# Expert Second Opinion
# Investigators Discuss the Role of Novel Treatment Approaches in the Care of Patients with Follicular Lymphoma and Diffuse Large B-Cell Lymphoma

*A CME-Accredited Friday Satellite Symposium Preceding the 67th ASH Annual Meeting*

**Friday, December 5, 2025**

**7:00 PM – 9:00 PM ET**

## Faculty

**Nancy L Bartlett, MD**
**John P Leonard, MD**
**Matthew Matasar, MD**
**Loretta J Nastoupil, MD**
**Professor Pier Luigi Zinzani**

## Moderator

**Neil Love, MD**

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# Faculty

**Nancy L Bartlett, MD**
Professor of Medicine
Koman Chair in Medical Oncology
Washington University School of Medicine
St Louis, Missouri

**John P Leonard, MD**
Laura and Isaac Perlmutter Professor of Hematology and Medical Oncology
Director, Division of Hematology and Medical Oncology
Director, Center for Blood Cancers
Senior Advisor to the Dean/CEO and Chief Clinical Officer for Enterprise Cancer Strategy and Operations
Interim Director, Laura and Isaac Perlmutter Cancer Center
NYU Grossman School of Medicine
NYU Langone Health
New York, New York

**Matthew Matasar, MD**
Chief, Division of Blood Disorders
Rutgers Cancer Institute
Hematologist/Oncologist
Professor
Rutgers Robert Wood Johnson Medical School
New Brunswick, New Jersey

**Loretta J Nastoupil, MD**
Oncologist
Southwest Oncology
CommonSpirit Mercy Hospital
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**Professor Pier Luigi Zinzani**
Professor of Hematology
Alma Mater Studiorum — University of Bologna
Head, “Seràgnoli” Institute of Hematology
IRCCS Azienda Ospedaliero-Universitaria di Bologna
Department of Medical and Surgical Sciences
Bologna University School of Medicine
Bologna, Italy

## Moderator

**Neil Love, MD**
Research To Practice
Miami, Florida

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# Dr Bartlett — Disclosures
# Faculty

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| **Contracted Research** | AbbVie Inc, ADC Therapeutics, Autolus, Bristol Myers Squibb, Celgene Corporation, Forty Seven Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Kite, A Gilead Company, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Seagen Inc, Takeda Pharmaceuticals USA Inc |

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# Dr Leonard — Disclosures
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# Dr Matasar — Disclosures
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# Dr Nastoupil — Disclosures
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# Prof Zinzani — Disclosures
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# CASES FROM THE COMMUNITY
# Investigators Discuss the Role of Antibody-Drug Conjugates in the Management of Triple-Negative and HR-Positive Metastatic Breast Cancer

*Part 1 of a 3-Part CME Satellite Symposium Series*

**Tuesday, December 9, 2025**

**7:00 PM – 8:30 PM CT (8:00 PM – 9:30 PM ET)**

## Faculty

**Javier Cortés, MD, PhD**

**Professor Peter Schmid, FRCP, MD, PhD**

**Rita Nanda, MD**

**Priyanka Sharma, MD**

## Moderator

**Neil Love, MD**

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# CASES FROM THE COMMUNITY
# Investigators Discuss the Optimal Management of HER2-Positive Breast Cancer

*Part 2 of a 3-Part CME Satellite Symposium Series*

**Wednesday, December 10, 2025**

**7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)**

## Faculty

**Professor Giuseppe Curigliano, MD, PhD**
**Nadia Harbeck, MD, PhD**
**Ian E Krop, MD, PhD**
**Nancy U Lin, MD**
**Joyce O'Shaughnessy, MD**

## Moderator

**Neil Love, MD**

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# CASES FROM THE COMMUNITY
# Investigators Discuss the Optimal Role of Endocrine-Based and Other Strategies in the Management of HR-Positive Breast Cancer

*Part 3 of a 3-Part CME Satellite Symposium Series*

**Thursday, December 11, 2025**

**7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)**

## Faculty

**Angela DeMichele, MD, MSCE**
**Komal Jhaveri, MD, FACP, FASCO**
**Erica Mayer, MD, MPH, FASCO**
**Hope S Rugo, MD**
**Seth Wander, MD, PhD**

## Moderator

**Neil Love, MD**

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# Cases from the Community: Investigators Discuss Available Research Guiding the Management of Relapsed/Refractory Multiple Myeloma — What Happened at ASH 2025?

*A CME/MOC-Accredited Live Webinar*

**Monday, December 15, 2025**

**5:00 PM – 6:00 PM ET**

## Faculty

**Sagar Lonial, MD, FACP, FASCO**

**María-Victoria Mateos, MD, PhD**

## Moderator

**Neil Love, MD**

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# Practical Perspectives on the Current and Future Management of Immune Thrombocytopenia — What Happened at ASH 2025?

*A CME/MOC-Accredited Live Webinar*

**Tuesday, December 16, 2025**

**5:00 PM – 6:30 PM ET**

## Faculty

**Hanny Al-Samkari, MD**

**Francesco Zaja, MD**

***Additional faculty to be announced***

## Moderator

**Neil Love, MD**

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# Practical Perspectives on the Current Role of Bispecific Antibodies in the Management of Lymphoma — What Happened at ASH 2025?

*A CME/MOC-Accredited Live Webinar*

**Wednesday, December 17, 2025**
**5:00 PM – 6:00 PM ET**

## Faculty

**Michael Dickinson, MD**
**Laurie H Sehn, MD, MPH**

## Moderator

**Neil Love, MD**

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# Grand Rounds

*CME/MOC-Accredited Interactive Series*

**Through April 2026**

## Three Series

**Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia**

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

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

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Save The Date

# Fifth Annual
# National General Medical Oncology Summit

***A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute***

**Friday to Sunday, April 24 to 26, 2026**

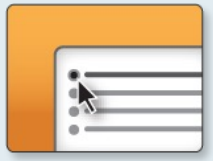
The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

**Moderated by Neil Love, MD**

# Clinicians in the Meeting Room

**Networked iPads are available.**

**Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.**



**Answer Survey Questions: Complete the pre- and postmeeting surveys.**

**Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.**

***For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.***

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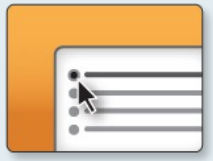
# Clinicians Attending via Zoom

**Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.**



**Answer Survey Questions: Complete the pre- and postmeeting surveys.**

**Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.**

**Get CME Credit: A credit link will be provided in the chat room at the conclusion of the program.**

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# About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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# RTP Playlist with Neil Love, MD

## BREAST CANCER

Dr Hope Rugo: Interview (28 min)

## SMALL CELL LUNG CANCER

Drs Stephen Liu and Charles Rudin: Cases (58 min)

## GASTROESOPHAGEAL CANCER

Drs Geoffrey Ku and Zev Wainberg: Cases (61 min)

## PROSTATE CANCER

Drs Emmanuel Antonarakis and Karim Fizazi: Year in Review (60 min)

## ENDOMETRIAL AND OVARIAN CANCER

Dr Shannon Westin: Interview (52 min)

## NEUROENDOCRINE TUMORS

Drs Simron Singh and Jonathan Strosberg: Meeting (50 min)

## NON-HODGKIN LYMPHOMA

Drs Jeremy Abramson, Joshua Brody, Christopher Flowers, Ann LaCasce and Tycel Phillips: Meeting, cases (59 min)

## CHRONIC LYMPHOCYTIC LEUKEMIA

Drs Jennifer Brown and Paolo Ghia: Year in Review (59 min)

## ACUTE MYELOID LEUKEMIA

Dr Jorge Cortes: Interview (43 min)

## MULTIPLE MYELOMA

Drs Natalie Callander and Sagar Lonial: Patient videos (59 min)

## IMMUNE THROMBOCYTOPENIA

Drs Hanny Al-Samkari, James Bussel and Nichola Cooper: Think Tank (117 min)

## OCULAR TOXICITES IN ONCOLOGY

Dr Neel Pasricha: Interview (54 min)

Feedback (Please!)
DrNeilLove@ResearchToPractice.com

## RTP Playlist with Neil Love, MD

**Webinar for patients and families on relapsed multiple myeloma with Drs Natalie Callander and Sagar Lonial.**

Relapsed Multiple Myeloma: Where We Were, Where We Are (4 min)

Common Questions from the Beginning (5 min)

Choosing Treatment Options (4 min)

Clinical Research Trials (6 min)

Neuropathy (5 min)

Chimeric Antigen Receptor (CAR) T-Cell Therapy (6 min)

Bispecific Antibodies (8 min)

Antibody-Drug Conjugates: Belantamab Mafadotin (8 min)

Interacting with the Oncology Team (5 min)

Other Questions (4 min)

Recording of Entire Webinar (62 min)

Feedback (Please!)
DrNeilLove@ResearchToPractice.com

# ASH and SABCS RTP Video Participants

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# ASH and SABCS RTP Participating Faculty

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**Neil Love, MD**

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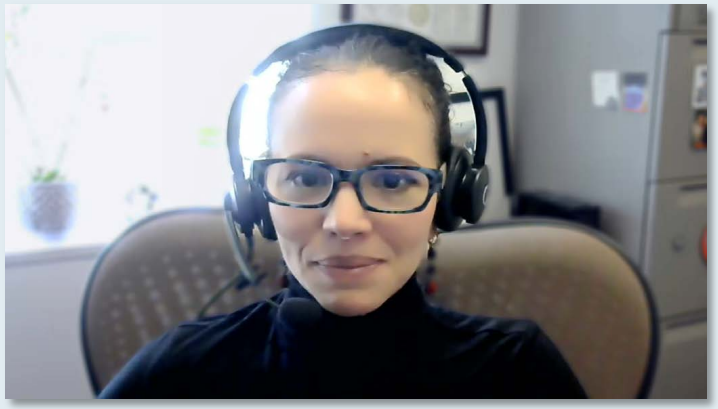
# Consulting Faculty



**Carla Casulo, MD**
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**Laurie H Sehn, MD, MPH**
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BC Cancer Centre for Lymphoid Cancer
Clinical Professor of Medicine
The University of British Columbia
Vancouver, British Columbia, Canada

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# Agenda

**Module 1:** Rational Incorporation of Antibody-Drug Conjugates into the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Matasar

**Module 2:** Clinical Utility of CD19-Directed Monoclonal Antibodies for DLBCL and Follicular Lymphoma (FL) — Dr Leonard

**Module 3:** Optimal Use of Antibody-Drug Conjugates in the Treatment of Relapsed/Refractory DLBCL — Prof Zinzani

**Module 4:** Bispecific Antibody Therapy for DLBCL — Dr Bartlett

**Module 5:** Bispecific Antibody Therapy for FL and Other Lymphoma Subtypes — Dr Nastoupil

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# Agenda

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**Module 4: Bispecific Antibody Therapy for DLBCL — Dr Bartlett**

**Module 5: Bispecific Antibody Therapy for FL and Other Lymphoma Subtypes — Dr Nastoupil**

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# Diffuse large B-cell lymphoma: Emerging strategies

Matt Matasar, MD

Chief of Blood Disorders, Rutgers Cancer Institute

Professor of Medicine, Rutgers RWJ Medical School

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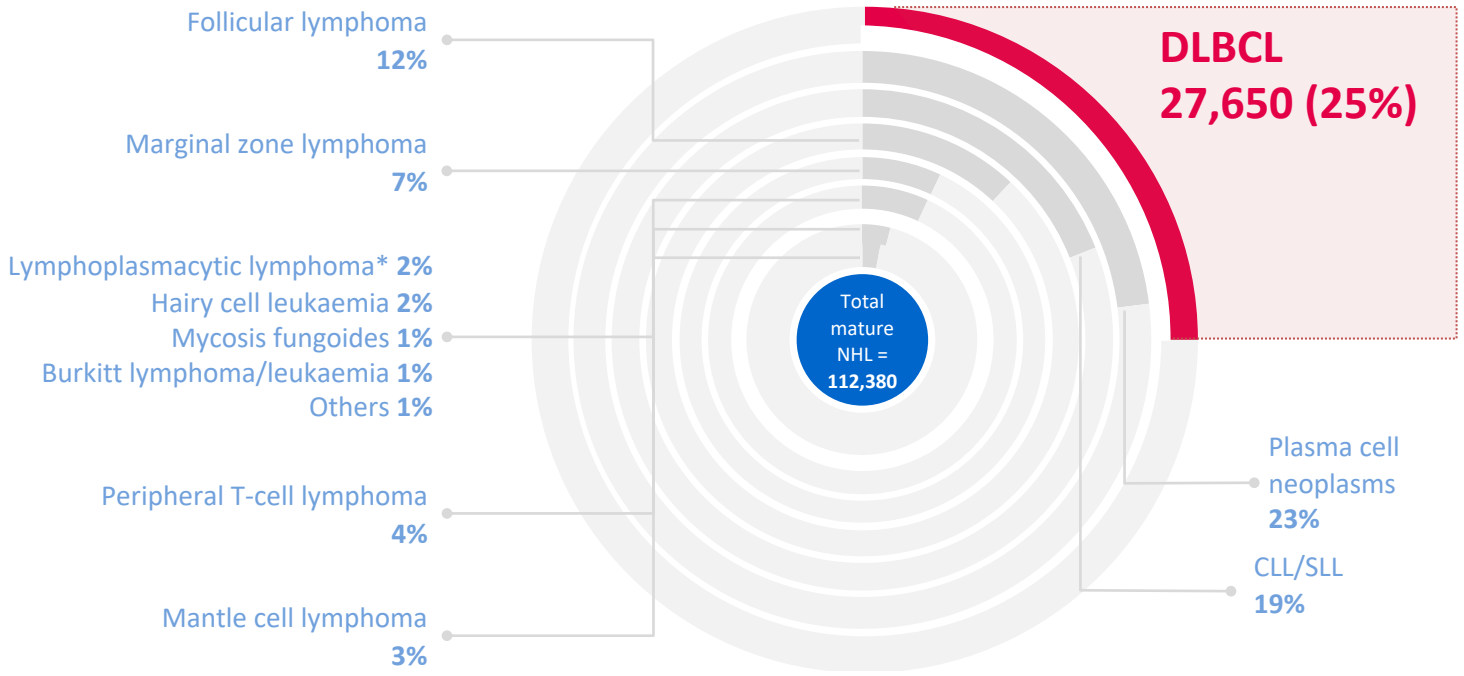
# DLBCL: An Aggressive, Common Lymphoma

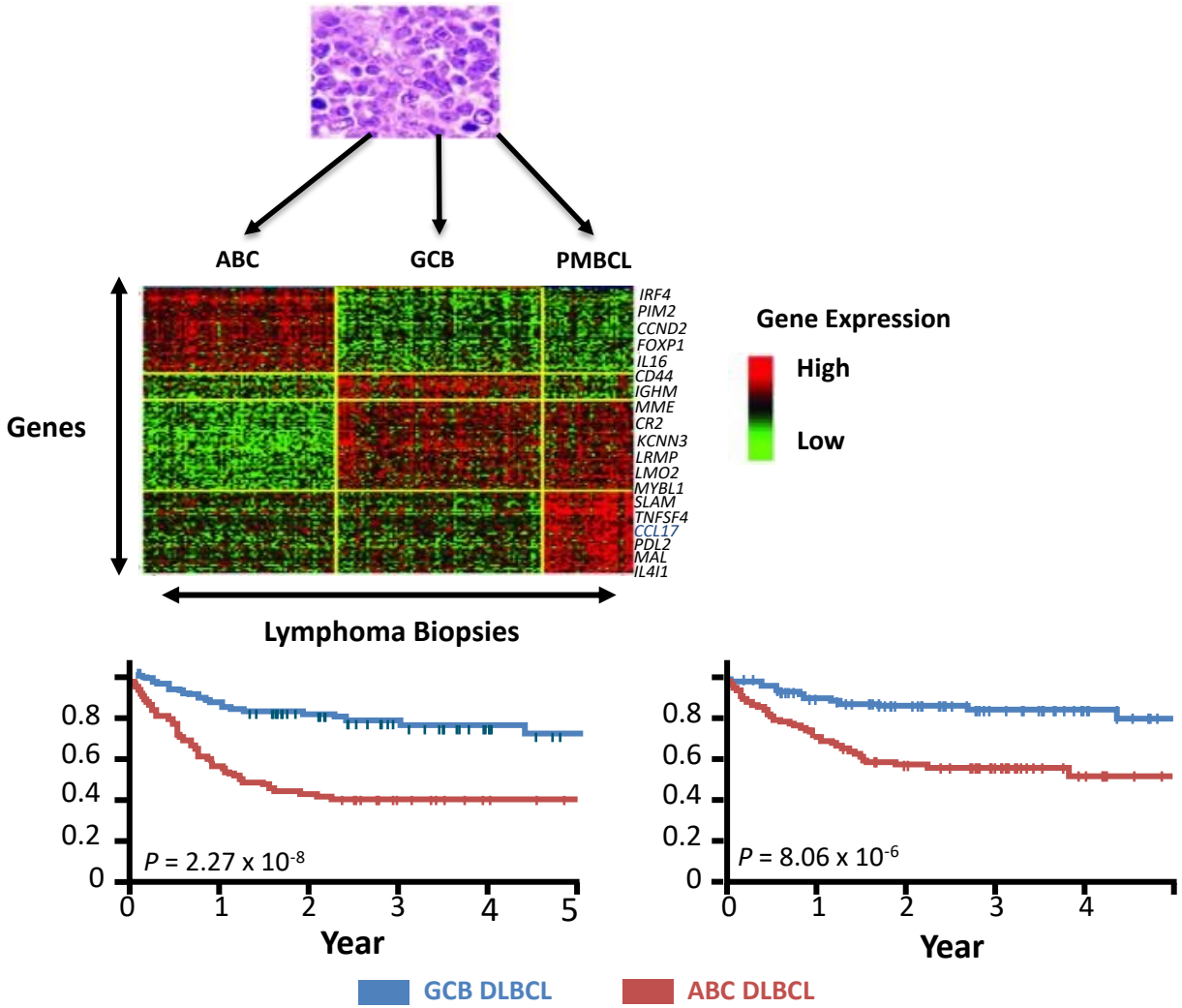
## Estimated cases and distribution of mature non-Hodgkin lymphoid neoplasm subtypes in the USA in 2016

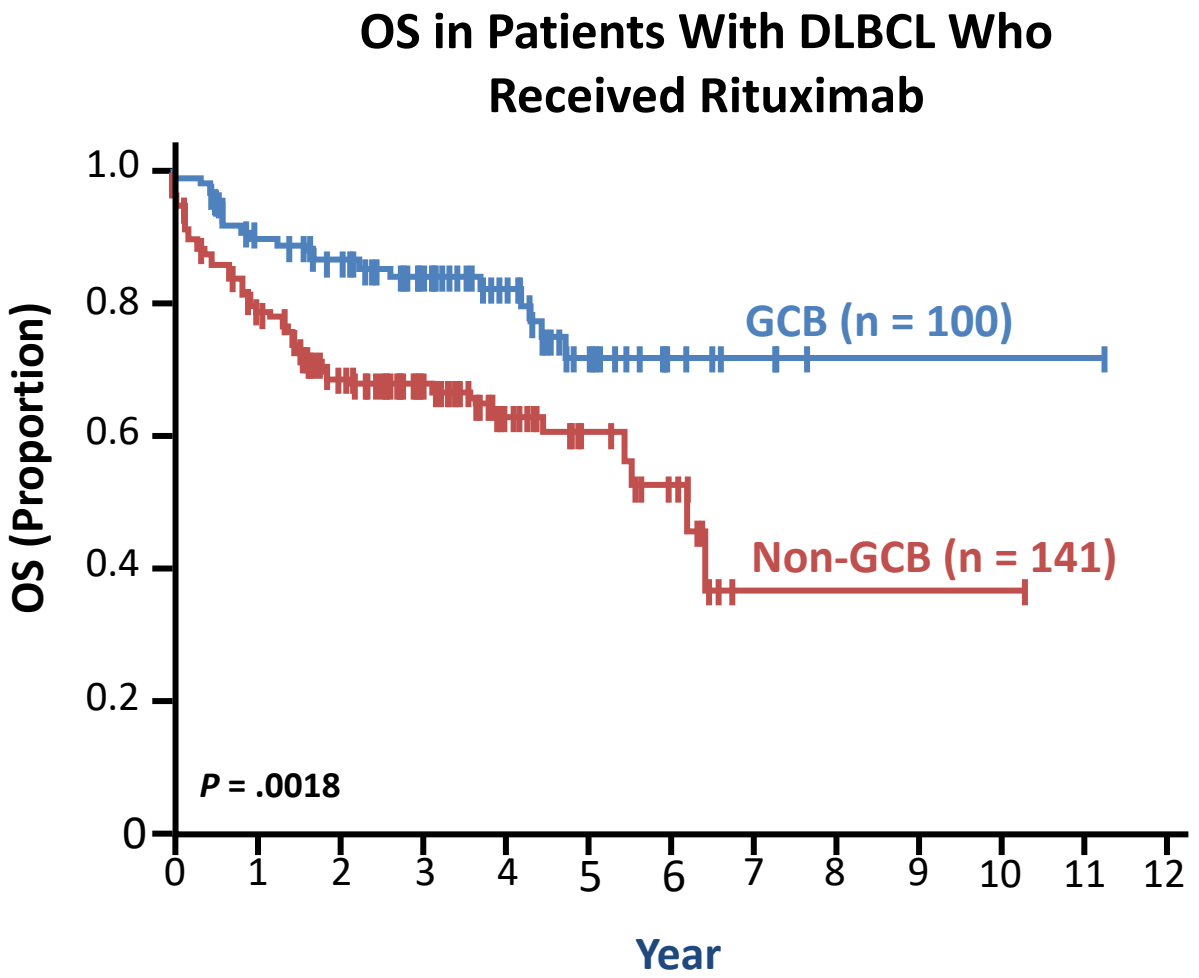



*Includes Waldenstrom macroglobulinemia. †Includes hairy cell leukemia variant CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; IPI, International Prognostic Index

BTKi = Bruton's tyrosine kinase inhibitor; DLBCL = diffuse large B-cell lymphoma; VA = Veterans Affairs; 1. Tilly H, et al. *Ann Oncol*. 2015;26(Suppl 5):v116-125. 2. Stewart BW, Wild CP. http://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-2014/. Accessed June 14, 2019. 3. The Non-Hodgkin's Lymphoma Classification Project. *Blood*. 1997;89:3909-3918. 4. Gascoyne RD, et al. WHO classification, Lyon 2017.

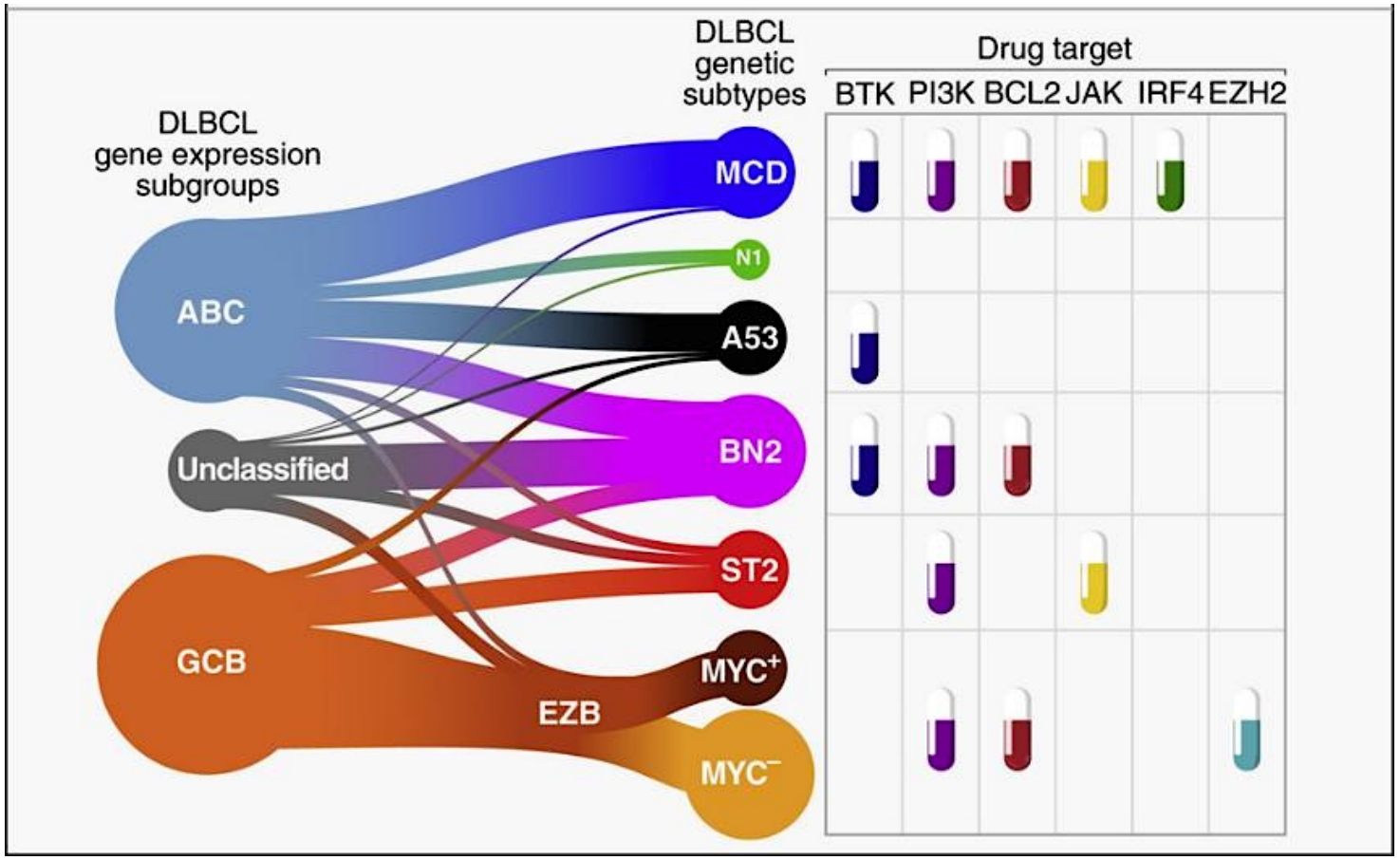
# DLBCL – Not One Disease




ABC = activated B-cell DLBCL; DLBCL = diffuse large b-cell lymphoma; GCB = germinal center B-cell-like DLBCL; OS = overall survival; PMBCL = primary mediastinal large B cell lymphoma; 1. Wilson WH. *Hematology Am Soc Hematol Educ Program*. 2013;2013:584-590. 2. Meyer PN, et al. *J Clin Oncol*. 2011;29(2):200-207.

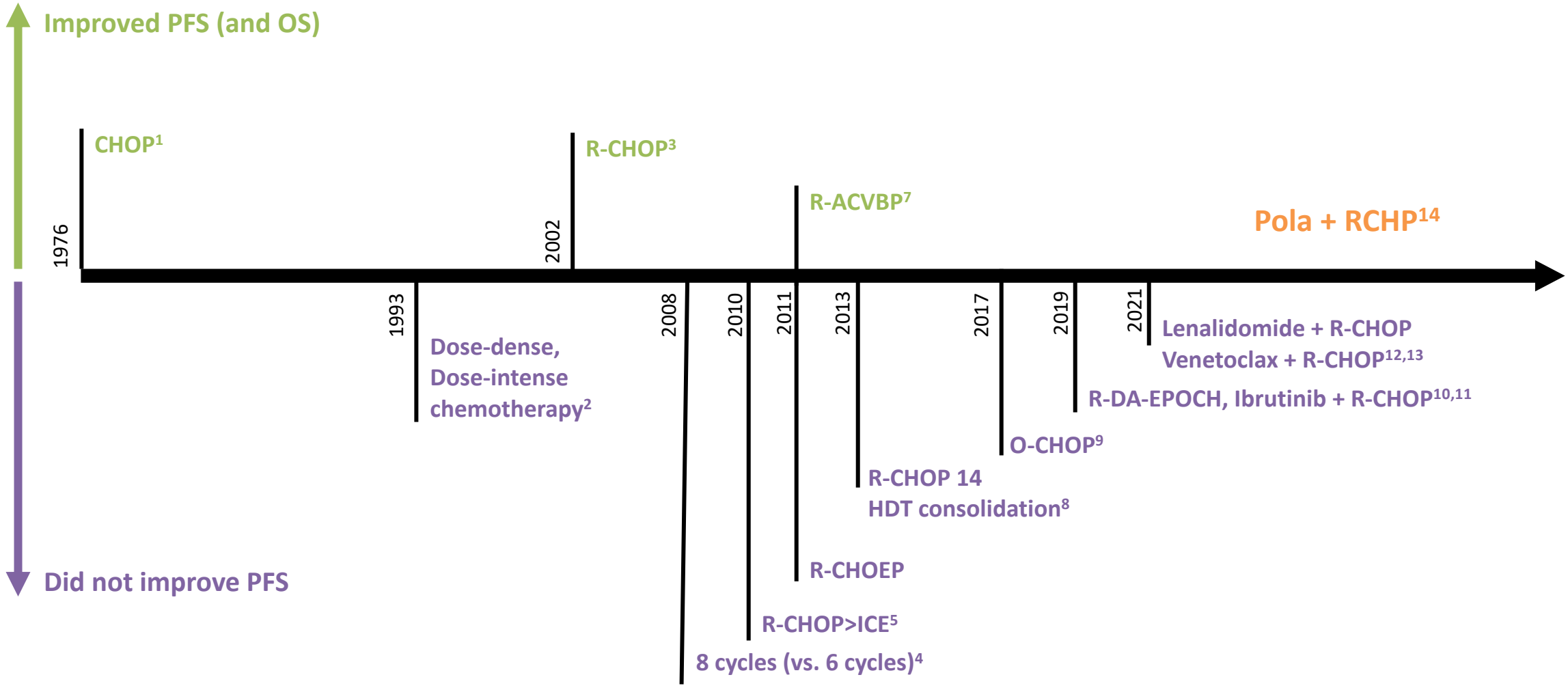
# LymphGen Molecular Classification




| Characteristics | OS |
|---|---|
| *MYD88 L265P* mutations and *CD79B* mutations<br>*CDKN2A* deletions | 40% |
| *NOTCH1* mutations. *BCOR, ikB* kinase β mutations | 27% |
| *TP53* mutations/deletions<br>Aneuploidy | 63% |
| *NOTCH2* mutations, *BLC6* translocation, *TNFAIP3 (A20),*<br>*BCL10, PRKCB* mutations | 67% |
| *SGK1* and *TET2* mutated | 84% |
| *EZH2, CREBP, KMT2D, EP300* mutations and<br>*BCL2, MYC, TP53, GNA13, FOX01* alterations | 48% |
| *EZH2, CREBP, KMT2D, EP300* mutations and<br>*BCL2* translocations<br>*CARD11, TNFAIP3 (A2)* alterations | 82% |

Wright GW. *Cancer Cell*. 2020;37(4):551-568.e14.

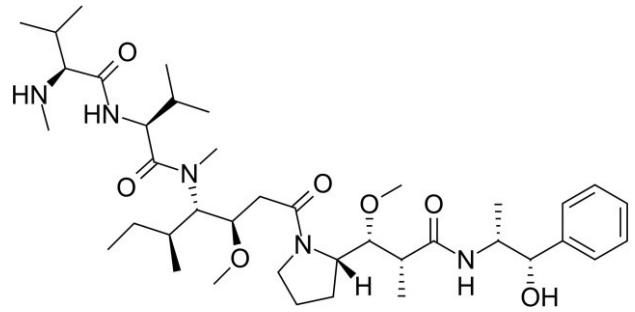
# Evolution of Standards




1. McKelvey EM, et al. Cancer. 1976;38(4):1484-1493. 2. Waits TM, et al. *J Clin Oncol*. 1993;11(5):943-949. 3. Coiffier B, et al. *N Engl J Med*. 2002;346(4):235-242. 4. Pfreundschuh M, et al. *Lancet Oncol*. 2008;9(2):105-116. 5. Moskowitz C, et al. *Blood*. 2010;116(21):420. 6. ??? 7. Récher C, et al. *Lancet*. 2011;378(9806):1858-1867. 8. Cunningham D, et al. *Lancet*. 2013;381(9880):1817-1826. 9. Peyrade F, et al. *Lancet Hematol*. 2017;4(1):e46-e55. 10. Bartlett NL, et al. *J Clin Oncol*. 2019;37(21). 11. Younes A, et al. *J Clin Oncol*. 2019;37(15):1285-1295. 12. Nowakowski GS, et al. *J Clin Oncol*. 2021;39(12):1317-1328. 13. Morschhauser F, et al. *Blood*. 2021;137(5):600-609. 14. Morschhauser F, et al. *J Clin Oncol*. 2025.

# Polatuzumab VEDOTIN

- Vedotin is MMAE + linker: monomethyl auristatin E
- Targets CD79, part of B-cell receptor
- Pan B-cell antigen and in precursors
- Binds to tubulin
- Cleavable linker
- 200x more potent than vincristine

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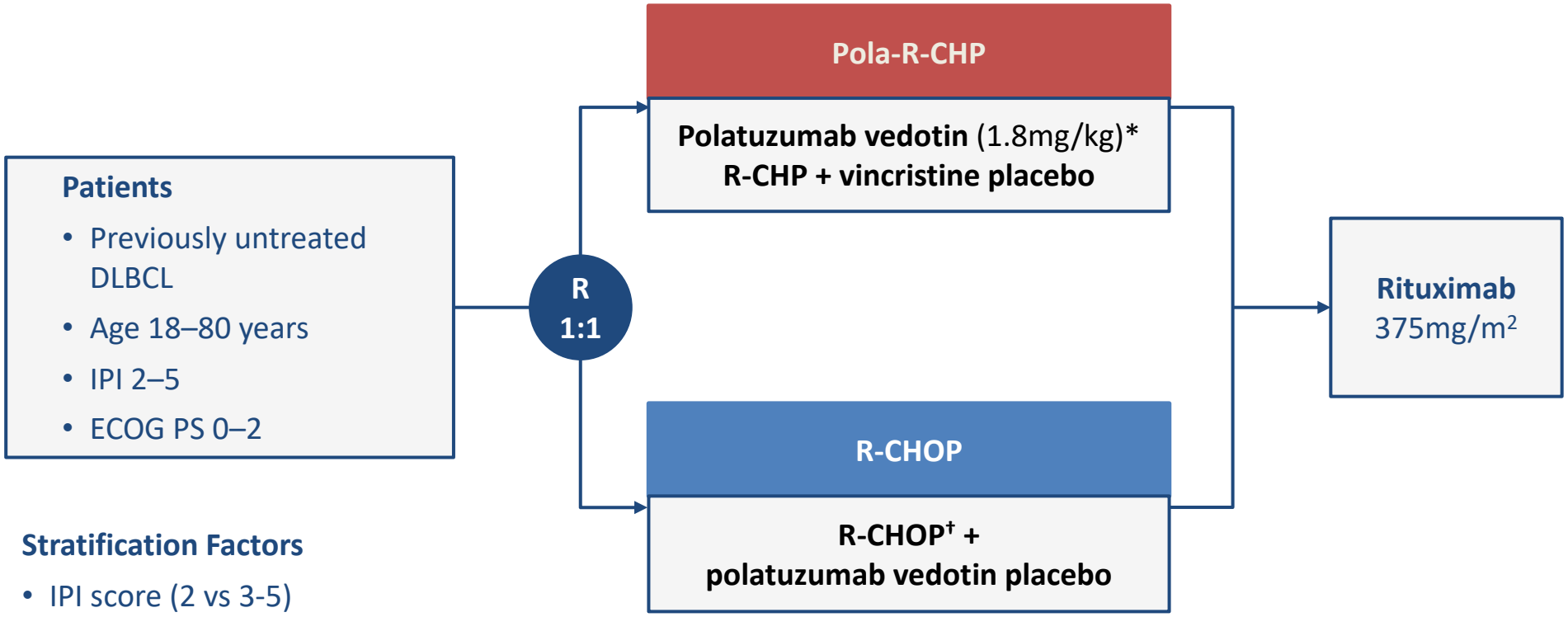
# POLARIX: Pola-R-CHP in Previously Untreated DLBCL



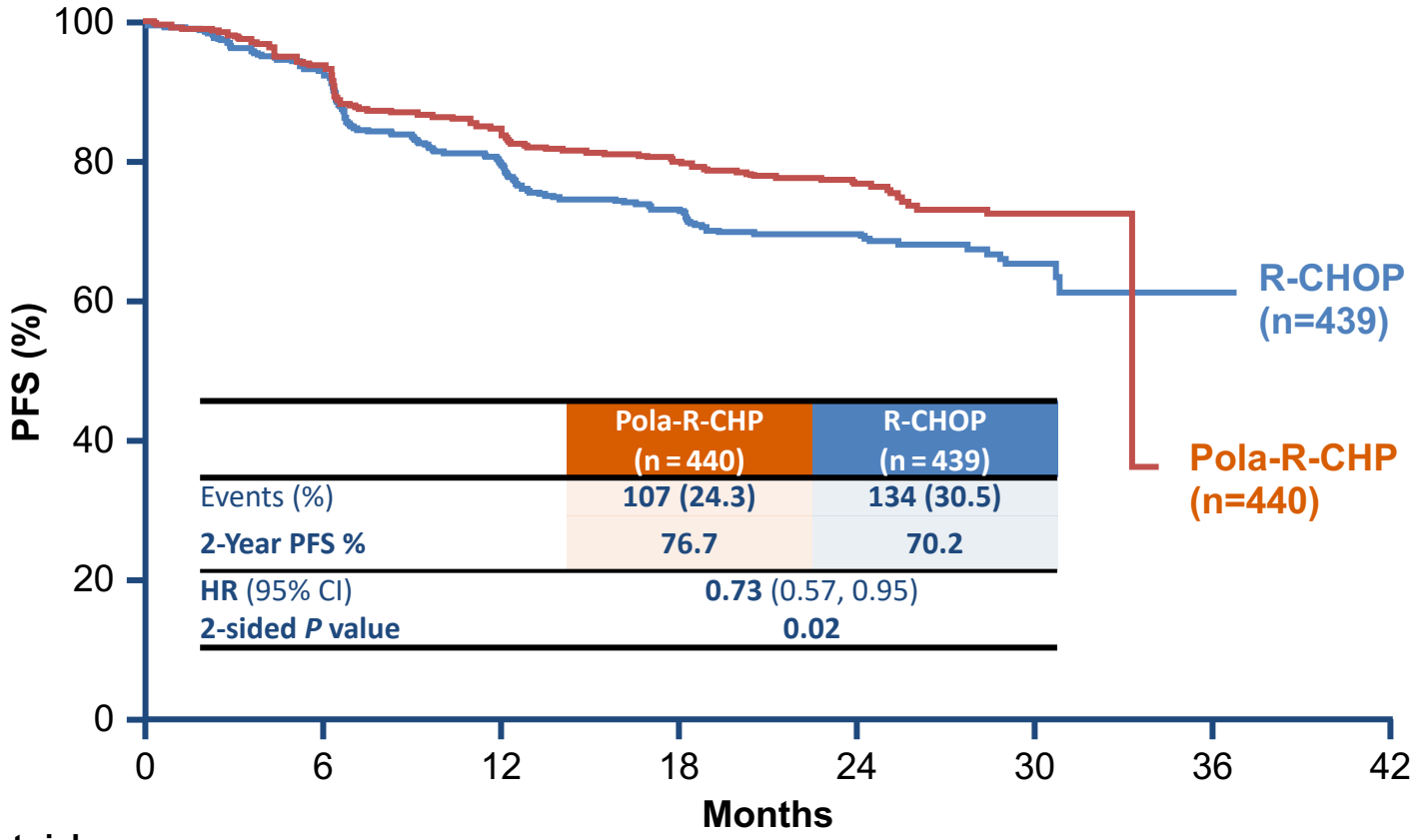

**Stratification Factors**

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

*IV on Day 1; †R-CHOP: IV rituximab 375mg/m$^2$, cyclophosphamide 750mg/m$^2$, doxorubicin 50mg/m$^2$, and vincristine 1.4mg/m$^2$ (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5. ECOG PS = Eastern Cooperative Oncology Group performance status; IPI = International prognostic index; R = randomized. Tilly H, et al. *N Engl J Med*. 2022;386:351-363.

