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Medical Oncology Update

A CME/MOC-Accredited Grand Rounds Event

Friday, August 28, 2026
2:30 PM – 4:45 PM

Faculty

Erica Stringer-Reasor, MD
Gilles Salles, MD, PhD

RTP
RESEARCH
TO PRACTICE

Agenda

- Hormone Receptor (HR)-Positive Localized Breast Cancer — Dr Stringer-Reasor
- Diffuse Large B-Cell Lymphoma (DLBCL) — Prof Salles

Agenda

- **Hormone Receptor (HR)-Positive Localized Breast Cancer — Dr Stringer-Reasor**
- **Diffuse Large B-Cell Lymphoma (DLBCL) — Prof Salles**

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

Erica Stringer-Reasor, MD
Associate Professor of Medicine
UAB O'Neal Comprehensive Cancer Center
Birmingham, Alabama

Disclosures

Advisory Committees and Consulting Agreements	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Gilead Sciences Inc, Lilly, Novartis, Pfizer Inc, Seagen Inc, Tesaro, A GSK Company
Contracted Research	Corcept Therapeutics Inc, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Lilly, Pfizer Inc, Seagen Inc

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Program Steering Committee

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Abramson Cancer Center
Co-Director, 2-PREVENT Breast Cancer Translational Center of Excellence
Senior Scholar, Center for Clinical Epidemiology and Biostatistics
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

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Patricia and James Cayne Chair for Junior Faculty
Associate Attending Physician
Breast Medicine Service and Early Drug Development Service
Section Head, Endocrine Therapy Research Program
Clinical Director, Early Drug Development Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
Associate Professor of Medicine
Weill Cornell College of Medicine
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Director, Division of Medical Oncology
Louisa and Rand Glenn Family Chair in Breast Cancer Research
Winship Cancer Institute at Emory University
Atlanta, Georgia

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Dana-Farber Cancer Institute
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SAB Chair of the Lobular Breast Cancer Alliance
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Director, Women's Cancers Program
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Professor, Department of Medical Oncology and Therapeutics Research
City of Hope Comprehensive Cancer Center
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Professor Emeritus, UCSF

Priyanka Sharma, MD
Frank B Tyler Professor in Cancer Research
Division of Medical Oncology, Department of Internal Medicine
Co-Program Leader
Drug Discovery, Delivery and Experimental Therapeutics Program
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Director of Breast Cancer Clinical Trials
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PROJECT CHAIR
Neil Love, MD
Research To Practice
Miami, Florida

Erica Stringer-Reasor, MD
Associate Professor of Medicine
UAB O'Neal Comprehensive Cancer Center
Birmingham, Alabama

Key Datasets

- Andre F et al. **Biomarkers** for **adjuvant endocrine and chemotherapy** in early-stage breast cancer: ASCO Guideline update. *J Clin Oncol* 2022;40:1816-37.
- Sparano JA et al. Trial Assigning Individualized Options for treatment **(TAILORx): An update** including 12-year event rates. San Antonio Breast Cancer Symposium 2022;Abstract GS1-05.
- Sparano JA et al. **Clinical** outcomes in early breast cancer with a **high 21-gene Recurrence Score** of 26 to 100 assigned to **adjuvant chemotherapy plus endocrine therapy**: A **secondary analysis of the TAILORx** randomized clinical trial. *JAMA Oncol* 2020;6(3):367-74.
- Chen N et al. **Impact of anthracyclines** in **genomic high-risk**, **node-negative, HR-positive/HER2-negative** breast cancer. *Ann Oncol* 2025;36(11):1356-65.
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- Sestak I et al. **Comparison** of the performance of 6 **prognostic signatures** for estrogen receptor-positive breast cancer: A **secondary analysis of a randomized clinical trial**. *JAMA Oncol* 2018;4(4):545-53.
- Noordhoek I et al. **Breast Cancer Index** predicts **extended endocrine benefit** to individualize selection of patients with HR+ early-stage breast cancer for **10 years of endocrine therapy**. *Clin Cancer Res* 2021;27(1):311-19.

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Key Datasets

- Woolpert KM et al. **Biomarkers predictive** of a response to **extended endocrine therapy** in breast cancer: A systematic review and meta-analysis. *Breast Cancer Res Treat* 2024;203(3):407-17.
- Johnston S et al. **monarchE**: **Primary overall survival** (OS) results of adjuvant abemaciclib + endocrine therapy (ET) for HR+, HER2-, high-risk early breast cancer (EBC). ESMO 2025;Abstract LBA13.
- Johnston S et al. **Overall survival** with **abemaciclib** in early breast cancer. *Ann Oncol* 2026;37(2):155-65.
- Cortés J et al. **monarchE**: **Subgroup analysis** of adjuvant abemaciclib + endocrine therapy for HR+, HER2-, high-risk early breast cancer by nodal status. San Antonio Breast Cancer Symposium 2025;Abstract PS1-08-08.
- Crown JP et al. **Adjuvant ribociclib** (RIB) **plus nonsteroidal aromatase inhibitor** (NSAI) in patients (pts) with HR+/HER2− early breast cancer (EBC): **NATALEE 5-year outcomes**. ESMO 2025;Abstract LBA14.
- Rugo HS et al. **Adjuvant abemaciclib** combined **with endocrine therapy** for high-risk early breast cancer: **Safety and patient-reported outcomes** from the **monarchE** study. *Ann Oncol* 2022;33(6):616-27.
- Barrios C et al. **NATALEE update**: **Safety and treatment (tx) duration** of **ribociclib** (RIB) + **nonsteroidal aromatase inhibitor** (NSAI) in patients (pts) with HR+/HER2− early breast cancer (EBC). ESMO Breast 2024;Abstract 113MO.
- Mayer EL et al. **TRADE:** A **phase II** trial to assess the **tolerability of abemaciclib dose escalation** in early-stage HR-positive/HER2-negative breast cancer. *Ann Oncol* 2025;31(1):117-24.
- Bardia A et al. **Giredestrant** vs standard-of-care endocrine therapy as **adjuvant treatment** for patients with estrogen receptor-positive, HER2-negative early breast cancer: **Results from the global phase III lidERA Breast Cancer trial**. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: Clinician Survey Results

Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer

Module 4: Clinician Survey Results

Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy

Module 6: Clinician Survey Results

Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

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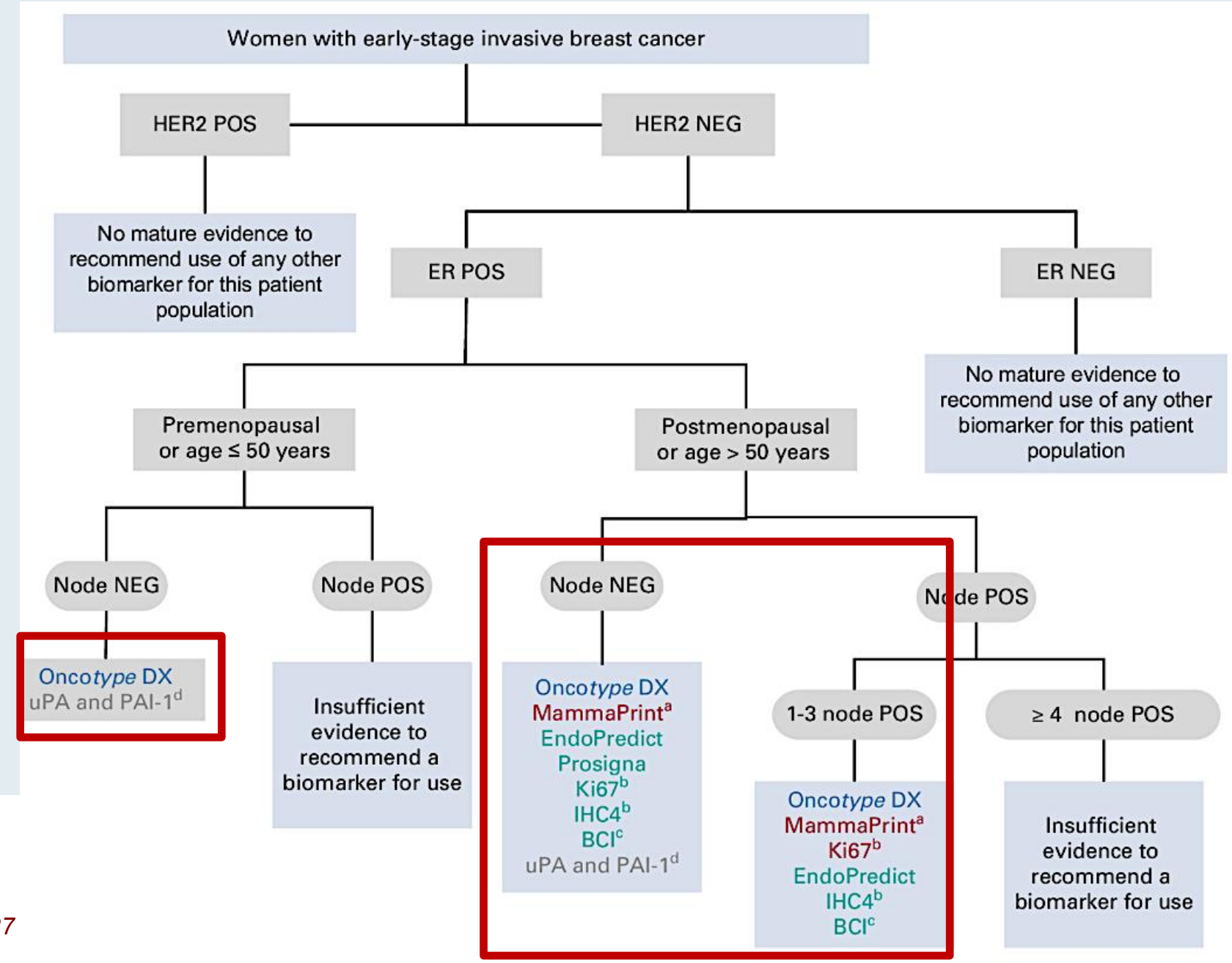
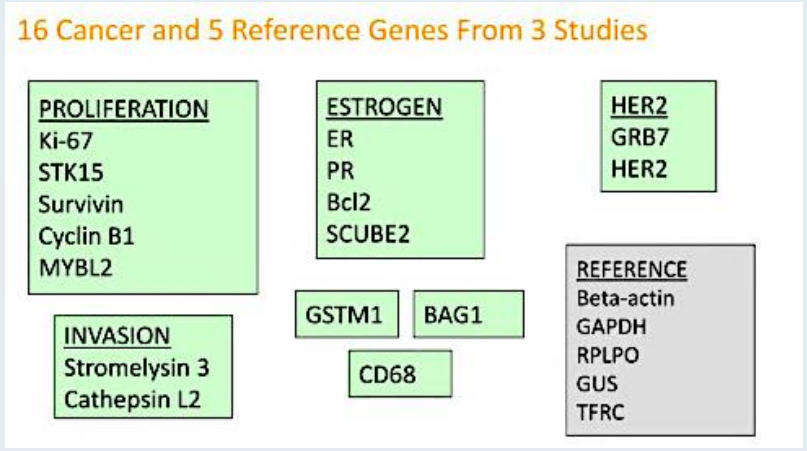
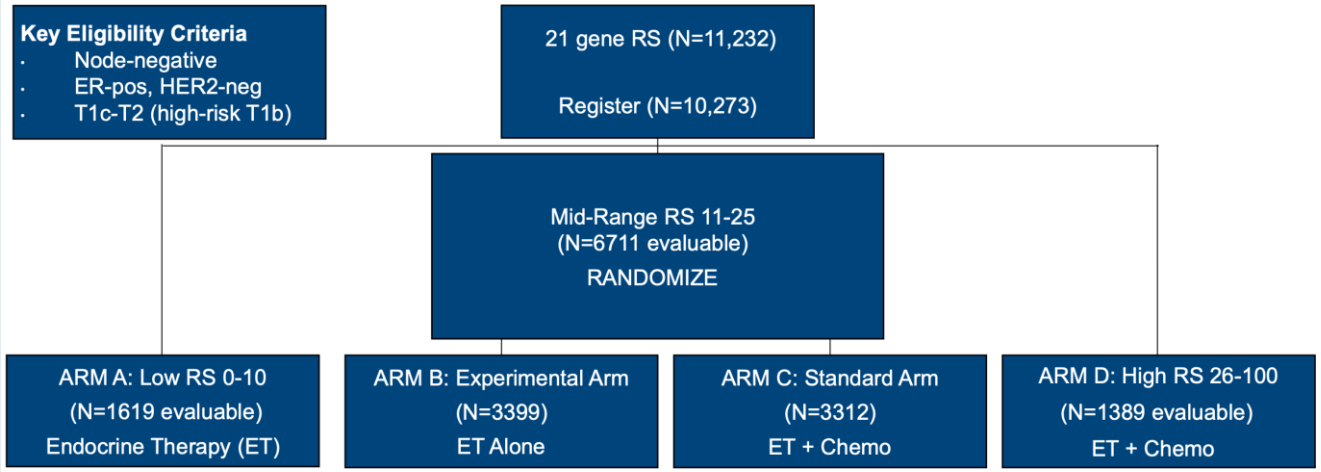


Andre F et al. J Clin Oncol. 2022;40:1816-1837

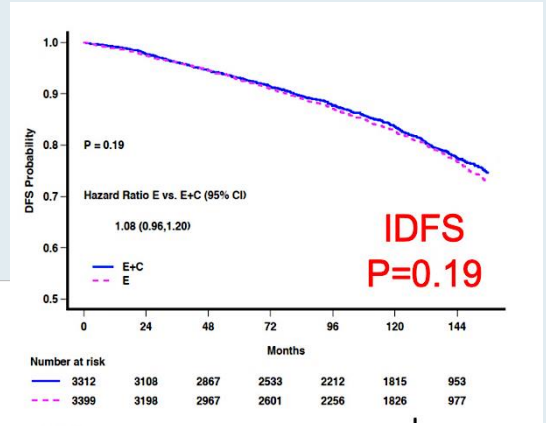
Oncotype DX®: TAILORx Trial Key Results for Node-Negative Disease

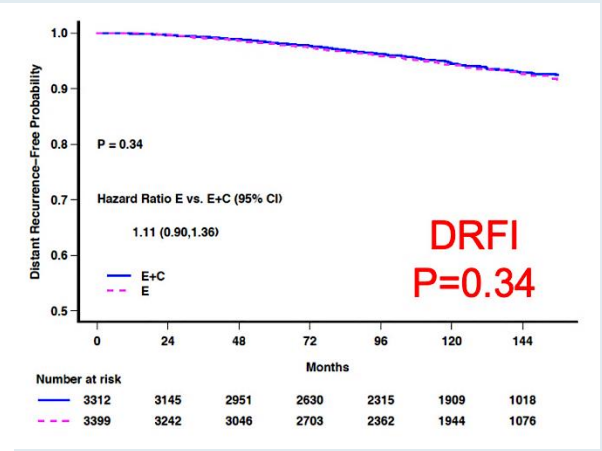


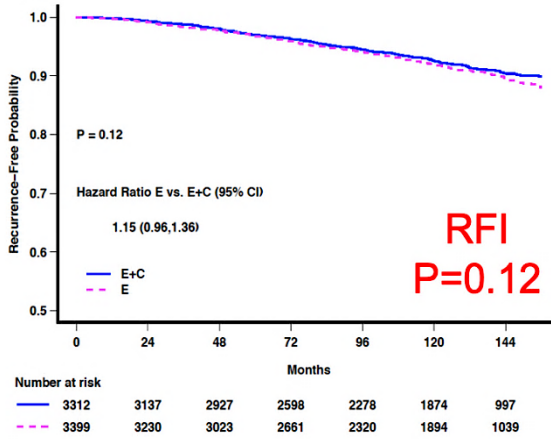
TAILORx Trial Design

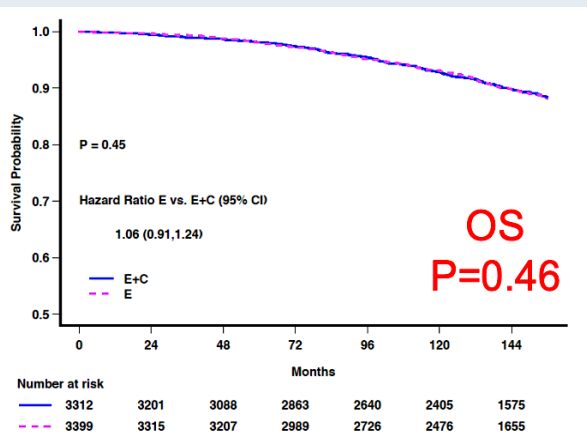


Intermediate risk (11-25): No overall benefit to chemotherapy (2022 update)





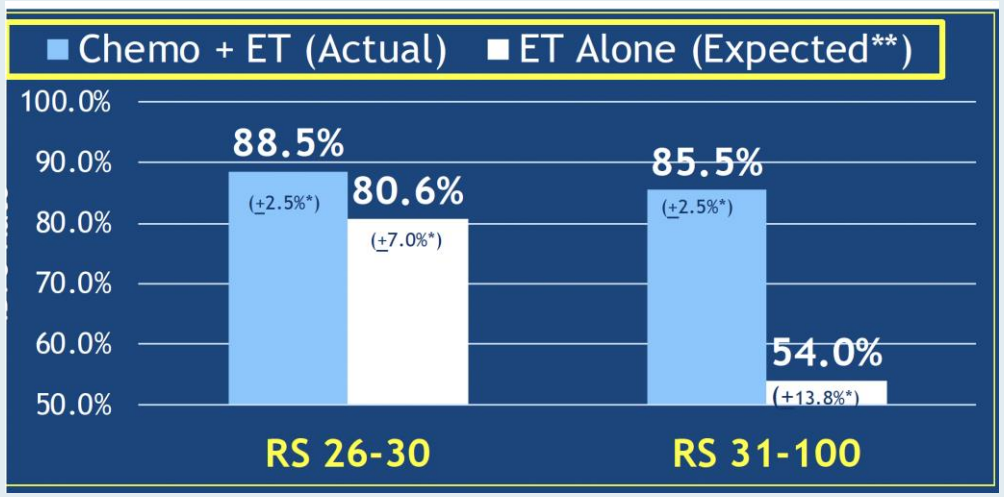


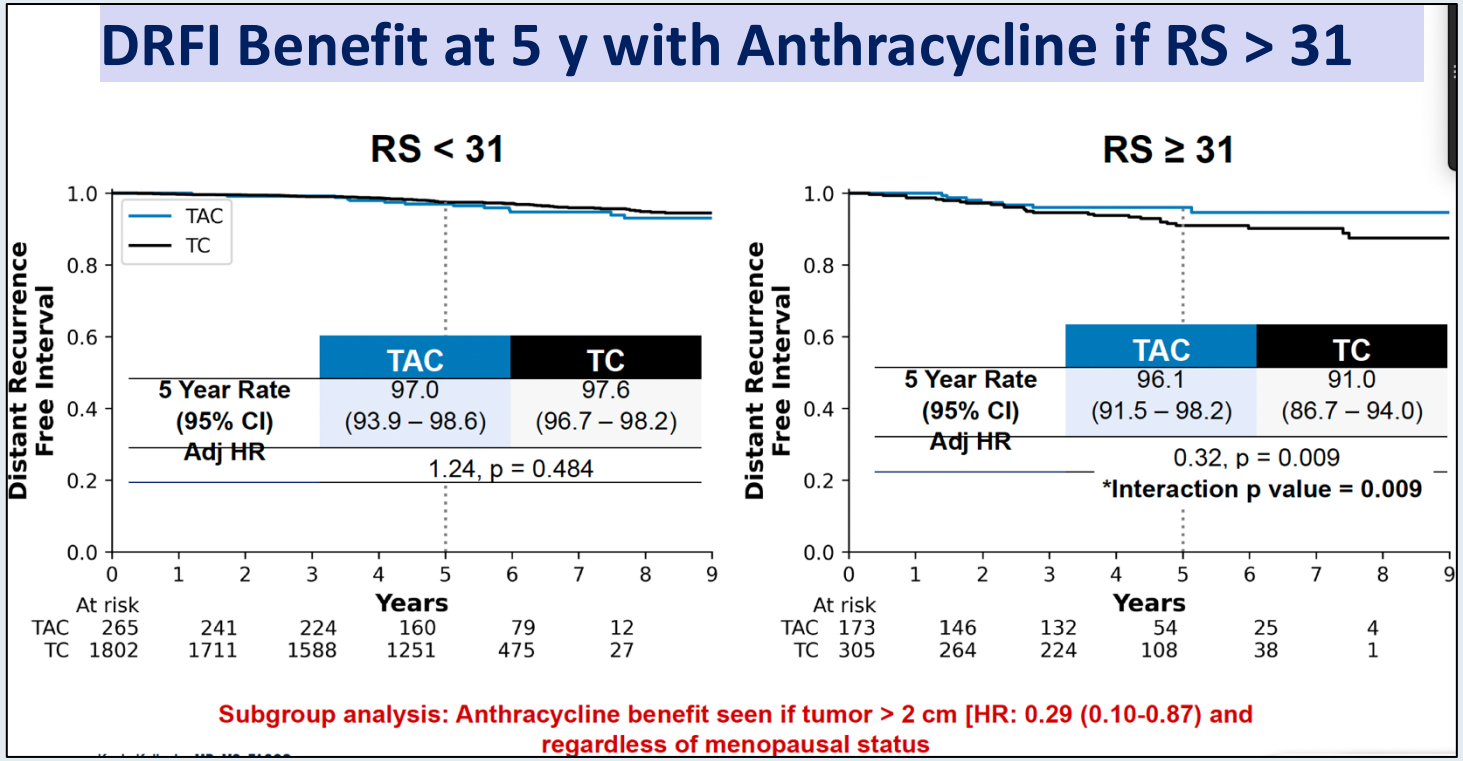


Sparano JA et al. SABCS 2022;Abstract GS1-05.

Chemotherapy and Anthracycline Benefits for Patients with High Recurrence Scores® (>25)

High Risk (RS > 25): Expected benefit with chemotherapy





"No chemotherapy" rates estimated by combining

- patient-specific distant recurrence risk information with
- patient-specific chemotherapy benefit information
- from the ERBB2-negative cohort of NSABP B20

TAILORx N = 2,549. T-AC vs TC

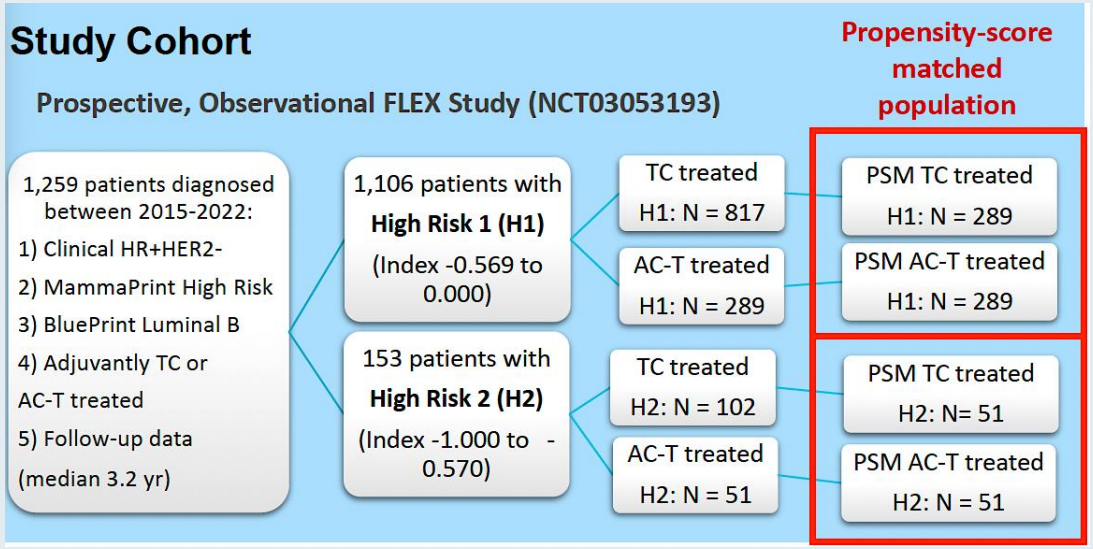
5-y DRFI 96.1 vs 91%, HR 0.31, *p* = 0.006

5-y DRFS 95.4% vs 89.8%, aHR 0.49, *p* = 0.032

OS NS

Sparano JA et al. *JAMA Oncol* 2020; Chen N et al. *Ann Oncol* 2025.

Propensity-Score Matched Analysis of Real-World FLEX Data: IDFS with Anthracycline-Based Therapy for Patients with MammaPrint® High 2, Luminal B, HR-Positive, HER2-Negative Localized Breast Cancer

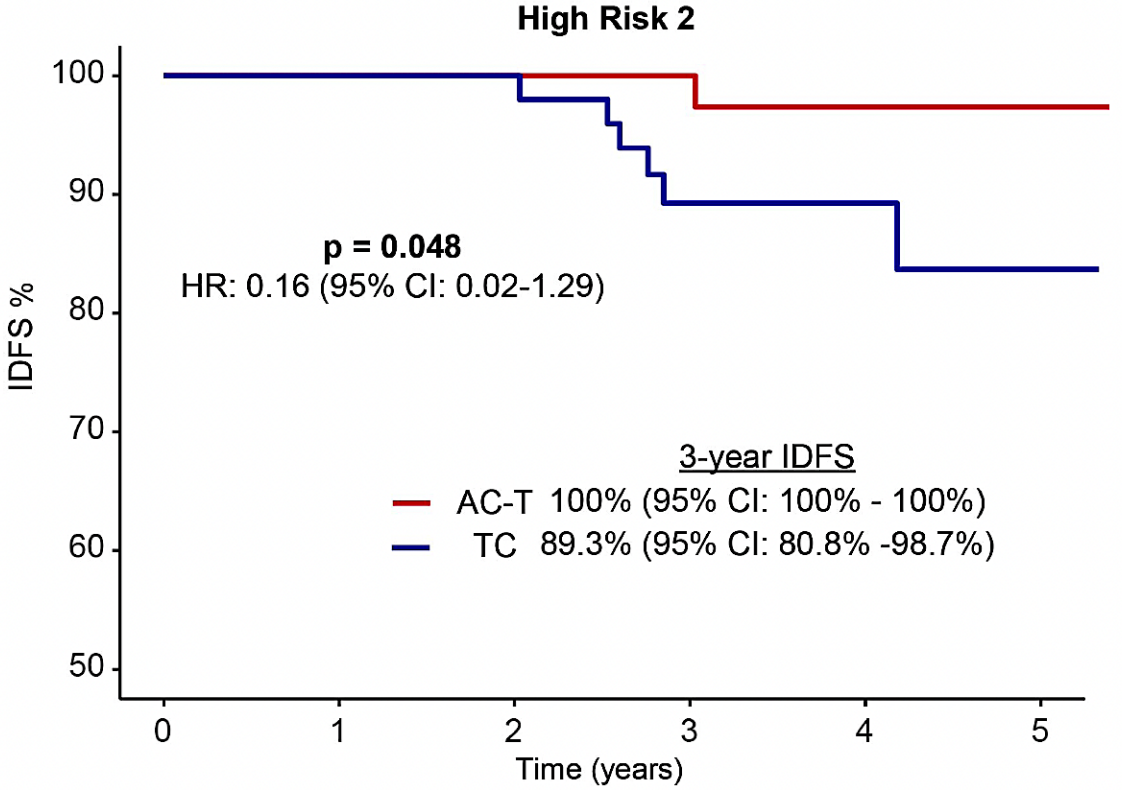


Conclusions

- In this PSM analysis of a non-randomized, prospective, real-world FLEX Study data with 3.2 years median follow-up, patients with H2, HR+HER2- cancer had significantly improved IDFS with AC-T compared to TC
- Although adjusted analyses were limited by few events, the direction and magnitude of benefit remained consistent
- In contrast, patients with H1 cancer did not benefit more from AC-T vs. TC
- These findings further support the utility of MammaPrint in informing chemotherapy selection in patients with HR+HER2- breast cancer

IDFS = invasive disease-free survival

Figure 2. IDFS in patients with High Risk 2 cancer: AC-T vs TC



Numbers at Risk

H2	0	1	2	3	4	5
AC–T	51	50	49	40	17	8
TC	51	51	50	30	16	9

O'Shaughnessy J et al. SABCS 2025;Abstract PS2-07-03.

Oncotype DX: RxPONDER Trial Results Summary
One to Three Positive Lymph Nodes

RxPONDER Trial Design

Key Entry Criteria
- Women age ≥ 18 yrs
- ER and/or PR ≥ 1%, HER2- breast cancer with 1*-3 LN+ without distant metastasis
- Able to receive adjuvant taxane and/or anthracycline-based chemotherapy**
- Axillary staging by SLNB or ALND

REGISTRATION

Recurrence Score 0-25

Recurrence Score > 25

Off Study
Chemotherapy Followed by Endocrine Therapy Recommended

RANDOMIZATION

N = 5,000 pts

Arm 1: Chemotherapy Followed by Endocrine Therapy

Arm 2: Endocrine Therapy Alone

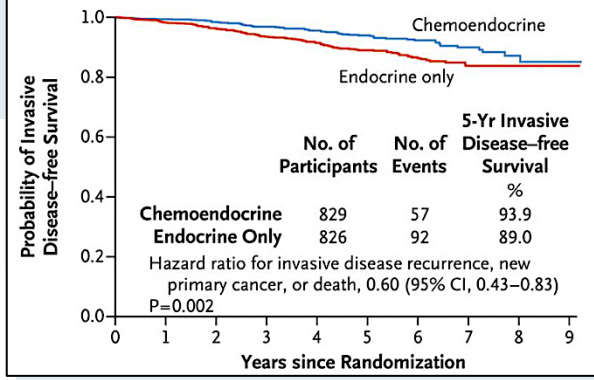
Stratification Factors
Recurrence Score: 0-13 vs.14-25
Menopausal Status: pre vs. post
Axillary Surgery: ALND vs. SLNB

RxPONDER Population

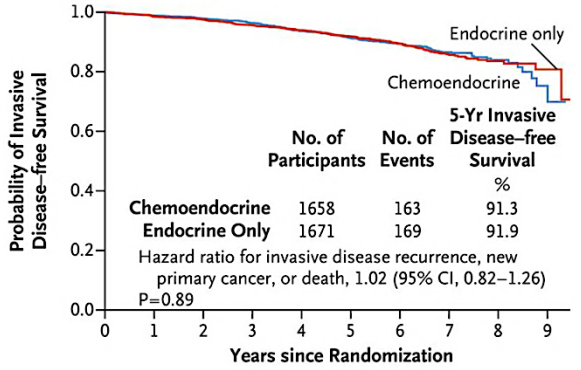
T1	58%	T3	5%
1 LN+	66%	3 LN+	9%
Grade 2	64%	Grade 3	10%
40-49 yrs	21%	< 40 yrs	3%

RxPONDER: Chemo Benefit Different by Menopausal Status if RS 0-25

Premenopausal (1/3rd Trial)



Postmenopausal (2/3rd Trial)



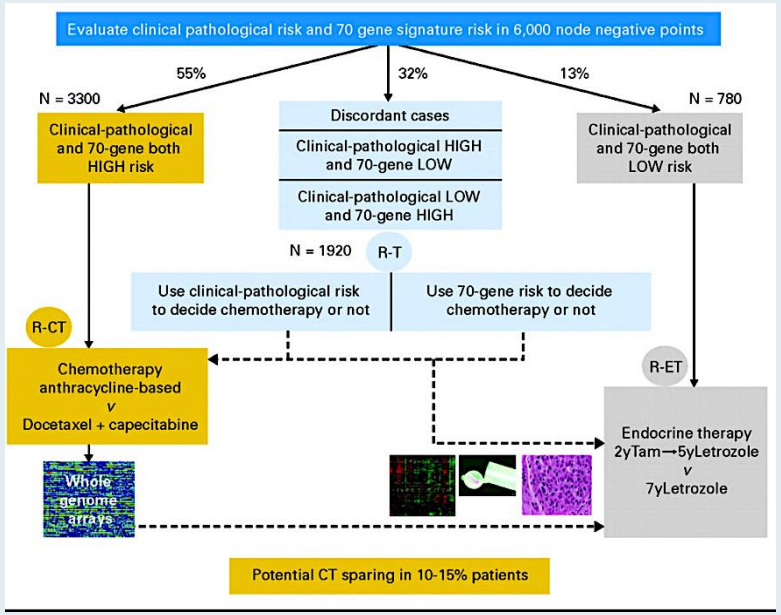
IDFS Benefit Modified by Score for Women Age ≤50

Women ≤50 yr			
≤10, endocrine only	145	91.0±2.6	0.31 (0.10–0.94)
≤10, chemoendocrine	135	97.9±1.5	
11–15, endocrine only	247	93.1±1.8	0.71 (0.33–1.51)
11–15, chemoendocrine	235	95.4±1.6	
16–20, endocrine only	227	85.1±2.6	0.58 (0.33–1.00)
16–20, chemoendocrine	224	92.2±2.0	
21–25, endocrine only	107	80.0±4.3	0.56 (0.27–1.17)
21–25, chemoendocrine	98	90.0±3.6	

Sparano JA et al. *JAMA Oncol* 2020; Chen N et al. *Ann Oncol* 2025.

MammaPrint: MindACT Trial Key Results

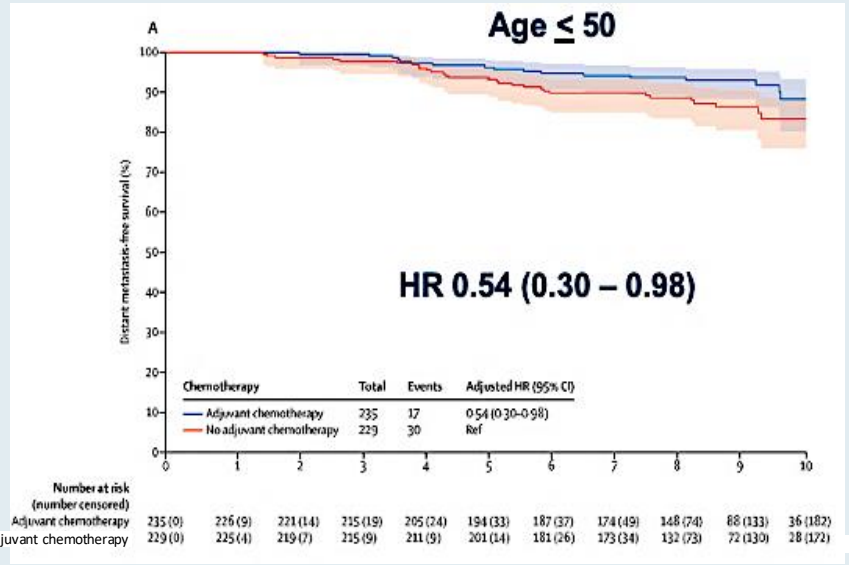
Clinical "high risk": <88% 10-yr BCSS
Modified Adjuvant! Online to determine
Model included: T size, Node (0-3), grade, ER status, age, comorbidity

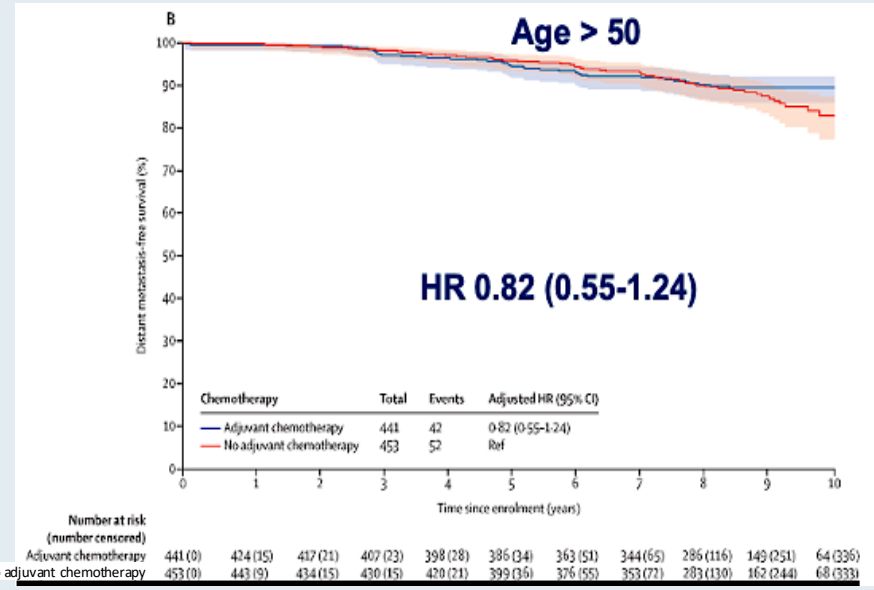


Met primary outcome: Lower bound of 95% CI >92% 5-y DMFS in the High Clinical/Low Genomic risk group

Chemo benefit increases over time overall. Lost in those age >50, maintained in those age <50

	ET	CET	Absolute diff
5-y DMFS	94.7% (92.5 – 96.2)	95.9% (94-97.2)	1.2%
8-yr DMFS	89.4% (86.8- 91,5)	92% (896-93.8)	2.6%





BCSS = breast cancer-specific survival; DMFS = distant metastasis-free survival

Cardoso F et al. *N Engl J Med* 2016; Piccart M et al. *Lancet Oncol* 2021.

Prosigna® ROR, EndoPredict® EPclin and Breast Cancer Index®

ROR (risk of recurrence, Prosigna)
- 50-gene RNA-based molecular subtyping assay
- ROR available in US; PAM50 not available

EPclin (EndoPredict)
- 12 genes – Proliferation and hormone receptor

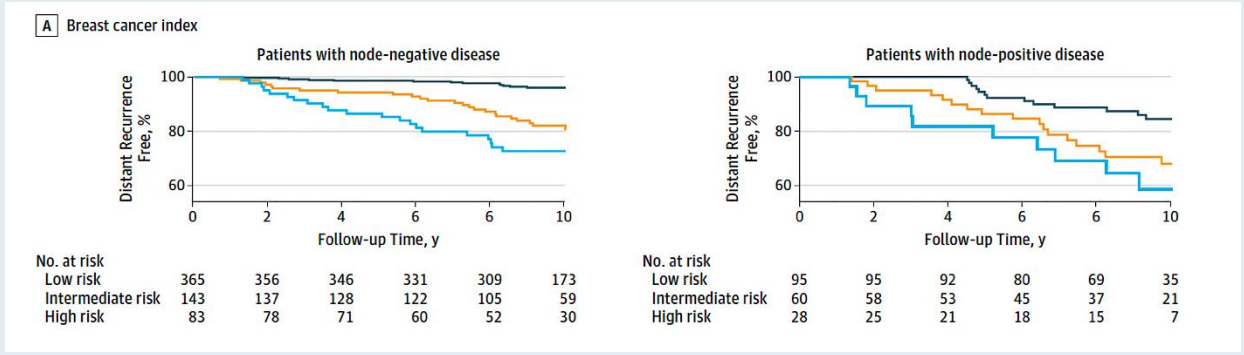
Breast Cancer Index (BCI)
- 7 genes – Proliferation and hormone receptor (HoxB13/IL17BR)

JAMA Oncology | Original Investigation

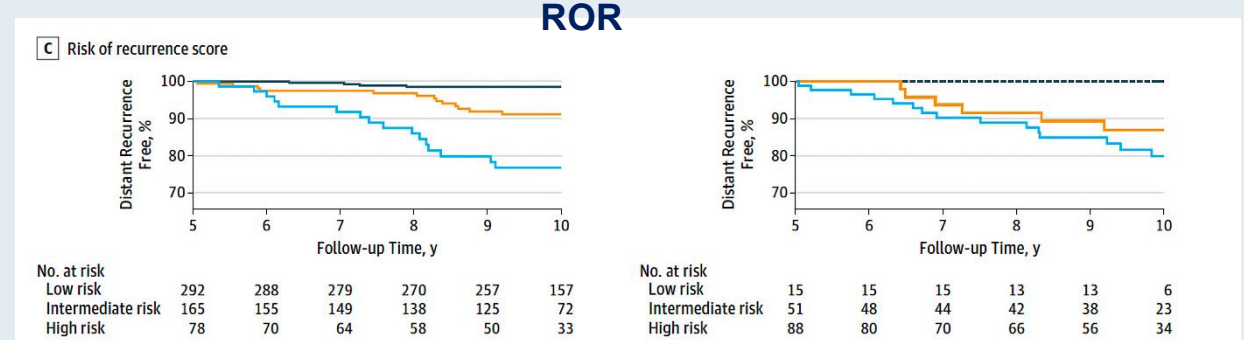
Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor–Positive Breast Cancer
A Secondary Analysis of a Randomized Clinical Trial

- Largest retrospective prognostic validation in TransATAC Trial (included Onco*type* DX and BCI as well)
- N = 535 node-negative, 154 node-positive
- Examined risk years 0 to 10
- ROR, EPclin and BCI provided most prognostic information
- ROR HR 2.56 (1.96-3.35)
- EPclin HR 2.14 (1.71-2.68)
- BCI HR 2.46 (1.88-3.23)

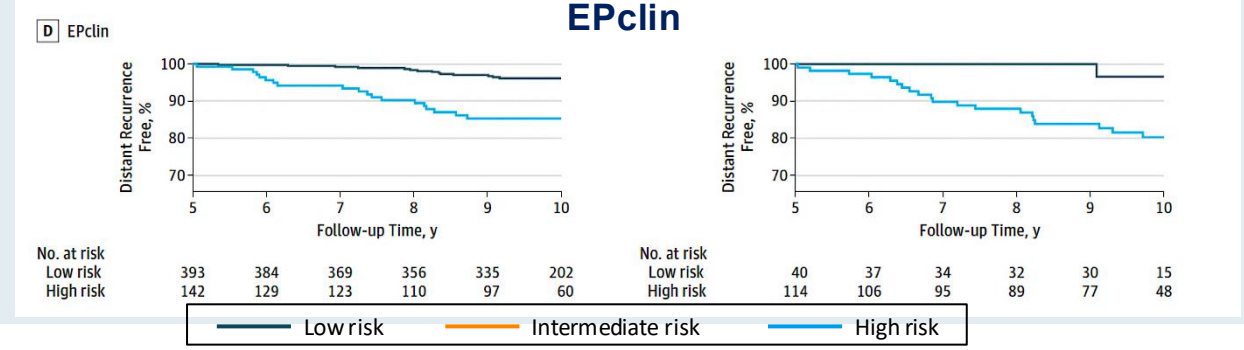
BCI



ROR



EPclin

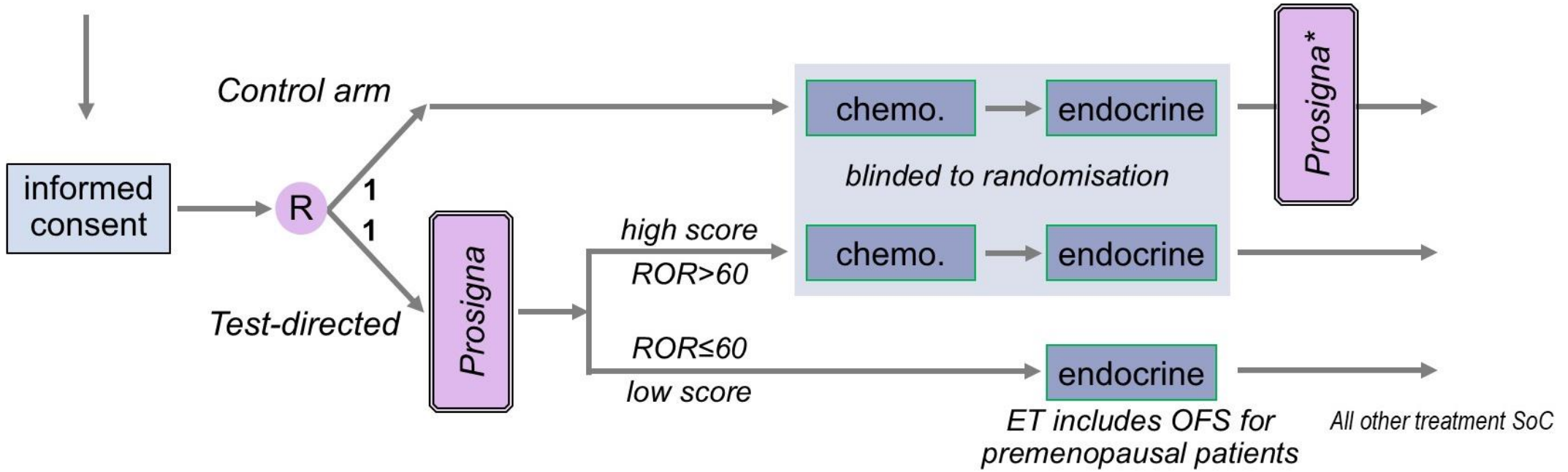


Sestak I et al. *JAMA Oncol* 2018;4(4):545-53.

Phase III OPTIMA Study Design

Main eligibility criteria

- Women & men age ≥40 with excised breast cancer
- ER-pos (IHC>10%) & HER2-neg
- Nodes: ▸0-9N+,
  ▸minimum T-size requirement if N0/ N1mi
- Neoadjuvant chemotherapy prohibited

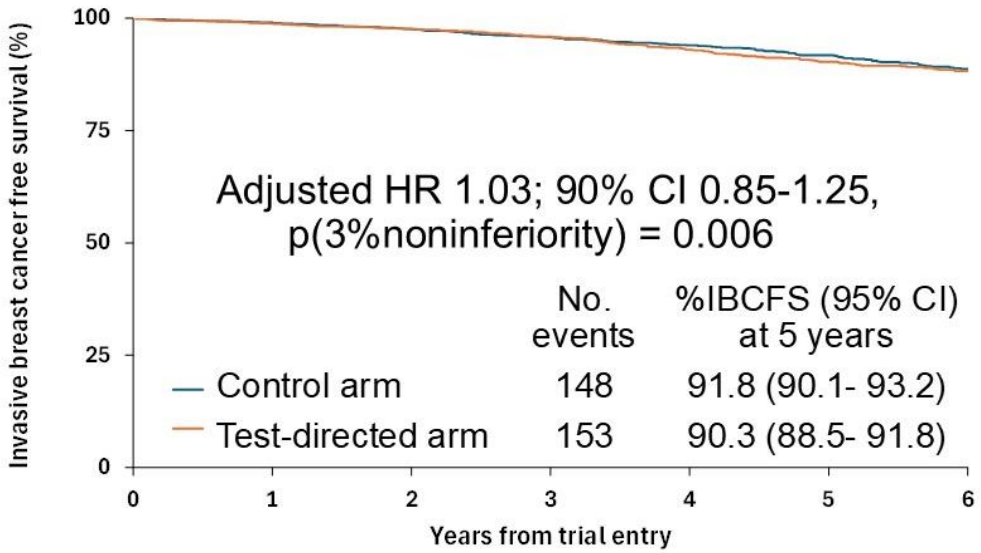


*Control arm Prosigna testing used for analysis only. U.K. control arm testing performed following recruitment completion

Stein R et al. ASCO 2026;Abstract 500.

Phase III OPTIMA: Invasive Breast Cancer-Free Survival (IBCFS)

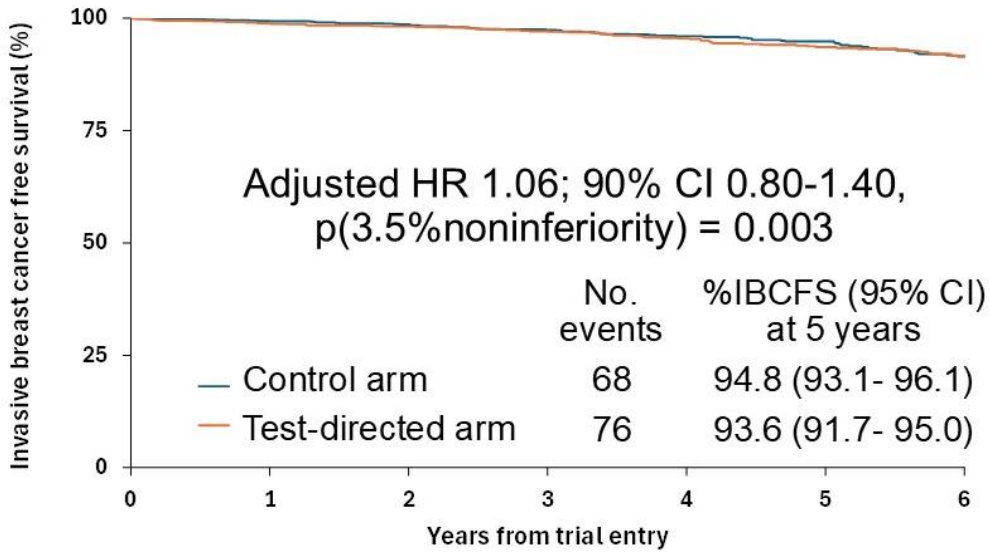
Complete Per Protocol population



Number at risk:							
Control	2059	1818	1563	1283	999	741	485
Test-directed	2094	1857	1591	1303	989	724	481

Demonstrated non-inferiority limit = 2%
No certainty of chemotherapy benefit
1.5% observed 5-year difference –favors chemotherapy

ROR ≤60 subpopulation



Number at risk:							
Control	1358	1207	1043	862	672	504	337
Test-directed	1421	1257	1086	905	694	503	342

Demonstrated non-inferiority limit = 2%
No certainty of chemotherapy benefit
1.2% observed 5-year difference –favors chemotherapy

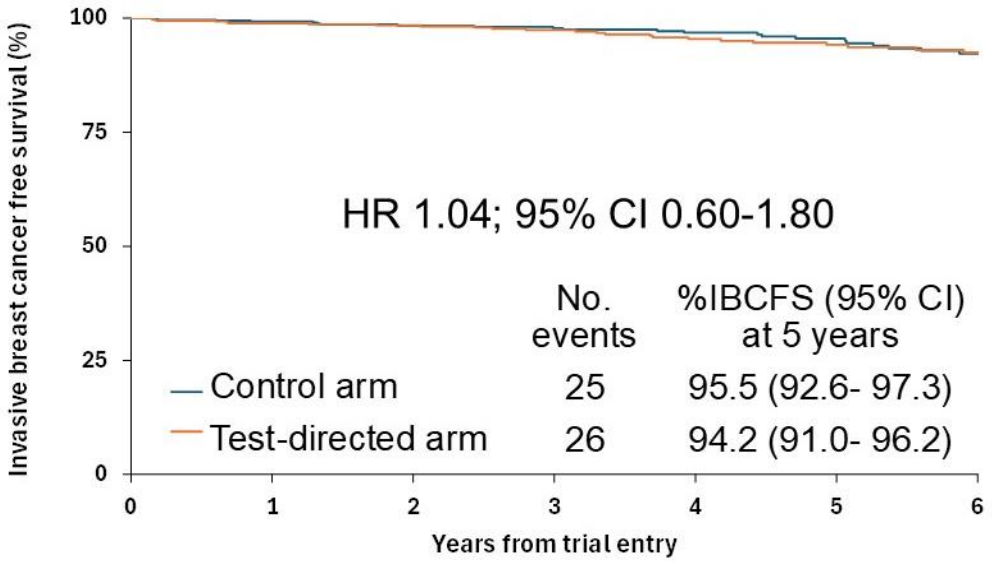
ROR = risk of recurrence

Stein R et al. ASCO 2026;Abstract 500.

