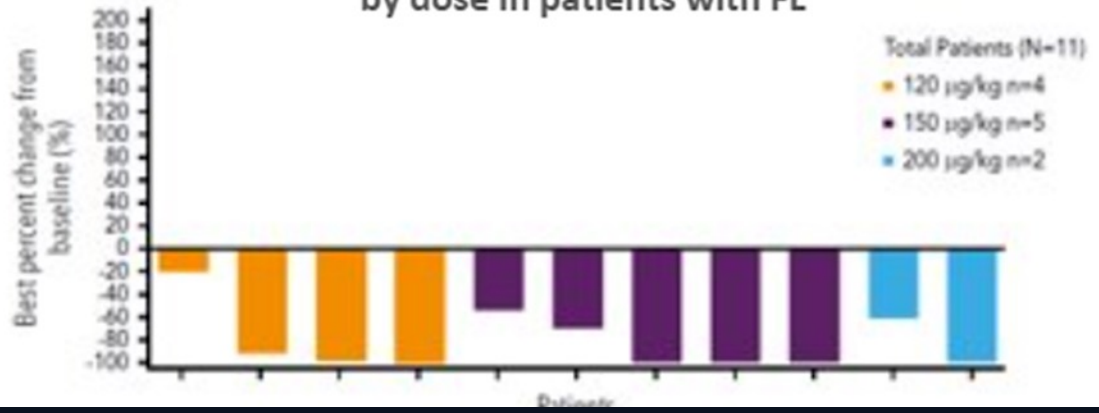
LOTIS-U: Playing Different Venues

LOTIS-1: Outcomes with Lonca[1]	FL (n = 14)	Total (N = 180)
ORR, n (%)	11 (78.6)	82 (45.6)
95% CI	49.2-95.3	38.1-53.1
CR	9 (64.3)	48 (26.7)
PR	2 (14.3)	34 (18.9)
Median DOR, months	NR	5.4
Median PFS, months	NR	3.1
Median OS, months	NR	8.3

LOTIS-1: Best percent change in tumor volume size by dose in patients with FL



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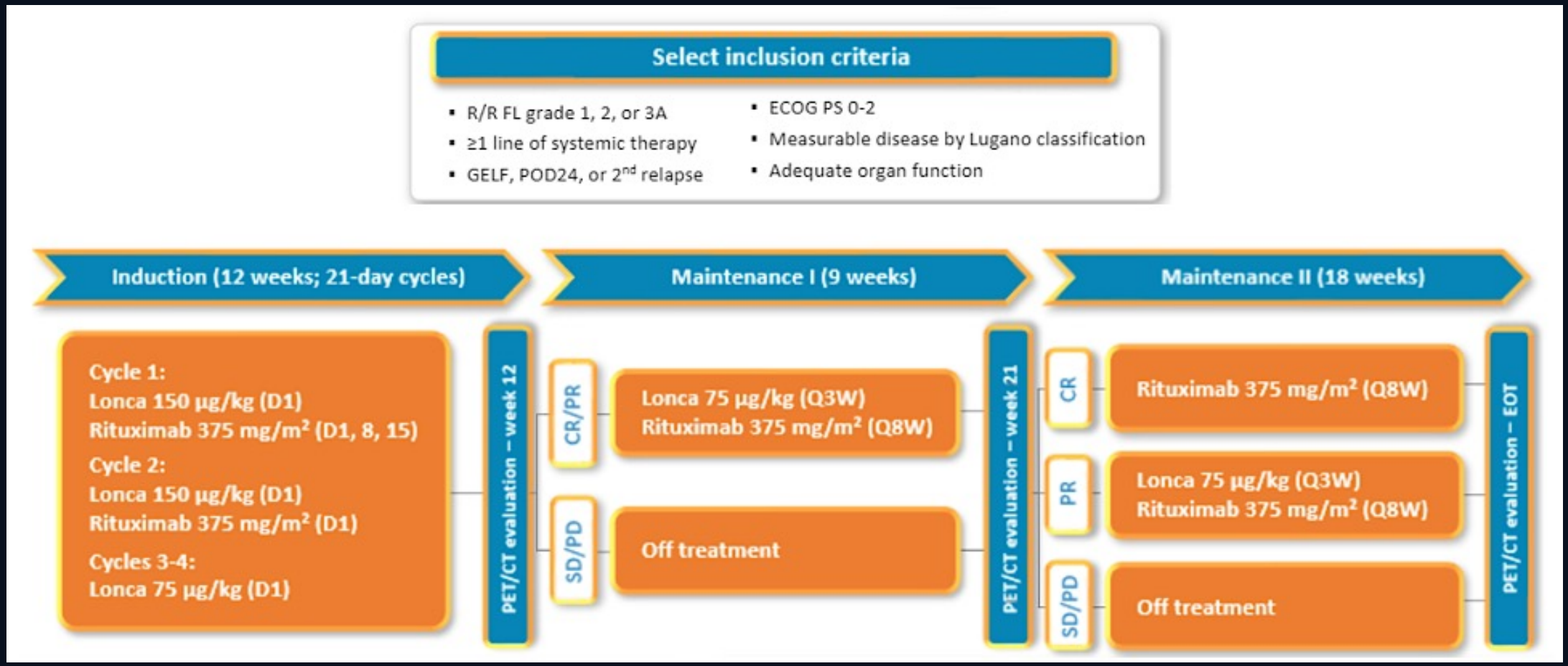
LOTIS-U: Playing Different Venues

Phase 2 Study of Lonca-T with R in High-risk Relapsed/Refractory FL



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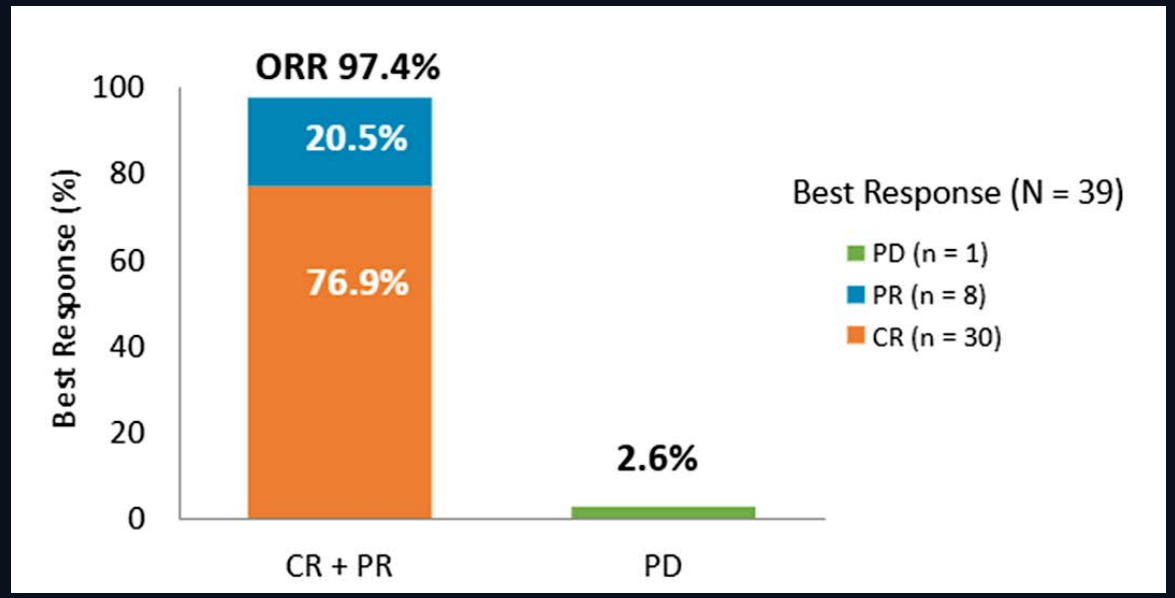
LOTIS-U: Playing Different Venues

Prior treatment characteristics (N = 39)	
Refractory to last therapy, n (%)	20 (51.3)
Relapsed FL, n (%)	19 (48.7)
Prior lines of therapy, median (range)	1 (1-6)
≥3 lines of prior therapy, n (%)	11 (28.2)
Prior frontline regimens, n (%)	
R-CHOP	22 (56.4)
Bendamustine with rituximab	10 (25.6)
Rituximab	6 (15.4)
Fludarabine, mitoxantrone, dexamethasone with rituximab	1 (2.6)



Post-hoc efficacy analyses			
	n	Best ORR, %	Best CR, %
POD24	20	100	85
High risk FLIPI score	24	96	67
Prior transformed FL	11	100	73
Rituximab with an alkylating agent	32	100	75

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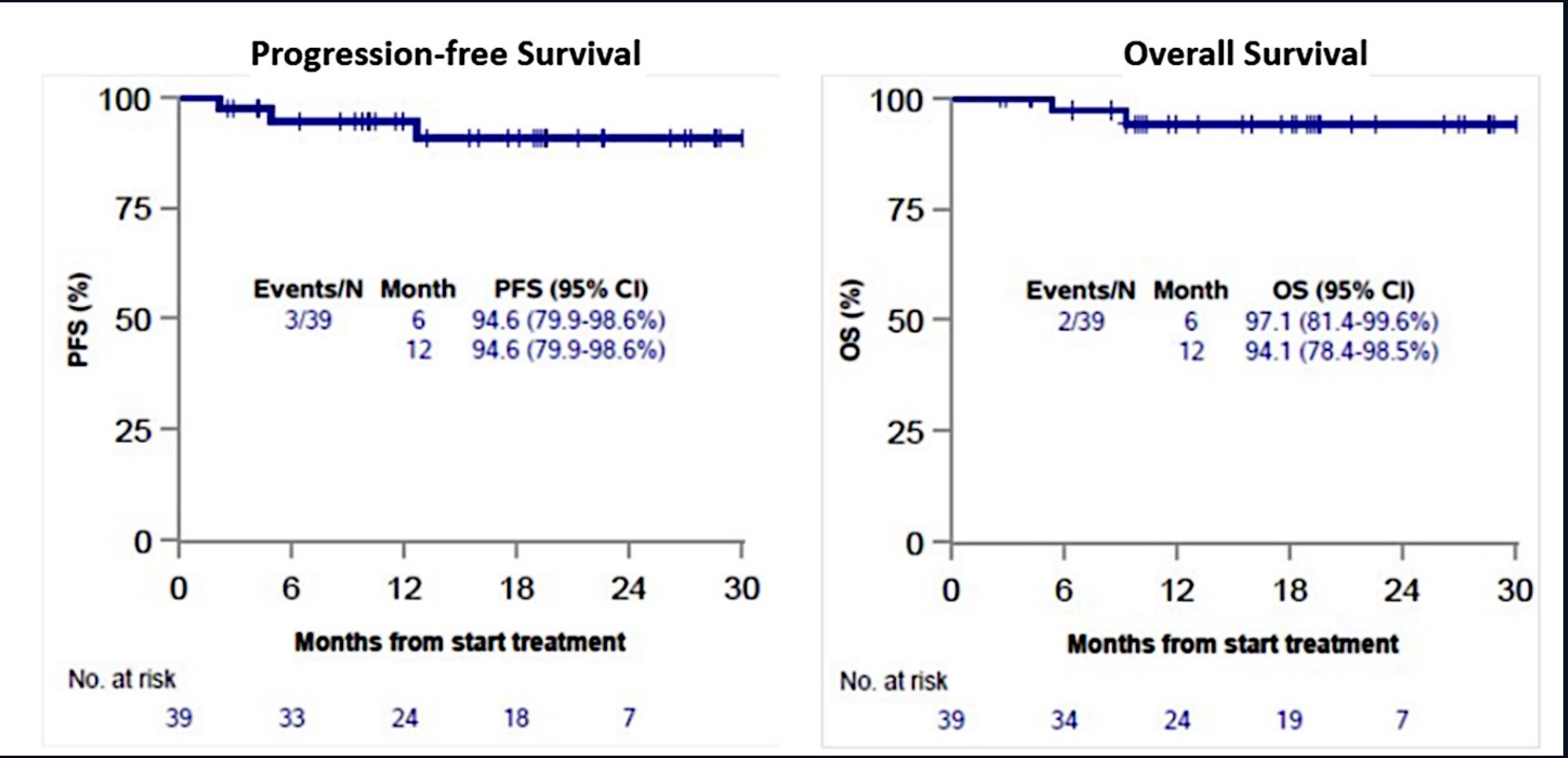
LOTIS-U: Playing Different Venues



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LOTIS-U: Playing Different Venues

Most Common TEAEs (≥10% for All Grades in 39 Evaluable Patients)				
AEs, n (%)	Any grade	Grade 1-2	Grade 3	Grade 4
Hematological AEs				
Neutropenia	15 (38.5)	10 (25.6)	4 (10.3)	1 (2.6)
Anemia	14 (35.9)	14 (35.9)	0 (0)	0 (0)
Lymphopenia	13 (33.3)	5 (12.8)	5 (12.8)	3 (7.7)
Thrombocytopenia	9 (23.1)	9 (23.1)	0 (0)	0 (0)
Non-hematological AEs				
Hyperglycemia	17 (43.6)	16 (41.0)	1 (2.6)	0 (0)
Increased ALP	16 (41.0)	16 (41.0)	0 (0)	0 (0)
Increased ALT	15 (38.5)	14 (35.9)	1 (2.6)	0 (0)
Fatigue	15 (38.5)	15 (38.5)	1 (2.6)	0 (0)
Increased AST	15 (38.5)	15 (38.5)	0 (0)	0 (0)
Rash maculo-papular	14 (35.9)	14 (35.9)	0 (0)	0 (0)
Localized edema	6 (15.4)	5 (12.8)	1 (2.6)	0 (0)
Photosensitivity	6 (15.4)	6 (15.4)	0 (0)	0 (0)
Generalized edema	6 (15.4)	5 (12.8)	1 (2.6)	0 (0)
Diarrhea	6 (15.4)	6 (15.4)	0 (0)	0 (0)
Pleural effusion	5 (12.8)	5 (12.8)	0 (0)	0 (0)
Dyspnea	5 (12.8)	4 (10.3)	1 (2.6)	0 (0)

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Second Opinion

Gilles Salles, MD, PhD

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Discussion Questions

How quickly do you observe responses in your patients with R/R DLBCL receiving loncastuximab tesirine? When do you start to evaluate for response with this agent?