# POLARIX: Pola-R-CHP in Previously Untreated DLBCL

## *Primary Endpoint: Progression-Free Survival*




| | Pola-R-CHP (n = 440) | R-CHOP (n = 439) |
|---|---|---|
| Events (%) | 107 (24.3) | 134 (30.5) |
| 2-Year PFS % | 76.7 | 70.2 |
| HR (95% CI) | 0.73 (0.57, 0.95) | |
| 2-sided *P* value | 0.02 | |

| No. at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Pola-R-CHP | 440 | 404 | 353 | 327 | 246 | 78 | NE | NE |
| R-CHOP | 439 | 389 | 330 | 296 | 220 | 78 | 3 | NE |

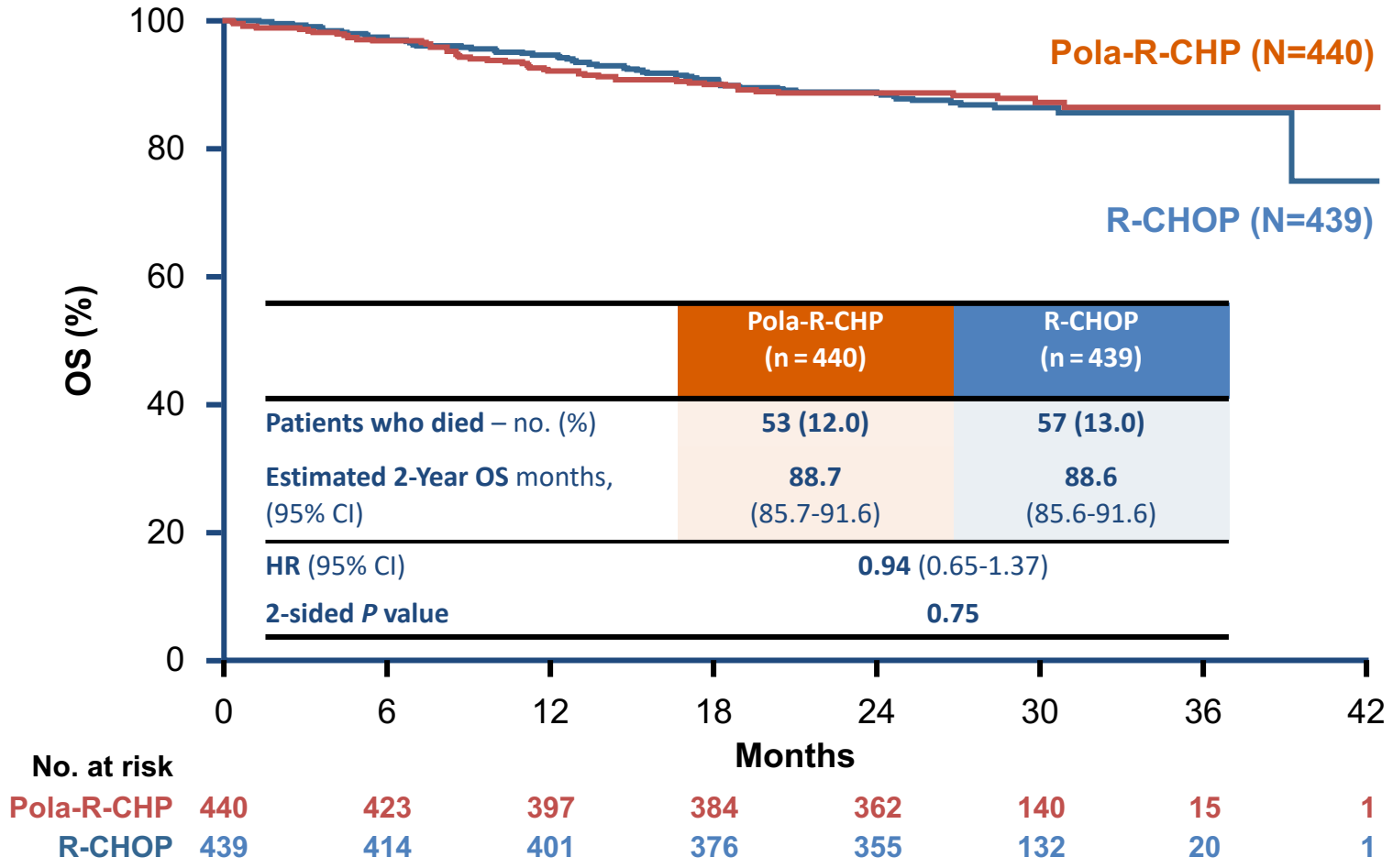
- **Pola-R-CHP significantly improved PFS versus R-CHOP**
- Pola-R-CHP demonstrated a 27% reduction in the relative risk of disease progression, relapse, or death versus R-CHOP
- 24-month-PFS:
  - 76.7% with Pola-R-CHP
  - 70.2% with R-CHOP (Δ=6.5%)
- Most common adverse events from Pola-R-CHP, R-CHOP consisted of peripheral neuropathy, nausea, neutropenia, diarrhea, anemia, constipation

CI = confidence interval; HR = hazard ratio; PFS = progression-free survival; Pola-R-CHP = polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, prednisone; R-CHOP = rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisone.

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

# POLARIX: Pola-R-CHP in Previously Untreated DLBCL

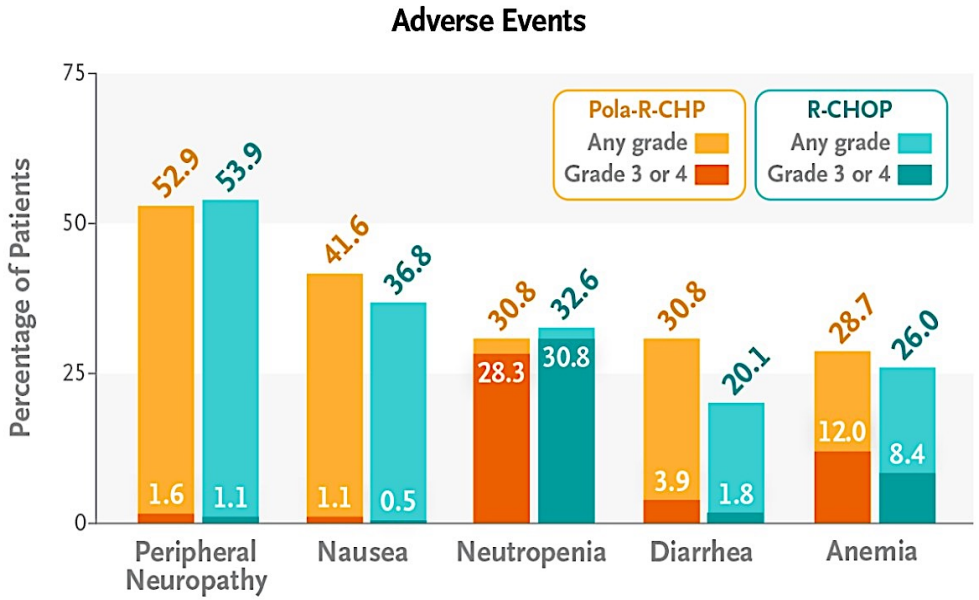
## *Overall Survival*




CI = confidence interval; HR = hazard ratio; No. = number; OS = overall survival; Pola-R-CHP = polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, prednisone; R-CHOP = rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisone. Tilly H, et al. *N Engl J Med*. 2022;386:351-363.

# Polatuzumab vedotin in combination:
# Safety Profile

## POLARIX Study




## G029365 Phase 1b/2 "PBR"

| AE, n (%)[a] | Pola-BR (n=39) All Grade | BR (n=39) All Grade | Pola-BR (n=39) Grade 3-4 | BR (n=39) Grade 3-4 |
|---|---|---|---|---|
| **Blood and lymphatic system disorders** | | | | |
| Anemia | 21 (54) | 10 (26) | **11 (28)** | 7 (18) |
| Neutropenia | 21 (54) | 15 (39) | **18 (46)** | 13 (33) |
| Thrombocytopenia | 19 (49) | 11 (28) | **16 (41)** | 9 (23) |
| **GI disorders** | | | | |
| Diarrhea | 15 (39) | 11 (28) | 1 (3) | 1 (3) |
| Nausea | 12 (31) | 16 (41) | 0 | 0 |
| Constipation | 7 (18) | 8 (21) | 0 | 1 (3) |
| **General disorders and administration site conditions** | | | | |
| Fatigue | 14 (36) | 14 (36) | 1 (3) | 1 (3) |
| Pyrexia | 13 (33) | 9 (23) | 1 (3) | 0 |
| **Metabolism and nutrition disorders** | | | | |
| Decreased appetite | 10 (26) | 8 (21) | 1 (3) | 0 |
| **Peripheral neuropathy** | | | | |
| Peripheral neuropathy[b] | **17 (44)** | 3 (8) | 0 | 0 |



RWJBarnabas HEALTH

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Rutgers Cancer Institute

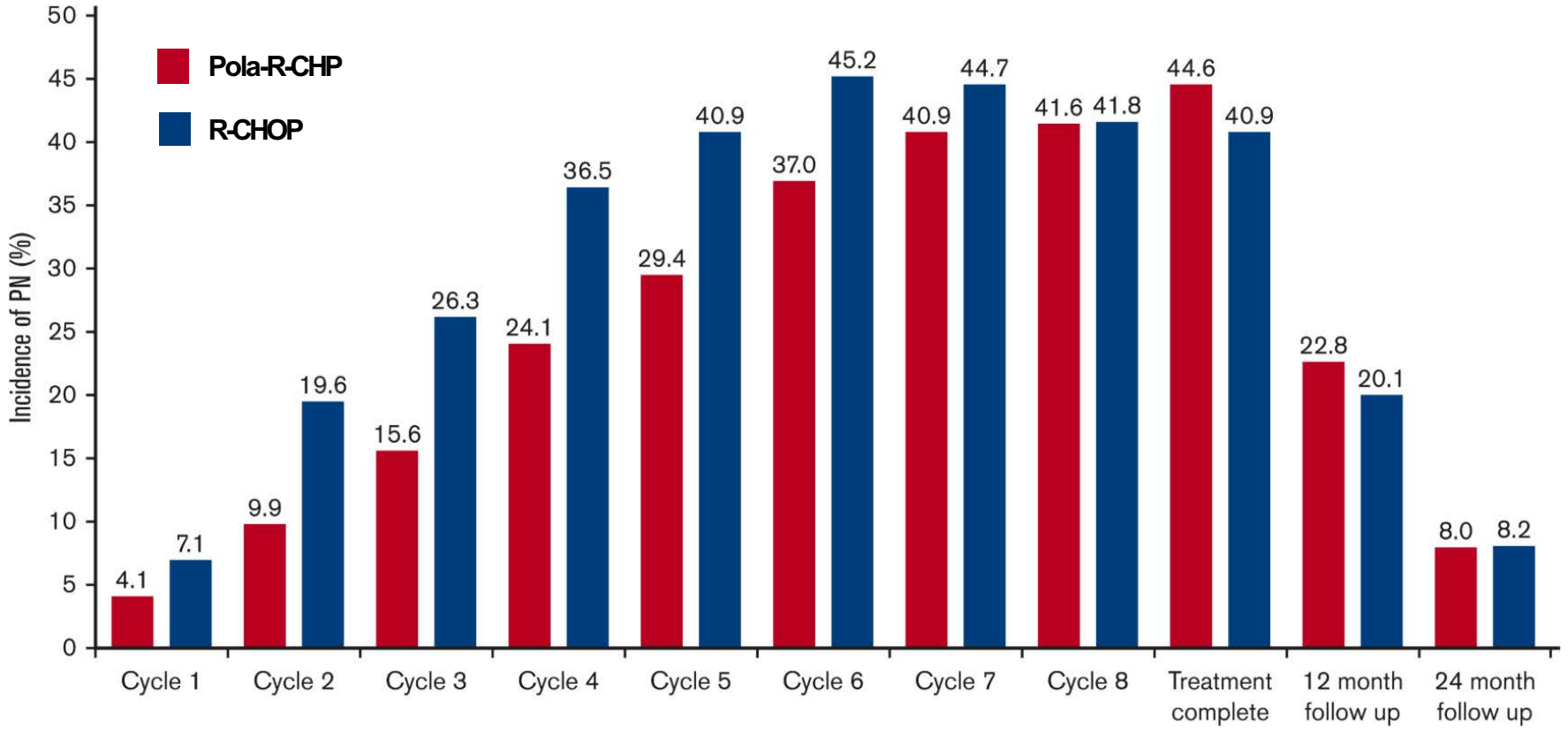
Tilly H et al, NEJM, 2022; Sehn L et al, JCO, 2020

# **Polatuzumab:** Peripheral Neuropathy

**Pola-RCHP**

40 – 50% of patients will develop some peripheral neuropathy

- Predominantly sensory
- Many reversible
- Severe cases can have motor impairment
- About 4 months to resolution
- 0.7% drug d/c
- 4% dose reduction




BEST PRACTICES IN
**DIFFUSE LARGE B-CELL LYMPHOMA**

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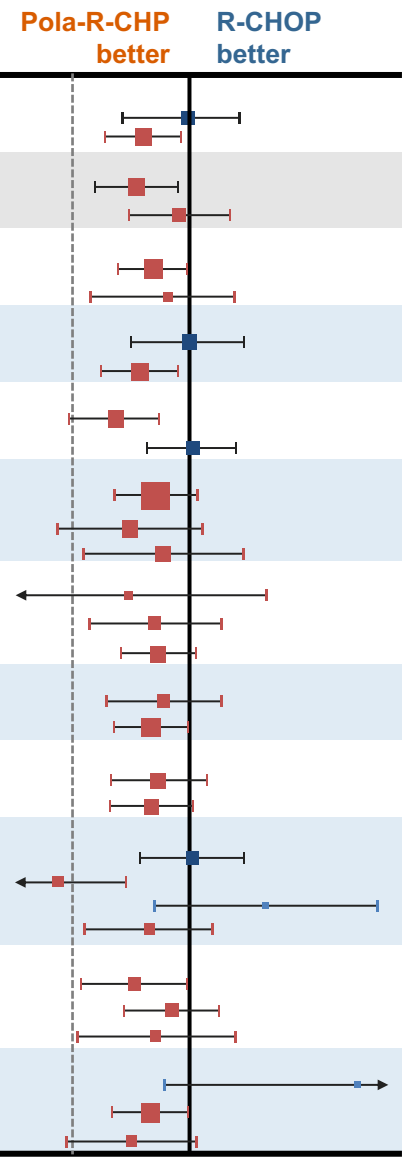
Rutgers Cancer Institute

Trneny et al, *Blood Advances* 2025

# POLARIX: Subgroup Analysis

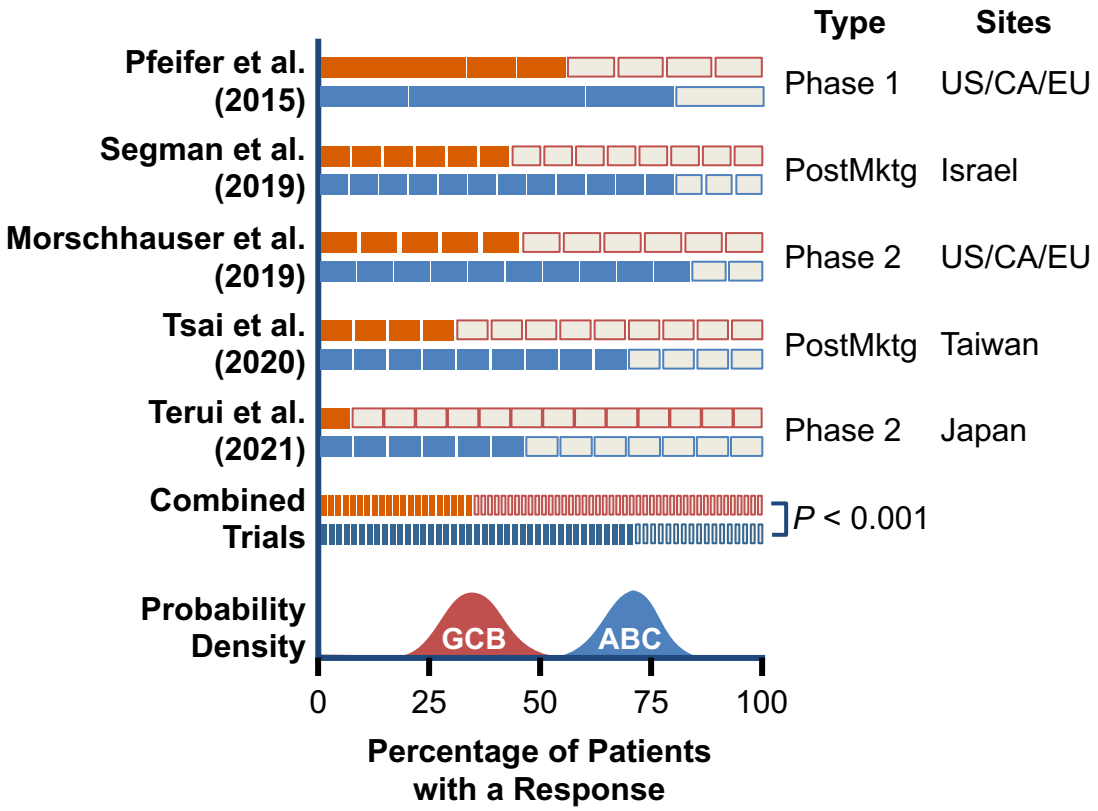
| Baseline Risk Factors | Total N | Pola-R-CHP (N = 440) n | Pola-R-CHP (N = 440) 2-yr Rate | R=CHOP (N = 439) n | R=CHOP (N = 439) 2-yr Rate | HR | 95% Wald CI |
|---|---|---|---|---|---|---|---|
| **Age group** | | | | | | | |
| ≤60 | 271 | 140 | 74.1 | 131 | 71.9 | 0.9 | (0.6-1.5) |
| >60 | 608 | 300 | 77.9 | 308 | 69.5 | 0.7 | (0.5-0.9) |
| **Sex** | | | | | | | |
| Male | 473 | 239 | 75.9 | 234 | 65.9 | 0.7 | (0.5-0.9) |
| Female | 406 | 201 | 77.7 | 205 | 75.2 | 0.9 | (0.6-1.4) |
| **ECOG PS** | | | | | | | |
| 0-1 | 737 | 374 | 78.4 | 363 | 71.2 | 0.8 | (0.6-1.0) |
| 2 | 141 | 66 | 67.2 | 75 | 65.0 | 0.8 | (0.5-1.4) |
| **IPI score** | | | | | | | |
| IPI 2 | 334 | 167 | 79.3 | 167 | 78.5 | 1.0 | (0.6-1.0) |
| IPI 3-5 | 545 | 273 | 75.2 | 272 | 65.1 | 0.7 | (0.5-1.4) |
| **Bulky disease** | | | | | | | |
| Absent | 494 | 247 | 82.7 | 247 | 70.7 | 0.6 | (0.4-0.8) |
| Present | 385 | 193 | 69.0 | 192 | 69.7 | 1.0 | (0.7-1.5) |
| **Geographic region** | | | | | | | |
| Western Europe, US, Canada, and Australia | 603 | 302 | 78.6 | 301 | 72.0 | 0.8 | (0.6-1.1) |
| Asia | 160 | 81 | 74.3 | 79 | 65.6 | 0.6 | (0.4-1.5) |
| Rest of world | 116 | 57 | 70.8 | 59 | 67.3 | 0.9 | (0.6-1.5) |
| **Ann Arbor stage** | | | | | | | |
| I-II | 99 | 47 | 89.1 | 52 | 85.5 | 0.6 | (0.2-1.8) |
| III | 232 | 124 | 80.7 | 108 | 73.6 | 0.8 | (0.5-1.3) |
| IV | 548 | 269 | 72.6 | 279 | 66.1 | 0.8 | (0.6-1.1) |
| **Baseline LDH** | | | | | | | |
| ≤ULN | 300 | 146 | 78.9 | 154 | 75.6 | 0.8 | (0.5-1.3) |
| >ULN | 575 | 291 | 75.4 | 284 | 67.2 | 0.7 | (0.5-1.0) |
| **No. of extranodal sites** | | | | | | | |
| 0-1 | 453 | 227 | 80.2 | 226 | 74.5 | 0.8 | (0.5-1.1) |
| ≥2 | 426 | 213 | 73.0 | 213 | 65.8 | 0.7 | (0.5-1.0) |
| **Cell-of-origin** | | | | | | | |
| GCB | 352 | 184 | 75.1 | 168 | 76.9 | 1.0 | (0.7–1.5) |
| ABC | 221 | 102 | 83.9 | 119 | 58.8 | 0.4 | (0.2-0.6) |
| Unclassified | 95 | 44 | 73.0 | 51 | 86.2 | 1.9 | (0.8-4.5) |
| Unknown | 211 | 110 | 73.8 | 101 | 64.3 | 0.7 | (0.4-1.2) |
| **Double expressor by IHC** | | | | | | | |
| DEL | 290 | 139 | 75.5 | 151 | 63.1 | .63 | (0.4-1.0) |
| Non DEL | 438 | 223 | 77.7 | 215 | 75.7 | 0.9 | (0.6-1.3) |
| Unknown | 151 | 78 | 76.0 | 73 | 69.8 | 0.8 | (0.4-1.5) |
| **Double- or triple-hit lymphoma** | | | | | | | |
| Yes | 45 | 26 | 69.0 | 19 | 88.9 | 3.8 | (0.8-17.6) |
| No | 620 | 305 | 76.8 | 315 | 70.3 | 0.7 | (0.5-1.0 |
| Unknown | 214 | 109 | 78.5 | 105 | 66.4 | 0.6 | (0.4-1.1) |



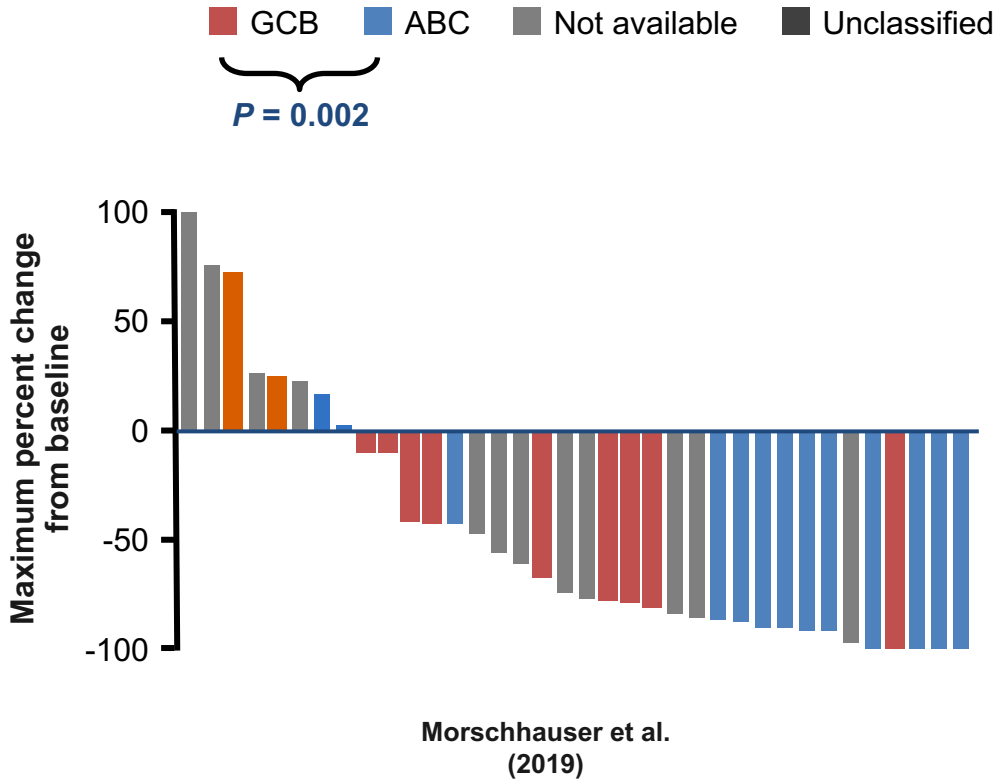

Pola-R-CHP = polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, prednisone; R-CHOP = rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisone. Tilly H, et al. *N Engl J Med*. 2022;386:351-363.

# Cell of Origin and Polatuzumab

**Cell of Origin and Response to Polatuzumab Vedotin in DLBCL**



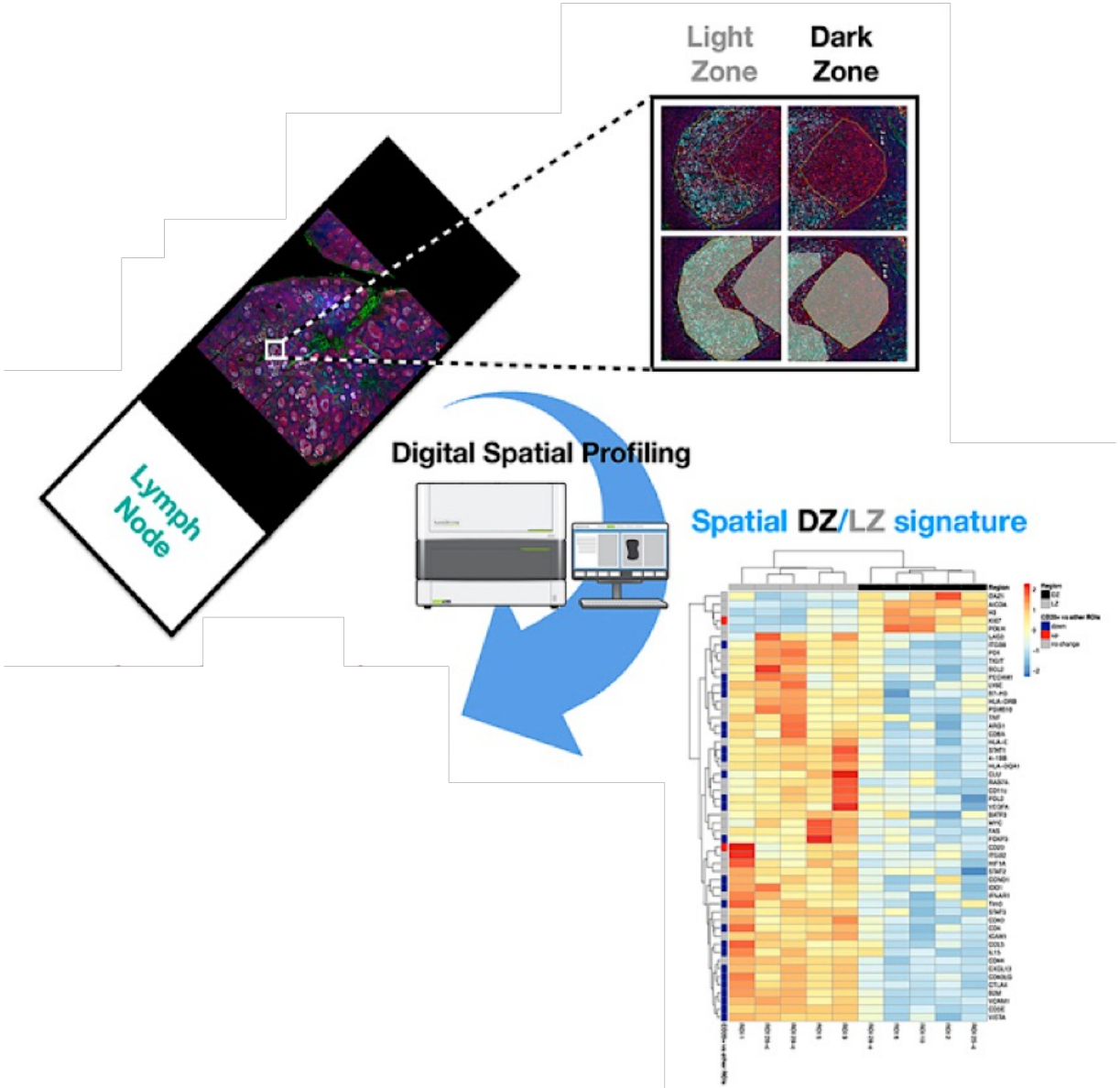

**Cell of Origin and Response to Polatuzumab Vedotin Combined with Rituximab**

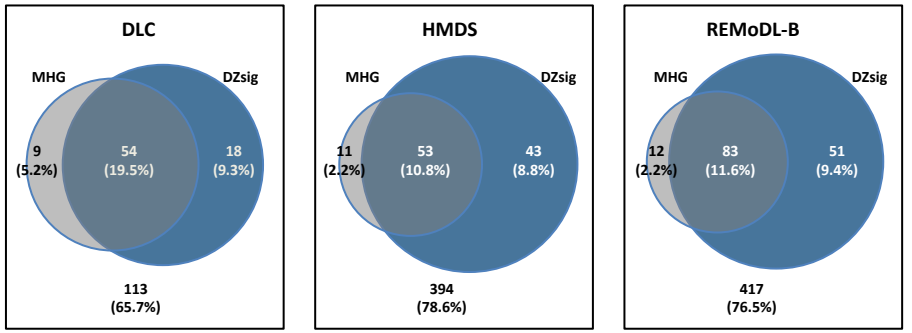


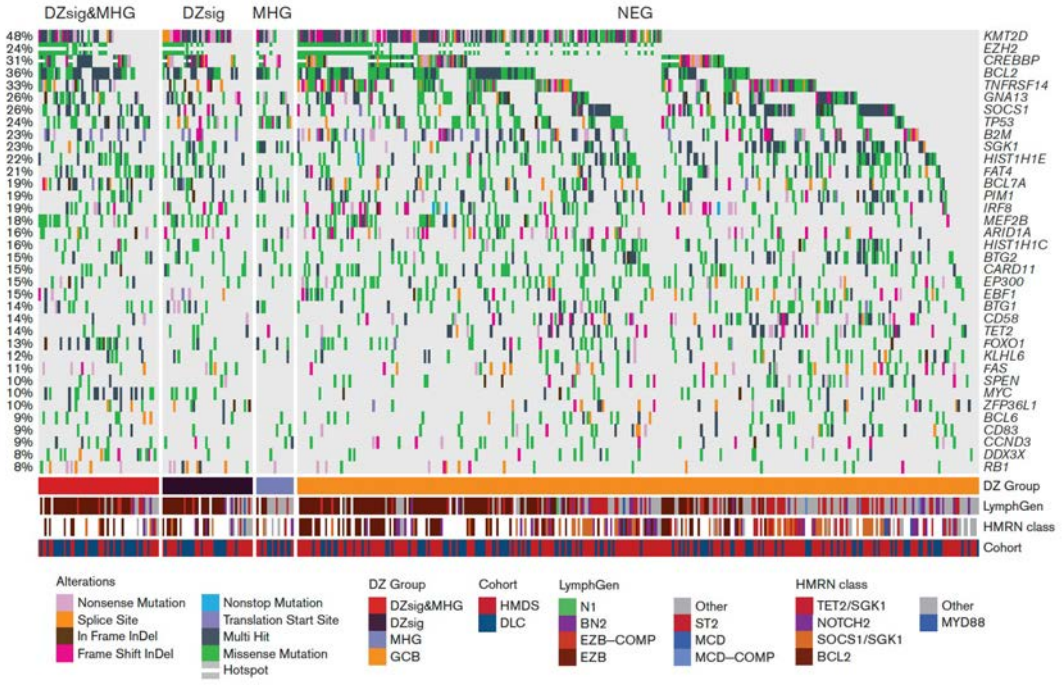

ABC, activated B-cell-like DLBCL; CA, Canada; DLBCL, diffuse large B-cell lymphoma; EU, European Union; GCB, germinal center B-cell-like DLBCL; PostMktg, Post-Marketing.

1. Palmer AC, et al. *N Engl J Med*. 2023;389(8):764-766.

# Germinal Center / EZH is not “One” Disease



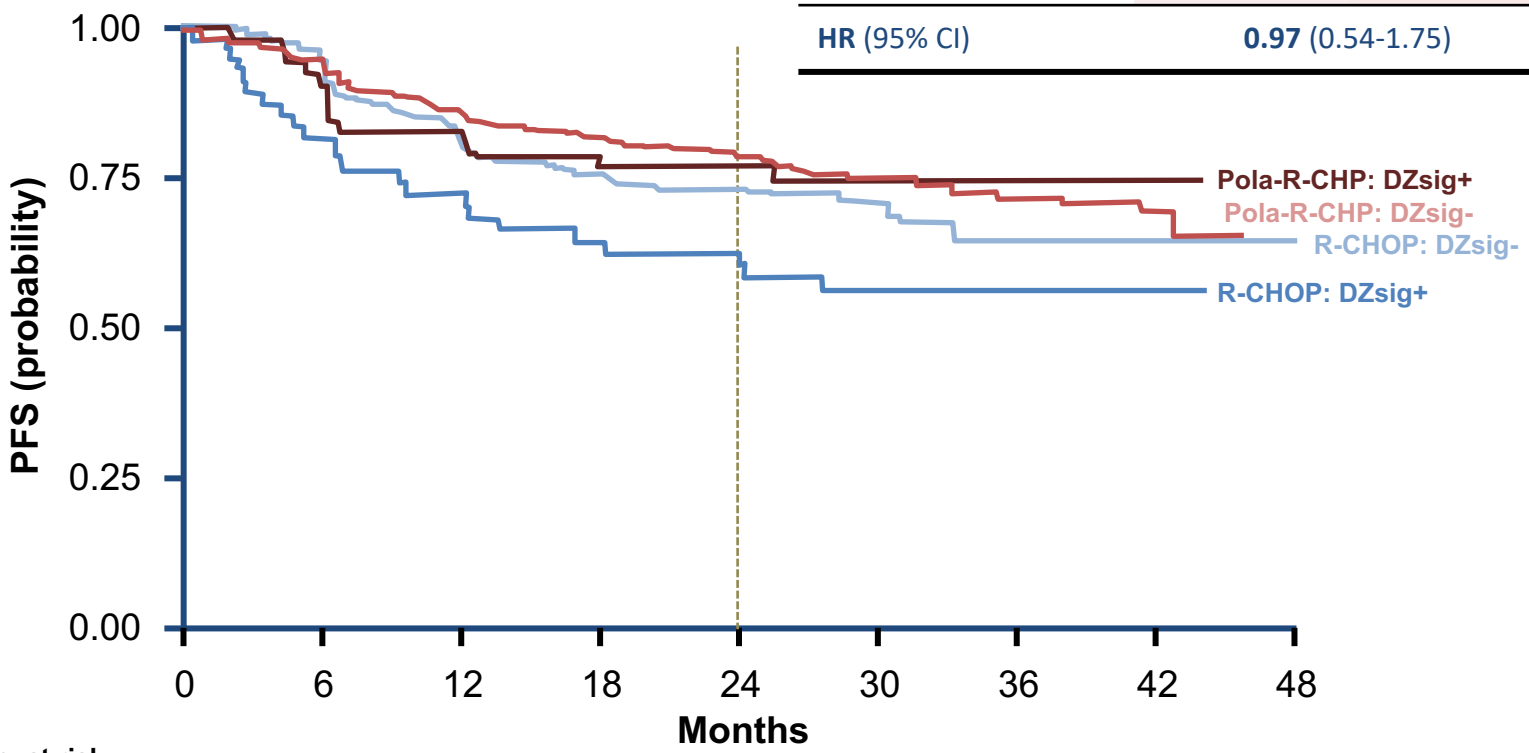




1. Tripodo C, et al. *iScience*. 2020;23(10):101562. 2. Davies, et al. *Blood Adv*. 2023 Oct 24;7(20):6156-6162.

# POLARIX: Benefit in "Dark Zone Signature" GCB/EZB

| | Pola-R-CHP DZsig+ | Pola-R-CHP DZsig- | R-CHOP DZsig+ | R-CHOP DZsig- |
|---|---|---|---|---|
| **2-yr PFS** (95% CI) | **79%** (74-84) | **77%** (66-89) | **62%** (51-77) | **73%** (68-79) |
| **HR** (95% CI) | **0.97** (0.54-1.75) | | **1.61** (1.02-2.56) | |




| No. at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Pola-R-CHP: DZsig+ | 52 | 48 | 42 | 40 | 37 | 31 | 10 | 9 | 0 |
| Pola-R-CHP: DZsig- | 279 | 259 | 231 | 215 | 203 | 152 | 70 | 42 | 0 |
| R-CHOP: DZsig+ | 56 | 45 | 37 | 32 | 31 | 18 | 11 | 10 | 0 |
| R-CHOP: DZsig- | 278 | 258 | 221 | 201 | 191 | 155 | 62 | 39 | 2 |

CI = confidence interval; HR = hazard ratio; PFS = progression-free survival; Morschhauser F, et al. *Blood*. 2023;142(Suppl 1):3000.