RTP RESEARCH TO PRACTICE

Phase III OPTIMA: IBCFS and Menopausal Status (Low ROR Score)

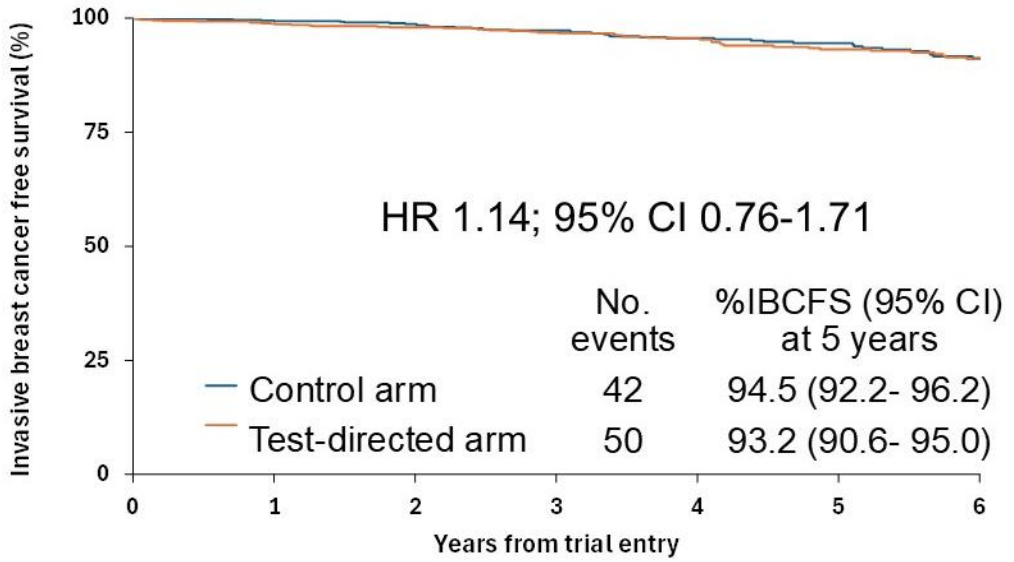
Premenopausal



Number at risk:							
Control	561	481	409	338	258	200	140
Test-directed	559	487	410	347	256	195	135

1.3% observed 5-year difference -favors chemotherapy

Postmenopausal



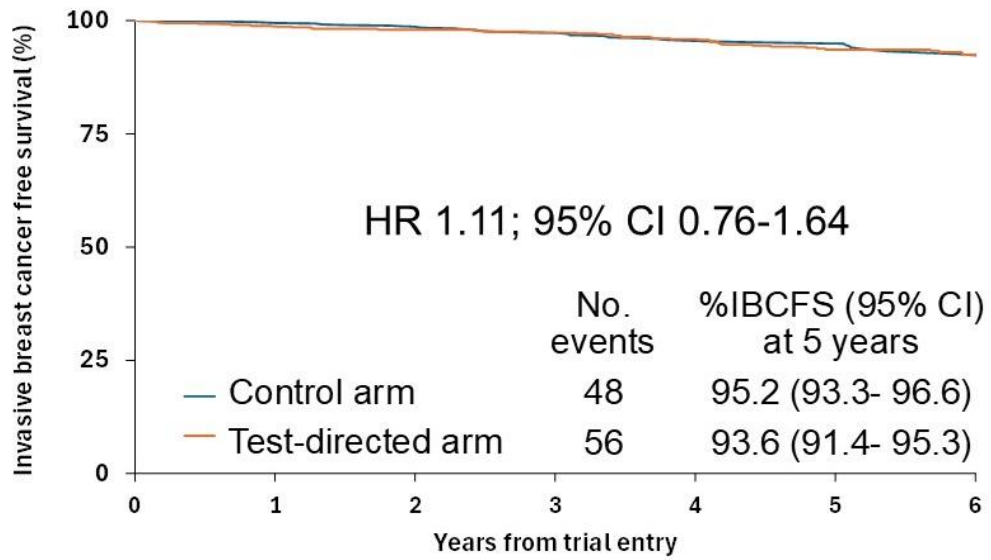
Number at risk:							
Control	791	721	631	522	414	304	197
Test-directed	858	766	673	556	437	307	207

1.3% observed 5-year difference -favors chemotherapy

Stein R et al. ASCO 2026;Abstract 500.

Phase III OPTIMA: IBCFS and Nodal Status (Low ROR Score)

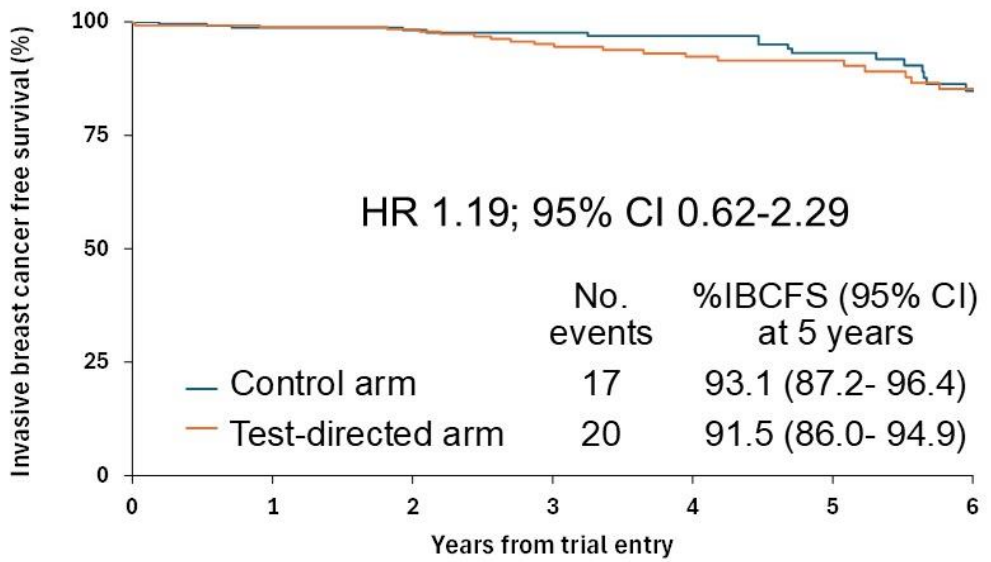
1-3 involved nodes



Number at risk:							
Control	1015	914	798	651	499	382	264
Test-directed	1063	953	829	700	539	389	270

1.6% observed 5-year difference -favors chemotherapy

4-9 involved nodes



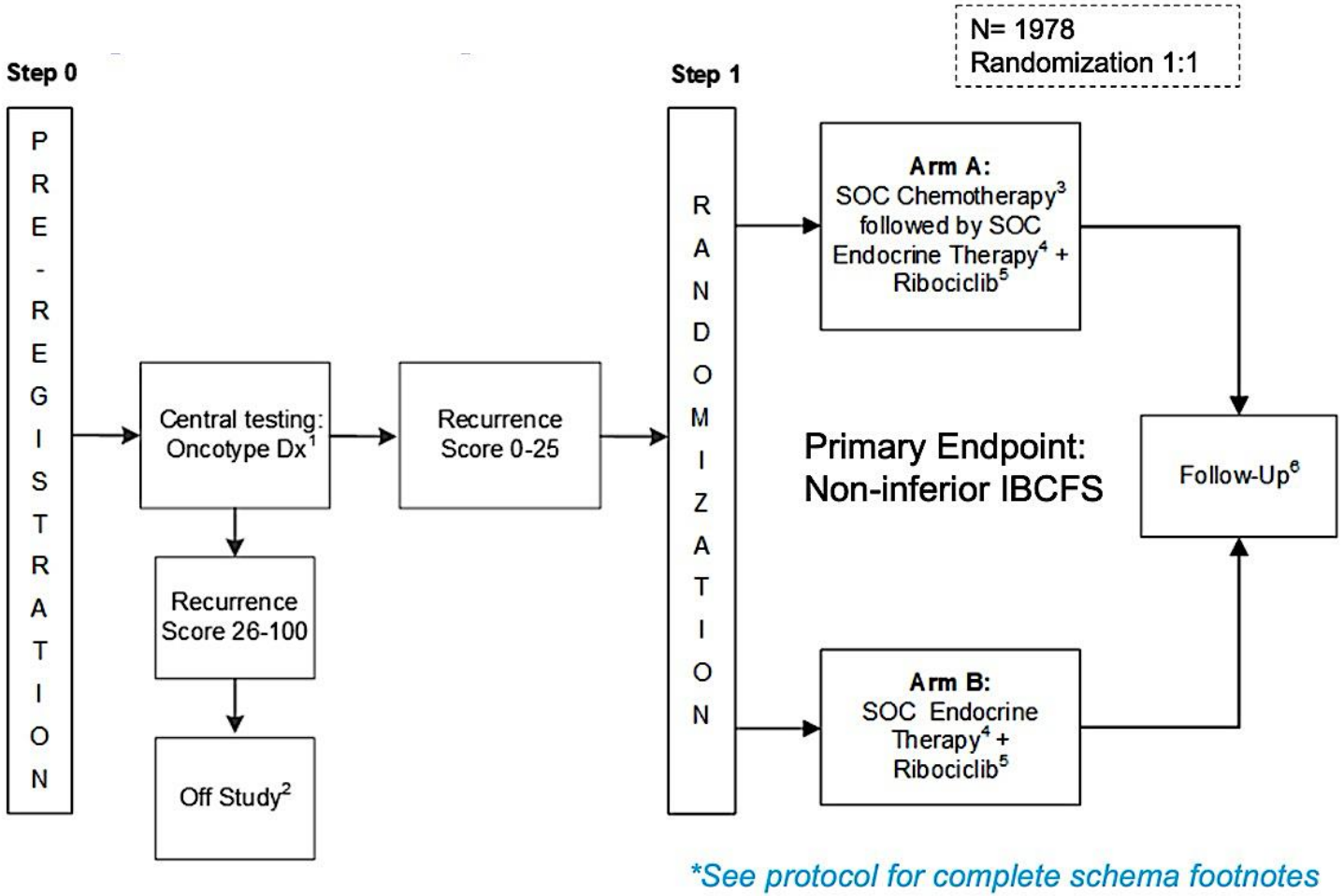
Number at risk:							
Control	243	214	181	155	125	84	48
Test-directed	269	232	197	158	118	86	49

1.6% observed 5-year difference -favors chemotherapy

Stein R et al. ASCO 2026;Abstract 500.

Phase III RxFINE-Low (EA1242) Study Design

- Postmenopausal
- Stage: pT0-T3 with 3 positive ipsilateral lymph nodes (micro-or macrometastatic disease) and no planned axillary lymph node dissection (ALND) after definitive surgery in the breast and axilla with curative intent
- pT0-T3 with N2 or N3
- pT3 with N0-N3
- Must have undergone axillary staging with sentinel lymph node biopsy (SLNB), targeted axillary dissection (TAD), or ALND



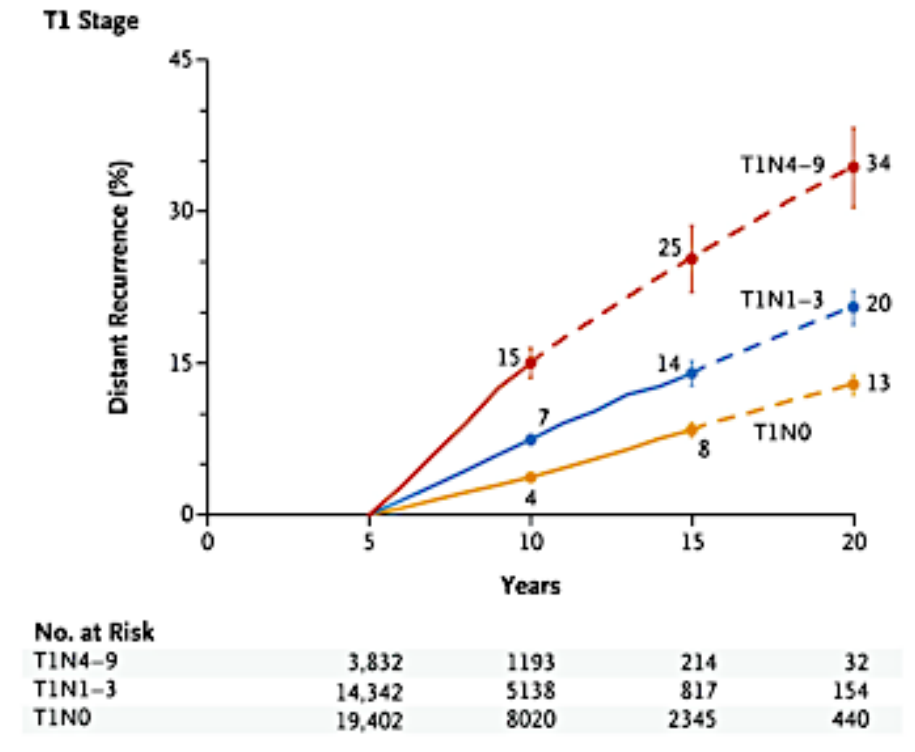
ECOG-ACRIN cancer research group

https://ecog-acrin.org/clinical-trials/ea1242-rxfine-low-breast-cancer/

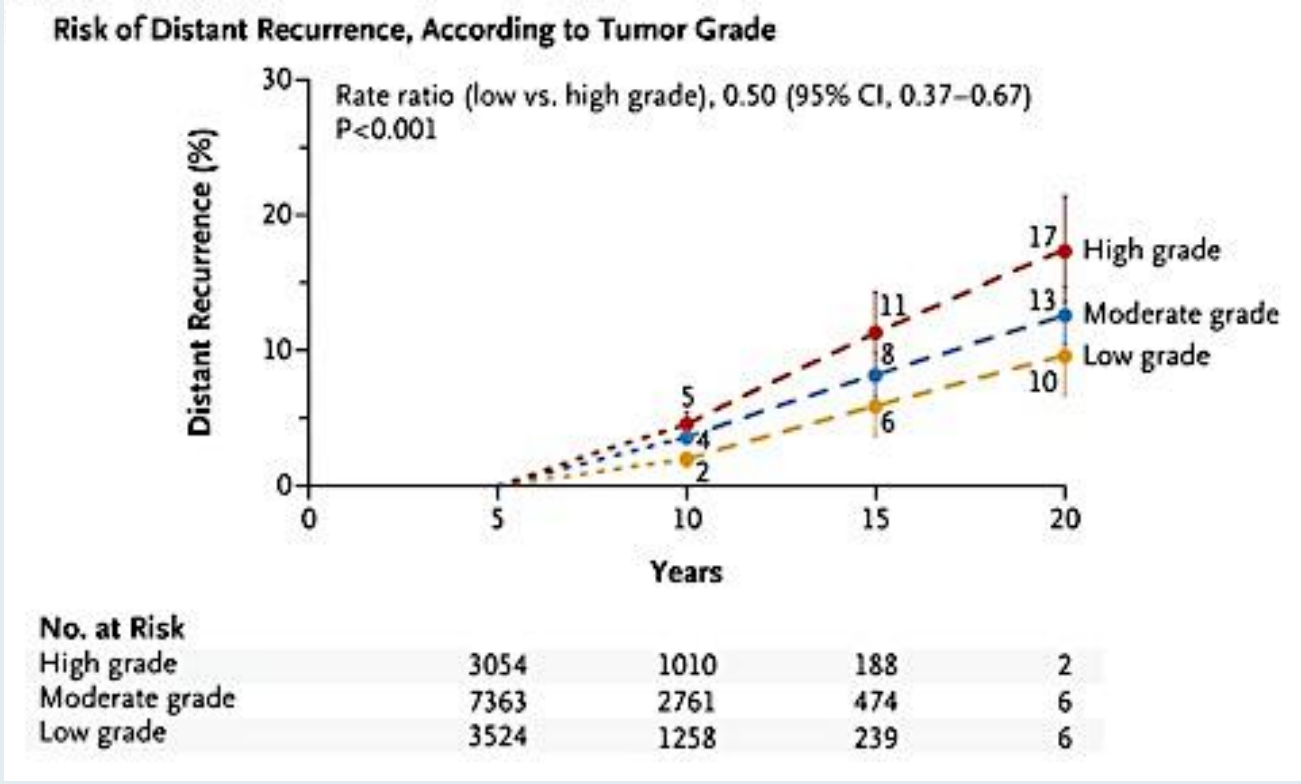
RTP RESEARCH TO PRACTICE

Persistent Long-Term Risk of Distant Recurrence

Risk of late distant recurrence after 5 years of adjuvant endocrine therapy persists across all clinical stages.



No. at Risk				
T1N4–9	3,832	1193	214	32
T1N1–3	14,342	5138	817	154
T1N0	19,402	8020	2345	440

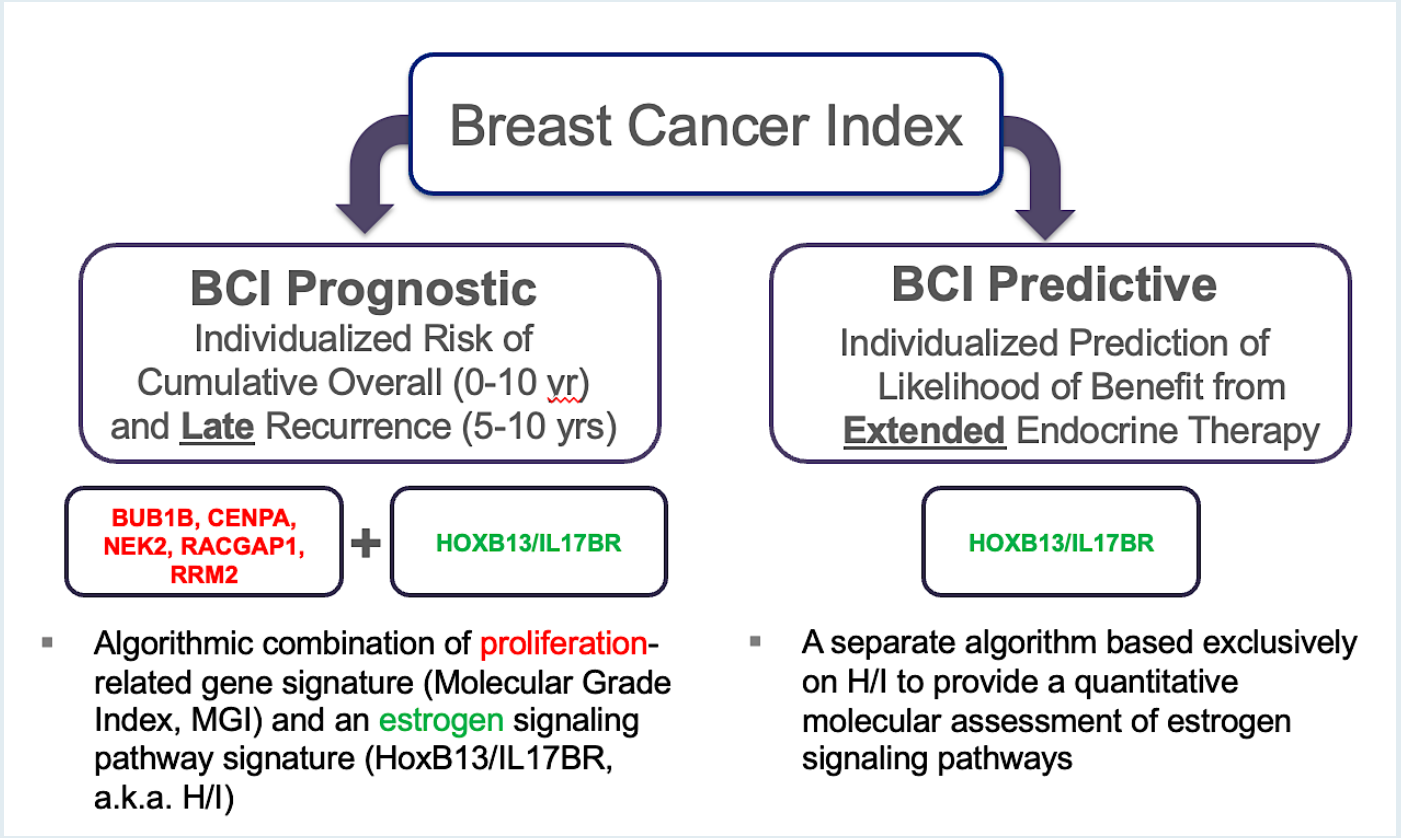


No. at Risk				
High grade	3054	1010	188	2
Moderate grade	7363	2761	474	6
Low grade	3524	1258	239	6

Pan H et al. *N Engl J Med* 2017;377(19):1836-46.

Breast Cancer Index (BCI)

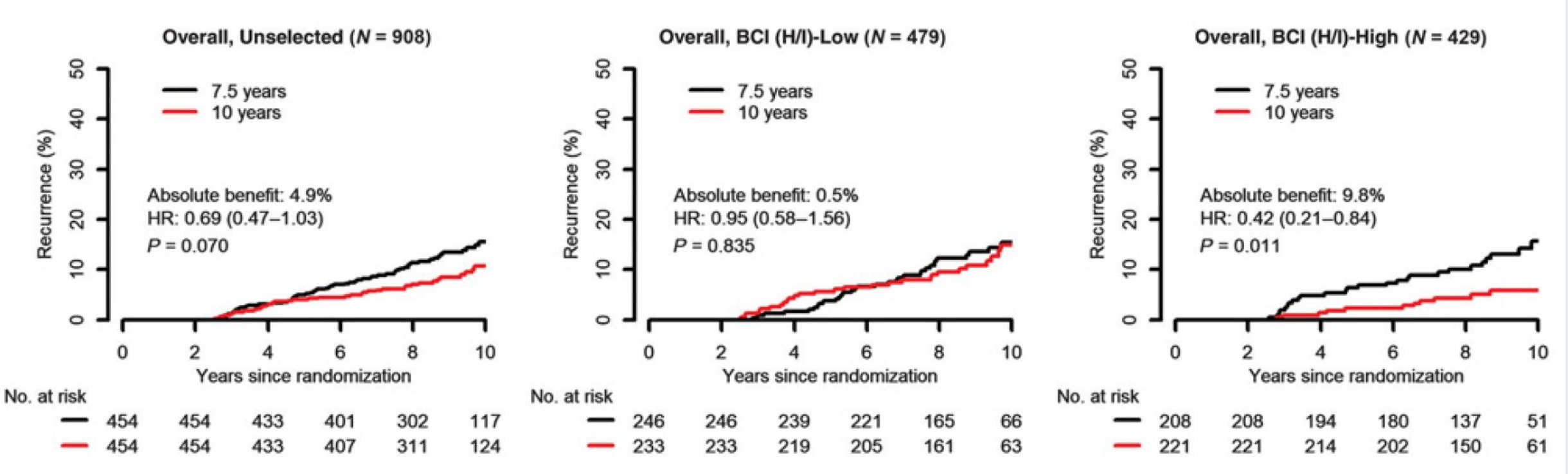
BCI Components



Distribution of BCI scores

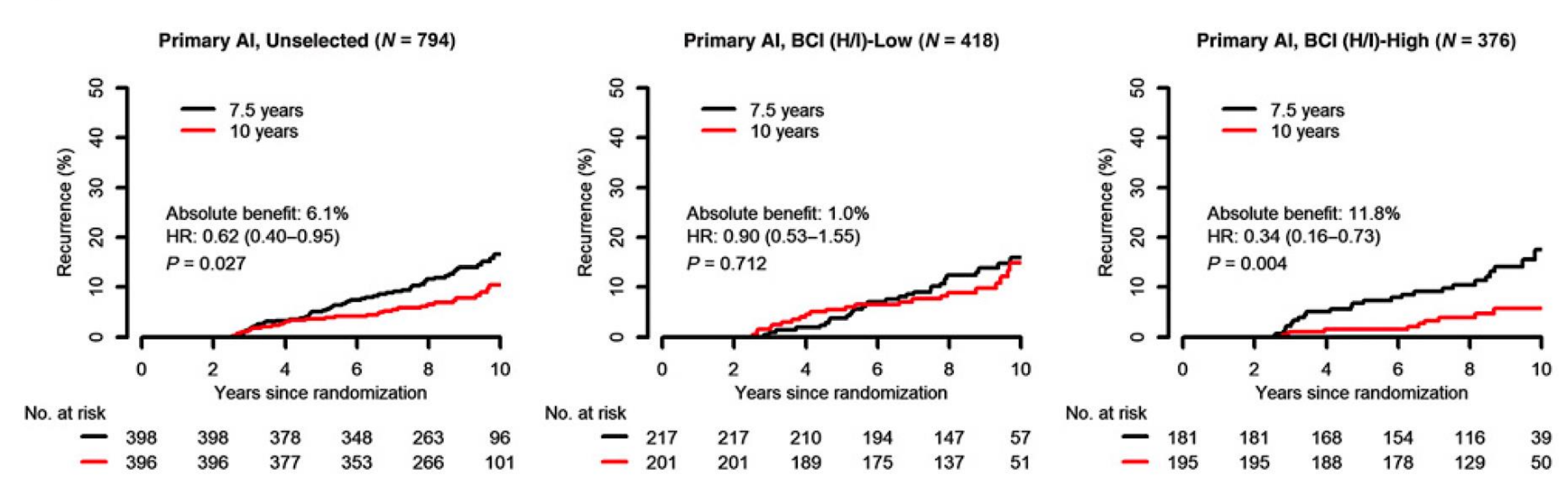
Sgroi DC et al. *J Natl Cancer Inst* 2013;105(14):1036-42.

Predictive Performance by BCI H/I Groups Based on Recurrence-Free Interval in the Overall Cohort of the Phase III IDEAL Trial



Noordhoek I et al. *Clin Cancer Res* 2021;27(1):311-19.

Predictive Performance by BCI H/I Groups Based on Recurrence-Free Interval in the Subset of Patients in the Phase III IDEAL Trial Who Received a Primary Aromatase Inhibitor (AI)



Noordhoek I et al. *Clin Cancer Res* 2021;27(1):311-19.

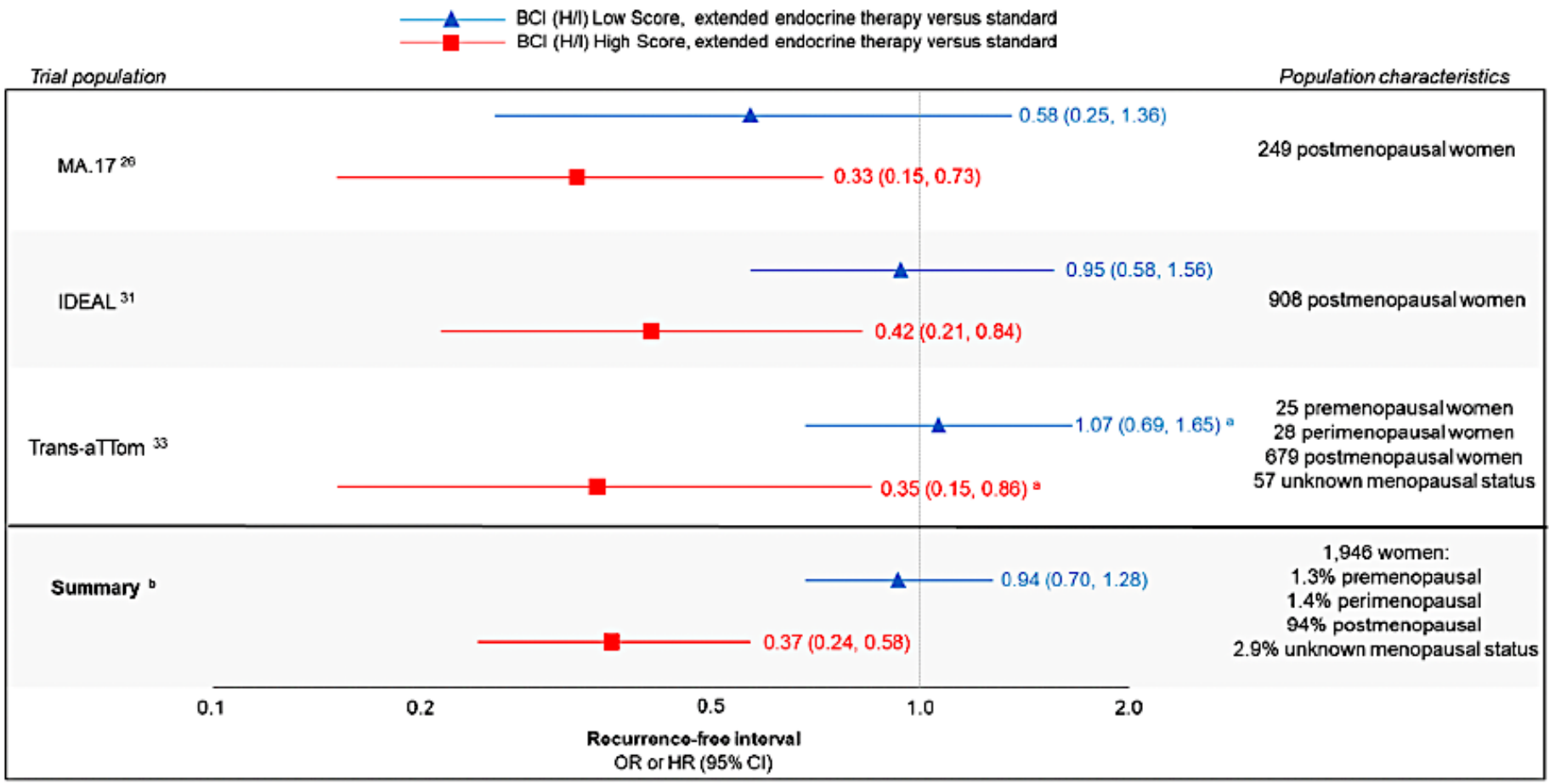
Risk of Recurrence at Year 10 Since Randomization for Patients Who Received 5 Years versus 2.5 Years of Additional Letrozole in the Overall Cohort and in the Primary AI Subset of the Phase III IDEAL Trial

Groups	5-year letrozole		2.5-year letrozole		HR (95% CI)*
	Number of Patients	10-year risk (95% CI)	Number of Patients	10-year risk (95% CI)	
Overall (N=908)					
Unselected	454 (100%)	10.6% (7.1-14.0)	454 (100%)	15.5% (11.5-19.3)	0.69 (0.47-1.03)
BCI (H/I)-High	221 (49%)	5.9% (2.3-9.3)	208 (46%)	15.7% (9.5-21.5)	0.42 (0.21-0.84)
BCI (H/I)-Low	233 (51%)	14.9% (9.1-20.3)	246 (54%)	15.4% (10.1-20.4)	0.95 (0.58-1.56)
Primary AI (N=794)					
Unselected	396 (100%)	10.5% (6.6-14.2)	398 (100%)	16.6% (12.1-20.8)	0.62 (0.40-0.95)
BCI (H/I)-High	195 (49%)	5.7% (1.9-9.4)	181 (45%)	17.5% (10.1-24.4)	0.34 (0.16-0.73)
BCI (H/I)-Low	201 (51%)	14.9% (8.2-21.1)	217 (55%)	15.9% (10.2-21.3)	0.90 (0.53-1.55)

*HR was calculated to compare 5-year letrozole vs. 2.5-year letrozole. HR=hazard ratio. CI=confidence interval.

Noordhoek I et al. *Clin Cancer Res* 2021;27(1):311-19.

BCI Validation in Extended-Adjuvant Therapy Trials



a. Estimates reported are from most recent update on results from this population.
b. Summary statistic calculated using a random effects model incorporating each study's OR or HR and its associated 95% confidence interval.

Woolpert KM et al. Breast Cancer Res Treat 2024;203(3):407-417.

ASCO Guideline: Extended Adjuvant Therapy

Extended Endocrine Therapy for ER-Positive HER2-Negative Breast Cancer

Oncotype DX, EndoPredict, Prosigna, Ki67, or IHC4.

Recommendation 1.23. If a patient has node-negative breast cancer and has had 5 years of endocrine therapy without evidence of recurrence, there is insufficient evidence to use Oncotype DX, EndoPredict, Prosigna, Ki67, or IHC4 scores to guide decisions about extended endocrine therapy (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).

Breast Cancer Index.

Recommendation 1.24. If a patient has node-negative or node-positive breast cancer with 1-3 positive nodes and has been treated with 5 years of primary endocrine therapy without evidence of recurrence, the clinician may offer the BCI test to guide decisions about extended endocrine therapy with either tamoxifen, an AI, or a sequence of tamoxifen followed by AI (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 1.25. If a patient has node-positive breast cancer with ≥ 4 positive nodes and has been treated with 5 years of primary endocrine therapy without evidence of recurrence, there is insufficient evidence to use the BCI test to guide decisions about extended endocrine therapy with either tamoxifen, an AI, or a sequence of tamoxifen followed by AI (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical treatment score post-5 years.

Recommendation 1.26. If a patient is postmenopausal and had invasive breast cancer and is recurrence-free after 5 years of adjuvant endocrine therapy, the clinical treatment score post-5 years (CTS5) web tool may be used to calculate the estimated risk of late recurrence (recurrence between years 5-10), which could assist in decisions about extended endocrine therapy (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).

Andre F et al. J Clin Oncol. 2022;40:1816-1837

Summary: ASCO Guideline 2022

ER+ and HER2–	Premenopausal or Age ≤ 50 Years (evidence quality/strength of recommendation)	Postmenopausal or Age > 50 Years (evidence quality/strength of recommendation)
Node-negative	Oncotype DX (*high/strong*)	Oncotype DX (*high/strong*) MammaPrint[a] (*intermediate/strong*) EndoPredict (*intermediate/moderate*) Prosigna (*intermediate/moderate*) Ki67[b] (*intermediate/moderate*) IHC4[b] (*intermediate/moderate*) BCI[c] (*intermediate/moderate*)
1-3 positive nodes	Insufficient evidence to recommend a biomarker for use	Oncotype DX (*high/strong*) MammaPrint[a] (*intermediate/strong*) EndoPredict (*intermediate/moderate*) Ki67[b] (*intermediate/strong*) IHC4[b] (*intermediate/moderate*) BCI[c] (*intermediate/moderate*)
≥ 4 positive nodes	Insufficient evidence to recommend a biomarker for use	
HER2+ (ER+ or ER–)	No mature evidence to recommend use of any other biomarker for this patient population	
ER–/HER2–	No mature evidence to recommend use of any other biomarker for this patient population	

Andre F et al. J Clin Oncol. 2022;40:1816-1837

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: Clinician Survey Results

Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer

Module 4: Clinician Survey Results

Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy

Module 6: Clinician Survey Results

Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

RTP
RESEARCH TO PRACTICE

Outside of a clinical trial, which genomic assay(s) do you routinely order to assist with decision-making regarding adjuvant systemic therapy for your patients with HR-positive, HER2-negative localized breast cancer (BC)?

 Dr Brufsky	Oncotype DX®, MammaPrint®, EndoPredict®, Breast Cancer Index®
 Dr DeMichele	Oncotype DX, MammaPrint, Breast Cancer Index
 Dr Kalinsky	Oncotype DX
 Dr Mahtani	Oncotype DX, MammaPrint, Breast Cancer Index
 Dr Mouabbi	Oncotype DX, MammaPrint, Breast Cancer Index
 Dr Rugo	Oncotype DX and MammaPrint
 Dr Sharma	Oncotype DX and MammaPrint
 Dr Stringer-Reasor	Oncotype DX and MammaPrint

RTP RESEARCH TO PRACTICE

Would you recommend adjuvant chemotherapy for a 40-year-old premenopausal patient with node-negative, HR-positive, HER2-negative localized BC and the 21-gene Recurrence Score® (RS) listed below?

	RS = 8	RS = 17	RS = 20
 Dr Brufsky	No	No	Yes, but offer OFS/OA as alternative
 Dr DeMichele	No	Yes, but offer OFS/OA as alternative	Yes
 Dr Kalinsky	No	No	Yes
 Dr Mahtani	No	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
 Dr Mouabbi	No	No	No
 Dr Rugo	No	No*	No*
 Dr Sharma	No	No	Yes, but offer OFS/OA as alternative
 Dr Stringer-Reasor	No	No	No

OFS/OA = ovarian function suppression/ovarian ablation; * Would offer OFS/OA

Would you recommend adjuvant chemotherapy for a 40-year-old premenopausal patient with HR-positive, HER2-negative localized BC with 3 positive nodes and the 21-gene RS listed below?

	RS = 8	RS = 17	RS = 20
 Dr Brufsky	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
 Dr DeMichele	Yes	Yes	Yes
 Dr Kalinsky	Yes	Yes	Yes
 Dr Mahtani	Yes	Yes	Yes
 Dr Mouabbi	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
 Dr Rugo	Yes	Yes	Yes
 Dr Sharma	Yes	Yes	Yes
 Dr Stringer-Reasor	Yes	Yes	Yes

OFS/OA = ovarian function suppression/ovarian ablation

Would you recommend adjuvant chemotherapy for a 65-year-old postmenopausal patient with HR-positive, HER2-negative localized BC with 3 positive nodes and the 21-gene RS listed below?

	RS = 8	RS = 17	RS = 20
 Dr Brufsky	No	No	No
 Dr DeMichele	No	No	No
 Dr Kalinsky	No	No	Yes
 Dr Mahtani	No	No	Yes
 Dr Mouabbi	No	No	No
 Dr Rugo	No	No	No
 Dr Sharma	No	No	No
 Dr Stringer-Reasor	No	No	No

Have you ordered or would you order a genomic assay to assist with treatment decision-making in the localized setting for any patients with HR-positive, HER2-negative localized BC and 4 or more positive nodes?

 Dr Brufsky	I have
 Dr DeMichele	I have not but would for the right patient
 Dr Kalinsky	I have not but would for the right patient
 Dr Mahtani	I have not and would not
 Dr Mouabbi	I have not and would not
 Dr Rugo	I have
 Dr Sharma	I have not and would not
 Dr Stringer-Reasor	I have

Outside of a clinical trial, which genomic assay(s) do you routinely order to assist with decision-making in the neoadjuvant setting for your patients with HR-positive, HER2-negative localized BC?

 Dr Brufsky	MammaPrint
 Dr DeMichele	MammaPrint**
 Dr Kalinsky	MammaPrint
 Dr Mahtani	MammaPrint
 Dr Mouabbi	MammaPrint
 Dr Rugo	MammaPrint and Oncotype DX*
 Dr Sharma	Oncotype DX and MammaPrint
 Dr Stringer-Reasor	MammaPrint

* All my patients with HR+ disease screen for I-SPY with rare exceptions and we order Mammaprint and BluePrint. I will occasionally order Oncotype DX. ** I-SPY only, I do not routinely order genomic assays in the neoadjuvant setting

RTP RESEARCH TO PRACTICE

Outside of a clinical trial, do you routinely employ Breast Cancer Index (BCI) to determine whether to continue adjuvant endocrine therapy beyond 5 years for patients with HR-positive, HER2-negative localized BC? If so, in which clinical situations?

 Dr Brufsky	Yes, for node-positive disease when MammaPrint not available
 Dr DeMichele	Yes, primarily for patients with intermediate risk disease who would like more information to assist with making the decision
 Dr Kalinsky	Yes, in situations where I'm on the fence about extending ET
 Dr Mahtani	Yes, for patients with N0 disease or up to 3 pos nodes
 Dr Mouabbi	Yes, for patients for whom we are considering extended ET
 Dr Rugo	No*
 Dr Sharma	Yes, for patients with high-risk, node-negative disease
 Dr Stringer-Reasor	Yes, for patients with HR-positive disease who may be lymph node-negative for whom extended therapy might be beneficial

ET = endocrine therapy; * No due to reimbursement issues, but I would for patients with poor tolerance to ET and high-risk disease

RTP RESEARCH TO PRACTICE

Approximately what proportion of the time would you estimate that having the results from BCI cause you to change your recommendation regarding extended-adjuvant endocrine therapy (ET)?

	Recommending ET to not recommending	Not recommending ET to recommending
 Dr Brufsky	25%	25%
 Dr DeMichele	20%	20%
 Dr Kalinsky	10%	10%
 Dr Mahtani	20%	20%
 Dr Mouabbi	80%	20%
 Dr Rugo	NA	NA
 Dr Sharma	10%	10%
 Dr Stringer-Reasor	10%	10%

NA = not applicable

Outside of a clinical trial, do you routinely employ any genomic assays other than Breast Cancer Index to determine whether to continue adjuvant endocrine therapy beyond 5 years for patients with HR-positive, HER2-negative localized BC?

 Dr Brufsky	Yes, MammaPrint
 Dr DeMichele	No
 Dr Kalinsky	No
 Dr Mahtani	No
 Dr Mouabbi	Yes, MammaPrint
 Dr Rugo	No
 Dr Sharma	No
 Dr Stringer-Reasor	Yes, MammaPrint

RTP RESEARCH TO PRACTICE

Have you ordered or would you order a circulating tumor DNA (ctDNA)-based molecular residual disease (MRD) assay to assist with clinical decision-making for a patient with localized BC? If you were to order a ctDNA-based MRD assay for a patient with localized BC, which specific assay(s) would you use?

	Order a ctDNA-based MRD assay?	Assay
 Dr Brufsky	I have	Signatera™
 Dr DeMichele	I have	Personalis® or Signatera
 Dr Kalinsky	I have not but would for the right patient	Signatera
 Dr Mahtani	I have not and would not	NA
 Dr Mouabbi	I have	Signatera
 Dr Rugo	I have	Signatera
 Dr Sharma	I have not and would not	NA
 Dr Stringer-Reasor	I have	Signatera or Guardant Reveal™

NA = not applicable

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

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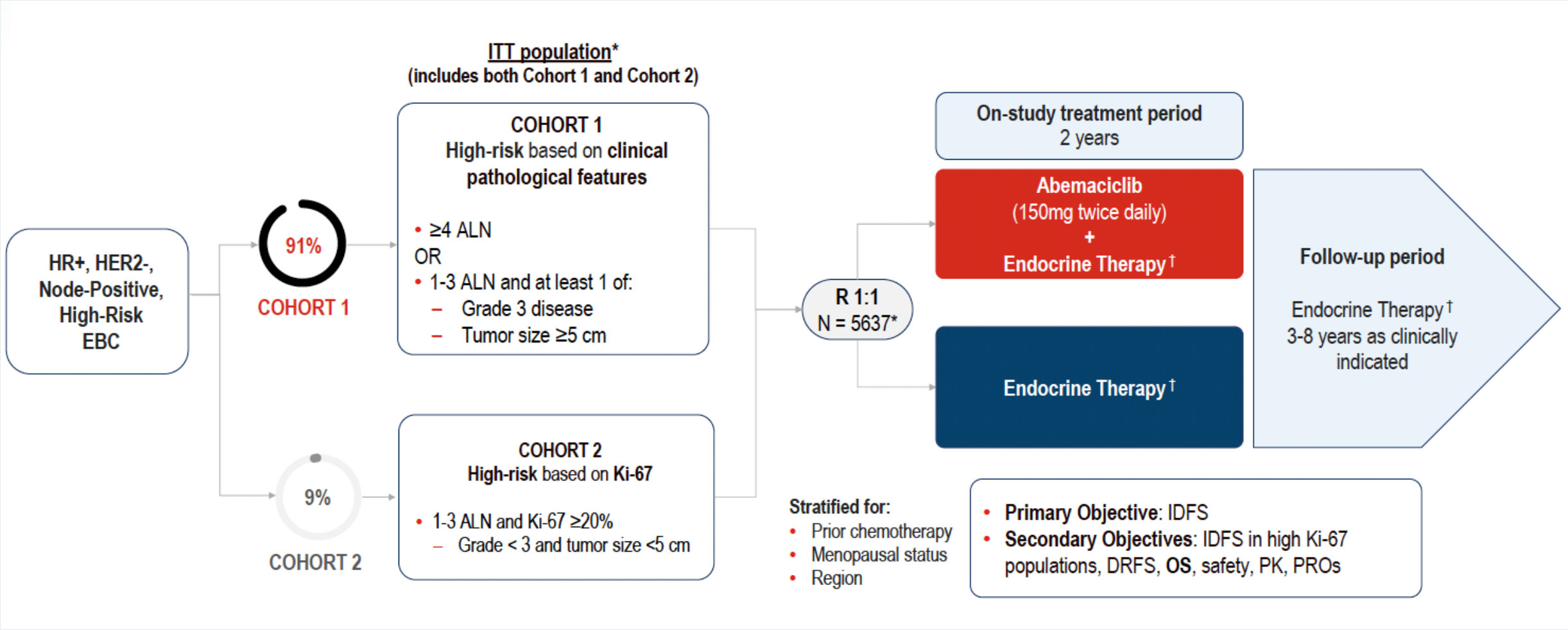
RTP
RESEARCH TO PRACTICE

Key Datasets

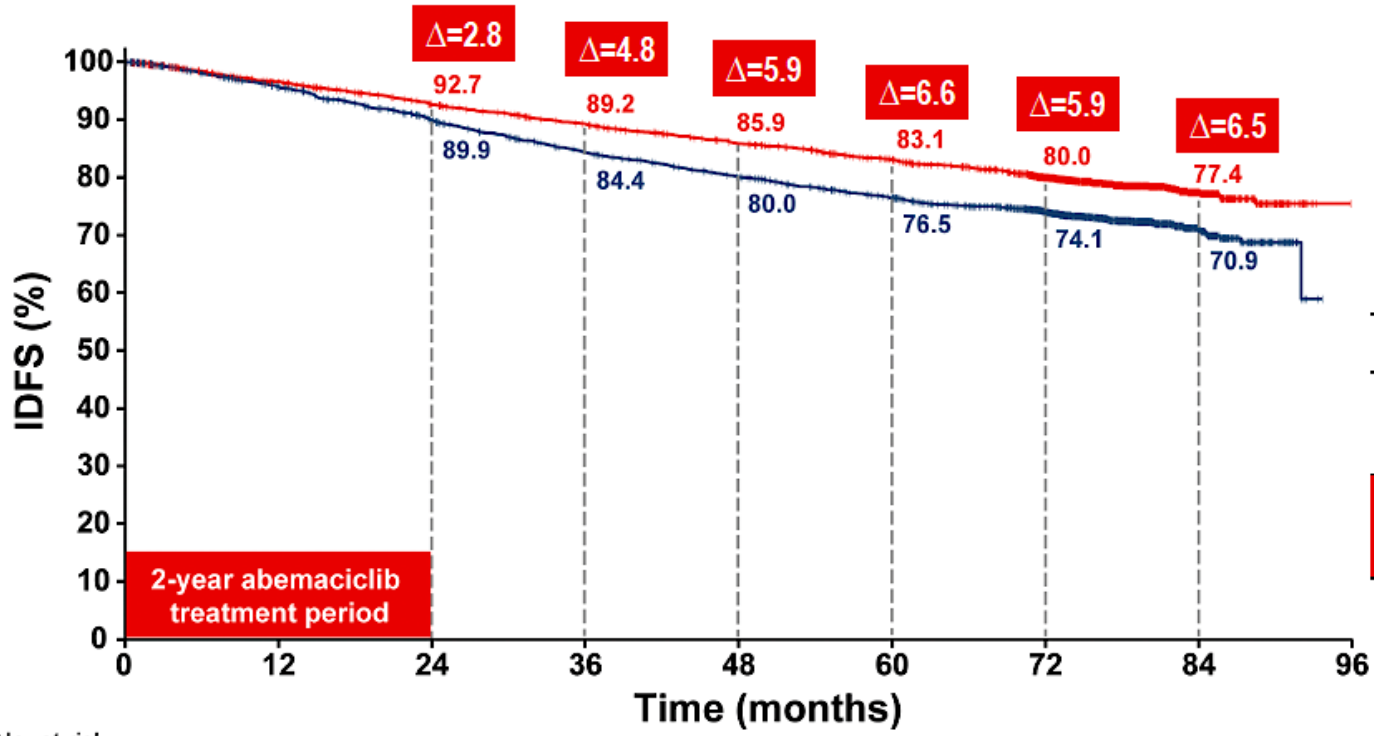
- Johnston S et al. **monarchE**: **Primary overall survival** (OS) results of adjuvant abemaciclib + endocrine therapy (ET) for HR+, HER2-, high-risk early breast cancer (EBC). ESMO 2025;Abstract LBA13.
- Johnston S et al. **Overall survival** with **abemaciclib** in early breast cancer. *Ann Oncol* 2026;37(2):155-65.
- Cortés J et al. **monarchE**: **Subgroup analysis** of adjuvant abemaciclib + endocrine therapy for HR+, HER2-, high-risk early breast cancer by nodal status. San Antonio Breast Cancer Symposium 2025;Abstract PS1-08-08.
- Crown JP et al. **Adjuvant ribociclib** (RIB) **plus nonsteroidal aromatase inhibitor** (NSAI) in patients (pts) with HR+/HER2− early breast cancer (EBC): **NATALEE 5-year outcomes**. ESMO 2025;Abstract LBA14.
- Chia SKL et al. Prognostic and predictive impact of baseline gene expression (exp) in the **NATALEE trial** of adjuvant (adj) ribociclib (RIB) + nonsteroidal aromatase inhibitor (NSAI) in HR+/HER2- early breast cancer (EBC). ASCO 2026;Abstract 501.

monarchE Study Design



Johnston S et al. ESMO 2025;Abstract LBA13. Johnston S et al. *Ann Oncol* 2026;37(2):155-65.

monarchE: Invasive Disease-Free Survival (IDFS) Outcomes



Number of IDFS events	
Abemaciclib + ET	ET
547	722

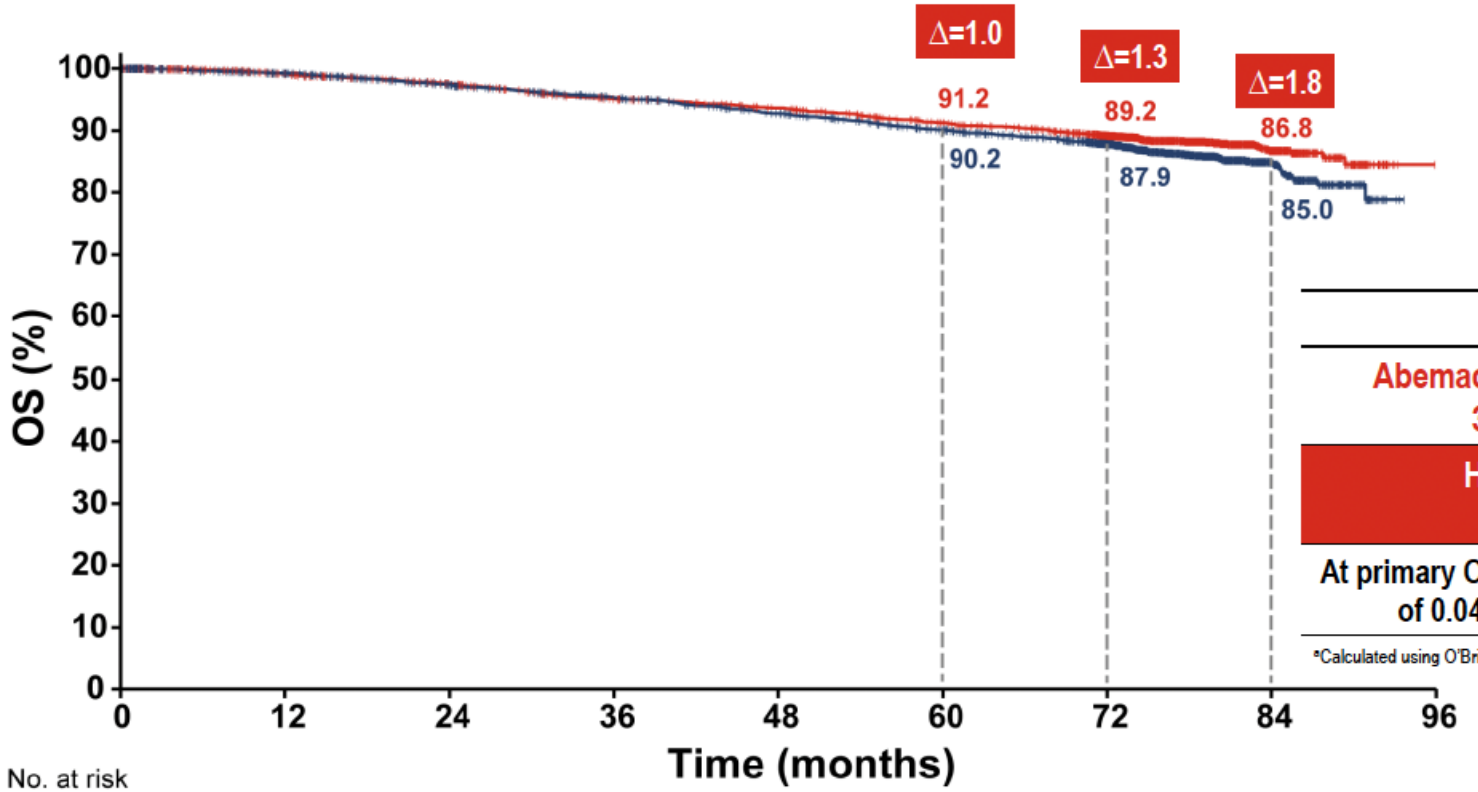
HR (95% CI): 0.734 (0.657, 0.820)
Nominal *P*<.0001