What is your experience with rash with loncastuximab tesirine? What do you generally offer in terms of prophylaxis and patient education? Are you using antibiotic prophylaxis with this drug?

What other tolerability issues do you most frequently encounter in patients receiving loncastuximab tesirine, and how do you mitigate and manage them?

RTP
RESEARCH
TO PRACTICE

Second Opinion

Ann LaCasce, MD, MMSc

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Discussion Questions

How would you think through next steps for a patient like this with aggressive FL and no response to CAR T-cell therapy? Is loncastuximab tesirine alone or in combination a reasonable option for patients like this?

Given that loncastuximab tesirine/rituximab was recently incorporated into the NCCN guidelines as a third- or later-line treatment option for FL, in which specific situations can you envision yourself employing this strategy?

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1: Rational Incorporation of CD79b-Targeted Antibody-Drug Conjugates into the Management of Newly Diagnosed and Relapsed/ Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Flowers

Module 2: Clinical Utility of CD19-Directed Monoclonal Antibodies in the Treatment of DLBCL and Follicular Lymphoma (FL) — Dr Smith

Module 3: Optimal Use of CD19-Directed Antibody-Drug Conjugates for R/R DLBCL and FL — Dr Lunning

Module 4: Current and Future Role of Bruton Tyrosine Kinase Inhibition in Therapy for Non-Hodgkin Lymphoma — Dr Kahl

RTP RESEARCH TO PRACTICE

BTK inhibitors in Lymphoma

Brad Kahl, MD

Professor of Medicine

SITEMAN CANCER CENTER
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BARNES-JEWISH Hospital
BJC HealthCare

Washington University in St. Louis
SCHOOL OF MEDICINE

SITEMAN Kids
AT ST. LOUIS Children's HOSPITAL
Washington University Physicians

NCI Designated Comprehensive Cancer Center

NCCN National Comprehensive Cancer Network®

BTK inhibitors

- First Generation
  - Ibrutinib
- Second Generation
  - Acalabrutinib
  - Zanubrutinib
- Third Generation
  - Pirtobrutinib

- Game changing therapy for management of CLL
- Evolving role in the management of Lymphoma

Current Use of BTKi in Lymphoma

FRONTLINE

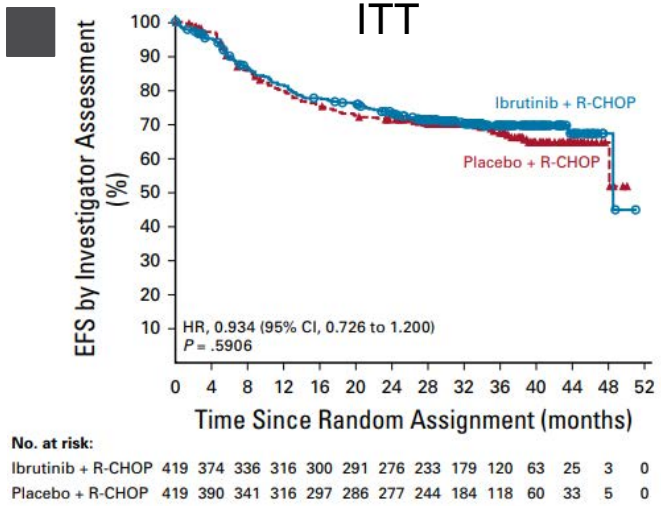
- DLBCL
  - None at present
- FL
  - None at present
- MZL
  - None at Present
- MCL
  - As part of ECHO regimen (Acalabrutinib)
  - As part of BOVEN regimen (Zanubrutinib)
  - As part of TRIANGLE regimen (either)

RELAPSE/REFRACTORY

- DLBCL
  - None at present
- FL
  - Zanubrutinib plus Obinutuzumab
- MZL
  - Single agent Zanubrutinib
- MCL
  - Single Agent Acalabrutinib
  - Single Agent Zanubrutinib
  - Single Agent Pirtobrutinib

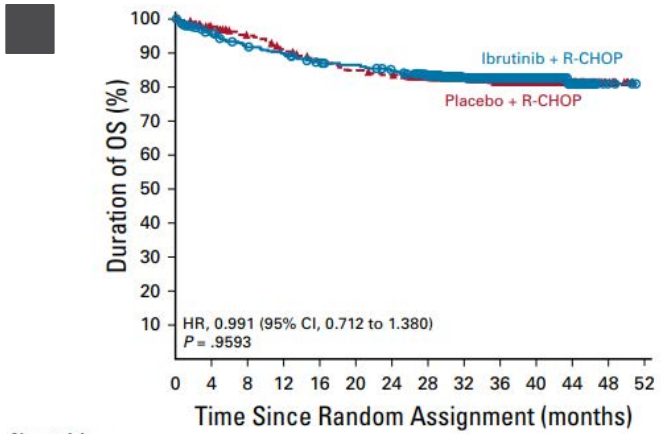
PHOENIX: R-CHOP +/– Ibrutinib in Non-GCB/ABC DLBCL

ITT



No. at risk:

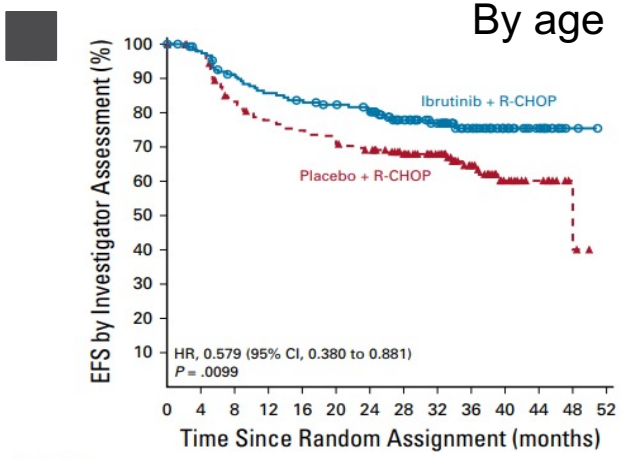
Ibrutinib + R-CHOP	419	374	336	316	300	291	276	233	179	120	63	25	3	0
Placebo + R-CHOP	419	390	341	316	297	286	277	244	184	118	60	33	5	0



No. at risk:

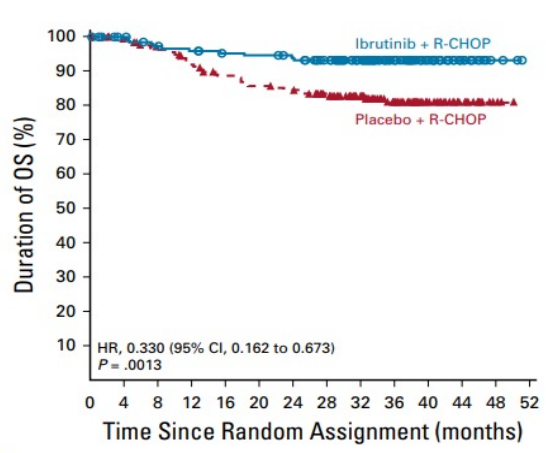
Ibrutinib + R-CHOP	419	384	365	356	342	337	328	309	236	159	100	38	4	0
Placebo + R-CHOP	419	400	382	363	347	335	329	301	237	157	99	51	12	0

By age



No. at risk:

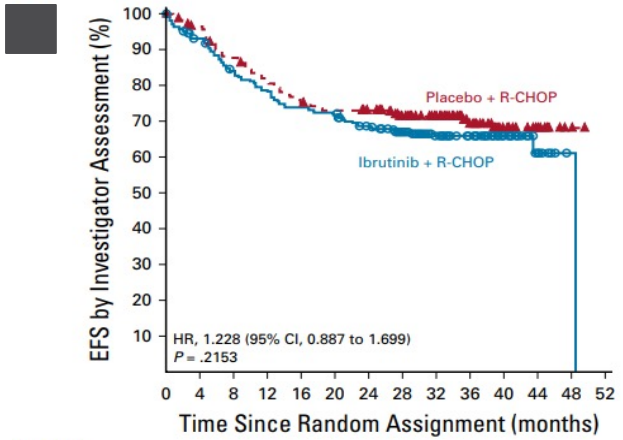
Ibrutinib + R-CHOP	156	146	133	125	121	117	113	93	72	44	27	13	2	0
Placebo + R-CHOP	186	177	148	137	132	127	120	104	78	52	24	16	3	0



No. at risk:

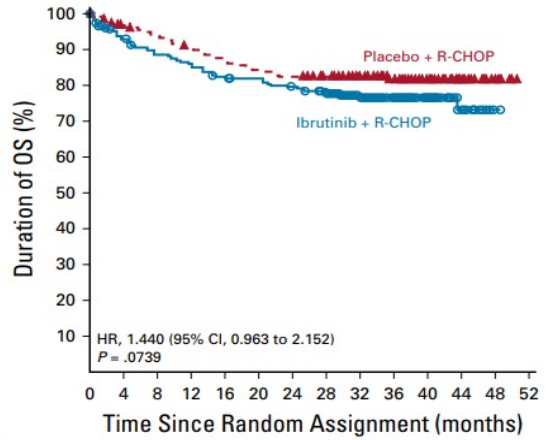
Ibrutinib + R-CHOP	156	151	145	142	138	137	134	125	96	62	39	18	3	0
Placebo + R-CHOP	186	181	173	161	153	148	145	130	101	70	38	21	5	0

Age <60



No. at risk:

Ibrutinib + R-CHOP	263	228	203	191	179	174	163	140	107	76	36	12	1	0
Placebo + R-CHOP	233	213	193	179	165	159	157	140	106	66	36	17	2	0



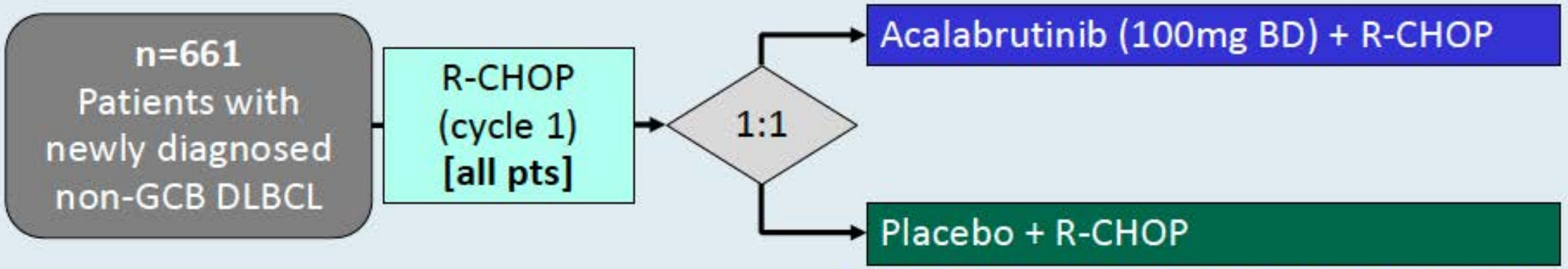
No. at risk:

Ibrutinib + R-CHOP	263	233	220	214	204	200	194	184	140	97	61	20	1	0
Placebo + R-CHOP	233	219	209	202	194	187	184	171	136	87	61	30	7	0

Age ≥60

Younes A et al. J Clin Oncol 2019;37(15):1285-1295.