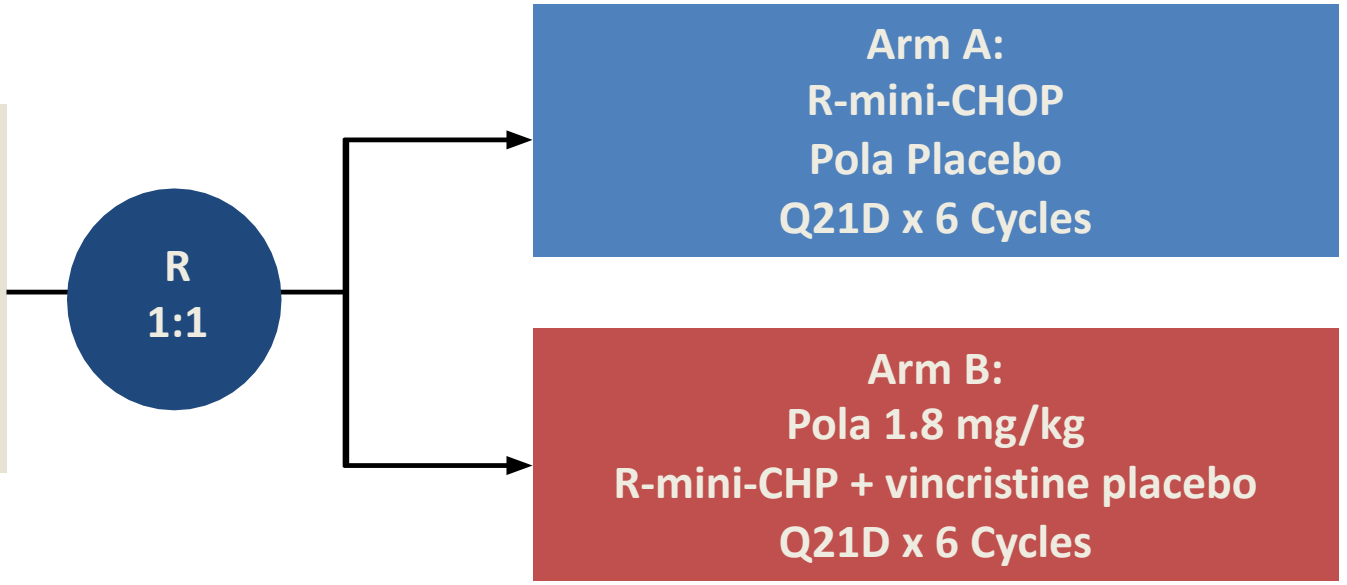
# POLAR BEAR: Study Design

Pola+R-mini-CHOP in Elderly DLBCL

**Patient Population:**

- Previously untreated DLBCL
- ≥ 80 years, or frail ≥ 75 years
- ECOG PS 0-3

N = 200

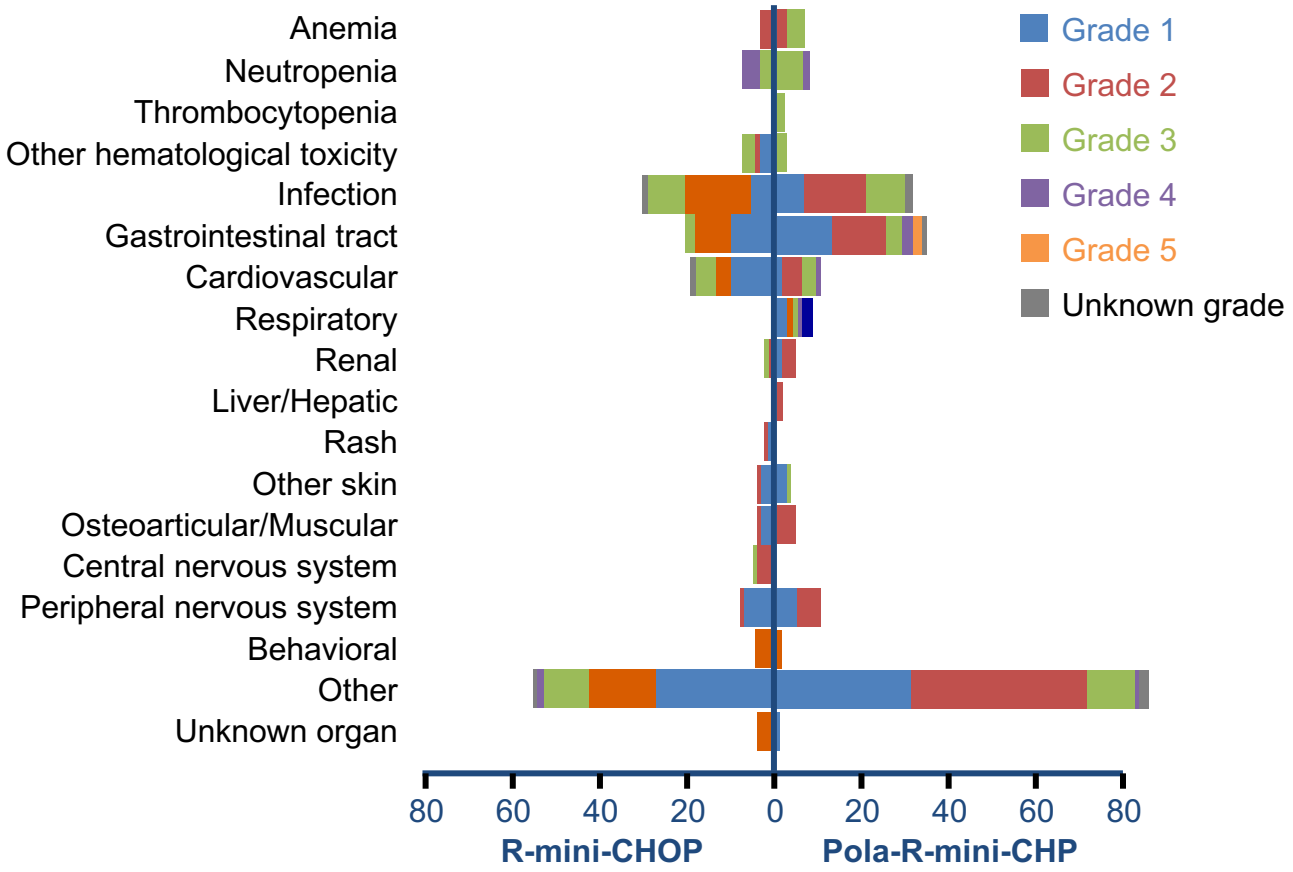



Primary endpoint: PFS

DLBCL = diffuse large B-cell lymphoma; ECOG PS = Eastern Cooperative Oncology Group performance status; PFS = progression-free survival; Pola = polatuzumab vedotin; Q21D = every 21 days; R = randomized; R-mini-CHP = rituximab, cyclophosphamide, doxorubicin, prednisone; R-mini-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; Jerkeman M, et al. *Hemasphere*. 2023;7(Suppl):e91359ec.

# POLAR BEAR:
# No Increased Toxicity Signal

- No difference in terms of grade 3-4 hematological toxicity between treatment groups
- Gastrointestinal toxicity > grade 1 occurred twice as frequently in the R-pola-miniCHP polatuzumab group than in recipients of standard R-miniCHP
- Relevant clinical consideration for select patients

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# Polatuzumab in 1L DLBCL: Bottom line

- POLARIX establishes Pola-R-CHP as a standard of care (but not *the* standard of care) in IPI 2+ DLBCL, PFS benefit without markedly increased toxicity
- Residual uncertainty regarding subset-based or biology-based patient selection for Pola-R-CHP (vs. R-CHOP)
- Data on the ability of Pola to improve outcomes in older and frailer patients are emerging
- How best to continue to incorporate Pola in the context of an evolving 1L treatment landscape needs to be defined

# Case Presentation: 58-year-old man who presents with left testicular swelling and abdominal discomfort is diagnosed with ABC-subtype Stage IV DLBCL

Dr Laurie Sehn (Vancouver, British Columbia)

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**How would you have managed care for this patient? Should he receive radiation therapy to the contralateral testis?**

**Would you have recommended CNS prophylaxis (if so, what type)?**

**Do you actively assess cell of origin in all your patients with DLBCL? Do you consider cell-of-origin testing when deciding on first-line treatment, and if so, are you comfortable with IHC testing using the Hans algorithm?**

# Discussion Questions

**Would you ever attempt to rechallenge with polatuzumab vedotin later in the treatment course for a patient who received it up front and experienced subsequent disease progression?**

# Agenda

**Module 1:** Rational Incorporation of Antibody-Drug Conjugates into the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Matasar

**Module 2: Clinical Utility of CD19-Directed Monoclonal Antibodies for DLBCL and Follicular Lymphoma (FL) — Dr Leonard**

**Module 3:** Optimal Use of Antibody-Drug Conjugates in the Treatment of Relapsed/Refractory DLBCL — Prof Zinzani

**Module 4:** Bispecific Antibody Therapy for DLBCL — Dr Bartlett

**Module 5:** Bispecific Antibody Therapy for FL and Other Lymphoma Subtypes — Dr Nastoupil

RTP RESEARCH TO PRACTICE

NYU Langone Health

Perlmutter Cancer Center

An NCI-designated Comprehensive Cancer Center

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


**John P. Leonard, M.D.**

Laura and Isaac Perlmutter Professor of Hematology and Medical Oncology

Director, Division of Hematology and Medical Oncology

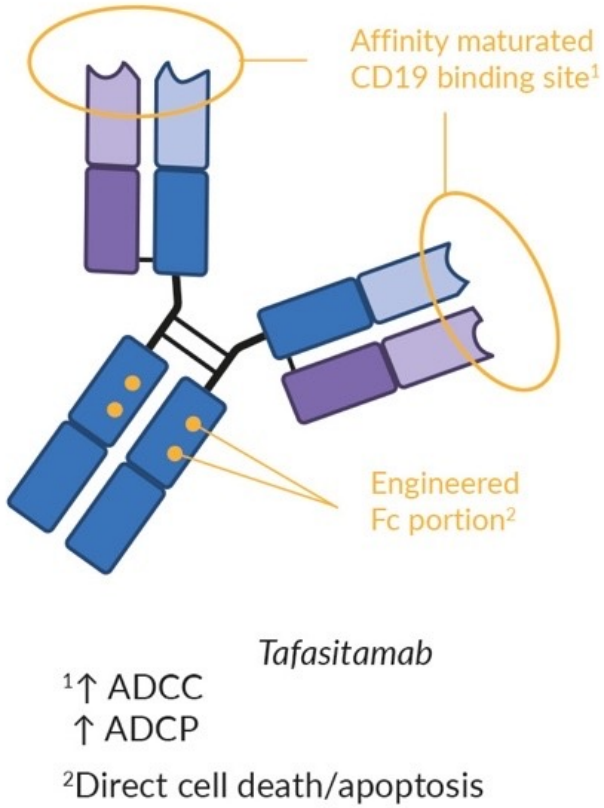
Director, Center for Blood Cancers

Senior Advisor to the Dean/CEO for Enterprise Cancer Strategy and Operations

Interim Director, Perlmutter Cancer Center

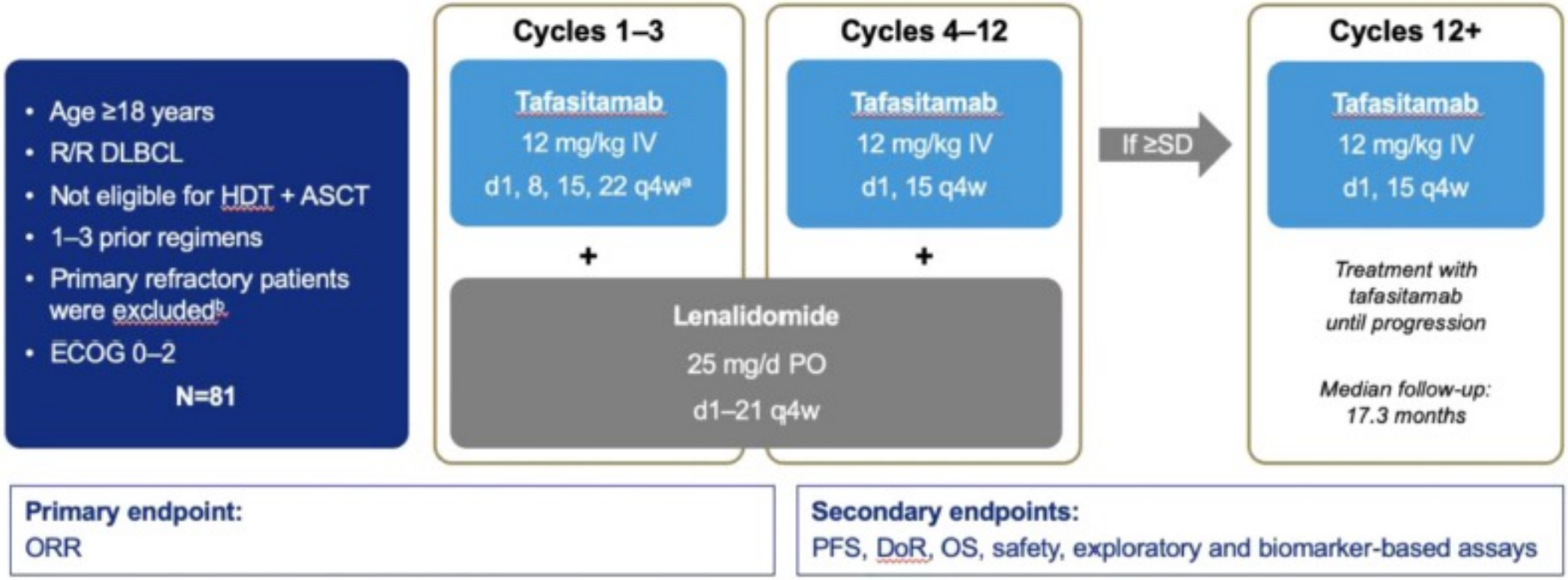
# CD19 mAb: Tafasitamab

- Humanized CD19-targeting monoclonal antibody (mAb)
- Induces direct cytotoxicity and enhances NK cell and macrophage immune-mediated mechanisms




Meisel A, et al. *Healthbook Times Oncol Hematol*. 2025;23(1):151-158.

# L-MIND treatment regimen for patients with recurrent DLBCL




Cheson et al, Blood Cancer J 2021

# L-MIND patient characteristics

| Characteristics | All patients: full analysis set | 1 prior line of therapy | ≥2 prior lines of therapy |
|---|---|---|---|
| N | 80 | 40 | 40 |
| Age in years, median (range) | 72.0 (41.0-86.0) | 72.0 (53.0-86.0) | 70.5 (41.0-82.0) |
| Age >70 years, N (%) | 45 (56.3) | 25 (62.5) | 20 (50.0) |
| Sex, N (%) | | | |
| Female | 37 (46.3) | 19 (47.5) | 18 (45.0) |
| Male | 43 (53.8) | 21 (52.5) | 22 (55.0) |
| Ann Arbor stage, N (%) | | | |
| I-II | 20 (25.0) | 11 (27.5) | 9 (22.5) |
| III-IV | 60 (75.0) | 29 (72.5) | 31 (77.5) |
| IPI score, N (%) | | | |
| 0-2 | 40 (50.0) | 25 (62.5) | 15 (37.5) |
| 3-5 | 40 (50.0) | 15 (37.5) | 25 (62.5) |
| Elevated LDH, N (%) | | | |
| Yes | 44 (55.0) | 18 (45.0) | 26 (65.0) |
| No | 36 (45.0) | 22 (55.0) | 14 (35.0) |
| Prior lines, N (%) | | | |
| 1 | 40 (50.0) | - | - |
| 2 | 34 (42.5) | - | - |
| 3 | 5 (6.3) | - | - |
| 4 | 1 (1.3) | - | - |
| Primary refractory*, N (%) | | | |
| Yes | 15 (18.8) | 6 (15.0) | 9 (22.5) |
| No | 65 (81.3) | 34 (85.0) | 31 (77.5) |
| Refractory to previous line of therapy, N (%) | | | |
| Yes | 35 (43.8) | 6 (15.0) | 29 (72.5) |
| No | 45 (56.3) | 34 (85.0) | 11 (27.5) |
| Prior ASCT, N (%) | | | |
| Yes | 9 (11.3) | 2 (5.0) | 7 (17.5) |
| No | 71 (88.8) | 38 (95.0) | 33 (82.5) |
| Cell of origin (by IHC), N (%) | | | |
| GCB | 38 (47.5) | 16 (40.0) | 22 (55.0) |
| Non-GCB | 22 (27.5) | 14 (35.0) | 8 (20.0) |
| Unknown/NE | 20 (25.0) | 10 (25.0) | 10 (25.0) |

Median age 73
50% IPI 3-5
50% 1 prior rx
43% refractory to last rx

Duell et al, Haematologica 2024

# L-MIND efficacy – 5 year update

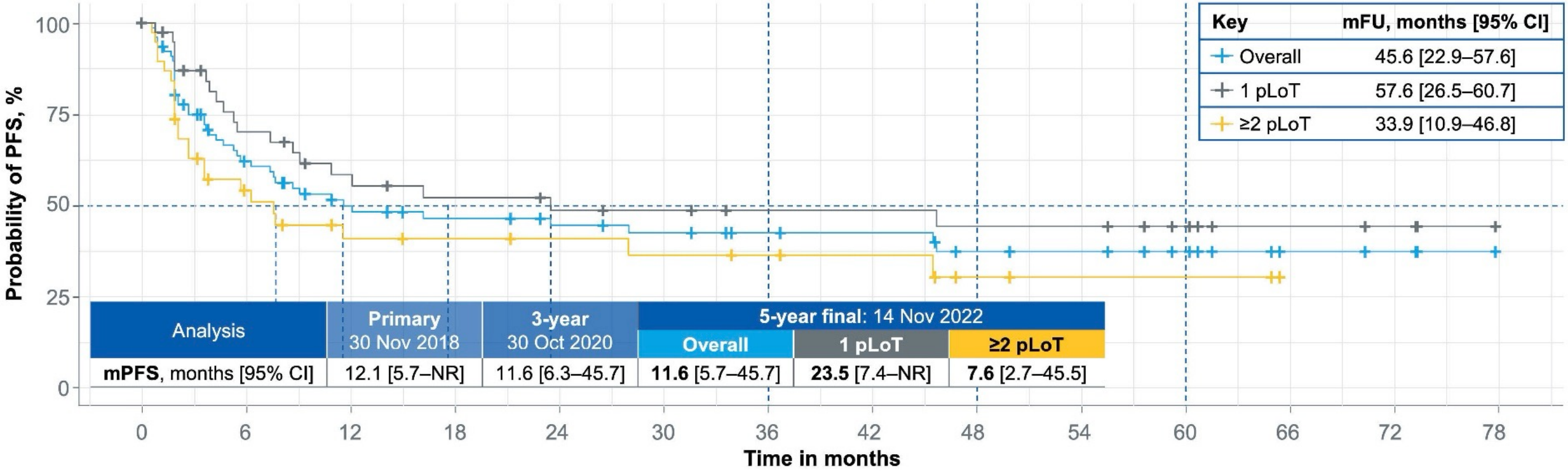
| Characteristics | Primary analysis | 3-year follow-up | Final 5-year data | 5-year data for patients with 1 prior line of therapy, N=40 | 5-year data for patients with ≥2 prior lines of therapy, N=40 |
|---|---|---|---|---|---|
| Data cut-off date | Nov 30, 2018 | Oct 30, 2020 | Nov 14, 2022 | Nov 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.

ORR 57%, CR 41%, Median PFS 11.6 m

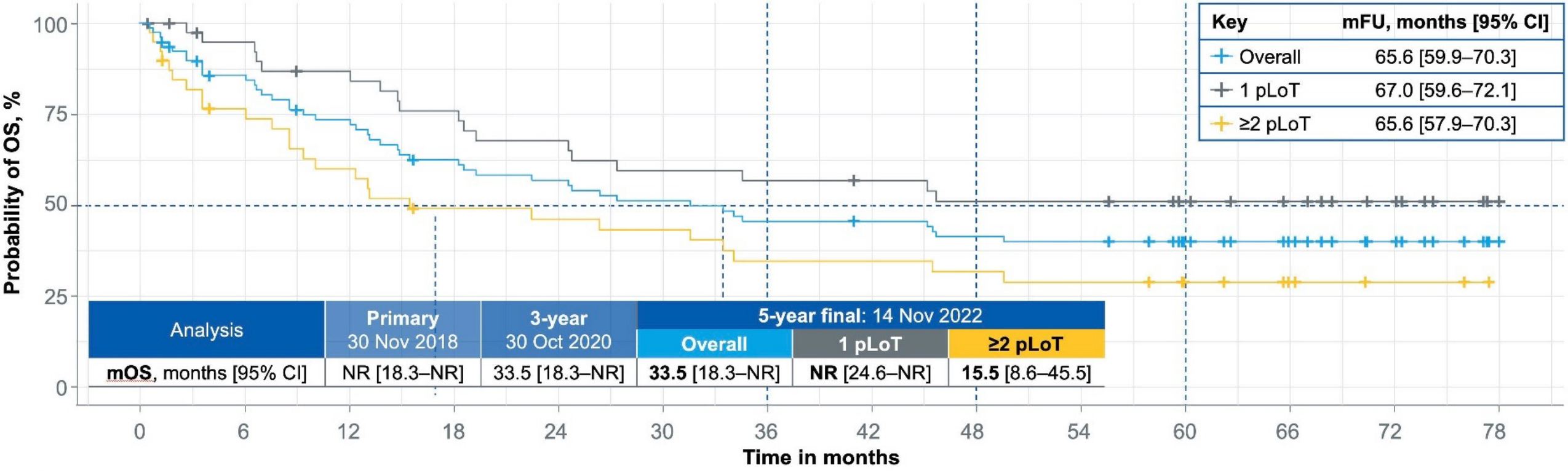
Duell et al, Haematologica 2024

# L-MIND efficacy – PFS – 5 year update



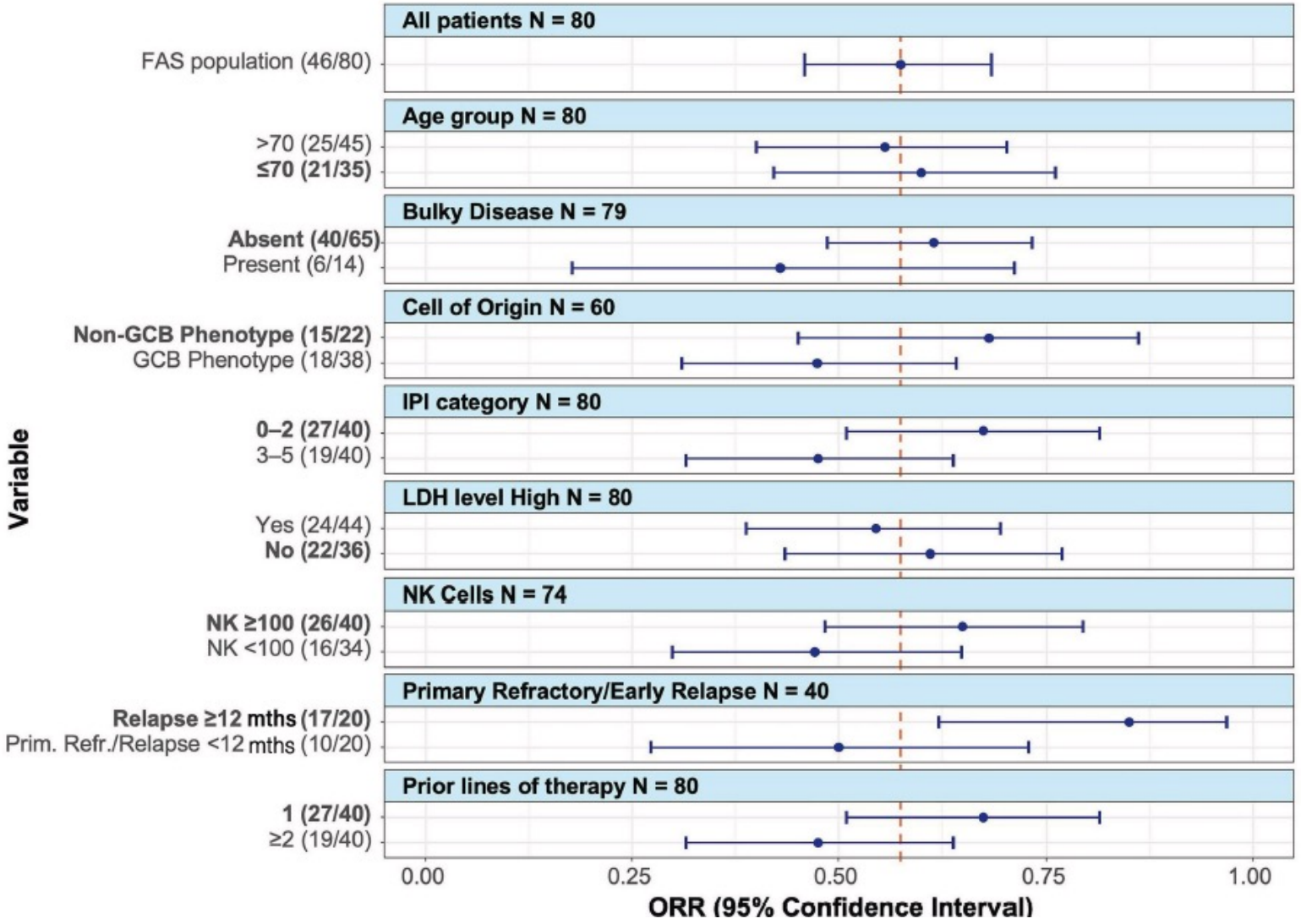

Duell et al,
Haematologica 2024

# L-MIND efficacy – OS – 5 year update



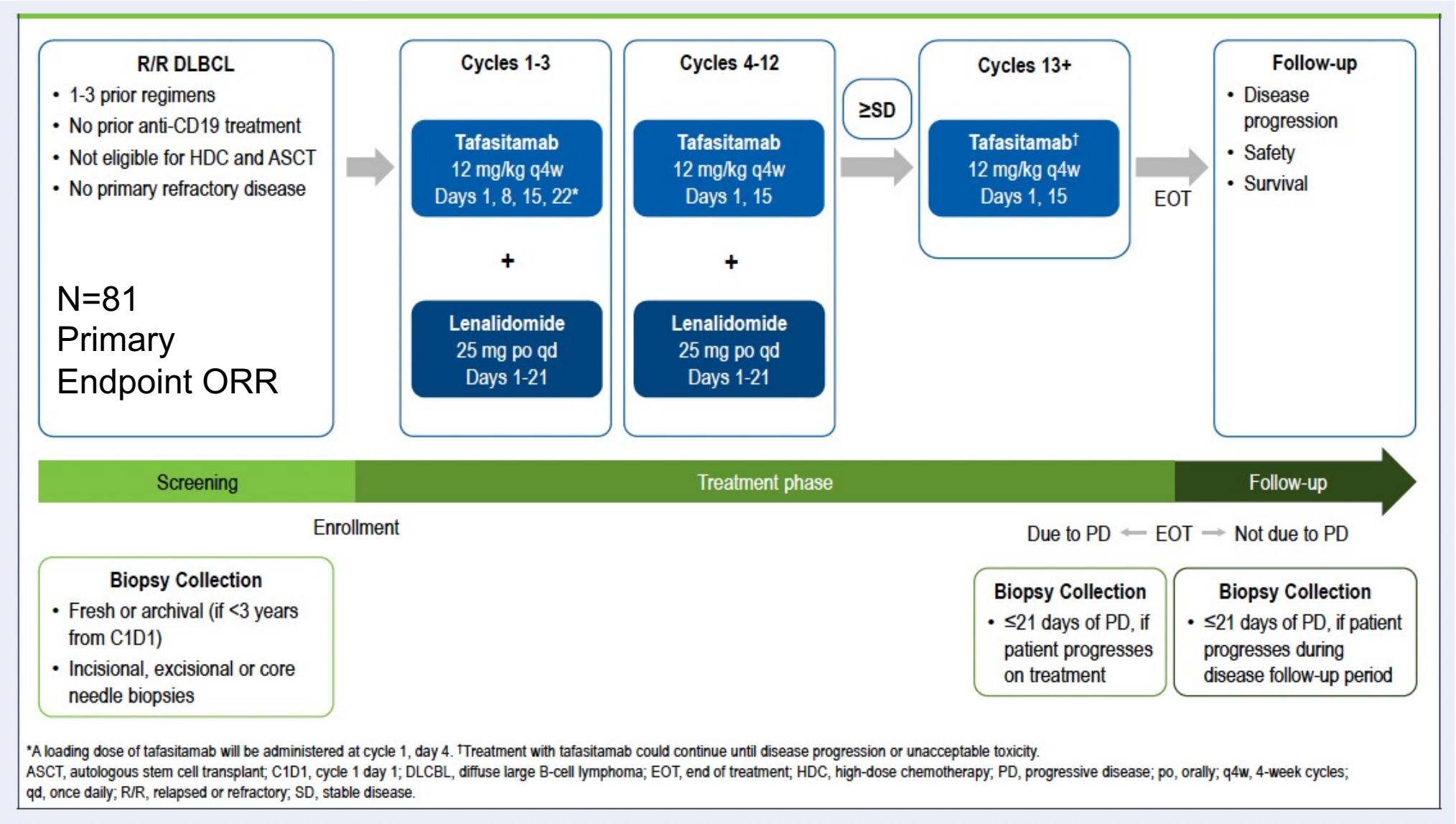

Duell et al,
Haematologica 2024

# L-MIND efficacy – subgroups




Duell et al,
Haematologica 2024

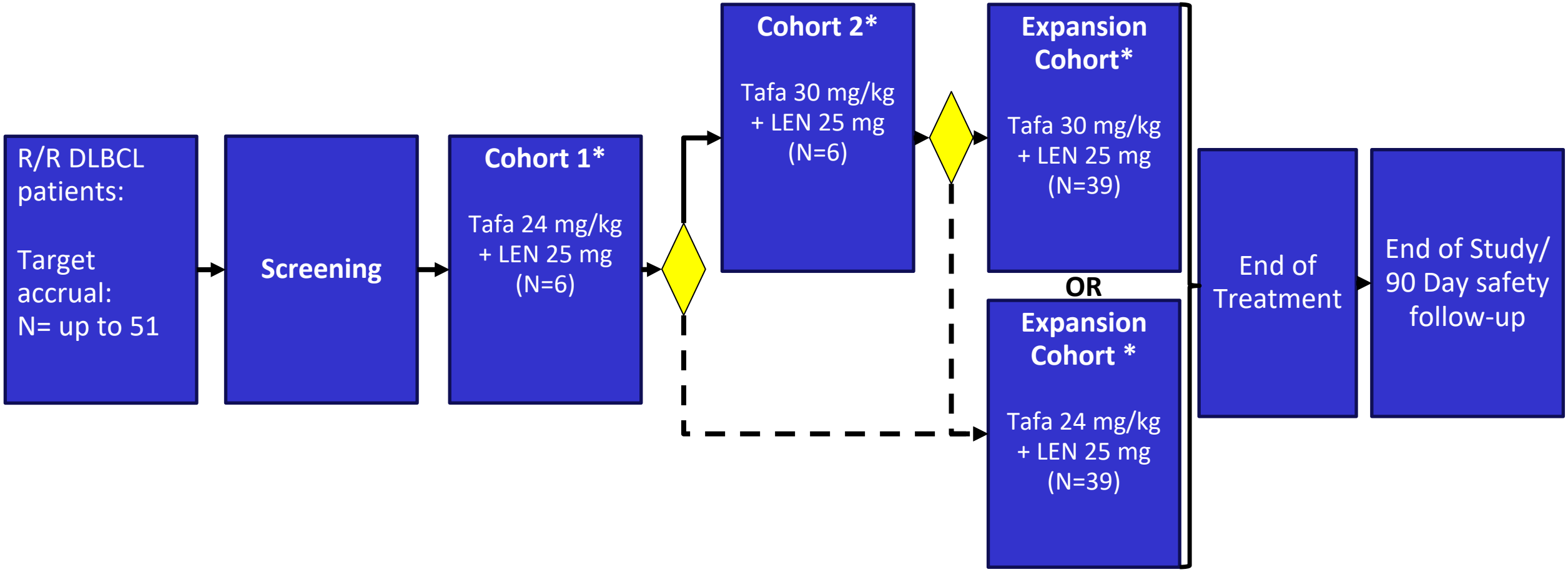
# Phase 3 Study of Tafasitamab Plus Lenalidomide in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma (firmMIND)




*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.

Arias DA et al. EHA 2024;Abstract P1234

# MINDway: Ph Ib/II dose optimization study (safety and PK) of tafasitamab + lenalidomide in pts with relapsed/refractory DLBCL



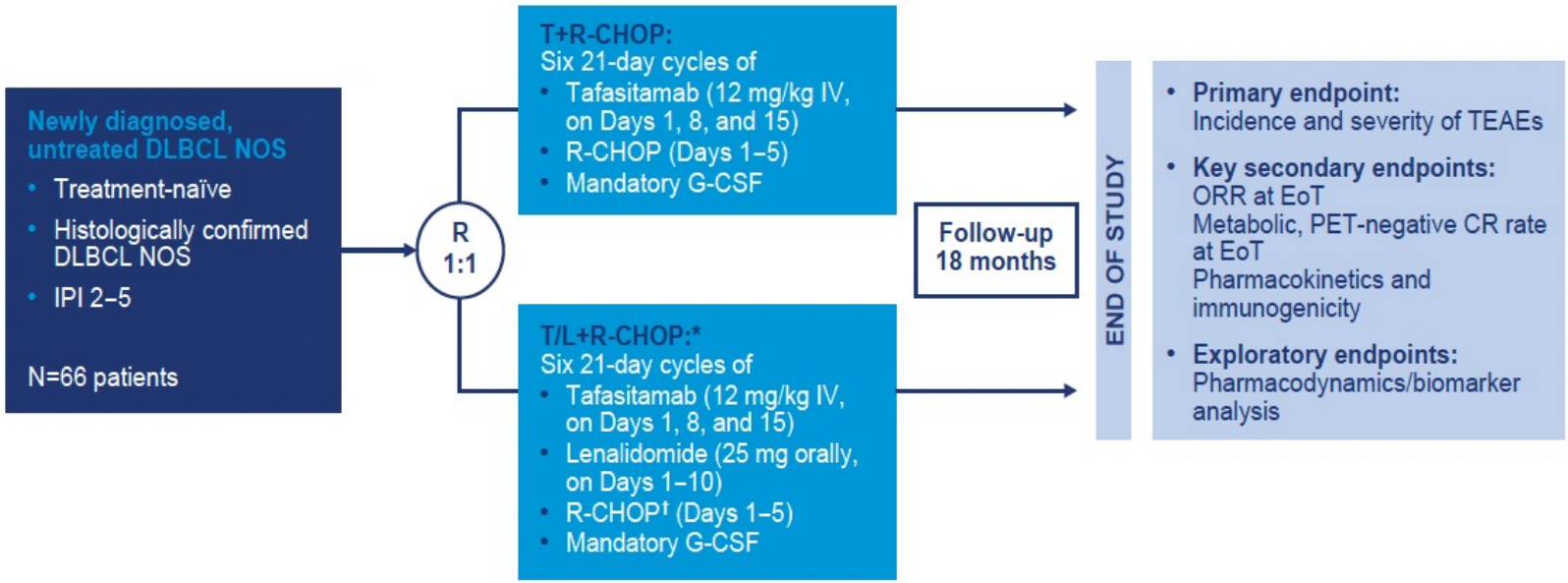

* In the first 28-day cycle (Cycle 1) tafasitamab is given on Day 1, Day 4 and Day 8 at a dose of 12 mg/kg

◆ Data and Safety Monitoring Committee Meeting

Goal to reduce infusion frequency from biweekly to monthly

Greil et al EHA 2022

# Tafasitamab +/- lenalidomide first-line + R-CHOP for DLBCL
# Phase Ib First-MIND study



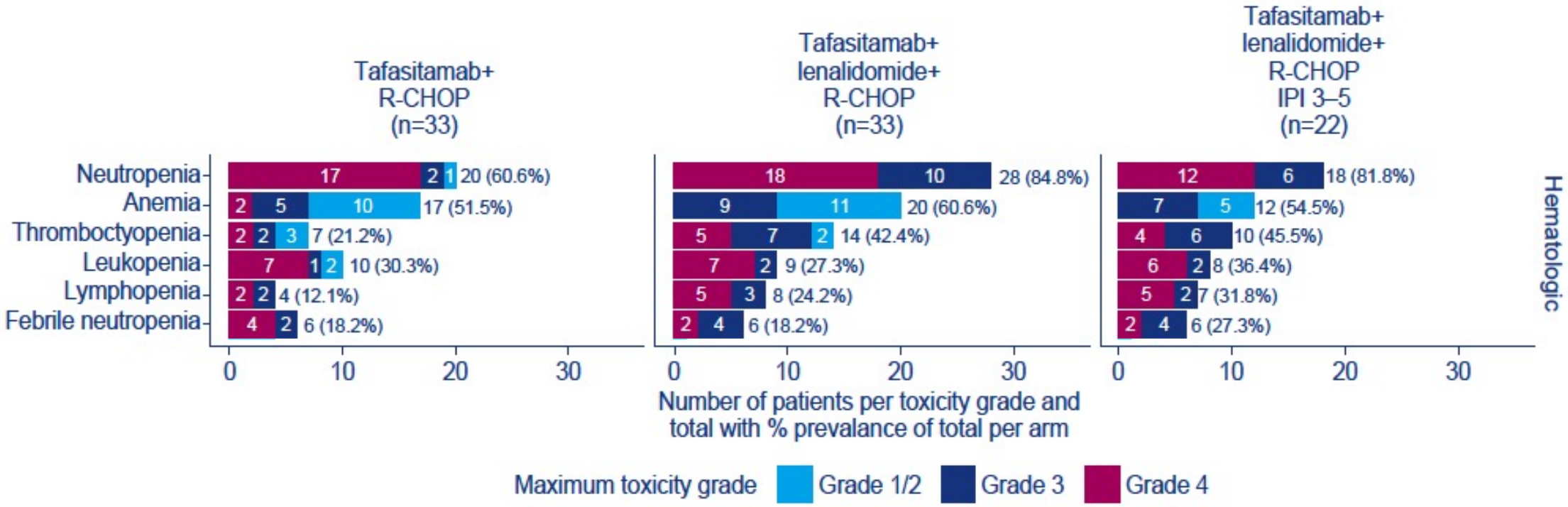

*In the lenalidomide arm, venous thromboembolism prophylaxis with either low-molecular weight heparins or aspirin is mandatory (according to institutional guidelines).

| Characteristics, n (%) | | T+R-CHOP (n=33) | T/L+R-CHOP (n=33) | T/L+R-CHOP IPI 3–5 (n=22) |
|---|---|---|---|---|
| Gender | Male/Female | 15 (45.5)/ 18 (54.5) | 13 (39.4)/ 20 (60.6) | 10 (45.5)/ 12 (54.5) |
| Age (screening) | ≤60 years/ >60 years | 12 (36.4)/ 21 (63.6) | 11 (33.3)/ 22 (66.7) | 7 (31.8)/ 15 (68.2) |
| Race | White/Other/ Not reported | 31 (93.9)/ 1 (3.0)/1 (3.0) | 33 (100.0)/ 0/0 | 22 (100) |
| IPI score | 2 | 13 (39.4) | 11 (33.3) | – |
| | 3 | 13 (39.4) | 16 (48.5) | 16 (72.7) |
| | 4 | 7 (21.2) | 4 (12.1) | 4 (18.2) |
| | 5 | 0 | 2 (6.1) | 2 (9.1) |
| | 3–5 | 20 (60.6) | 22 (66.7) | 22 (100) |
| ECOG PS | 0 | 19 (57.6) | 12 (36.4) | 7 (31.8) |
| | 1 | 12 (36.4) | 17 (51.5) | 12 (54.5) |
| | 2 | 2 (6.1) | 4 (12.1) | 3 (13.6) |
| Cell of origin (assessed locally) | GCB | 9 (27.3) | 10 (30.3) | 12 (54.5) |
| | Non-GCB | 15 (45.5) | 14 (42.4) | 9 (40.9) |
| | Missing or not evaluable | 9 (27.3) | 9 (27.3) | 1 (4.5) |
| Ann Arbor disease stage | I | 2 (6.1) | 1 (3.0) | – |
| | II | 0 | 1 (3.0) | – |
| | III | 8 (24.2) | 7 (21.2) | 3 (13.6) |
| | IV | 23 (69.7) | 24 (72.7) | 19 (86.4) |
| | I & II | 2 (6.1) | 2 (6.1) | – |
| | III & IV | 31 (93.9) | 31 (93.9) | 22 (100) |

Most IPI 2-3
63% over age 60

Nowakowski GS et al. ASH 2022;Abstract 1619

# Tafasitamab +/- lenalidomide first-line + R-CHOP for DLBCL
# Phase Ib First-MIND study



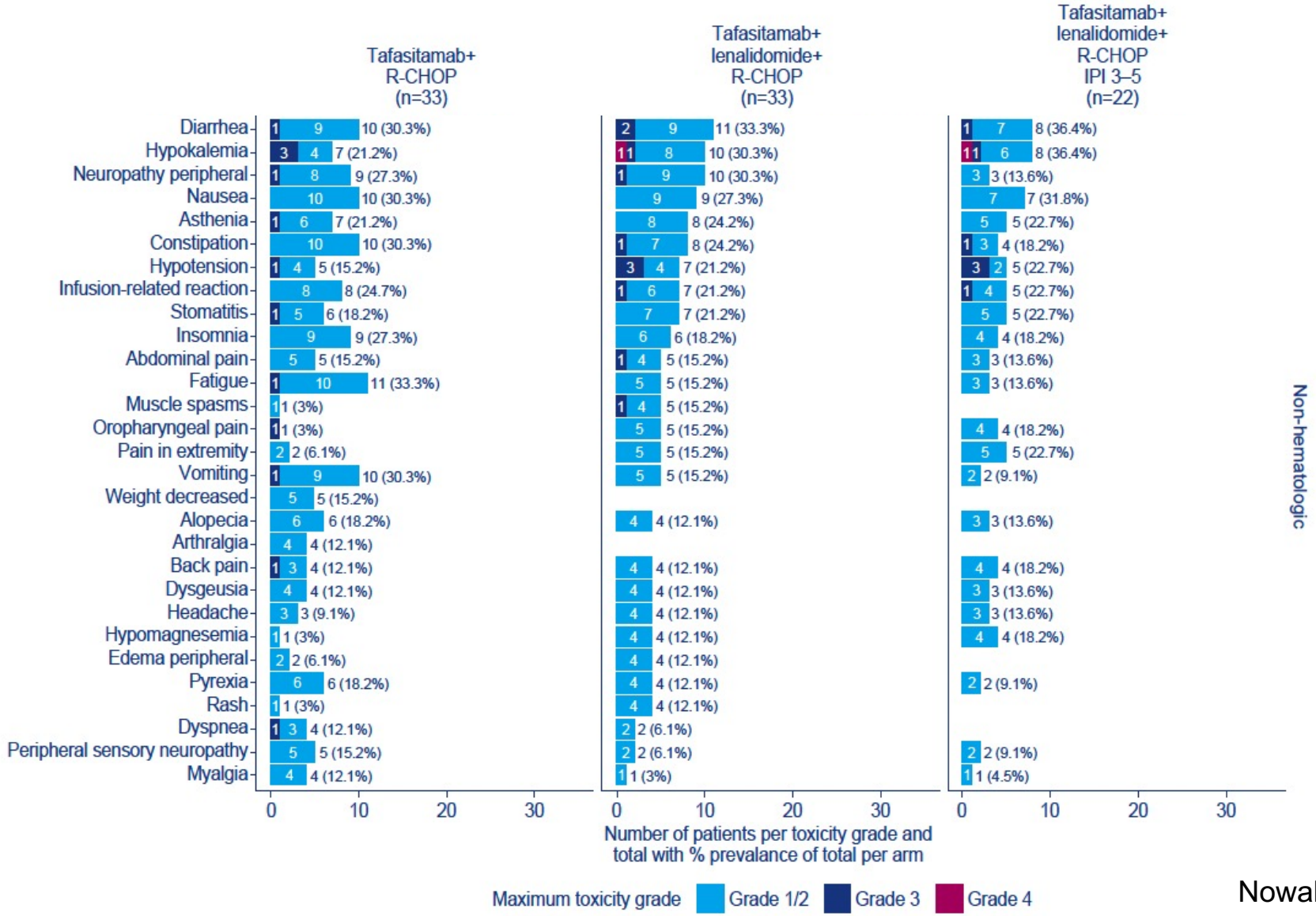

IPI, International Prognostic Index; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; TEAE, treatment-emergent adverse events.