Abemaciclib + ET reduced the risk of IDFS events by 26.6% compared to ET alone

ET = endocrine therapy

Johnston S et al. ESMO 2025;Abstract LBA13. Johnston S et al. *Ann Oncol* 2026;37(2):155-65.

monarchE: Overall Survival (OS) Outcomes



Number of OS events	
Abemaciclib + ET	ET
301	360

HR (95% CI): 0.842 (0.722, 0.981)
***P*=0.0273**

At primary OS testing, OS in ITT met the critical boundary of 0.0434 (2-sided)[a] for statistical significance

[a]Calculated using O'Brien-Fleming type stopping boundary based on the observed number of events

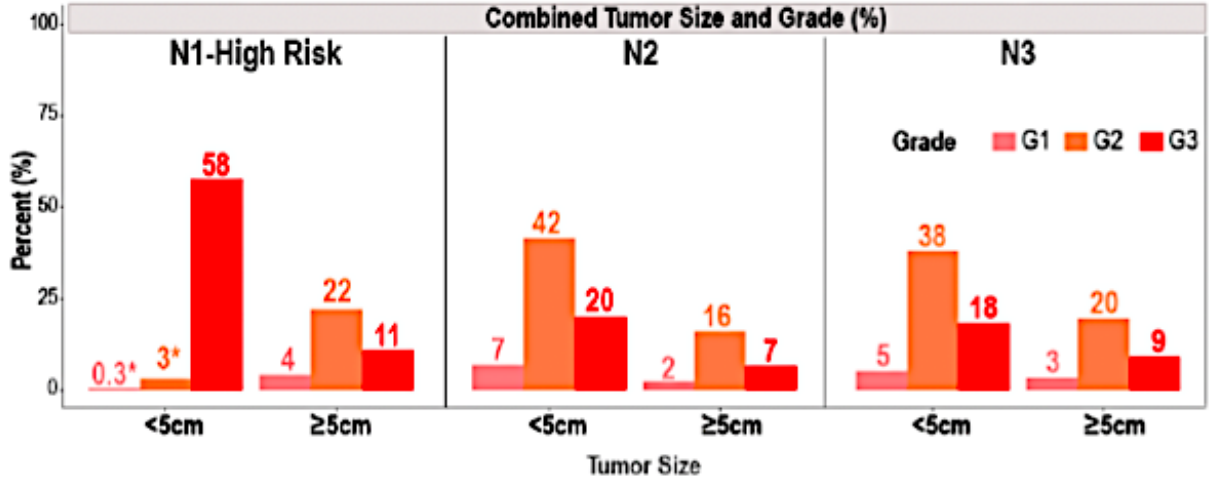
At a median follow-up of 6.3 years, abemaciclib + ET reduced the risk of death by 15.8% compared to ET alone

Johnston S et al. ESMO 2025;Abstract LBA13. Johnston S et al. *Ann Oncol* 2026;37(2):155-65.

monarchE: Subgroup Analysis by Nodal Status

Tumor Characteristics in Cohort 1

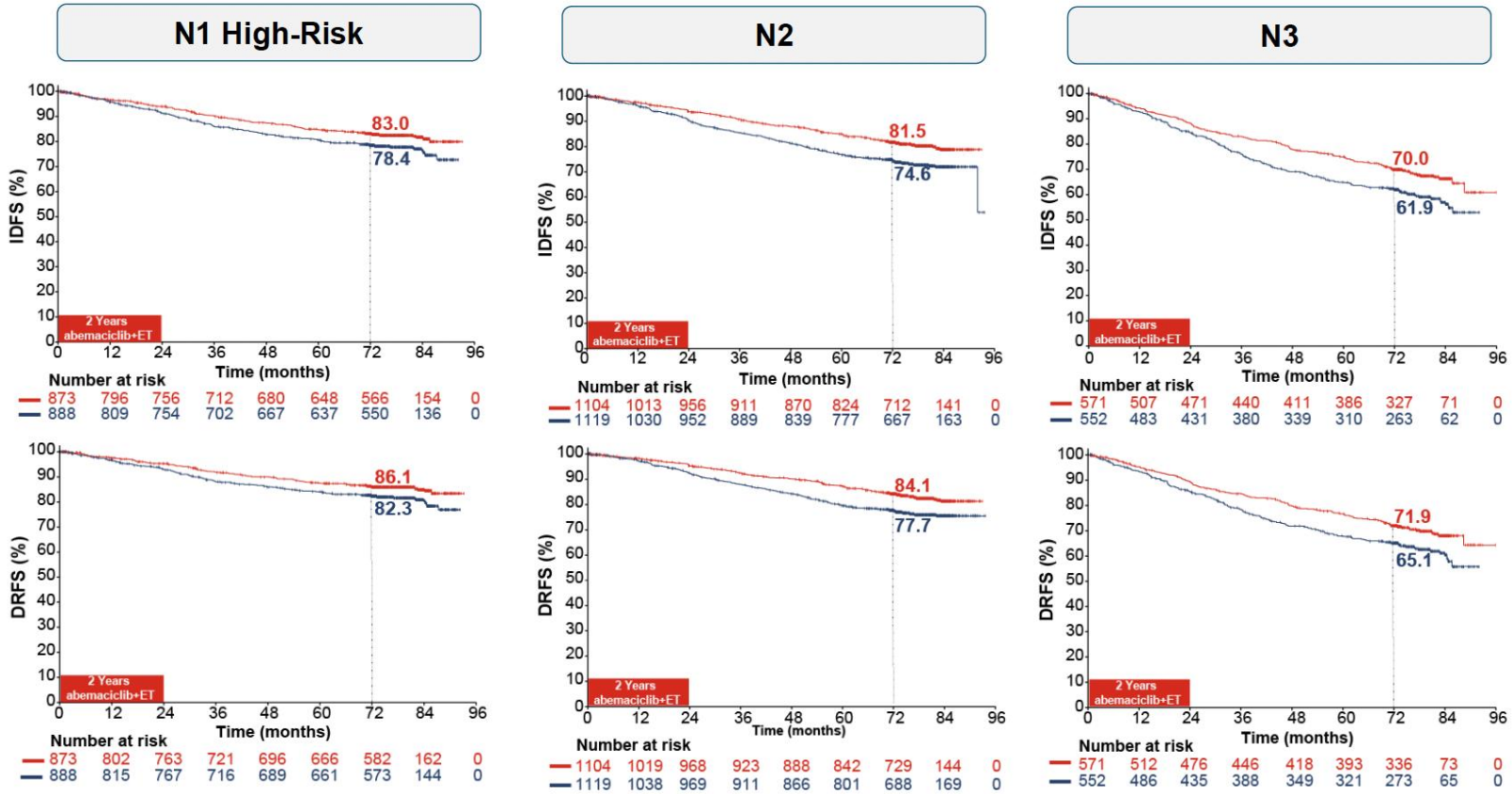
	N1-High Risk	N2	N3
Ki-67 (%)			
<20%	29	43	41
≥20%	49	33	36
Missing	23	24	24
Histology (%)			
Lobular	11	13	20
Ductal	72	68	62
Other	17	20	18



- monarchE eligible patients with N1 high risk disease presented more Grade 3 tumors and Ki-67 ≥20% compared to N2 and N3
- Distribution of ductal/lobular histology was similar in N1-high risk and N2 while N3 had more lobular tumors
- Over 40% of patients with N1-High risk disease received neoadjuvant chemotherapy compared to less than 30% of those with N3 disease
- Conversely, the use of adjuvant chemotherapy and radiation therapy was higher among patients with N2 and N3 disease

Cortés J et al. San Antonio Breast Cancer Symposium 2025;Abstract PS1-08-08.

monarchE: IDFS and DRFS by Nodal Status

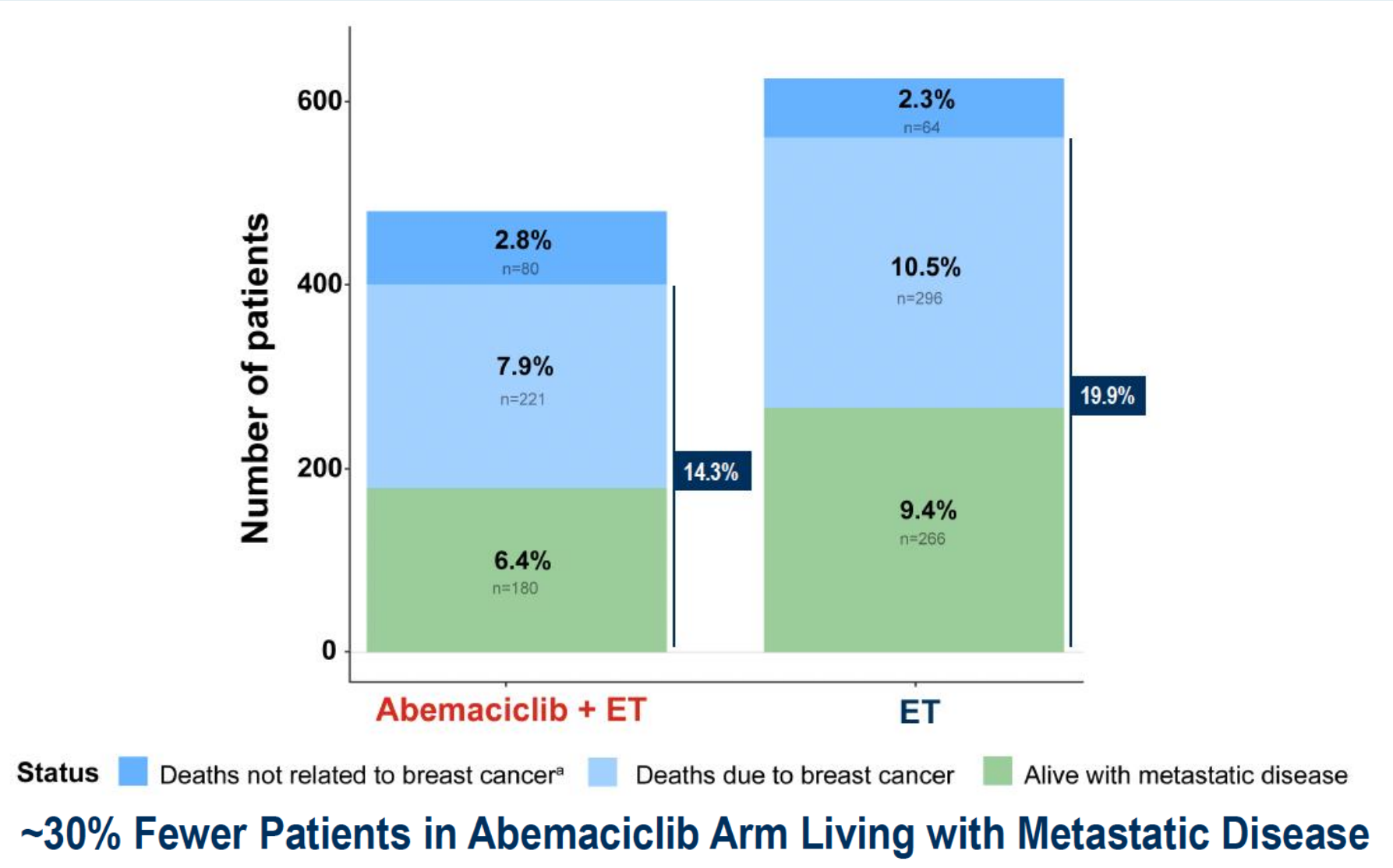


- In the ET alone arm, patients with N1-High risk and N2 disease had comparable risk of recurrence and death, while higher risk was observed in N3 subgroup
- Abemaciclib plus ET reduced the risk of IDFS events by 24.8% (N1), 31.5% (N2) and 27.4% (N3), compared to ET

DRFS = distant relapse-free survival

Cortés J et al. San Antonio Breast Cancer Symposium 2025;Abstract PS1-08-08.

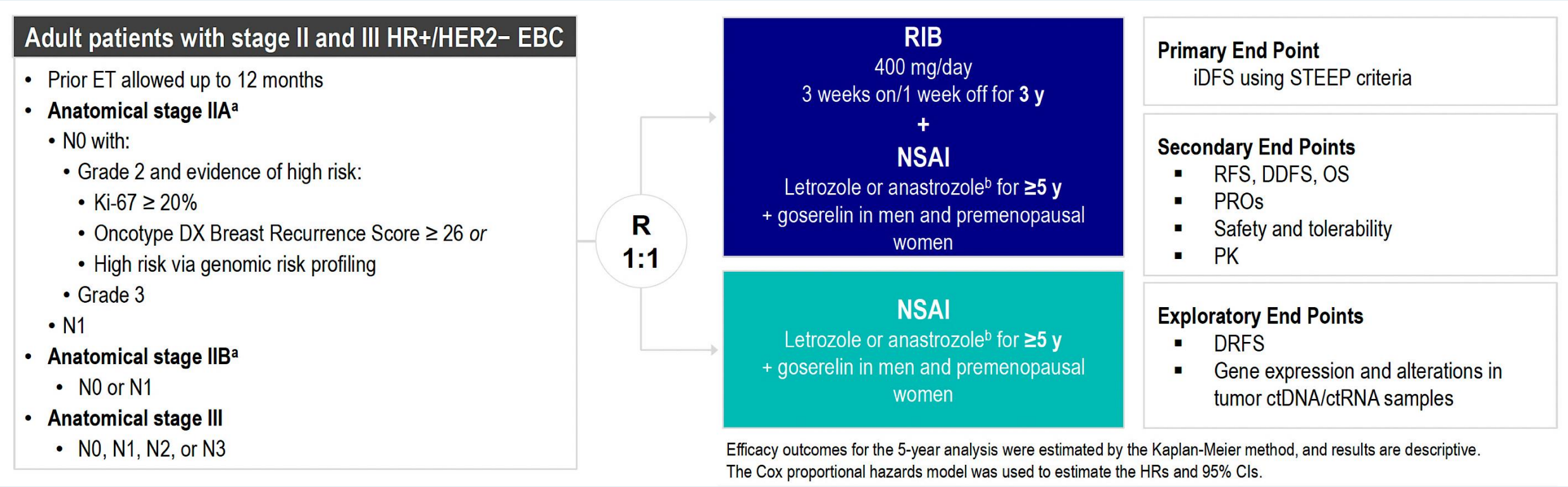
monarchE: Survival Status



~30% Fewer Patients in Abemaciclib Arm Living with Metastatic Disease

Johnston S et al. ESMO 2025;Abstract LBA13. Johnston S et al. *Ann Oncol* 2026;37(2):155-65.

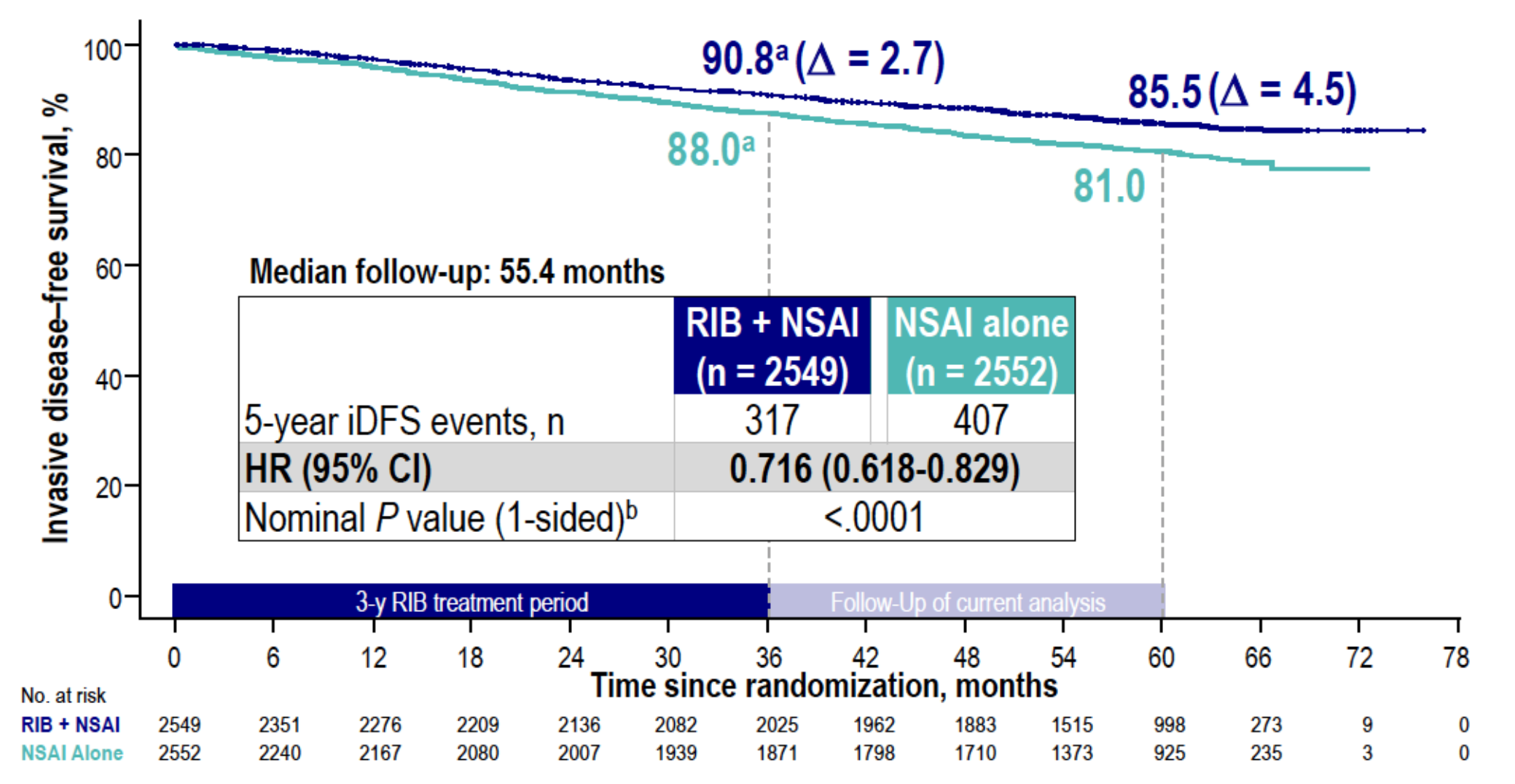
NATALEE Study Design



RIB = ribociclib; NSAI = nonsteroidal aromatase inhibitor

Crown JP et al. ESMO 2025;Abstract LBA14.

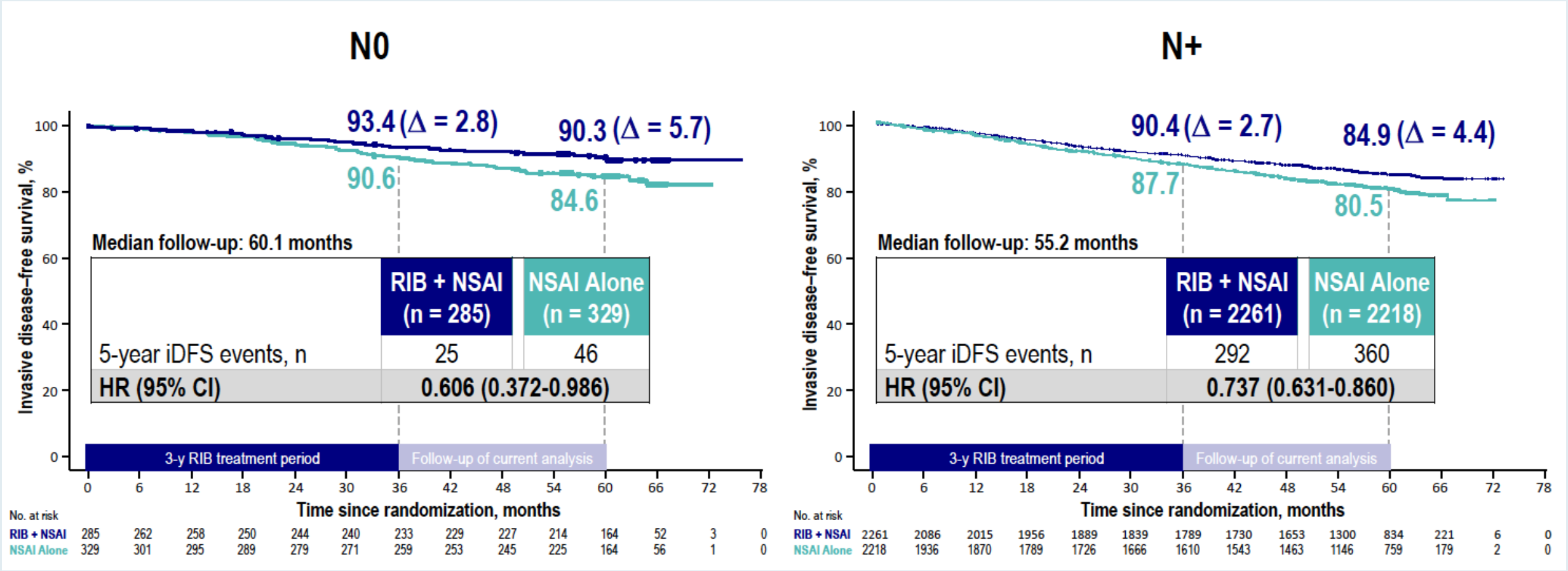
NATALEE: IDFS Outcomes



RIB = ribociclib; NSAI = nonsteroidal aromatase inhibitor

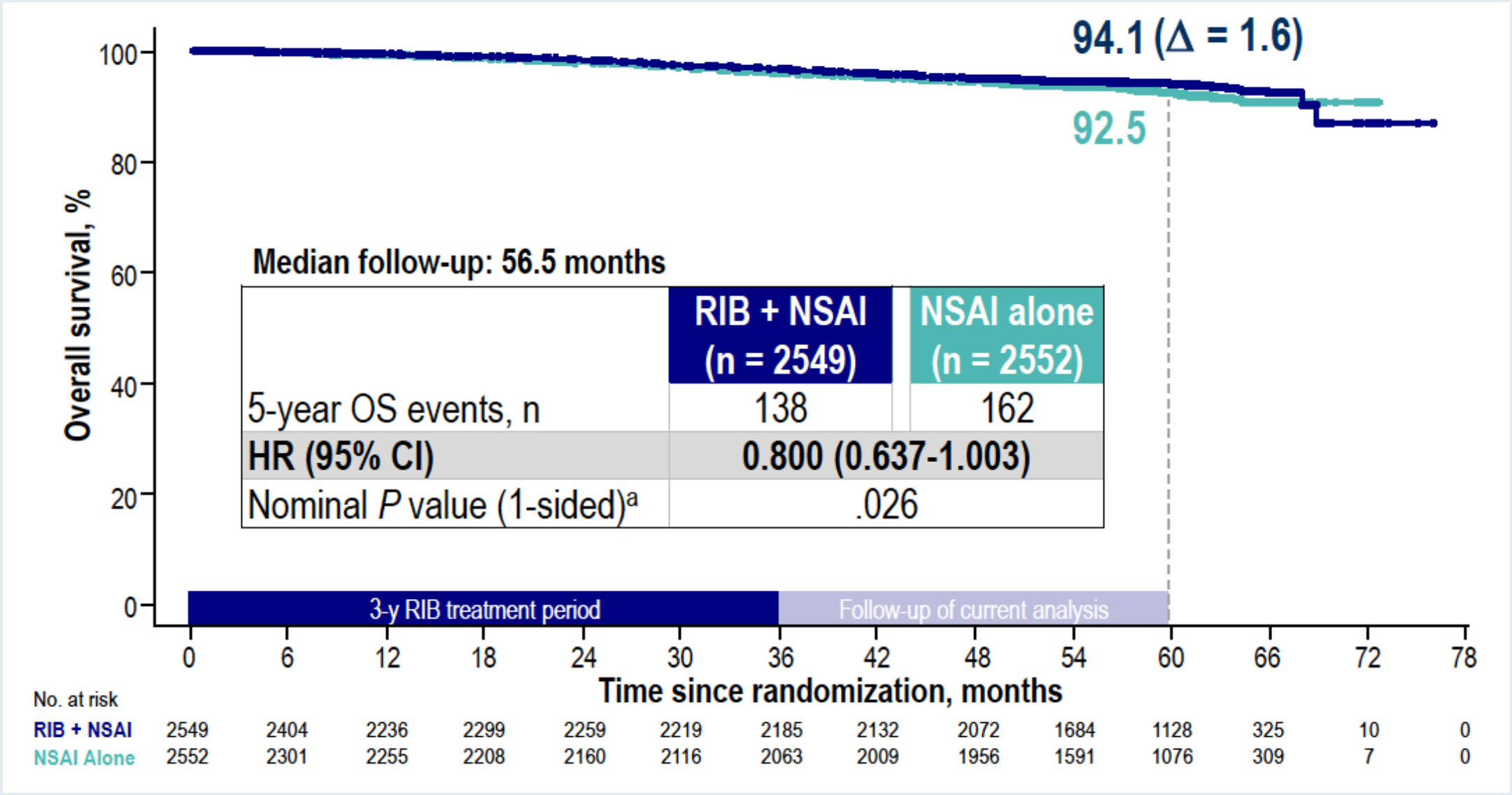
Crown JP et al. ESMO 2025;Abstract LBA14.

NATALEE: IDFS by Nodal Status



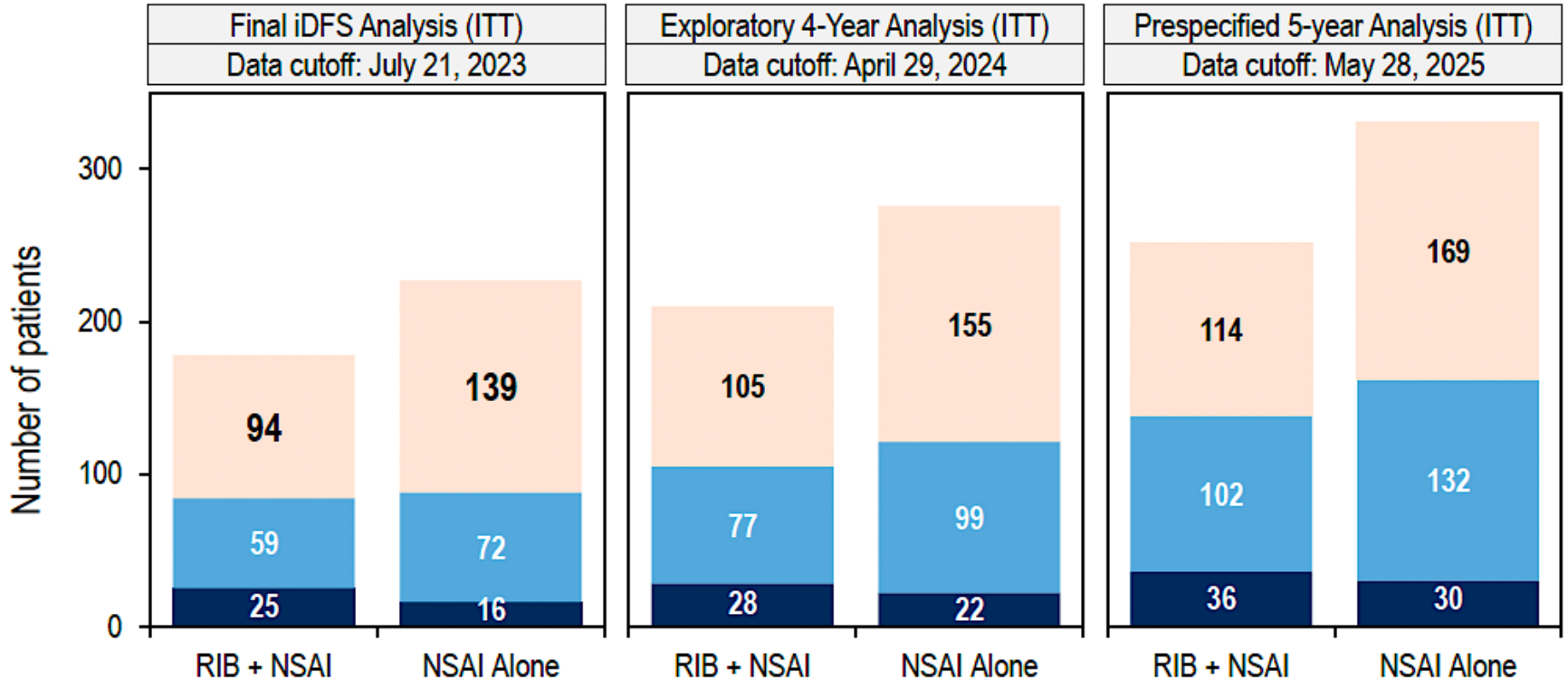
Crown JP et al. ESMO 2025;Abstract LBA14.

NATALEE: OS Outcomes



Crown JP et al. ESMO 2025;Abstract LBA14.

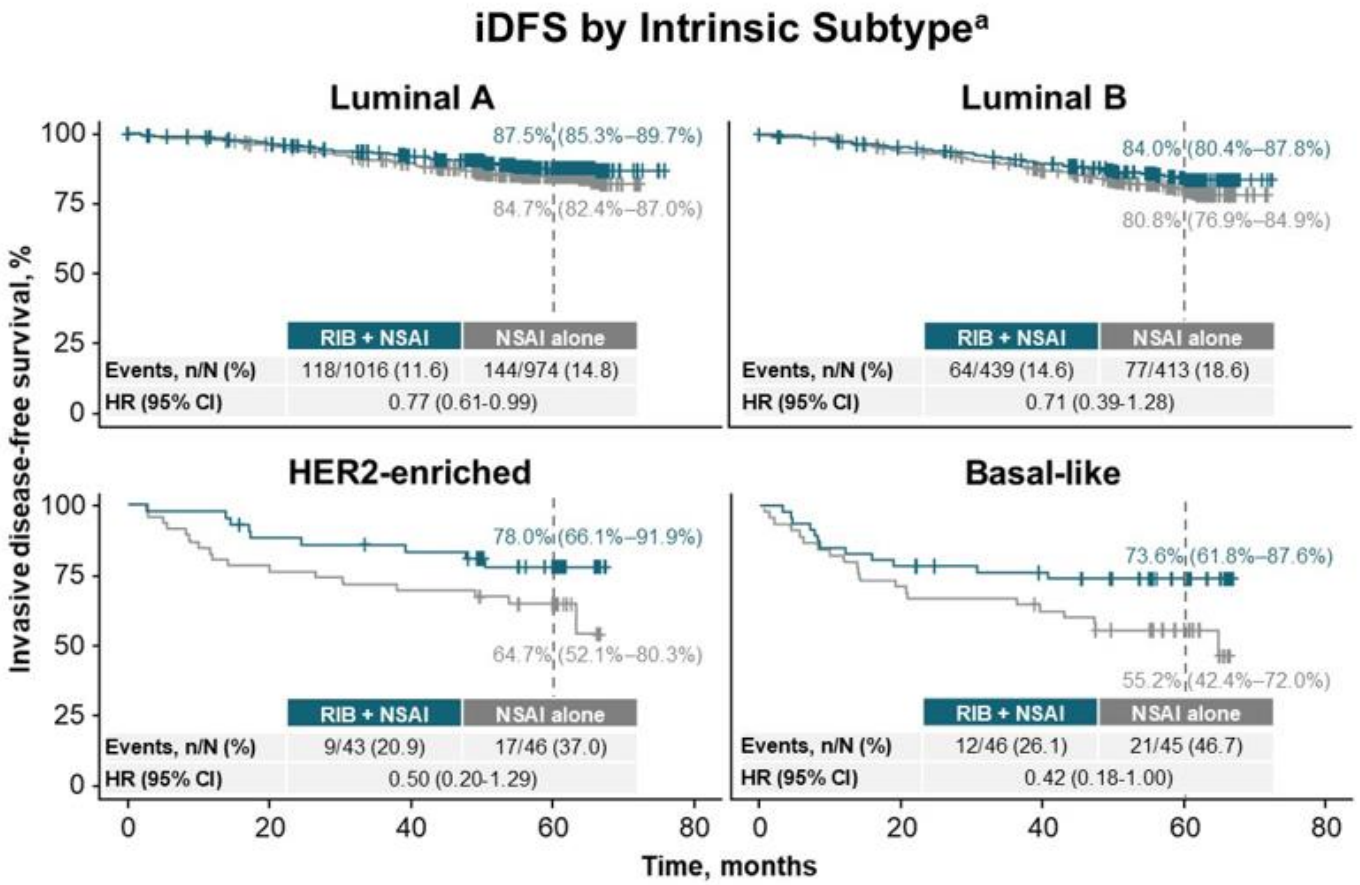
NATALEE: Survival Status over Time

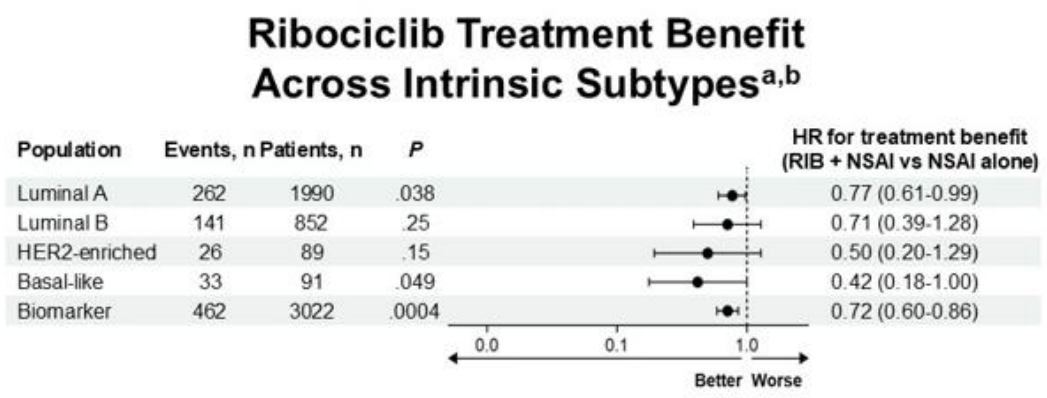


Approximate median follow-up (months)	36	44	57
OS HR (95% CI)	0.89 (0.66-1.20)	0.83 (0.64-1.07)	0.800 (0.637-1.003)

Crown JP et al. ESMO 2025;Abstract LBA14.

NATALEE: Ribociclib Treatment Benefit Is Observed Across PAM50-Based Intrinsic Subtypes



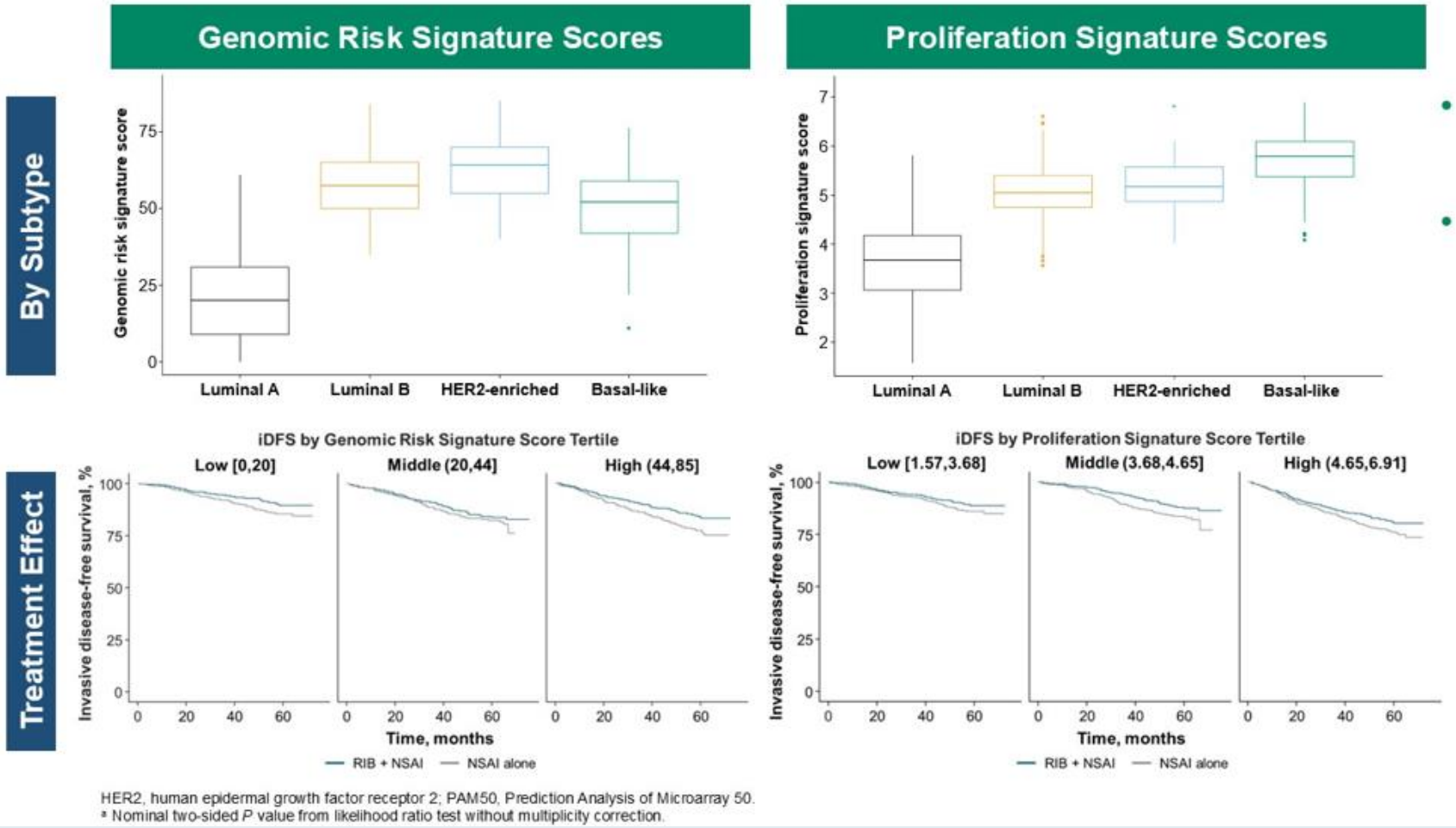


- Across treatment arms, PAM50 subtypes were strongly prognostic (hazard ratio vs luminal A: luminal B, 1.39; HER2-enriched, 2.62; basal-like, 3.92[c])
- No significant interaction between subtype and treatment was observed (*P*=.34[d])

HER2, human epidermal growth factor receptor 2; HR, hazard ratio; iDFS, invasive disease–free survival; NSAI, nonsteroidal aromatase inhibitor; PAM50, Prediction Analysis of Microarray 50; RIB, ribociclib.
[a] HRs were estimated using Cox proportional hazards models stratified by the four main strata and including a term for biomarker-by-treatment interaction. [b] The p-values for treatment effects within individual biomarker subgroups are model-based nominal two-sided Wald p-values without multiplicity correction. [c] HRs were obtained from Cox proportional hazards models stratified by the four main strata and adjusted for treatment group. [d] Nominal two-sided p-value from likelihood ratio test without multiplicity correction.

Chia SKL et al. ASCO 2026;Abstract 501.

NATALEE: Higher Genomic Risk Signature and Proliferation Signature Scores Are Associated with Increased Ribociclib Benefit

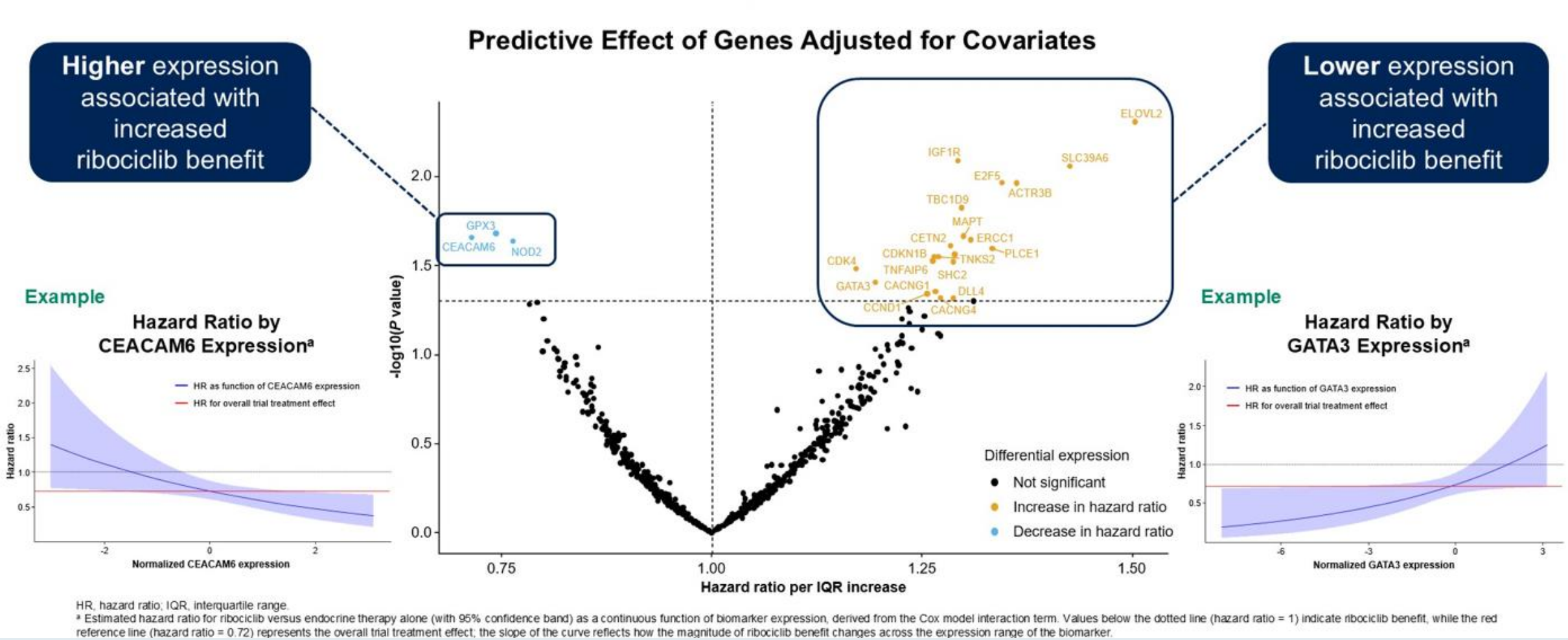


HER2, human epidermal growth factor receptor 2; PAM50, Prediction Analysis of Microarray 50.
[a] Nominal two-sided *P* value from likelihood ratio test without multiplicity correction.

- Gene signatures were associated with PAM50 subtypes
- Higher genomic risk signature or proliferation signature scores showed a trend for increased ribociclib benefit, with no significant treatment interaction (*P*=.42 and *P*=.84, respectively[a])
- Of note, patients with N0 disease had significantly higher genomic risk scores and proliferation scores than those with N1-N3 disease

Chia SKL et al. ASCO 2026;Abstract 501.

NATALEE: Differential Gene Expression Affects Ribociclib Benefit



HR, hazard ratio; IQR, interquartile range.
[a] Estimated hazard ratio for ribociclib versus endocrine therapy alone (with 95% confidence band) as a continuous function of biomarker expression, derived from the Cox model interaction term. Values below the dotted line (hazard ratio = 1) indicate ribociclib benefit, while the red reference line (hazard ratio = 0.72) represents the overall trial treatment effect; the slope of the curve reflects how the magnitude of ribociclib benefit changes across the expression range of the biomarker.

Chia SKL et al. ASCO 2026;Abstract 501.

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: Clinician Survey Results

Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer

Module 4: Clinician Survey Results

Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy

Module 6: Clinician Survey Results

Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, would you generally recommend an adjuvant CDK4/6 inhibitor in addition to adjuvant endocrine therapy to a patient with 5.5-cm, Grade 2, HR-positive, HER2-negative localized BC and the following nodal status?

	Node-negative	2 positive nodes	4 positive nodes
 Dr Brufsky	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
 Dr DeMichele	Yes, ribociclib	Yes, either	Yes, abemaciclib
 Dr Kalinsky	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
 Dr Mahtani	Yes, ribociclib	Yes, either	Yes, either
 Dr Mouabbi	Yes, ribociclib	Yes, either	Yes, either
 Dr Rugo	Yes, ribociclib	Yes, either	Yes, abemaciclib
 Dr Sharma	Yes, ribociclib	Yes, either	Yes, either
 Dr Stringer-Reasor	Yes, ribociclib	Yes, ribociclib	Yes, either

Regulatory and reimbursement issues aside, would you generally recommend an adjuvant CDK4/6 inhibitor in addition to adjuvant endocrine therapy to a patient with 2.5-cm Grade 2, HR-positive, HER2-negative localized BC and the following nodal status?

	Node-negative	2 positive nodes	4 positive nodes
 Dr Brufsky	No	No	Yes, abemaciclib
 Dr DeMichele	No	Yes, either	Yes, abemaciclib
 Dr Kalinsky	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
 Dr Mahtani	No	Yes, ribociclib	Yes, either
 Dr Mouabbi	No	Yes, either	Yes, either
 Dr Rugo	Yes, ribociclib	Yes, either	Yes, abemaciclib
 Dr Sharma	No	Yes, either	Yes, either
 Dr Stringer-Reasor	Yes, ribociclib	Yes, ribociclib	Yes, either

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: Clinician Survey Results

Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer

Module 4: Clinician Survey Results

Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy

Module 6: Clinician Survey Results

Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

RTP
RESEARCH TO PRACTICE

Key Datasets

- Rugo HS et al. **Adjuvant abemaciclib** combined **with endocrine therapy** for high-risk early breast cancer: **Safety and patient-reported outcomes** from the **monarchE** study. *Ann Oncol* 2022;33(6):616-27.
- Barrios C et al. **NATALEE update**: **Safety and treatment (tx) duration** of **ribociclib** (RIB) + **nonsteroidal aromatase inhibitor** (NSAI) in patients (pts) with HR+/HER2− early breast cancer (EBC). ESMO Breast 2024;Abstract 113MO.
- Mayer EL et al. **TRADE:** A **phase II** trial to assess the **tolerability of abemaciclib dose escalation** in early-stage HR-positive/HER2-negative breast cancer. *Ann Oncol* 2025;31(1):117-24.