Phase III ESCALADE (ACE-LY-312) Study Design



*All patients will receive primary prophylaxis with G-CSF accompanying all R-CHOP cycles.

Primary endpoint:
PFS

Secondary endpoints:
EFS, CR rate, OS, pharmacokinetics, safety

GCB = germinal center B-cell-like; CR = complete response; G-CSF = granulocyte-colony stimulating factor

Sehn LH et al. ASCO 2021;Abstract TPS7572.

Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab: Primary Analysis of the Phase 2 Randomized ROSEWOOD Trial

Key Eligibility Criteria

- Adults with grade 1-3a FL
- R/R disease, previously treated with ≥2 systemic treatments including an anti-CD20 antibody and an appropriate alkylator-based combination therapy
- Measurable disease
- ECOG PS 0-2
- Adequate organ functions
- No prior BTK inhibitor

ClinicalTrials.gov: NCT03332017

Arm A
Zanubrutinib[a] plus obinutuzumab[b]
N=145
Until PD/unacceptable toxicity

Randomization 2:1
Stratification factors
- Number of prior lines
- Rituximab refractory status
- Geographic region

Arm B
Obinutuzumab[b]
N=72
Option to crossover to combination if PD centrally confirmed or no response at 12 months

Primary Endpoint
- ORR assessed by ICR according to Lugano classification[1]

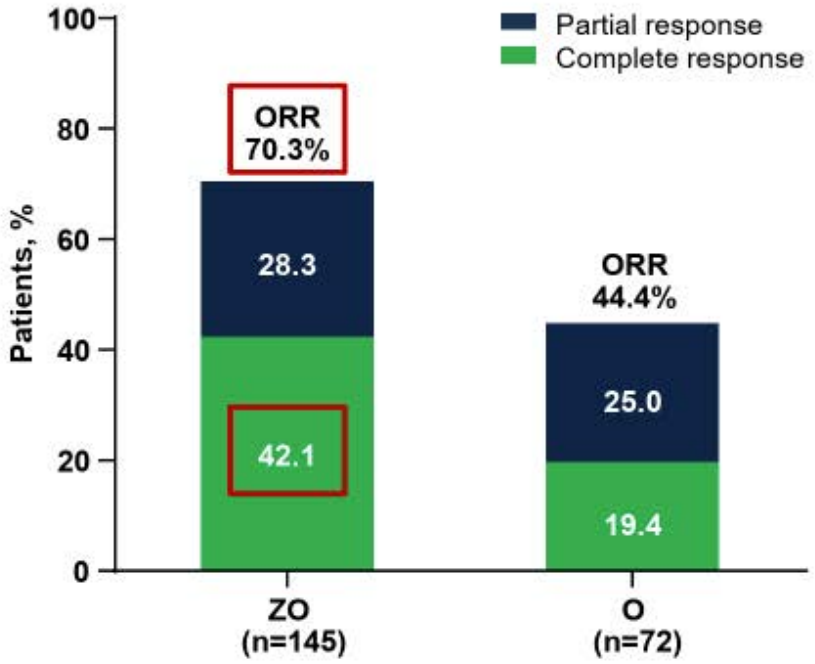
Select Secondary Endpoints
- ORR assessed by investigator
- DOR and PFS determined by ICR and investigator assessment
- Overall survival

- Patients were randomized between November 2017 and June 2021
- Median study follow-up: 20.2 months

1. Cheson et al. *J Clin Oncol* 2014;32(27):3059-68.
[a]Zanubrutinib was given orally at 160 mg twice a day; [b]Obinutuzumab was given in both arms on days 1, 8, and 15 of cycle 1, day 1 of cycles 2-6, and then every 8 weeks up to 20 doses maximum.
BTK, Bruton tyrosine kinase; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; ICR, independent central review; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; R/R, relapsed or refractory

ROSEWOOD – Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab: ORR

- The study met its primary endpoint
  - ORR per ICR was **70.3%** with zanubrutinib plus obinutuzumab vs **44.4%** with obinutuzumab



- ORRs per INV were similar to ORRs per IRC (ZO, 68.3%; O, 43.1%)

	ZO (n=145)	O (n=72)
Overall response rate, n (%)	102 (**70.3**)	32 (**44.4**)
95% CI	62.2-77.6	32.7-56.6
Risk difference (95% CI), %	25.5 (11.8-39.3)	
2-sided *P* value[a]	.0003	
Complete response rate, n (%)	61 (**42.1**)	14 (**19.4**)
95% CI	33.9-50.5	11.1-30.5
2-sided *P* value[a]	.0009	
Other responses, n (%)		
Stable disease	21 (14.5)	14 (19.4)
Indeterminate due to zanubrutinib hold	1 (0.7)	0
Non-progressive disease[b]	6 (4.1)	9 (12.5)
Progressive disease	13 (9.0)	16 (22.2)
Discontinued prior to first assessment/NE	2 (1.4)	1 (1.4)

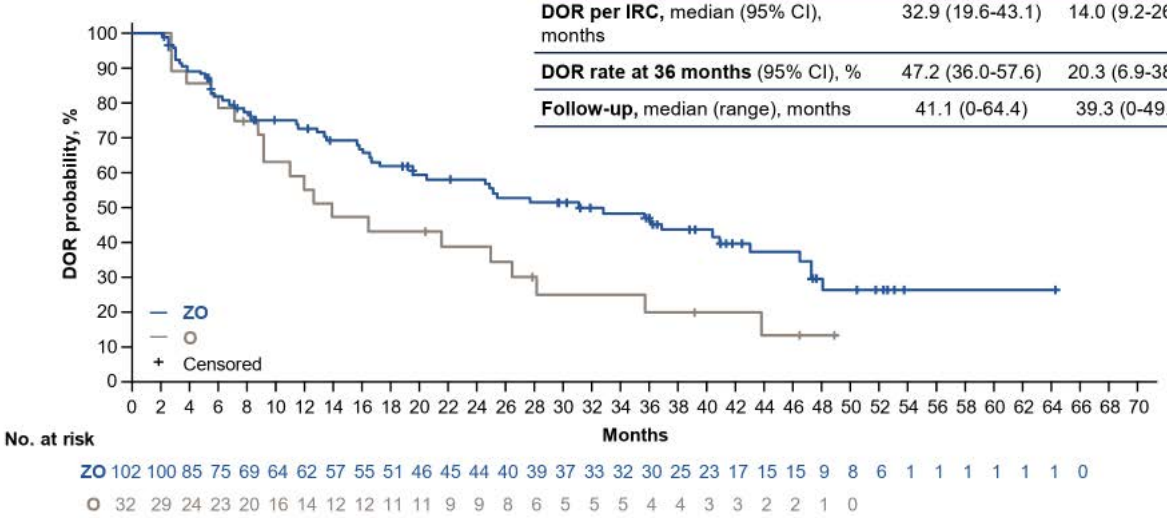
[a]*P* value is descriptive. [b]Defined as PET assessment missing or not evaluable, and CT assessment showed no progressive disease.
CT, computed tomography; INV, investigator; IRC, independent review committee; O, obinutuzumab; ORR, overall response rate; PET, positron emission tomography; ZO, zanubrutinib + obinutuzumab.

Zinzani PL et al. ASH 2025, Abstract 227.

ROSEWOOD – Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab: DoR and PFS

DoR

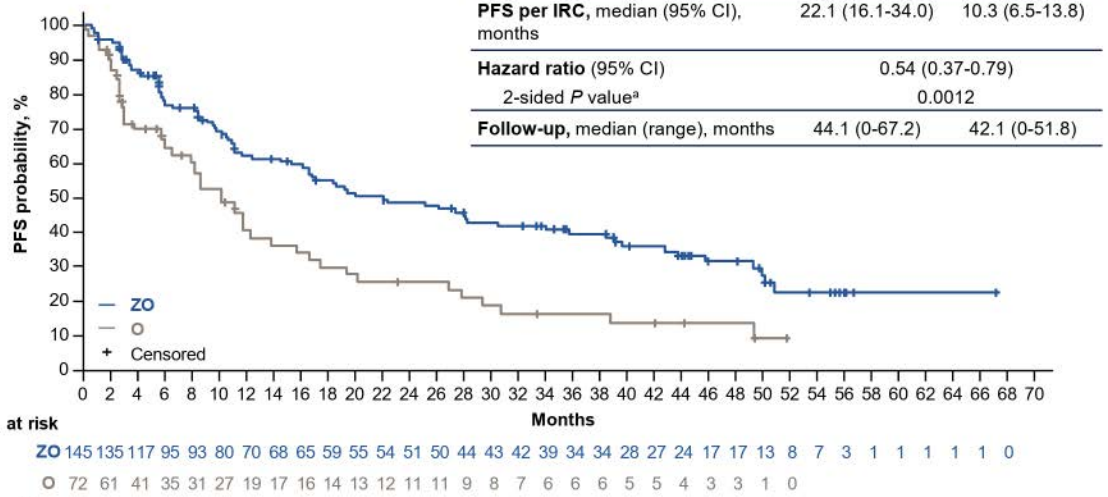
	ZO	O
DOR per IRC, median (95% CI), months	32.9 (19.6-43.1)	14.0 (9.2-26.5)
DOR rate at 36 months (95% CI), %	47.2 (36.0-57.6)	20.3 (6.9-38.6)
Follow-up, median (range), months	41.1 (0-64.4)	39.3 (0-49.0)



DOR, duration of response; IRC, independent review committee; O, obinutuzumab; ZO, zanubrutinib + obinutuzumab.

PFS

	ZO	O
PFS per IRC, median (95% CI), months	22.1 (16.1-34.0)	10.3 (6.5-13.8)
Hazard ratio (95% CI)	0.54 (0.37-0.79)	
2-sided *P* value[a]	0.0012	
Follow-up, median (range), months	44.1 (0-67.2)	42.1 (0-51.8)



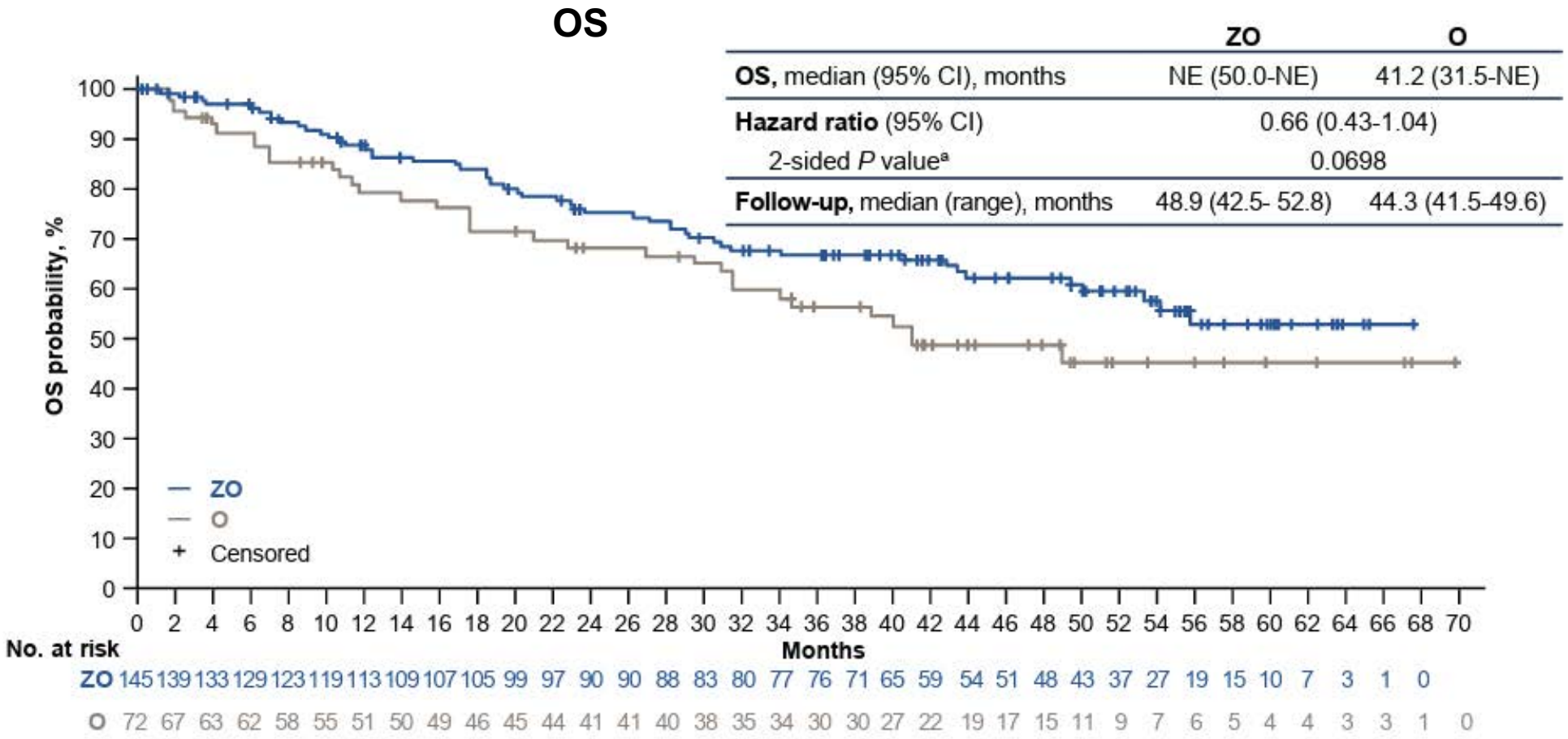
[a]*P* value is descriptive.
IRC, independent review committee; O, obinutuzumab; PFS, progression-free survival; ZO, zanubrutinib + obinutuzumab.