Most common AE neutropenia, febrile neutropenia in 18%+

Nowakowski GS et al. ASH 2022;Abstract 1619

# Tafasitamab +/- lenalidomide first-line + R-CHOP for DLBCL

## Phase Ib First-MIND study




Most common non-heme AE
Under 10% pts

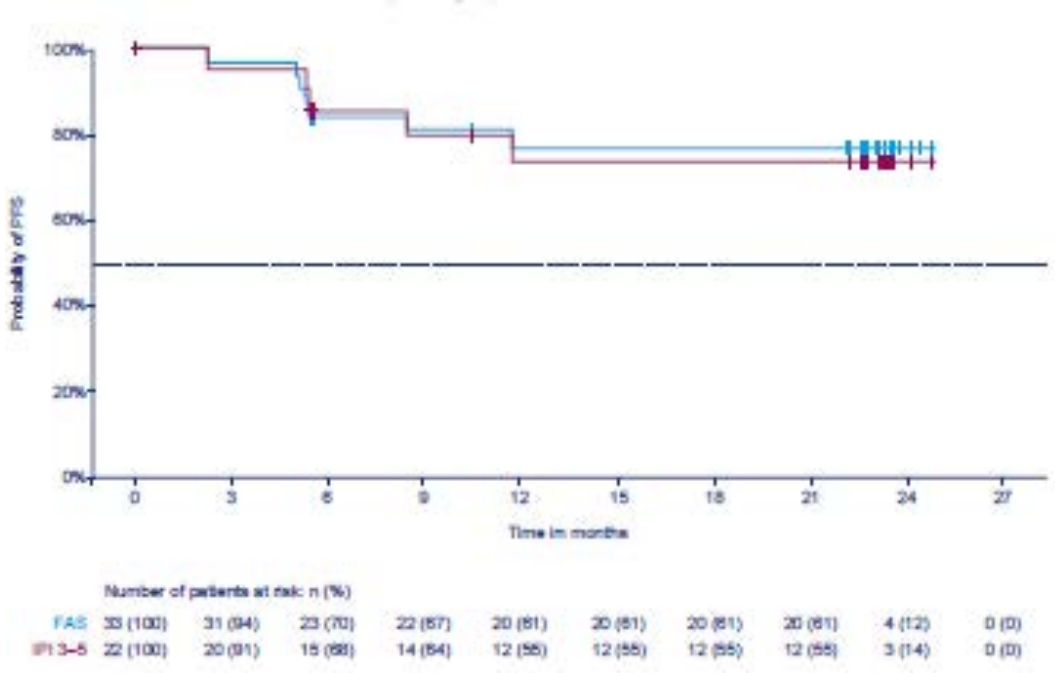
Nowakowski GS et al. ASH 2022;Abstract 1619

# Tafasitamab +/- lenalidomide first-line + R-CHOP for DLBCL
# Phase Ib First-MIND study

| Event | T+R-CHOP (n=33) | T/L+R-CHOP (n=33) | T/L+R-CHOP IPI 3–5 (n=22) |
|---|---|---|---|
| ORR, n (%) [95% CI] | | | |
| CR or PR (at EoT) | 25 (75.8) [57.7, 88.9] | 27 (81.8) [64.5, 93.0] | 18 (81.8) [59.7, 94.8] |
| CR or PR (best response across all visits) | 30 (90.9) [75.7, 98.1] | 31 (93.9) [79.8, 99.3] | 20 (90.9) [70.8, 98.9] |
| 18-month DoR rate, % [95% CI] | 72.7 [52.7, 85.3] | 78.7 [58.5, 89.9] | 76.6 [48.8, 90.5] |
| 18-month DoCR rate, % [95% CI] | 74.5 [53.8, 87.0] | 86.5 [63.8, 95.5] | 80.0 [50.0, 93.1] |
| 24-month PFS rate, % [95% CI] | 72.7 [52.7, 85.3] | 76.8 [57.1, 88.3] | 73.6 [47.3, 88.2] |
| 24-month OS rate, % [95% CI] | 90.3 [72.9, 96.8] | 93.8 [77.3, 98.4] | 95.2 [70.7, 99.3] |

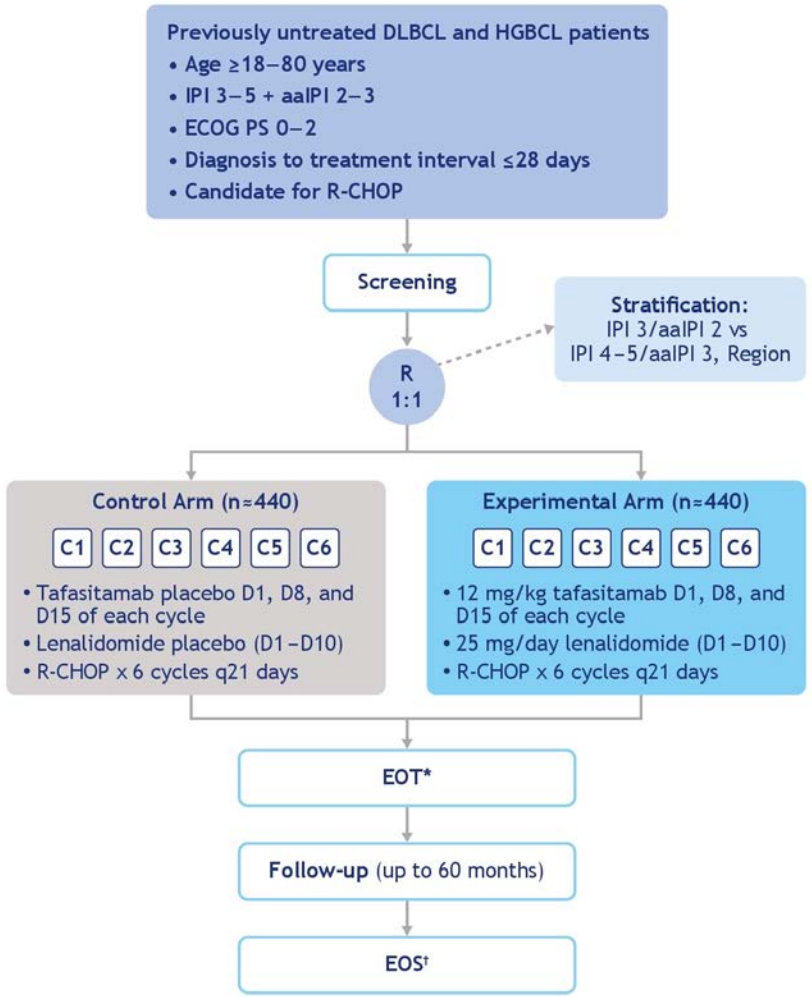
CI, confidence interval; CR, complete response; DoCR, duration of complete response; DoR, duration of response; EoT, end of treatment; IPI, International Prognostic Index; L, lenalidomide; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; T, tafasitamab.

ORR 75%-81%
24 mo PFS 72%-75%




Nowakowski GS et al. ASH 2022;Abstract 1619

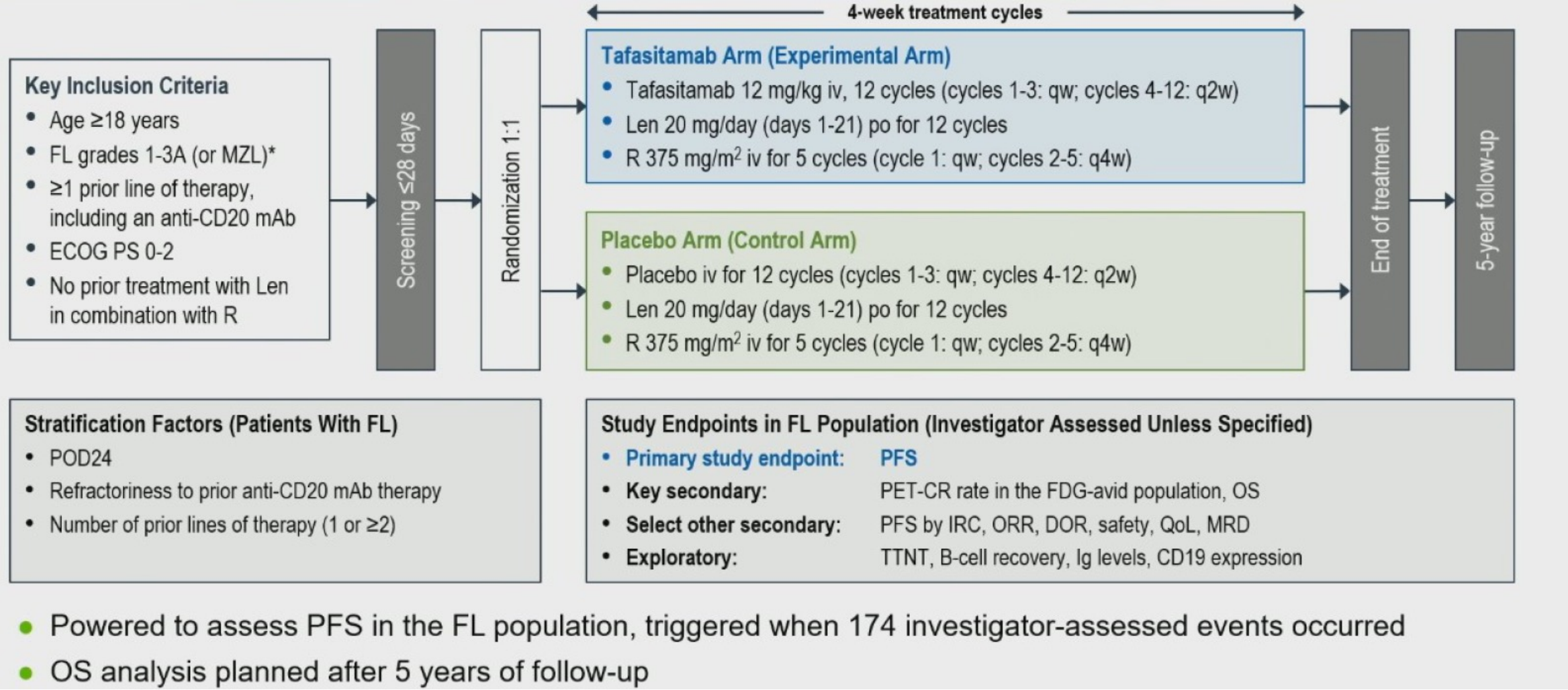
# frontMIND: Phase 3 randomized study of R-CHOP +/- Tafasitamab + lenalidomide first-line + R-CHOP for DLBCL IPI 3-5




| Assessments | Screening | Treatment Period | | | | | | | | | | | | | | | | | | | EOT*/ ETD | Follow-up period |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | D(−28) to D(−1) | Cycle 1 (21 days) | | | Cycle 2 (21 days) | | | Cycle 3 (21 days) | | | | Cycle 4 (21 days) | | | Cycle 5 (21 days) | | | Cycle 6 (21 days) | | | | |
| | | D1 | D8† | D15 | D1 | D8 | D15 | D1 | D8 | D15 | D18 | D1 | D8 | D15 | D1 | D8 | D15 | D1 | D8 | D15 | 6±2 wks | |
| **Efficacy** | | | | | | | | | | | | | | | | | | | | | | |
| Tumor tissue | X | | | | | | | | | | | | | | | | | | | | | |
| PET/CT or PET/MRI‡ | X | | | | | | | | | | | | | | | | | | | | X | |
| CT or MRI‡ | | | | | | | | | | | X | | | | | | | | | | | |
| **Safety** | | | | | | | | | | | | | | | | | | | | | | |
| AE, SAE, AESI and pregnancy reporting | X | X | X | X | X | X | X | X | X | | X | X | X | X | X | X | X | X | X | X | X | X |
| Survival follow-up§ | | | | | | | | | | | | | | | | | | | | | | X |
| **Quality of life assessment** | | | | | | | | | | | | | | | | | | | | | | |
| EORTC-QLQ-C30, EQ-5D-5L, FACT-Lym | X | X | | | X | | | X | | | | | | | X | | | | | | X | X |

Vitolo U et al. ASCO 2022;Abstract TPS7590

# inMIND Phase 3 Study: Lenalidomide + Rituximab +/- Tafasitamab in pts with recurrent FL




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

Sehn LH, et al. *Blood*. 2024;144(Suppl 2):LBA-1

# inMIND Phase 3 Study: Lenalidomide + Rituximab +/- Tafasitamab in pts with recurrent FL

| Variable | Tafasitamab + Len + R (n=273) | Placebo + Len + R (n=275) | Total (N=548) |
|---|---|---|---|
| Median age, years (range) | 64.0 (36, 88) | 64.0 (31, 85) | 64.0 (31, 88) |
| ≥75, n (%) | 54 (19.8) | 54 (19.6) | 108 (19.7) |
| Male sex, n (%) | 150 (54.9) | 149 (54.2) | 299 (54.6) |
| Median time since initial diagnosis of FL, years (range) | 5.2 (0, 34) | 5.5 (1, 33) | 5.3 (0, 34) |
| ECOG PS at screening, n (%) | | | |
| 0 | 181 (66.3) | 192 (69.8) | 373 (68.1) |
| 1-2 | 92 (33.7) | 83 (30.2) | 175 (31.9) |
| Ann Arbor stage, n (%) | | | |
| I or II | 52 (19.0) | 50 (18.2) | 102 (18.6) |
| III or IV | 221 (81.0) | 225 (81.8) | 446 (81.4) |
| FL grade, n (%) | | | |
| 1 or 2 | 203 (74.4) | 203 (73.8) | 406 (74.1) |
| 3A | 67 (24.5) | 71 (25.8) | 138 (25.2) |
| B symptoms, n (%) | 63 (23.1) | 67 (24.4) | 130 (23.7) |
| FLIPI score, n (%) | | | |
| 0-1 | 57 (20.9) | 57 (20.7) | 114 (20.8) |
| 2 | 79 (28.9) | 67 (24.4) | 146 (26.6) |
| 3-5 | 137 (50.2) | 150 (54.5) | 287 (52.4) |
| GELF criteria, n (%) | 222 (81.3) | 232 (84.4) | 454 (82.8) |
| FL diagnosis confirmed by central pathology, n (%) | 256 (93.8) | 259 (90.5) | 505 (92.2) |

Sehn LH, et al. *Blood*. 2024;144(Suppl 2):LBA-1

# inMIND Phase 3 Study: Lenalidomide + Rituximab +/- Tafasitamab in pts with recurrent FL

| Variable | Tafasitamab + Len + R (n=273) | Placebo + Len + R (n=275) | Total (N=548) |
|---|---|---|---|
| Median number of prior lines of therapy (range) | 1.0 (1, 7) | 1.0 (1, 10) | 1.0 (1, 10) |
| Number of prior lines of therapy, n (%) | | | |
| 1 | 147 (53.8) | 153 (55.6) | 300 (54.7) |
| 2 | 66 (24.2) | 71 (25.8) | 137 (25.0) |
| 3 | 39 (14.3) | 30 (10.9) | 69 (12.6) |
| ≥4 | 21 (7.7) | 21 (7.6) | 42 (7.7) |
| Time since last anti-lymphoma therapy, n (%) | | | |
| ≤2 years | 147 (53.8) | 157 (57.1) | 304 (55.5) |
| >2 years | 126 (46.2) | 118 (42.9) | 244 (44.5) |
| POD24, n (%) | 85 (31.1) | 88 (32.0) | 173 (31.6) |
| Relapsed/refractory status to last therapy, n (%) | | | |
| Relapsed | 148 (54.2) | 164 (59.6) | 312 (56.9) |
| Refractory | 112 (41.0) | 97 (35.2) | 209 (38.1) |
| Undetermined | 13 (4.8) | 14 (5.1) | 27 (4.9) |
| Refractory to prior anti-CD20 therapy, n (%) | 118 (43.2) | 115 (41.8) | 233 (42.5) |

55% 1 prior rx, 31% POD24

Sehn LH, et al. *Blood*. 2024;144(Suppl 2):LBA-1

# inMIND Phase 3 Study: Lenalidomide + Rituximab +/- Tafasitamab in pts with recurrent FL

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

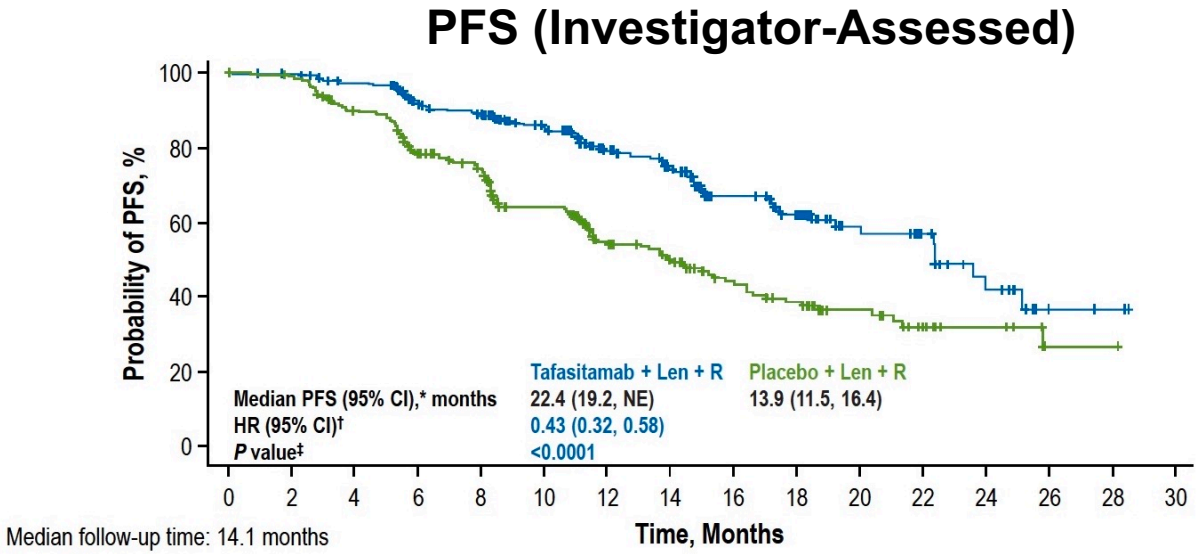
| Preferred Term, n (%) | Tafasitamab + Len + R (n=274)* | Placebo + Len + R (n=272)† | Total (n=546) |
|---|---|---|---|
| Neutropenia | 109 (39.8) | 102 (37.5) | 211 (38.6) |
| Pneumonia | 23 (8.4) | 14 (5.1) | 37 (6.8) |
| Thrombocytopenia | 17 (6.2) | 20 (7.4) | 37 (6.8) |
| Neutrophil count decreased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

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

Sehn LH, et al. *Blood*. 2024;144(Suppl 2):LBA-1

# inMIND Phase 3 Study: Lenalidomide + Rituximab +/- Tafasitamab in pts with recurrent FL

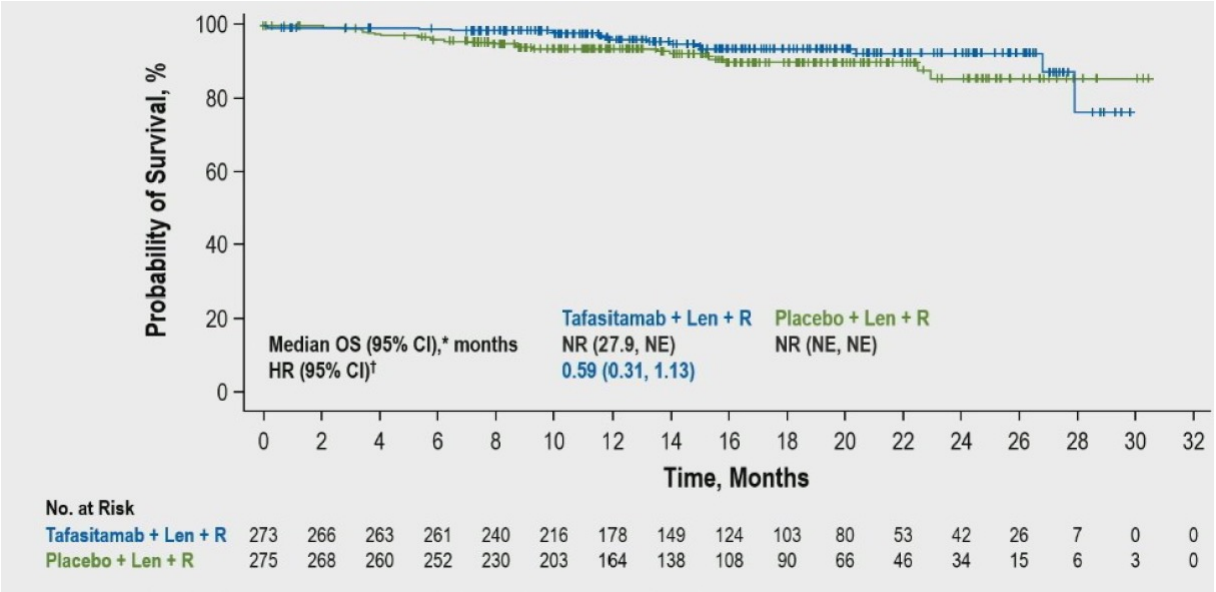
| ORR (ITT Population) | Tafasitamab + Len + R | Placebo + Len + R |
|---|---|---|
| Patients, n | 273 | 275 |
| Best overall response, n (%)‡ | | |
| CR | 142 (52.0) | 112 (40.7) |
| PR | 86 (31.5) | 87 (31.6) |
| SD | 28 (10.3) | 46 (16.7) |
| PD | 7 (2.6) | 20 (7.3) |
| NE | 2 (0.7) | 0 |
| Not done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

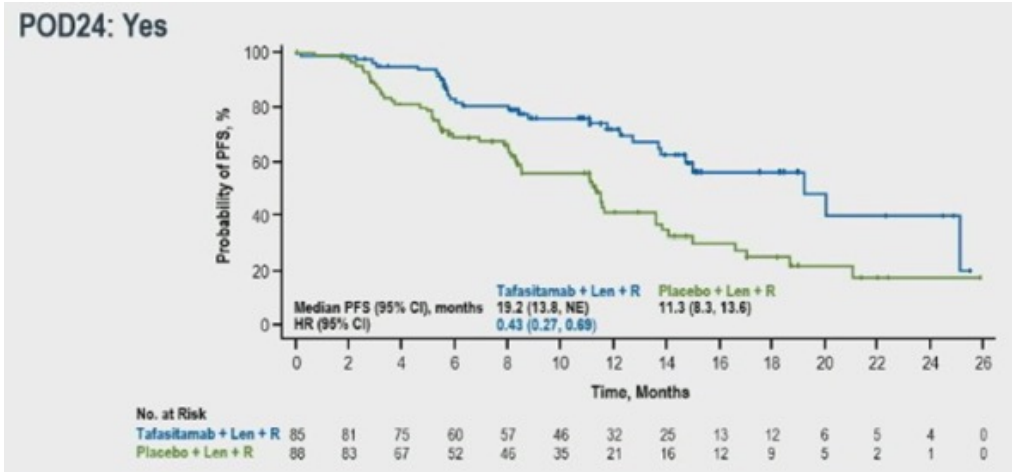


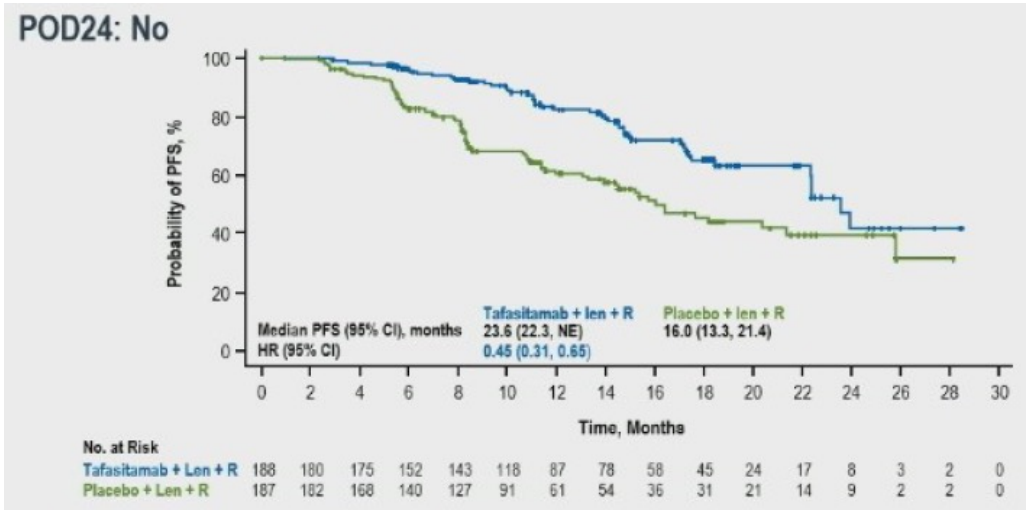

Median PFS 22.4 vs 13.9 mo

Sehn LH, et al. *Blood*. 2024;144(Suppl 2):LBA-1
Sehn L et al. ICML 2025;Abstract 028

# inMIND Phase 3 Study: Lenalidomide + Rituximab +/- Tafasitamab in pts with recurrent FL




Sehn LH, et al. *Blood*. 2024;144(Suppl 2):LBA-1

# Key ASH 2025 data

**Duell et al, Abst 5515 - CD19 expression is preserved following CD19-directed monoclonal antibody therapy with tafasitamab**

- **57 of 58 B-NHL pts that were CD19 pos pre-rx were pos post-rx**

# Conclusions

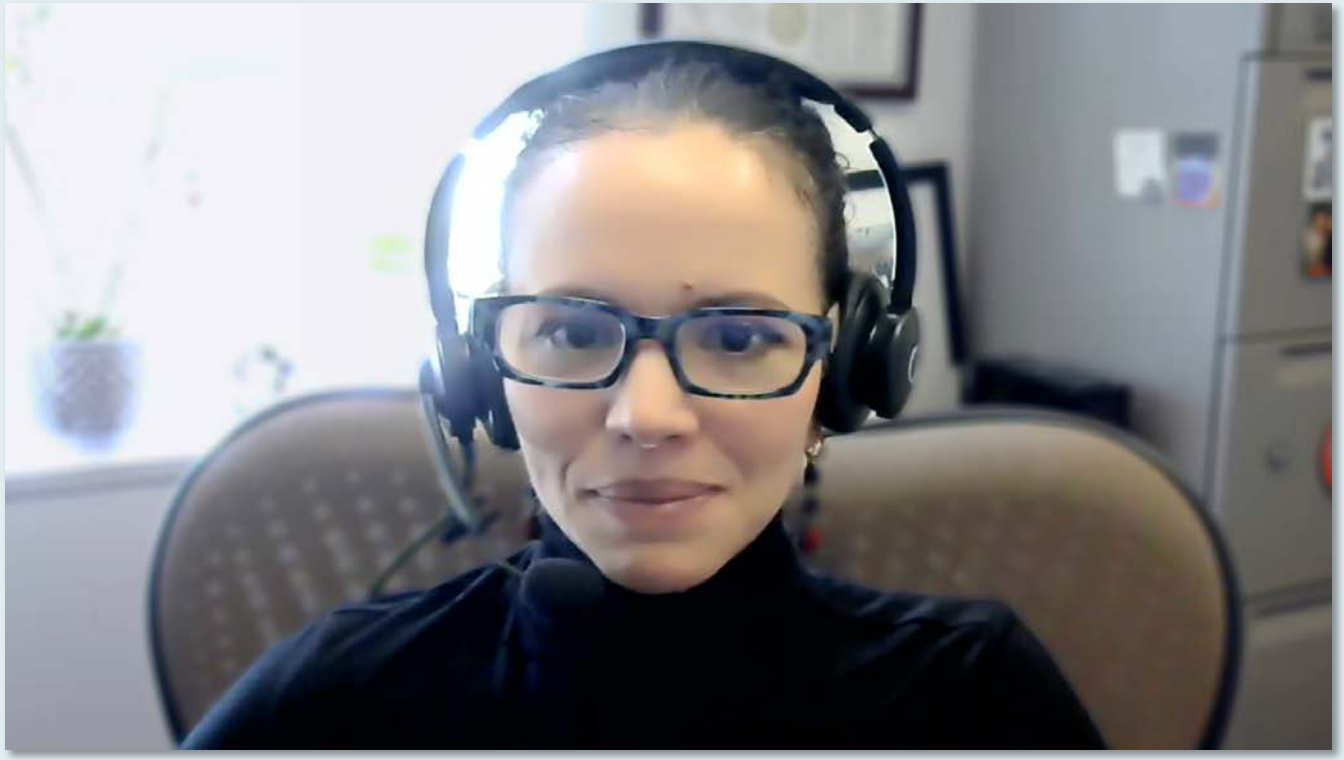
**Tafa-Len active in DLBCL**

**Combinations underway with R-CHOP**

**Tafa-Len-R improves outcomes vs Len-R**

**CD19 “preservation” reassuring**

# Case Presentation: 80-year-old woman with refractory DLBCL receives tafasitamab/lenalidomide



Dr Carla Casulo (Rochester, New York)

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**Currently, in which situations do you utilize tafasitamab for patients with DLBCL? Which tafasitamab combinations do you use?**

**Where do you see tafasitamab "landing" in the next 5 years in the management of DLBCL?**

# Discussion Questions

**Currently, in which situations do you utilize tafasitamab for patients with FL? Which tafasitamab combinations do you use?**

**Where do you see tafasitamab "landing" in the next 5 years in the management of FL?**

# Case Presentation: 78-year-old man with chronic renal disease and relapsed cutaneous DLBCL receives tafasitamab and dose-reduced lenalidomide

Dr Matthew Lunning (Omaha, Nebraska)

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**How would you have managed therapy for this patient, and how would you address the issue of chronic renal disease?**

**How, if at all, do lenalidomide dose reductions affect the activity of tafasitamab/lenalidomide?**

**How do you decide between liso-cel (PILOT trial) and tafasitamab/lenalidomide (L-MIND trial) in late-relapsed LBCL?**

# Agenda

**Module 1:** Rational Incorporation of Antibody-Drug Conjugates into the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Matasar

**Module 2:** Clinical Utility of CD19-Directed Monoclonal Antibodies for DLBCL and Follicular Lymphoma (FL) — Dr Leonard

**Module 3: Optimal Use of Antibody-Drug Conjugates in the Treatment of Relapsed/Refractory DLBCL — Prof Zinzani**

**Module 4:** Bispecific Antibody Therapy for DLBCL — Dr Bartlett

**Module 5:** Bispecific Antibody Therapy for FL and Other Lymphoma Subtypes — Dr Nastoupil

RTP RESEARCH TO PRACTICE

# Optimal Use of Antibody-Drug Conjugates in the Treatment of R/R DLBCL

Pier Luigi Zinzani
*Department of Medical and Surgical Sciences – University of Bologna*
*IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinico «Sant'Orsola-Malpighi»*
*Institute of Hematology «L. e A. Seràgnoli»*

# *Agenda*

- POLARGO: polatuzumab vedotin in combination with R-GemOx in R/R DLBCL
- LOTIS-2: loncastuximab tesirine in R/R DLBCL
- LOTIS-7: glofitamab + loncastuximab tesirine in R/R DLBCL
- Loncastuximab tesirine in R/R follicular lymphoma
- ECHELON-3: brentuximab vedotin + $R^2$ in R/R DLBCL

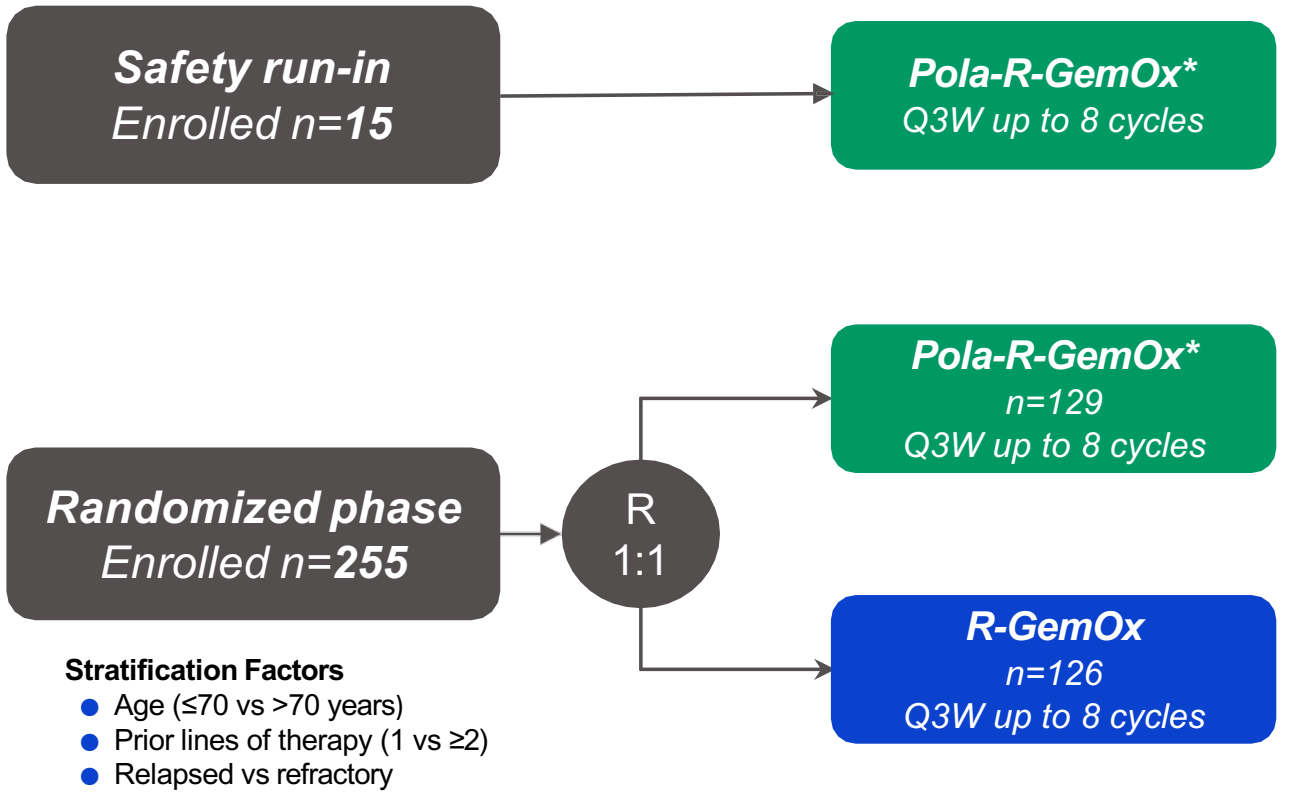
# *Agenda*

- POLARGO: polatuzumab vedotin in combination with R-GemOx in R/R DLBCL
- LOTIS-2: loncastuximab tesirine in R/R DLBCL
- LOTIS-7: glofitamab + loncastuximab tesirine in R/R DLBCL
- Loncastuximab tesirine in R/R follicular lymphoma
- ECHELON-3: brentuximab vedotin + $R^2$ in R/R DLBCL

# Polatuzumab Vedotin, Rituximab, Gemcitabine And Oxaliplatin for Relapsed/Refractory Diffuse Large B-cell Lymphoma: Results from the Randomized Phase III POLARGO Trial

**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




*Polatuzumab vedotin (1.8 mg/kg) plus R-GemOx (R, 375 mg/m²; Gem, 1000 mg/m²; Ox, 100 mg/m²).