RTP
RESEARCH TO PRACTICE

monarchE: Overall Safety Profile

Table 1. Clinically relevant adverse events observed in the abemaciclib + ET arm regardless of causality

	Abemaciclib + ET (*N* = 2791)				ET alone (*N* = 2800)			
	Any grade	G1	G2	G ≥ 3	Any grade	G1	G2	G ≥ 3
≥10% in the abemaciclib + ET arm								
Patients with ≥1 AE,[a] *n* (%)	2745 (98.4)	165 (5.9)	1192 (42.7)	1388 (49.7)	2486 (88.8)	634 (22.6)	1396 (49.9)	456 (16.3)
Diarrhea	2331 (83.5)	1255 (45.0)	857 (30.7)	219 (7.8)[b]	242 (8.6)	184 (6.6)	52 (1.9)	6 (0.2)
Infections[c]	1429 (51.2)	245 (8.8)	1029 (36.9)	155 (5.6)	1102 (39.4)	229 (8.2)	790 (28.2)	83 (3.0)[d]
Neutropenia	1278 (45.8)	178 (6.4)	554 (19.8)	546 (19.6)	157 (5.6)	66 (2.4)	68 (2.4)	23 (0.8)
Fatigue	1133 (40.6)	632 (22.6)	421 (15.1)	80 (2.9)	499 (17.8)	378 (13.5)	117 (4.2)	4 (0.1)
Nausea	824 (29.5)	623 (22.3)	187 (6.7)	14 (0.5)	252 (9.0)	198 (7.1)	52 (1.9)	2 (0.1)
Anemia	681 (24.4)	383 (13.7)	241 (8.6)	57 (2.0)	104 (3.7)	75 (2.7)	19 (0.7)	10 (0.4)
Headache	546 (19.6)	415 (14.9)	123 (4.4)	8 (0.3)	421 (15.0)	321 (11.5)	95 (3.4)	5 (0.2)
Vomiting	491 (17.6)	375 (13.4)	101 (3.6)	15 (0.5)	130 (4.6)	98 (3.5)	29 (1.0)	3 (0.1)
Stomatitis[e]	385 (13.8)	309 (11.1)	72 (2.6)	4 (0.1)	151 (5.4)	133 (4.8)	18 (0.6)	0 (0.0)
Thrombocytopenia	373 (13.4)	276 (9.9)	61 (2.2)	36 (1.3)	52 (1.9)	40 (1.4)	8 (0.3)	4 (0.1)
Decreased appetite	329 (11.8)	243 (8.7)	70 (2.5)	16 (0.6)	68 (2.4)	53 (1.9)	13 (0.5)	2 (0.1)
Alopecia	313 (11.2)	283 (10.1)	30 (1.1)	N/A	75 (2.7)	68 (2.4)	7 (0.3)	0 (0.0)
Alanine aminotransferase increase (ALT)	343 (12.3)	184 (6.6)	82 (2.9)	77 (2.8)	157 (5.6)	113 (4.0)	25 (0.9)	19 (0.7)
Aspartate aminotransferase increase (AST)	330 (11.8)	220 (7.9)	58 (2.1)	52 (1.9)	137 (4.9)	103 (3.7)	19 (0.7)	15 (0.5)
Rash	312 (11.2)	239 (8.6)	61 (2.2)	11 (0.4)	127 (4.5)	104 (3.7)	23 (0.8)	0 (0.0)
Other AEs of interest—composite terms								
VTE[f]	71 (2.5)	2 (0.1)	31 (1.1)	38 (1.4)[h]	17 (0.6)	0 (0.0)	9 (0.3)	8 (0.3)
PE[g]	28 (1.0)	N/A	N/A	28 (1.0)[i]	4 (0.1)	N/A	N/A	4 (0.1)
ILD[j]	89 (3.2)	44 (1.6)	34 (1.2)	11 (0.4)	37 (1.3)	26 (0.9)	10 (0.4)	1 (0.0)
Pneumonitis	49 (1.8)	21 (0.8)	21 (0.8)	7 (0.3)	10 (0.4)	7 (0.3)	3 (0.1)	0 (0.0)
Radiation pneumonitis	25 (0.9)	13 (0.5)	10 (0.4)	2 (0.1)	15 (0.5)	9 (0.3)	5 (0.2)	1 (0.0)
Increased transaminases[k]	433 (15.5)	241 (8.6)	94 (3.4)	98 (3.5)	209 (7.5)	143 (5.1)	38 (1.4)	28 (1.0)

Rugo HS et al. *Ann Oncol* 2022;33(6):616-27.

monarchE: Serious and Fatal Adverse Events (AEs) in Long-Term Follow-Up

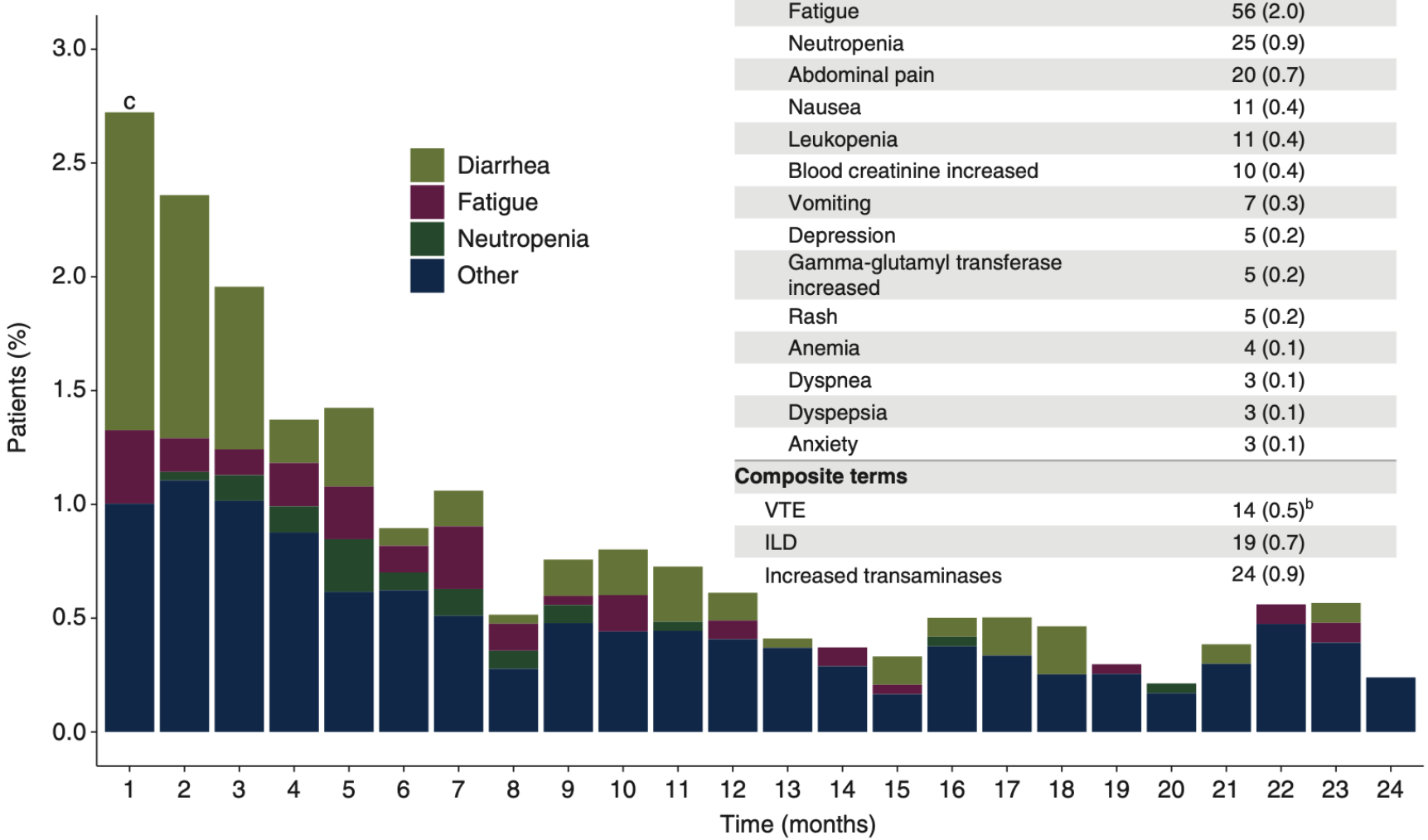
	Abemaciclib + ET N=2791, n (%)		ET N=2800, n (%)	
	On Therapy[a]	Post-Discontinuation[b]	On Therapy[a]	Post-Discontinuation[b]
≥1 SAE* LTFU, regardless of causality	**NA**	**197 (7.5)**	**NA**	**213 (8.1)**
Deaths due to AE by SOC and PT[c]	**15 (0.5)**	**44 (1.6)**	**11 (0.4)**	**30 (1.1)**
Infections and infestations	3 (0.1)	13 (0.5)	5 (0.2)	5 (0.2)
COVID-19	3 (0.1)	6 (0.2)	1 (<0.1)	2 (0.1)
Second primary neoplasm	0 (0)	13 (0.5)	1 (<0.1)	7 (0.3)
Cardiac disorders	5 (0.2)	6 (0.2)	0 (0)	9 (0.3)

Consistent safety results from prior analyses, as all treated patients completed treatment ≥ 4 years ago
No relevant differences between treatment arms in causes of deaths due to AEs

SAE = serious adverse event; LTFU = long-term follow-up; SOC = standard of care

Johnston S et al. ESMO 2025;Abstract LBA13. Johnston S et al. *Ann Oncol* 2026;37(2):155-65.

monarchE: AEs Leading to Discontinuation

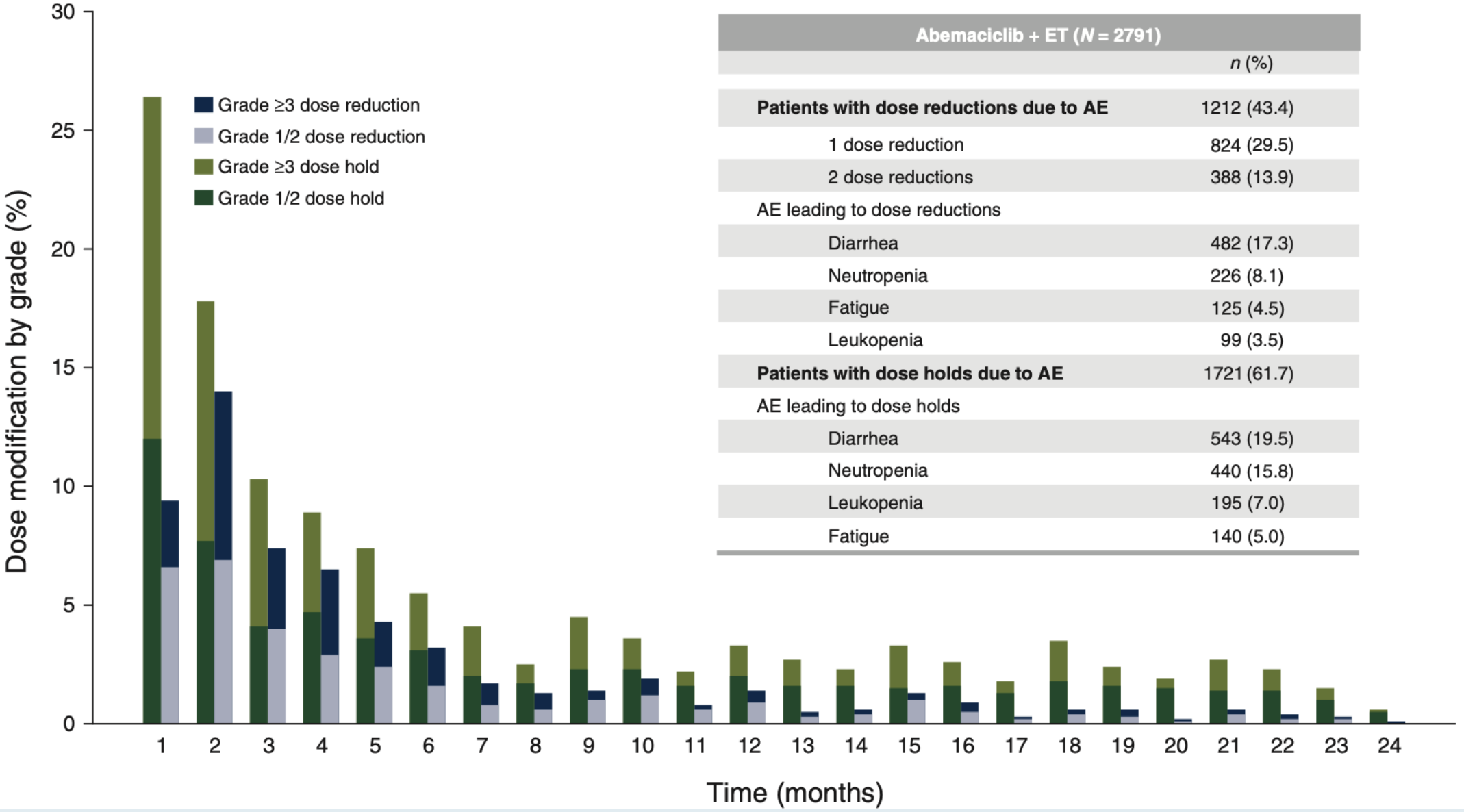


Abemaciclib + ET (*N* = 2791)	
AEs leading to discontinuation	***n* (%)**
Diarrhea	147 (5.3)
Fatigue	56 (2.0)
Neutropenia	25 (0.9)
Abdominal pain	20 (0.7)
Nausea	11 (0.4)
Leukopenia	11 (0.4)
Blood creatinine increased	10 (0.4)
Vomiting	7 (0.3)
Depression	5 (0.2)
Gamma-glutamyl transferase increased	5 (0.2)
Rash	5 (0.2)
Anemia	4 (0.1)
Dyspnea	3 (0.1)
Dyspepsia	3 (0.1)
Anxiety	3 (0.1)
Composite terms	
VTE	14 (0.5)[b]
ILD	19 (0.7)
Increased transaminases	24 (0.9)

Rugo HS et al. *Ann Oncol* 2022;33(6):616-27.

VTE = venous thromboembolism; ILD = interstitial lung disease

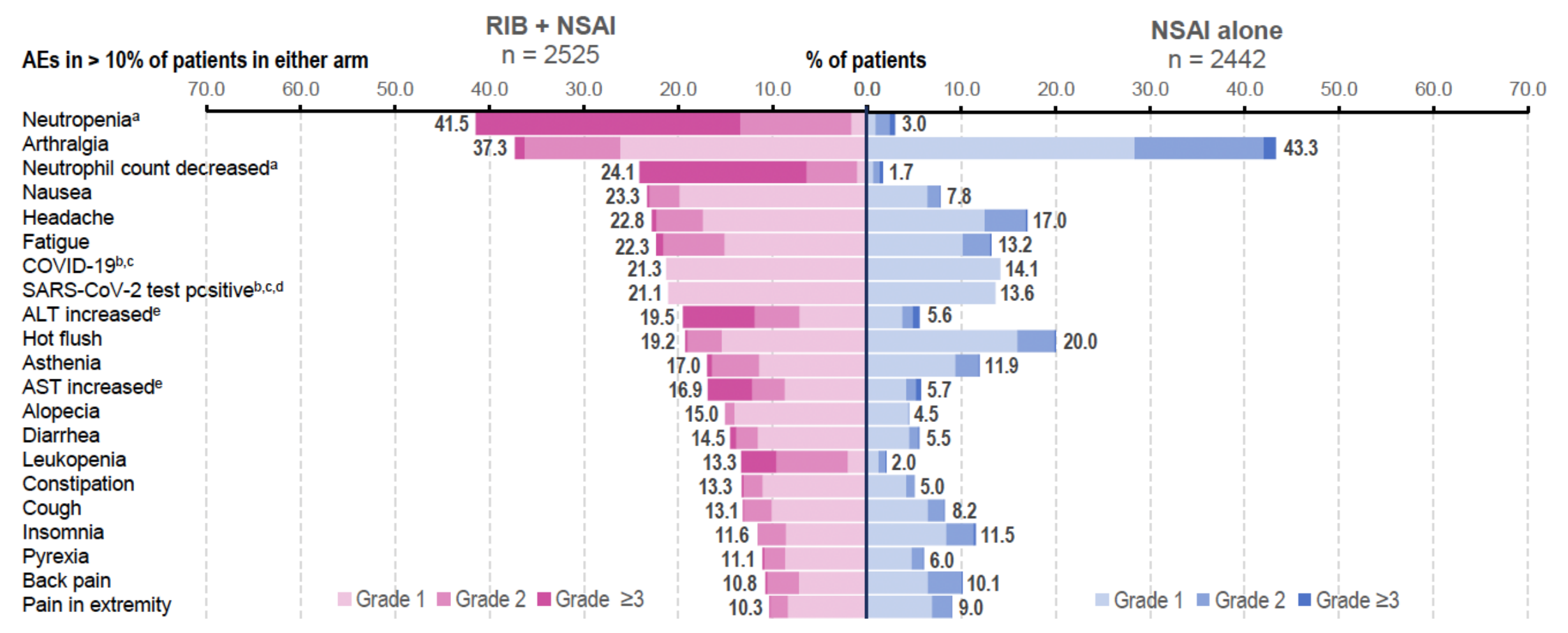
monarchE: AEs Leading to Dose Modifications



Abemaciclib + ET (*N* = 2791)	*n* (%)
Patients with dose reductions due to AE	1212 (43.4)
1 dose reduction	824 (29.5)
2 dose reductions	388 (13.9)
AE leading to dose reductions	
Diarrhea	482 (17.3)
Neutropenia	226 (8.1)
Fatigue	125 (4.5)
Leukopenia	99 (3.5)
Patients with dose holds due to AE	1721 (61.7)
AE leading to dose holds	
Diarrhea	543 (19.5)
Neutropenia	440 (15.8)
Leukopenia	195 (7.0)
Fatigue	140 (5.0)

Rugo HS et al. *Ann Oncol* 2022;33(6):616-27.

NATALEE: Overall Safety Profile



ALT = alanine aminostransferase; AST = aspartate aminotransferase

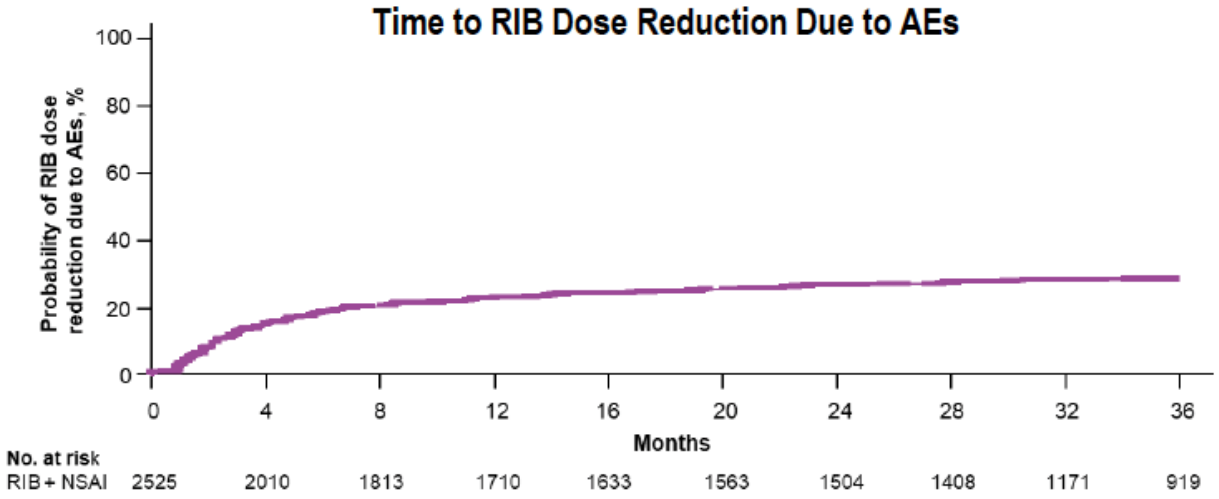
Barrios C et al. ESMO Breast 2024;Abstract 113MO.

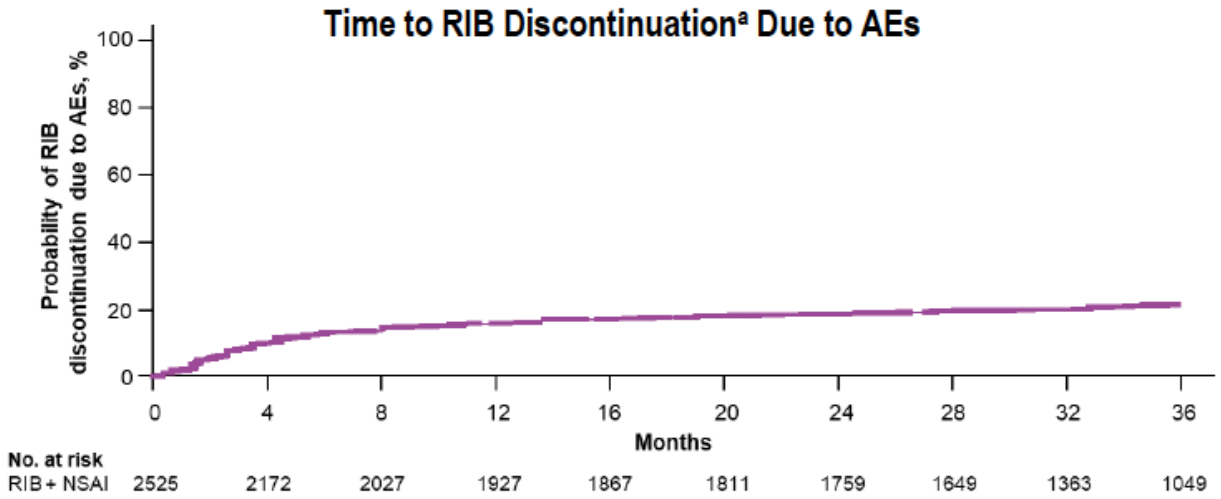
NATALEE: AEs of Special Interest (AESIs)

AESIs (grouped terms)	Neutropenia[a]		Liver-related AEs[c]		QT interval prolongation[d]	
	RIB + NSAI	NSAI alone	RIB + NSAI	NSAI alone	RIB + NSAI	NSAI alone
All grade	1579 (62.5)	113 (4.6)	667 (26.4)	273 (11.2)	134 (5.3)	34 (1.4)
Grade ≥3	1118 (44.3)	22 (0.9)	217 (8.6)	42 (1.7)	26 (1.0)	15 (0.6)
Time to first grade ≥2 based on laboratory values, median mo. (range)	1.0 (0.9-1.0)[b]	NE	2.8 (0.5-36.7)	9.1 (0.5-33.3)	0.5 (0.5-1.5)	1.4 (0.9-2.8)
Time to resolution of grade ≥2 to ≤1 based on laboratory values, median mo. (95% CI)	1.0 (NE)	1.0 (1.0-1.0)	0.9 (0.7-1.0)	1.4 (1.0-2.5)	0.2 (0.0-0.5)	1.1 (0.5-NE)
Dose reductions, RIB, %	14.2	0	2.6	0	0.1	0
Discontinuations, any component, %	1.1	0	8.9	0.1	0.4	0

Barrios C et al. ESMO Breast 2024;Abstract 113MO.

NATALEE: AE-Related Dose Reduction and Discontinuation





- AE-related RIB dose reductions occurred in 22.8% of patients
  - Most commonly due to neutropenia (8.5%) and neutrophil count decreased (5.6%)
- Median time to AE-related RIB dose reduction: 3.15 months (range, 0.26-34.17 months)
- Median RDI during RIB treatment: 94%

- Most common AEs leading to discontinuation: ALT increased (7.1%) and AST increased (2.8%)
- Of 19.7% who discontinued due to AEs, 14.0% discontinued without prior dose reduction and 5.7% had their dose reduced before discontinuing
- Median time to AE-related RIB discontinuation: 4.17 months (range, 0.10-35.75 months)

RDI = relative dose intensity

Barrios C et al. ESMO Breast 2024;Abstract 113MO.

AEs and Dosing Must Be Considered: Distinct AE Profiles and Dosing Schedules of CDK4/6 Inhibitors for Localized Breast Cancer

Abemaciclib

Adverse Events

- Neutropenia (41%-46%)
- Diarrhea (81%-86%)
- Increased ALT (13%-16%)
- Increased AST (12%-15%)
- Thromboembolic events (5%)

Schedule

Continuous daily dosing

Dosing

Starting dose in EBC: 150 mg BID
1st dose reduction: 100 mg BID
2nd dose reduction: 50 mg BID

Ribociclib

Adverse Events

- Neutropenia (69%-78%)
- Diarrhea (29%-35%)
- Increased ALT (15%-46%)
- Increased AST (13%-44%)
- QTc prolongation (6%)

Schedule

3 wk on/1 wk off

Dosing

Starting dose in EBC: 400 mg/day
1 (and only) dose reduction option available in EBC: 200 mg/day

Breast Cancer Status	CDK4/6i	Trial(s)	Discontinuation Rate Due to AE
HR+/HER2– EBC	Abemaciclib	monarchE[1,a]	**19%**
	Ribociclib	NATALEE[2,3]	**19%**

1. Rugo HS, et al. *Ann Oncol.* 2022;33(6):616-627. 2. Slamon D, et al. *N Engl J Med.* 2024 Mar 21;390(12):1080-1091. 3. Hortobagyi GN, et al. SABCS 2023. Abstract GS03-03.

Content courtesy of Komal Jhaveri, MD, FACP, FASCO

EBC = early breast cancer

TRADE: Abemaciclib Dose Escalation

Patient disposition in monarchE		
Outcome in monarchE	By 12 weeks	Overall at 2 years
Discontinued abemaciclib for any reason	10%	30.6%
• Discontinued for adverse events	7%	18.5%
Required abemaciclib dose reduction	27%	43.4%

- HR-positive, HER2-negative, early breast cancer
- Adjuvant abemaciclib is indicated based on patient risk/stage

Screening

N=90

Adjuvant Endocrine Therapy

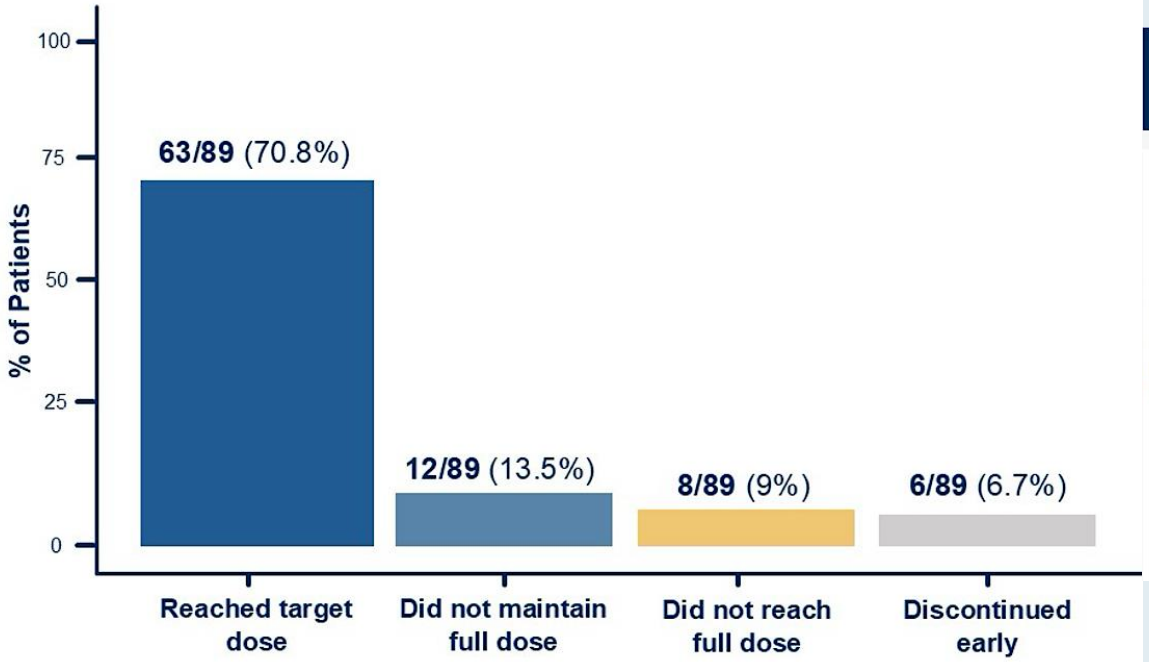
Abemaciclib **50mg BID** (Days 1 – 14) → Abemaciclib **100mg BID** (Days 15 – 28) → Abemaciclib **150mg BID** (> 28 Days)

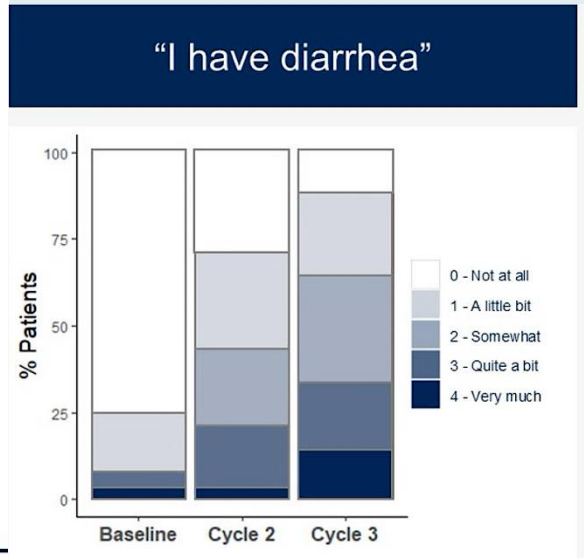
⟹ **Endocrine Therapy + up to 2 years Abemaciclib**

Intra-patient dose escalation requirements: Absence of ongoing grade 3/4 or persistent grade 2 toxicity

Supportive care, including anti-diarrhea medication, provided as needed

Primary endpoint: composite AE rate (discontinuation of adjuvant abemaciclib for any reason and/or need to dose reduce by 12 weeks of therapy)





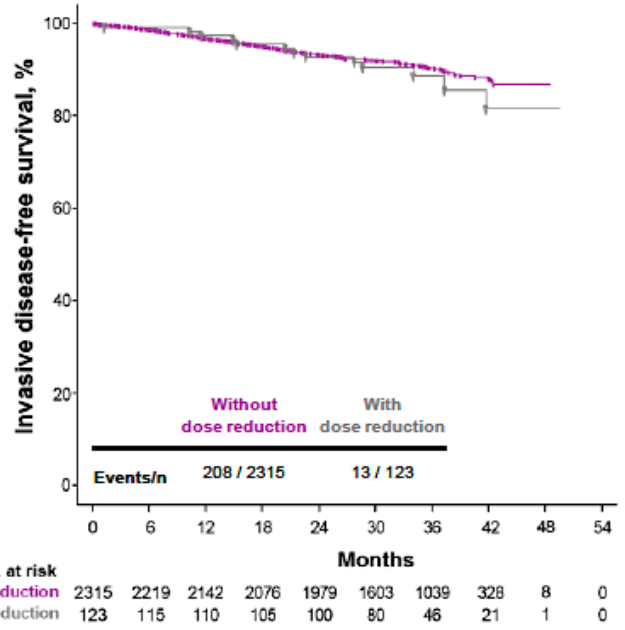
Courtesy of Komal Jhaveri, MD, FACP, FASCO

Mayer EL et al. *Ann Oncol* 2025

NATALEE: IDFS by Dose Reductions

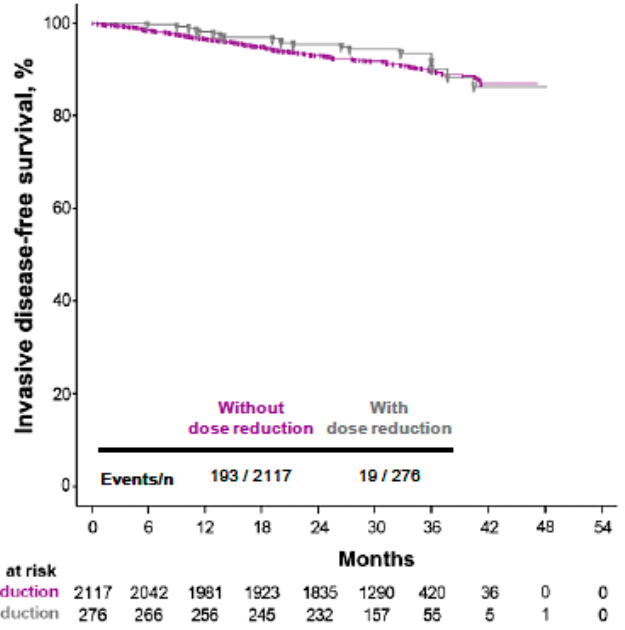
Landmark analysis revealed that RIB dose reduction due to AEs did not impact efficacy

iDFS by Dose Reduction at 25th Percentile[a] (1.87 mo.)



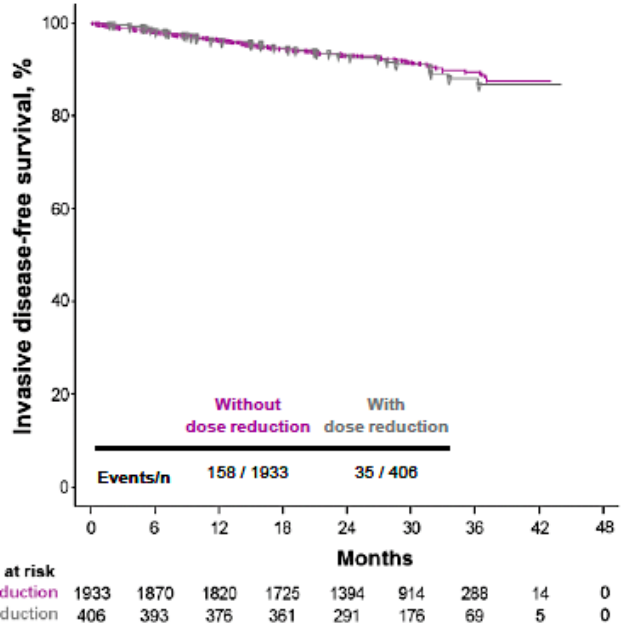
No. at risk										
Without dose reduction	2315	2219	2142	2076	1979	1603	1039	328	8	0
With dose reduction	123	115	110	105	100	80	46	21	1	0

iDFS by Dose Reduction at 50th Percentile[a] (3.17 mo.)



No. at risk										
Without dose reduction	2117	2042	1981	1923	1835	1290	420	36	0	0
With dose reduction	276	266	256	245	232	157	55	5	1	0

iDFS by Dose Reduction at 75th Percentile[a] (7.28 mo)



No. at risk										
Without dose reduction	1933	1870	1820	1725	1394	914	288	14	0	
With dose reduction	406	393	376	361	291	176	69	5	0	

Barrios C et al. ESMO Breast 2024;Abstract 113MO.

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: Clinician Survey Results

Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer

Module 4: Clinician Survey Results

Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy

Module 6: Clinician Survey Results

Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

RTP RESEARCH TO PRACTICE

Have you employed or would you employ an initial dose-escalation strategy rather than initiating therapy at the recommended starting dose for any of your patients with HR-positive localized BC receiving an adjuvant CDK4/6 inhibitor?

 Dr Brufsky	I have not but would for the right patient
 Dr DeMichele	I have
 Dr Kalinsky	I have
 Dr Mahtani	I have
 Dr Mouabbi	I have
 Dr Rugo	I have
 Dr Sharma	I have
 Dr Stringer-Reasor	I have

RTP RESEARCH TO PRACTICE

Assuming eligibility to receive abemaciclib or ribociclib, which CDK4/6 inhibitor would you prefer in the adjuvant setting for a patient with HR-positive localized BC and a history of …?

	Colitis	Chronic liver disease	Chronic renal disease
 Dr Brufsky	Ribociclib	Abemaciclib	Ribociclib
 Dr DeMichele	Ribociclib	Abemaciclib	No preference
 Dr Kalinsky	Ribociclib	Abemaciclib	No preference
 Dr Mahtani	Ribociclib	Abemaciclib	No preference
 Dr Mouabbi	Ribociclib	Abemaciclib	Ribociclib
 Dr Rugo	Ribociclib	Abemaciclib	No preference
 Dr Sharma	Ribociclib	Abemaciclib	Ribociclib
 Dr Stringer-Reasor	Ribociclib	Abemaciclib	No preference

Assuming eligibility to receive abemaciclib or ribociclib, which CDK4/6 inhibitor would you prefer in the adjuvant setting for a patient with HR-positive localized BC and a history of …?

	COPD	NYHA Class I congestive heart failure
 Dr Brufsky	No preference	Abemaciclib
 Dr DeMichele	No preference	Abemaciclib
 Dr Kalinsky	No preference	Abemaciclib
 Dr Mahtani	No preference	Abemaciclib
 Dr Mouabbi	Ribociclib	Abemaciclib
 Dr Rugo	No preference	Abemaciclib
 Dr Sharma	No preference	No preference
 Dr Stringer-Reasor	No preference	No preference

COPD = chronic obstructive pulmonary disease

Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer

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Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy

Module 6: Clinician Survey Results

Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

RTP RESEARCH TO PRACTICE

Key Datasets

- Bardia A et al. **Giredestrant** vs standard-of-care endocrine therapy as **adjuvant treatment** for patients with estrogen receptor-positive, HER2-negative early breast cancer: **Results from the global phase III lidERA Breast Cancer trial**. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

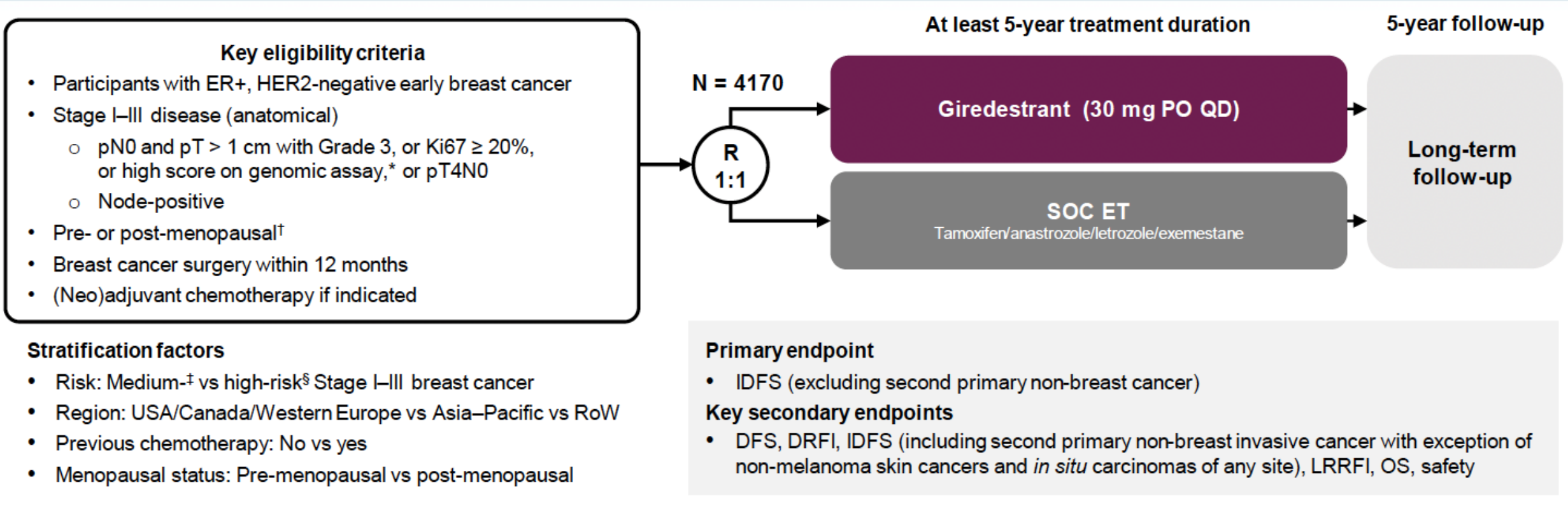
SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Giredestrant vs standard-of-care endocrine therapy as adjuvant treatment for patients with estrogen receptor-positive, HER2-negative early breast cancer: Results from the global Phase III lidERA Breast Cancer trial

Presenting author: Aditya L. Bardia, MD
University of California, Los Angeles, Los Angeles, CA, USA

Abstract GS1-10

lidERA Breast Cancer Study Design



DRFI = distant recurrence-free interval; LRRFI = locoregional recurrence-free interval

Bardia A et al. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

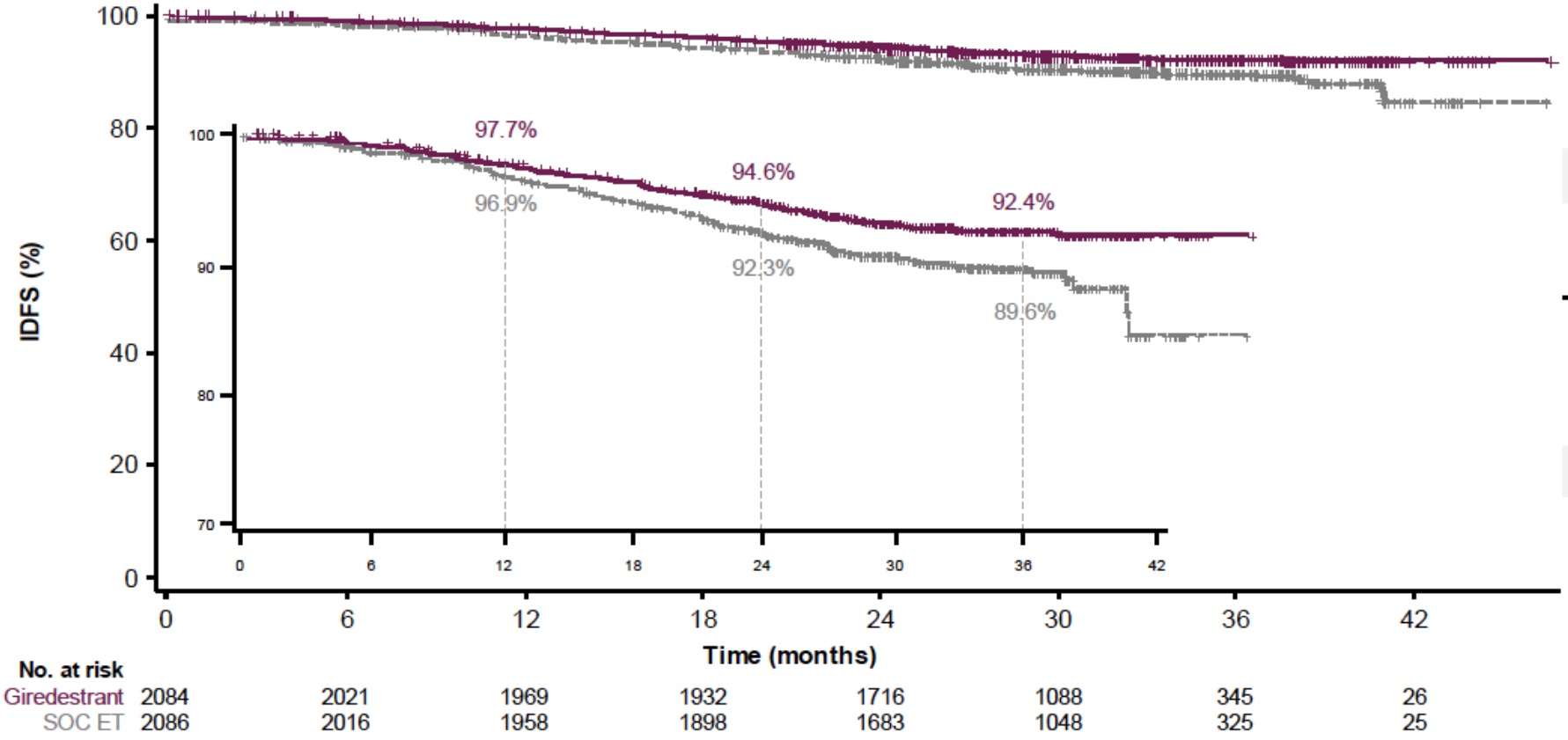
lidERA Breast Cancer: Patient Demographics

	Giredestrant n = 2084	SOC ET n = 2086
Median age, years (range)	54.0 (22–91)	54.0 (25–89)
Female sex, n (%)	2073 (99.5)	2075 (99.5)
Race, n (%)		
American Indian or Alaska Native	77 (3.7)	62 (3.0)
Asian	461 (22.1)	467 (22.4)
Black or African American	50 (2.4)	50 (2.4)
Other*	263 (12.6)	232 (11.1)
White	1233 (59.2)	1275 (61.1)
Region, n (%)		
Asia–Pacific	544 (26.1)	544 (26.1)
USA/Canada/Western Europe	860 (41.3)	905 (43.4)
Latin America/Africa/Eastern Europe	680 (32.6)	637 (30.5)
Menopausal status, n (%)†		
Pre-menopausal	849 (41.0)	838 (40.4)
Post-menopausal	1220 (59.0)	1236 (59.6)

	Giredestrant n = 2084	SOC ET n = 2086
ER status, n (%)‡		
Low-positive (1–10% of cells positive)	45 (2.2)	52 (2.5)
Positive (> 10% of cells positive)	2030 (97.8)	2031 (97.5)
AJCC stage at surgery, n (%)§		
I	254 (12.3)	283 (13.6)
II	1013 (49.0)	950 (45.7)
III	799 (38.7)	844 (40.6)
Nodal status, n (%) on surgical specimen‖		
pN0	449 (21.6)	441 (21.2)
pN1	968 (46.6)	953 (45.7)
pN2–3	662 (31.8)	691 (33.1)
Risk, n (%)		
High	1448 (69.5)	1447 (69.4)
Medium	636 (30.5)	639 (30.6)
Previous chemotherapy, n (%)		
No	396 (19.0)	450 (21.6)
Yes	1688 (81.0)	1636 (78.4)

Bardia A et al. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

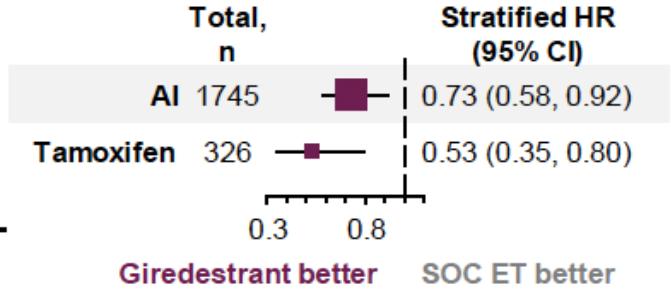
lidERA Breast Cancer: IDFS Outcomes



No. at risk								
Giredestrant	2084	2021	1969	1932	1716	1088	345	26
SOC ET	2086	2016	1958	1898	1683	1048	325	25

	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	140 (6.7)	196 (9.4)
Stratified HR (95% CI)	**0.70** (0.57, 0.87); **p = 0.0014***	

Exploratory analysis: IDFS by SOC ET



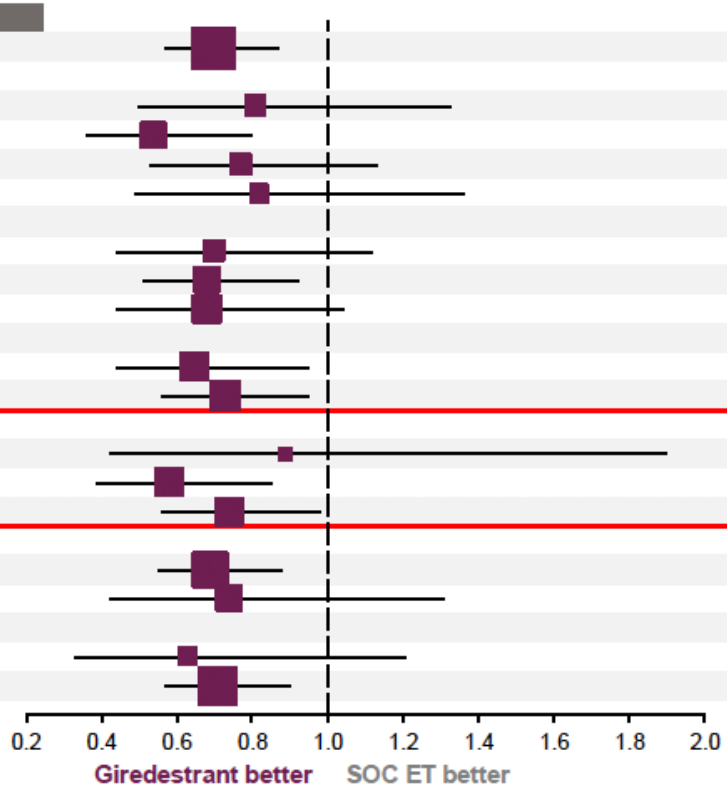
Median follow-up: 32.3 months

Statistically significant and clinically meaningful improvement in IDFS:
Giredestrant reduced the risk of invasive disease recurrence or death by 30% compared with SOC ET

Bardia A et al. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

lidERA Breast Cancer: IDFS in Key Subgroups

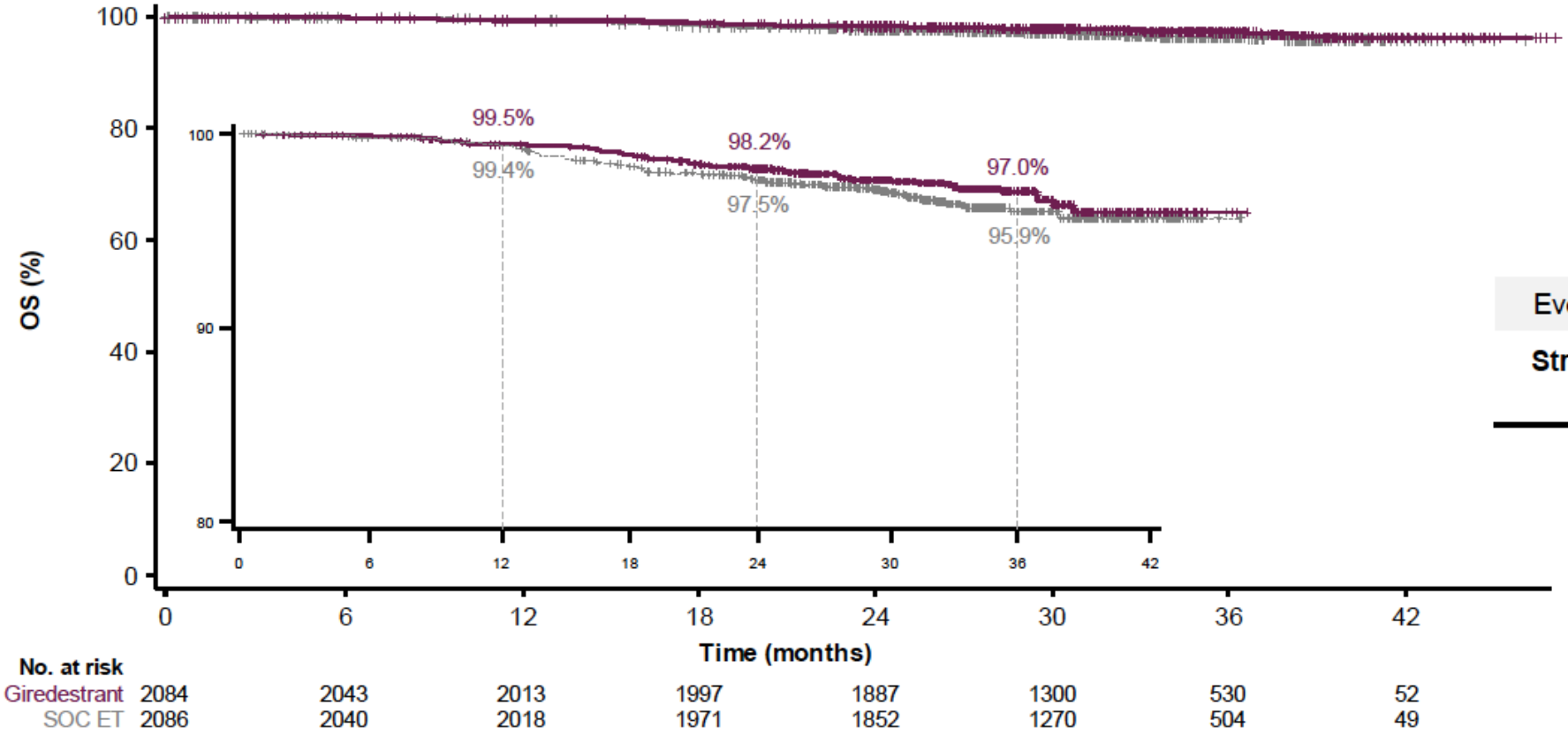
	Total, n	Patients, n: Giredestrant	Patients, n: SOC ET	HR (95% CI)
All patients	4170	2084	2086	0.70 (0.57, 0.87)
Age group, years				
≤ 45	906	472	434	0.81 (0.50, 1.33)
> 45 to ≤ 55	1355	660	695	0.54 (0.36, 0.80)
> 55 to ≤ 65	1118	567	551	0.77 (0.53, 1.13)
> 65	791	385	406	0.82 (0.49, 1.36)
Region				
Asia–Pacific	1088	544	544	0.70 (0.44, 1.12)
Latin America/Africa/Eastern Europe	1317	680	637	0.68 (0.51, 0.92)
USA/Canada/Western Europe	1765	860	905	0.68 (0.44, 1.04)
Menopausal status				
Pre-menopausal	1680	841	839	0.65 (0.44, 0.95)
Post-menopausal	2490	1243	1247	0.73 (0.56, 0.95)
AJCC stage at surgery*				
I	537	254	283	0.89 (0.42, 1.90)
II	1963	1013	950	0.58 (0.39, 0.85)
III	1643	799	844	0.74 (0.56, 0.98)
Risk				
High	2895	1448	1447	0.69 (0.55, 0.88)
Medium	1275	636	639	0.74 (0.42, 1.31)
Previous chemotherapy				
No	787	392	395	0.63 (0.33, 1.21)
Yes	3383	1692	1691	0.71 (0.57, 0.90)



IDFS benefit was consistent across key prespecified subgroups

Bardia A et al. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

lidERA Breast Cancer: OS Outcomes



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	57 (2.7)	71 (3.4)
Stratified HR (95% CI)	**0.79** (0.56, 1.12); p = 0.1863*	

No. at risk								
Giredestrant	2084	2043	2013	1997	1887	1300	530	52
SOC ET	2086	2040	2018	1971	1852	1270	504	49

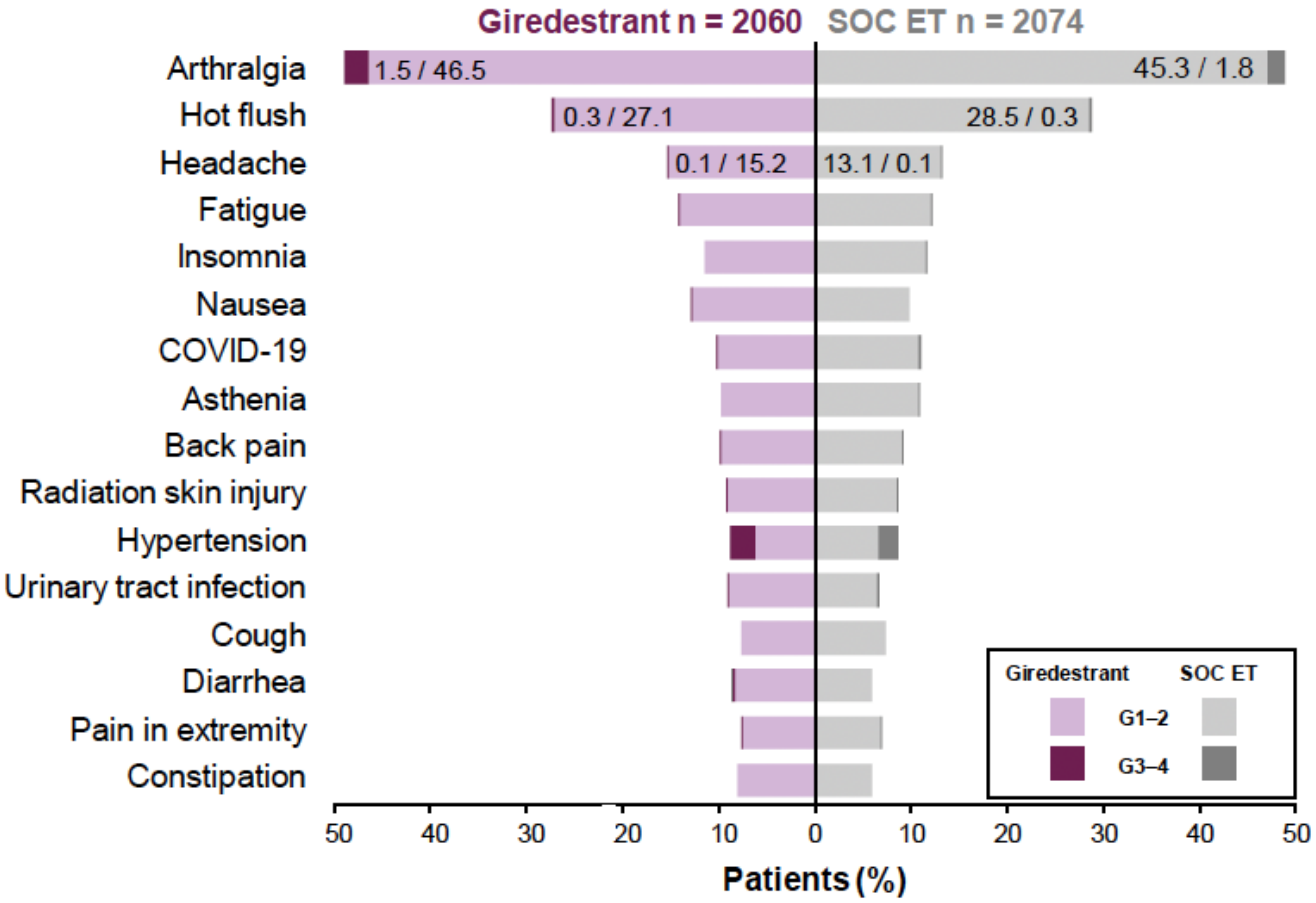
Median follow-up: 32.3 months

While OS data were immature, a clear positive trend was observed. OS testing will continue at future analyses

Bardia A et al. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

lidERA Breast Cancer: Safety Profile

Common TEAEs (≥ 7.5% of patients in either arm at any grade)



Selected AEs

	Giredestrant n = 2060	SOC ET n = 2074
Patients, n (%) with treatment discontinuations due to AEs		
Musculoskeletal disorders	38 (1.8)	92 (4.4)
• Arthralgias (PT)	32 (1.6)	76 (3.7)
Vasomotor disorders	2 (< 0.1)	18 (0.9)
• Hot flush (PT)	1 (< 0.1)	16 (0.8)

	Giredestrant n = 2060			SOC ET n = 2074		
Patients, n (%) with selected AEs by medical concept*						
	G1	**G2**	**G3–4**	**G1**	**G2**	**G3–4**
Bradycardia†	217 (10.5)	15 (0.7)	0	64 (3.1)	2 (< 0.1)	0
Venous thromboembolic events	4 (0.2)	12 (0.6)	2 (< 0.1)‡	3 (0.1)	7 (0.3)	7 (0.3)

Bardia A et al. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

Based on recently presented findings from the Phase III lidERA trial, would you like to have access to adjuvant giredestrant today for your patients with HR-positive, HER2-negative localized BC?