- The 36-month DOR rate was **47.2%** in the zanubrutinib plus obinutuzumab arm vs **20.3%** in the obinutuzumab arm

- Zanubrutinib plus obinutuzumab was associated with a **46%** reduction of risk of progression or death compared with obinutuzumab

Zinzani PL et al. ASH 2025, Abstract 227.

ROSEWOOD – Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab: OS



[a]*P* value is descriptive.
NE, not estimable; O, obinutuzumab; OS, overall survival; ZO, zanubrutinib + obinutuzumab.

Zinzani PL et al. ASH 2025, Abstract 227.

CONCLUSIONS

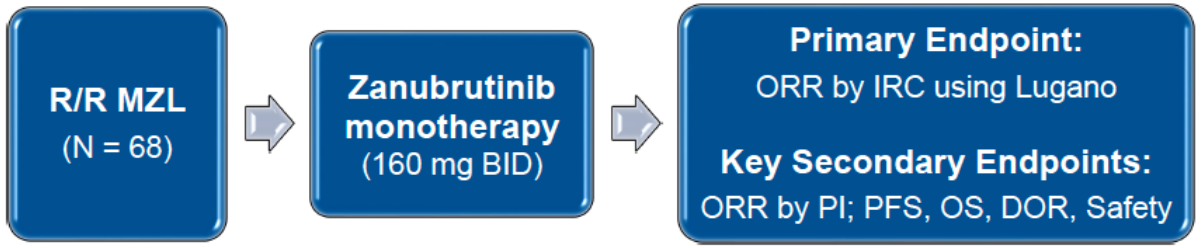
- The favorable risk-benefit profile of ZO in heavily pretreated patients with R/R FL was sustained
- Compared with O monotherapy, combination treatment with ZO demonstrated substantially
  - ✓ higher ORR and CR rate
  - ✓ longer DOR and PFS
- ZO had a manageable, consistent safety profile, with no new safety signals
- With a long median follow-up (34.6 months), these data support the potential benefit of ZO as a novel combination therapy for patients with R/R FL

CR, complete response; DOR, duration of response; FL, follicular lymphoma; O, obinutuzumab; ORR, overall response rate; PFS, progression-free survival; R/R, relapsed/refractory; Z, zanubrutinib; ZO, zanubrutinib + obinutuzumab.

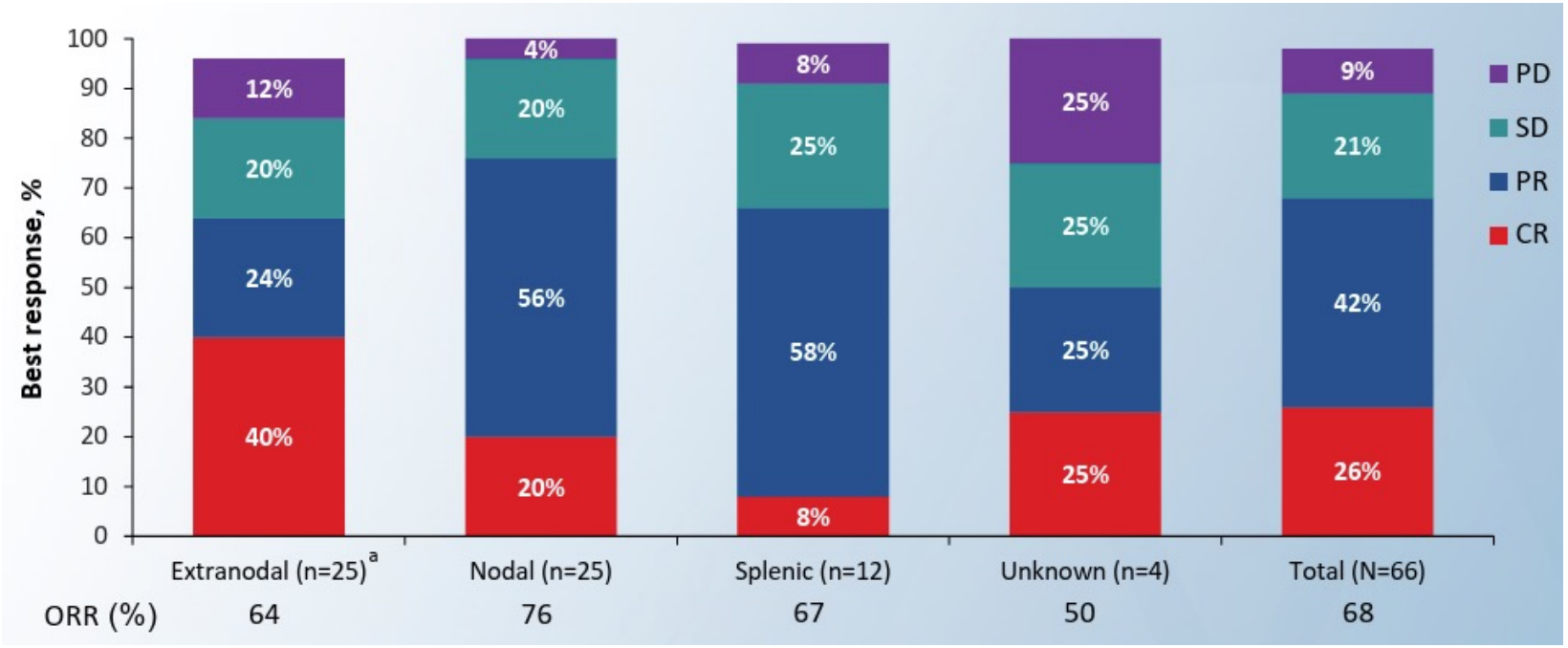
Zinzani PL et al. ASH 2025, Abstract 227.

Zinzani et al. ROSEWOOD EHA 2022

Zanubrutinib for MZL: MAGNOLIA Trial

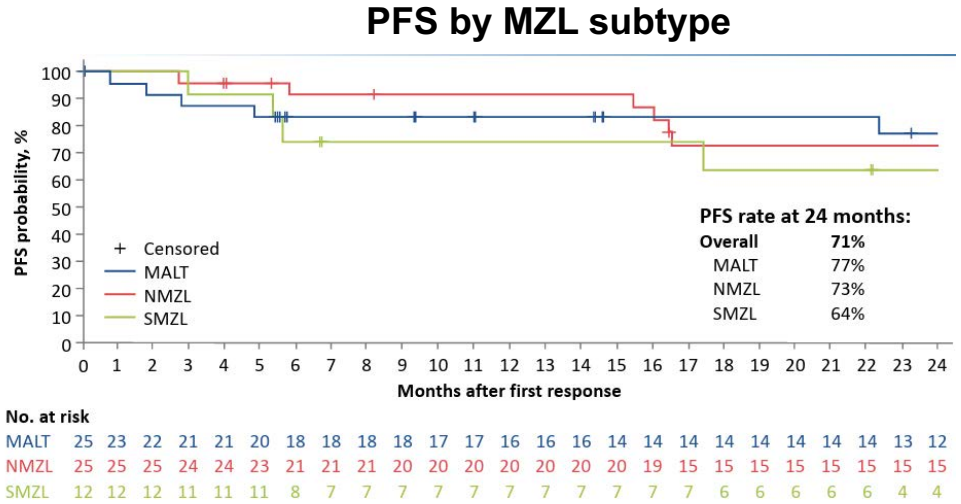


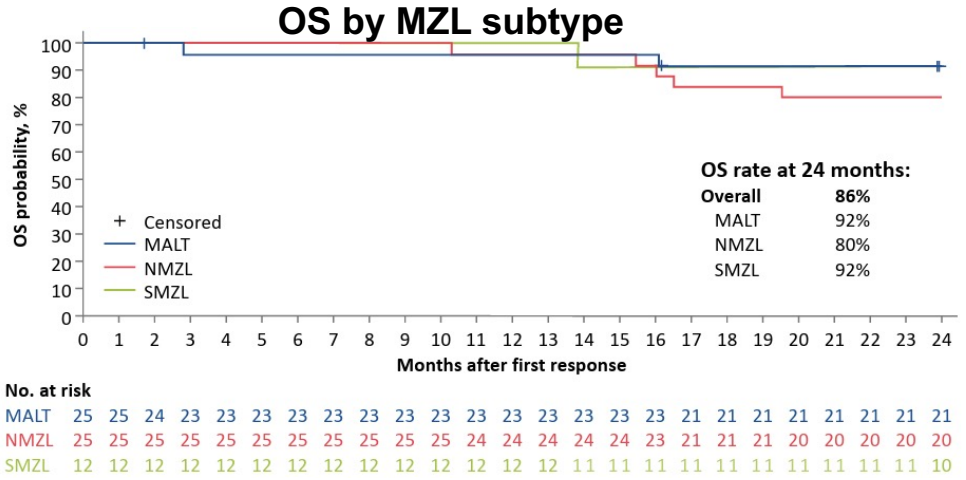
Best Overall Response by IRC and MZL Subtypes

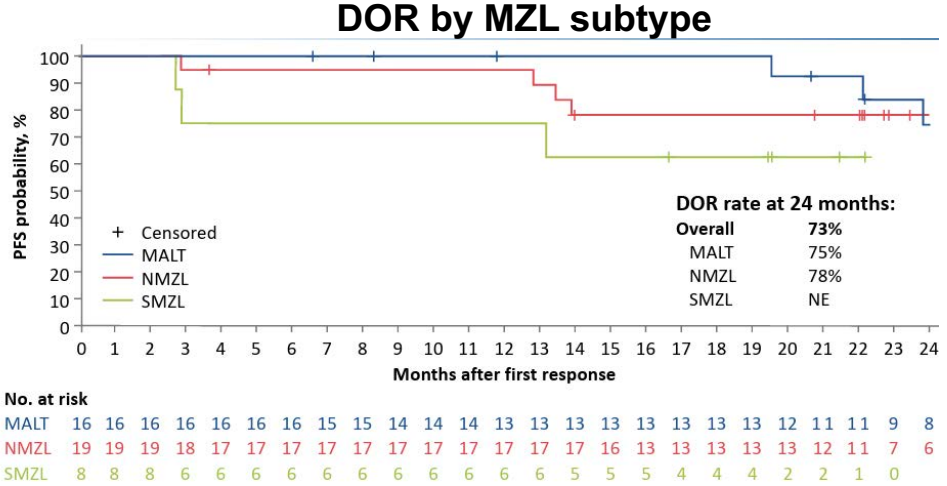


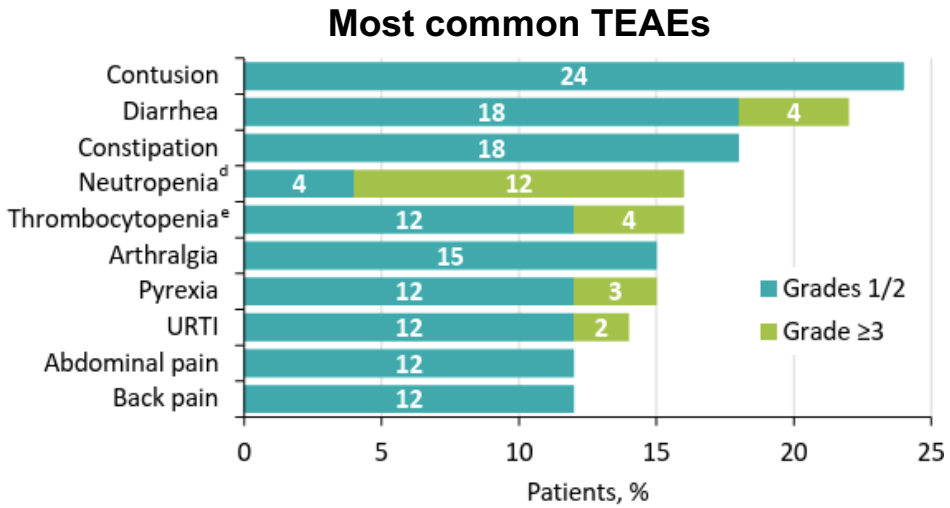
Opat et al, Clinical Cancer Res, 2021; Opal et al, Blood 2023, Abstract P1084.