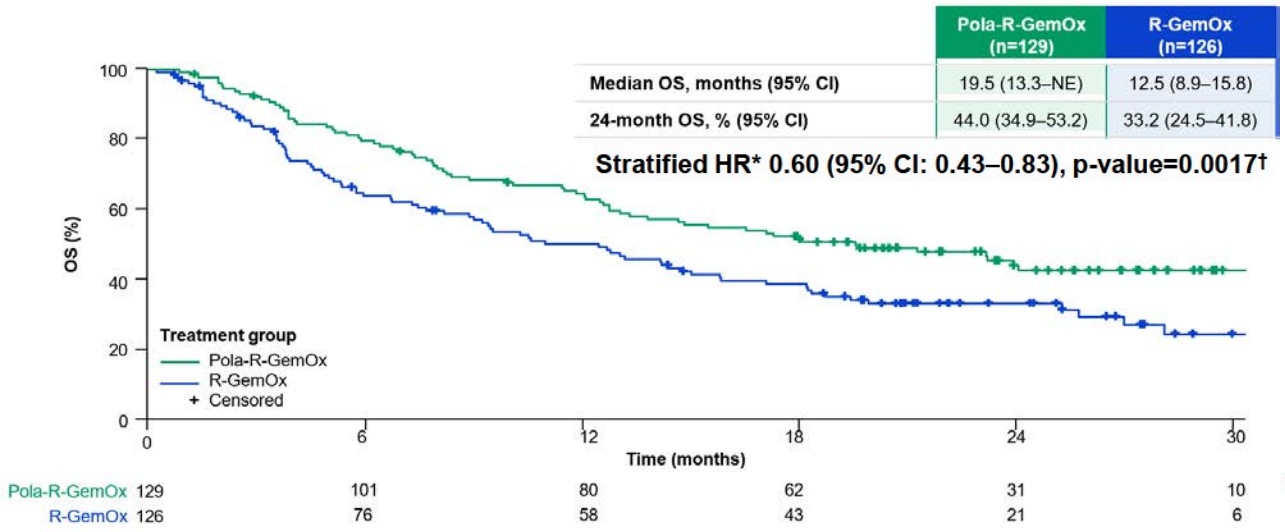
Matasar M. *EHA*, 2025; S101

# Polatuzumab Vedotin, Rituximab, Gemcitabine And Oxaliplatin for Relapsed/Refractory Diffuse Large B-cell Lymphoma: Results from the Randomized Phase III POLARGO Trial

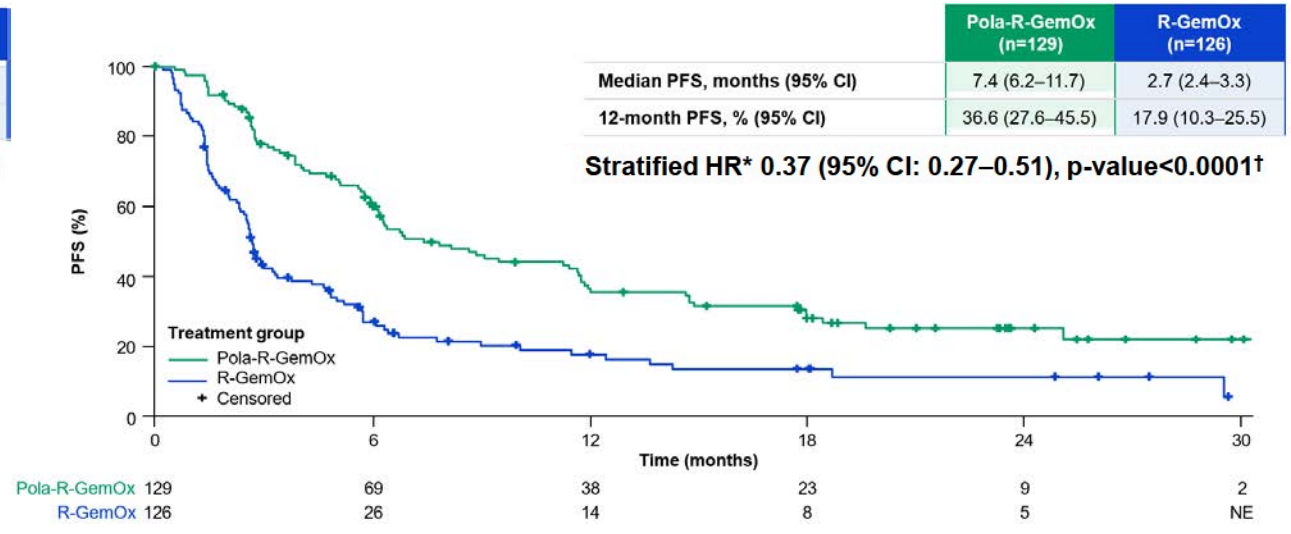
| n (%), unless otherwise stated | | Pola-R-GemOx (n=129) | R-GemOx (n=126) |
|---|---|---|---|
| **Age, years** | Median (range) | 67 (20–85) | 64 (24–89) |
| | >70 years | 45 (34.9) | 44 (34.9) |
| **Geographical region** | Western Europe, United States, Canada | 32 (24.8) | 37 (29.4) |
| | China, South Korea | 42 (32.6) | 34 (27.0) |
| | Brazil, Mexico, India, Turkey | 55 (42.6) | 55 (43.7) |
| **ECOG PS** | 0–1 | 115 (89.1) | 110 (87.3) |
| | 2 | 14 (10.9) | 16 (12.7) |
| **Ann Arbor stage** | I–II | 32 (24.8) | 28 (22.2) |
| | III–IV | 97 (75.2) | 98 (77.8) |
| **IPI risk factor** | 0–2 | 66 (51.2) | 63 (50.0) |
| | 3–5 | 63 (48.8) | 63 (50.0) |
| **Histopathologic diagnosis** | DLBCL, NOS | 116 (89.9) | 116 (92.1) |
| | Transformation from indolent disease | 13 (10.1) | 10 (7.9) |
| **Bulky disease (≥7.5cm)** | Present | 23 (17.8) | 25 (19.8) |
| **Prior lines of therapy for lymphoma** | 1 | 81 (62.8) | 81 (64.3) |
| | ≥2 | 48 (37.2) | 45 (35.7) |
| **Primary refractory (DLBCL, NOS)** | Yes | 65/116 (56.0) | 71/116 (61.2) |
| **R/R to last prior therapy** | Refractory | 85 (65.9) | 83 (65.9) |
| **Cell of origin (central, GEP)** | ABC | 41 (31.8) | 45 (35.7) |
| | GCB | 48 (37.2) | 50 (39.7) |
| | Unclassified | 11 (8.5) | 9 (7.1) |
| | Unknown | 29 (22.5) | 22 (17.5) |

Matasar M. *EHA*, 2025; S101

# Polatuzumab Vedotin, Rituximab, Gemcitabine And Oxaliplatin for Relapsed/Refractory Diffuse Large B-cell Lymphoma: Results from the Randomized Phase III POLARGO Trial




*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.

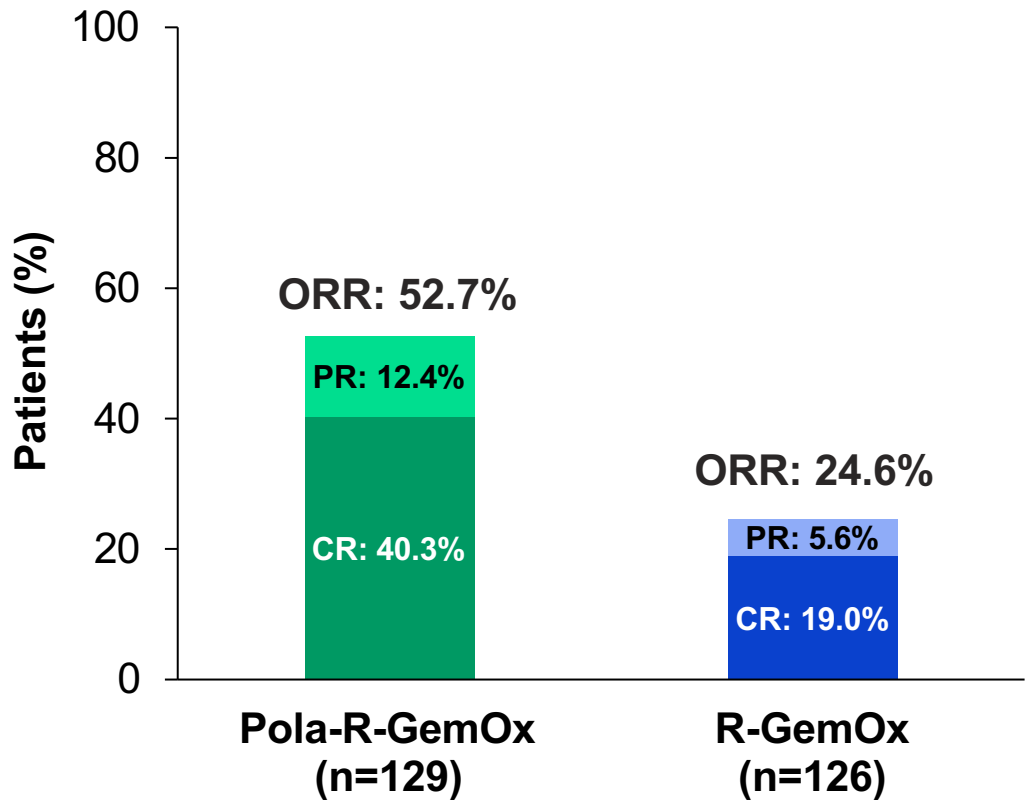



PFS is censored at earliest subsequent therapy or two or more missing tumor assessments.
*Stratified for age (≤70 vs >70 years), prior lines of systemic therapy (1 vs ≥2), outcome of last systemic therapy (relapsed vs refractory). †Log rank.

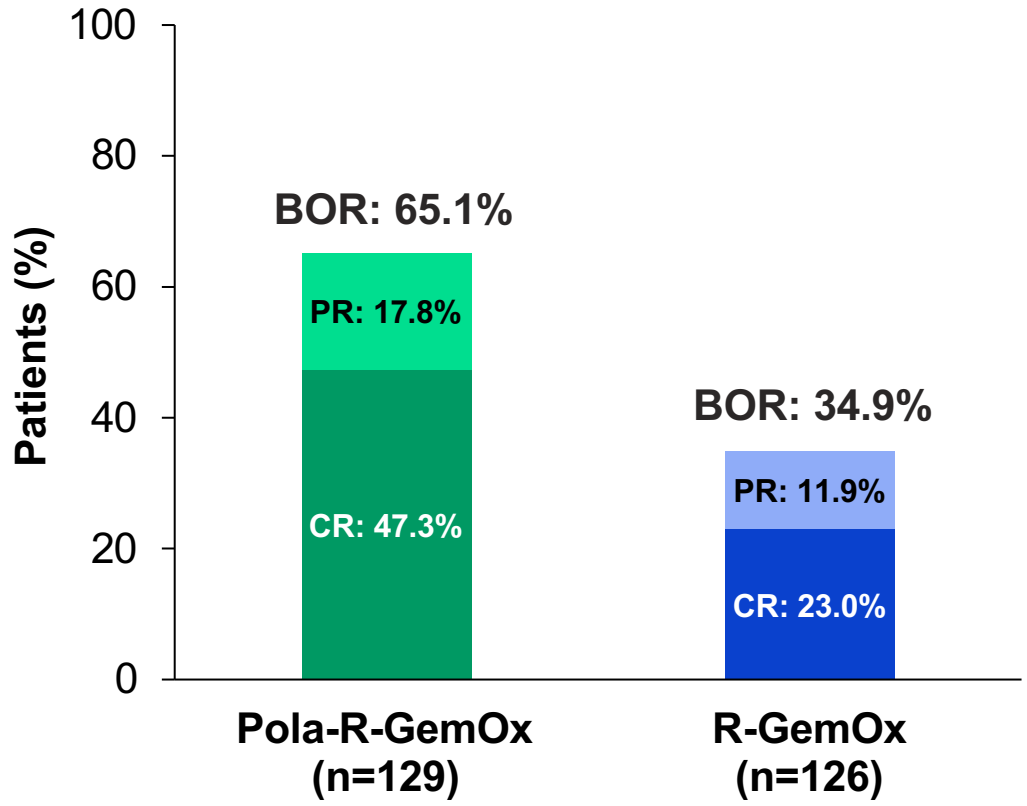
Matasar M. *EHA*, 2025; S101

# Polatuzumab Vedotin, Rituximab, Gemcitabine And Oxaliplatin for Relapsed/Refractory Diffuse Large B-cell Lymphoma: Results from the Randomized Phase III POLARGO Trial

## Response rates by PET-CT at EOT (IRC-assessed)




## Best response rates (INV-assessed)




Matasar M. *EHA*, 2025; S101

# Polatuzumab Vedotin, Rituximab, Gemcitabine And Oxaliplatin for Relapsed/Refractory Diffuse Large B-cell Lymphoma: Results from the Randomized Phase III POLARGO Trial

| n (%), unless otherwise stated | Pola-R-GemOx (n=128) | R-GemOx (n=125) |
|---|---|---|
| **Number of cycles**, median (range) | 7.5 (1–8) | 4 (1–8) |
| **Treatment duration (months)**, median (range) | 4.8 (0–7.6) | 2.1 (0–6.2) |
| **Any AEs**<br>Treatment-related<br>Grade 3–4 AE as highest grade | 125 (97.7)<br>118 (92.2)<br>73 (57.0) | 117 (93.6)<br>103 (82.4)<br>73 (58.4) |
| **Serious AEs**<br>Treatment-related | 49 (38.3)<br>36 (28.1) | 39 (31.2)<br>28 (22.4) |
| **Grade 5 AEs**<br>Treatment-related | 15 (11.7)<br>4 (3.1) | 5 (4.0)<br>3 (2.4) |
| **AEs leading to any study drug discontinuation** | 30 (23.4) | 10 (8.0) |
| **AE leading to any dose reduction** | 31 (24.2) | 14 (11.2) |
| **Any Grade Peripheral neuropathy**<br>Grade 1<br>Grade 2<br>Grade 3 | 73 (57.0)<br>48 (37.5)<br>20 (15.6)<br>5 (3.9) | 36 (28.8)<br>29 (23.2)<br>7 (5.6)<br>0 |

Matasar M. *EHA*, 2025; S101

# *Agenda*

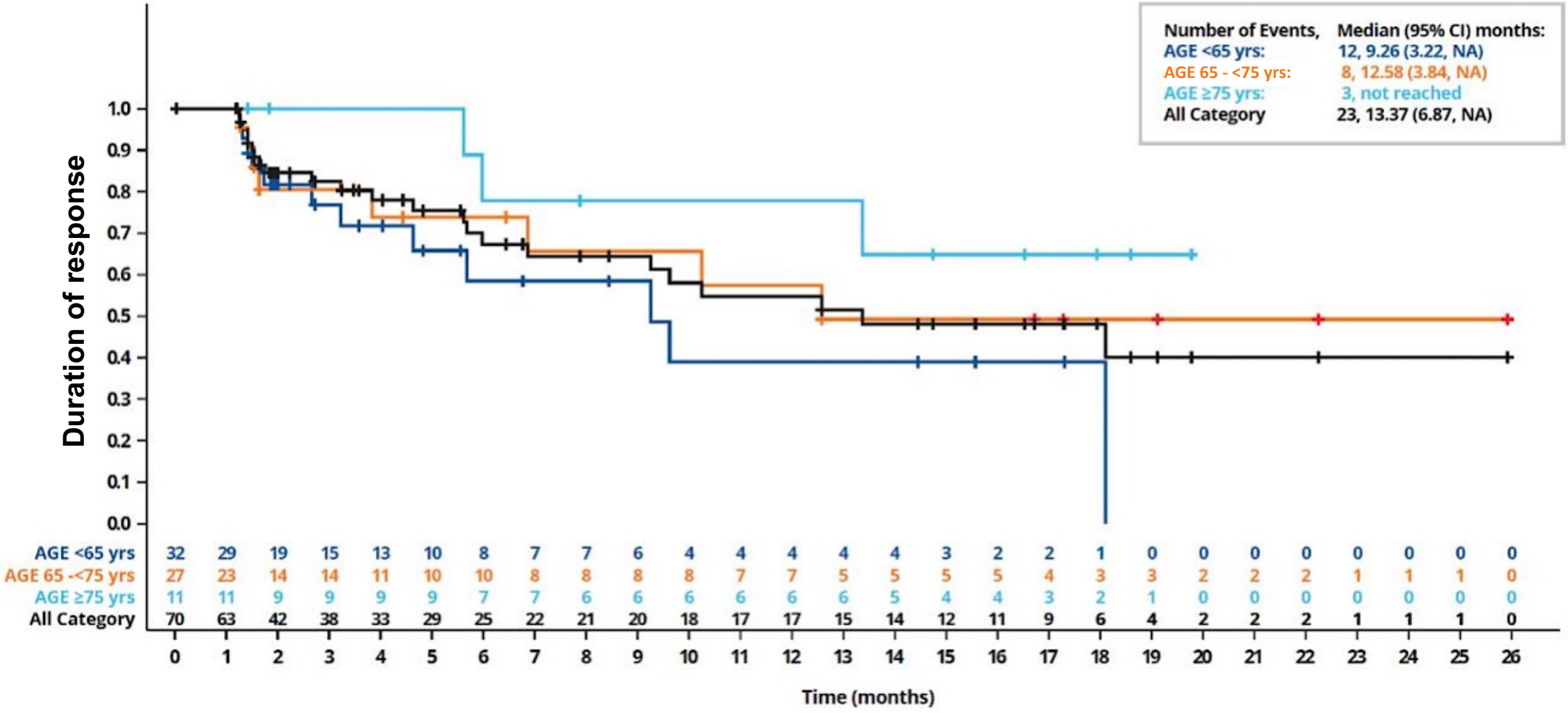
- POLARGO: polatuzumab vedotin in combination with R-GemOx in R/R DLBCL
- LOTIS-2: loncastuximab tesirine in R/R DLBCL
- LOTIS-7: glofitamab + loncastuximab tesirine in R/R DLBCL
- Loncastuximab tesirine in R/R follicular lymphoma
- ECHELON-3: brentuximab vedotin + $R^2$ in R/R DLBCL

# Clinical outcomes of older and younger patients treated with loncastuximab tesirine in the LOTIS-2 clinical trial

| | <70 y (n = 95) | ≥70 y (n = 50) | Total (N = 145) |
|---|---|---|---|
| **BOR, n (%)** | | | |
| CR | 21 (22.1) | 15 (30.0) | 36 (24.8) |
| PR | 25 (26.3) | 9 (18.0) | 34 (23.4) |
| Stable disease | 16 (16.8) | 6 (12.0) | 22 (15.2) |
| PD | 18 (18.9) | 12 (24.0) | 30 (20.7) |
| Not evaluable | 15 (15.8) | 8 (16.0) | 23 (15.9) |
| **ORR (CR + PR)** | 46 (48.4) | 24 (48.0) | 70 (48.3) |
| 95% CI for ORR | 38.0-58.9 | 33.7-62.6 | 39.9-56.7 |
| 95% CI for CR | 14.2-31.8 | 17.9-44.6 | 18.0-32.7 |
| | **<70 y (n = 46)** | **≥70 y (n = 24)** | **Total (N = 70)** |
| Time to CR/PR, d, median (min, max) | 41.5 (35, 247) | 41.0 (36, 142) | 41.0 (35, 247) |
| | **<70 y (n = 21)** | **≥70 y (n = 15)** | **Total (N = 36)** |
| Time to CR, d, median (min, max) | 42.0 (37, 247) | 41.0 (36, 59) | 42 (36, 247) |
| | **<70 y (n = 49)** | **≥70 y (n = 24)** | **Total (N = 73)** |
| Median PFS, mo (95% CI) | 3.81 (2.69-8.08) | 7.36 (2.99-NA) | 4.93 (2.89-8.31) |
| | **<70 y (n = 17)** | **≥70 y (n = 6)** | **Total (N = 23)** |
| Median DOR, mo (95% CI) | 9.26 (4.63-NA) | NR | 13.37 (6.87-NA) |
| | **<70 y (n = 63)** | **≥70 y (n = 33)** | **Total (N = 96)** |
| Median OS, mo (95% CI) | 9.89 (6.14-12.09) | 8.90 (6.74-12.42) | 9.53 (6.93-11.47) |

Hamadani M... Zinzani PL. *Blood Adv*, 2024; 8: 93-98

# Clinical outcomes of older and younger patients treated with loncastuximab tesirine in the LOTIS-2 clinical trial




Hamadani M... Zinzani PL. *Blood Adv*, 2024; 8: 93-98

# *Agenda*

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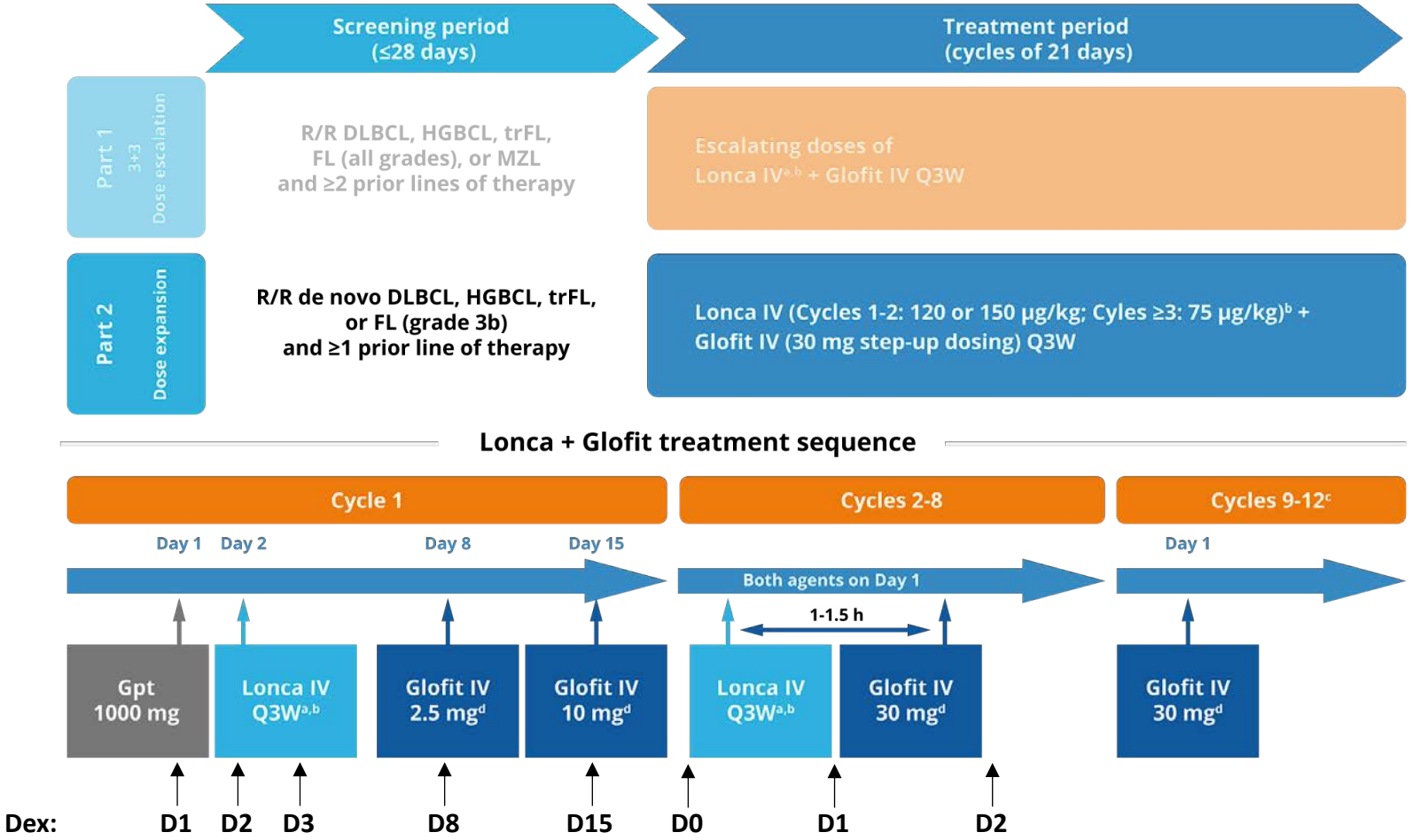
- Loncastuximab tesirine in R/R follicular lymphoma
- ECHELON-3: brentuximab vedotin + $R^2$ in R/R DLBCL

# 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)




## 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. *Hematol Oncol (18-ICML meeting abstracts)*, 2025; 43 (S3): 78

# 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)

| | Glofit + Lonca, 120 µg/kg (n=20) | Glofit + Lonca, 150 µg/kg (n=21) | All dose levels (N=41) |
|---|---|---|---|
| **Age, median (range), y** | 70 (50-82) | 74 (26-85) | 71 (26-85) |
| **Male sex, n (%)** | 11 (55.0) | 12 (57.1) | 23 (56.1) |
| **ECOG PS score, n (%)** | | | |
| **0** | 9 (45.0) | 14 (66.7) | 23 (56.1) |
| **1** | 10 (50.0) | 7 (33.3) | 17 (41.5) |
| **2** | 1 (5.0) | 0 | 1 (2.4) |
| **Ann Arbor disease stage, n (%)** | | | |
| **Stage I/II** | 3 (15.0) | 3 (14.3) | 6 (14.6) |
| **Stage III/IV** | 17 (85.0) | 18 (85.7) | 35 (85.4) |
| **IPI score, n (%)** | | | |
| **0-2** | 9 (45.0) | 10 (46.7) | 19 (46.3) |
| **3-5** | 11 (55.0) | 11 (52.4) | 22 (53.7) |
| **Bulky disease, n (%)** | 2 (10.0) | 2 (9.5) | 4 (9.8) |
| **LDH levels high, n (%)** | 11 (55.0) | 10 (47.6) | 21 (51.2) |
| **LBCL histology, n (%)** | | | |
| **de novo DLBCL** | 13 (65.0) | 17 (81.0) | 30 (73.2) |
| **HGBCL** | 4 (20.0) | 2 (9.5) | 6 (14.6) |
| **trFL** | 2 (10.0) | 2 (9.5) | 4 (9.8) |
| **FL grade 3b** | 1 (5.0) | 0 | 1 (2.4) |

| | Glofit + Lonca, 120 µg/kg (n=20) | Glofit + Lonca, 150 µg/kg (n=21) | All dose levels (N=41) |
|---|---|---|---|
| **DLBCL subtype, n (%)** | | | |
| **GCB** | 10 (50.0) | 11 (52.4) | 21 (51.2) |
| **non-GCB** | 5 (25.0) | 8 (38.1) | 13 (31.7) |
| **Double or triple hit, n (%)** | 3 (15.0) | 5 (23.8) | 8 (19.5) |
| **Number of prior LOT** | | | |
| **Median (range)** | 2 (1-4) | 2 (1-5) | 2 (1-5) |
| **1, n (%)** | 10 (50.0) | 10 (47.6) | 20 (48.8) |
| **≥2, n (%)** | 10 (50.0) | 11 (52.4) | 21 (51.2) |
| **Refractory status, n (%)** | | | |
| **Refractory to primary therapy** | 8 (40.0) | 13 (61.9) | 21 (51.2) |
| **Refractory to last prior therapy** | 7 (35.0) | 13 (61.9) | 20 (48.8) |
| **Prior stem cell transplant, n (%)** | 3 (15.0) | 1 (4.8) | 4 (9.8) |
| **Prior CAR-T therapy, n (%)** | 4 (20.0) | 4 (19.0) | 8 (19.5) |

Alderuccio JP. *Hematol Oncol (18-ICML meeting abstracts)*, 2025; 43 (S3): 78

# 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)

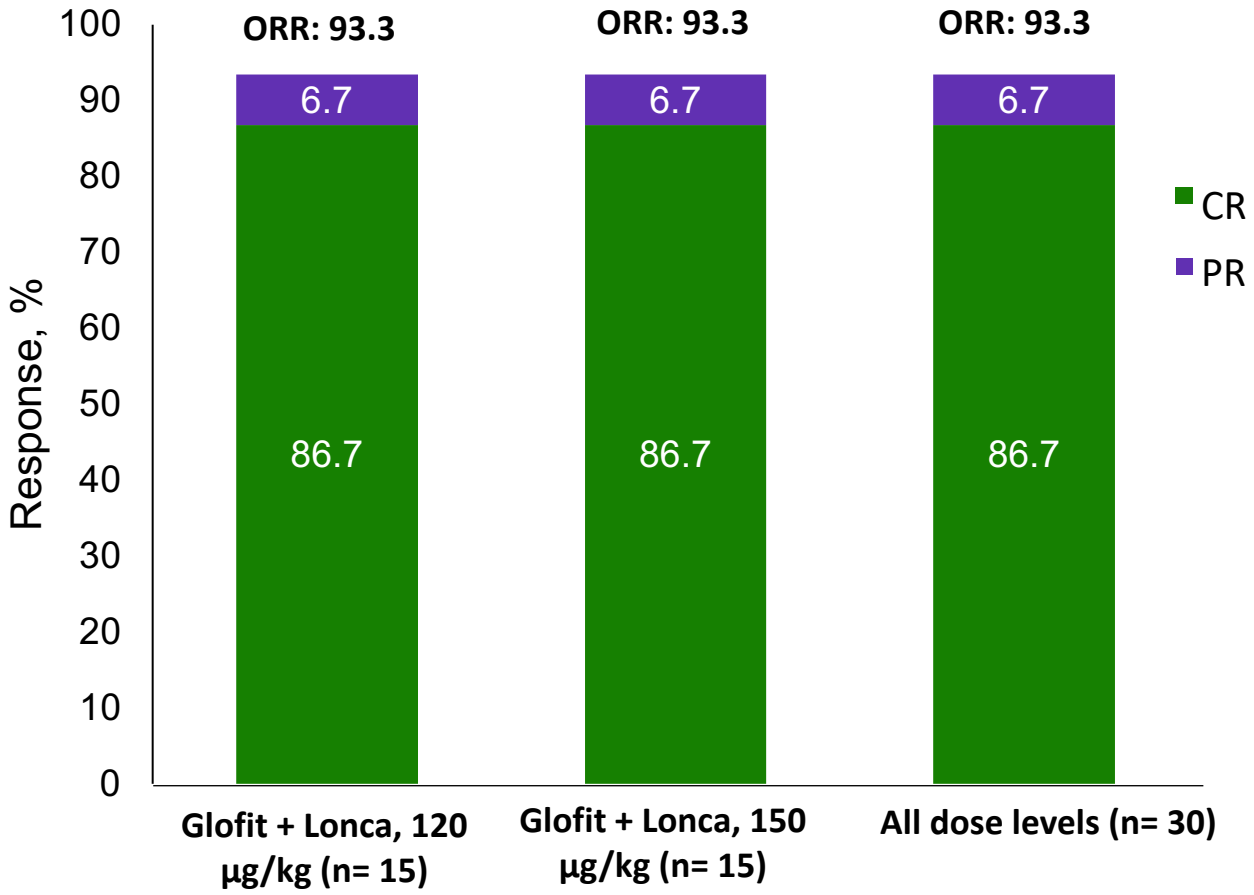
| Safety Results | 120 µg/kg n = 20 | 150 µg/kg n = 21 | All n = 41 |
|---|---|---|---|
| **Grade 3/4 TEAEs (> 5% of patients)[a]** | **11 (55%)** | **12 (57.1%)** | **23 (56.1%)** |
| Neutropenia | 4 (20%) | 6 (28.6%) | 10 (24.4%) |
| Anemia | 1 (5%) | 3 (14.3%) | 4 (9.8%) |
| AST increased | 2 (10%) | 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** | | |

| Safety Results | 120 µg/kg n = 20 | 150 µg/kg n = 21 | All n = 41 |
|---|---|---|---|
| **Cytokine Release Syndrome** | | | |
| **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** | | | |
| **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 |

Alderuccio JP. *Hematol Oncol (18-ICML meeting abstracts)*, 2025; 43 (S3): 78

# 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)

## Best overall response




## Duration of response

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

Alderuccio JP. *Hematol Oncol (18-ICML meeting abstracts)*, 2025; 43 (S3): 78

# *Agenda*

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- Loncastuximab tesirine in R/R follicular lymphoma
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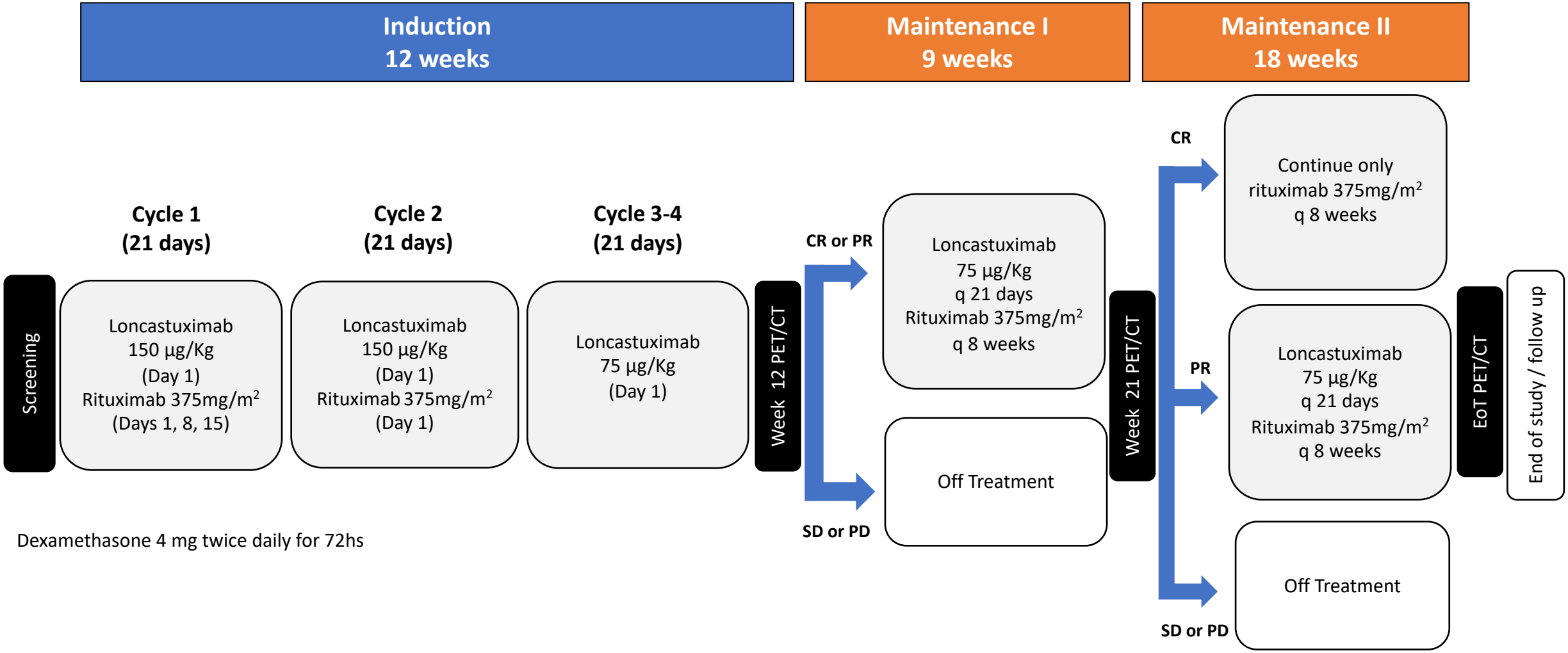
# Loncastuximab tesirine with rituximab in patients with relapsed or refractory follicular lymphoma: a single-centre, single-arm, phase 2 trial




Dexamethasone 4 mg twice daily for 72hs

**Data cutoff: September 13, 2024**
**Median follow-up: 18 (95% CI 12-19.3) months**

Alderuccio JP. *Lancet Haematol*, 2025; 12: e23-e34

# Loncastuximab tesirine with rituximab in patients with relapsed or refractory follicular lymphoma: a single-centre, single-arm, phase 2 trial

| | | n = 39 | % |
|---|---|---|---|
| **Median age, years (range)** | | 68 (47-89) | |
| **Male** | | 21 | 53.8 |
| **Hispanic** | | 22 | 56.4 |
| **Prior transformed FL** | | 11 | 28.2 |
| **FL grade 3A** | | 11 | 28.2 |
| **Bone marrow involvement** | | 13 | 33.3 |
| **ECOG performance status** | 0 / 1 | 29 / 10 | 74.3 / 25.7 |
| **Elevated β2-microglobulin** | | 27 | 69.2 |
| **Ann-Arbor stage** | II / III-IV | 7 / 32 | 17.9 / 79.1 |
| **FLIPI risk score** | 0-1 / 2 / 3-5 | 9 / 6 / 24 | 23 / 15.4 / 61.6 |
| **Progression of disease within 24 months** | | 20 | 51.5 |
| **High-tumor burden by GELF criteria** | | 36 | 92 |
| **Bulky disease (>7cm)** | | 9 | 23 |
| **Refractory to last therapy** | | 20 | 51 |
| **Relapsed FL** | | 19 | 49 |
| **Median no, of prior lines, n (range)** | | 1 (1-6) | |
| **≥3 lines of therapy** | | 11 | 28 |

Alderuccio JP. *Lancet Haematol*, 2025; 12: e23-e34

# Loncastuximab tesirine with rituximab in patients with relapsed or refractory follicular lymphoma: a single-centre, single-arm, phase 2 trial

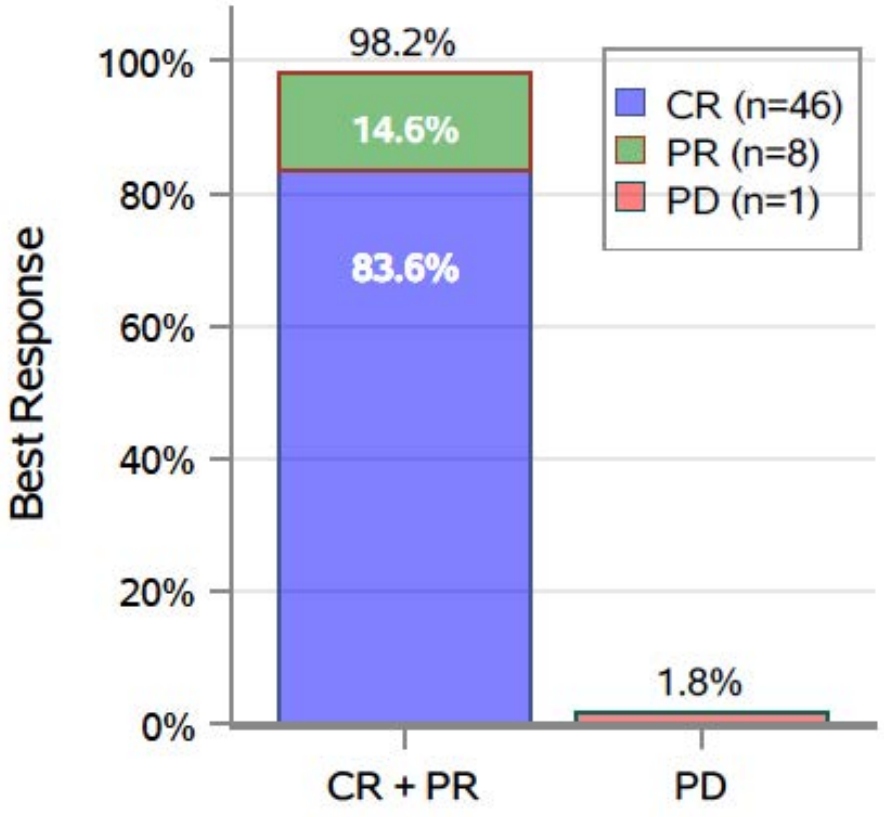
| | n | Best ORR | Best CR rate |
|---|---|---|---|
| POD24* | 20 | 100% | 85% |
| High risk FLIPI score | 24 | 96% | 67% |
| Prior transformed FL | 11 | 100% | 73% |
| Rituximab with an alkylating agent | 32 | 100% | 75% |

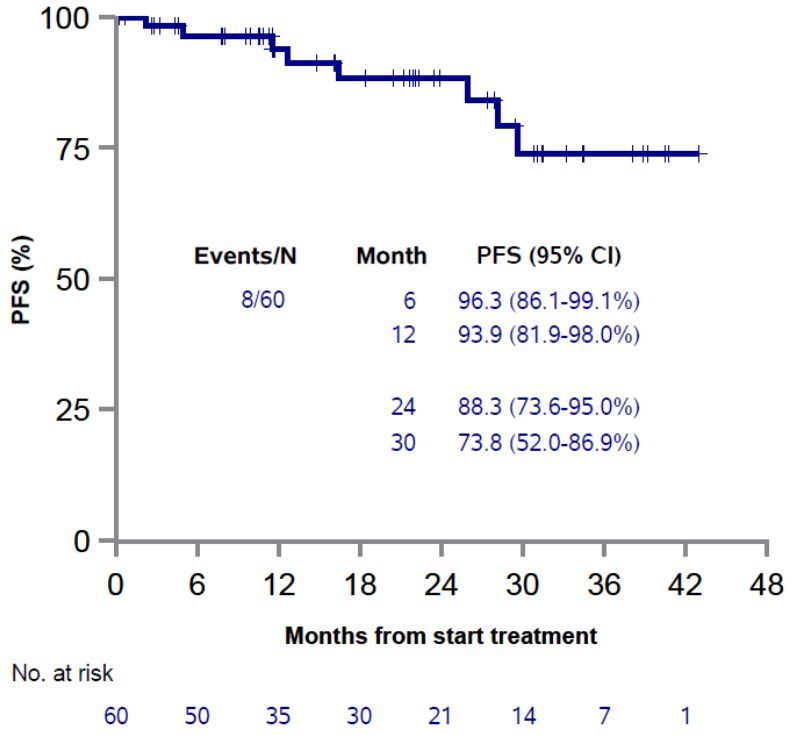
**Previously treated with rituximab and an alkylating agent*