 Dr Brufsky	Yes, for patients with higher-risk disease
 Dr DeMichele	Yes, for those who can't tolerate a CDK4/6i or unable to tolerate an AI or in place of tamoxifen for a premenopausal patient with high-risk disease
 Dr Kalinsky	Yes, for patients with higher-risk disease after CDK4/6i or if cannot tolerate standard ET
 Dr Mahtani	Yes, for patients with high-risk disease
 Dr Mouabbi	Yes, for patients who are receiving AI monotherapy
 Dr Rugo	Yes, for high-risk disease as defined in the trial
 Dr Sharma	Yes, for patients that match eligibility of the lidERA trial
 Dr Stringer-Reasor	Yes, for patients with node-negative disease and those with difficulty tolerating AI, after use of CDK 4/6i

ET = endocrine therapy; CDK4/6i = CDK4/6 inhibitor

RTP RESEARCH TO PRACTICE

If giredestrant were available, regulatory and reimbursement issues aside, what would you generally recommend for patients who met the criteria for both an adjuvant CDK4/6 inhibitor and adjuvant giredestrant?

 Dr Brufsky	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr DeMichele	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr Kalinsky	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr Mahtani	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr Mouabbi	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr Rugo	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr Sharma	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i
 Dr Stringer-Reasor	CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i

ET = endocrine therapy; CDK4/6i = CDK4/6 inhibitor

RTP RESEARCH TO PRACTICE

Questions?

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Agenda

- Hormone Receptor (HR)-Positive Localized Breast Cancer — Dr Stringer-Reasor
- **Diffuse Large B-Cell Lymphoma (DLBCL) — Prof Salles**

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Gilles Salles, MD, PhD
Service Chief, Lymphoma Service
Steven Greenberg Chair
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Disclosures

Advisory Committees	AbbVie Inc, BeOne, Bristol Myers Squibb, Foresight Diagnostics, a wholly-owned subsidiary of Natera Inc, Genentech, a member of the Roche Group, Genmab US Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Kite, A Gilead Company, Lilly, Merck, Novartis, Nurix Therapeutics Inc, Pfizer Inc, SERB Pharmaceuticals
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RESEARCH TO PRACTICE

Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Clinician Survey Results

Module 3: Current and Future Roles of Monoclonal and Bispecific Antibodies in Therapy for Relapsed/Refractory (R/R) DLBCL

Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

RTP
RESEARCH TO PRACTICE

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Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Key Datasets

- Morschhauser F et al. **Five-year outcomes** of the **POLARIX study** comparing **Pola-R-CHP and RCHOP in patients with diffuse large B-cell lymphoma**. *J Clin Oncol* 2025 December 10;43(35):3698-705.
- Trněný M et al. Analysis of **peripheral neuropathy in the POLARIX** study using **clinician- and patient-reported outcomes**. *Blood Adv* 2025 July 8;9(13):3263-7.
- Lenz G et al. **frontMIND: Phase 3** study of **tafasitamab (Tafa) plus lenalidomide (Len) and R-CHOP** for patients (pts) with **newly diagnosed diffuse large B-cell lymphoma (DLBCL)**. ASCO 2026;Abstract LBA700.
- Sehn LH et al. **ESCALADE:** A **phase 3** study of **acalabrutinib in combination** with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for **patients ≤65y** with **untreated non-germinal center B-cell–like (non-GCB) diffuse large B-cell lymphoma (DLBCL)**. ASCO 2021;Abstract TPS7572.

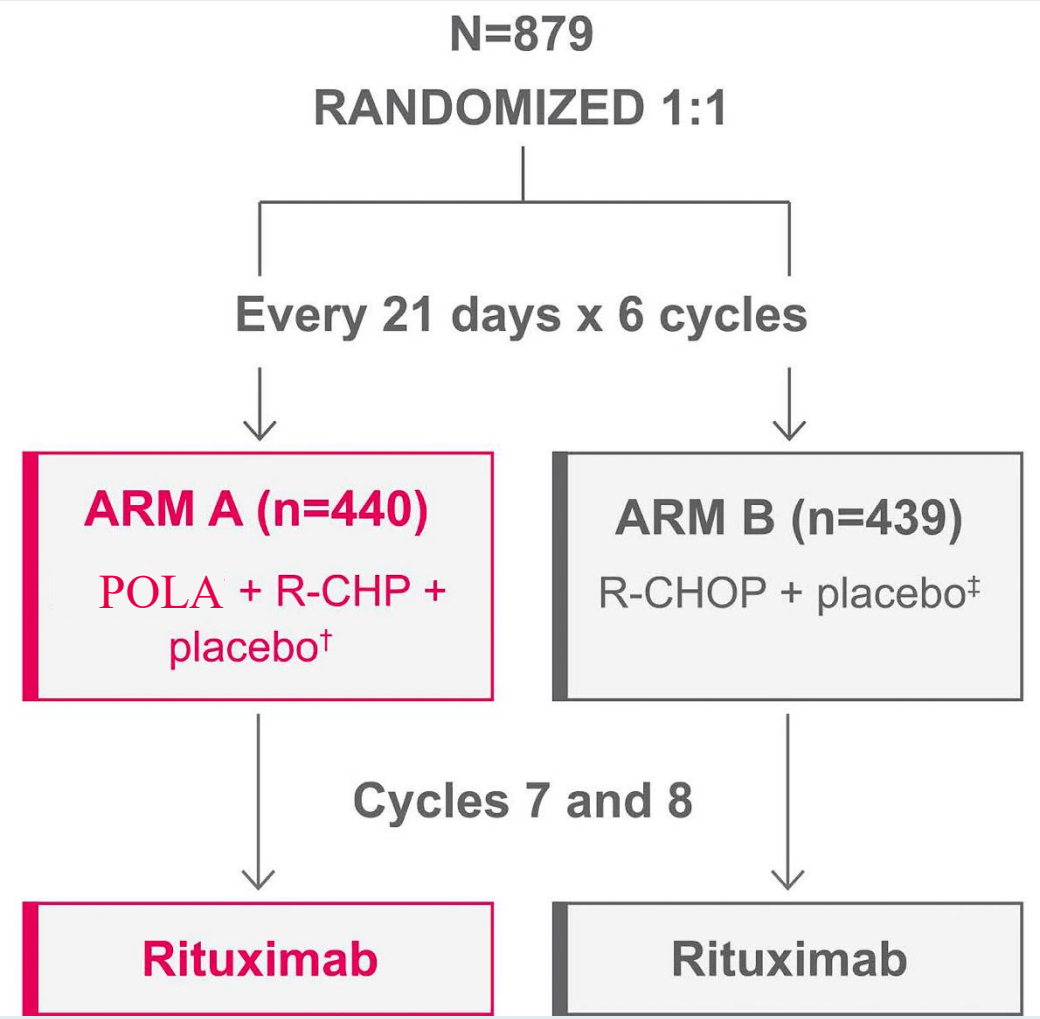
Phase III POLARIX Study Design

Eligibility Criteria:

- Previously untreated LBCL
- Aged 18-80 years
- IPI score 2-5
- ECOG PS 0-2

Primary endpoint:
Investigator-assessed PFS

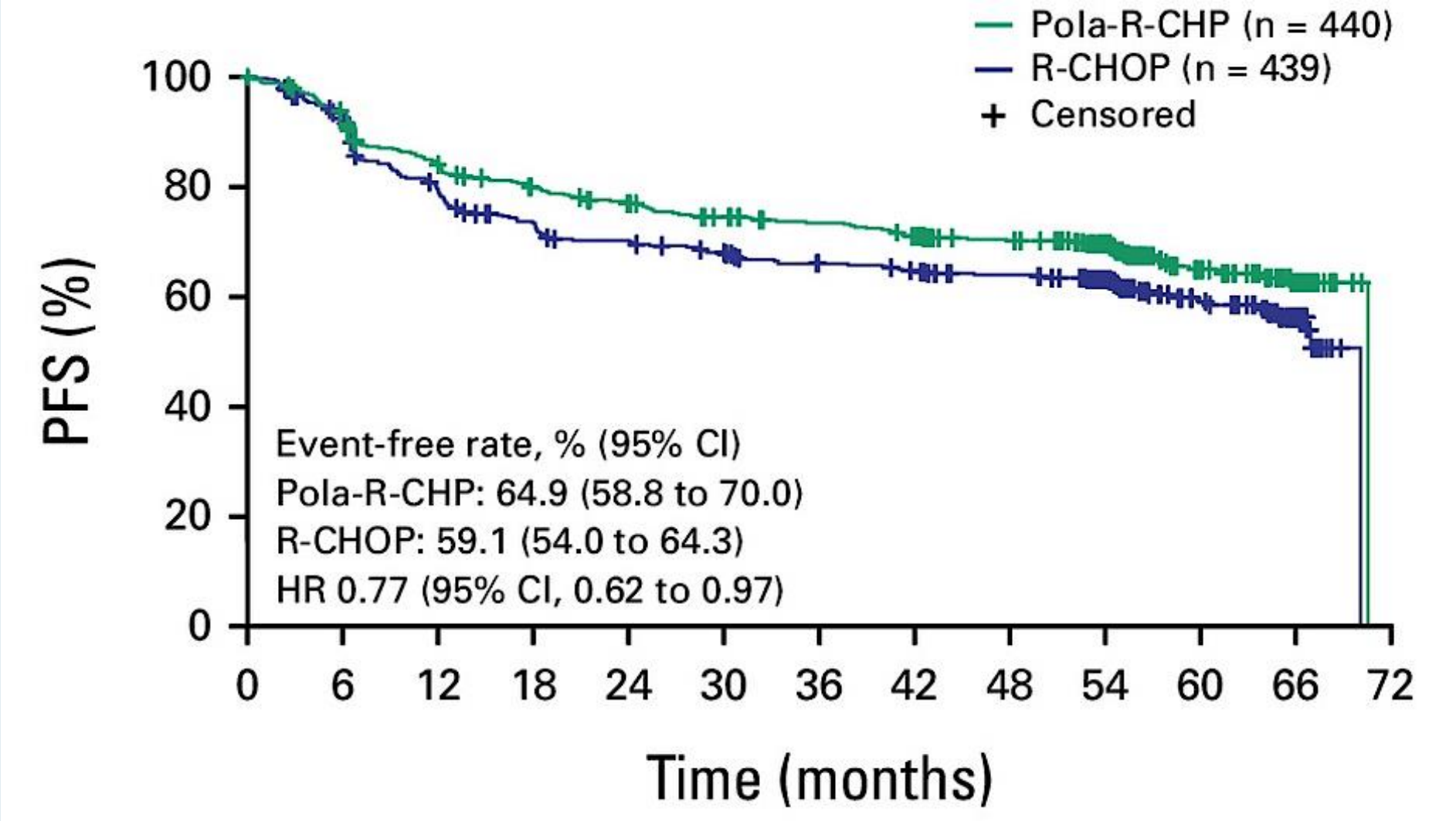
Secondary endpoints:
Investigator-assessed EFS, ORR, OS



LBCL = large B-cell lymphoma; PFS = progression-free survival; EFS = event-free survival; ORR = overall response rate; OS = overall survival

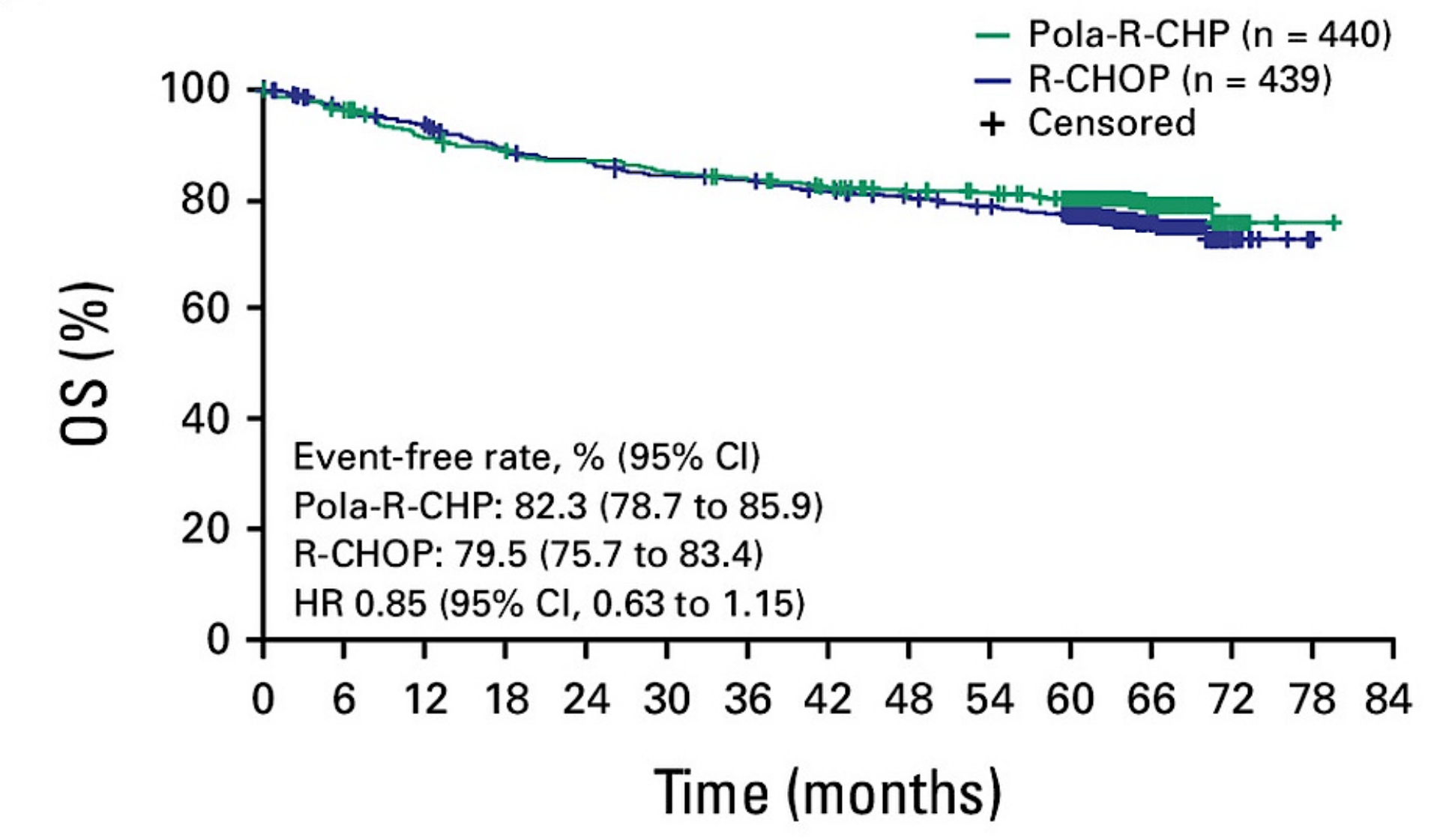
[from the manufacturer's website]

Phase III POLARIX: 5-Year PFS (Global Population)



Morschhauser F et al. *J Clin Oncol* 2025 December 10;43(35):3698-705.

Phase III POLARIX: 5-Year OS (Global Population)



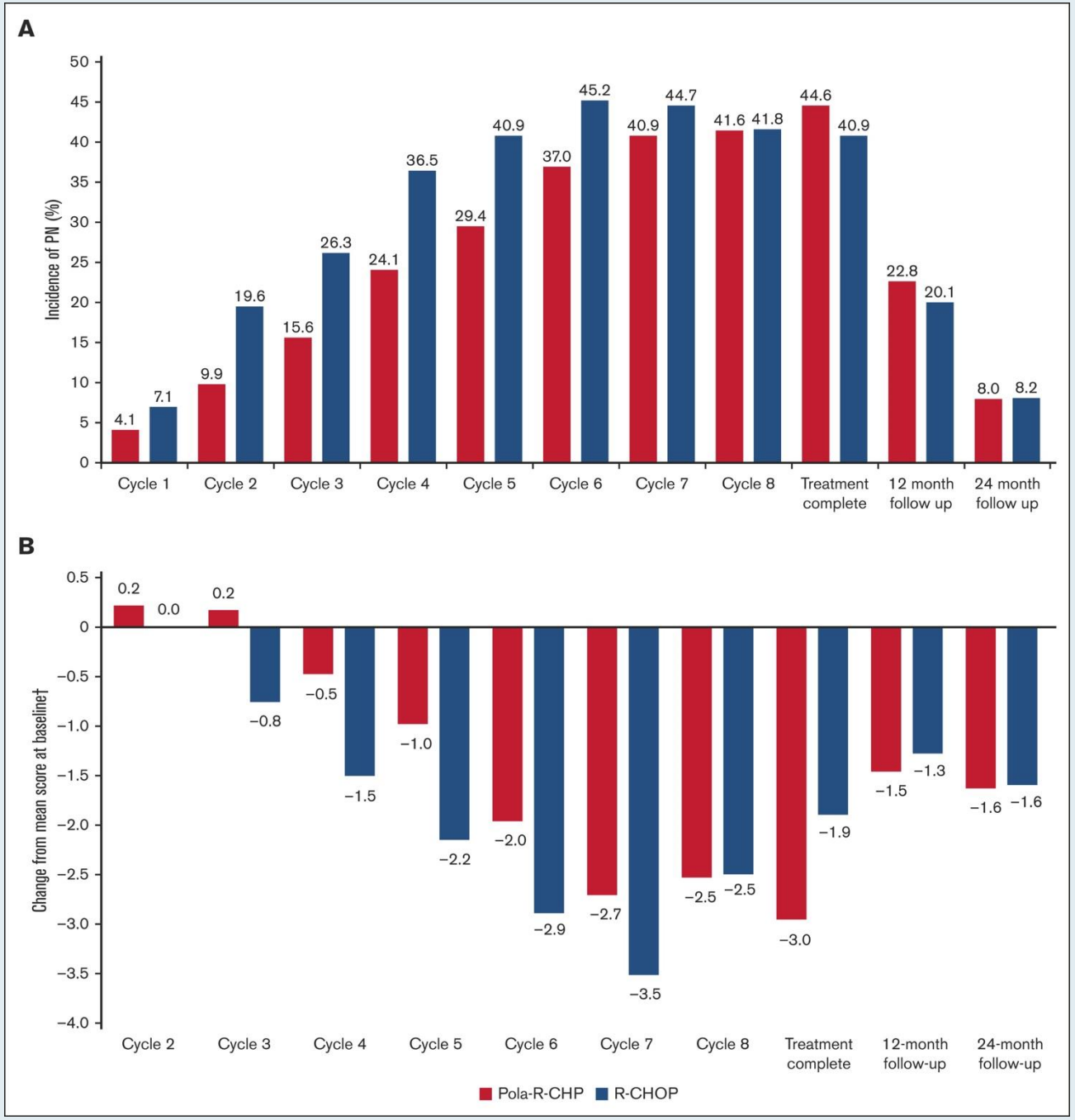
Morschhauser F et al. *J Clin Oncol* 2025 December 10;43(35):3698-705.

Phase III POLARIX: Adverse Events of Interest

Patients, n (%)	Pola-R-CHP (n=495)	R-CHOP (n=498)
Peripheral neuropathy		
All grade	249 (50.3)	261 (52.4)
Grade 3–5	7 (1.4)	5 (1.0)
Resolved[a]	170 (68.3)	195 (74.7)
Ongoing/Unresolved[b]	79 (31.7)	66 (25.3)
Neutropenia		
All grade	240 (48.5)	228 (45.8)
Grade 3–5	216 (43.6)	205 (41.2)
Infections		
All grade	237 (47.9)	219 (44.0)
Grade 3–5	75 (15.2)	66 (13.3)
Anemia		
All grade	165 (33.3)	150 (30.1)
Grade 3–5	56 (11.3)	49 (9.8)
Thrombocytopenia		
All grade	89 (18.0)	86 (17.3)
Grade 3–5	32 (6.5)	31 (6.2)
Cardiac arrhythmias		
All grade	18 (3.6)	26 (5.2)
Grade 3–5	3 (0.6)	5 (1.0)
Secondary malignancies[c]		
All grade	5 (1.0)	12 (2.4)
Grade 3–5	5 (1.0)	9 (1.8)

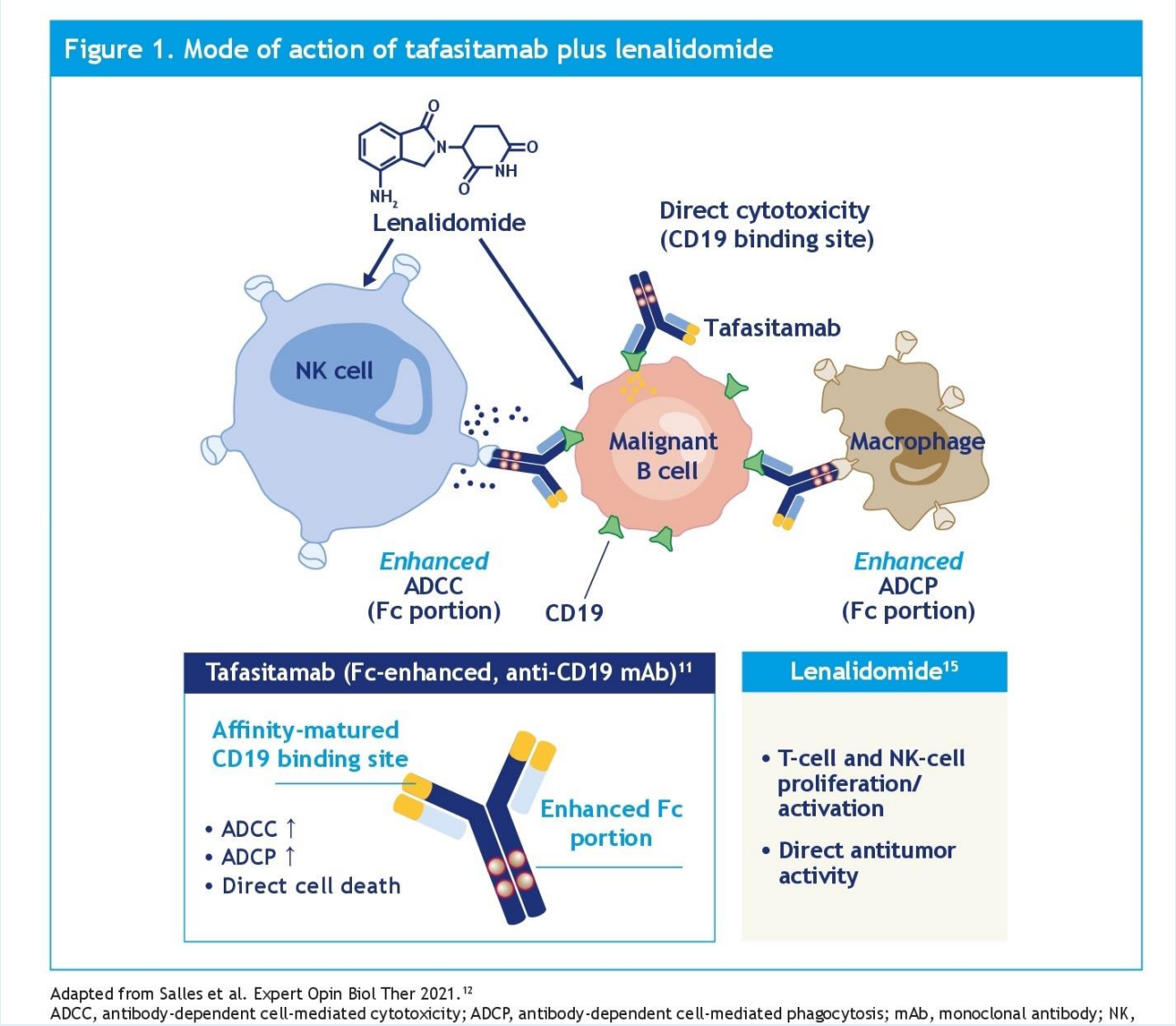
Morschhauser F et al. *J Clin Oncol* 2025 December 10;43(35):3698-705.

Phase III POLARIX: Peripheral Neuropathy



Trněný M et al. *Blood Adv* 2025 March 17;9(13):3263-7.

Rationale for Tafasitamab and Lenalidomide Combination Therapy



Adapted from Salles et al. Expert Opin Biol Ther 2021.[12]
ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; mAb, monoclonal antibody; NK,

Vitolo U et al. ASCO 2022;Abstract TPS7590.

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

Georg Lenz,[1] Marek Trněný,[2] John M. Burke,[3] Grzegorz S. Nowakowski,[4] Christopher P. Fox,[5] Annalisa Chiappella,[6] Johannes Duell,[7] Young Woo Jeon,[8] Chan Y. Cheah,[9] Jason Westin,[10] Joseph Z. Ye,[11] Priscilla B. Caguioa,[12] David Belada,[13] Ho-Jin Shin,[14] Sung Yong Oh,[15] Sandy Amorim,[16] Andreas Rosenwald,[17] Roberto Chiarle,[18] Philomena Colucci,[19] Sonia Ioannidis,[20] Lulu Cheng,[19] and Umberto Vitolo[21]

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Presented at the 2026 ASCO Annual Meeting • Chicago, IL, USA & Online • May

Tafasitamab plus lenalidomide and R-CHOP versus R-CHOP for first-line treatment of patients with high-risk diffuse large B-cell lymphoma (frontMIND): a global, phase 3, randomised, double-blind, placebo-controlled trial

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***Lancet* 2026 May 30;[Online ahead of print].**

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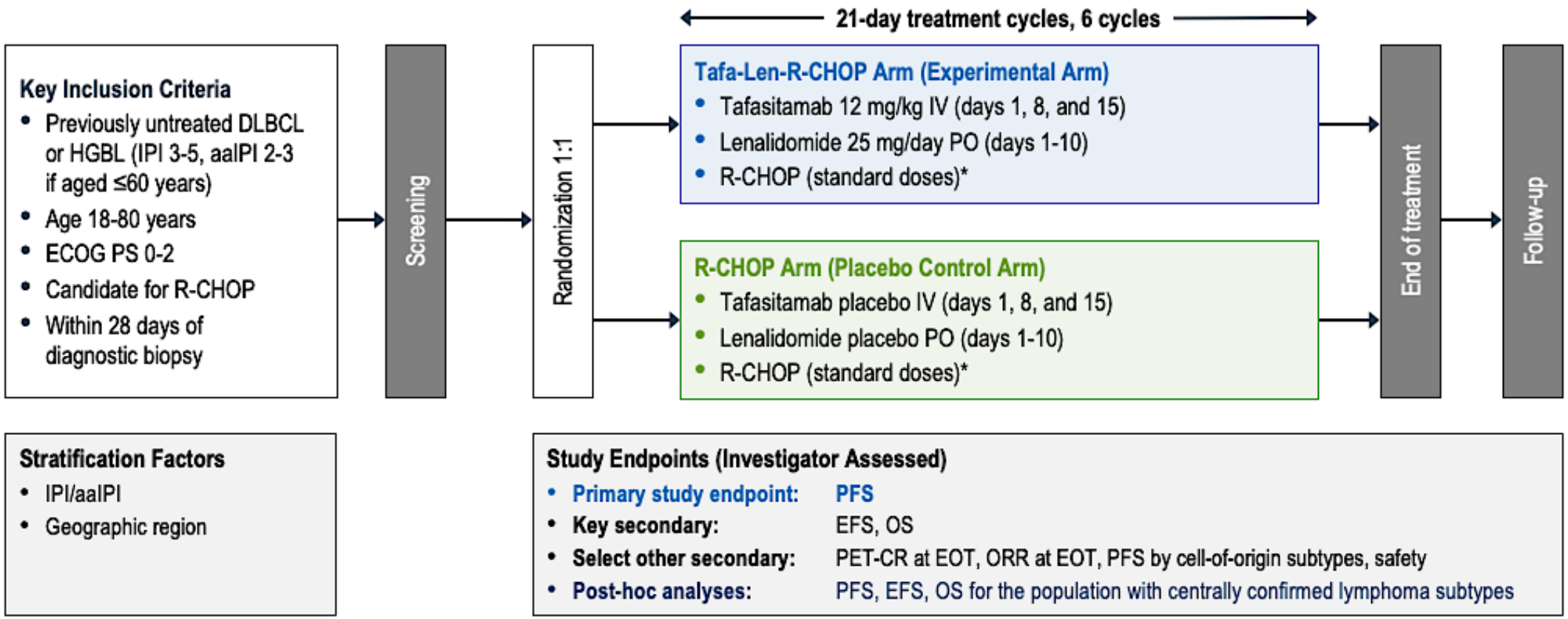
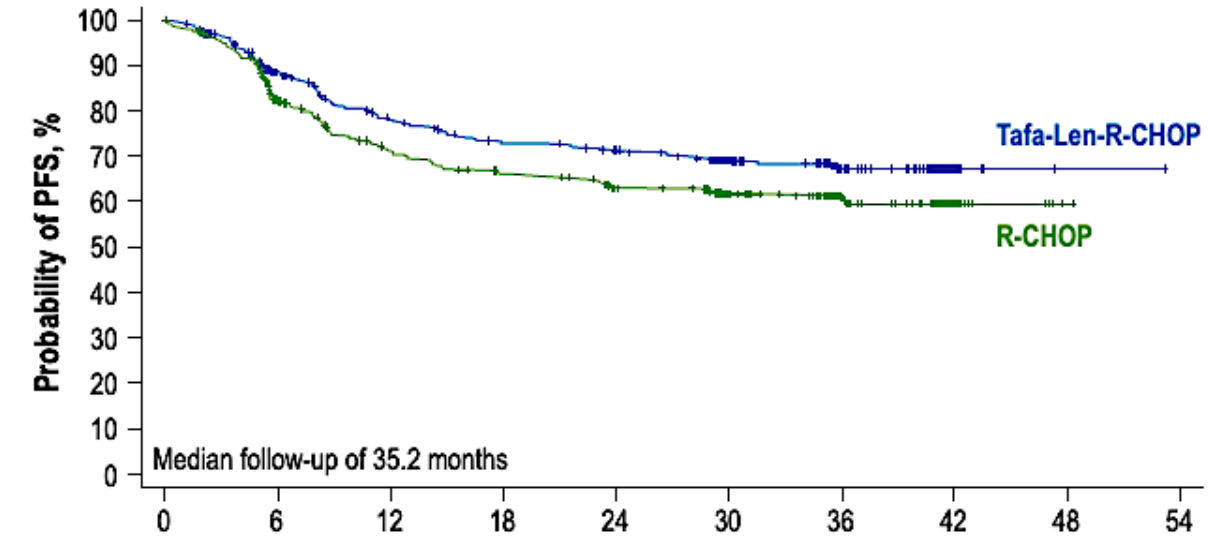
Phase III frontMIND Study Design



*Rituximab administered at 375 mg/m^2 IV (day 1); cyclophosphamide, doxorubicin, and vincristine administered IV (day 1); prednisone/prednisolone administered PO (days 1-5).
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.

Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet*. 2026 Jun 20;407(10547):2528-2541.

frontMIND Primary Endpoint: Investigator-Assessed Progression-Free Survival



No. at Risk										
Tafa-Len-R-CHOP	448	333	282	259	248	191	107	13	1	0
R-CHOP	451	320	266	244	222	182	101	19	1	0

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

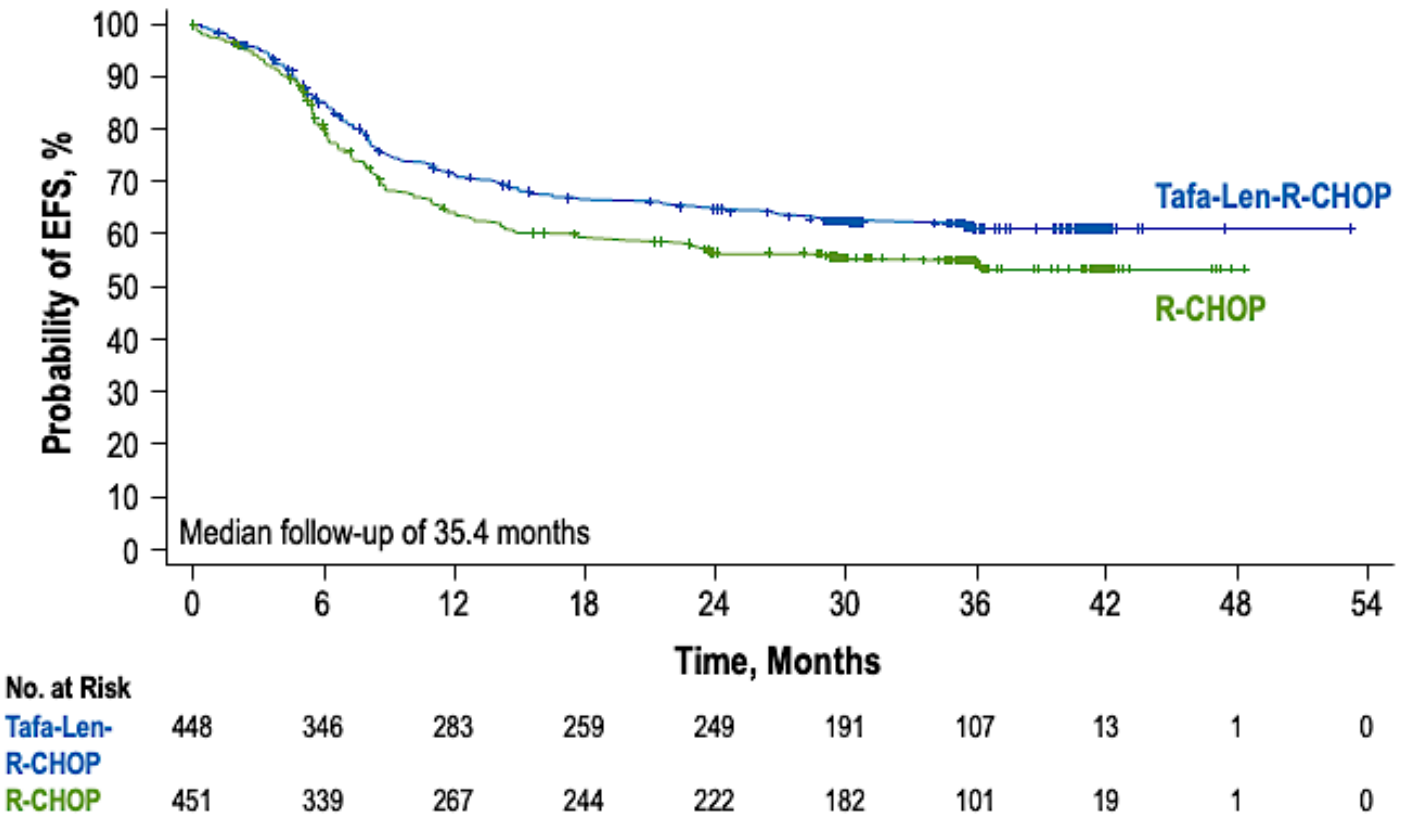
- A **25% reduction in risk of progression or death** demonstrated with Tafa-Len-R-CHOP vs R-CHOP
- **2-year PFS:** 71.1% with Tafa-Len-R-CHOP vs 62.9% with R-CHOP (Δ=**8.2%**)
- **3-year PFS:** 67.3% with Tafa-Len-R-CHOP vs 60.7% with R-CHOP (Δ=**6.6%**)

ITT population. *Calculated using a stratified Cox proportional hazards model.
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.

In key prespecified subgroup analyses, point estimates suggested trends toward PFS advantage with Tafa-Len-R-CHOP

Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet* 2026 June 20;407(10547):2528-41.

frontMIND Key Secondary Endpoint: Investigator-Assessed Event-Free Survival



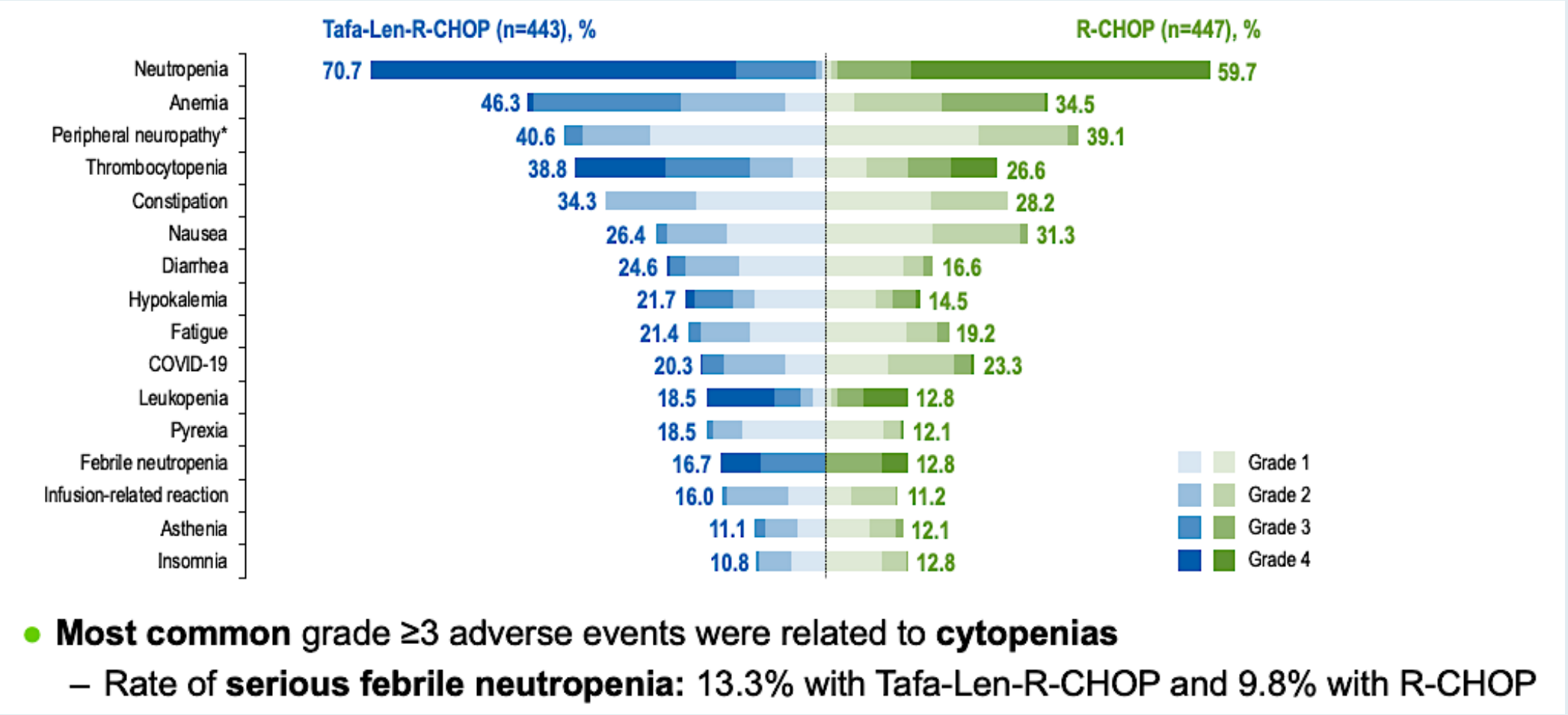
HR 0.79* (*P*=0.0260)
95% CI: 0.64, 0.97

- **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.

Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet* 2026 June 20;407(10547):2528-41.

frontMIND: Most Frequent Treatment-Emergent Adverse Events



- **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 events with Tafa-Len-R-CHOP were manageable and did not affect the delivery of the R-CHOP backbone

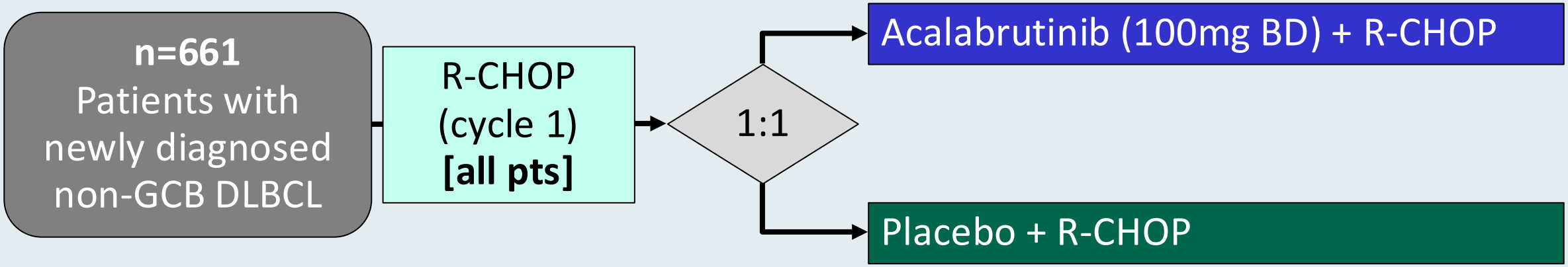
Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet* 2026 June 20;407(10547):2528-41.

Studies Supporting the ESCALADE Study

- **ACCEPT — Davies et al. ASH 2020**
  - "There is a strong rationale for combining A with R-CHOP in pts with untreated DLBCL, and safety of A + R-CHOP has been shown in a phase 1b/2 study"
- **PHOENIX — Younes et al. *J Clin Oncol* 2019;37:1285-9.**
  - "In untreated non-GCB DLBCL pts, [PHOENIX] showed that addition of the BTKi ibrutinib to R-CHOP (R-CHOP-I) did not improve outcomes in the intent-to-treat population. However, pts age <60y treated with R-CHOP-I had significantly improved progression-free survival (PFS) and overall survival (OS) compared with those receiving R-CHOP alone."

Sehn LH et al. ASCO 2021;Abstract TPS7572.

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.

Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Clinician Survey Results

Module 3: Current and Future Roles of Monoclonal and Bispecific Antibodies in Therapy for Relapsed/Refractory (R/R) DLBCL

Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

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Which first-line therapy would you generally recommend for an otherwise healthy patient with Stage IV germinal center B-cell (GCB)-type diffuse large B-cell lymphoma (DLBCL) with an International Prognostic Index (IPI) score of 3?

	65-year-old	80-year-old
 Dr Abramson	R-CHP + polatuzumab vedotin	Dose-reduced R-CHP + polatuzumab vedotin
 Dr Flowers	R-CHP + polatuzumab vedotin	R-CHP + polatuzumab vedotin
 Dr Kamdar	R-CHP + polatuzumab vedotin	R-mini-CHOP
 Dr LaCasce	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Matasar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Phillips	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Prof Salles	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Westin	R-CHOP	R-mini-CHOP

R-CHP = rituximab/cyclophosphamide/doxorubicin/prednisone; R-mini-CHOP = rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone (attenuated)

Which first-line therapy would you generally recommend for an otherwise healthy patient with Stage IV activated B-cell (ABC)-type DLBCL with an IPI score of 3?

	65-year-old	80-year-old
 Dr Abramson	R-CHP + polatuzumab vedotin	Dose-reduced R-CHP + polatuzumab vedotin
 Dr Flowers	R-CHP + polatuzumab vedotin	R-CHP + polatuzumab vedotin
 Dr Kamdar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr LaCasce	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Matasar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Phillips	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Prof Salles	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Westin	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin

A 75-year-old woman with a history of congestive heart failure and a LVEF of 45% presents with Stage IV DLBCL with an IPI of 3. Which initial therapy would you most likely recommend if she had the DLBCL molecular subtype below?

	GCB-type	ABC-type, high-risk
 Dr Abramson	R-CHOP + dexrazoxane	Pola-R-CHP + dexrazoxane
 Dr Flowers	R-CHP + polatuzumab vedotin (dose adjustments PRN, cardiac monitoring)	R-CHP + polatuzumab vedotin (dose adjustments PRN, cardiac monitoring)
 Dr Kamdar	Dose-adjusted R-EPOCH	Pola-R-CHP + dexrazoxane
 Dr LaCasce	R-GCVP	Pola-R-CGP
 Dr Matasar	R-GCVP	R-GCVP
 Dr Phillips	Dose-adjusted R-EPOCH	R-CP + Pola + infusional doxorubicin
 Prof Salles	R-GCVP	R-mini-CGemP-Pola
 Dr Westin	R-CEOP	RCEP-Pola

R = rituximab; C = cyclophosphamide; E = etoposide; O = vincristine; P = prednisone; G = gemcitabine; V = vincristine; Pola = polatuzumab vedotin

Optimizing the Use of Novel Therapies for Patients with DLBCL

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Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

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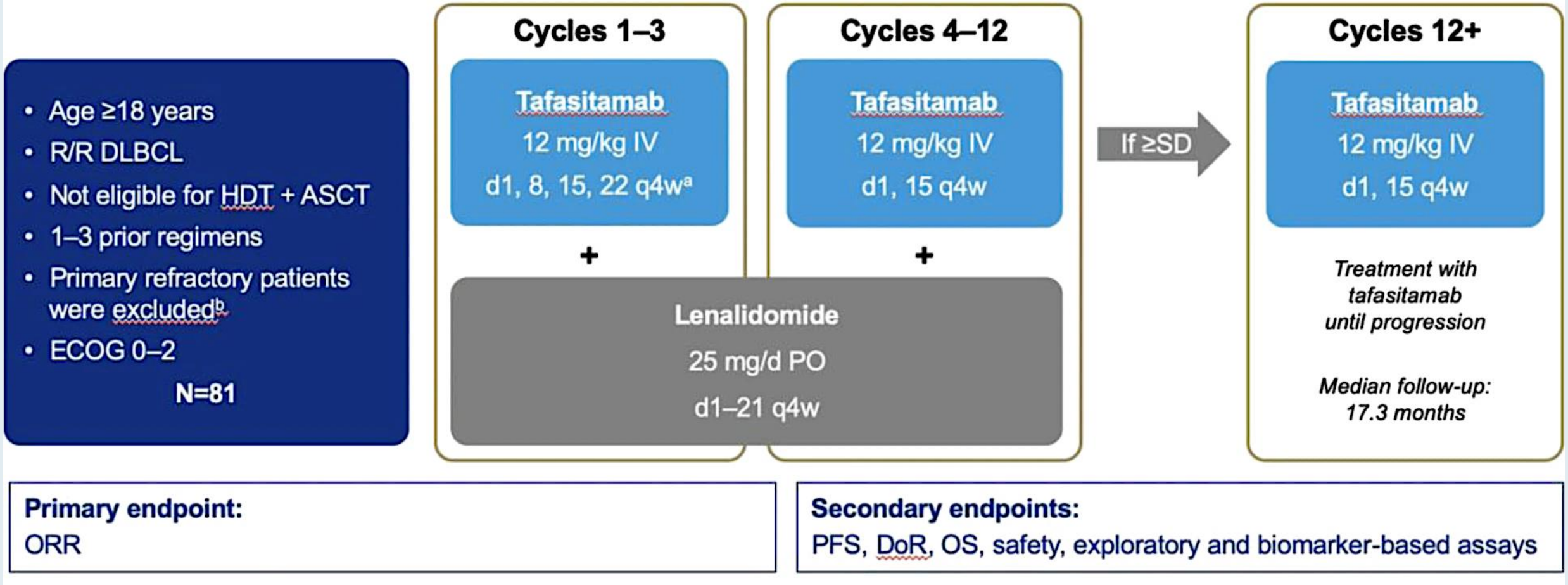
Key Datasets

- Duell J et al. **Tafasitamab** for patients with **relapsed or refractory diffuse large B-cell lymphoma: Final 5-year efficacy and safety findings** in the phase II **L-MIND** study. *Haematologica* 2024 February 1;109(2):553-66.
- Arias DA et al. **CD19 expression** persists in **diffuse large B-cell lymphoma** patient biopsies after treatment with **tafasitamab**. EHA 2024;Abstract P1234.
- Kim TM et al. **Safety and efficacy** of **AZD0486**, a **CD19xCD3 T-cell engager**, in **relapsed or refractory diffuse large B-cell lymphoma**. ASCO 2025;Abstract 7046.
- Dickinson MJ et al. **Glofitamab** for **relapsed or refractory diffuse large B-cell lymphoma**. *N Engl J Med* 2022 December 15;387(24):2220-31.
- Karimi YH et al. **3-year update** from the **Epcore NHL-1 trial**: **Epcoritamab** leads to deep and durable responses in **relapsed or refractory large B-cell lymphoma.**. ASH 2024;Abstract 4480.
- Fox CP et al. Results from **EPCORE DLBCL-1**: Randomized **phase 3** study of **epcoritamab vs investigator's choice chemoimmunotherapy** in patients with **relapsed/refractory large B-cell lymphoma**. EHA 2026;Abstract S235.
- Abramson JS et al. **Glofitamab plus gemcitabine and oxaliplatin (GemOx)** versus rituximab-GemOx for **relapsed or refractory diffuse large B-cell lymphoma (STARGLO):** A global **phase 3**, randomised, **open-label** trial. *Lancet* 2024 November 16;404(10466):1940-54.

Phase II L-MIND Study Design



HDT = high-dose therapy; ASCT = autologous stem cell transplant; SD = stable disease; DoR = duration of response

Duell J et al. *Haematologica* 2024 February 1;109(2):553-66.