Efficacy/Toxicity









Zanubrutinib received accelerated approval for R/R MZL September 2021.

Opal et al, Blood 2023, Abstract P1084.

MCL: Reasonable Standards of Care in 2026

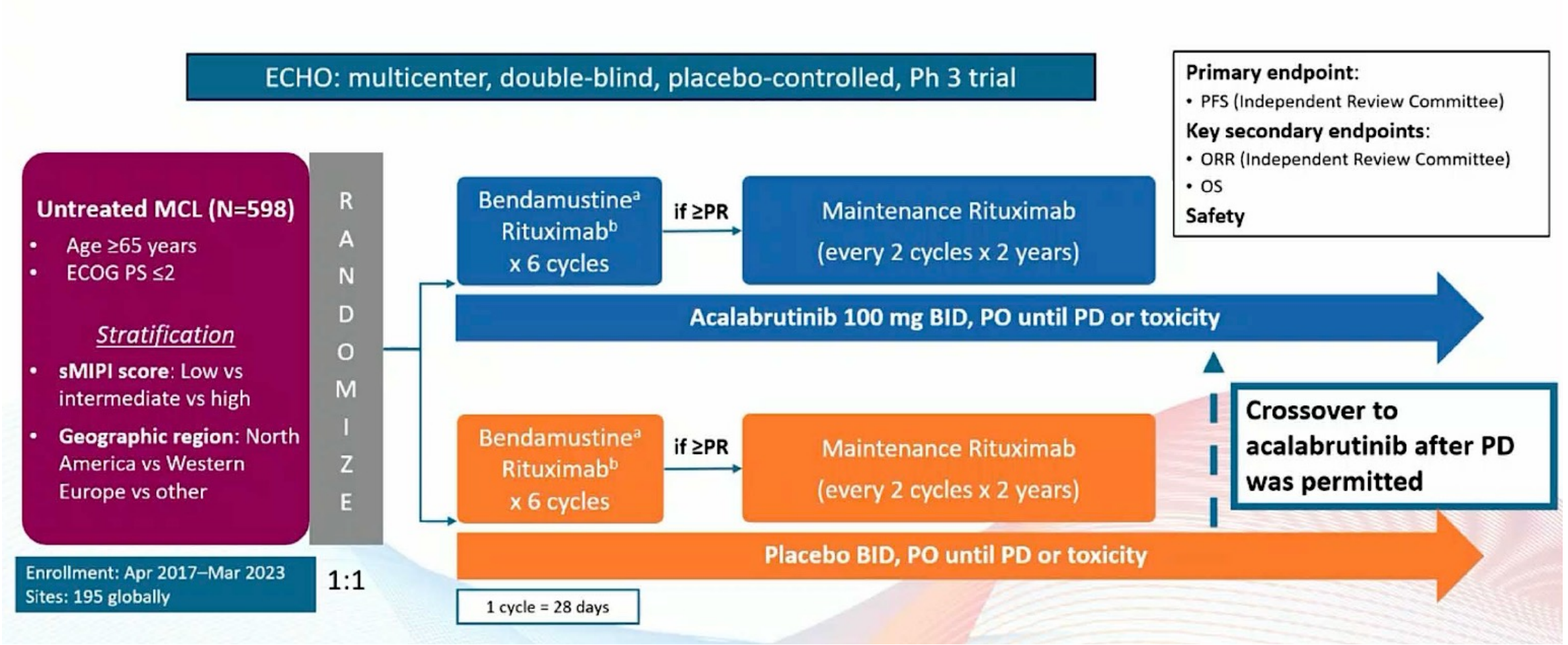
FRONTLINE MANAGEMENT

- Older/Less Fit
  - Bendamustine-Rituximab (BR) Induction + Maintenance Rituximab
  - Can consider adding a BTKi (ala ECHO)
- Younger/Fit
  - A TRIANGLE type approach (will clarify)
- p53 mutated
  - BOVEN regimen (or something similar)

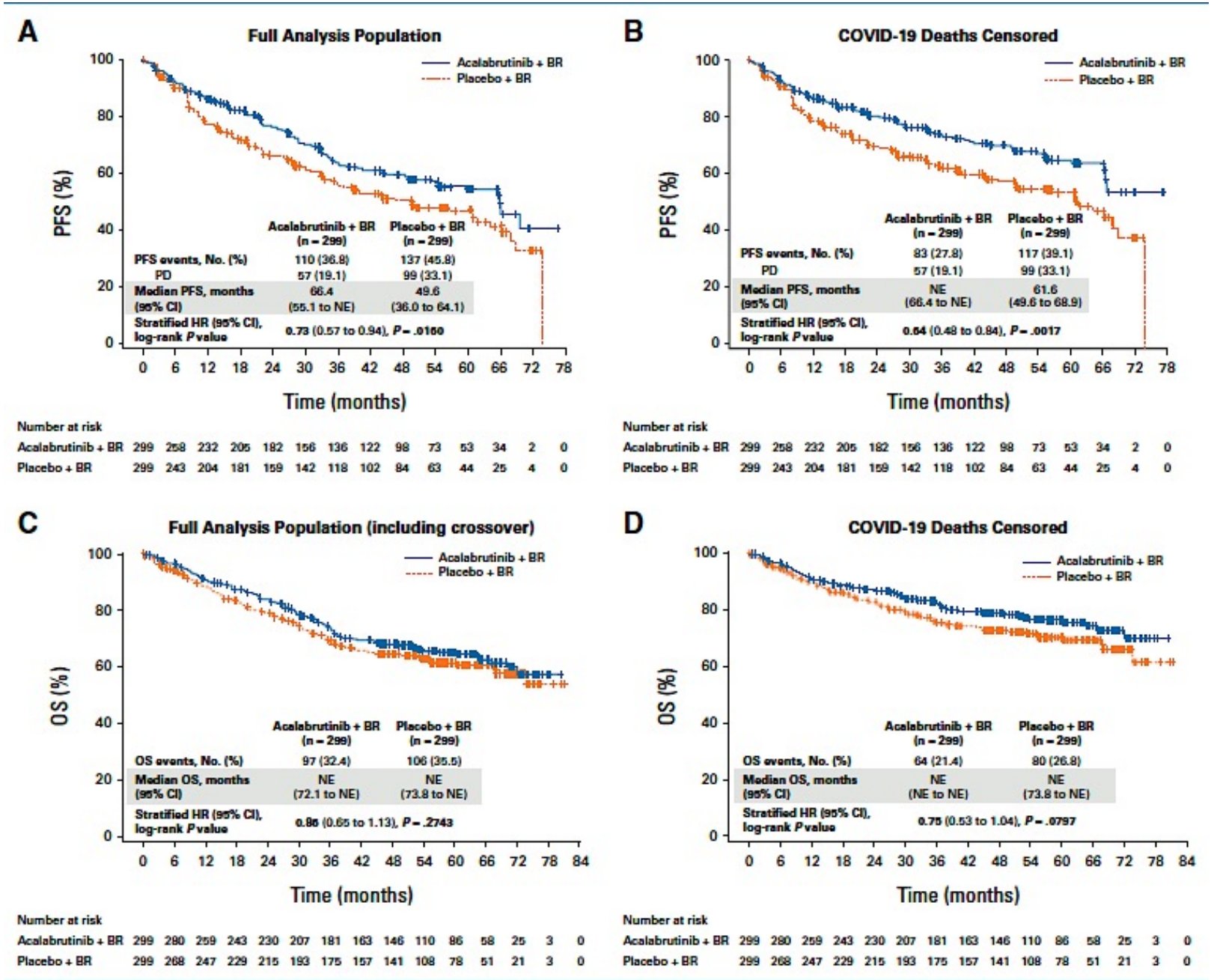
RELAPSED DISEASE

- Single agent 2nd generation BTKi
  - Acalabrutinib
  - Zanubrutinib
- Third generation BTKi
  - Pirtobrutinib
- CART
  - Liso-cel
  - Brexu-cel

ACALABRUTINIB PLUS BR IN MANTLE CELL LYMPHOMA: RESULTS FROM THE PHASE 3 ECHO TRIAL.



Wang, et al. JCO 2025



Wang, et al. JCO 2025

ECHO Results in MCL

- No difference in OS
  - Fewer MCL deaths on Acal arm
  - More COVID deaths on Acal arm
- Results fairly similar to SHINE
  - Same design, used ibrutinib
- Acalabrutinib approval in older MCL first-line in 2025, should you use it?
  - PFS benefit without OS benefit
  - cBTKi given until PD, meaning not available for 2nd line

Chemofree vs. SOC in older MCL

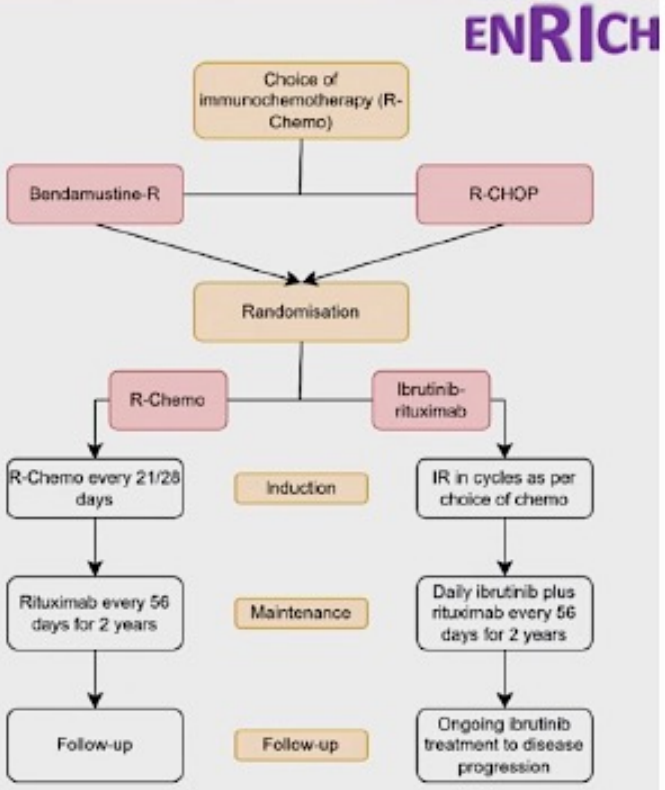
ENRICH STUDY

Trial design

Inclusion criteria
- 60 years or older
- Pathologically confirmed MCL, including either cyclin D1 overexpression or t(11;14)(q13;q32)
- Previously untreated, measurable (>1.5cm), stage II-IV MCL in need of treatment
- ECOG 0-2

Exclusion criteria
- Considered fit for stem cell transplantation
- CNS involvement
- Known serological positivity for HBC/HCV/HIV

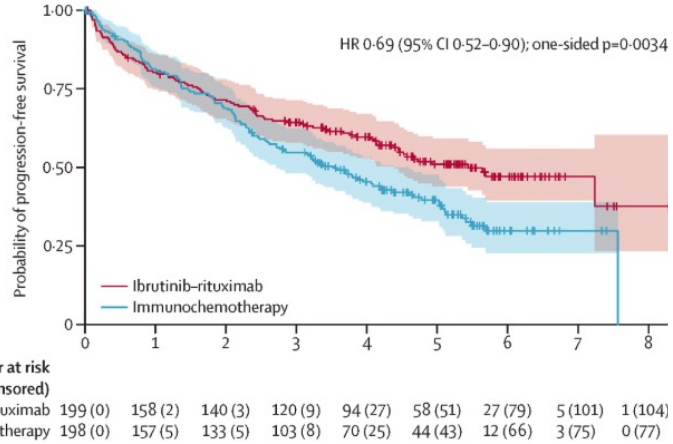
Rituximab 375mg/m²
Ibrutinib - 560mg od
Bendamustine 90mg/m² D1+D2 of 28 day cycle
CHOP - (Cyclophosphamide 750mg/m², Doxorubicin 50mg/m², Vincristine 1.4mg/m², Prednisolone 100mg *5 days) 21 day cycle
Maintenance rituximab - 1400mg sc every 56 days



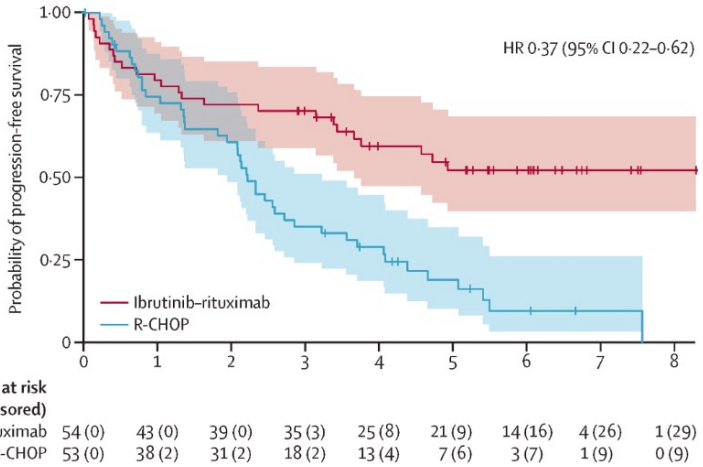
Lewis et al. ASH 2024, Abstract 235; Lewis et al, Lancet 2025.