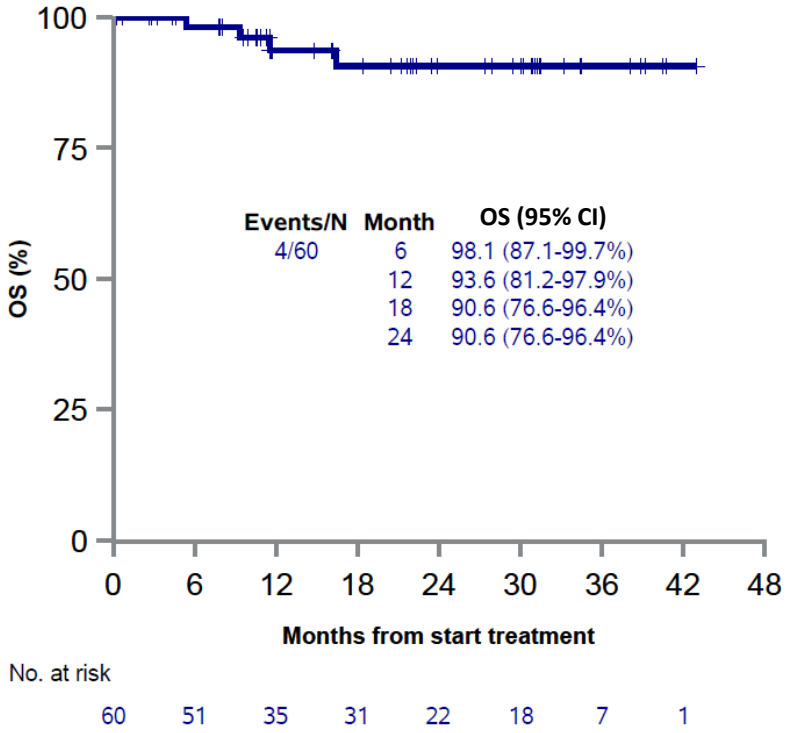
Alderuccio JP. *Lancet Haematol*, 2025; 12: e23-e34

# Loncastuximab tesirine with rituximab in patients with relapsed or refractory follicular lymphoma: a single-centre, single-arm, phase 2 trial

## Updated efficacy analysis (*n*=60)




***Median follow-up of 28 months (September 10th, 2025)***

Alderuccio JP. *Lancet Haematol*, 2025; 12: e23-e34

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- Loncastuximab tesirine in R/R follicular lymphoma
- ECHELON-3: brentuximab vedotin + $R^2$ in R/R DLBCL

# Brentuximab Vedotin Combination for Relapsed Diffuse Large B-Cell Lymphoma

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

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

Randomization 1:1

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

**Treatment groups**

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

### Primary endpoint
- OS in ITT population

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

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

- Per protocol, G-CSF prophylaxis was required

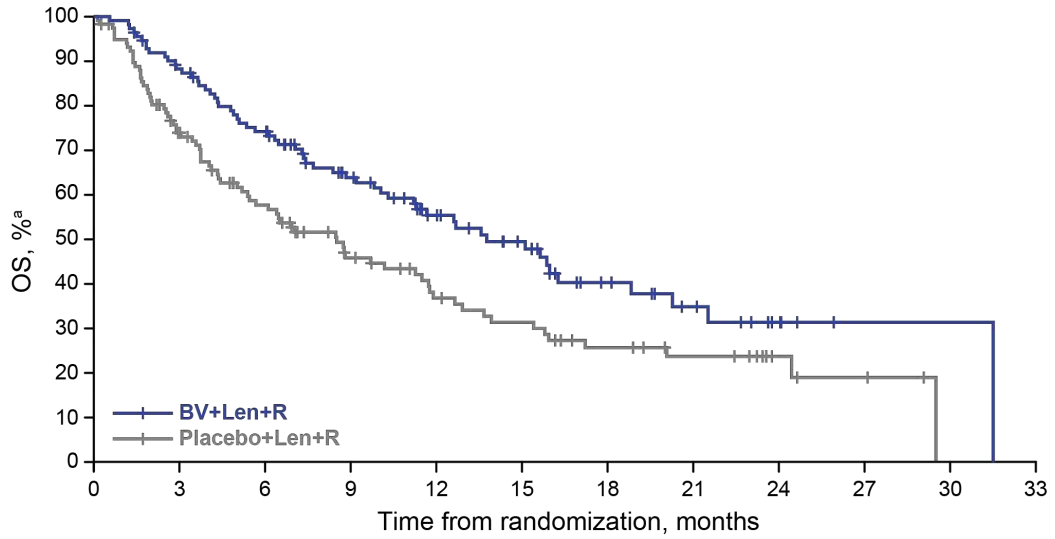
Bartlett NL. *J Clin Oncol*, 2025; 43: 1061-1072

# Brentuximab Vedotin Combination for Relapsed Diffuse Large B-Cell Lymphoma

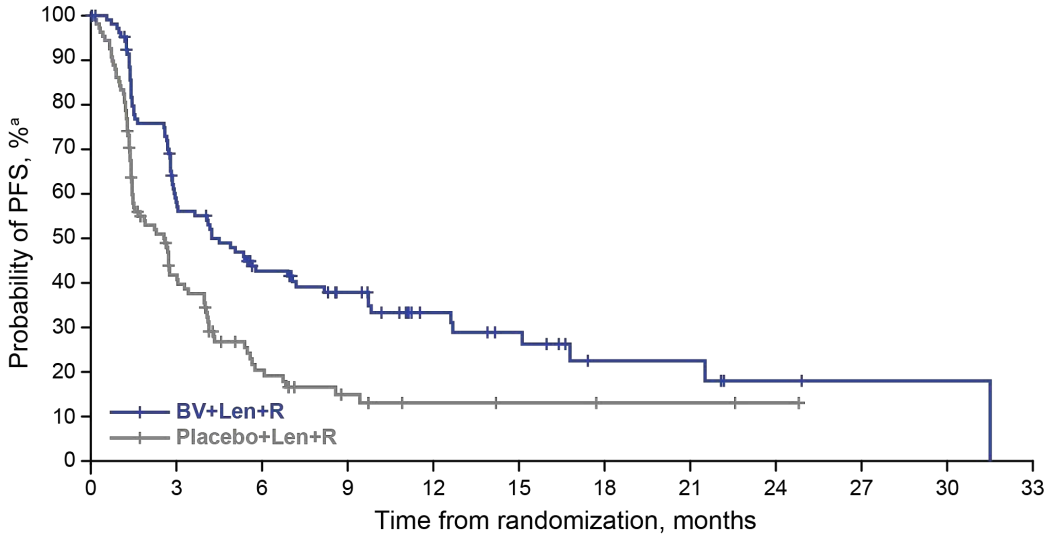
| | BV+Len+R (n=112) | Placebo+Len+R (n=118) |
|---|---|---|
| **Patient characteristics** | | |
| Age, median (range), years | 74.0 (29-87) | 70.0 (21-89) |
| Age, n (%) | | |
| ≥65 years | 79 (71) | 76 (64) |
| ≥80 years | 23 (21) | 15 (13) |
| Male, n (%) | 60 (54) | 70 (59) |
| ECOG PS 2, n (%) | 12 (11) | 13 (11) |
| **Prior treatments** | | |
| Lines of systemic therapies, median (range) | 3 (2-8) | 3 (2-7) |
| Systemic therapies received, n (%) | | |
| Previous anthracycline | 110 (98) | 115 (97) |
| Previous anti-CD20 antibody | 110 (98) | 114 (97) |
| CAR T-cell therapy | 32 (29) | 35 (30) |
| Bispecific antibody | 14 (13) | 20 (17) |
| HSCT | 10 (9) | 18 (15) |
| **CD30 status** | | |
| ≥1% | 36 (32) | 38 (32) |
| <1% | 76 (68) | 80 (68) |

Bartlett NL. *J Clin Oncol*, 2025; 43: 1061-1072

# Brentuximab Vedotin Combination for Relapsed Diffuse Large B-Cell Lymphoma




| No. at risk | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BV+Len+R | 112 | 96 | 79 | 57 | 40 | 30 | 17 | 11 | 5 | 1 | 1 | 0 |
| Placebo+Len+R | 118 | 81 | 58 | 39 | 28 | 23 | 16 | 12 | 5 | 3 | 0 | 0 |



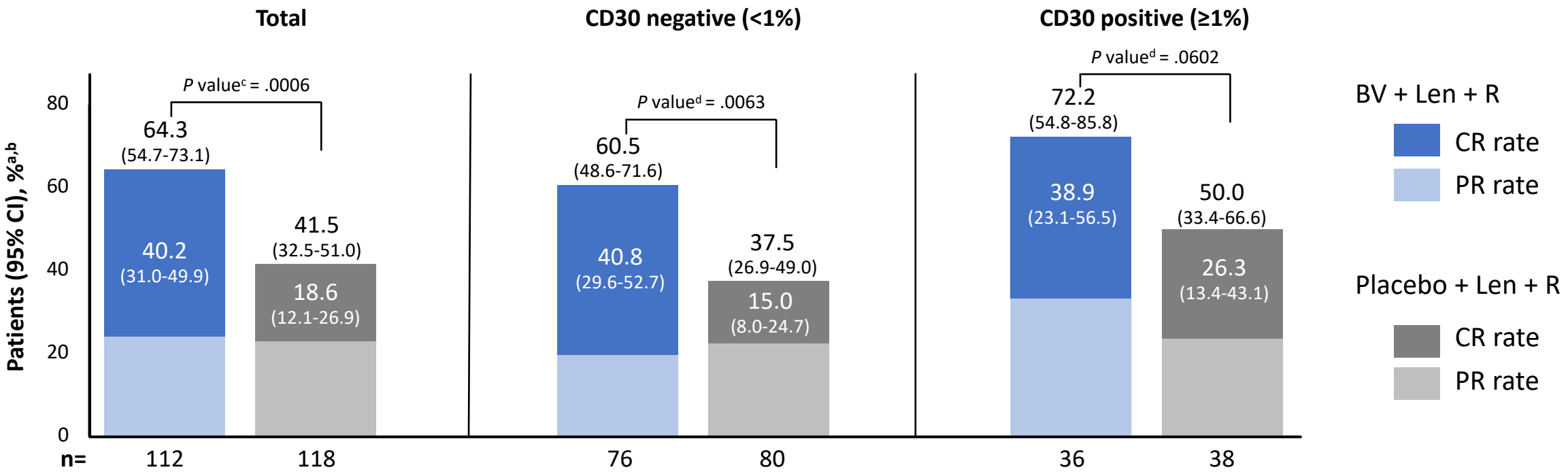

| No. at risk | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BV+Len+R | 112 | 58 | 38 | 27 | 15 | 11 | 5 | 5 | 2 | 1 | 1 | 0 |
| Placebo+Len+R | 118 | 40 | 16 | 8 | 4 | 3 | 2 | 2 | 1 | 0 | 0 | 0 |

| | 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 (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) |

Bartlett NL. *J Clin Oncol*, 2025; 43: 1061-1072

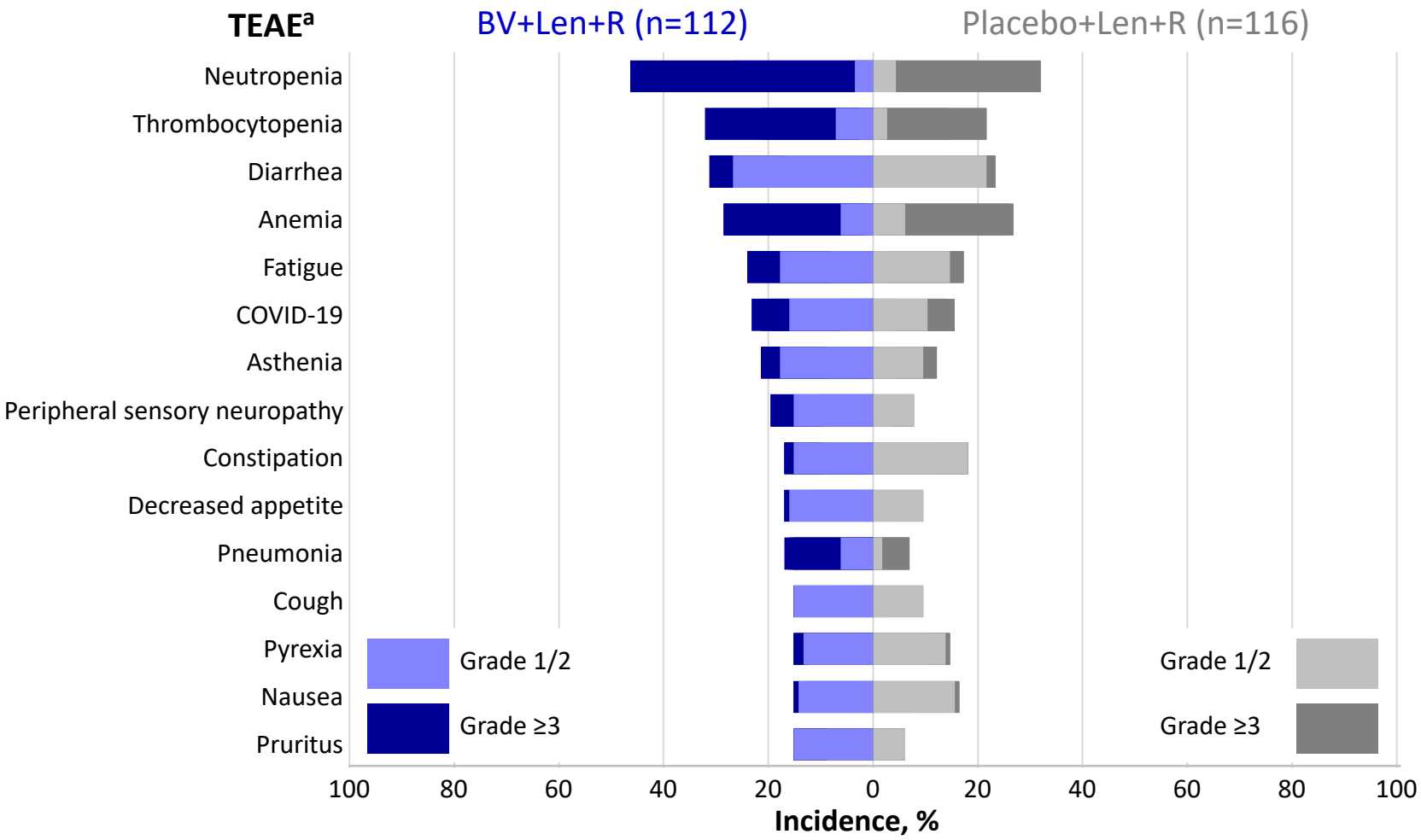
# Brentuximab Vedotin Combination for Relapsed Diffuse Large B-Cell Lymphoma




- 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


Bartlett NL. *J Clin Oncol*, 2025; 43: 1061-1072
Kim JA et al. ASCO 2024;Abstract LBA7005

# Brentuximab Vedotin Combination for Relapsed Diffuse Large B-Cell Lymphoma




- 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

Bartlett NL. *J Clin Oncol*, 2025; 43: 1061-1072

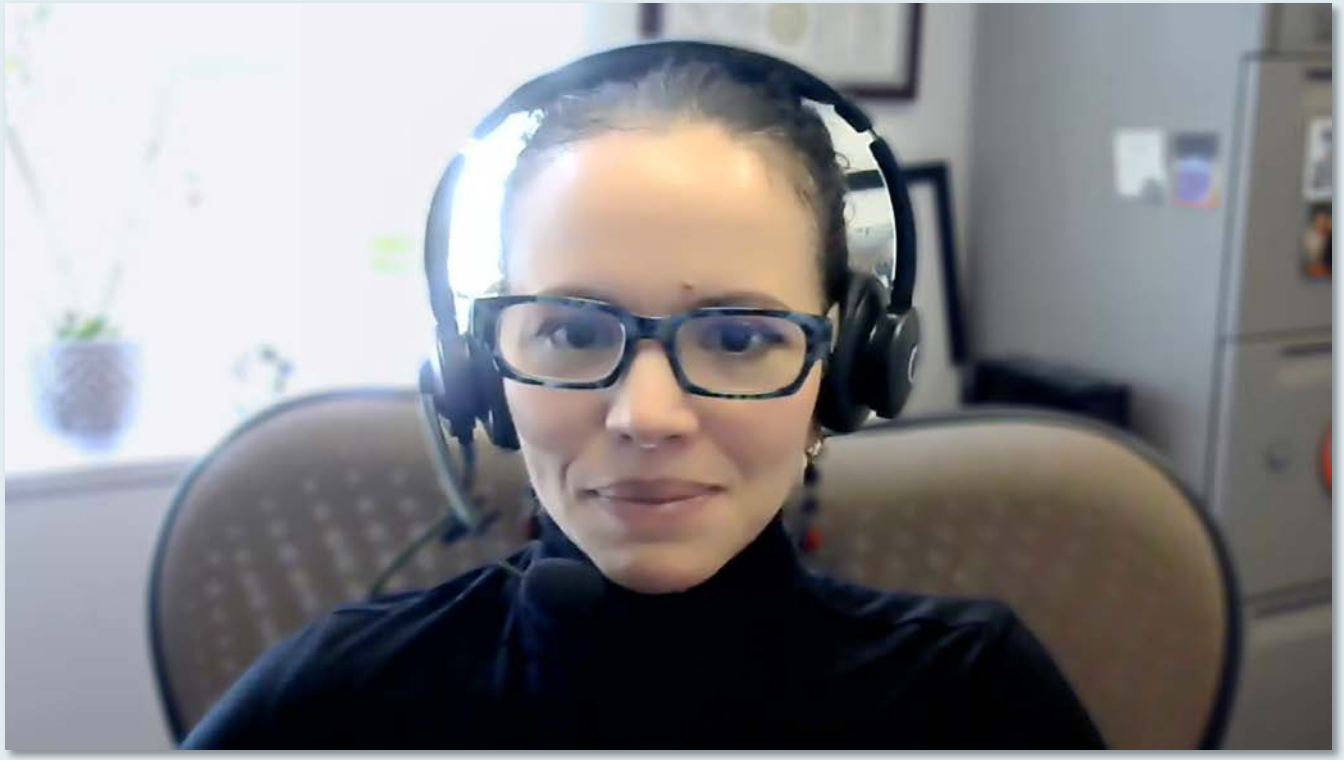
# *Take home messages*

- Pola-R-GemOx significantly improved outcomes, including a 40% reduction in relative risk of death compared with R-GemOx in patients with transplant-ineligible R/R DLBCL.
- The POLARGO data reinforce the benefit of combining polatuzumab vedotin with chemotherapy in the treatment of DLBCL.

- Loncastuximab-based combinations are demonstrating encouraging efficacy in 2-line+ LBCL, especially in combination with glofitamab.
- Similar encouraging results are observed in combination with rituximab in 2-line+ FL.

- BV has modest activity in R/R DLBCL, with no clear association with CD30 expression.
- BV+Len (+R) increases effectiveness regardless of COO or CD30 status.
- BV+Len-R improved survival vs Len-R. Reasonable choice in CART/BsAb failed or ineligible/inaccessible.

# Case Presentation: 69-year-old woman with relapsed DLBCL s/p Pola-BR receives loncastuximab tesirine with PR but develops skin rash



Dr Carla Casulo (Rochester, New York)

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**Currently, in which situations do you utilize loncastuximab tesirine for patients with DLBCL?**

**Do you see a role for loncastuximab tesirine in combination with a bispecific antibody in DLBCL?**

**Which tolerability/toxicity issues have you encountered with this agent, and how are they ameliorated?**

**Do you currently see a role for loncastuximab tesirine in FL?**

# Case Presentation: 41-year-old woman with multiregimen-relapsed GCB-type DLBCL and PD on loncastuximab tesirine receives brentuximab vedotin/R$^2$

Dr Matthew Lunning (Omaha, Nebraska)

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**What is your experience with sun- or UV-associated rash with loncastuximab tesirine? What about hepatic toxicity?**

**Do you generally re-biopsy after CAR T-cell therapy to assess for antigen escape?**

**If CD19 expression was low after CAR T-cell therapy, would you consider loncastuximab tesirine/dexamethasone?**

# Discussion Questions

**For which patients with DLCBL are you currently using BV/$R^2$ in your practice?**

**Would you hesitate to use BV for a patient who had received prior treatment with polatuzumab vedotin?**

# Agenda

**Module 1:** Rational Incorporation of Antibody-Drug Conjugates into the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Matasar

**Module 2:** Clinical Utility of CD19-Directed Monoclonal Antibodies for DLBCL and Follicular Lymphoma (FL) — Dr Leonard

**Module 3:** Optimal Use of Antibody-Drug Conjugates in the Treatment of Relapsed/Refractory DLBCL — Prof Zinzani

**Module 4: Bispecific Antibody Therapy for DLBCL — Dr Bartlett**

**Module 5:** Bispecific Antibody Therapy for FL and Other Lymphoma Subtypes — Dr Nastoupil

RTP RESEARCH TO PRACTICE

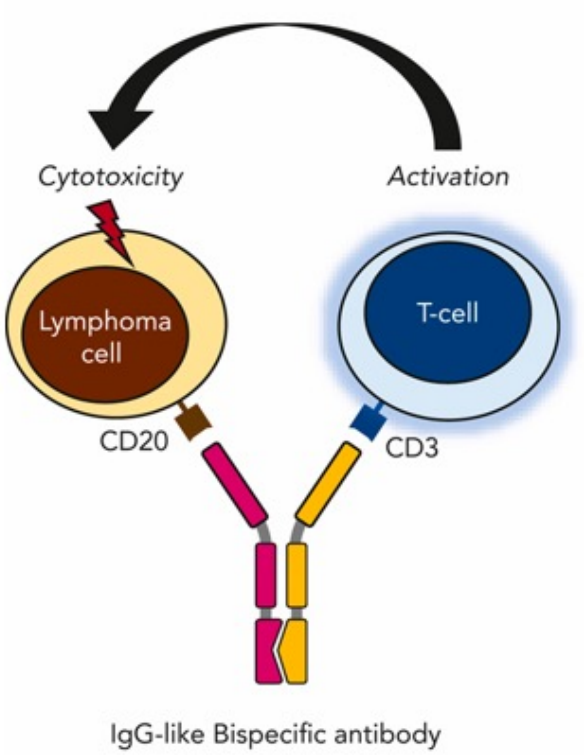

# Bispecific Antibody Therapy for DLBCL

Nancy L. Bartlett, MD
Washington University in St. Louis
Siteman Cancer Center
ASH Symposium
December 5, 2025

# Pharmacologic similarities and differences among the approved CD20 x CD3 bispecific antibodies

# Similarities

## Mechanism of Action




## Half-life

| | |
|---|---|
| Glofit | 10 d |
| Epcor | 9 d |
| Mosun | 6-11 d |
| Odro | 14 d |

## Clearance

- Similar to natural IgG antibodies
- Engineered to bind effectively to neonatal FcRn preventing rapid degradation
- Silencing FcγR mutations slows clearance
- No kidney/liver clearance

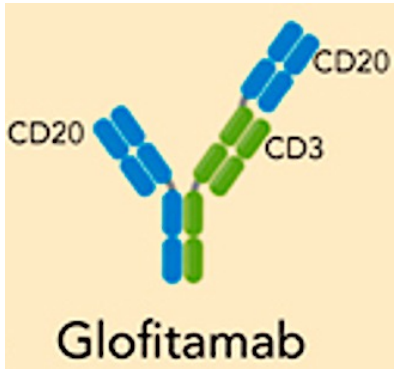
All incorporate weekly or twice weekly step-up dosing with dex pre-med Cycle 1

Falchi et al. Blood 2023;141:467 Li T et al Clin Pharmacol Ther 2025;117:1437 Minson et al. Haematologica 2025;110:1483

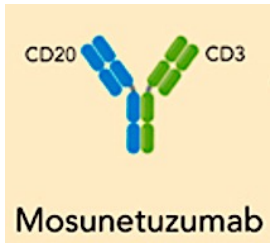
# Differences

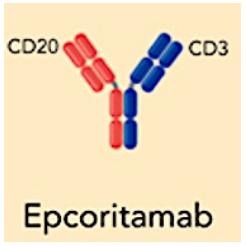
## Structure CD20:CD3

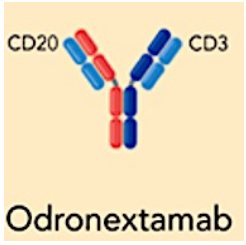
2:1




Glofit requires Obinu D -7 to ↓ CRS




1:1

| Agent | CD20 epitope | Mode of admin. | Schedule | Duration |
|---|---|---|---|---|
| **Glofit** | Obinutuzumab | IV | C1 Q7d<br>C2+ Q21d | FIXED x12 |
| **Epcor** | Ofatumumab | SC | C1-3 Q7d<br>C4-9 Q14d<br>C≥10 Q28d | Until PD /intolerance |
| **Mosun** | Rituximab | IV<br>(SC soon) | C1 Q7d<br>C2-8 Q21d | FIXED x 8 |
| **Odron** | Ofatumumab | IV<br>(SC in dev) | C1 2d/wk<br>C2-4 Q7d<br>C≥5 Q14d | Until PD /intolerance |

Falchi et al. Blood 2023;141:467
Li T et al Clin Pharmco Ther 2025;117:1437
Minson et al. Haematologica 2025;110:1483

# Efficacy and safety outcomes from pivotal registration studies of glofitamab and epcoritamab monotherapy in R/R DLBCL

# Efficacy CD20xCD3 BsAb in 3rd line or later R/R DLBCL

## Best CR rates ≈ 40%

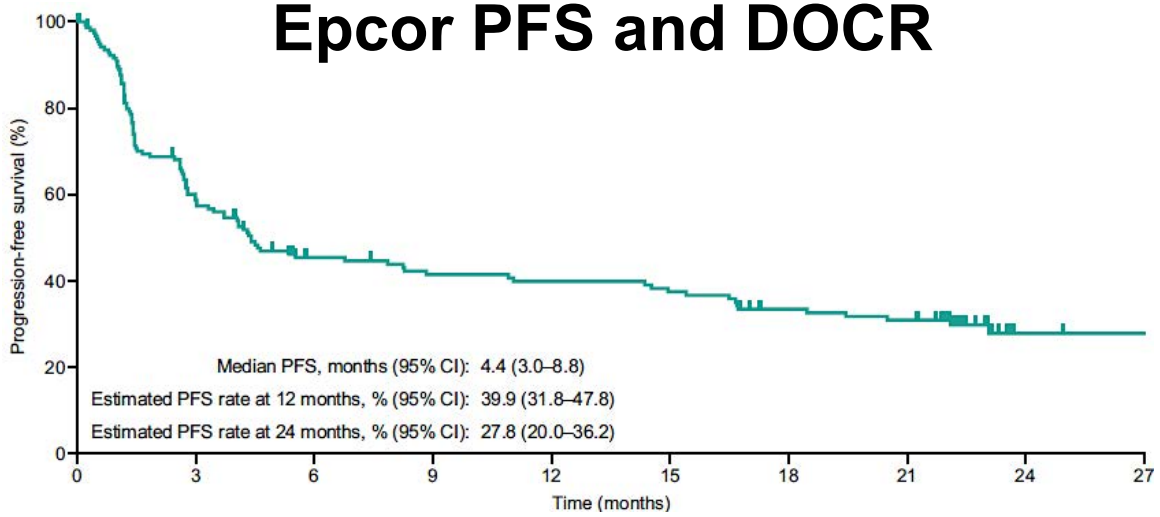
| | Agent | #pts | ORR% | CR% | DOCR | PFS |
|---|---|---|---|---|---|---|
| Approved FDA, EU | **Epcoritamab[1,2]** | 157 | 63 | **40** | **52% 3-yr** | 28% 2-yr |
| | **Glofitamab[3,4]** | 154 | 52 | **40** | **57% 2-yr** | 37% 1-yr |
| | | | | | | |
| Approved EU | Odronextamab[5,6] | 127 | 52 | 32 | 51% 3-yr | 18% 3-yr |
| | Mosunetuzumab[7] | 88 | 42 | 24 | 70% 1-yr | 23% 1-yr |

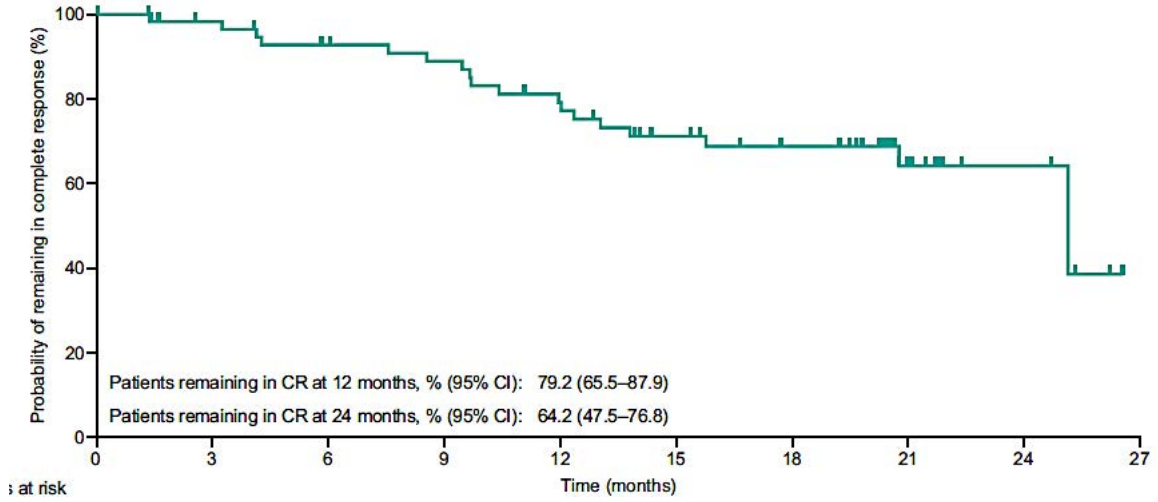
Approximately half of CRs appear durable at 2-3 yrs.

1. Thieblemont et al JCO 2023;41:2238-2247; 2. Thieblemont et al Leukemia 2024;38:2653-2662; 3. Dickinson et al NEJM 2022;387:2220-2231; 4. Dickinson et al ASH 2024; 5. Kim et al Nature Cancer 2025;6:528-539 6. Allan et al ASH 2024; 7. Bartlett et al Blood 2023;7:4926-4935

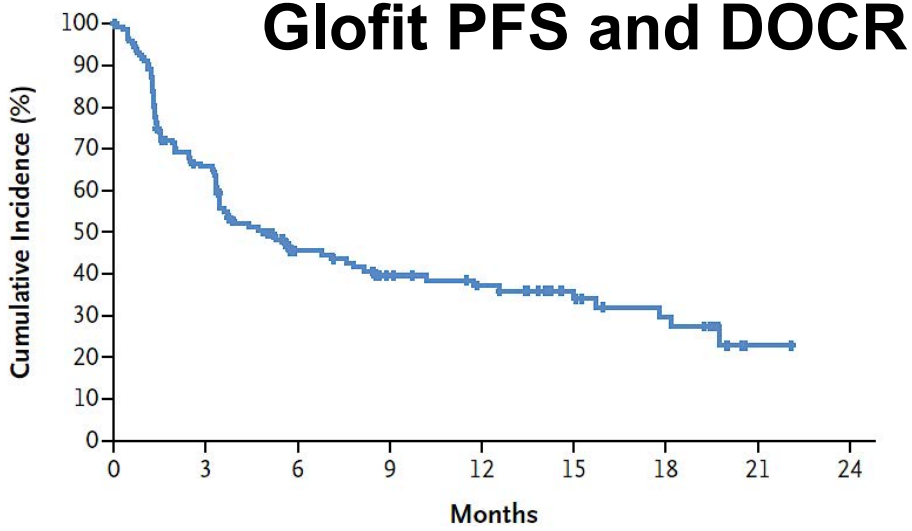
# PFS in R/R DLBCL: A chance for cure?

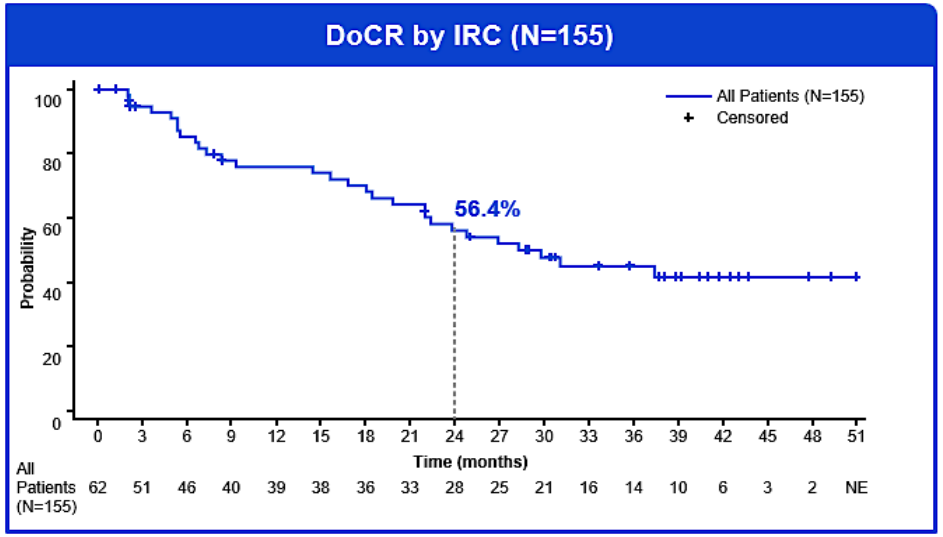
## Epcor PFS and DOCR




## Glofit PFS and DOCR




Thieblemont et al Leukemia 2024;38:2653-2662, Dickinson et al NEJM 2022;387:2220-2231, Dickinson et al ASH 2024

# Toxicities of Special Interest: R/R DLBCL

| Agent | CRS Rate | | Neurotoxicity Rate | | Gr 3+ Infections | Tocilizumab Required |
|---|---|---|---|---|---|---|
| | Any Gr | Gr 3+ | Any Gr | Gr 3+ | | |
| **Epcoritamab**[1] | 50% | 3% | 6% | <1% | **15%** | 28% |
| **Glofitamab**[2] | 63% | 4% | 8% | 3% | **15%** | 32% |
| | | | | | | |
| Odronextamab[3] | 55% | 5% | 43% | 4% | **39%** | 25% |
| Mosunetuzumab[4] | 26% | 2% | 0 | 0 | **13%** | 6% |

1. Thieblemont et al Leukemia 2024;38:2653-2662; 2. Dickinson et al NEJM 2022;387:2220-2231;
3. Kim et al Nature Cancer 2025;6:528-539 ; 4. Bartlett et al Blood 2023;7:4926-4935

# Non-lymphoma deaths: BsAb in R/R DLBCL

Many deaths reported as “not related” to treatment.
**Should assume most are related.**

| Agent | Non-lymphoma deaths | Available Descriptions of Deaths |
|---|---|---|
| **Epcoritamab[1]** | **4%** | 2 COVID, 1 ICANS, 1 hepatotoxicity, 1 MI |
| **Glofitamab[2,3]** | **7.1%** | 6 COVID, 2 sepsis, 1 delirium, 1 AML |
| Odronextamab[4] | 15.7% | 15 Infection (COVID 5, pneumonia 3, sepsis 3, PJP 1, CMV 2, pseudomonas 1), 1 HLH, 1 ILD,1 Multiorgan failure 1 GI bleed, 1 unk |
| Mosunetuzumab[5] | 3% | 1 pneumonia, 1 sepsis, 1 cholangitis |

1. Thieblemont et al Leukemia 2024;38:2653-2662; 2. Dickinson et al NEJM 2022;387:2220-2231 3. Dickinson et al ASH 2024
4. Kim et al Nature Cancer 2025;6:528-539 ; 5. Bartlett et al Blood 2023;7:4926-4935

# Bispecific antibodies in combination with other anticancer therapies and in earlier settings in DLBCL

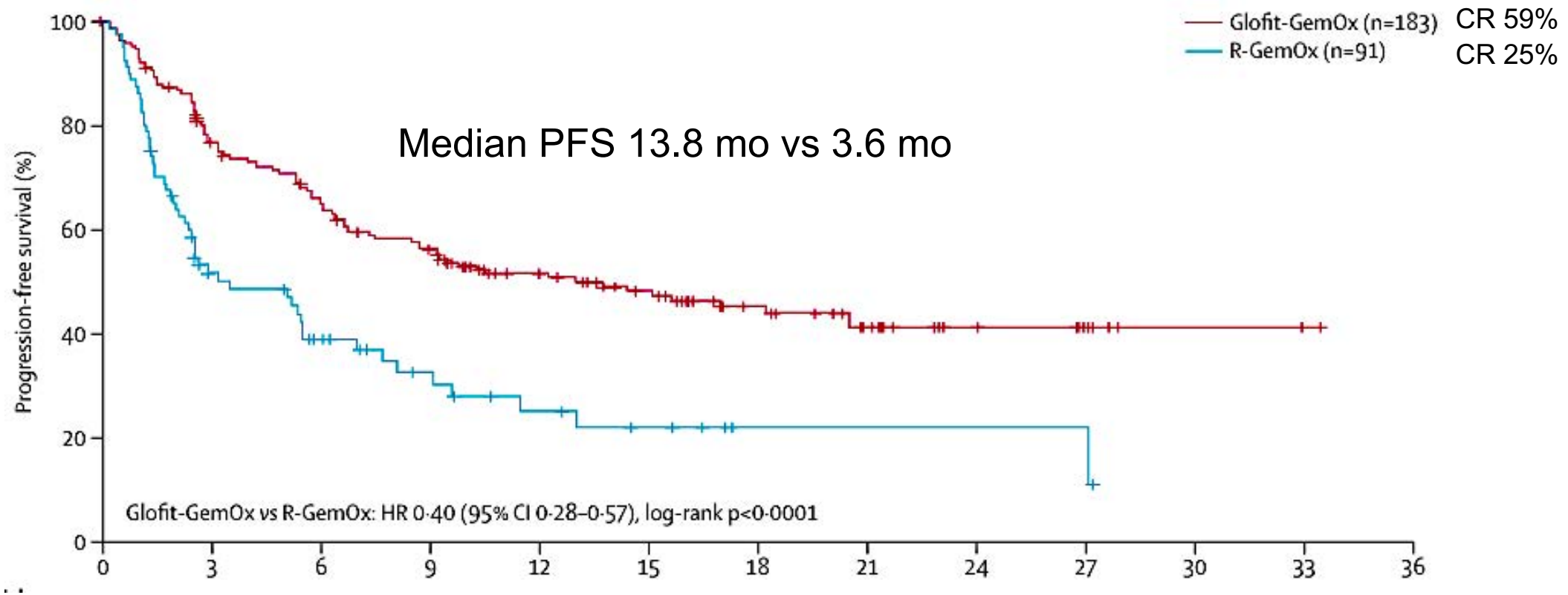
# BsAb + Chemo/ADC combos in 2nd line or later R/R DLBCL

| Agent | Ph | #pts | ORR% | CR% | Median DOCR (mo) | Median PFS (mo) |
|---|---|---|---|---|---|---|
| **Glofit-GemOx vs** R-GemOx[1,2] | III **(STARGLO)** | 183<br>91 | 68<br>41 | 59<br>**25** | NR<br>24.2 | 14.4<br>**3.3** |
| **Epco-GemOx**[3,4] | I/II | 103 | 81 | 60 | 27.3 | 16.3 |
| | | | | | | |
| **Mosun-Pola vs** R-GemOx[5] | III **(SUNMO)** | 138<br>70 | 70<br>40 | 51<br>**24** | **NR**<br>**9.5** | 11.5<br>**3.8** |
| **Glofit-Pola**[6] | I/II | 129 | 78 | 60 | 37.8 | 12.3 |
| **Glofit-Lonca**[7] | I/II | 30 | 93 | 87 | - | - |

1. Abramson et al Lancet 2024;404:1940; 2.Abramson et al ASH 2025, 3. Brody et al Blood 2025;145:1621; 4. Brody et al ASH 2025
5. Budde et al, JCO 2025; 10.1200/JCO-25-01957; 6. Hutchings et al, JCO 2025;10.1200/JCO-25-00992; 7. Alderuccio JP et al EHA 2025