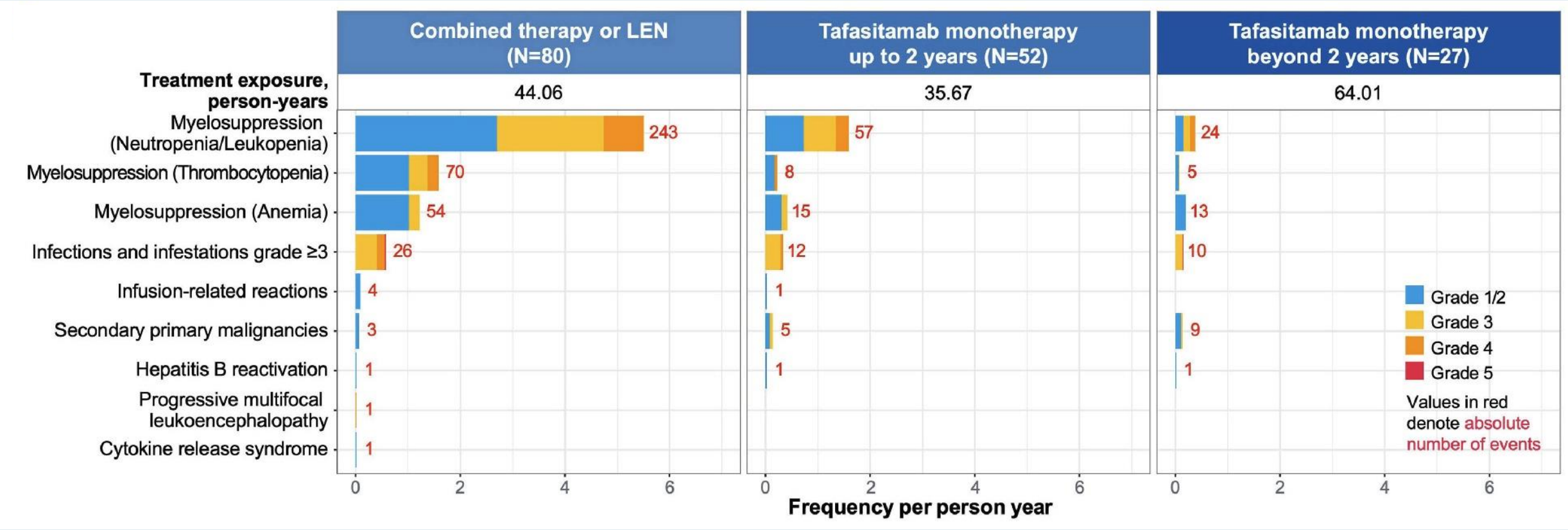
Phase II L-MIND: Efficacy Outcomes (Primary, 3-Year, 5-Year Analyses)

Characteristics	Primary analysis	3-year follow-up	Final 5-year data	5-year data for patients with 1 prior line of therapy, N=40	5-year data for patients with ≥2 prior lines of therapy, N=40
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022	Nov 14, 2022	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6-46.5]
PR rate, N (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
Median DoR in months [95% CI]	21.7 [21.7-NR]	43.9 [26.1-NR]	NR [33.8-NR]	NR [9.1-NR]	NR [26.1-NR]
Median PFS in months [95% CI]	12.1 [5.7-NR]	11.6 [6.3-45.7]	11.6 [5.7-45.7]	23.5 [7.4-NR]	7.6 [2.7-45.5]
Median OS in months [95% CI]	NR [18.3-NR]	33.5 [18.3-NR]	33.5 [18.3-NR]	NR [24.6-NR]	15.5 [8.6-45.5]

ORR: objective response rate; 95% CI: 95% confidence interval; CR: complete response; PR: partial response; DoR: duration of response; NR: not reached; PFS: progression-free survival; OS: overall survival.

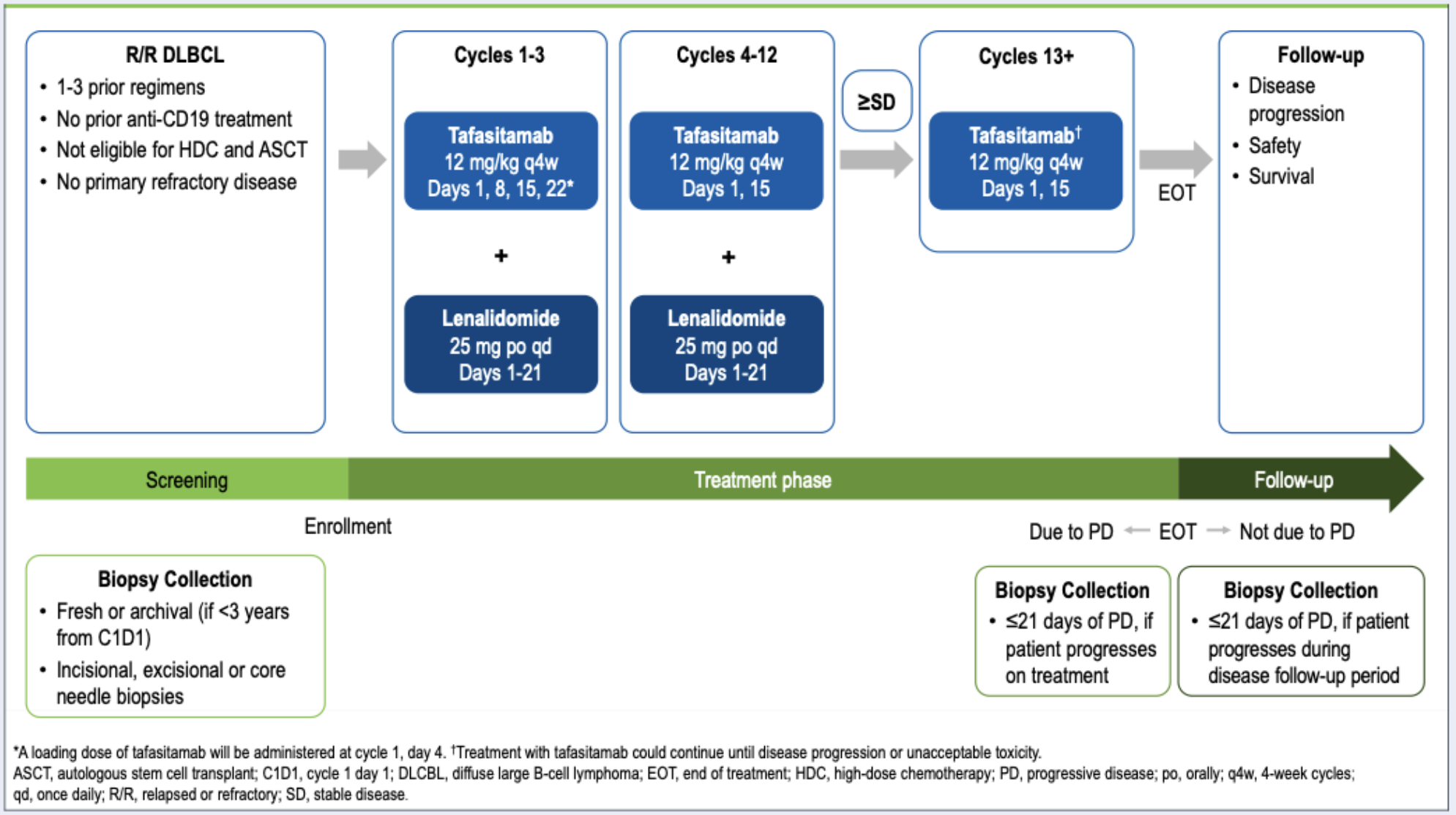
Duell J et al. *Haematologica* 2024 February 1;109(2):553-66.

Phase II L-MIND: Adverse Events of Special Interest



Duell J et al. *Haematologica* 2024 February 1;109(2):553-66.

Phase III firmMIND Study Design

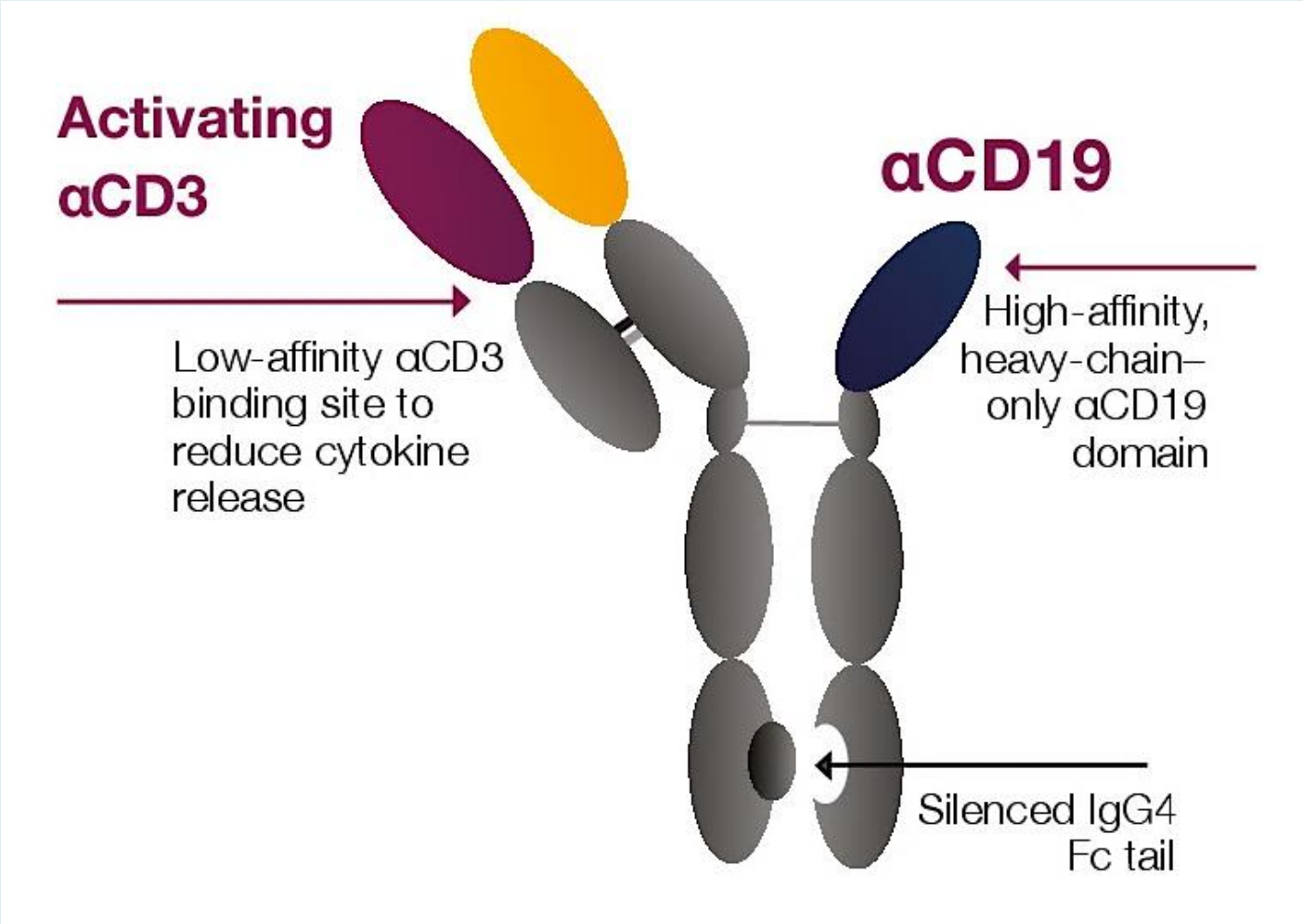


*A loading dose of tafasitamab will be administered at cycle 1, day 4. †Treatment with tafasitamab could continue until disease progression or unacceptable toxicity.
ASCT, autologous stem cell transplant; C1D1, cycle 1 day 1; DLCBL, diffuse large B-cell lymphoma; EOT, end of treatment; HDC, high-dose chemotherapy; PD, progressive disease; po, orally; q4w, 4-week cycles; qd, once daily; R/R, relapsed or refractory; SD, stable disease.

Estimated completion (primary): 2026-04-01

Arias DA et al. EHA 2024;Abstract P1234.

AZD0486: A CD19 x CD3 Bispecific T-Cell Engager



Le Gouill S et al. ASCO 2025;Abstract TPS7083.

Phase I AZD0486 Study: Responses by Target Dose (≥7.2 mg)

	Overall (N=58)			CAR-T Naive (n=31)			CAR-T Exposed (n=27)		
	n	ORR	CR rate	n	ORR	CR rate	n	ORR	CR rate
7.2 mg	24	46%	33%	9	67%	44%	15	33%	27%
15 mg	26	62%	39%	16	75%	38%	10	40%	40%
25 mg	8	75%	63%	6	83%	67%	2	50%	50%

Kim TM et al. ASCO 2025;Abstract 7046.

Phase I AZD0486 Study: Safety

Most common AEs (≥15%)	Any grade	Grade 3	Grade 4
CRS	42 (49)	0	0
Infections and infestations[b]	39 (45)	10 (12)	1 (1)
Neutropenia	29 (34)	9 (10)	15 (17)
Constipation	21 (24)	0	0
Anemia	20 (23)	14 (16)	0
Fatigue	20 (23)	3 (3)	0
ICANS	17 (20)	5 (6)	0
Hypogammaglobulinemia	16 (19)	0	0
Nausea	16 (19)	1 (1)	0
Diarrhea	14 (16)	0	0
Pyrexia	13 (15)	0	0

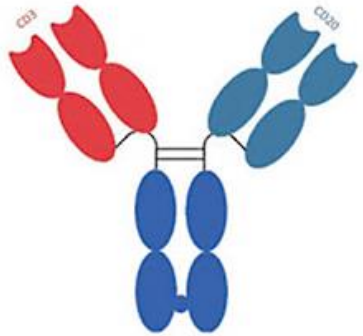
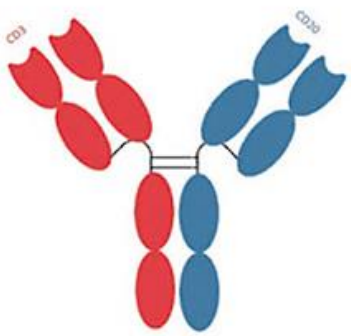
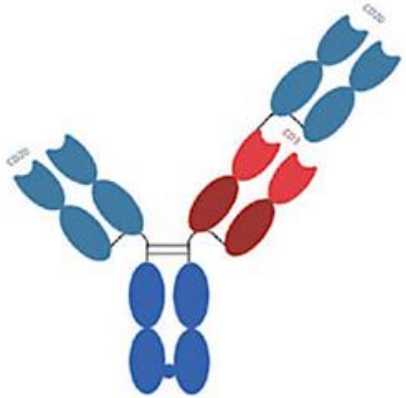
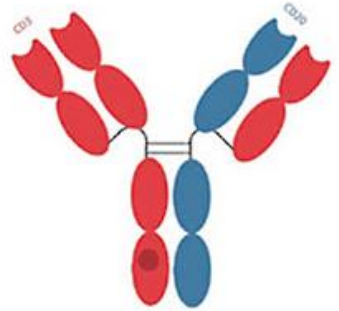
Values are n (%).
[a]All patients eventually received TD.
[b]Grouped by system organ class. One grade 5 event reported (pneumonia). COVID-19 infections reported in 9 (10%) patients (n=3 grade 1; n=6 grade 2).

AEs = adverse events; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

AZD0486 2SUD cohort (n=70), n (%)	Grade 1	Grade 2	Grade 3	Grade ≥4	Total
CRS	30 (43)	4 (6)	0	0	34 (49)
ICANS	4 (6)	6 (9)	4 (6)	0	14 (20)

Kim TM et al. ASCO 2025;Abstract 7046.

Bispecifics for DLBCL

	BLINATUMOMAB	MOSUNETUZUMAB	EPCORITAMAB	GLOFITAMAB	ODRONEXTAMAB
TARGET	CD3xCD19	CD3xCD20	CD3xCD20	CD3x$(CD20)_2$	CD3xCD20
DESIGN					
	• Monovalent CD3 and monovalent CD19 binding • Two murine scFv-joined by a glycine–serine linker	• Monovalent CD3 and monovalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and monovalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and bivalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and monovalent CD20 binding • Fully human IgG4-based antibody

Brijs J et al. *Belg J Hematol* 2023;14(2):67-72.

Glofitamab for R/R DLBCL Study: Efficacy (IRC- and Investigator-Assessed)

Outcome	Assessment According to Independent Review Committee (N=155)	Assessment According to Investigator (N=155)
Complete response		
No. of patients with response	61	58
Percentage of patients (95% CI)	39 (32–48)	37 (30–46)
Objective response		
No. of patients with response	80	89
Percentage of patients (95% CI)	52 (43–60)	57 (49–65)
Duration of complete response†		
Median (95% CI) — mo	NR (16.8–NR)	19.8 (18.2–NR)
Complete response at 12 mo (95% CI) — %	78 (64–91)	72 (59–86)
Duration of objective response‡		
Median (95% CI) — mo	18.4 (13.7–NR)	10.4 (6.8–NR)
Objective response at 12 mo (95% CI) — %	64 (51–76)	49 (37–61)
Median time to first complete response (range) — days†	42 (31–308)	43 (31–274)
Progression-free survival		
Median (95% CI) — mo	4.9 (3.4–8.1)	3.8 (3.3–5.4)
Alive without progression at 12 mo (95% CI) — %	37 (29–46)	30 (22–38)
Overall survival		
Median (95% CI) — mo	—	11.5 (7.9–15.7)
Alive at 12 mo (95% CI) — %	—	50 (41–58)

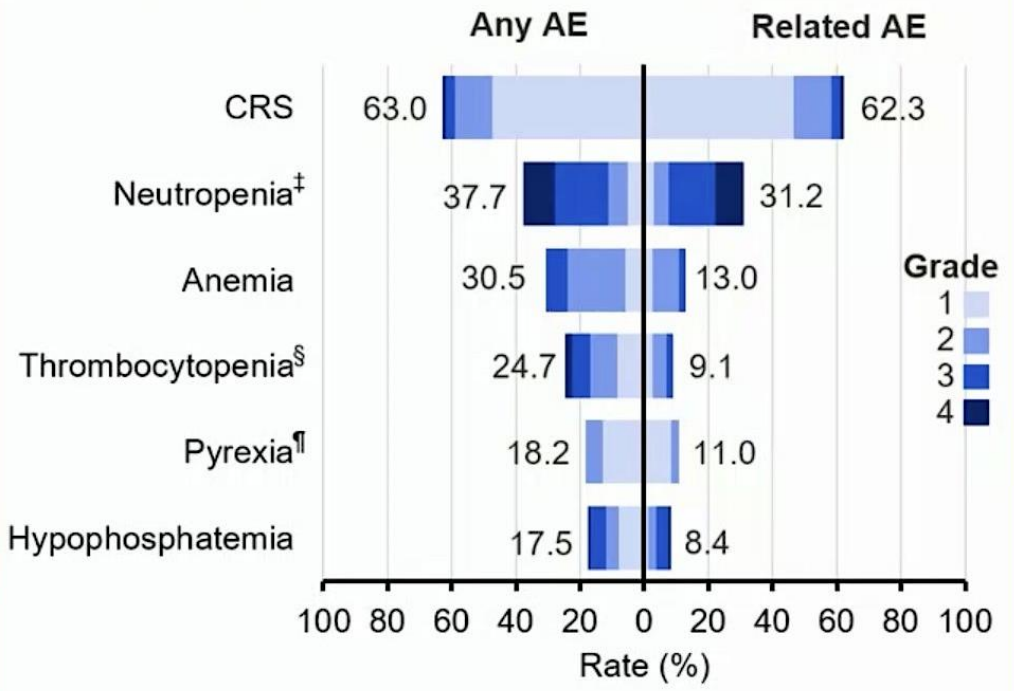
Dickinson MJ et al. *N Engl J Med* 2022 December 15;387(24):2220-31.

IRC = independent review committee

Glofitamab for R/R DLBCL: Safety

n (%)*	N=154
Median no. of cycles received (range)	5 (1–13)
Median relative dose intensity, % (range)	100 (94–100)
AE	152 (98.7)
Related AE	140 (90.9)
Grade 3–4 AE	87 (56.5)
Related AE	64 (41.6)
Serious AE	73 (47.4)
Related AE	46 (29.9)
Grade 5 (fatal AE)	8 (5.2)†
Related AE	0
AE leading to treatment discontinuation	14 (9.1)
Related AE	5 (3.2)

AEs (≥15%) by grade and relationship with glofitamab

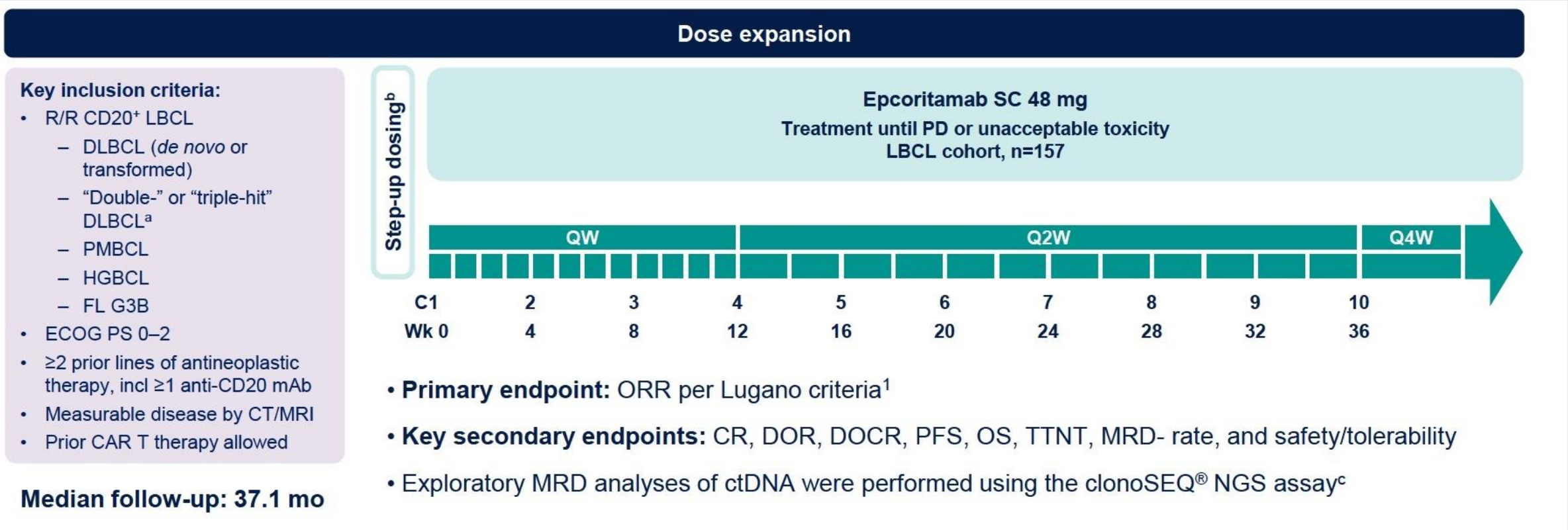


Glofitamab was well tolerated, with a favorable safety profile

*unless otherwise specified; †COVID-19/COVID-19 pneumonia (n=5); sepsis (n=2); delirium (n=1);
‡includes neutrophil count decreased; §includes platelet count decreased; ¶pyrexia events separate from CRS.

Dickinson MJ et al. EHA 2022;Abstract S220.

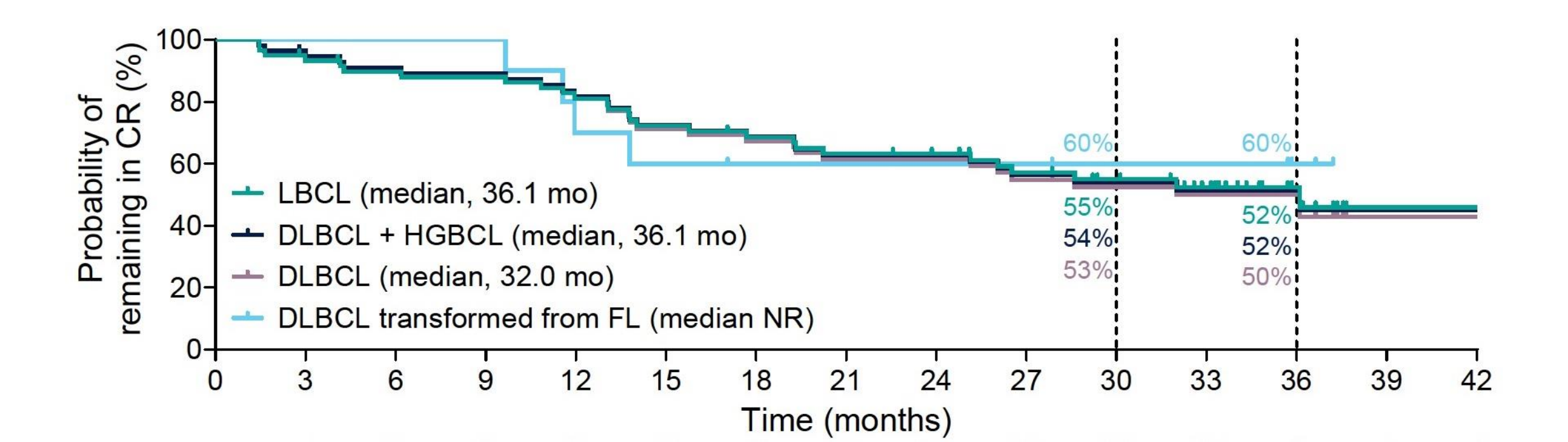
Phase II EPCORE NHL-1 Study Design



PMBCL = primary mediastinal B-cell lymphoma; HGBCL = high-grade B-cell lymphoma; FL = follicular lymphoma; DOCR = duration of complete response; TTNT = time to next treatment; MRD = minimal residual disease; ctDNA = circulating tumor DNA

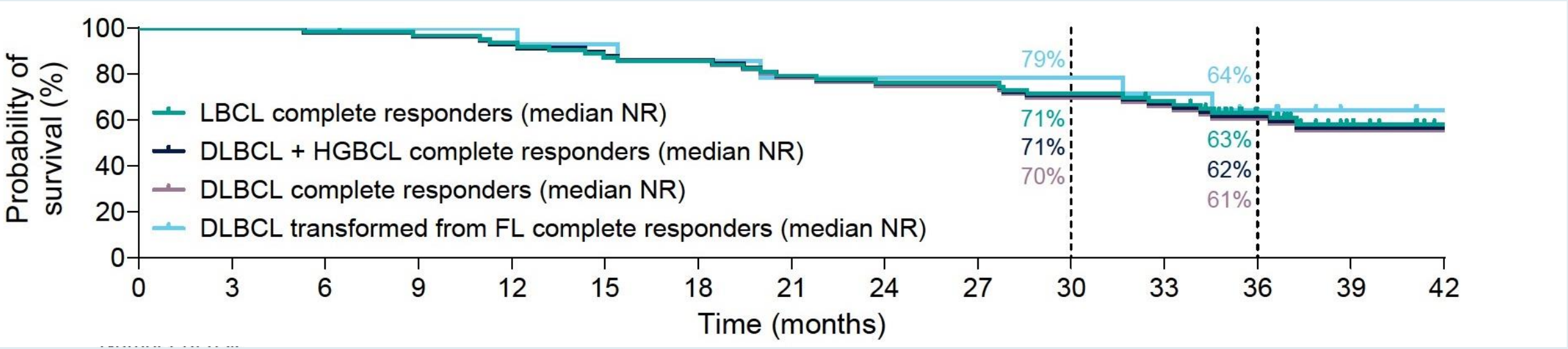
Karimi YH et al. ASH 2024;Abstract 4480.

Phase II EPCORE NHL-1: Responses



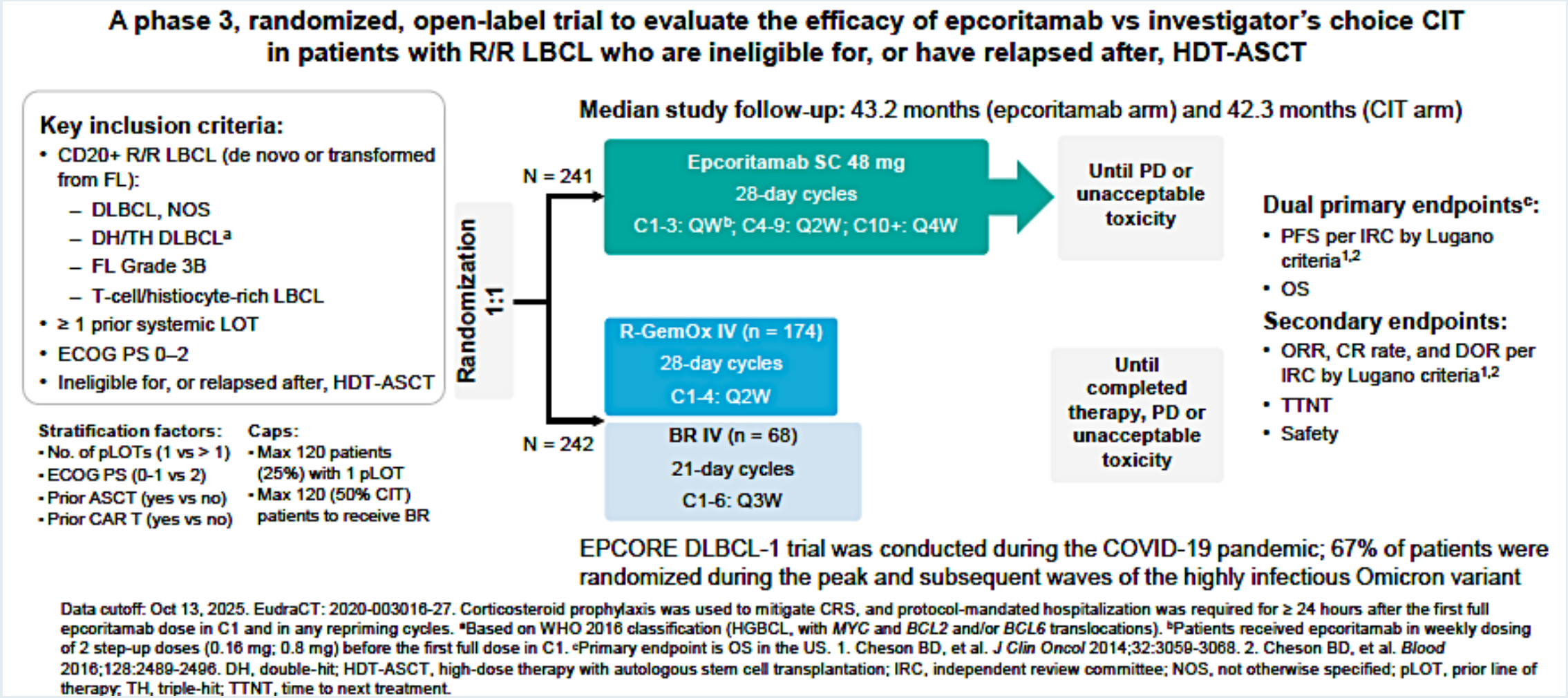
Karimi YH et al. ASH 2024;Abstract 4480.

Phase II EPCORE NHL-1: Overall Survival



Karimi YH et al. ASH 2024;Abstract 4480.

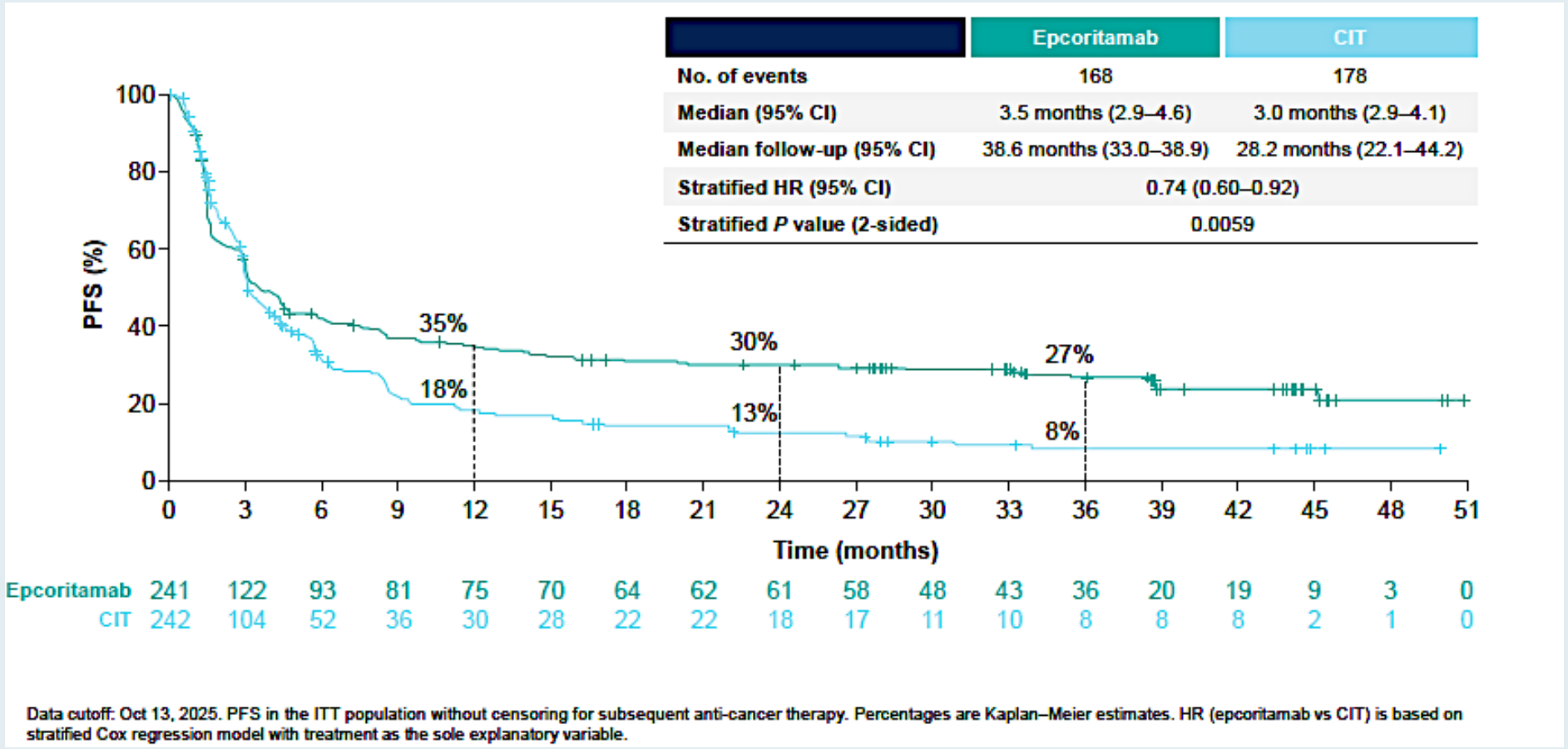
EPCORE DLBCL-1 Phase III Trial of Epcoritamab versus Investigator's Choice Chemoimmunotherapy (CIT) for R/R LBCL



Data cutoff: Oct 13, 2025. EudraCT: 2020-003016-27. Corticosteroid prophylaxis was used to mitigate CRS, and protocol-mandated hospitalization was required for ≥ 24 hours after the first full epcoritamab dose in C1 and in any repriming cycles. [a]Based on WHO 2016 classification (HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations). [b]Patients received epcoritamab in weekly dosing of 2 step-up doses (0.16 mg; 0.8 mg) before the first full dose in C1. [c]Primary endpoint is OS in the US. 1. Cheson BD, et al. *J Clin Oncol* 2014;32:3059-3068. 2. Cheson BD, et al. *Blood* 2016;128:2489-2496. DH, double-hit; HDT-ASCT, high-dose therapy with autologous stem cell transplantation; IRC, independent review committee; NOS, not otherwise specified; pLOT, prior line of therapy; TH, triple-hit; TTNT, time to next treatment.

Fox CP et al. EHA 2026;Abstract S235.

EPCORE DLBCL-1: Efficacy Summary



Data cutoff: Oct 13, 2025. PFS in the ITT population without censoring for subsequent anti-cancer therapy. Percentages are Kaplan–Meier estimates. HR (epcoritamab vs CIT) is based on stratified Cox regression model with treatment as the sole explanatory variable.

- Epcoritamab resulted in clinically meaningful improvement in CR, DOR and DOCR
- OS was not significantly different; confounded by COVID-19 mortality and higher use of effective subsequent treatments in the CIT arm

Fox CP et al. EHA 2026;Abstract S235.

EPCORE DLBCL-1: Most Common Treatment-Emergent Adverse Events

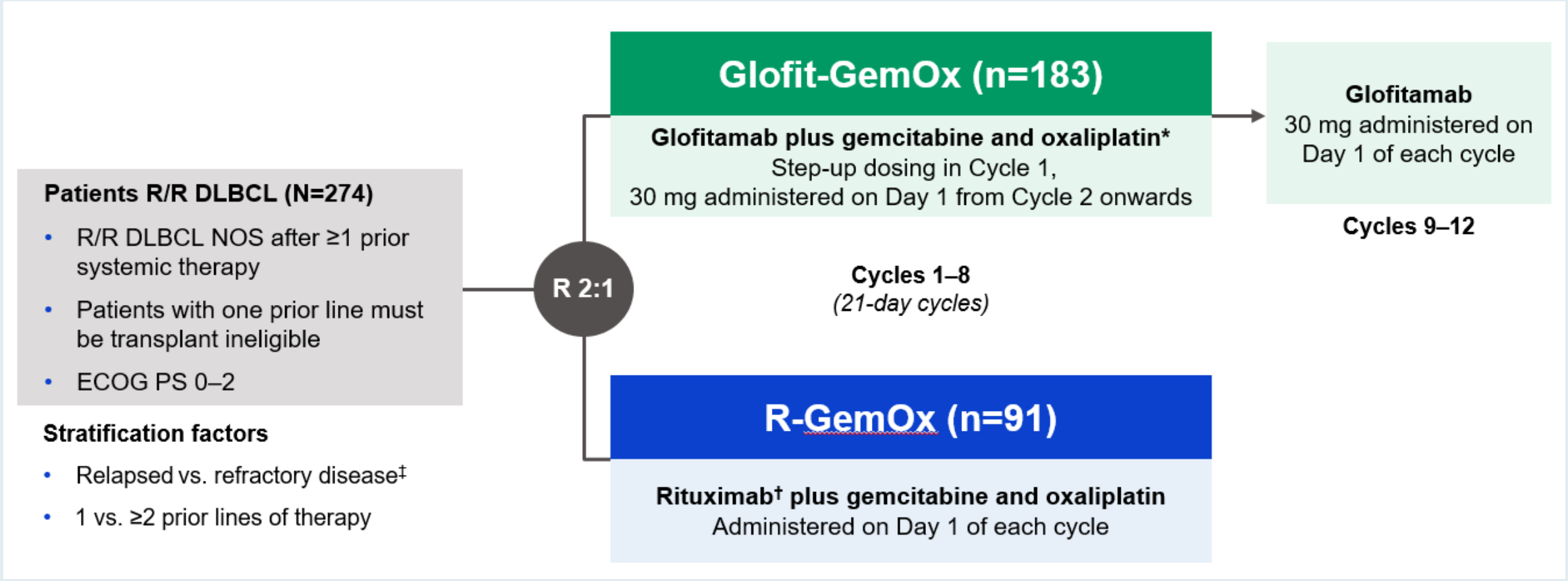
	Epcoritamab (N = 236)	CIT (N = 237)	Epcoritamab (N = 236)	CIT (N = 237)
	n (%)	n (%)	EAER[a]	EAER[a]
CRS[b]	124 (53)	NA	NA	NA
COVID-19[c]	88 (37)	28 (12)	4.8	3.9
Neutropenia[d]	84 (36)	109 (46)	6.4	30.1
Pyrexia	62 (26)	30 (13)	3.1	4.4
Anemia	61 (26)	84 (35)	2.6	15.6
Injection site reactions[e]	51 (22)	NA	NA	NA
Diarrhea	47 (20)	30 (13)	2.1	4.3
Thrombocytopenia[f]	42 (18)	125 (53)	1.9	28.3
Nausea	32 (14)	74 (31)	1.4	11.3

- Higher rates of grade 3–4 infections (30% vs 12%) were reported in the epcoritamab vs the CIT arm, with grade 3–4 infection EAERs of 4.3 vs 4.9, respectively
- Febrile neutropenia was reported in 2% of patients in the epcoritamab arm and 5% in the CIT arm; EAERs were 0.2 vs 1.7, respectively
- ICANS events were reported in 9 patients (grade 1–2, in 7; grade 3–4 in 2) in the epcoritamab arm

Data cutoff: Oct 13, 2025. [a]EAER equals the number of events*100/patient-months of exposure. [b]Most CRS events were grade 1–2 (117/124 [94%]) with the remaining 7/124 (6%) grade 3. [c]Includes preferred terms COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [d]Includes preferred terms neutropenia and neutrophil count decreased. [e]Includes preferred terms injection site reaction, injection site reaction erythrema, injection site reaction pain, injection site reaction pruritus, injection site reaction rash, injection site reaction inflammation, injection site reaction swelling. [f]Includes preferred terms platelet count decreased and thrombocytopenia. EAER, exposure-adjusted event rate.

Fox CP et al. EHA 2026;Abstract S235.

Phase III STARGLO Study Design



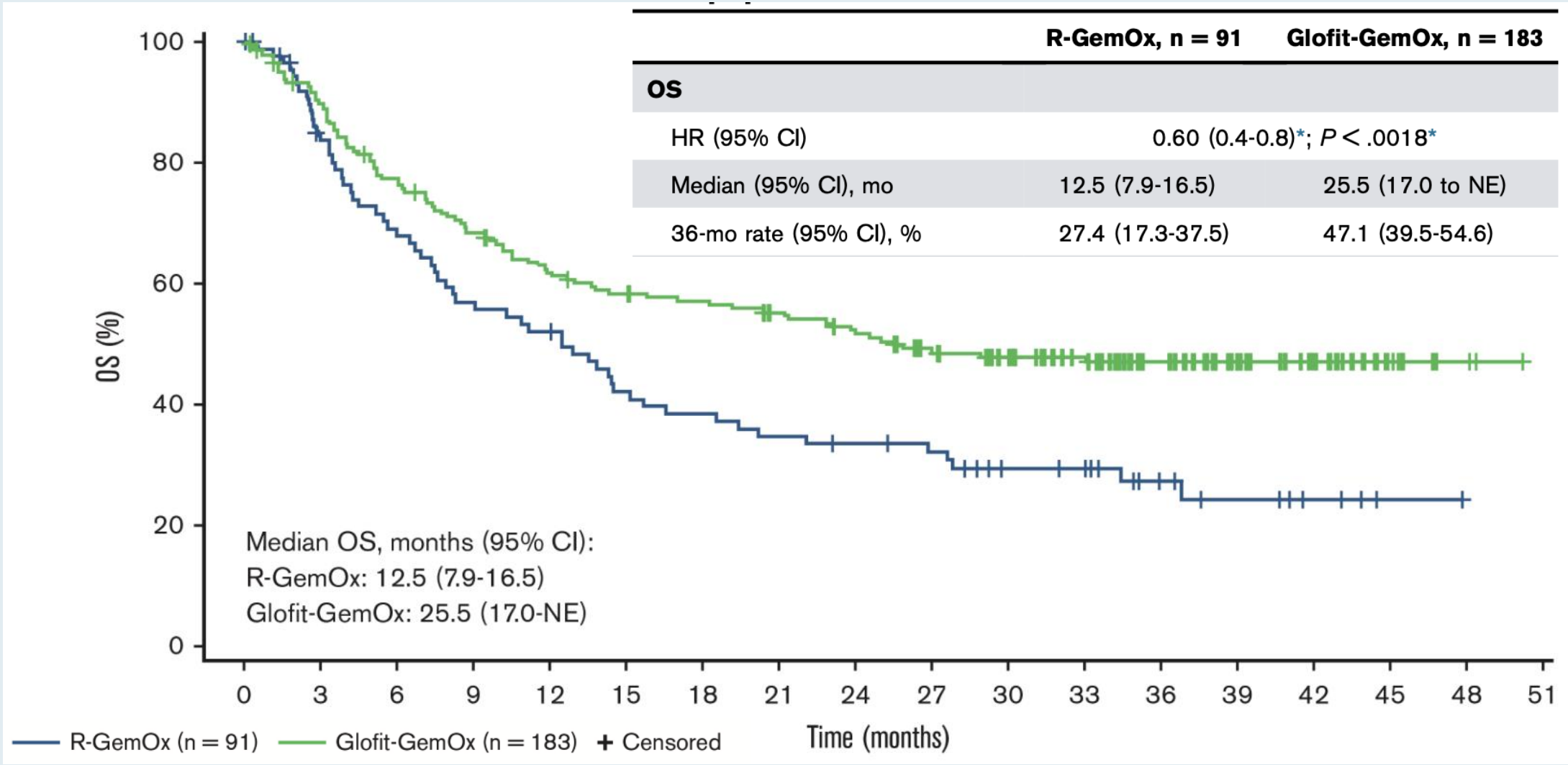
Primary endpoint:
Overall survival

Secondary endpoints:
Progression-free survival, ORR, DoR

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

Phase III STARGLO 3-Year Follow-Up: Overall Survival (OS; Primary Endpoint)

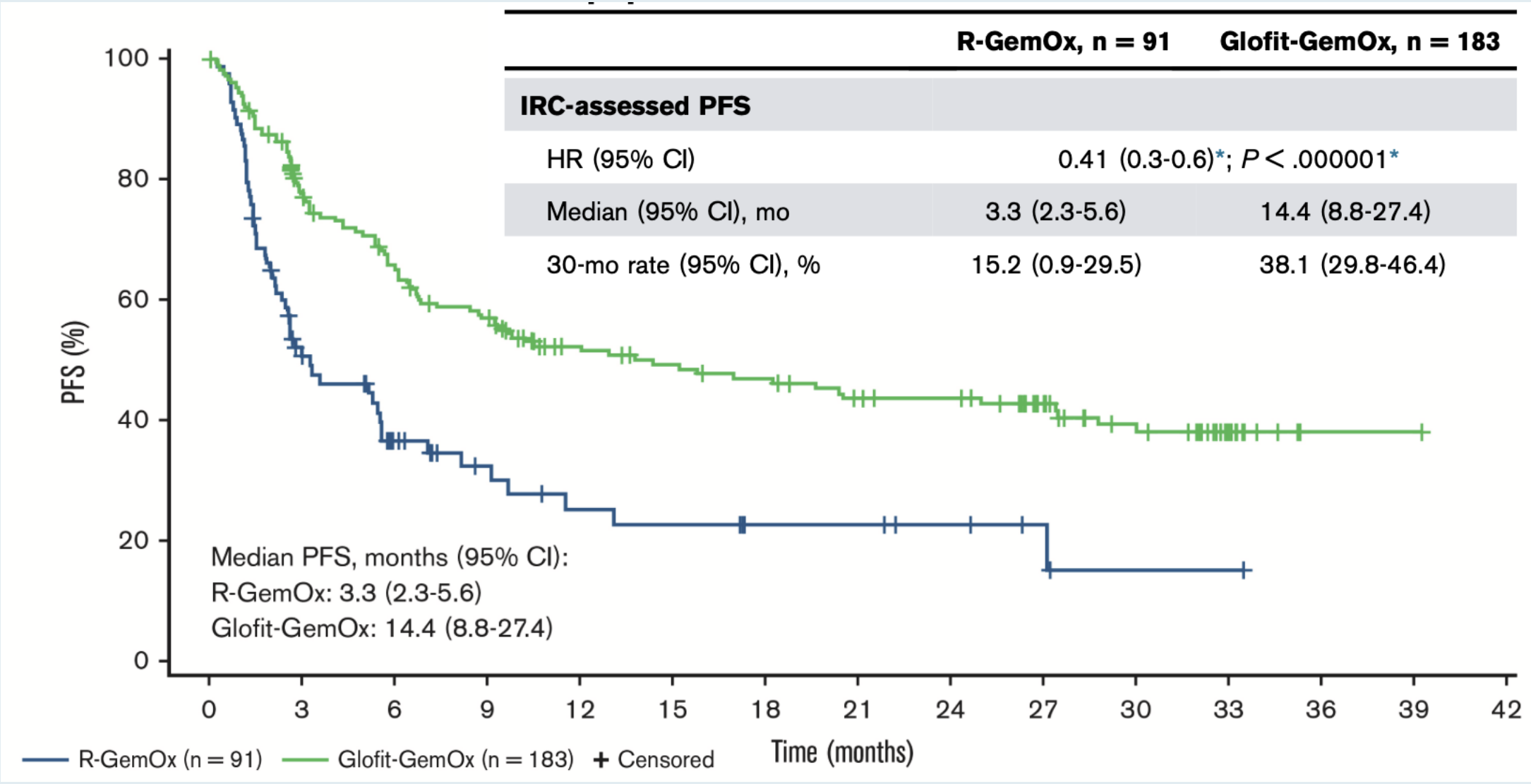
	R-GemOx, n = 91	Glofit-GemOx, n = 183
OS		
HR (95% CI)	0.60 (0.4-0.8)*; $P < .0018$*	
Median (95% CI), mo	12.5 (7.9-16.5)	25.5 (17.0 to NE)
36-mo rate (95% CI), %	27.4 (17.3-37.5)	47.1 (39.5-54.6)



Abramson JS et al. *Blood Adv* 2026 August 11;10(15):5367-77.

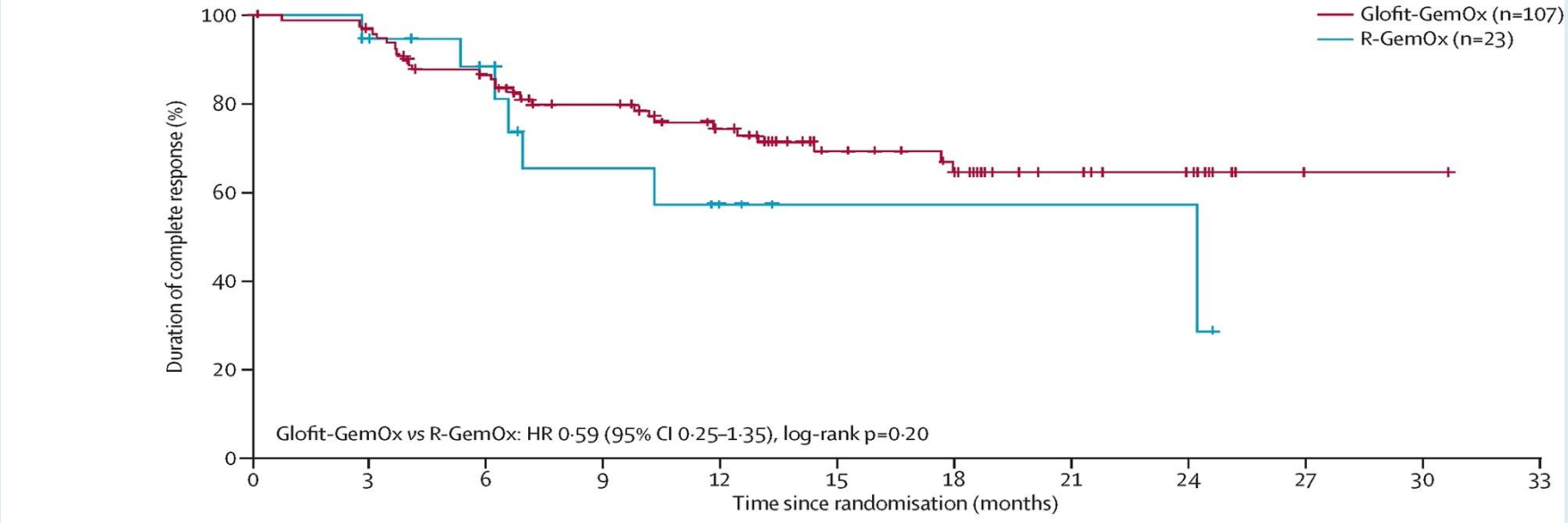
Phase III STARGLO 3-Year Follow-up: Progression-Free Survival (PFS)

	R-GemOx, n = 91	Glofit-GemOx, n = 183
IRC-assessed PFS		
HR (95% CI)	0.41 (0.3-0.6)*; $P < .000001$*	
Median (95% CI), mo	3.3 (2.3-5.6)	14.4 (8.8-27.4)
30-mo rate (95% CI), %	15.2 (0.9-29.5)	38.1 (29.8-46.4)



Abramson JS et al. *Blood Adv* 2026 August 11;10(15):5367-77.