ENRICH Study – Chemo-free vs SOC in Older MCL: PFS

PFS: Ibrutinib-rituximab vs immunochemotherapy

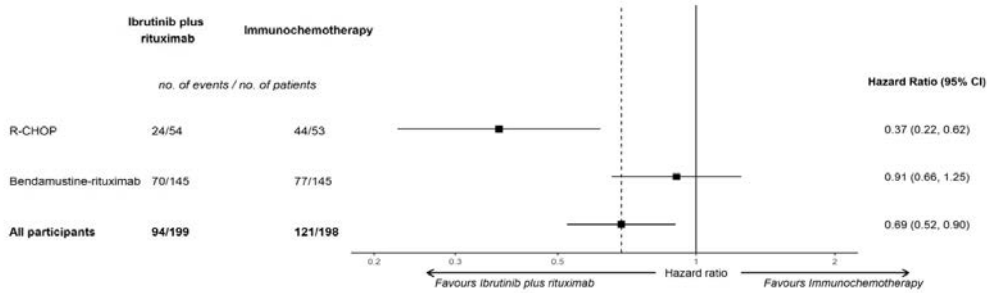


PFS: Ibrutinib-rituximab vs R-CHOP

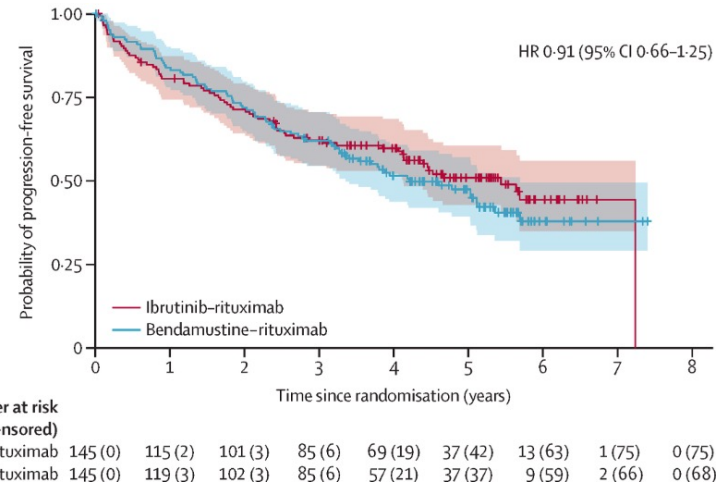


Pre-randomization choice of immunochemotherapy

P value for interaction between treatment effect and choice of chemotherapy = 0.0038



PFS: Ibrutinib-rituximab vs bendamustine-rituximab



Median Follow up: 47.9 months

Lewis et al. ASH 2024, Abstract 235; Lewis et al, Lancet 2025.

Chemofree triplet options in frontline older MCL

1. Acalabrutinib + Lenalidomide + Rituximab[1] (N = 24)
   - ORR after 12 cycles 100%. CR 83%. 4yr PFS 76%.
   - Rash 42%

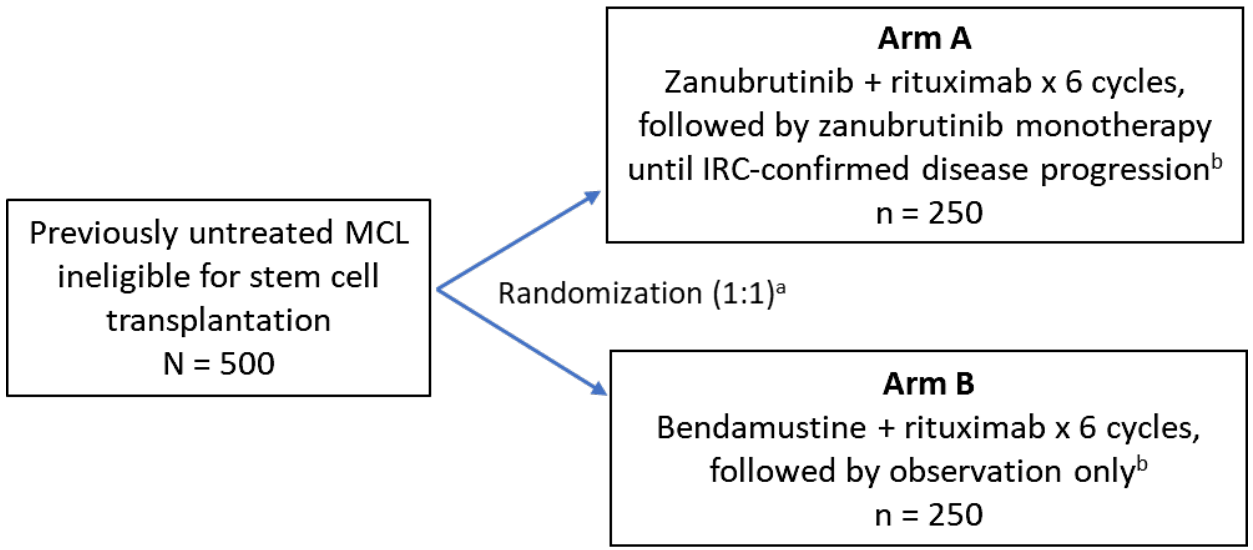
2. Acalabrutinib + Venetoclax + Rituximab[2] (N = 108)
   - ORR 95%. CR 86%
   - 12 month PFS 95%

3. BOVEN (Zanu-Venetoclax-Obinutuzumab)[3] (N = 50)
   - ORR 98%. CR96%.
   - 2 year PFS 86%

1. Ruan et al, Blood Adv 2026. 2. Hawkes, ASH 2025 3. Kumar ASH 2025

MCL Treatment: The Horizon for Older MCL

MANGROVE



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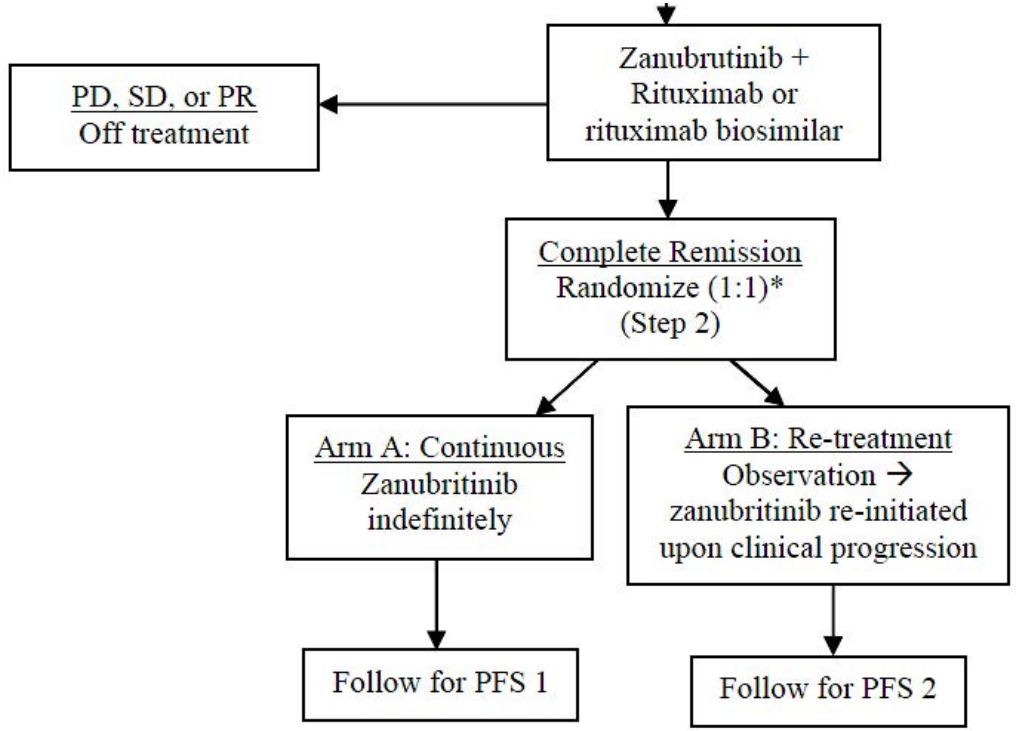
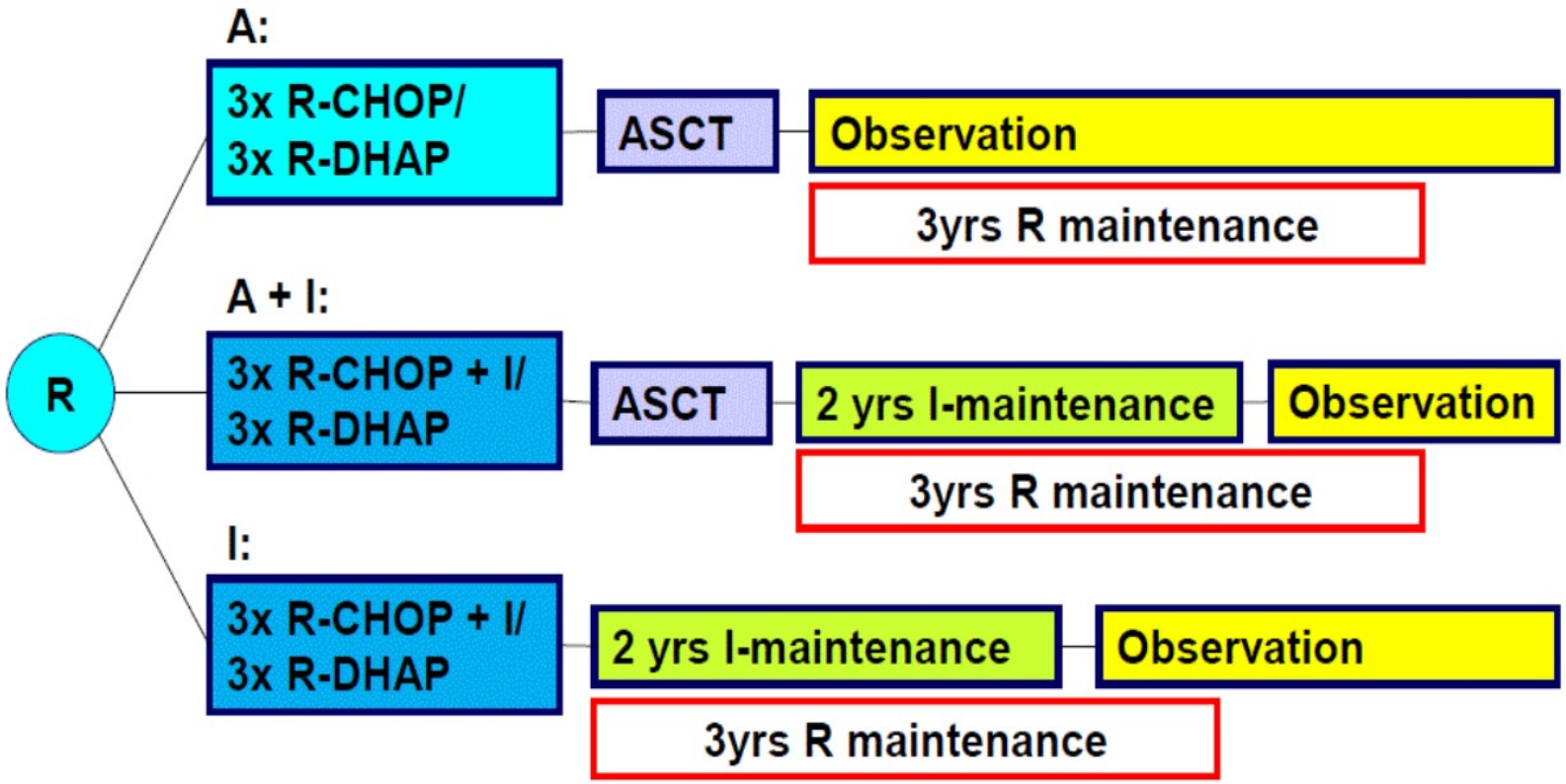


* Patients will be stratified by age (60-69 years vs. ≥70 years) and MCL IPI score (low, intermediate, or high)