# PFS: Phase 3 STARGLO: Glofit-GemOx vs R-GemOx, 2L+ R/R DLBCL

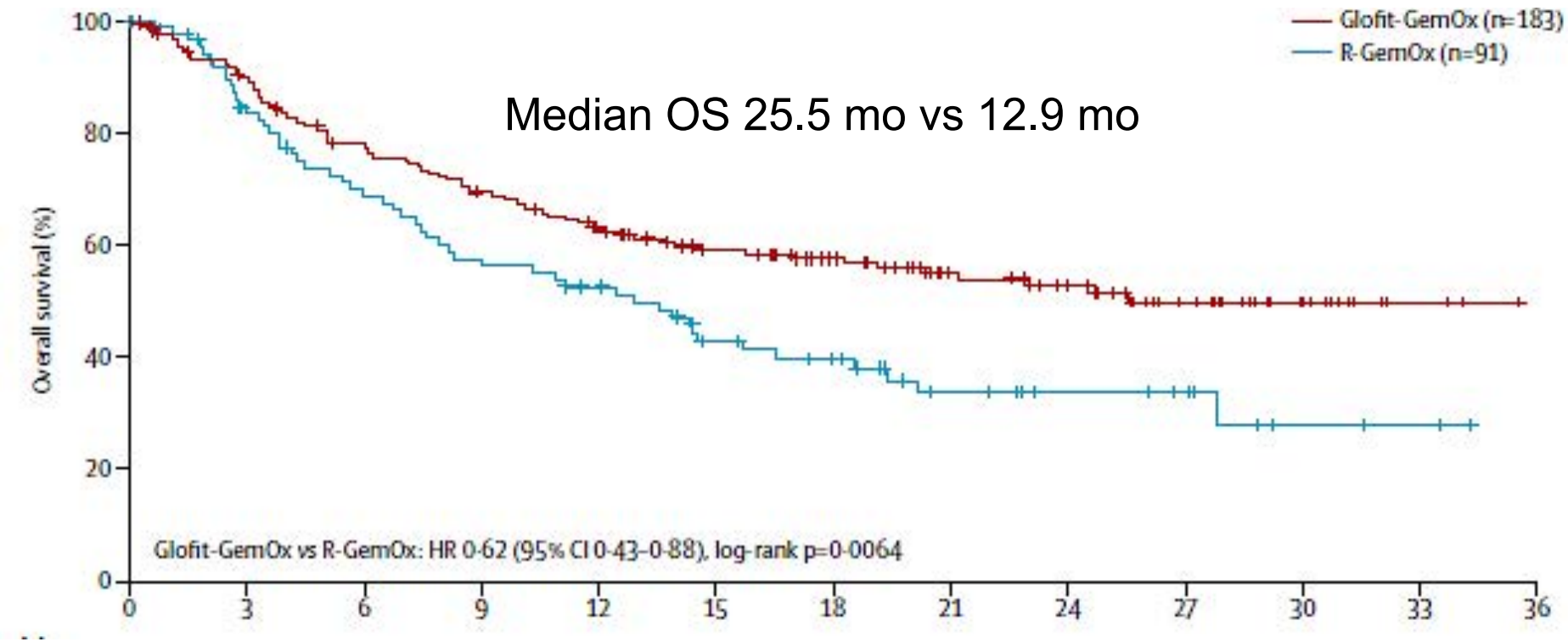
## Efficacy differed between geographic regions




| | |
|---|---|
| HR **0.27** (0.17 - 0.42) | China, Taiwan, Korea, Australia (n=161, 59%) |
| HR 0.84 (0.44 - 2.59) | Europe (n=88) |
| HR 2.25 (0.48 - 10.5) | North America (n=25) |

Abramson et al Lancet 2024;404:1940–54

# OS: Phase 3 STARGLO: Glofit-GemOx vs R-GemOx




Median OS 25.5 mo vs 12.9 mo

| | |
|---|---|
| HR **0.41** (0.27 - 0.64) | China, Taiwan, Korea, Australia (n=161, 59%) |
| HR 1.09 (0.54 - 2.18) | Europe (N=88) |
| HR 2.62 (0.56 - 12.3) | North America (n=25) |

Abramson et al Lancet 2024;404:1940–54

# Toxicity: STARGLO

| AE | Glofit-GemOx | R-GemOx |
|---|---|---|
| Neutropenia | 42% | 31% |
| **Serious infect** | **26%** | **13%** |
| Gr 5 infect | 6% | 3% |
| **Gr 5** | **8%** | **5%** |
| Gr 1-2 CRS | 42% | 0 |
| Gr 3 CRS | 2% | 0 |

**FDA Ruling: Not Approved**
Results are not applicable to US population (9% of study population).

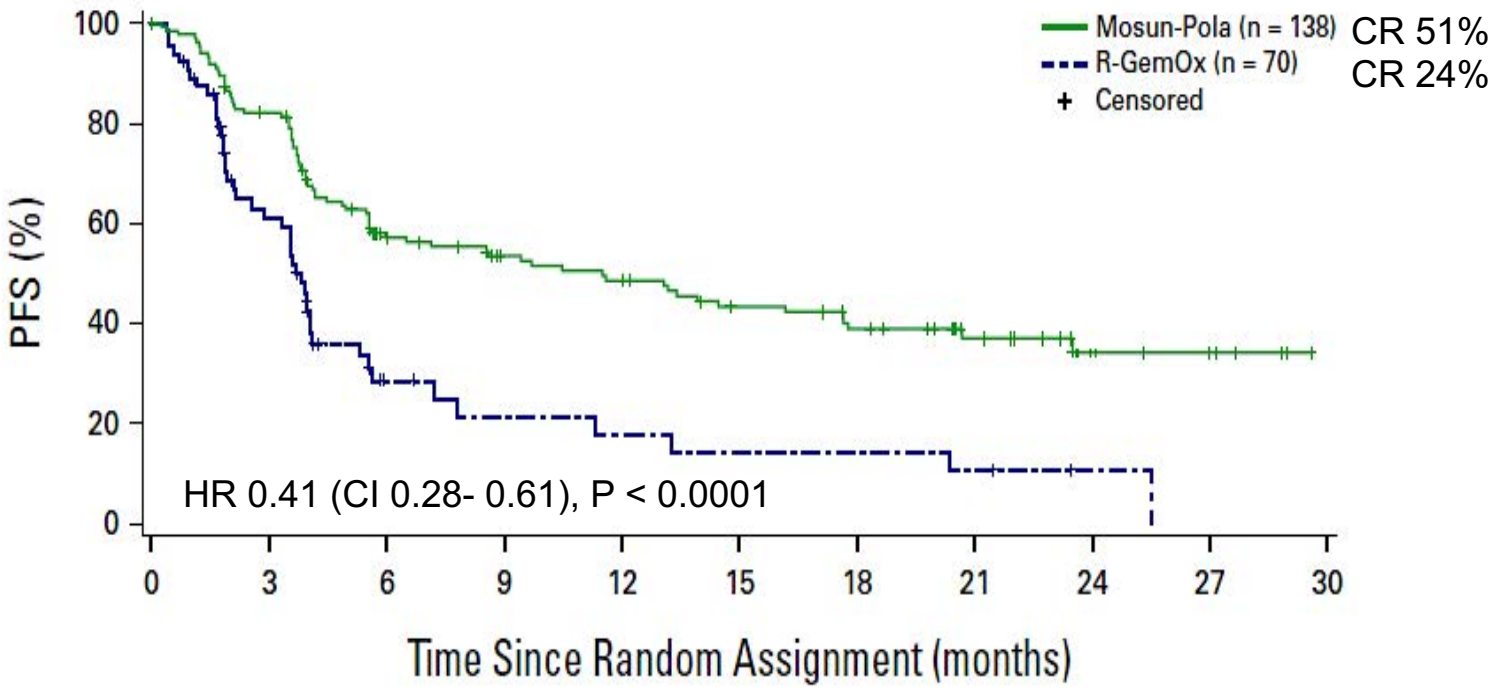
**Approved by European Commission**

**Added to NCCN Guidelines**

Abramson et al Lancet 2024;404:1940–54

# Phase 3 SUNMO: Mosun + Pola vs R-GemOx
# 2L+ R/R DLBCL, ASCT ineligible

Median PFS 11.5 mo vs 3.8 mo

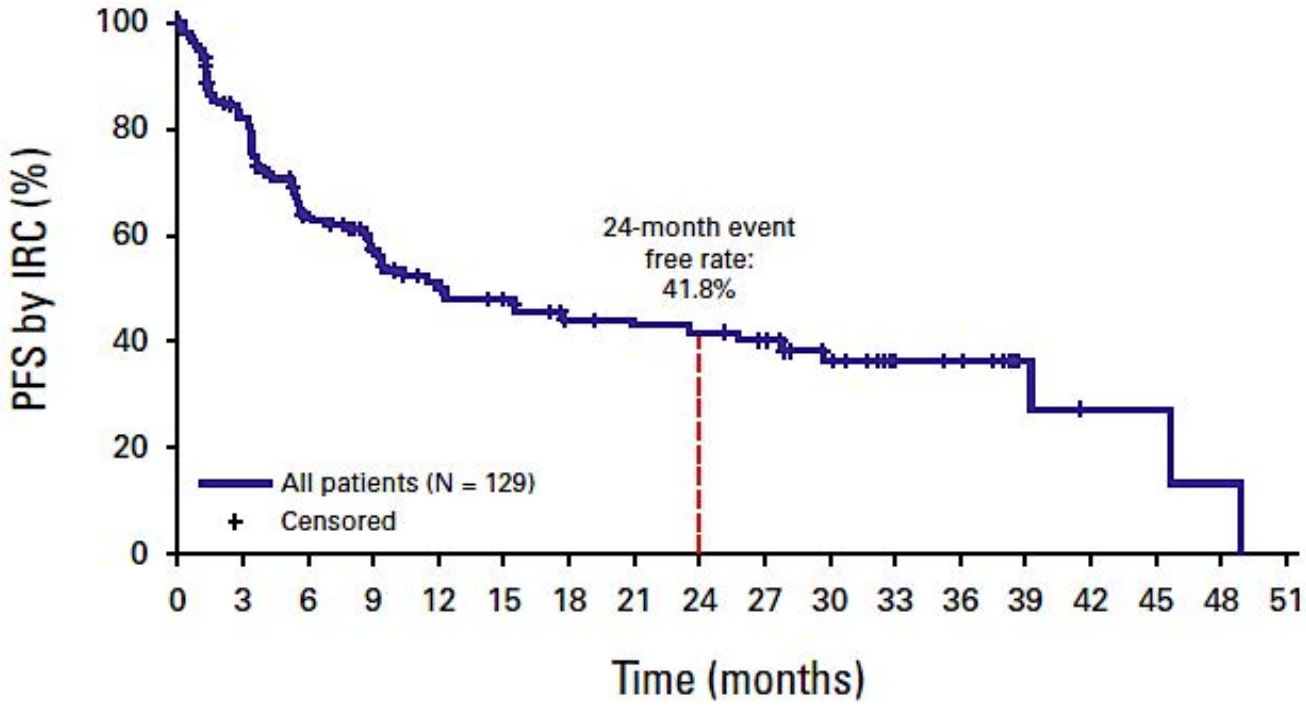



## Toxicity

| AE | Mosun-Pola | R-GemOx |
|---|---|---|
| Neutropenia | 46% | 55% |
| Serious infect | 16% | 14% |
| Gr 5 infect | 3% | 6% |
| Gr 5 | 6% | 7% |
| Gr 1-2 CRS | 25% | 0 |
| Gr 3 CRS | <1% | 0 |

Budde et al JCO 2025;10.1200/JCO-25-01957

# Phase Ib/II Glofit-Pola in ≥ 2L R/R DLBCL/HGBCL



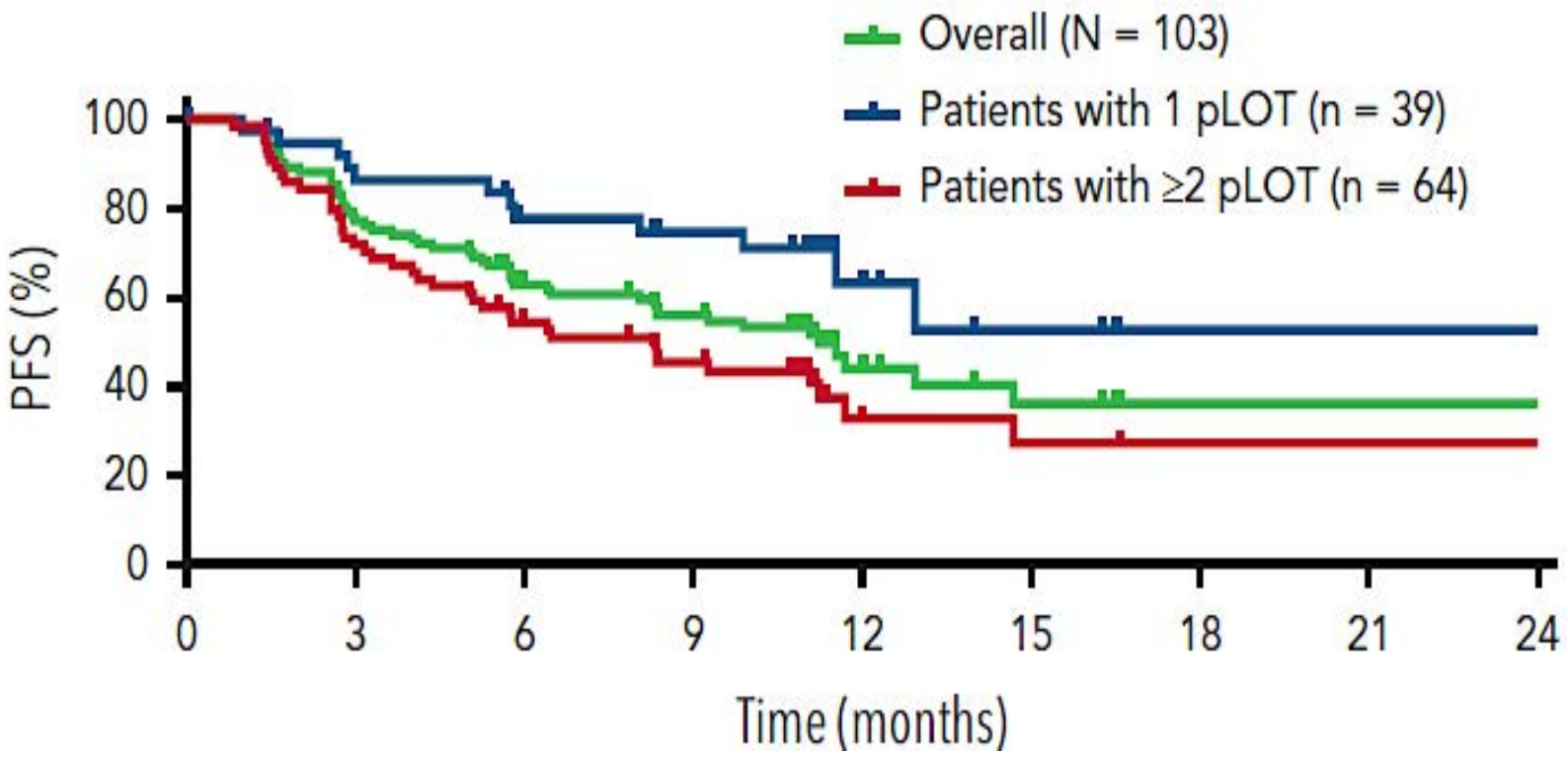

## Toxicity

| AE | Glofit-Pola |
|---|---|
| Neutropenia | 42% |
| Serious infect | 23% |
| Gr 5 infect | 5% |
| Gr 5 | 9% |
| Gr 1-2 CRS | 43% |
| Gr ≥3 CRS | 1.9% (1pt Gr5) |

Hutchings, JCO 2025; 10.1200/JCO-25-00992

# Phase Ib/II EPCORE NHL-2 Trial: Epcor-GemOx ≥ 2L R/R DLBCL

## 2nd vs later line of therapy significantly affected outcomes




12mo PFS 63%
12mo PFS 44%
12mo PFS 33%

Brody et al Blood 2025;145:1621–1631

# Phase 1-2 Trials of BsAb combinations in 1L DLBCL


| Agent | Phase | #pts | ORR% | CR% | DOCR | PFS |
|---|---|---|---|---|---|---|
| Glofit + RCHOP[1]<br>Glofit + Pola-RCHP | II | 40<br>40 | 100<br>100 | 98<br>98 | -<br>- | 24 mo 86%<br>24 mo 86% |
| Mosun + Pola-CHP[2]<br>R + Pola-CHP | II<br>(rand) | 40<br>22 | 75<br>86 | **73**<br>**77** | -<br>- | **24 mo 71%**<br>**24 mo 82%** |
| Epcor + R-CHOP[3] | II | 47 | 98 | 85 | 33-mo 75% | 33 mo 80% |
| Epcor + Pola-RCHP[4] | I/II | 35 | 100 | 97 | - | 21 mo 97% |

Phase 2 studies suggest addition of BsAb does not compromise chemo doses and CRS is lower grade and less frequent than single agent studies

1. Minson et al JCO 2025;43:2595-2605 2. Westin et al Blood Adv 2025;9:2461-72; 3.Falci et al ASH 2025; 4. Lavie et al ICML 2025

# Ongoing Phase III studies of bispecifics in combination with other therapies and in earlier settings in DLBCL

# Active Phase 3 trials
# BsAb + Chemo combinations in ≥2L DLBCL

| Agent | #pts | Pt Population | NCT number |
|---|---|---|---|
| Epcor + Len<br>vs R-GemOx<br>(EPCORE DLBCL-4) | 360 | ≥1 prior tx<br>ASCT rel/ref<br>CAR T ineligible | NCT06508658 |
| Epcor vs<br>R-GemOx or BR<br>(EPCORE DLBCL-1) | 480 | ≥1 prior tx<br>Failed/ineligible ASCT | NCT04628494 |
| Odron vs<br>SOC salvage + ASCT<br>(OLYMPIA-4) | 216 | Primary ref or rel ≤12 mo,<br>1 prior tx, ASCT eligible | NCT06230224 |

Accrual complete

# Active Ph3 trials
# BsAb + Chemo combinations in 1L DLBCL

| | Agent | #pts | Pt population | NCT number |
|---|---|---|---|---|
| Accrual complete | Epcor + R-CHOP<br>vs R-CHOP (EPCORE DLBCL-2) | 900 | Fit , IPI 2-5 | NCT05578976 |
| | Glofit + Pola-RCHP<br>vs Pola-RCHP (SKYGLO) | 1130 | Fit , IPI 2-5 | NCT06047080 |
| Accrual complete | Odron + R-CHOP<br>vs R-CHOP (OLYMPIA-3) | 900 | Fit , IPI 2-5 | NCT06091865 |

# Case Presentation: 66-year-old man with DLBCL and early relapse on axicabtagene ciloleucel receives glofitamab

**Dr Laurie Sehn (Vancouver, British Columbia)**

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**For which patients with R/R DLBCL are you prioritizing the use of bispecific antibodies (BSAbs), and in which line of therapy are you generally administering these agents?**

**How do you choose between CAR T-cell therapy and a BSAb for a patient with R/R DLBCL who is eligible to receive both?**

**Do you have any hesitation administering a BSAb after CAR T-cell therapy or vice versa for a patient with R/R DLBCL?**

# Discussion Questions

**How do you compare the efficacy, tolerability and convenience of the available BSAbs for DLBCL?**

**For patients with R/R DLBCL to whom you plan to administer a BSAb, how do you choose between glofitamab and epcoritamab?**

# Case Presentation: 68-year-old man with Type 2 diabetes, CHF and COPD receives glofitamab monotherapy after glofitamab + GEMOX for relapsed GCB-type double-hit DLBCL

**Dr Matthew Lunning (Omaha, Nebraska)**

RTP RESEARCH TO PRACTICE

# Discussion Questions

**What is your experience with glofitamab, gemcitabine and oxaliplatin, and in which situations do you utilize this combination? What toxicities have you observed?**

**Where do you see BSAb “landing” in the next five years in DLBCL?**

# Agenda

**Module 1:** Rational Incorporation of Antibody-Drug Conjugates into the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Matasar

**Module 2:** Clinical Utility of CD19-Directed Monoclonal Antibodies for DLBCL and Follicular Lymphoma (FL) — Dr Leonard

**Module 3:** Optimal Use of Antibody-Drug Conjugates in the Treatment of Relapsed/Refractory DLBCL — Prof Zinzani

**Module 4:** Bispecific Antibody Therapy for DLBCL — Dr Bartlett

**Module 5: Bispecific Antibody Therapy for FL and Other Lymphoma Subtypes — Dr Nastoupil**

RTP RESEARCH TO PRACTICE

# Bispecific Antibodies FL, MZL and MCL

Loretta J. Nastoupil, MD

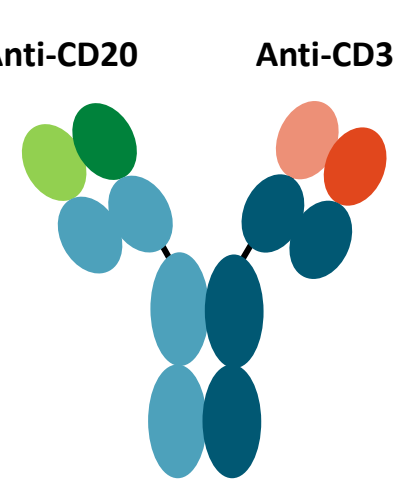
*Southwest Oncology*

*Durango, CO*

CommonSpirit

# CD20xCD3 Bispecific Antibodies: Structure and Function

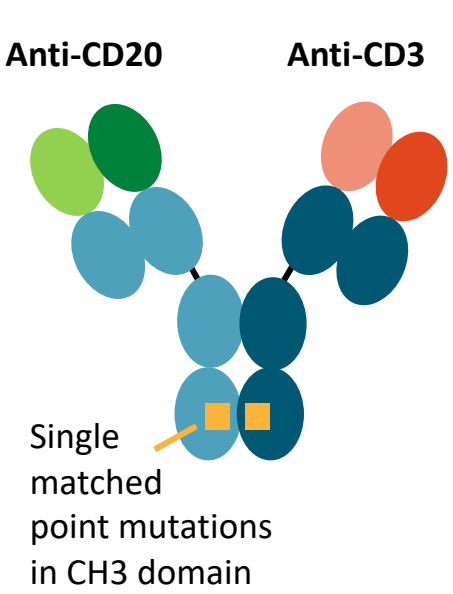
*Humanized mouse IgG1-based mAbs*




## Mosunetuzumab (IV*)

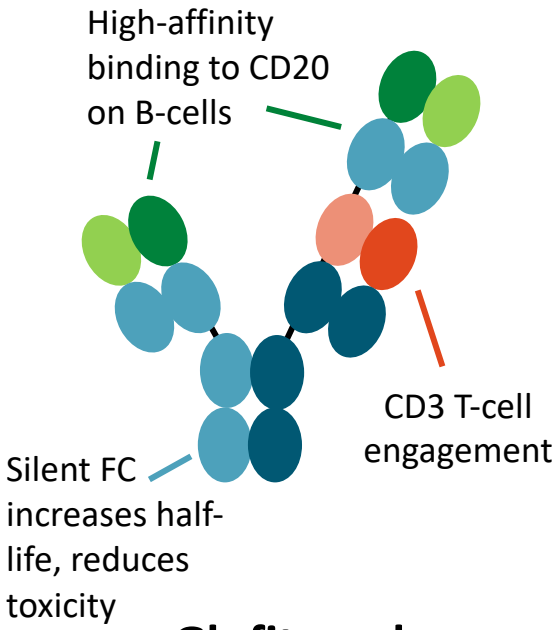
*SC formula under investigation.

**FDA accelerated approval: 3L+ R/R FL**



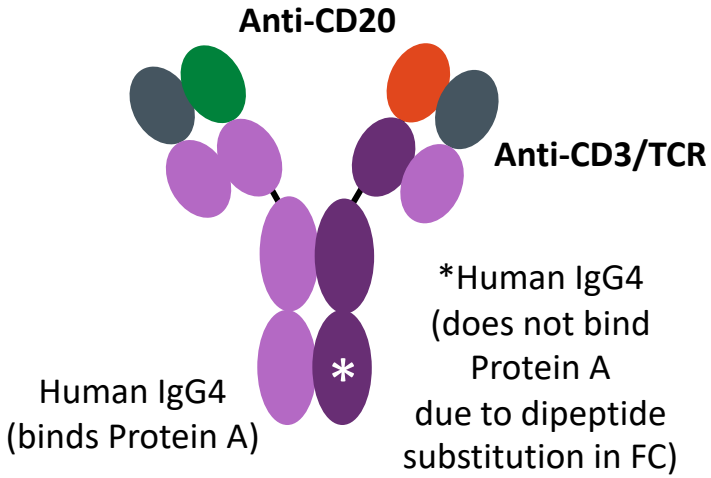

## Epcoritamab (SC)

**FDA full approval: monotherapy 3L+ FL and 2L+ in combo with R2**




## Glofitamab (IV)

**FDA accelerated approval: 3L+ LBCL arising from FL**



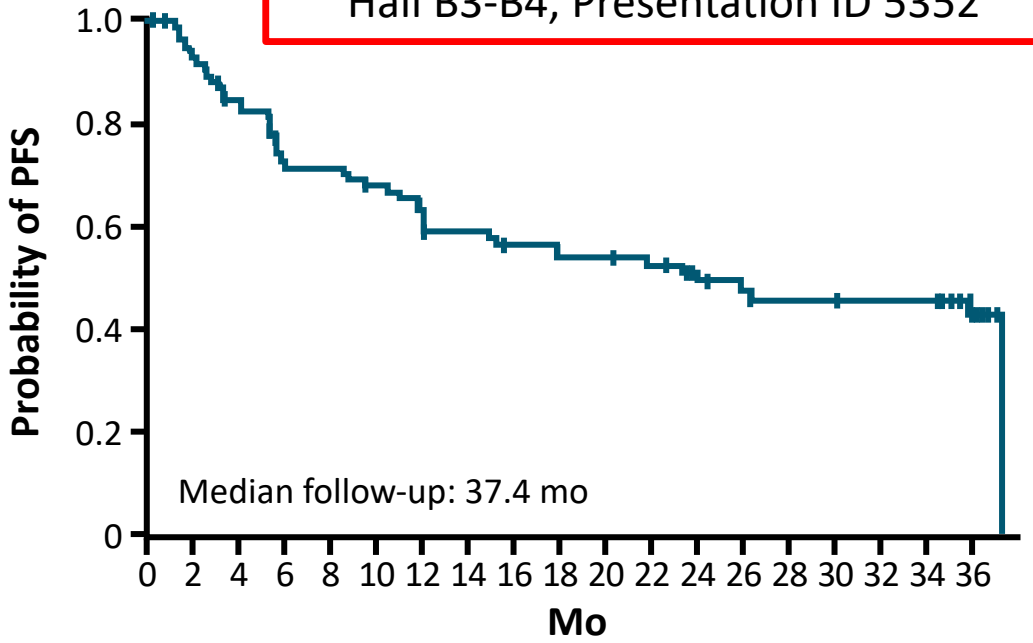

## Odronextamab (IV)

**EU approval: 2L+ R/R FL**

Mosunetuzumab PI; Epcoritamab PI; Glofitamab PI; Blair HA. Drugs. 2024;84:1651-1658; Falchi. Blood. 2023;141:467.

# Mosunetuzumab Phase II Study in R/R FL: 3-Yr Update

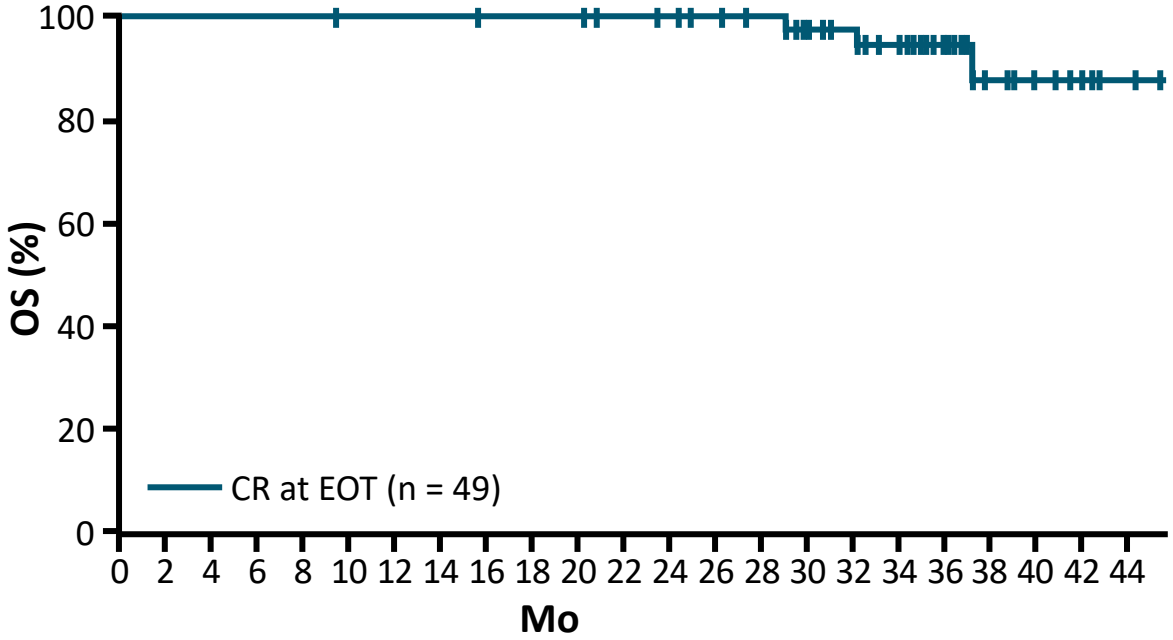
Monday, 12/8/25, 6:00-8:00PM, West Hall B3-B4, Presentation ID 5352




**Patients at Risk, n**

90 81 72 60 59 55 47 46 43 40 40 38 30 27 25 25 24 24 13

| Outcome, Mo (95% CI) | Mosunetuzumab (n = 90) |
|---|---|
| Median PFS | 24.0 (12.0-NR) |
| 36-mo PFS | 43.2 (31.3-55.2) |



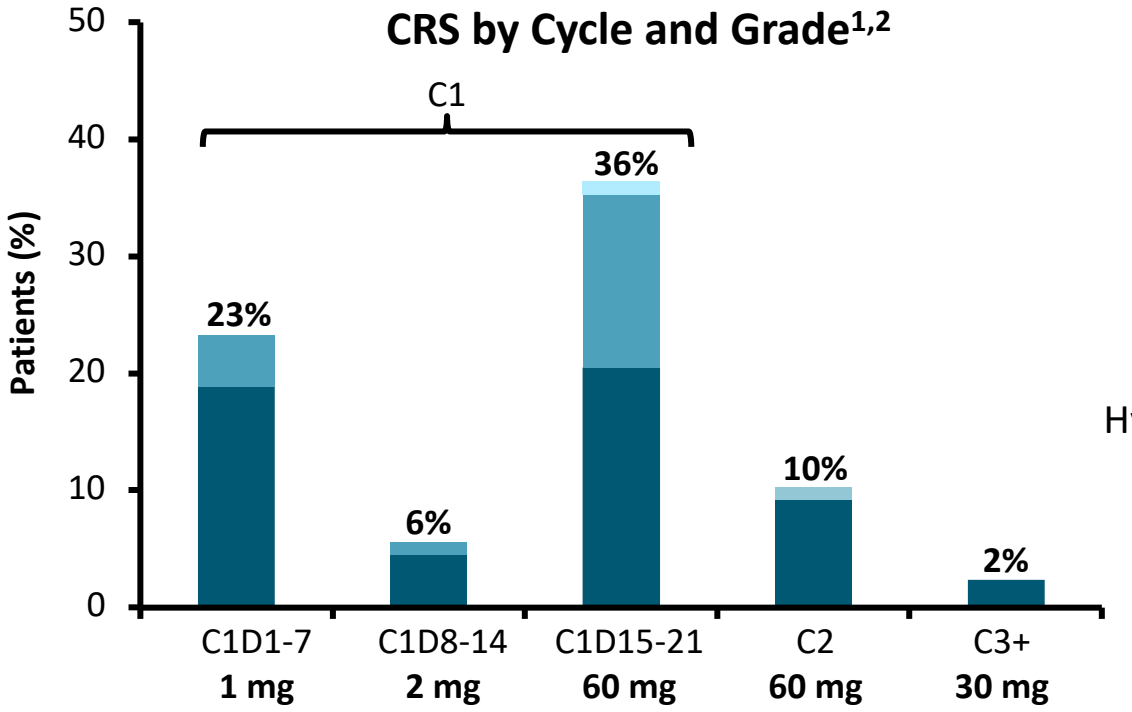

**Patients at Risk, n**

49 49 49 49 49 48 48 48 47 47 47 45 44 42 40 35 32 29 21 11 8 6 3

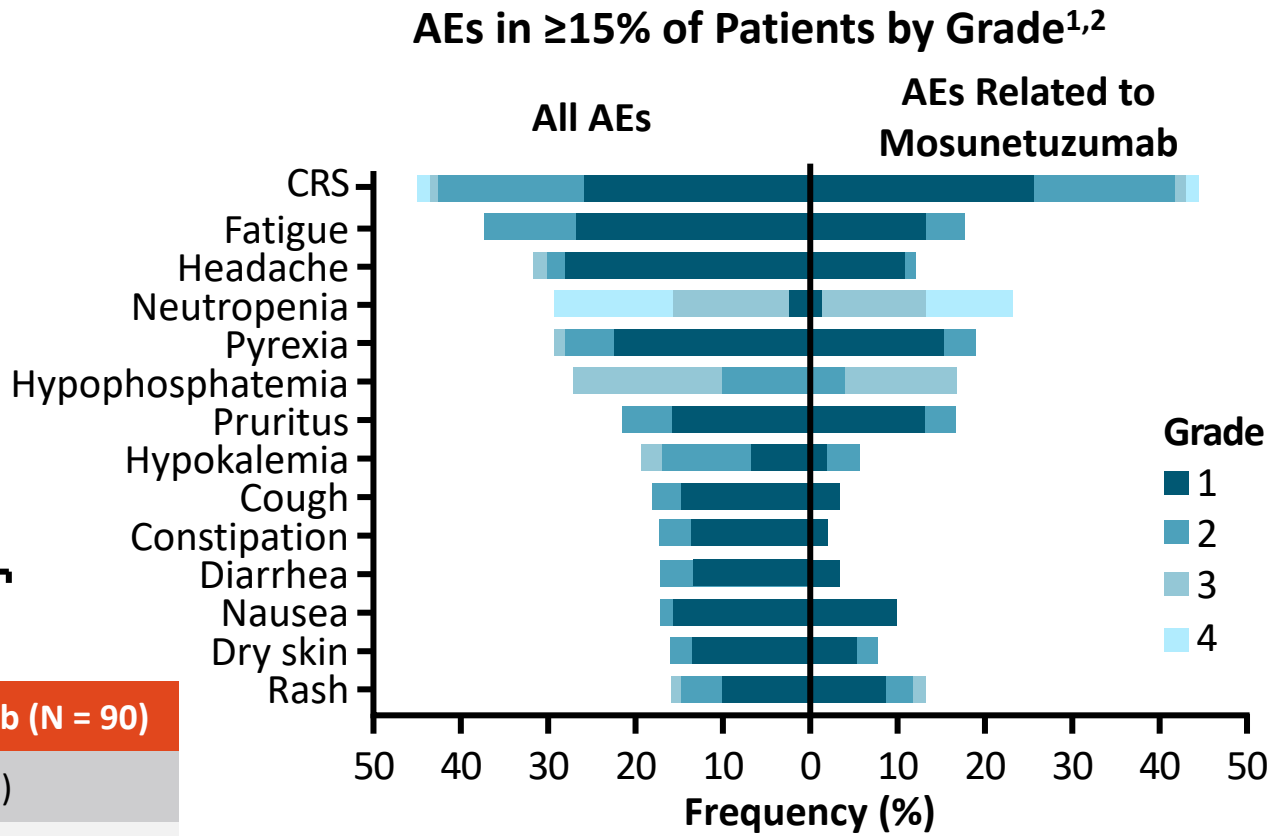
| Outcome, Mo (95% CI) | Mosunetuzumab (n = 90) |
|---|---|
| Median OS | NR (NE-NE) |
| 36-mo OS | 82.4 (73.8-91.0) |

Sehn. Blood. 2025;145:708.

# Single-Agent Mosunetuzumab in R/R FL: Safety




| CRS per ASTCT Criteria | Mosunetuzumab (N = 90) |
|---|---|
| Median duration, days (range)[1,2] | 3 (1-29) |
| Patients who received tx for CRS (n = 40), n (%)[2] | |
| ▪ Corticosteroids only | 6 (15) |
| ▪ Tocilizumab only | 3 (8) |
| ▪ Both | 4 (10) |




*Fatal AEs: malignant neoplasm progression (n = 1) and unexplained (n = 1). †D/c: mosunetuzumab related, CRS (n = 2); unrelated to mosunetuzumab, EBV viremia (n = 1), Hodgkin disease (n = 1).

1. Bartlett. ASH 2022. Abstr 610. 2. Budde. Lancet Oncol. 2022;23:1055.

# ASH 2025 Update: Mosunetuzumab 5-Year Follow-Up

PRESENTATION ID 5352
OCCC - West Halls B3-B4
Monday, December 8
06:00 PM - 08:00 PM EST

**Fixed treatment duration mosunetuzumab continues to demonstrate clinically meaningful outcomes in patients with relapsed/refractory (R/R) follicular lymphoma (FL) after ≥2 prior therapies: 5-year follow-up of a pivotal Phase II study**

Elizabeth Budde, MD PhD

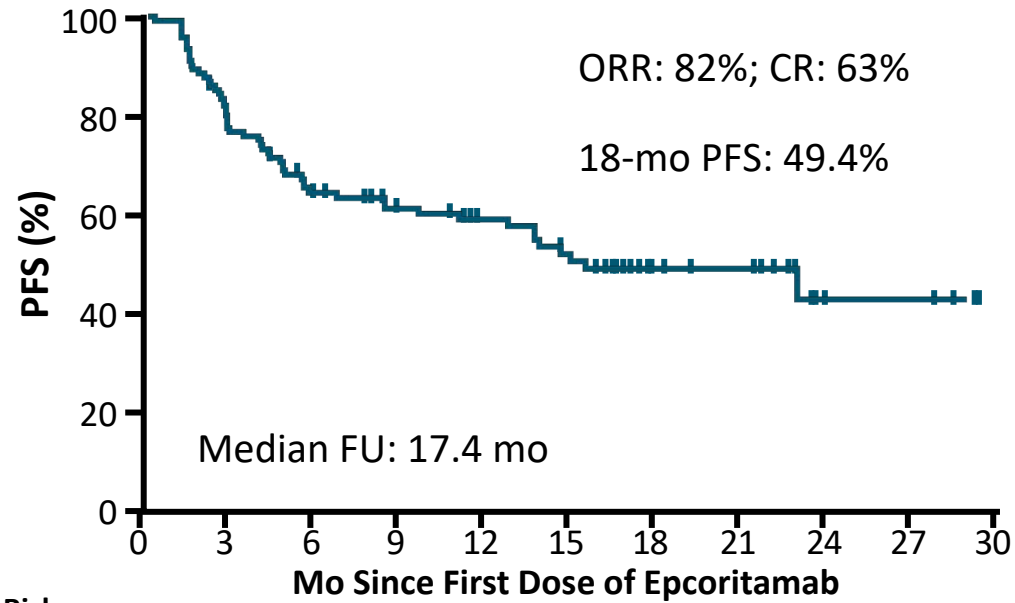
**Key Results:**

Ninety patients with R/R FL were enrolled, of whom 52% had a history of disease progression within 24 months from the start of first-line therapy (POD24) and 53% were double refractory.