Phase III STARGLO: Responses



	R-GemOx (n=91)	Glofit-GemOx (n=183)	p value*
Secondary endpoints			
IRC-assessed best overall response‡, %	..	..	..
Objective response	40·7 (30·5–51·5)	68·3 (61·0–75·0)	p<0·0001†
Complete response	25·3 (16·8–35·5)	58·5 (51·0–65·7)	p<0·0001†
Investigator-assessed best overall response‡, %	..	..	..
Objective response	37·4 (27·4–48·1)	69·9 (62·7–76·5)	p<0·0001†
Complete response	23·1 (14·9–33·1)	57·4 (49·9–64·6)	p<0·0001†
IRC-assessed duration of complete response	n=23	n=107	..
HR	..	0·59 (0·25–1·35)§	p=0·20§
Median, months	24·2 (6·9–NE)	NE (NE–NE)	..
IRC-assessed duration of objective response	n=37	n=125	..
HR	..	0·57 (0·30–1·10)§	p=0·089§
Median, months	10·3 (6·5–NE)	NE (17·6–NE)	..

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

Phase III STARGLO: Safety

	R-GemOx (n=88)	Glofit-GemOx (n=180)
Any adverse event	84 (96%)	180 (100%)
Most common adverse event (≥30% patients in either group)		
Thrombocytopenia*	42 (48%)	87 (48%)
CRS†	NA	76 (44%)†
Neutropenia‡	27 (31%)	76 (42%)
Anaemia	19 (22%)	73 (41%)
Nausea	35 (40%)	71 (39%)
Peripheral neuropathy§	23 (26%)	64 (36%)
Diarrhoea	24 (27%)	62 (34%)
Aspartate transferase increased	17 (19%)	59 (33%)
Alanine transaminase increased	19 (22%)	57 (32%)
Any glofitamab-related or rituximab-related adverse event	58 (66%)	149 (83%)
Any grade ≥3 adverse event	36 (41%)	140 (78%)
Any glofitamab-related or rituximab-related grade ≥3 adverse event	20 (23%)	85 (47%)
Any serious adverse event	15 (17%)	98 (54%)
Any glofitamab-related or rituximab-related serious adverse event	7 (8%)	62 (34%)
Any adverse event of special interest	69 (78%)	176 (98%)
CRS†	NA	76 (44%)†
Grade 1	NA	54 (31%)†
Grade 2	NA	18 (11%)†
Grade 3	NA	4 (2%)†
Neurological adverse event (grade ≥2)	11 (13%)	55 (31%)
Serious infections	11 (13%)	46 (26%)
Febrile neutropenia	1 (1%)	6 (3%)
Tumour flare (grade ≥2)	1 (1%)	1 (1%)
Any grade 5 adverse event	4 (5%)	15 (8%)

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

RTP RESEARCH TO PRACTICE

Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Clinician Survey Results

Module 3: Current and Future Roles of Monoclonal and Bispecific Antibodies in Therapy for Relapsed/Refractory (R/R) DLBCL

Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which second-line therapy would you generally recommend for an older (85-year-old) patient with DLBCL who experienced disease relapse 18 months after first-line R-CHOP and who was …

	CAR T eligible but transplant ineligible	Transplant *and* CAR T ineligible
 Dr Abramson	CAR T-cell therapy	Mosunetuzumab/polatuzumab vedotin
 Dr Flowers	Mosunetuzumab/polatuzumab vedotin	Mosunetuzumab/polatuzumab vedotin
 Dr Kamdar	CAR T-cell therapy	Tafasitamab/lenalidomide or glofitamab/GemOx
 Dr LaCasce	CAR T-cell therapy	Mosunetuzumab/polatuzumab vedotin
 Dr Matasar	CAR T-cell therapy	Glofitamab/GemOx
 Dr Phillips	Mosunetuzumab/polatuzumab vedotin	Mosunetuzumab/polatuzumab vedotin
 Prof Salles	Glofitamab/GemOx	Glofitamab/GemOx
 Dr Westin	CAR T-cell therapy	Tafasitamab/lenalidomide or mosunetuzumab/polatuzumab vedotin

GemOx = gemcitabine/oxaliplatin

Regulatory and reimbursement issues aside, which third-line therapy would you generally recommend for a 65-year-old patient with DLBCL who received first-line R-CHOP and subsequently experienced disease progression on second-line CAR T-cell therapy?

 Dr Abramson	Glofitamab/GemOx
 Dr Flowers	Glofitamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Polatuzumab vedotin/R-GemOx
 Dr Phillips	Glofitamab/polatuzumab vedotin
 Prof Salles	Glofitamab/GemOx or polatuzumab vedotin/glofitamab
 Dr Westin	Glofitamab/GemOx or polatuzumab vedotin/glofitamab

R-GemOx = rituximab/gemcitabine/oxaliplatin

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which third-line therapy would you generally recommend for a 65-year-old patient with DLBCL who received first-line polatuzumab vedotin/R-CHP and subsequently experienced disease progression on second-line CAR T-cell therapy?

 Dr Abramson	Glofitamab/GemOx
 Dr Flowers	Glofitamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Loncastuximab tesirine
 Dr Phillips	Glofitamab/GemOx
 Prof Salles	Glofitamab/GemOx
 Dr Westin	Glofitamab/GemOx

Regulatory and reimbursement issues aside, which third-line therapy would you generally recommend for an 85-year-old patient with DLBCL who received first-line R-mini-CHOP and subsequently experienced disease progression on second-line polatuzumab vedotin with bendamustine/rituximab (BR)?

 Dr Abramson	Glofitamab
 Dr Flowers	Epcoritamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Glofitamab/GemOx
 Dr Phillips	Glofitamab or epcoritamab
 Prof Salles	Glofitamab/GemOx
 Dr Westin	Glofitamab or epcoritamab

Assuming equal access, which bispecific antibody would you prefer to use when administering one of these agents as monotherapy for your patients with R/R DLBCL?

 Dr Abramson	Glofitamab
 Dr Flowers	No preference
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Glofitamab
 Dr Phillips	No preference
 Prof Salles	Glofitamab
 Dr Westin	Glofitamab

RTP RESEARCH TO PRACTICE

Based on the published literature and your clinical experience, would you like to have access to surovatamig for your patients with R/R DLBCL today?

 Dr Abramson	Yes, for patients with CD20-negative disease
 Dr Flowers	Yes, as part of second-line combinations prior to CAR T; third-line+ relapse
 Dr Kamdar	Yes, for CAR T-ineligible pts in the second-line setting
 Dr LaCasce	Yes, for patients who are ineligible for CD19 CAR T
 Dr Matasar	No
 Dr Phillips	Yes, after CAR T-cell therapy
 Prof Salles	Yes, for patients with PD on CD3 x CD20 combinations or monotherapy, and for those with CD20-negative disease
 Dr Westin	Yes, for patients with CD20 loss and non-CAR T eligible

RTP RESEARCH TO PRACTICE

If surovatamig were granted regulatory approval, would you employ a CD20 x CD3 bispecific antibody and surovatamig in sequence for the same patient with R/R DLBCL?

 Dr Abramson	Yes
 Dr Flowers	Yes
 Dr Kamdar	Yes
 Dr LaCasce	Maybe
 Dr Matasar	Yes
 Dr Phillips	Yes
 Prof Salles	Yes
 Dr Westin	Yes

RTP RESEARCH TO PRACTICE

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Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Key Datasets

- Sehn LH et al. **Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL): Final results of a phase Ib/II randomized study and single-arm extension (ext) study**. ASH 2022;Abstract 4260.
- Matasar M et al. **Polatuzumab vedotin, rituximab, gemcitabine and oxaliplatin (Pola-R-GemOx) for relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL): Results** from the randomized **phase III POLARGO** trial. EHA 2025;Abstract S101.
- Kim W et al. **Mosunetuzumab plus polatuzumab vedotin (Mosun-Pola)** versus rituximab, gemcitabine and oxaliplatin (R-GemOx) in patients with **relapsed/refractory large B-cell lymphoma (R/R LBCL): Updated efficacy and safety from the phase 3 SUNMO study** including in second-line (2L) versus third-line plus (3L+) patient subgroups. ASCO 2026;Abstract 7007.
- Kim JA et al. **Brentuximab vedotin in combination with lenalidomide and rituximab** in patients with **relapsed/refractory diffuse large B-cell lymphoma: Results** from the **phase 3 ECHELON-3** study**.** ASCO 2024;Abstract LBA7005.
- Caimi PF et al. **Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: Long-term efficacy and safety from the phase II LOTIS-2 study.** *Haematologica* 2024 April 1;109(4):1184-93.
- Carlo-Stella C et al. **Updated safety run-in results** from **LOTIS-5:** A **phase 3,** randomized trial of **loncastuximab tesirine with rituximab** versus immunochemotherapy in patients with **R/R DLBCL/HGBL**. EHA 2025;Abstract PS1957.
- Alderuccio JP et al. **Initial results from LOTIS-7: A phase 1b** study of **loncastuximab tesirine plus glofitamab** in patients with **relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL)**. ICML 2025;Abstract 078.

RTP RESEARCH TO PRACTICE

Phase Ib/II GO29365 Study Final Results: Efficacy

Outcome*	Randomized		Extension
	Pola+BR (n=40)	BR (n=40)	Pola+BR (n=106)
ORR, % (95% CI)	42.5 (27.0–59.1)	17.5 (7.3–32.8)	43.4 (33.8–53.4)
CR, % (95% CI)	42.5 (27.0–59.1)	17.5 (7.3–32.8)	39.6 (30.3–49.6)
BOR, % (95% CI)	62.5 (45.8–77.3)	25.0 (12.7–41.2)	57.5 (47.6–67.1)
BCR, % (95% CI)	52.5 (36.1–68.5)	22.5 (10.8–38.5)	53.8 (43.8–63.5)
Median DOR, months (95% CI)	10.9 (5.7–40.7)	10.6 (4.0–19.7)	13.4 (8.6–20.0)
Median PFS, months (95% CI)	9.2 (6.0–13.9)	3.7 (2.1–4.5)	7.0 (5.1–9.8)
Median OS, months (95% CI)	12.4 (9.0–32.0)	4.5 (3.7–6.0)	12.3 (8.3–17.0)

*All endpoints were determined by IRC, except OS, which was INV-determined.
BCR, best complete response; BOR, best overall response; BR, bendamustine + rituximab; CI, confidence interval; CR, complete response; DOR, duration of response; INV, investigator; IRC, independent review committee; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Pola, polatuzumab vedotin.

Sehn LH et al. ASH 2022;Abstract 4260.

Phase Ib/II GO29365 Final Results: Safety

	Randomized		Extension
	Pola+BR (n=39*)	BR (n=39*)	Pola+BR (n=106)
Any-grade AEs, n (%)	39 (100.0)	38 (97.4)	105 (99.1)
Grade 3–4 AEs, n (%)	34 (87.2)	28 (71.8)	83 (78.3)
Neutropenia	18 (46.2)	13 (33.3)	31 (29.2)
Thrombocytopenia	15 (38.5)	9 (23.1)	15 (14.2)
Serious AEs, n (%)	27 (69.2)	24 (61.5)	57 (53.8)
Pyrexia	5 (12.8)	0 (0.0)	7 (6.6)
Pneumonia	4 (10.3)	4 (10.3)	6 (5.7)
Febrile neutropenia	4 (10.3)	4 (10.3)	9 (8.5)
Sepsis	2 (5.1)	2 (5.1)	7 (6.6)
Grade 5 AEs, n (%)	11 (28.2)	10 (25.6)	6 (5.7)
Any-grade PN, n (%)	17 (43.6)	3 (7.7)	29 (27.4)
Grade ≥2 PN	6 (15.4)	2 (5.1)	16 (15.1)
AEs leading to delay of any drug, n (%)	21 (53.8)	14 (35.9)	53 (50.0)
AEs leading to discontinuation of any drug, n (%)	13 (33.3)	5 (12.8)	16 (15.1)

*One patient in each group did not receive study treatment and so was excluded from the safety-evaluable population.

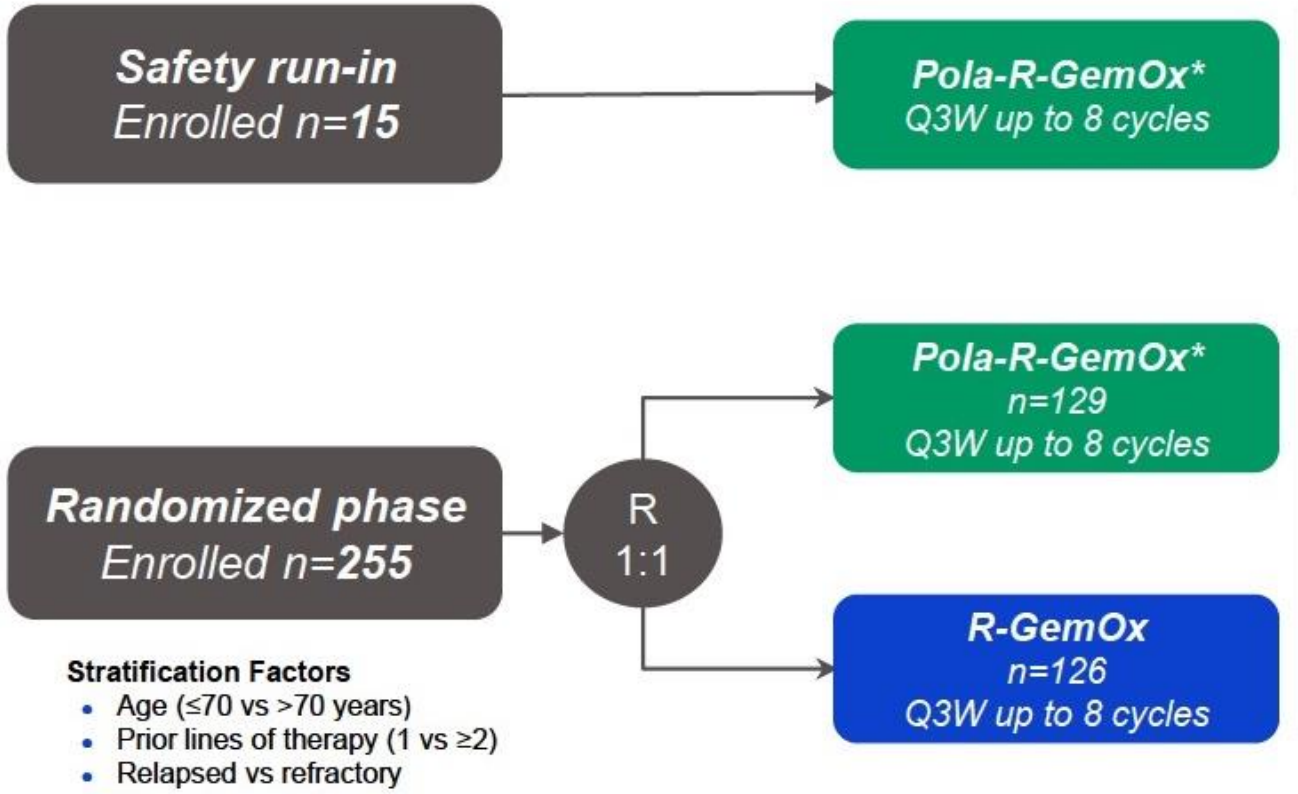
AE, adverse event; BR, bendamustine + rituximab; PN, peripheral neuropathy; Pola, polatuzumab vedotin.

Sehn LH et al. ASH 2022;Abstract 4260.

Phase III POLARGO Study Design

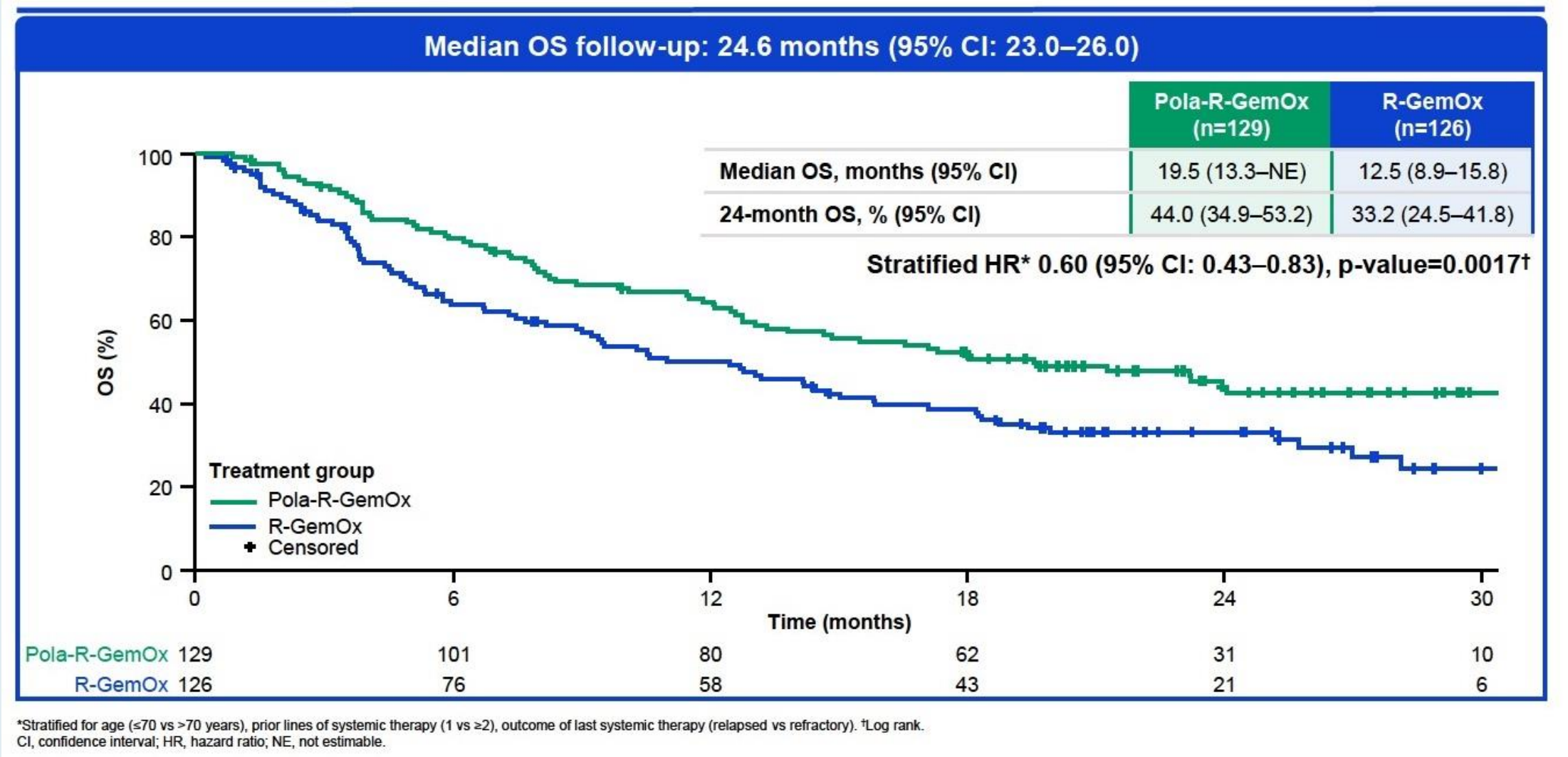
Key eligibility criteria

- DLBCL, NOS or history of transformation of indolent disease to DLBCL
- R/R disease after ≥1 prior line of treatment
- Ineligible for transplant



Matasar M et al. EHA 2025;Abstract S101.

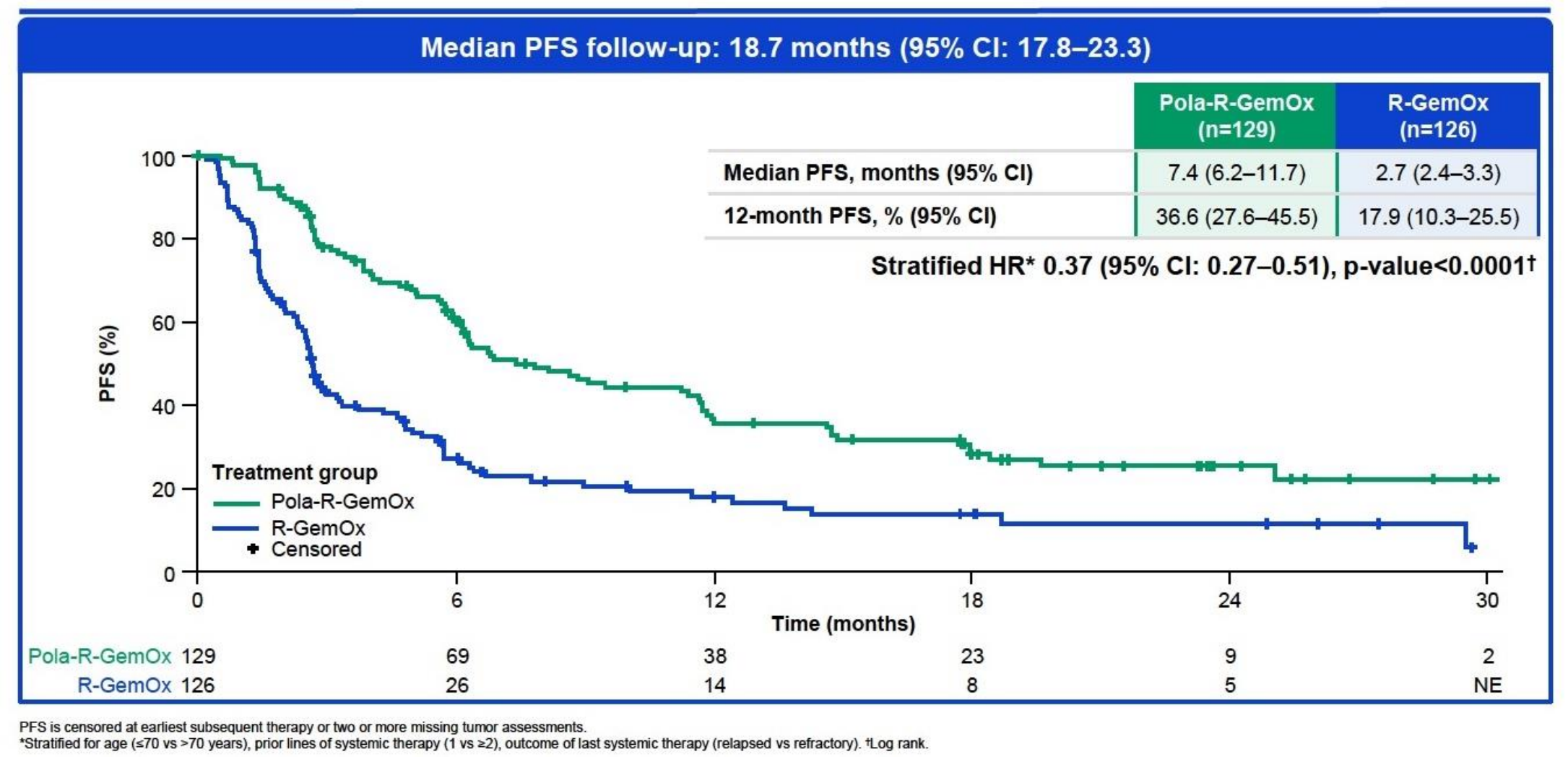
Phase III POLARGO Overall Survival



*Stratified for age (≤70 vs >70 years), prior lines of systemic therapy (1 vs ≥2), outcome of last systemic therapy (relapsed vs refractory). †Log rank.
CI, confidence interval; HR, hazard ratio; NE, not estimable.

Matasar M et al. EHA 2025;Abstract S101.

Phase III POLARGO: Progression-Free Survival



PFS is censored at earliest subsequent therapy or two or more missing tumor assessments.
*Stratified for age (≤70 vs >70 years), prior lines of systemic therapy (1 vs ≥2), outcome of last systemic therapy (relapsed vs refractory). †Log rank.

Matasar M et al. EHA 2025;Abstract S101.

Phase III POLARGO: Select AEs

n (%)	Pola-R-GemOx (n=128)	R-GemOx (n=125)
Thrombocytopenia*	68 (53.1)	51 (40.8)
Grade ≥3	44 (34.4)	33 (26.4)
Neutropenia*	53 (41.4)	52 (41.6)
Grade ≥3	43 (33.6)	38 (30.4)
Febrile neutropenia†	3 (2.3)	3 (2.4)
Grade ≥3	3 (2.3)	3 (2.4)
Anemia*	48 (37.5)	35 (28.0)
Grade ≥3	17 (13.3)	19 (15.2)
Infections*	53 (41.4)	39 (31.2)
Grade ≥3	28 (21.9)	12 (9.6)
Hepatic toxicity*	41 (32.0)	25 (20.0)
Grade ≥ 3	11 (8.6)	2 (1.6)

*Custom grouped terms. †Based on preferred term.

Matasar M et al. EHA 2025;Abstract S101.

RTP RESEARCH TO PRACTICE

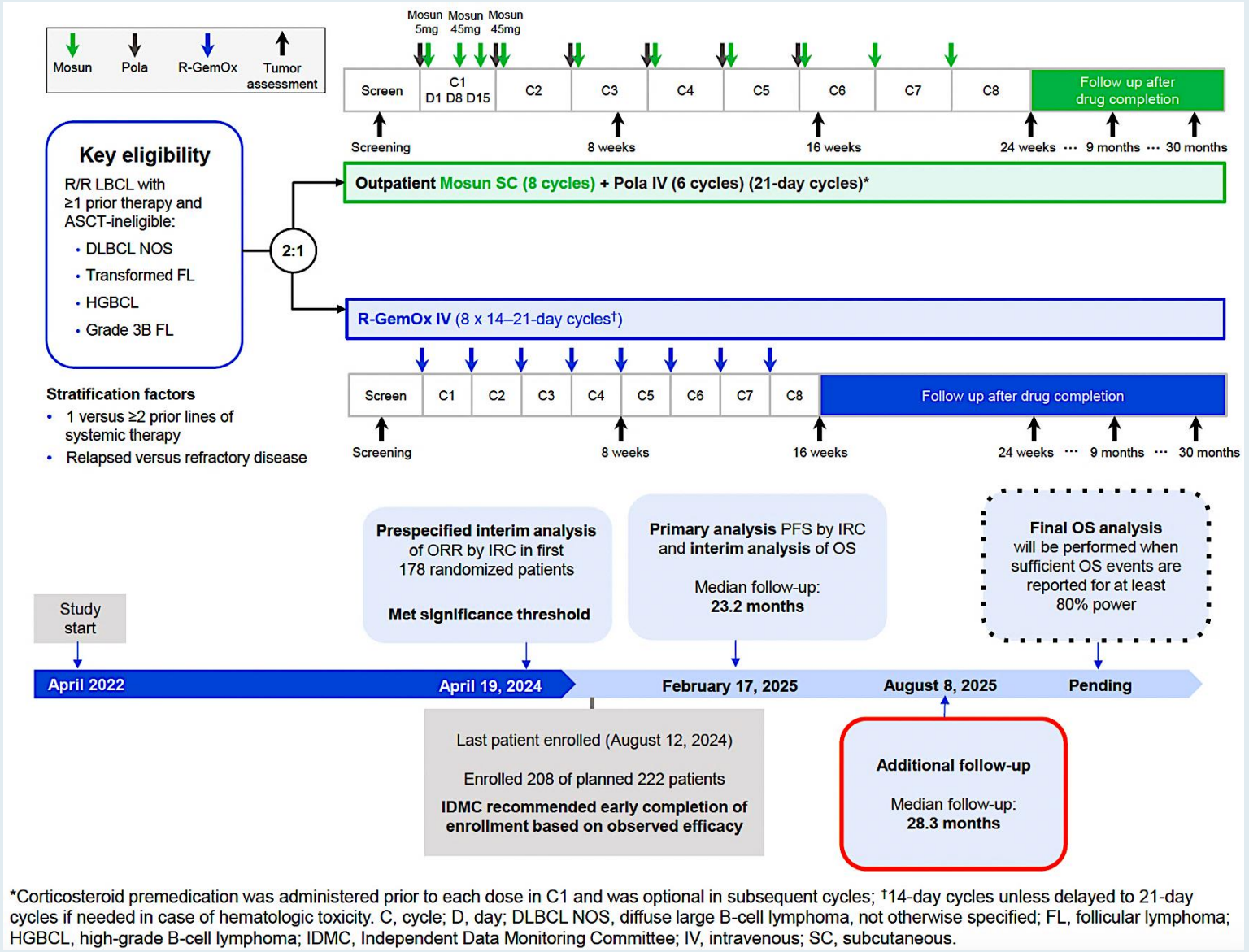
Phase III POLARGO: Peripheral Neuropathy

n (%), unless otherwise specified	Pola-R-GemOx (n=128)	R-GemOx (n=125)
Any Grade PN*	73 (57.0)	36 (28.8)
Grade 1	48 (37.5)	29 (23.2)
Grade 2	20 (15.6)	7 (5.6)
Grade 3	5 (3.9)	0
Median time to onset, months (range)	1.6 (0–8.0)	0.9 (0–4.4)
PN AEs leading to any study drug discontinuation	4 (3.1)	0
Polatuzumab vedotin discontinuation	3 (2.3)	N/A
Number of PN AEs leading to any dose reduction	13 (10.2)	4 (3.2)
Polatuzumab vedotin reduction	13 (10.2)	N/A
Patients with all PN AEs resolved or improved	37 (50.7)	21 (58.3)
Patients with all PN AEs resolved	28 (38.4)	21 (58.3)

*Custom grouped terms.
N/A, not applicable; PN, peripheral neuropathy.

Matasar M et al. EHA 2025;Abstract S101.

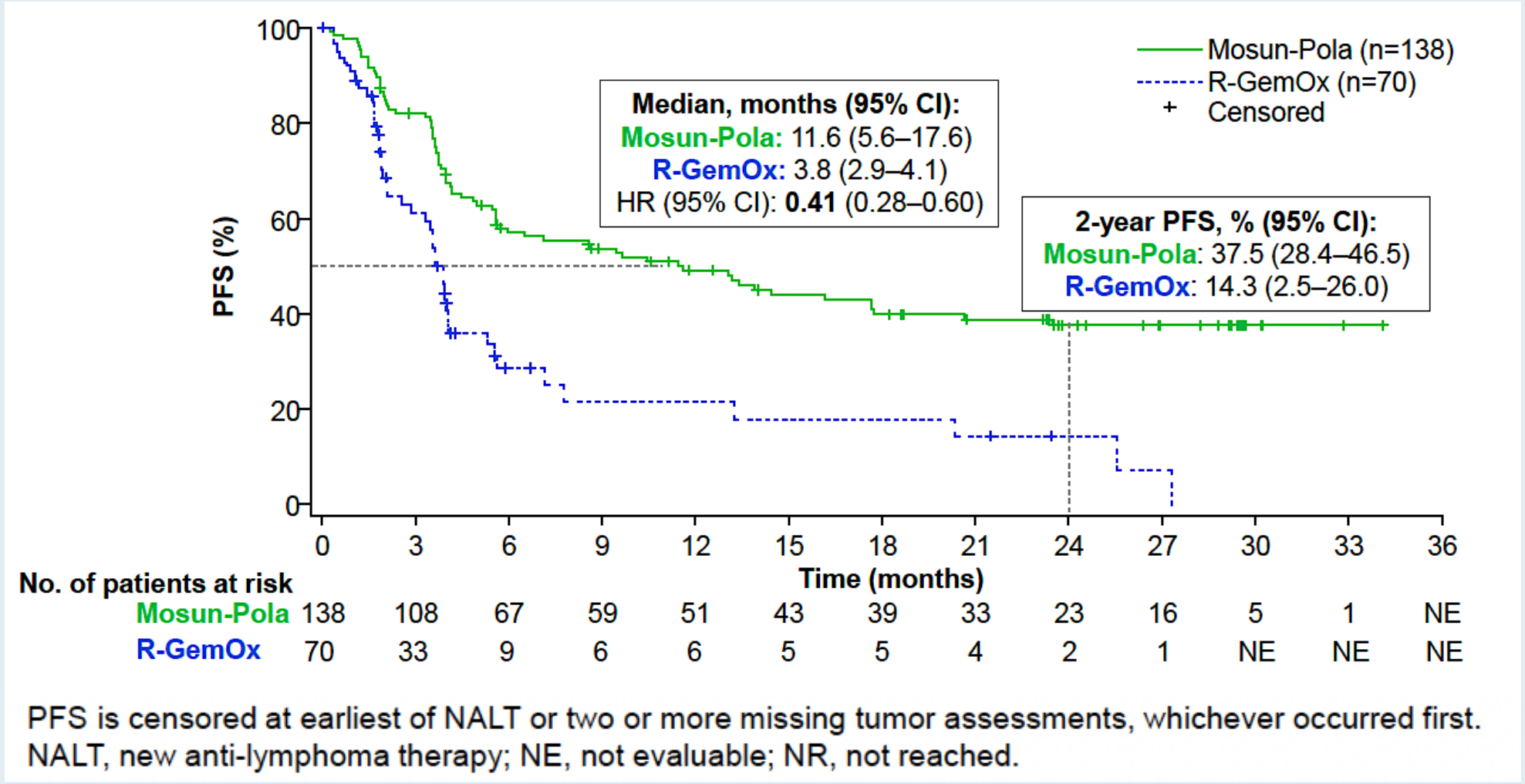
Phase III SUNMO Study Design



*Corticosteroid premedication was administered prior to each dose in C1 and was optional in subsequent cycles; †14-day cycles unless delayed to 21-day cycles if needed in case of hematologic toxicity. C, cycle; D, day; DLBCL NOS, diffuse large B-cell lymphoma, not otherwise specified; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IDMC, Independent Data Monitoring Committee; IV, intravenous; SC, subcutaneous.

Budde LE et al. EHA 2026;Abstract PF968.

Phase III SUNMO Primary Endpoint: PFS by IRC in the Intention-to-Treat Population (28.3-Month Follow-Up)



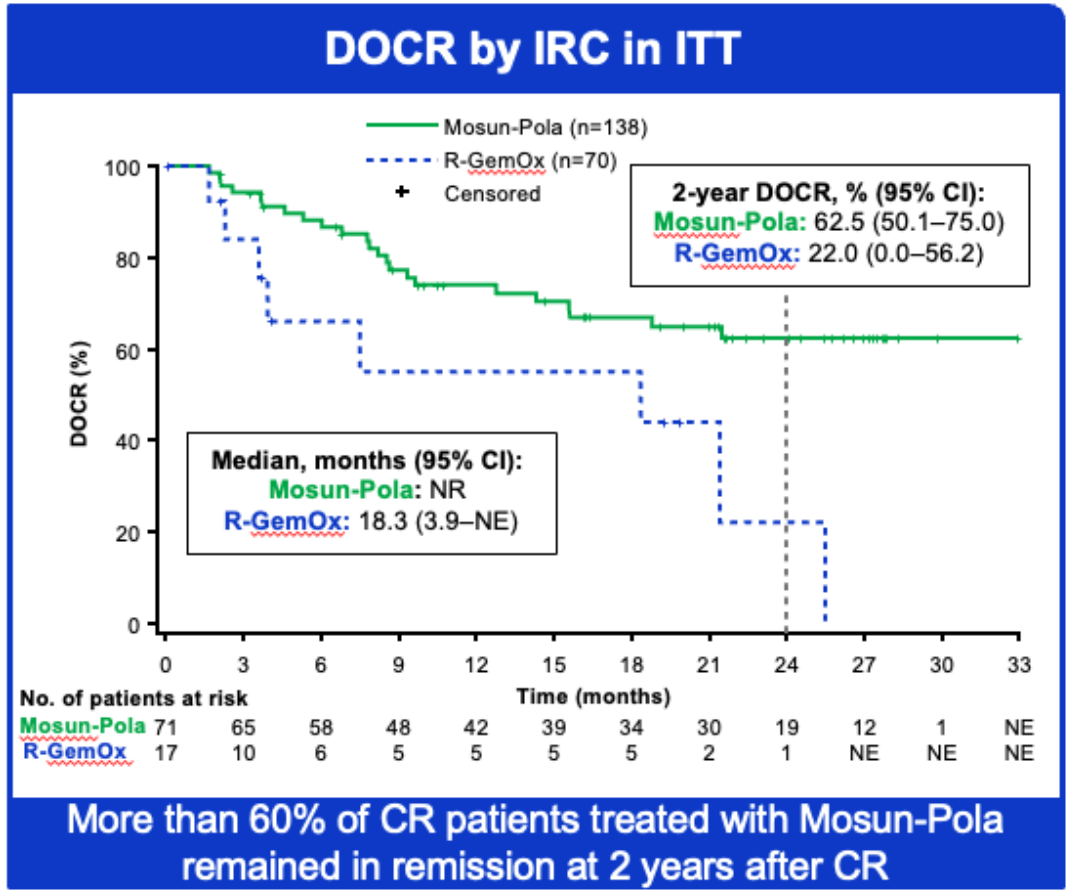
PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first.
NALT, new anti-lymphoma therapy; NE, not evaluable; NR, not reached.

Efficacy and safety of mosun-pola were comparable across age groups

Budde LE et al. EHA 2026;Abstract PF968.

Phase III SUNMO: Overall Response Rate and Duration of Complete Response

IRC-assessed efficacy % (95% CI), unless otherwise stated	Mosun-Pola (n=138)	R-GemOx (n=70)
ORR	70.3% (61.9–77.8)	40.0% (28.5–52.4)
CR	51.4% (42.8–60.0)	24.3% (14.8–36.0)
DOR		
Median, months	18.8 (11.5–NE)	6.0 (3.7–23.9)
2-year rate	47.9% (37.0–58.8)	15.4% (0.0–39.8)
DOCR		
Median, months	NR	18.3 (3.9–NE)
2-year rate	62.5% (50.1–74.9)	22.0% (0.0–56.2)



Clinical cut-off date: August 8, 2025.
DOCR, duration of complete response; DOR, duration of response; NR, not reached.

Kim W et al. ASCO 2026;Abstract 7007.

Phase III SUNMO: Efficacy in the Second-Line Setting

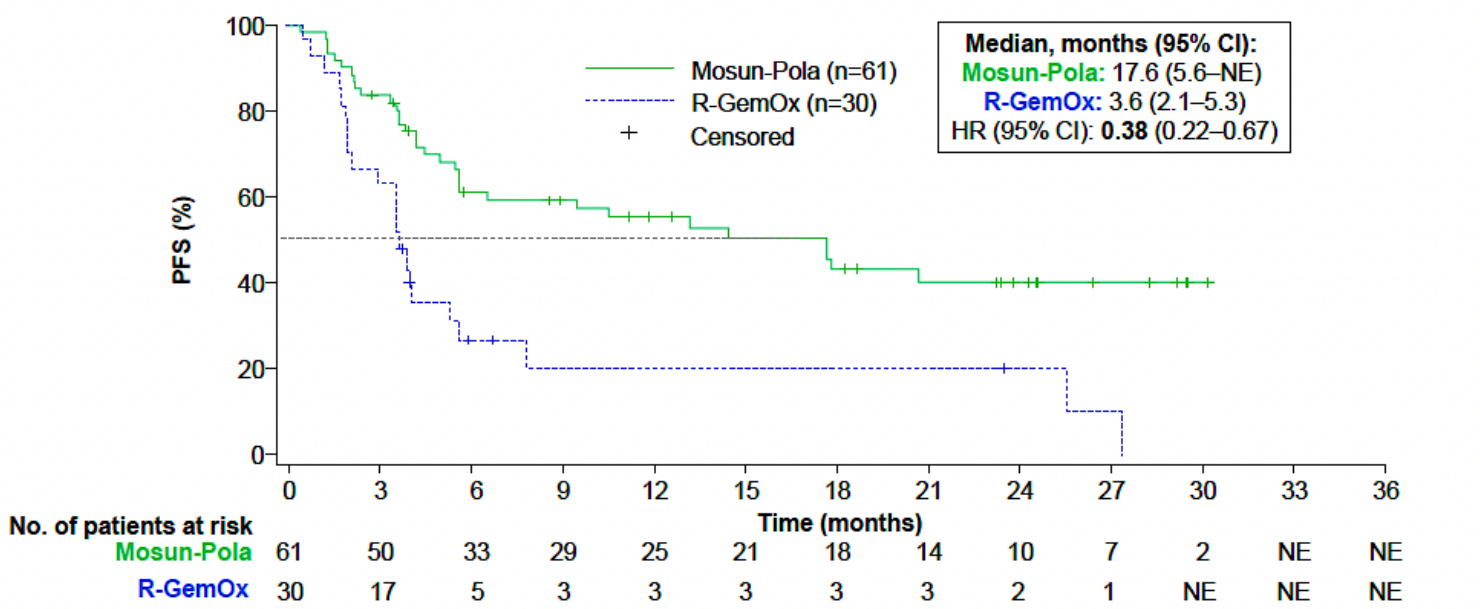


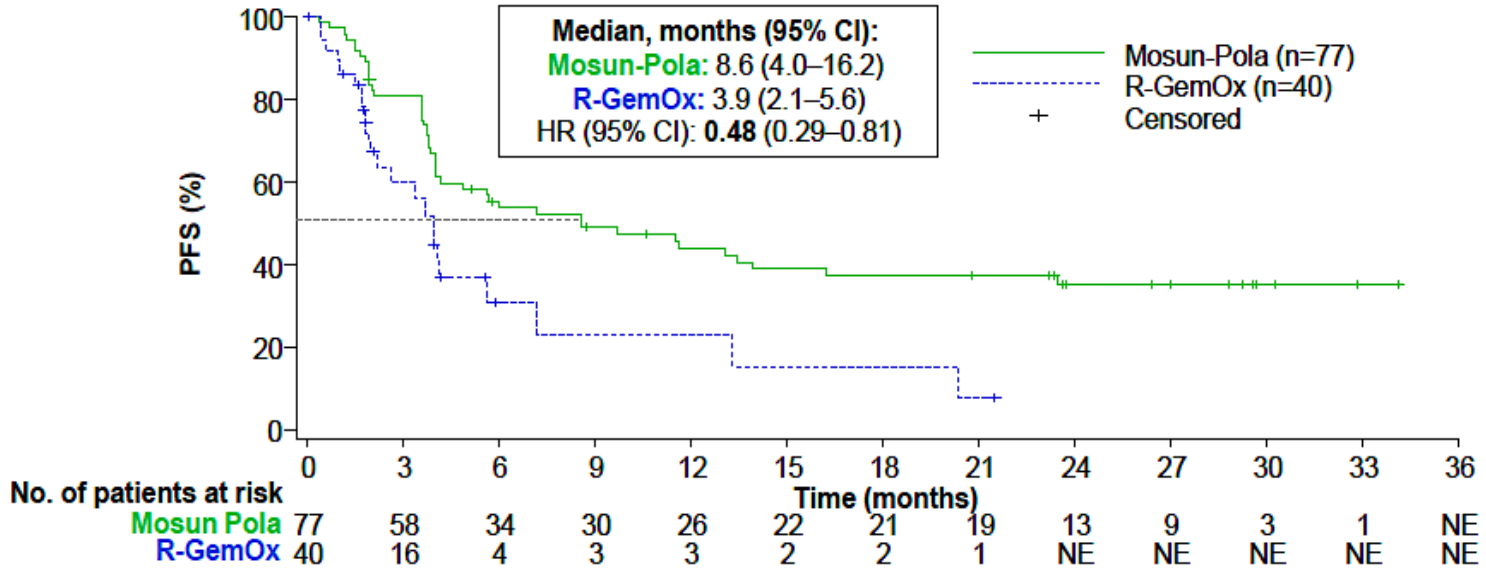
Table 3. Summary of IRC-assessed efficacy endpoints in the 2L setting

% (95% CI), unless otherwise stated	2L Mosun-Pola (n=61)	2L R-GemOx (n=30)
Median PFS, months (95% CI)	17.6 (5.6–NE)	3.6 (2.1–5.3)
ORR	75.4% (62.7–85.5)	36.7% (19.9–56.1)
CR	60.7% (47.3–72.9)	20.0% (7.7–38.6)
Median DOR, months (95% CI)	18.8 (11.3–NE)	6.0 (3.9–NE)
Median DOCR, months (95% CI)	NR (15.6–NE)	21.4 (3.9–NE)

ORR = objective response rate; CR = complete response;
DOR = duration of response; DOCR = duration of complete response

Budde LE et al. EHA 2026;Abstract PF968.

Phase III SUNMO: Efficacy in the Third-Line and Beyond Setting

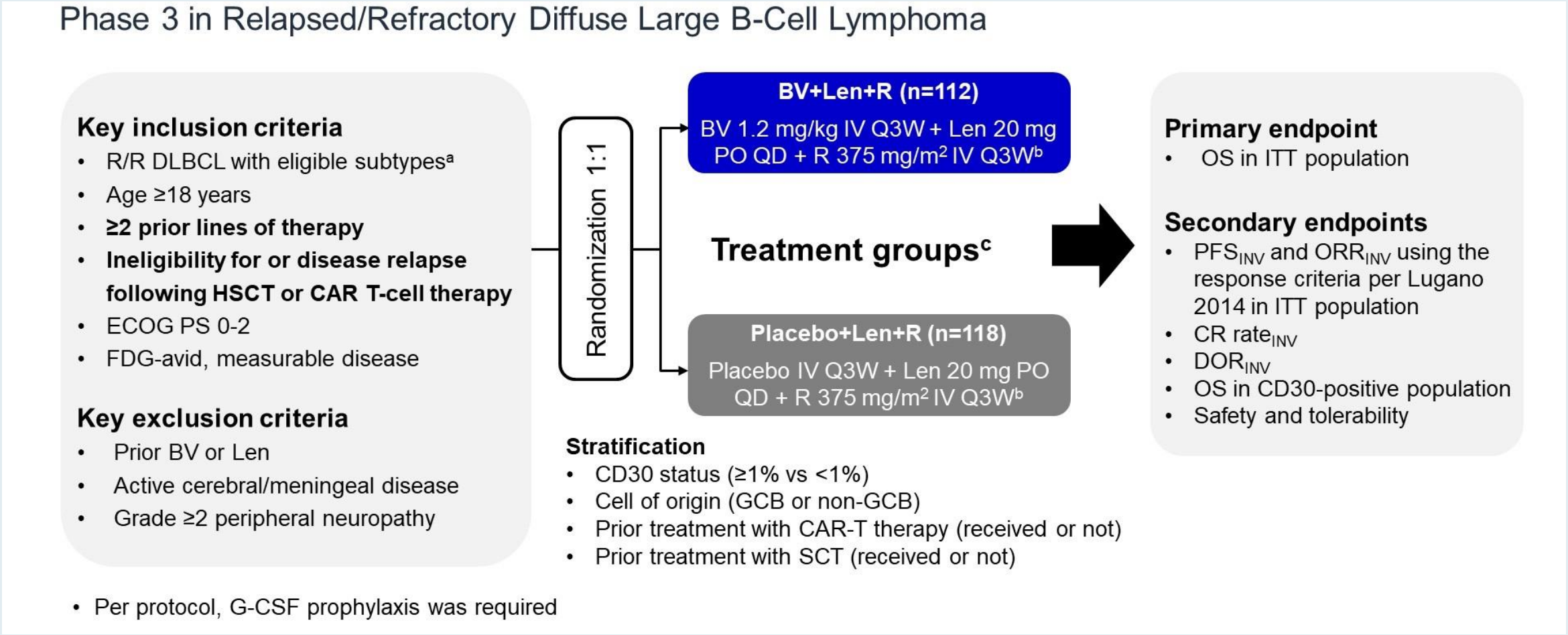


% (95% CI), unless otherwise stated	3L+ Mosun-Pola (n=77)	3L+ R-GemOx (n=40)
Median PFS, months (95% CI)	8.6 (4.0–16.2)	3.9 (2.1–5.6)
ORR	66.2% (54.6–76.6)	42.5% (27.0–59.1)
CR	44.2% (32.8–55.9)	27.5% (14.6–43.9)
Median DOR, months (95% CI)	21.5 (9.5–NE)	5.4 (2.3–18.3)
Median DOCR, months (95% CI)	NR (21.5–NE)	7.5 (2.3–NE)

ORR = objective response rate

Budde LE et al. EHA 2026;Abstract PF968.

Phase III ECHELON-3 Study Design

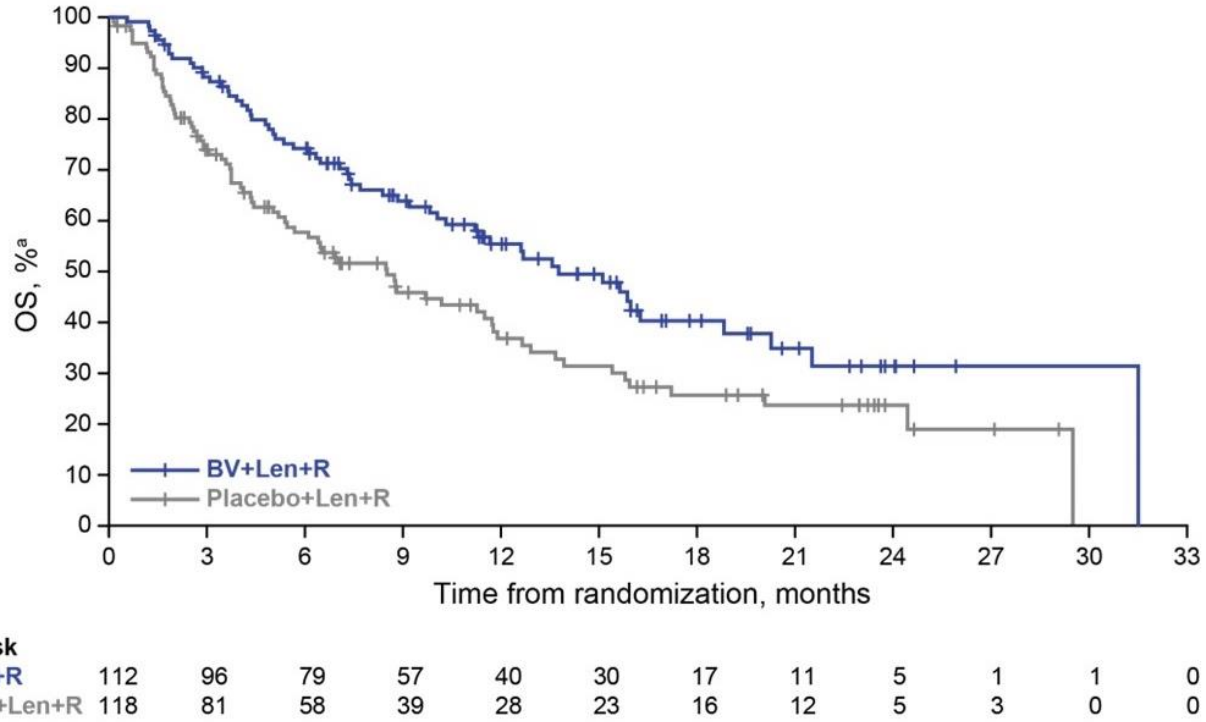


HSCT = hematopoietic stem cell transplantation; FDG = fluorodeoxyglucose; ITT = intent to treat; SCT = stem cell transplant

Kim JA et al. ASCO 2024;Abstract LBA7005.