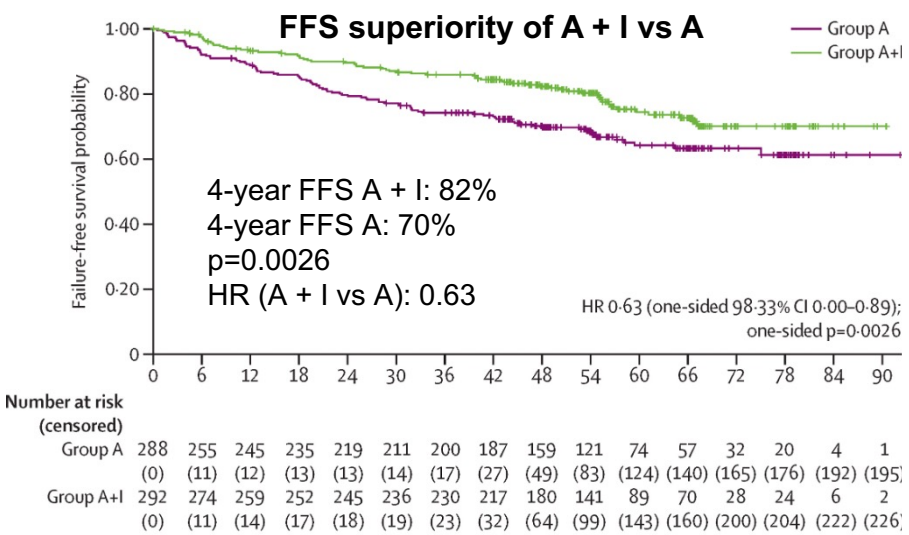
https://clinicaltrials.gov/study/NCT04002297; https://clinicaltrials.gov/study/NCT05976763

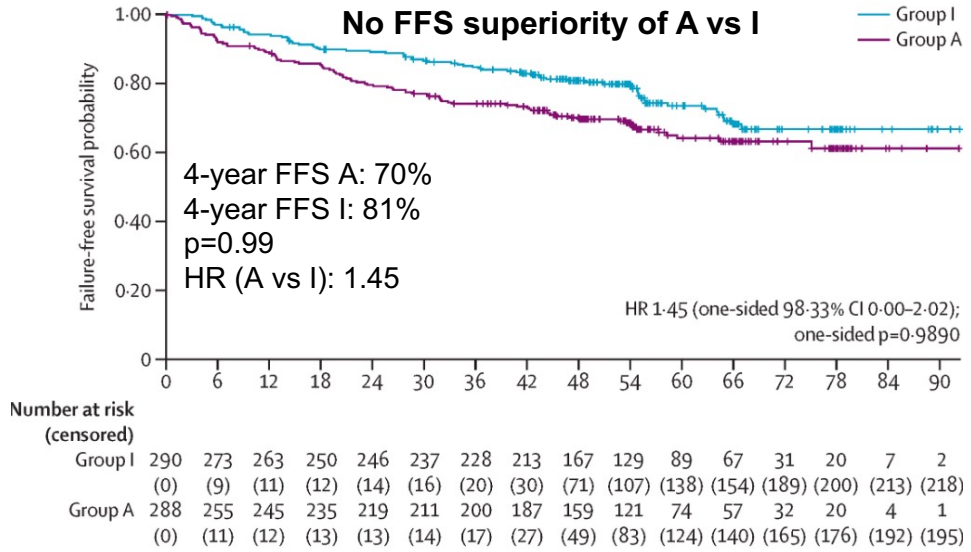
TRIANGLE Trial (European MCL Network)

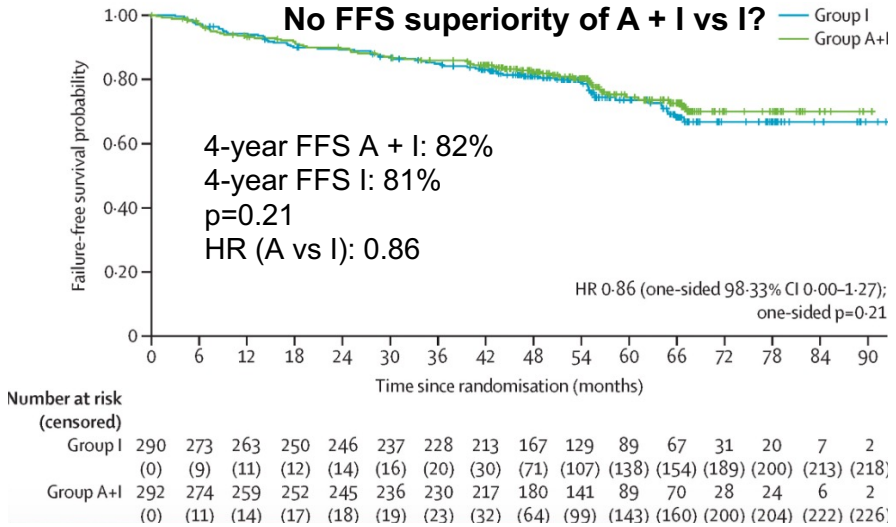
- Target 870 pts (290 per arm)
- Activated Oct 2017
- Completed accrual Dec 2020
- 1st results ASH 2022
- Published 2024 in Lancet
- Updated ASH 2024
- Updated 2026 in Lancet



TRIANGLE – ASCT + Ibrutinib-Containing 1L Treatment: FFS





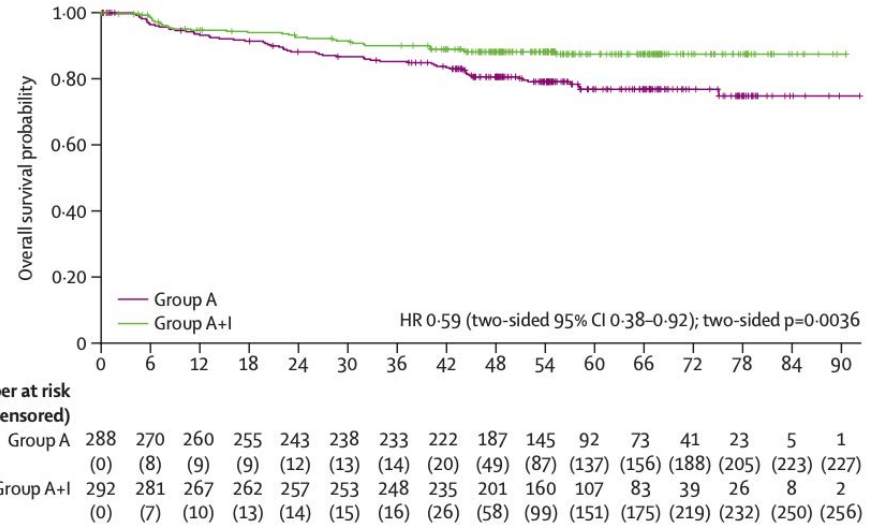


Median Follow up: 55 months

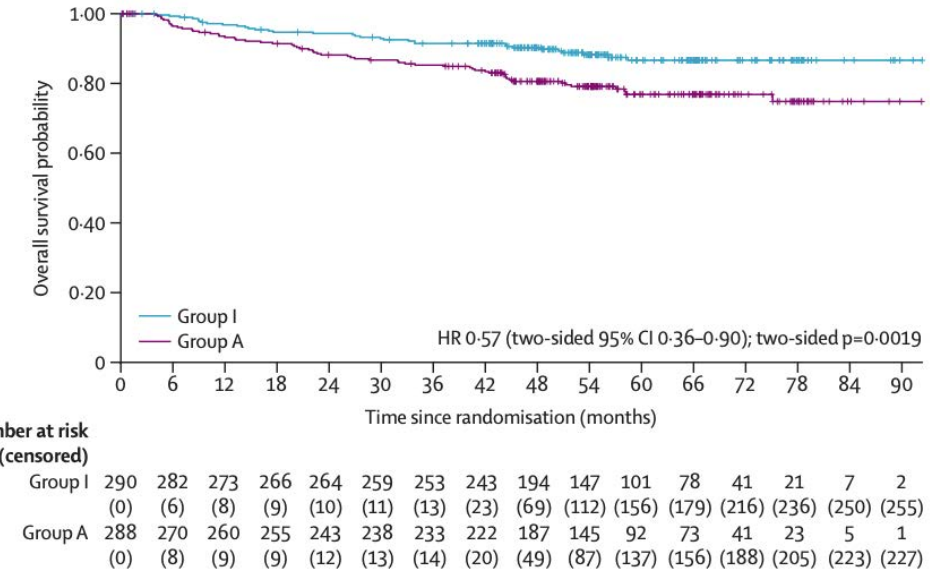
Dreyling M et al. The Lancet 2026; 407(10542):1953-1967.

TRIANGLE – ASCT + Ibrutinib-Containing 1L Treatment: OS

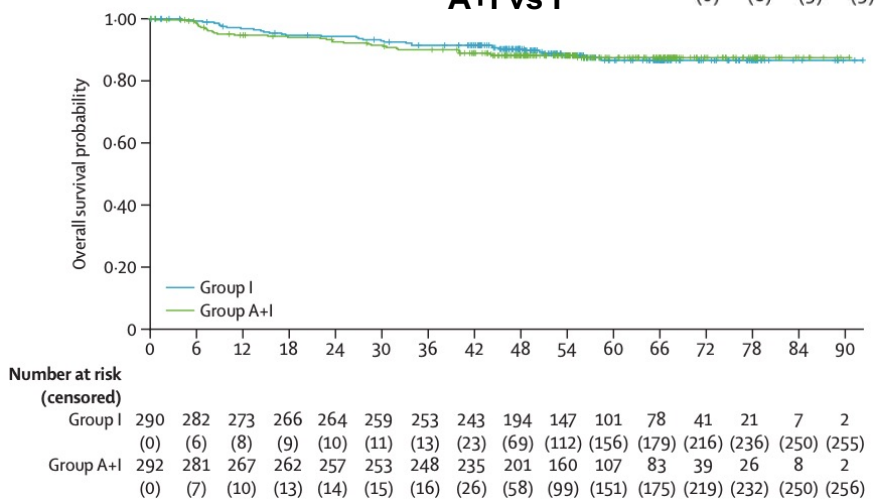
A+I vs A



A vs I



A+I vs I



4-year OS

- A: 81%
- A + I: 88%
- I: 90%

Two-sided test

- A + I vs A: p=0.0036; HR=0.59
- A vs I: p=0.0019; HR=0.57
- A + I vs I: ongoing

Dreyling M et al. The Lancet 2026; 407(10542):1953-1967.

TRIANGLE Trial Impact

- Addition of BTKi obviates needs for ASCT in frontline MCL

- Caveats
  - Ibrutinib pulled from US market in spring 2023
  - May substitute acalabrutinib or zanubrutinib (NCCN guidelines just say BTKi)
  - I am comfortable with this extrapolation

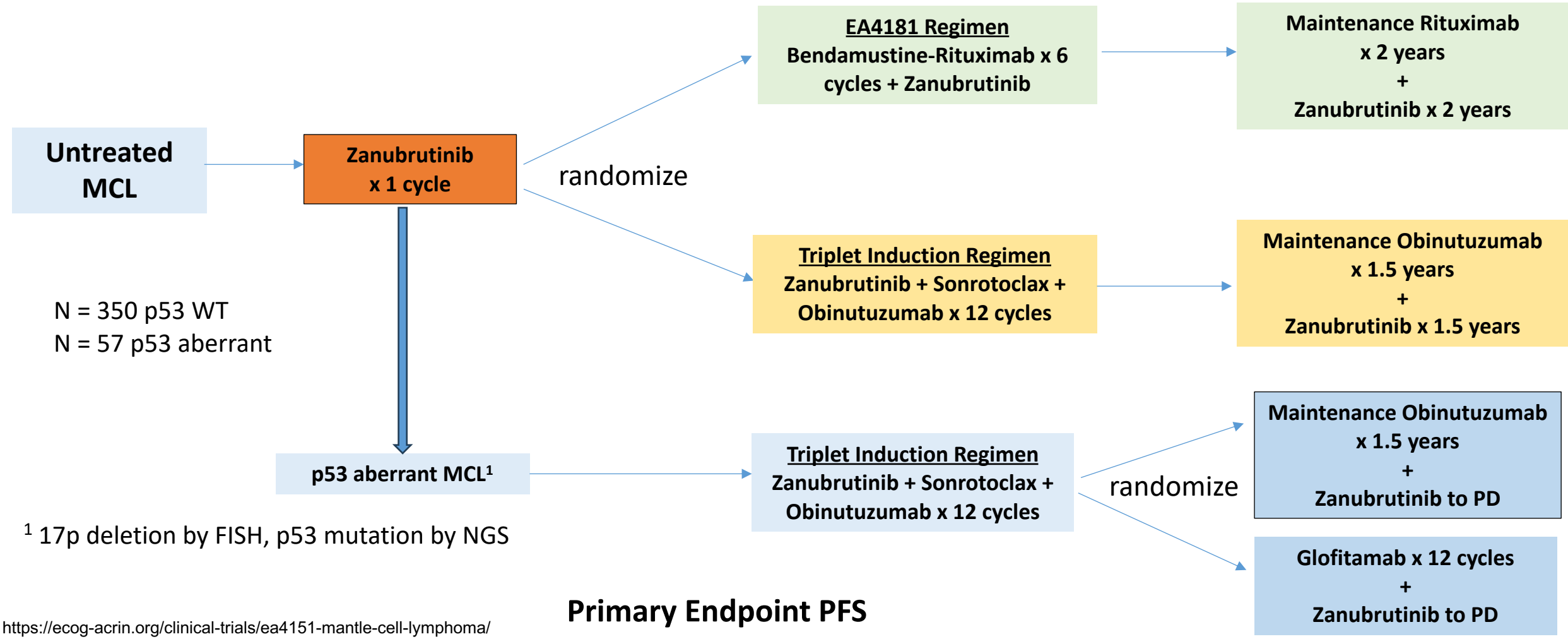
- A major appeal here is the BTKi exposure is **TIME LIMITED**

- **The new standard of care for young/fit MCL**

TRIANGLE Ongoing Questions

- What about maintenance rituximab?
  - Some patients received it, some did not, based upon national policy.
  - Re-analysis shows MR adds FFS benefit on top of BTKi benefit
- Are there subgroups who still benefit from ASCT?
  - PR after induction? MRD+ after induction? Ki-67 > 50%? p53 aberrant?
  - Unclear at this time.
- Do we still need to give high dose cytarabine in induction?
  - Just showed ASCT can be subtracted with BTKi
  - Can the HiDAC be subtracted?

EA4251: North American TRIANGLE approach versus Chemotherapy Free Approach



[1] 17p deletion by FISH, p53 mutation by NGS

Primary Endpoint PFS

https://ecog-acrin.org/clinical-trials/ea4151-mantle-cell-lymphoma/

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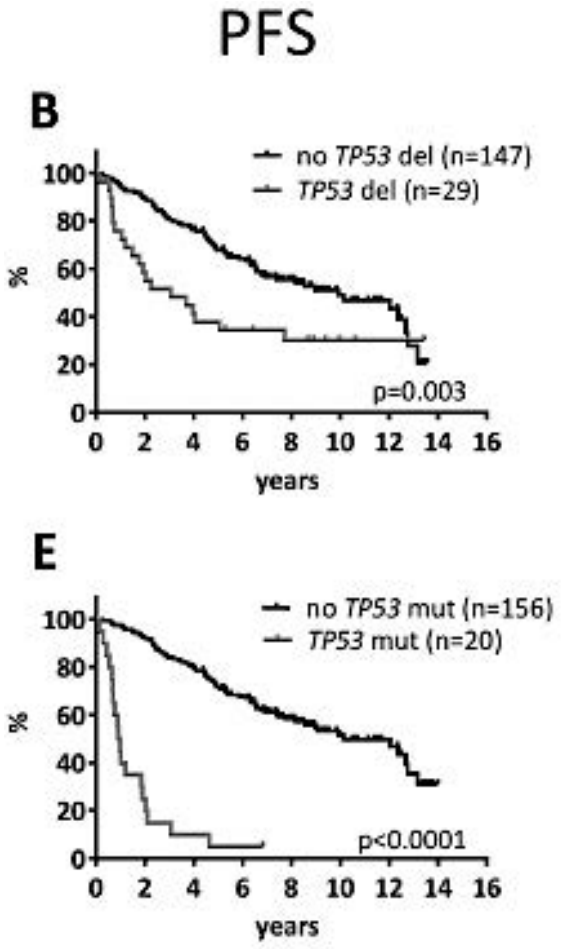
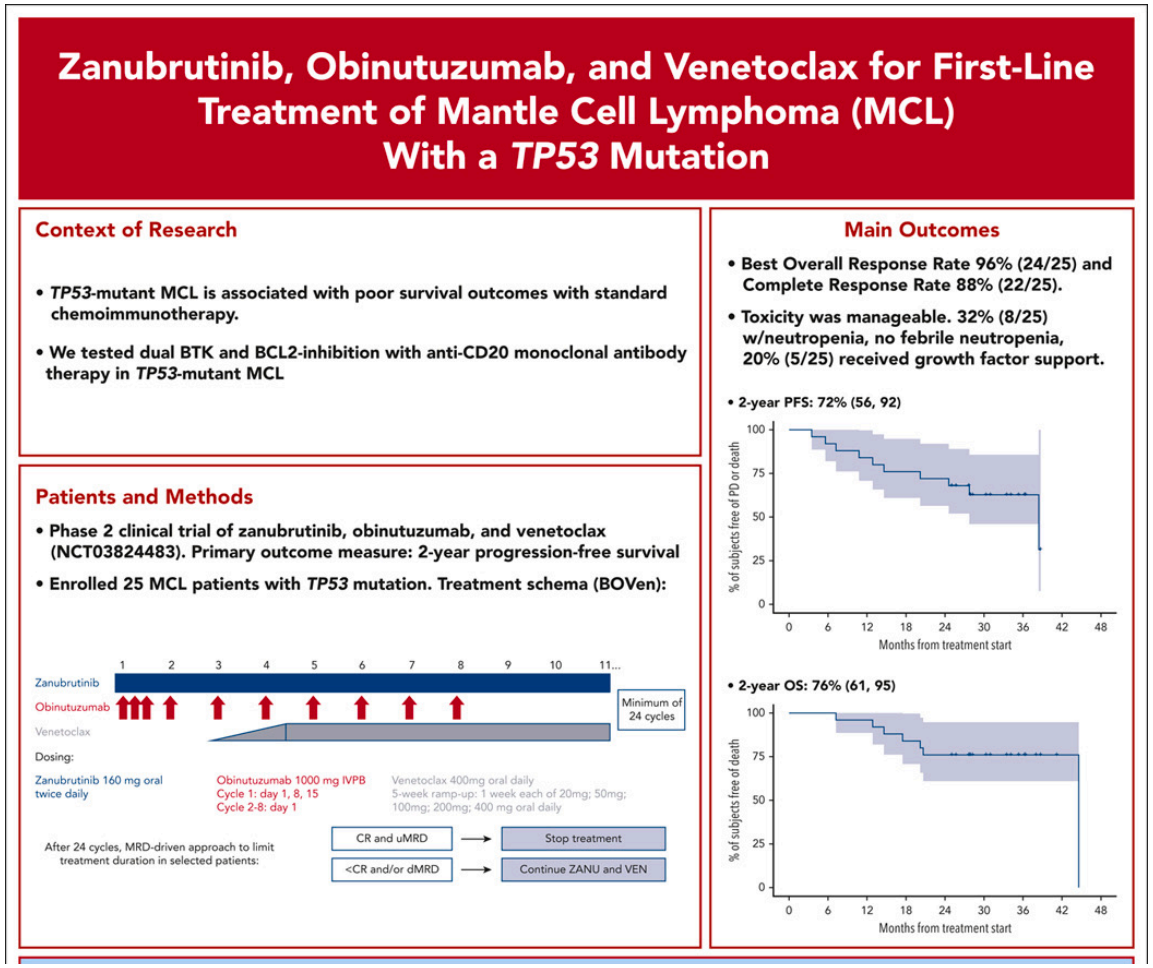
The vexing problem of p53 mutated MCL

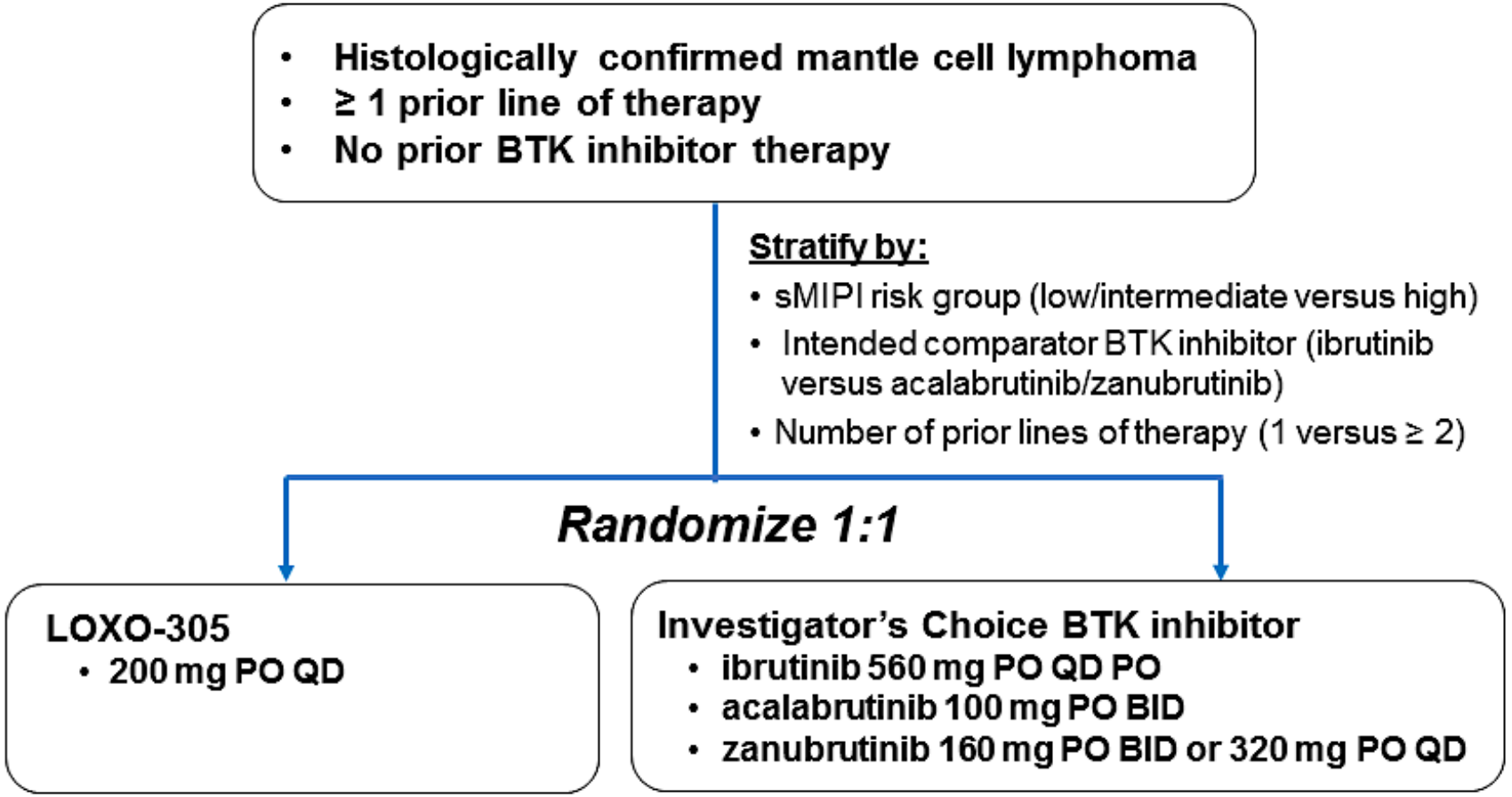


Eskelund et al, Blood online Aug 17, 2017



Kumar et al, Blood 2025

BRUIN MCL 321 Trial for R/R MCL: Pirtobrutinib vs. Investigators Choice BTKi



Eyre TA et al. Future Oncology 2022; 18(36): 3961-3969.

Second Opinion

Ann LaCasce, MD, MMSc

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Discussion Questions

In the contemporary era, how do you approach initial treatment for elderly patients with MCL? When do you employ first-line acalabrutinib/BR? When do you prefer a chemotherapy-free combination (eg, a BTK inhibitor in combination with rituximab)? What about a single-agent BTK inhibitor? Which specific BTK inhibitor do you prefer for your patients with MCL?

How does the need for anticoagulation affect your approach to up-front therapy for these patients?

How are you employing BTK inhibitors in other NHL subtypes? How are you sequencing zanubrutinib/obinutuzumab relative to other evidence-based options for patients with R/R FL? Do you anticipate that BTK inhibitors will eventually have a role in DLBCL management?

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TO PRACTICE

Consensus or Controversy? Documenting and Discussing Investigators' Approaches to the Management of Myelofibrosis

A CME/MOC-Accredited Virtual Event Held
Adjunct with the 2026 ASCO® Annual Meeting

Tuesday, June 2, 2026
4:00 PM – 5:00 PM CT (5:00 PM – 6:00 PM ET)

Faculty

Professor Claire Harrison
Raajit K Rampal, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!
Your feedback is very important to us.

Please complete the survey currently up on the iPads for attendees in the room and on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.

How to Obtain CME Credit

In-person attendees: Please refer to the program syllabus for the CME credit link or QR code. Online/Zoom attendees: The CME credit link is posted in the chat room.

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