Phase III ECHELON-3: Overall Survival (Primary Endpoint)

BV+Len+R reduced risk of death by 37% compared with placebo+Len+R



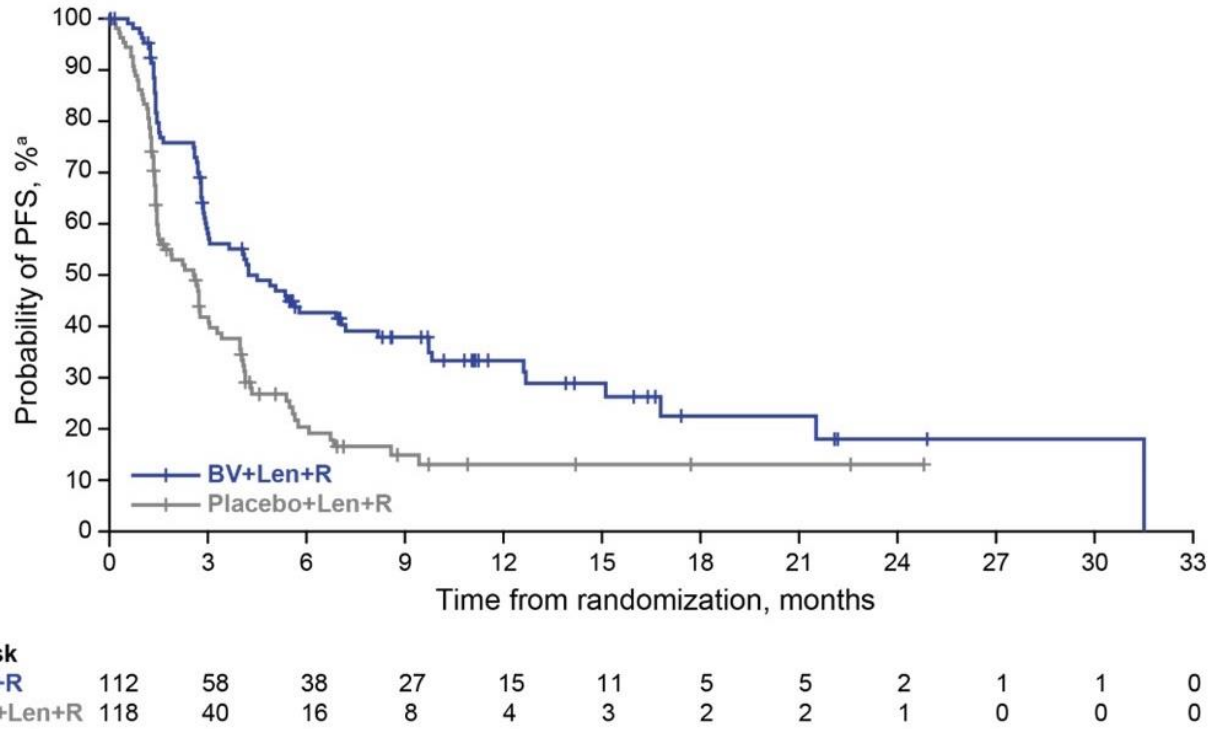
	BV+Len+R (n=112)	Placebo+Len+R (n=118)
OS, median (95% CI), months	**13.8** (10.3-18.8)	**8.5** (5.4-11.7)
Hazard ratio (95% CI)[b]	0.629 (0.445-0.891)	
Log-rank *P* value[c]	.0085	
Events (deaths)	58	76
Follow-up, median (95% CI), months	15.5 (12.2-18.1)	18.9 (12.2-23.2)

- BV+Len+R prolonged median OS by 5.3 months compared with placebo+Len+R
- Prespecified O'Brien-Fleming efficacy boundary was crossed at this interim analysis

Kim JA et al. ASCO 2024;Abstract LBA7005.

Phase III ECHELON-3: PFS (Key Secondary Endpoint)

BV+Len+R reduced risk of disease progression or death by 47% compared with placebo+Len+R



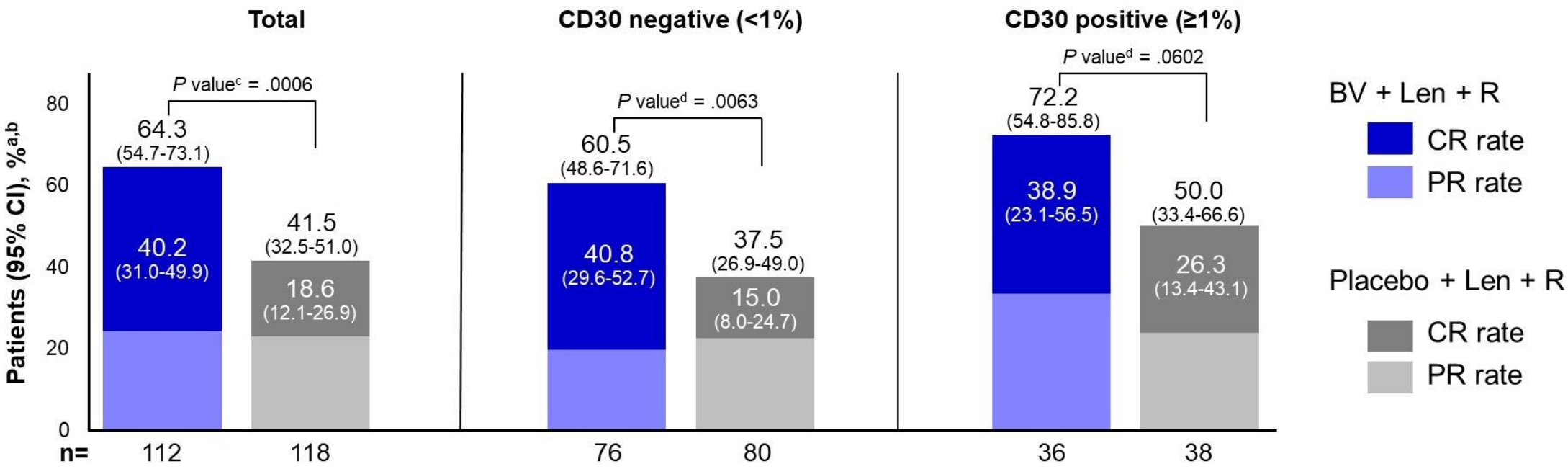
	BV+Len+R (n=112)	Placebo+Len+R (n=118)
PFS, median (95% CI), months	**4.2** (2.9-7.1)	**2.6** (1.4-3.1)
Hazard ratio (95% CI)[b]	0.527 (0.380-0.729)	
Log-rank *P* value[c]	<.0001	
Events	71	85
Follow-up, median (95% CI), months	11.1 (8.6-14.2)	8.8 (6.9-10.9)

- PFS was an alpha controlled key secondary endpoint

Kim JA et al. ASCO 2024;Abstract LBA7005.

Phase III ECHELON-3: Responses

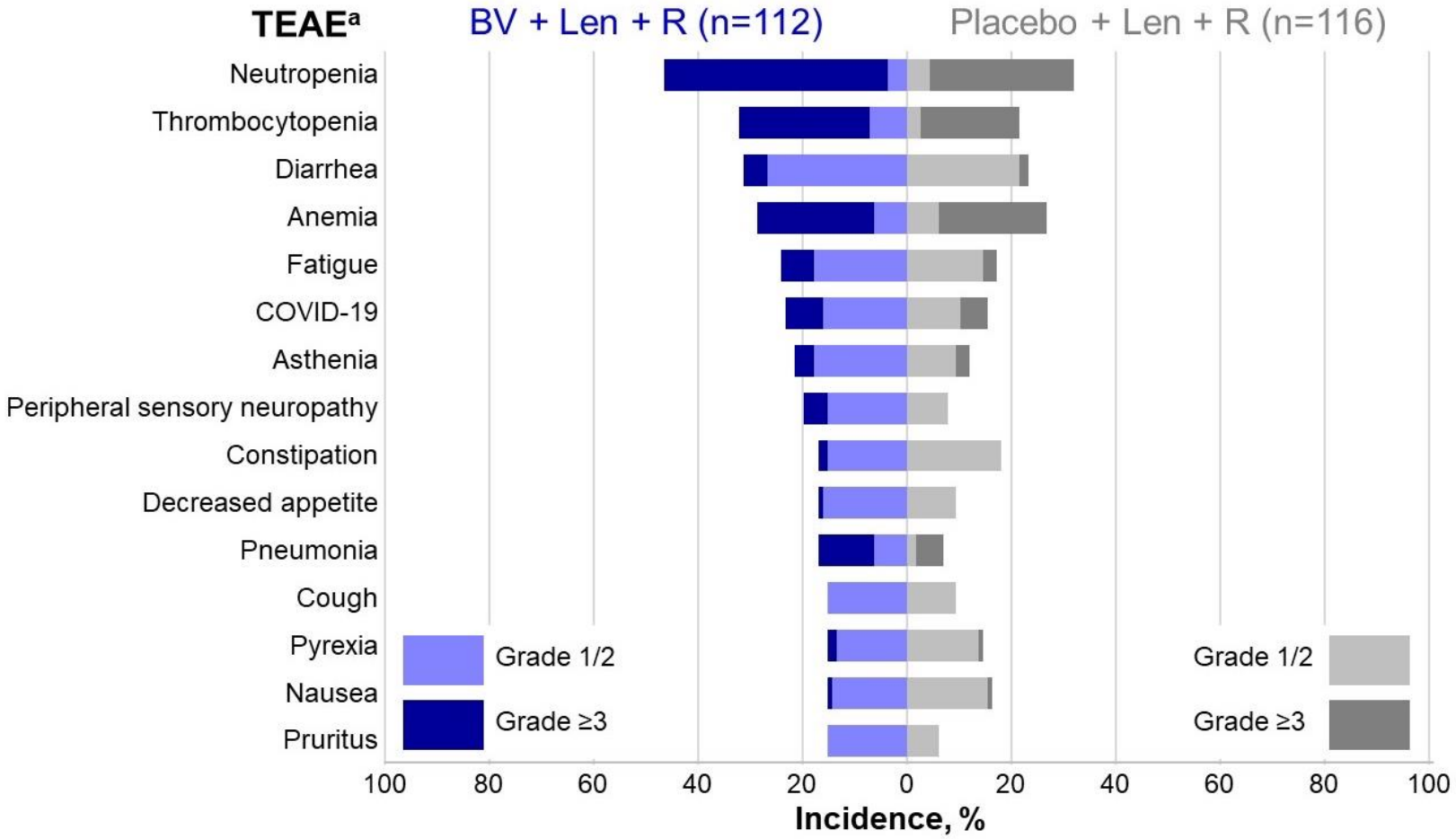
40% CR rate with BV+Len+R and ORR improvement regardless of CD30 expression



- In the total population, the median DOR (95% CI) was longer with BV+Len+R: 8.3 months (4.2-15.3 months) vs 3.0 months (2.8-5.4 months)
  - In patients who had a CR, the median DOR (95% CI) was 18.9 months (11.1 months-NR) with BV+Len+R and NR (2.8 months-NR) with placebo+Len+R
  - The median time to CR onset (range) was 1.58 months (1.2-7.3 months) with BV+Len+R and 1.61 months (0.7-4.6 months) with placebo+Len+R

Kim JA et al. ASCO 2024;Abstract LBA7005.

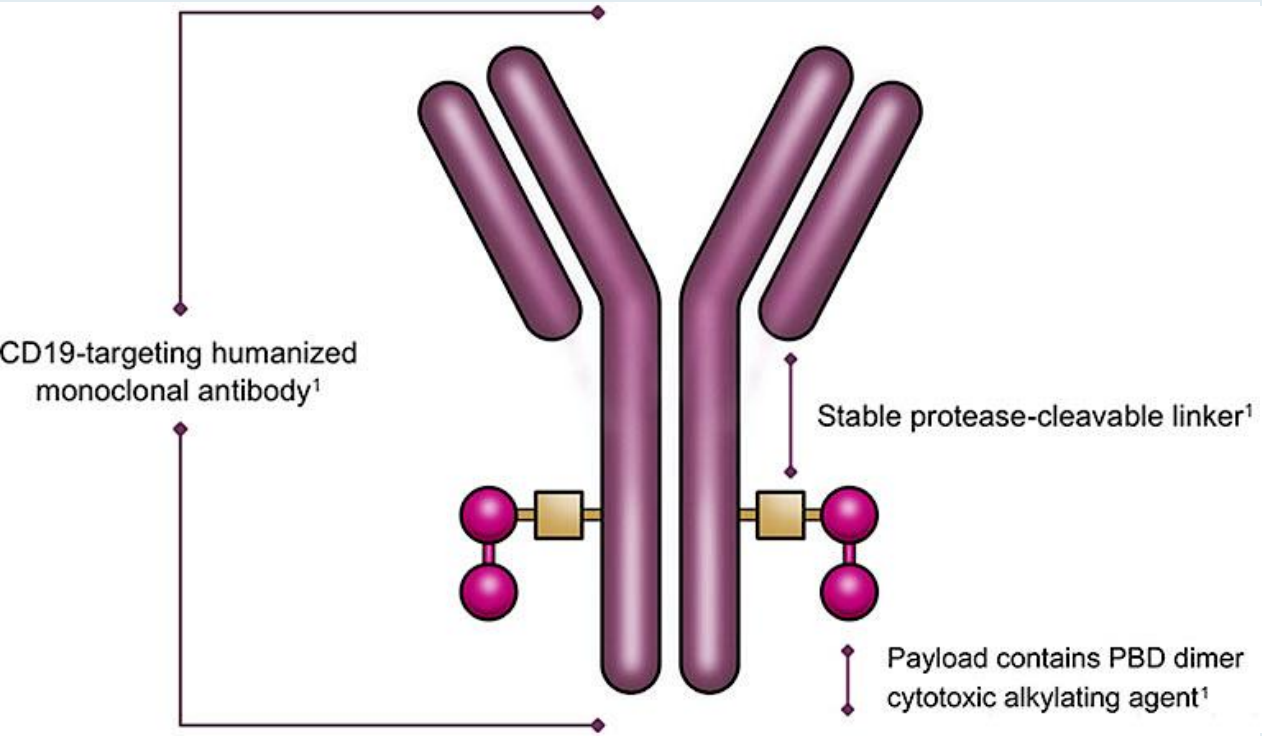
Phase III ECHELON-3: Safety



- TEAEs of any grade occurred in 97% of patients with each treatment
- Grade ≥3 TEAEs:
  - 88% with BV+Len+R
  - 77% with placebo+Len+R
  - 9% febrile neutropenia in each group
- Grade 5 TEAEs:
  - 12% with BV+Len+R
  - 8% with placebo+Len+R
- Any grade peripheral neuropathy TEAEs
  - 31% with BV+Len+R
  - 24% with placebo+Len+R
- Relative dose intensity
  - 94.4% for BV
  - 99.7% for placebo

Kim JA et al. ASCO 2024;Abstract LBA7005.

Loncastuximab Tesirine: A CD19-Directed Antibody-Drug Conjugate



Upon binding to CD19, Loncastuximab tesirine is internalized into the tumor cell and the PBD dimer cytotoxin is released into the cell[1]

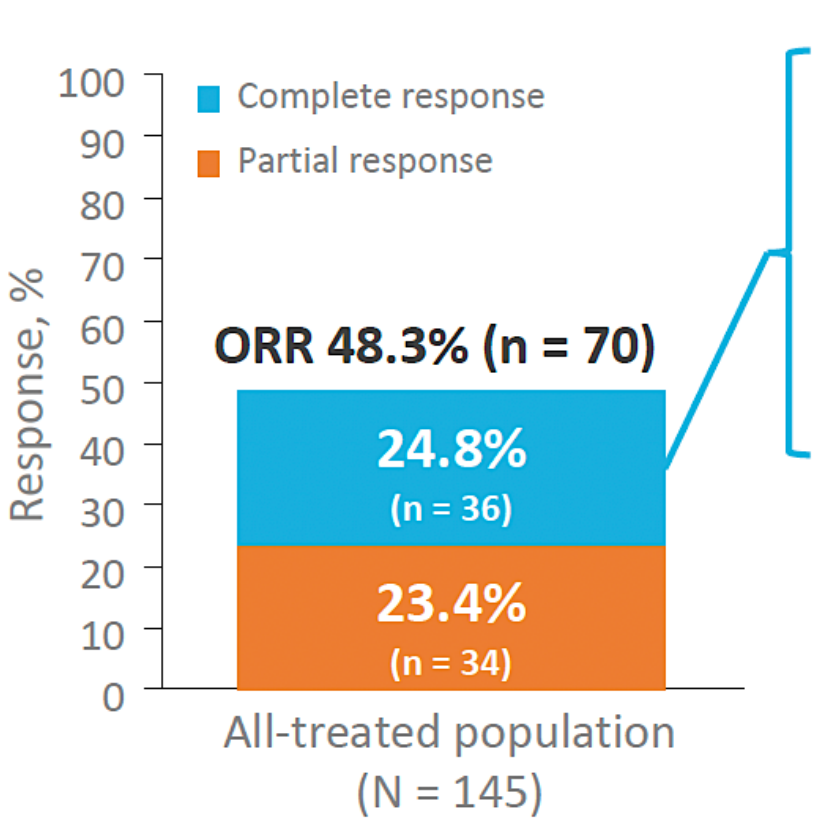
PBD dimer—an alkylating agent—binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks[1]

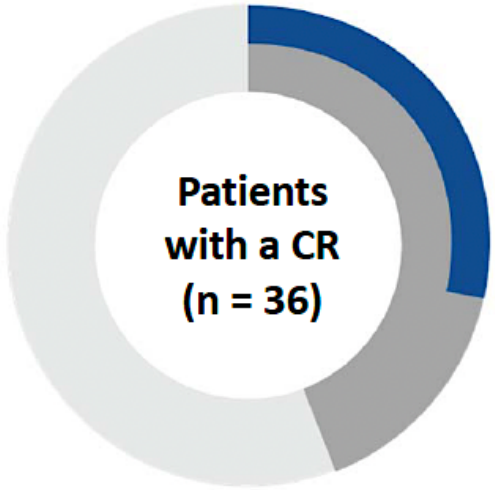
DNA interstrand crosslinks subsequently induce tumor cell death[1]

ADC = antibody-drug conjugate; PBD = pyrrolobenzodiazepine.

[Loncastuximab tesirine manufacturer prescribing information].

Phase II LOTIS-2 Study: Overall Response Rate (ORR) and Long-Term Responses — All-Treated Population





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

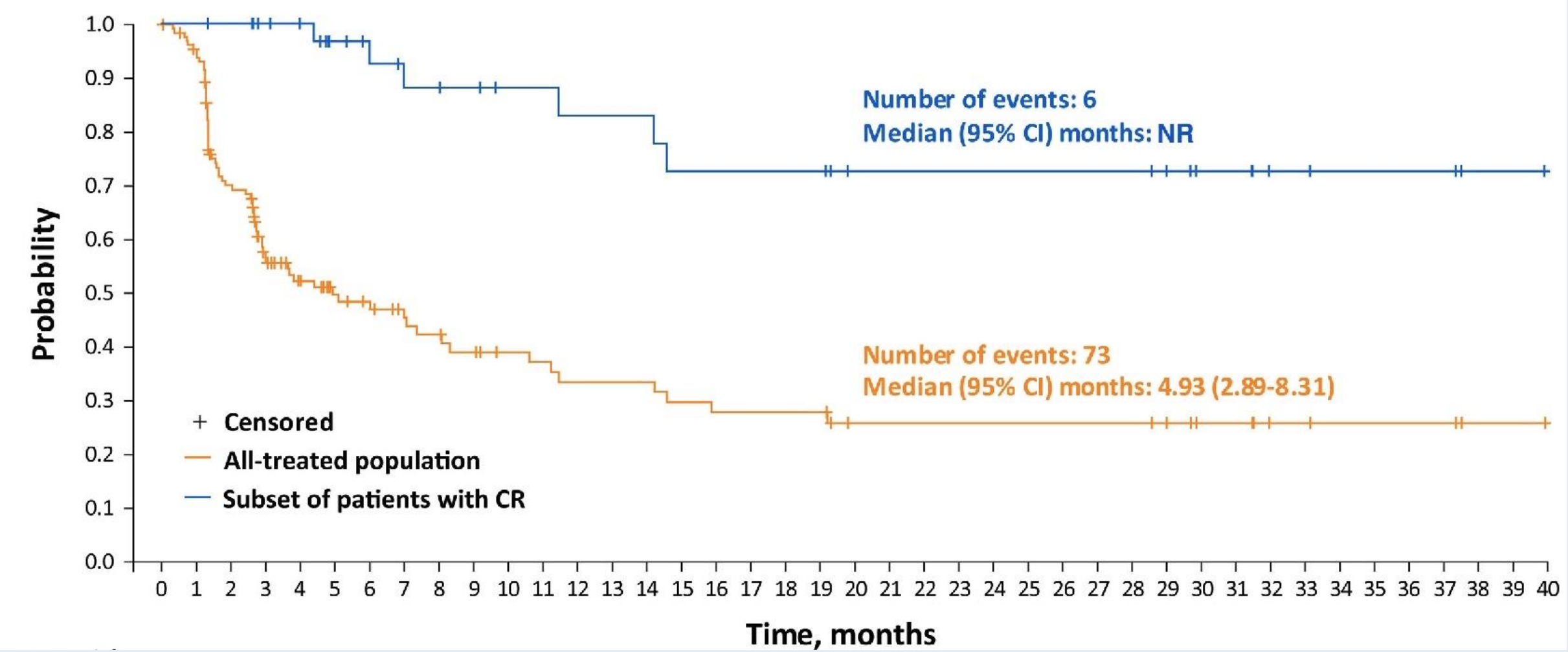
Of the patients with a CR, 31% (11 of 36) were event-free for ≥2 years.

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)

No new safety signals were identified during the long-term follow-up

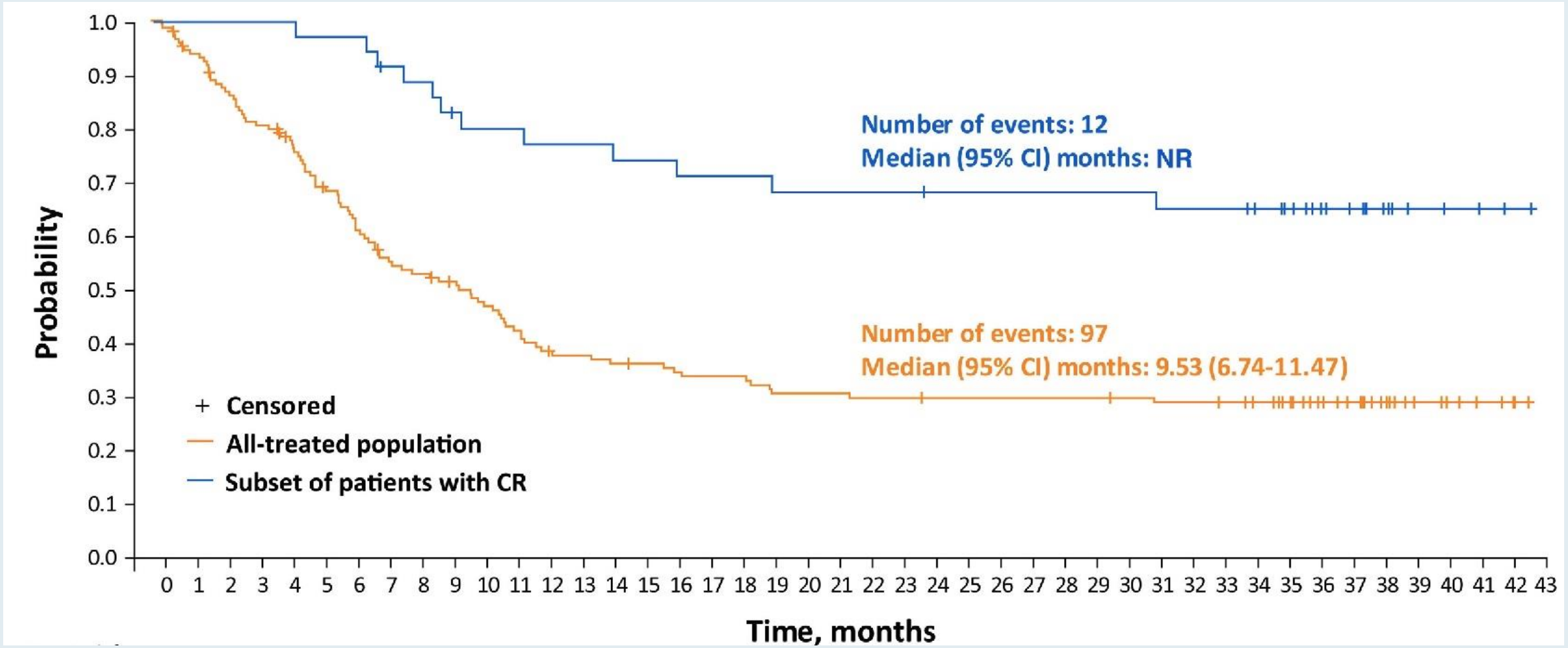
Caimi PF et al. EHA 2023;Abstract P1132.

Phase II LOTIS-2: Progression-Free Survival



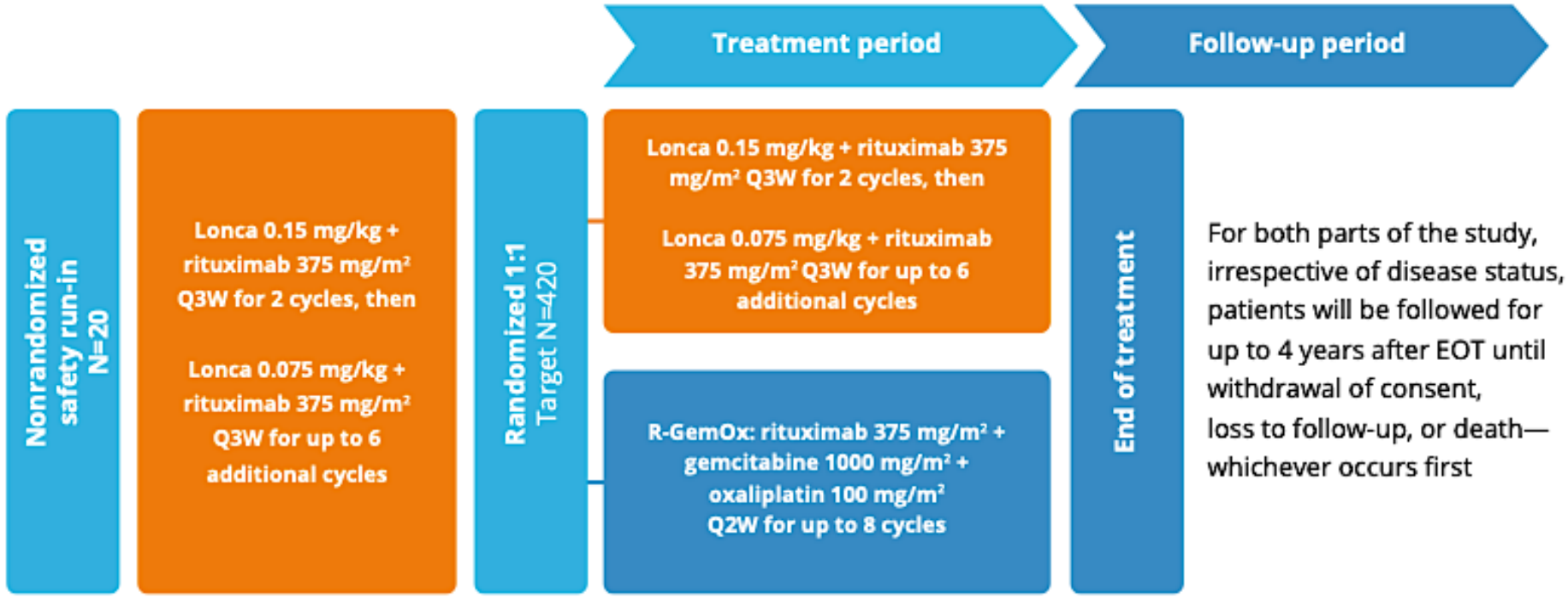
Caimi PF et al. *Haematologica* 2024 April 1;109(4):1184-93.

Phase II LOTIS-2: Overall Survival



Caimi PF et al. *Haematologica* 2024 April 1;109(4):1184-93.

Phase III LOTIS-5 Study Design



EOT, end of treatment; Lonca, loncastuximab tesirine; QXW, every X weeks.

Study Endpoints

- The primary endpoint is progression-free survival (PFS) by independent central review
- Secondary endpoints include OS, overall response rate (ORR), CR rate, duration of response (DOR), safety, PK parameters, Lonca ADAs, and patient-reported outcomes (PROs)
- Exploratory endpoints include correlations between clinical activity and Lonca exposure (ie, Lonca dose and PK metrics) and tumor and/or blood biomarkers

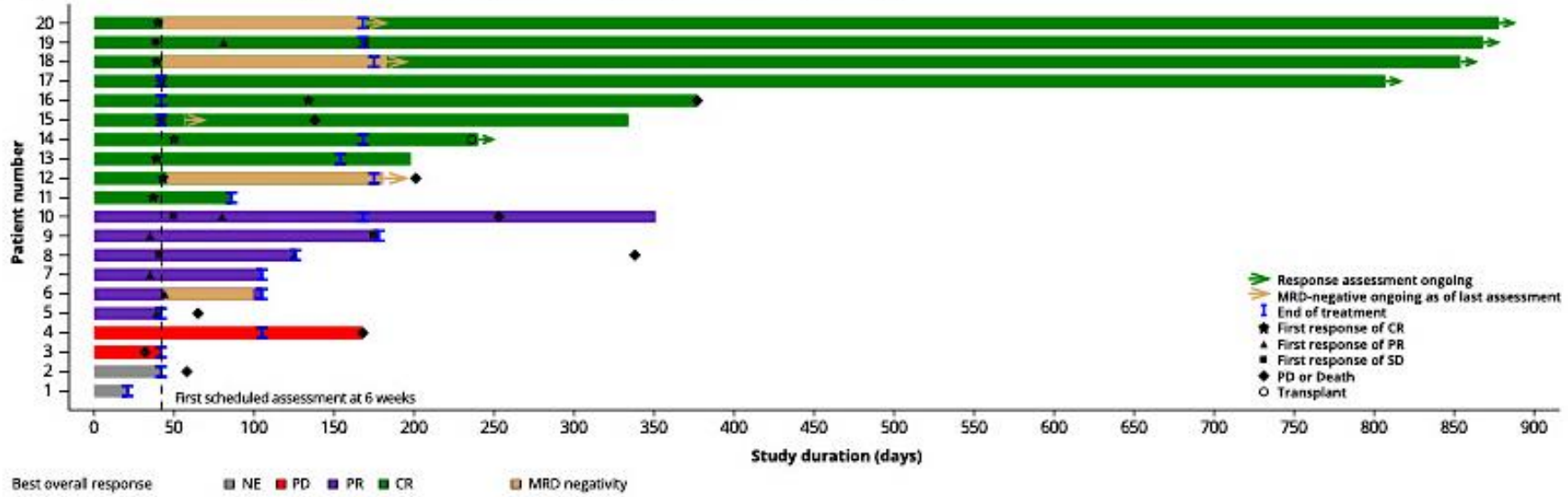
Carlo-Stella C et al. EHA 2025;Abstract PS1957.

Phase III LOTIS-5: Efficacy

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)
Efficacy outcomes in complete responders (n=10)	
Median DOR, months (95% CI)	NE (3.19-NE)
Events, n (%)	3 (30.0)
MRD results in patients with ctDNA measurements (n=8)	
CR and MRD negative, n (%)	4 (50.0)
MRD negative at end of treatment, n (%)	4 (50.0)

CRR, complete response rate; ctDNA, circulating tumor DNA; DOR, duration of response; MRD, minimal residual disease; NE, not estimable; ORR, overall response rate; PFS, progression-free survival.

Figure 2. Swimmer plot of safety run-in population (N=20)



Each bar represents one patient in the study. Response is determined by independent reviewer.
CR, complete response; MRD, minimal residual disease; NE, not estimable; PD, progressive disease; PR, partial response.

Carlo-Stella C et al. EHA 2025;Abstract PS1957.

Phase III LOTIS-5: Safety

Safety endpoint, n (%)	N=20
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)
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 decompression	1 (5)
TEAEs leading to any study drug withdrawal	8 (40)

GGT, gamma-glutamyl transferase; TEAE, treatment-emergent adverse event.

Carlo-Stella C et al. EHA 2025;Abstract PS1957.

Results from LOTIS-5 Phase III Confirmatory Clinical Trial of Loncastuximab Tesirine-lpyl in Combination with Rituximab for R/R DLBCL

Press Release: June 3, 2026

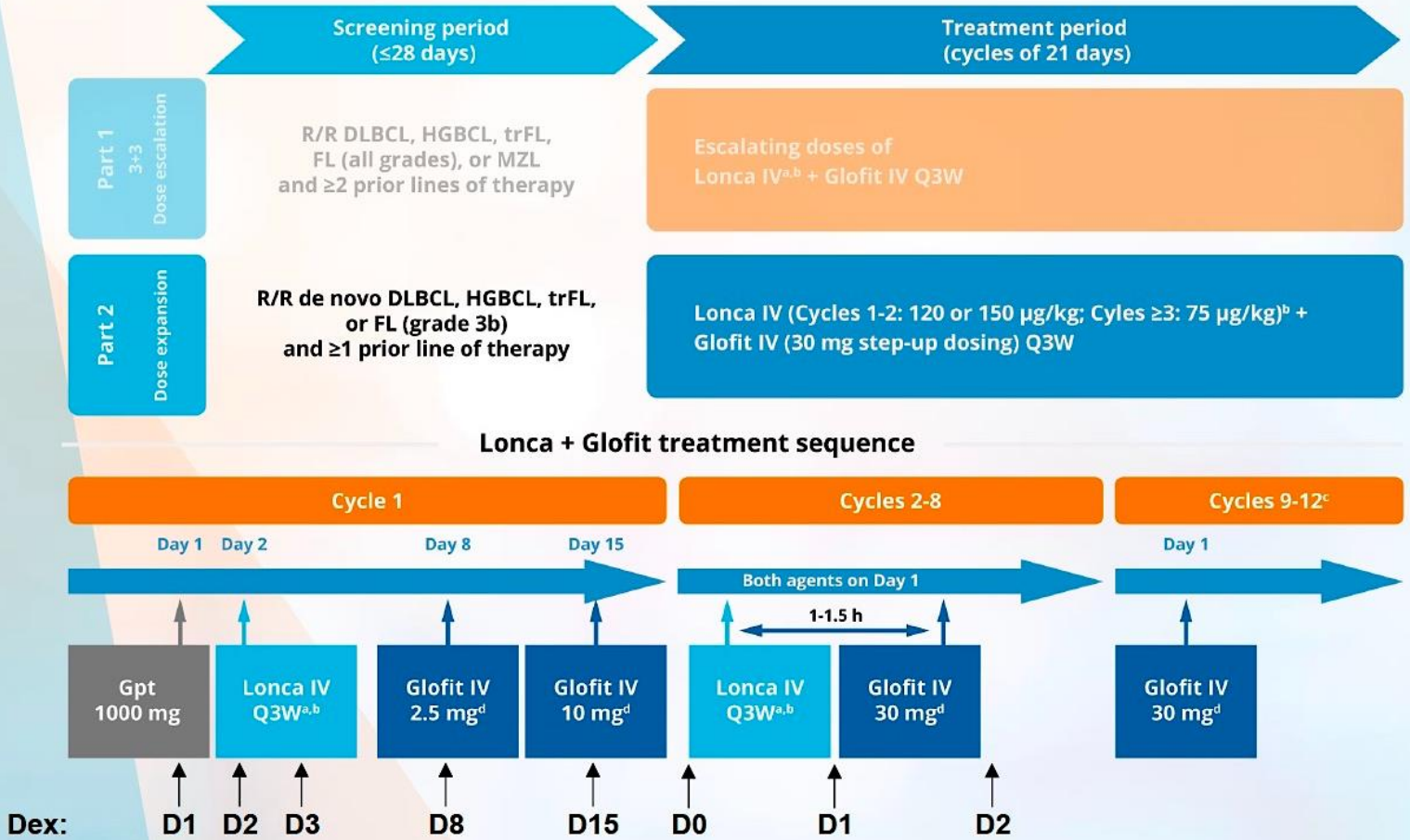
"[The manufacturer] today announced topline data from its Phase 3 LOTIS-5 confirmatory trial evaluating loncastuximab tesirine-lpyl in combination with rituximab in patients with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL). Loncastuximab tesirine-lpyl plus rituximab achieved statistical significance on the trial's primary endpoint of progression-free survival (PFS) and demonstrated no detrimental effect on the key secondary efficacy endpoint of overall survival (OS). In addition, a higher complete response (CR) rate and duration of CRs (DoCR) were observed with loncastuximab tesirine-lpyl plus rituximab.

Overall, treatment emergent adverse event (TEAE) rates were similar between arms. Similar rates of overall Grade ≥3 TEAEs greater than 5% were observed across both arms, with hematologic TEAEs higher in the control arm and infection, hepatotoxicity, and edema/effusion higher in the test arm. Serious adverse events (SAEs), TEAEs leading to study drug withdrawal, and Grade 5 events were higher in the test arm, with the majority of Grade 5 TEAEs in the test arm occurring in patients aged 75 years or older."

https://ir.adctherapeutics.com/2026-06-03-ADC-Therapeutics-Announces-Results-From-LOTIS-5-Phase-3-Confirmatory-Clinical-Trial-of-ZYNLONTA-R-in-Combination-with-Rituximab-in-Relapsed-or-Refractory-Diffuse-Large-B-Cell-Lymphoma

RTP RESEARCH TO PRACTICE

Phase Ib LOTIS-7 Study Design



Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

Endpoints

- **Primary**: safety and tolerability; MTD and/or RDE
- **Secondary**: ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory**: Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: Safety Outcomes

TREATED POPULATION (N=41)

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Grade 3/4 TEAEs (> 5% of patients)[a]	**11 (55%)**	**12 (57.1%)**	**23 (56.1%)**
Neutropenia	4 (20%)	6 (28.6%)	10 (24.4%)
Anemia	1 (5%)	3 (14.3%)	4 (9.8%)
AST increased	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 3/4 AESI (all patients)[a]			
Febrile neutropenia	0	1 (4.8%)	1 (2.4%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Generalized oedema	1 (5%)	1 (4.8%)	2 (4.9%)
Rash	1 (5%)	0	1 (2.4%)
Photosensitivity reaction	0	1 (4.8%)	1 (2.4%)
Sepsis	1 (5%)	0	1 (2.4%)
Upper respiratory infection	1 (5%)	0	1 (2.4%)
Pneumonia	1 (5%)	0	1 (2.4%)
Serious TEAE	**11 (55%)**	**9 (42.9%)**	**20 (48.8%)**
No Grade 5 TEAEs occurred			

[a]As per Investigator reported adverse events. [b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
TEAE = treatment emergent adverse event; AESI = adverse event of special interest | Data cutoff: 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: CRS and ICANS

TREATED POPULATION (N=41)

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Cytokine Release Syndrome[a]			
Any grade	11 (55%)	5 (23.8%)	16 (39.0%)
Grade 1	7 (35%)	5 (23.8%)	12 (29.3%)
Grade 2	3 (15%)	0	3 (7.3%)
Grade 3	1 (5%)	0	1 (2.4%)
Grade 4/5	0	0	0
ICANS[a]			
Any grade	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 1	1 (5%)	0	1 (2.4%)
Grade 2	1 (5%)	1 (4.8%)	2 (4.9%)
Grade ≥ 3	0	0	0

Any-grade CRS was less frequent at the Lonca 150 µg/kg starting dose[b] (23.8%) than at 120 µg/kg starting dose[b] (55.0%)

- Grade 1 and 2 CRS cases managed with tocilizumab, corticosteroids, acetaminophen, and/or fluid bolus, without ICU admittance or pressor support
- Grade 3 CRS case managed with tocilizumab, acetaminophen, dexamethasone, norepinephrine. ICU admittance

- All patients with ICANS had complete resolution of symptoms
  - Two patients resumed treatment and ultimately achieved a CR
  - One patient elected to discontinue treatment
- ICANS managed primarily with corticosteroids

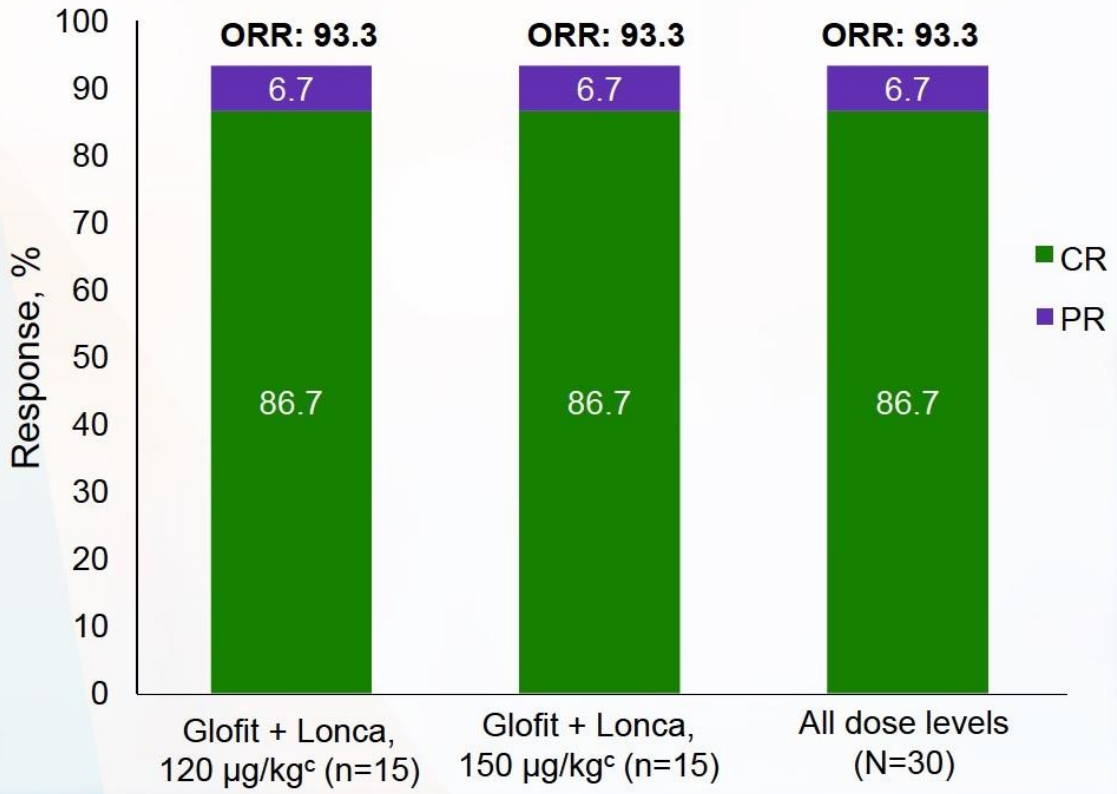
[a]Number of patients who experienced at least 1 event per ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells; worst grade reported if applicable
[b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
Data Cutoff 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: Best Overall Responses, DoR

EFFICACY EVALUABLE POPULATION (N=30)[a]

Best overall response[b]



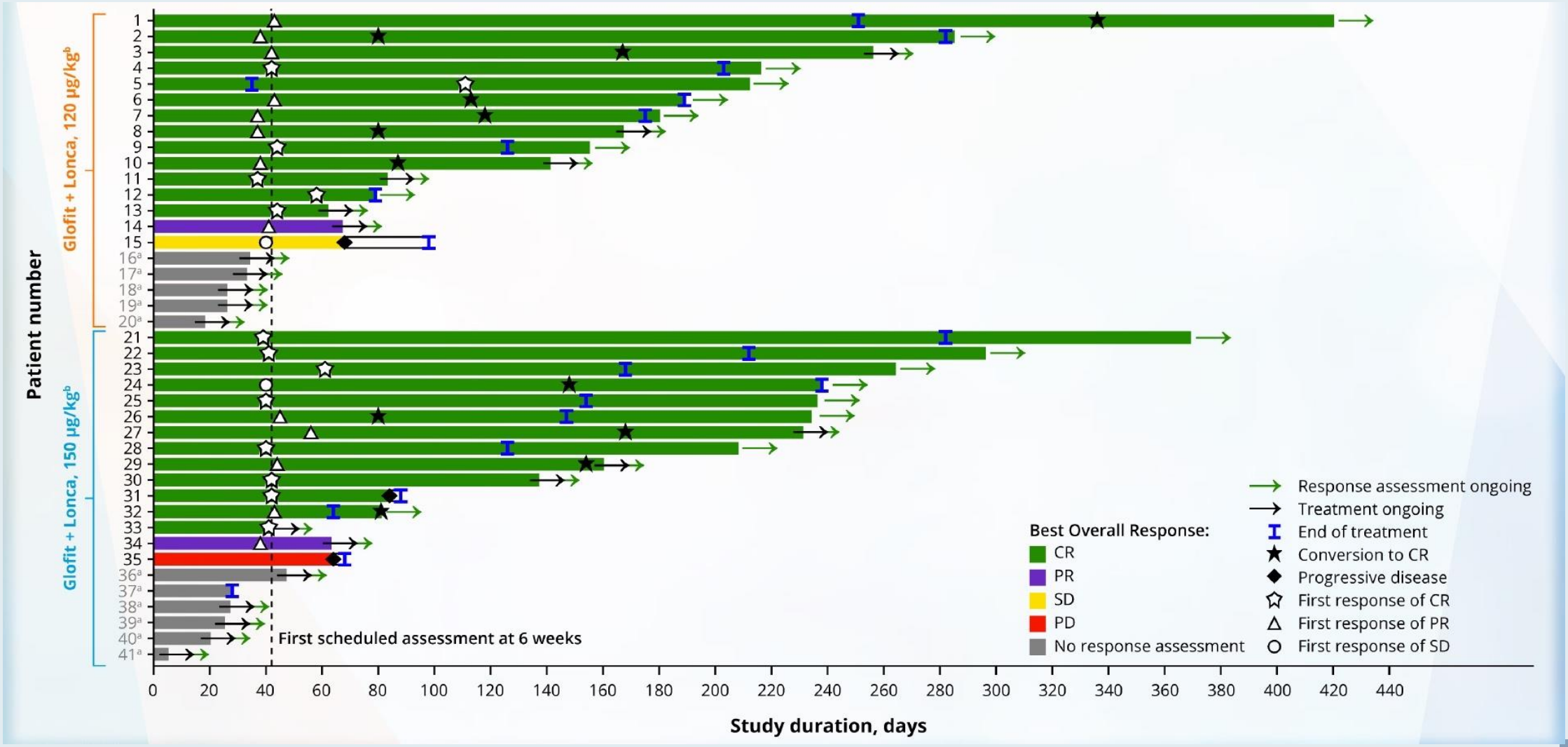
Duration of response

Characteristic, n (%)	Glofit + Lonca, 120 µg/kg[c] (n=15)	Glofit + Lonca, 150 µg/kg[c] (n=15)	All dose levels (N=30)
DOR[d] Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5

Data cutoff: April 14, 2025.
CR, complete response; DOR, duration of response; Glofit, glofitamab; Lonca, loncastuximab tesirine; NE, not estimable; ORR, overall response rate; PR, partial response.
[a]The efficacy evaluable population (N=30) included all patients who received ≥1 dose of the study drug with a valid baseline and ≥1 valid postbaseline disease assessment. Patients who did not have a postbaseline assessment owing to early clinical progression or death were also included. [b]Percentages do not add up to total due to rounding. [c]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3. [d]In the efficacy evaluable population, the DOR and probability of maintaining an event-free response were evaluated in responders (n=28), including all patients who had a best response of CR or PR.

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: Efficacy over Time



Alderuccio JP et al. ICML 2025;Abstract 078.

Updated Data Announced from LOTIS-7 Phase Ib Trial of Loncastuximab Tesirine in Combination with Bispecific Antibody Supporting Potential Best-in-Class Regimen for R/R DLBCL

Press Release: December 3, 2025

"On December 3, 2025, [the manufacturer] announced updated data from the LOTIS-7 Phase 1b open-label clinical trial evaluating the safety and efficacy of loncastuximab tesirine in combination with the bispecific antibody glofitamab in patients with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL). The updated data is based on investigator assessment and reflects the 49 efficacy-evaluable patients with a minimum of 6 months of follow-up from treatment initiation.

Enrollment in the LOTIS-7 clinical trial is ongoing, with complete enrollment of approximately 100 patients at the selected 150 µg/kg dose expected during the first half of 2026. The Company plans to share full data at a medical meeting and submit for publication by the end of 2026. In addition, the Company plans to assess regulatory and compendia strategies."

https://ir.adctherapeutics.com/2025-12-03-ADC-Therapeutics-Announces-Updated-Data-from-LOTIS-7-Phase-1b-Clinical-Trial-of-ZYNLONTA-R-in-Combination-with-Bispecific-Antibody-Supporting-Potential-Best-in-Class-Regimen-in-Patients-with-Relapsed-Refractory-Diffuse-Large-B-cell-Lymphoma

RTP RESEARCH TO PRACTICE

Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Clinician Survey Results

Module 3: Current and Future Roles of Monoclonal and Bispecific Antibodies in Therapy for Relapsed/Refractory (R/R) DLBCL

Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Outside of a clinical trial, would you partner polatuzumab vedotin with other systemic therapies beyond BR for patients with R/R DLBCL under any circumstances?

 Dr Abramson	Yes, mosunetuzumab and glofitamab
 Dr Flowers	Yes, mosunetuzumab
 Dr Kamdar	Yes, mosunetuzumab and glofitamab
 Dr LaCasce	Yes, mosunetuzumab and glofitamab
 Dr Matasar	Yes, R-GemOx, R-ICE, mosunetuzumab and glofitamab
 Dr Phillips	Yes, mosunetuzumab and glofitamab
 Prof Salles	Yes, mainly glofitamab
 Dr Westin	Yes, mosunetuzumab

R-ICE = rituximab/ifosfamide/carboplatin/etoposide

RTP RESEARCH TO PRACTICE

Where in the treatment course do you typically employ loncastuximab tesirine for your patients with R/R DLBCL? Would you administer it to a patient who has experienced disease progression on one or more other CD19-directed approaches?

	When	After PD on other CD19-directed tx?
 Dr Abramson	After CAR T and BsAb therapies	Yes, but only after assessing CD19 expression
 Dr Flowers	Fourth line or later	Yes, but only after assessing CD19 expression
 Dr Kamdar	After CAR T and BsAb therapies	Yes, but only after assessing CD19 expression
 Dr LaCasce	After CD20 BsAb therapy	Yes, but only after assessing CD19 expression
 Dr Matasar	3L+ especially post-CAR T with residual CD19+	Yes, but only after assessing CD19 expression
 Dr Phillips	3L+, after PD on CAR T (early relapse) or BsAb (late relapse after CAR T)	Yes, but only after assessing CD19 expression
 Prof Salles	When first-line, CAR T and bispecific Ab treatments have failed	Yes, but only after assessing CD19 expression
 Dr Westin	If CAR T ineligible and unable/ unwilling/relapsed after BsAb	Yes, but only after assessing CD19 expression

PD = disease progression; BsAb = bispecific antibody

Approximately what proportion of your patients with R/R DLBCL receiving loncastuximab tesirine derive meaningful clinical benefit? What is the longest duration of response that you have observed with loncastuximab tesirine in your own practice?

	Patients with clinical benefit	Longest duration of response
 Dr Abramson	30%	>1 year
 Dr Flowers	15%	3 months
 Dr Kamdar	20%	9 months
 Dr LaCasce	10%	3 months
 Dr Matasar	50%	4 years+
 Dr Phillips	30%	>1 year
 Prof Salles	30%	6 months
 Dr Westin	45%	>1 year

Approximately what proportion of your patients with DLBCL receiving loncastuximab tesirine develop clinically significant peripheral edema? In general, how do you manage peripheral edema in patients who are receiving loncastuximab tesirine?

	Patients with significant peripheral edema	Management
 Dr Abramson	25%	Dexamethasone prophylaxis, diuretics
 Dr Flowers	40%	Add spironolactone; dose reduce
 Dr Kamdar	30%	Dexamethasone prophylaxis, diuretics
 Dr LaCasce	20%	Peri-drug dexamethasone per label, diuretics
 Dr Matasar	25%	Diuretics
 Dr Phillips	50%	Initiate preventative diuretic in most patients, hold/stop drug if AE
 Prof Salles	20%	Diuretic and prophylactic steroids, then diuretic alone
 Dr Westin	33%	Diuretics and steroids

AE = adverse event

Would you administer brentuximab vedotin/R^2 to a patient with CD30-negative R/R DLBCL?

 Dr Abramson	Yes
 Dr Flowers	No
 Dr Kamdar	Yes
 Dr LaCasce	No
 Dr Matasar	No
 Dr Phillips	No
 Prof Salles	No
 Dr Westin	No

R^2 = lenalidomide/rituximab

RTP RESEARCH TO PRACTICE

Questions?