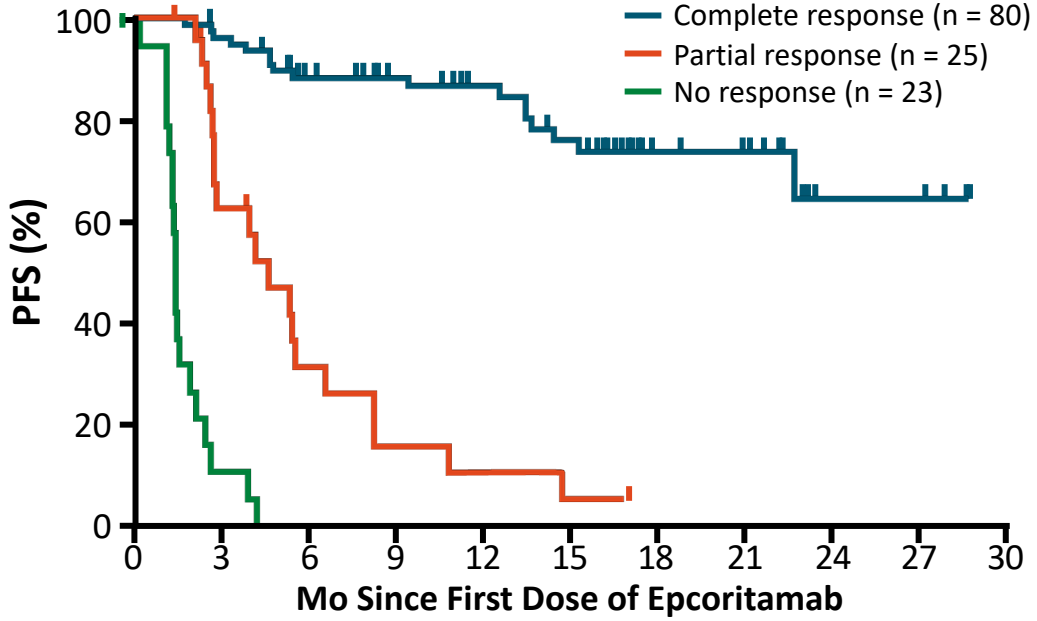
In the overall population (N=90), the ORR and CR rate were 78% and 60%, respectively; median DOR (n=70) was 46.4 months (95% confidence interval [CI]: 18.7–not estimable [NE]), and median DOCR (n=54) was not reached (95% CI: 44.1–NE). The 54-month DOR and DOCR rates were 46% (95% CI: 33.8–59.1) and 52% (95% CI: 36.2–67.9), respectively.

Median PFS was 24.0 months (95% CI: 12.0–53.2) in all patients, and 61.0 months (95% CI: 47.6–NE) in patients who achieved CR. The 5-year PFS rates were 36% (95% CI: 25.3–47.7) and 57% (95% CI: 42.0–71.6) in all patients and patients with CR, respectively. Median OS was not reached (95% CI: NE), and the 5-year OS rate was 78% (95% CI: 69.6–87.4).

# Epcoritamab in R/R Follicular Lymphoma




| Patients at Risk, n (number censored) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Pivotal cohort | 128 (0) | 90 (10) | 67 (19) | 57 (26) | 43 (38) | 35 (40) | 14 (60) | 12 (62) | 4 (69) | 4 (69) | 0 (73) |



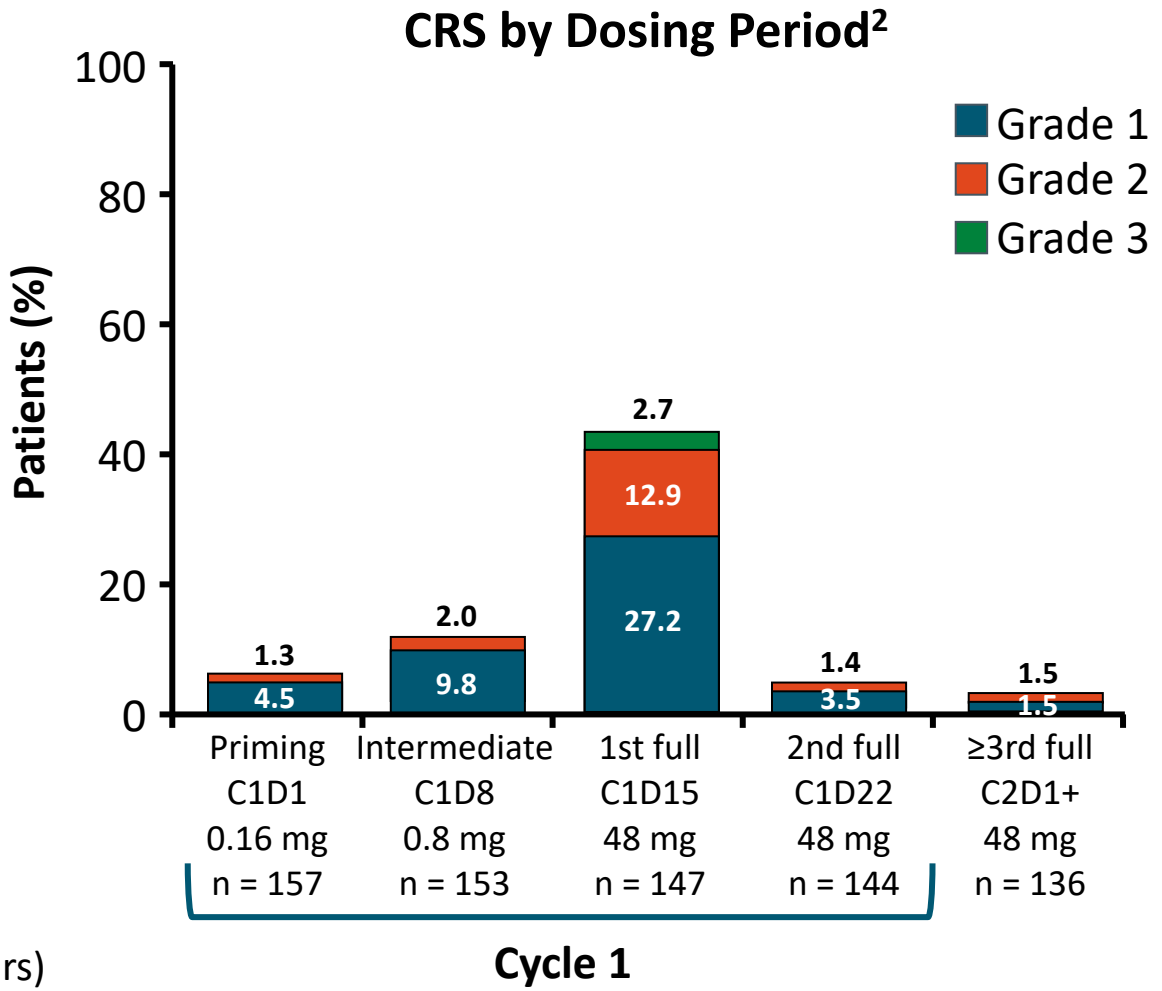

| Patients at Risk, n (number censored) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Complete response | 80 (0) | 75 (2) | 61 (10) | 54 (17) | 41 (29) | 34 (31) | 14 (50) | 12 (52) | 4 (59) | 4 (59) | 0 (63) |
| Partial response | 25 (0) | 13 (4) | 6 (5) | 3 (5) | 2 (5) | 1 (5) | 0 (6) | 0 (6) | 0 (6) | 0 (6) | 0 (6) |
| No response | 23 (0) | 2 (4) | 0 (4) | 0 (4) | 0 (4) | 0 (4) | 0 (4) | 0 (4) | 0 (4) | 0 (4) | 0 (4) |

Linton. Lancet Haematol 2024;11:E593.

# Epcoritamab in R/R FL: CRS and ICANS

| CRS Parameter,[1] n (%) | LBCL (N = 157) |
|---|---|
| Events<br>▪ Grade 1<br>▪ Grade 2<br>▪ Grade 3 | 80 (51)<br>50 (32)<br>25 (16)<br>5 (3) |
| Resolution, n/n (%) | 79/80 (99) |
| Median onset from first full dose, hr | 20 |
| Median duration, days (range) | 2 (1-27) |
| Received anti-cytokine treatment | 23 (15) |
| Led to treatment discontinuation | 1 (1) |

- Median follow-up: 20 mo
- Tocilizumab primarily used to address grade 2/3 CRS
- **ICANS**: 6.4%[2,3]
  - Median follow-up: ~11 mo
  - All grade 1/2, except 1 grade 5 (with multiple confounders)




1. Karimi. ASCO 2023. Abstr 7525. 2. Thieblemont. EHA 2022. Abstr LBA 2364. 3. Thieblemont. JCO. 2023;41:223.

# Epcoritamab in R/R FL: Safety in the Pivotal vs Optimization Cohorts

| Event, n (%) | Pivotal Cohort (n = 128) | | | |
|---|---|---|---|---|
| | Grade 1/2 | Grade 3 | Grade 4 | Grade 5 |
| CRS | 83 (65) | 2 (2) | 0 | 0 |
| Injection-site reaction | 73 (57) | 0 | 0 | 0 |
| COVID-19 | 27 (21) | 18 (14) | 0 | 6 (5) |
| Fatigue | 36 (28) | 3 (2) | 0 | 0 |
| Neutropenia | 4 (3) | 16 (13) | 16 (13) | 0 |
| Diarrhea | 32 (25) | 2 (2) | 0 | 0 |
| Pyrexia | 29 (23) | 3 (2) | 0 | 0 |
| Headache | 25 (20) | 0 | 0 | 0 |

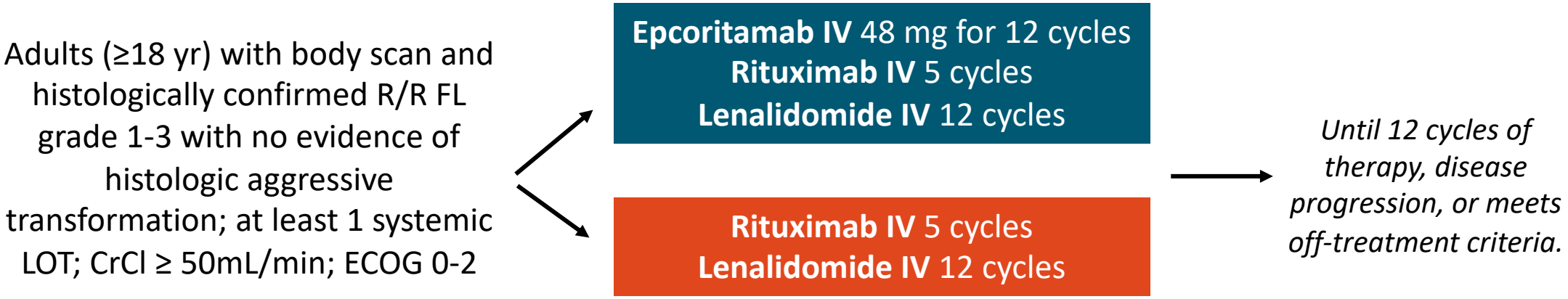
| Event n (%) | Cycle 1 Optimization Cohort (n = 86) | | | |
|---|---|---|---|---|
| | Grade 1/2 | Grade 3 | Grade 4 | Grade 5 |
| CRS | 42 (49) | 0 | 0 | 0 |
| Injection-site reaction | 28 (33) | 0 | 0 | 0 |
| Constipation | 18 (21) | 0 | 0 | 0 |
| COVID-19 | 13 (15) | 5 (6) | 0 | 0 |
| Neutropenia | 1 (1) | 9 (10) | 8 (9) | 0 |
| Fatigue | 17 (20) | 0 | 0 | 0 |
| Cough | 14 (16) | 0 | 0 | 0 |
| Headache | 11 (13) | 1 (1) | 0 | 0 |

- In the cycle 1 optimization cohort, a second intermediate dose of 3 mg was administered on Day 15

Linton. Lancet Haematol 2024;11:E593.

# EPCORE FL-1: Trial in Patients With R/R FL

- Global, multicenter, open-label phase III study




- **Primary endpoints:** ORR, and PFS as assessed by IRC per Lugano criteria
- **Key secondary endpoints:** CRR, BOR, OS, MRD
- The trial met the primary endpoints; full FDA approval.

FDA approves epcoritamab-bysp for follicular lymphoma indications. November 18, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-epcoritamab-bysp-follicular-lymphoma-indications; NCT05409066.

# ASH 2025 Update: Epcoritamab in EPCORE FL-1

PRESENTATION ID 466
OCCC - West Hall D2
**primary Phase 3 results from the epcore FL-1 trial of epcoritamab with rituximab and lenalidomide (R2) versus R2 for relapsed or refractory follicular lymphoma**
Lorenzo Falchi, MD

Sunday, December 7
09:30 AM - 11:00 AM EST

**Key Results:**

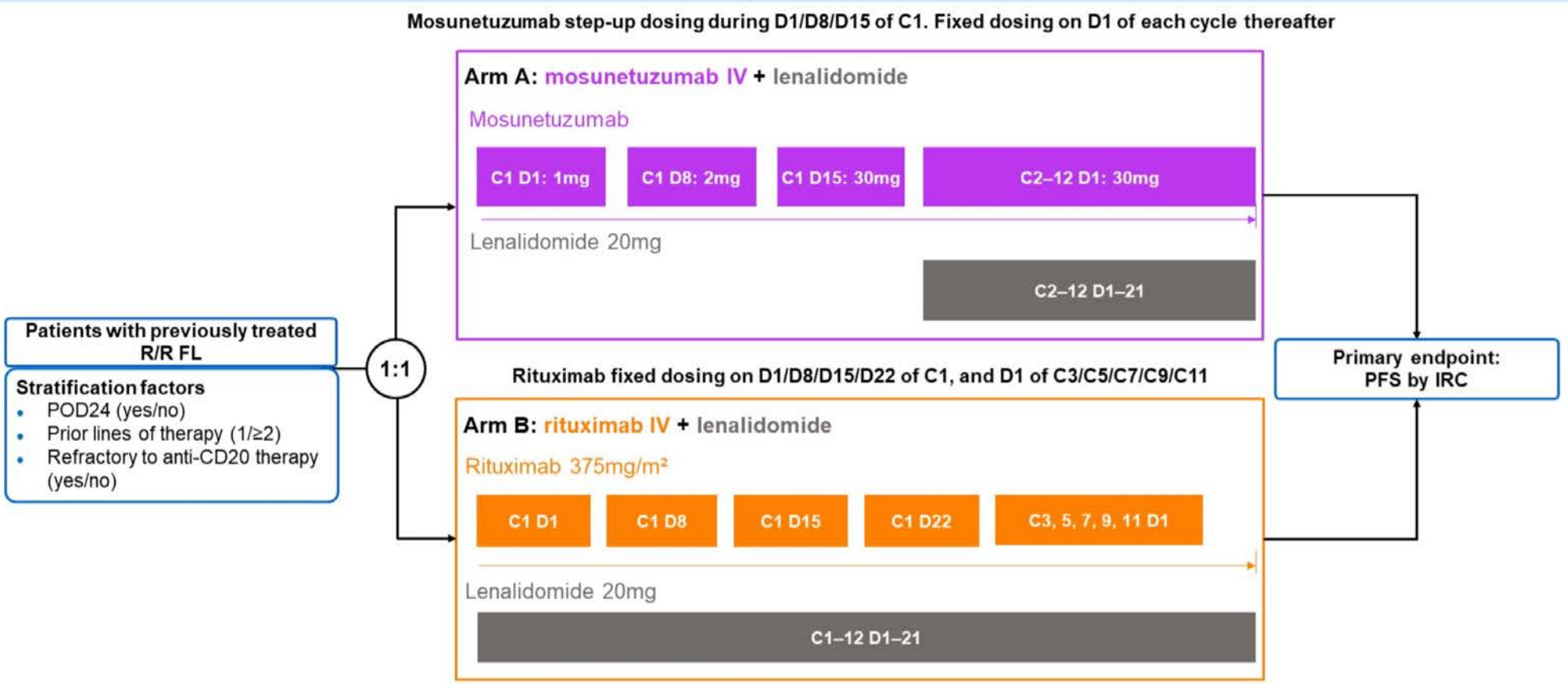
As of the Jan 10, 2025 data cut-off, 488 pts were randomized to receive E+$R^2$ (N=243) or $R^2$ alone (N=245). The median duration of follow-up was 10.4 months (95% CI: 9.8, 11.1).

A preplanned interim analysis was conducted after the first 232 pts achieved 12 months of follow-up post-randomization, and the ORR was significantly improved in pts treated with E+$R^2$ (95.7% [95% CI: 90.2, 98.6]) vs $R^2$ (81.0% [95% CI: 72.7, 87.7]; P<.0001). The 12-month DOR was 91.4% (95% CI: 84.0, 95.4) vs 57.0% (95% CI: 44.2, 68.0), respectively.

In the full ITT population (N=488), PFS was significantly longer in pts treated with E+$R^2$ vs those treated with $R^2$ (hazard ratio [HR] 0.21; 95% CI: 0.13, 0.33; P<.0001). Additionally, E+$R^2$ led to a significant improvement in CRR vs $R^2$ (74.5% [95% CI: 68.5, 79.8] vs 43.3% [95% CI: 37.0, 49.7]; P<.0001).

# Phase III CELESTIMO: Mosunetuzumab + Lenalidomide

**CELESTIMO** (NCT04712097) is a randomized, multicenter, open-label, Phase III study evaluating the efficacy and safety of M-Len versus rituximab plus Len (R-Len) in patients with R/R FL.




C, cycle; D, Day; FL, follicular lymphoma; IRC, independent review committee; IV, intravenous; PFS, progression-free survival; POD24, progression of disease within 24 months of first-line chemoimmunotherapy; R/R, relapsed/refractory.

Nastoupil L et al. ASCO 2022;Abstract TPS7588.

# ASH 2025 Update: Mosunetuzumab/Lenalidomide in CELESTIMO

PRESENTATION ID 1800
OCCC - West Halls B3-B4
Saturday, December 6
05:30 PM - 07:30 PM EST

**Promising response rates and manageable safety with mosunetuzumab plus lenalidomide (Mosun-Len) in patients with relapsed/refractory (R/R) follicular lymphoma (FL): US extension cohort from the Phase III CELESTIMO study**

Dahlia Sano

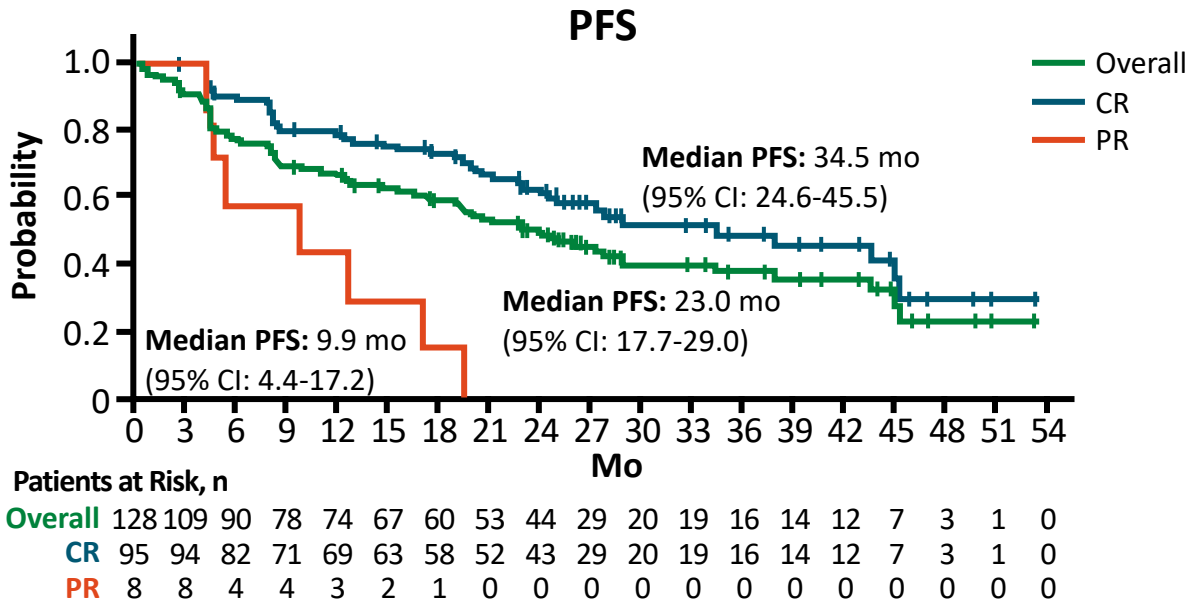
**Key Results:**

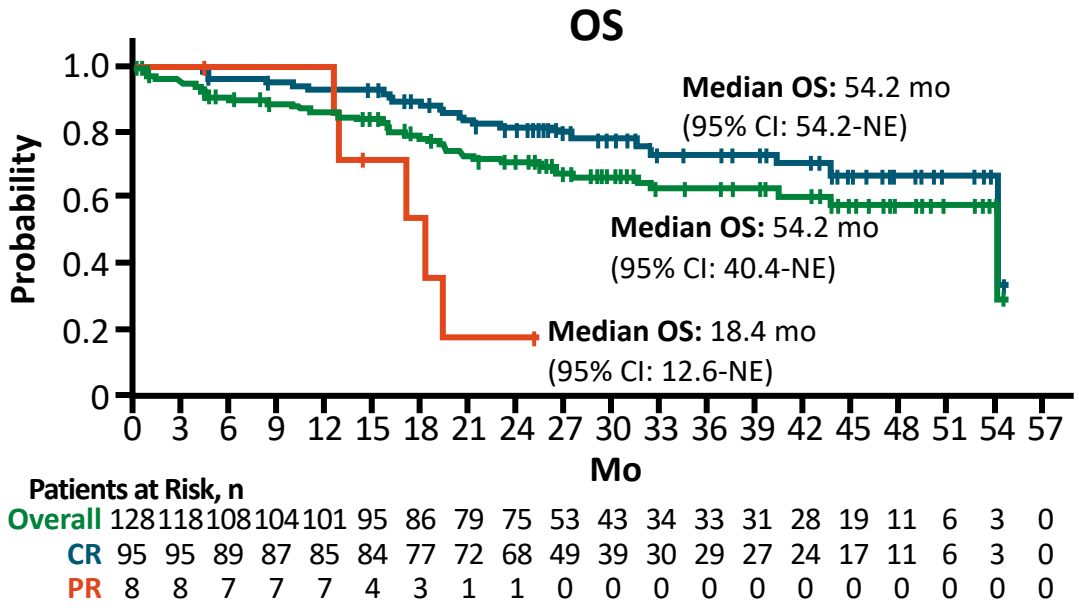
At data cut-off (June 9, 2025), 54 patients were enrolled in the US extension Arm C of the CELESTIMO trial. Median age was 62 years (range: 37–82); 59.3% (32/54) of patients were male; 40.4% (21/52) had a Follicular Lymphoma International Prognostic Index score of ≥3; 29.6% (16/54) had progressive disease within 24 months of first systemic therapy; 39.6% (19/48) were refractory to prior anti-CD20 therapy; and 17.0% (9/53) of patients had double-refractory disease.

Median duration of follow-up was 12.7 months (range: 5–20). ORR was 96.3% (n=52/54; 95% confidence interval [CI] 90.3–100.0) and CRR was 87.0% (n=47/54; 95% CI 75.1–94.6).

CRS was reported in 27.8% of patients (Gr 1, 22.2%; Gr 2, 3.7%; Gr 3, 1.9%); all CRS events resolved. Median duration of CRS was 4 days (range: 1–23). Neutropenia occurred in 40.7% of patients (Gr 1, 3.7%; Gr 2, 3.7%, Gr 3, 22.2%; Gr 4, 11.1%) and febrile neutropenia occurred in 3.7% of patients (all Gr 3). Infections were reported in 57.4% of patients (most common: COVID-19, 20.4%; sinusitis, 18.5%; upper respiratory tract infection, 16.7%) and were mainly Gr 2 (44.4%) in severity.

# ELM-2 Odronextamab in R/R FL: PFS and OS




| PFS Rate, % (95% CI) | N = 128 | CR (n = 95) | PR (n = 8) |
|---|---|---|---|
| 24 mo | 49.8 (40.1-58.73) | 62.8 (51.6-72.2) | 0 (NE-NE) |
| 36 mo | 37.5 (27.2-47.8) | 48.8 (35.9-60.6) | 0 (NE-NE) |

| OS Rate, % (95% CI) | N = 128 | CR (n = 95) | PR (n = 8) |
|---|---|---|---|
| 24 mo | 70.9 (61.7-78.3) | 81.1 (71.3-87.8) | 17.9 (0.8-53.8) |
| 36 mo | 62.6 (52.1-71.5) | 73.2 (61.0-82.1) | NE (NE-NE) |

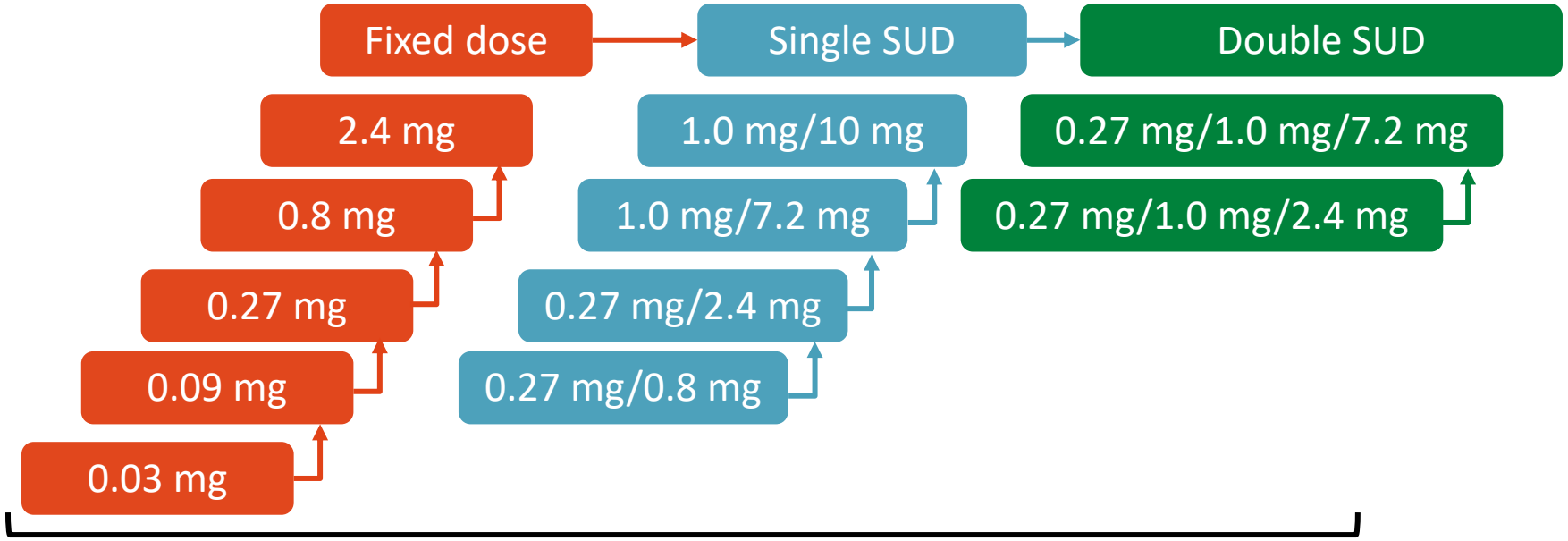
Median PFS in patients who were event-free at:

- 1 year (n = 74): 43.7 mo (95% CI: 27.8-NE)
- 2 years (n = 44): 45.5 mo (95% CI: 38.0-NE)

Luminari. EHA 2025. Abstr S235.

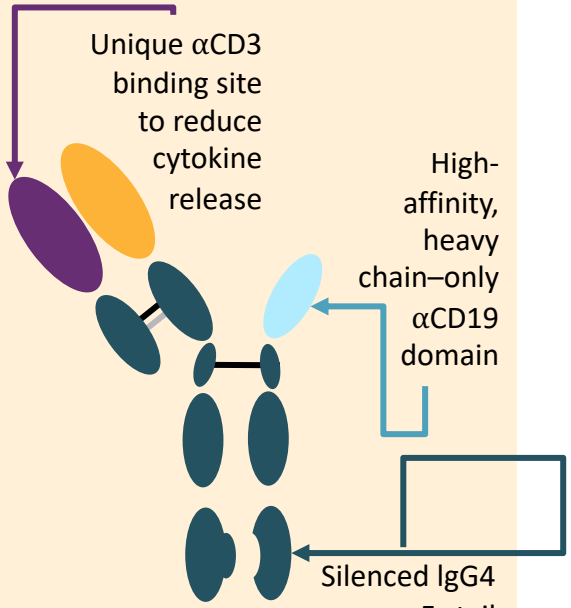
# Surovatamig (AZD-0486) in R/R FL: Double Step-up Dosing

## Study Design




**Enrollment for each dose may be expanded for up to N = 15 for dose optimization and RP2D selection**

## Activating αCD3




## Treatment Schedule

- AZD-0486 administered by IV infusion every 2 wk (28-day cycles) for up to 2 yr
  - In cycle 1 for double SUD, step-up dosing occurred in D1 and D8, with target dose on D15
- Q4W dosing was considered for patients in CR after C6

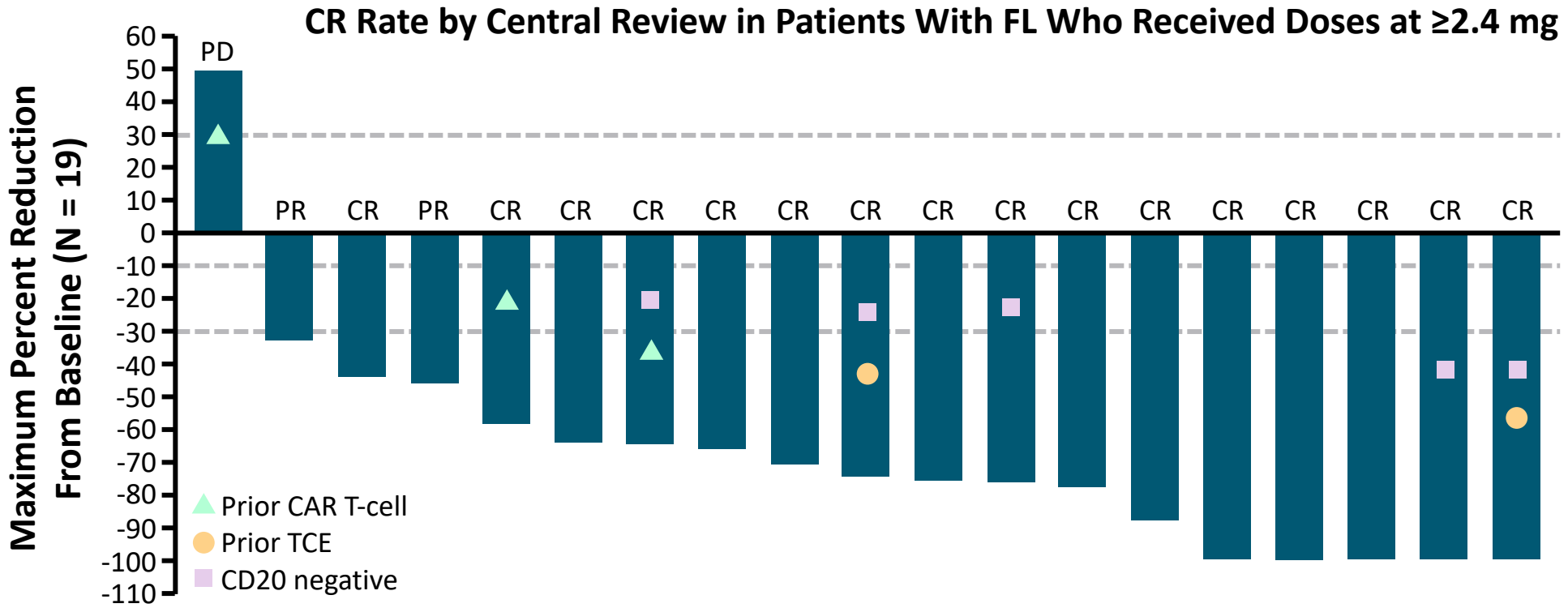
## Endpoints

- **Primary:** safety, tolerability, PK/PD
- **Secondary:** antitumor activity

Devata. EHA 2024. Abstr P1131.

# Surovatamig (AZD-0486): Efficacy in R/R FL

Monday, 12/8/25, 4:30-6:00 PM, Tangerine Ballroom 2, Presentation ID 1005

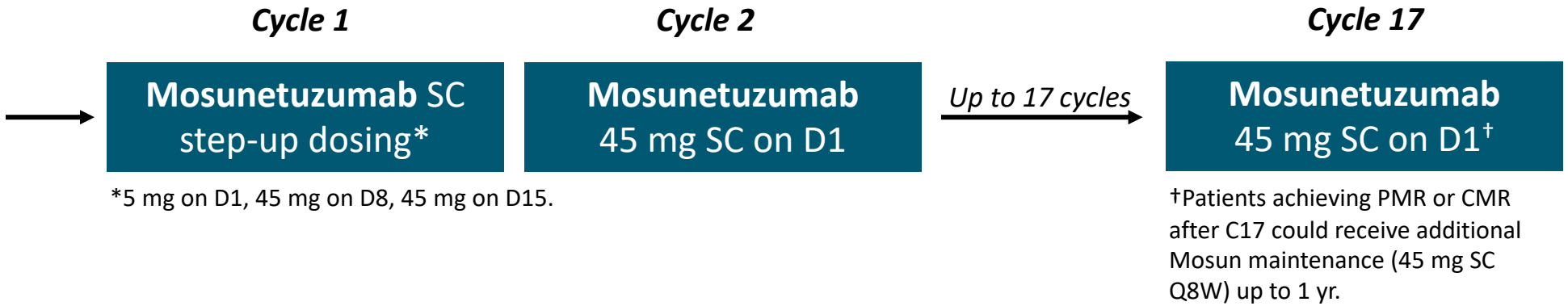



Devata. EHA 2024. Abstr P1131.

# MorningSun: Subcutaneous Mosunetuzumab in Patients With Previously Untreated FL

- Multicenter, multicohort, open-label phase II trial in patients with NHL

FL Cohort:
Adults with previously untreated FL; high tumor burden by GELF criteria; ECOG PS 0-2
(N = 102)



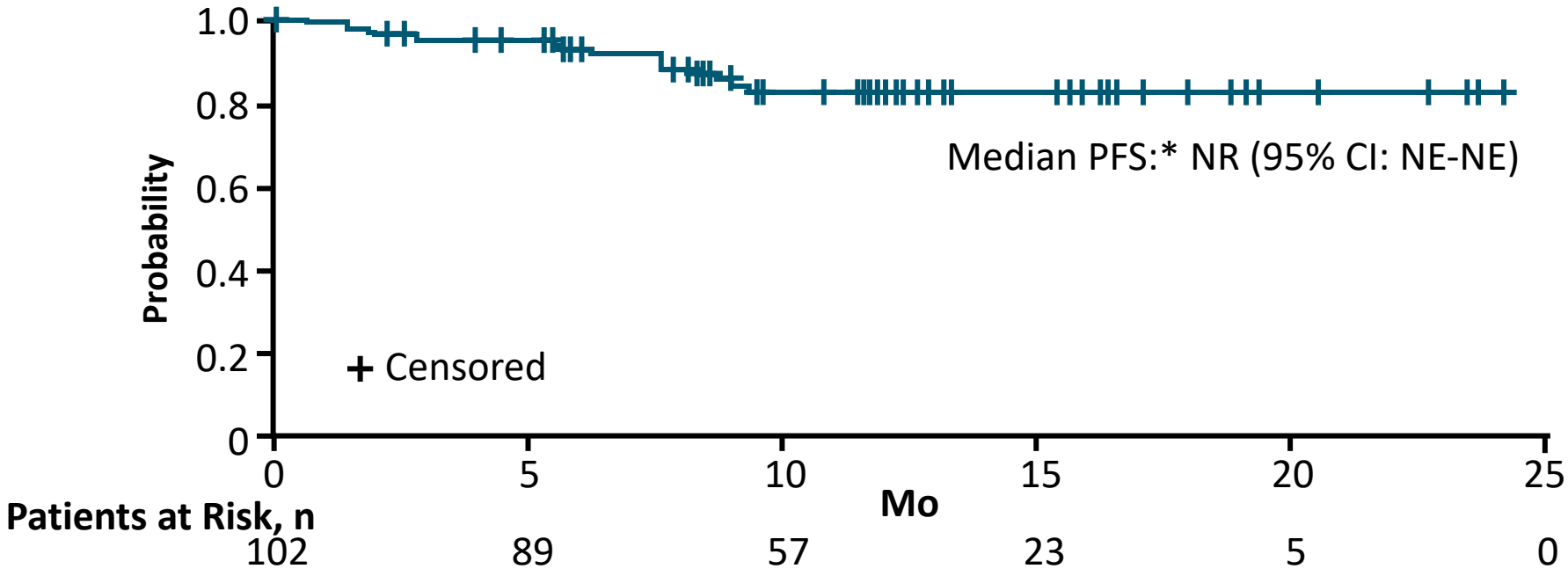

*5 mg on D1, 45 mg on D8, 45 mg on D15.

†Patients achieving PMR or CMR after C17 could receive additional Mosun maintenance (45 mg SC Q8W) up to 1 yr.

- **Primary endpoint:** PFS at 24 mo
- **Key secondary endpoints:** ORR, TTR, safety

Flinn. ASCO 2025. Abstr 7014. NCT05207670.

# MorningSun 1L FL Cohort: PFS with Mosunetuzumab SC



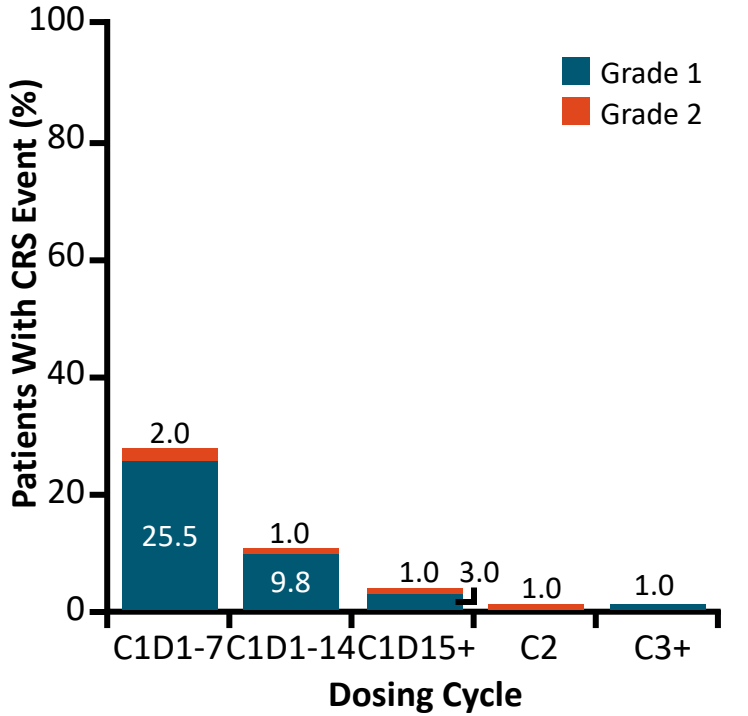

| | N = 102 |
|---|---|
| 12-month PFS rate, % (95% CI) | 82.8 (73.0-89.3) |
| Patients with progressive disease/relapse, n (%) | 10 (9.8) |
| Patients who died, n (%) | 5 (4.9) |

Flinn. ASCO 2025. Abstr 7014.

# MorningSun 1L FL Cohort: Safety with Mosunetuzumab SC

| n (%) | N = 102 |
|---|---|
| Any grade CRS* | 35 (34.3) |
| ▪ Grade 1 | 30 (29.4) |
| ▪ Grade 2 | 5 (4.9) |
| Median time to CCRS onset, days (range) | 2.0 (1-8) |
| Median CRS duration, days (range) | 2.5 (1-15) |
| CRS management | |
| ▪ Corticosteroids | 8 (7.8) |
| ▪ Tocilizumab | 6 (5.9) |
| ▪ Corticosteroids + tocilizumab | 3 (2.9) |
| CRS resolution | 35 (100) |
| Any grade AE | 102 (100) |
| Most common AEs of any grade (≥30%) | |
| ▪ Injection site reaction | 66 (64.7) |
| ▪ Fatigue | 43 (42.2) |
| ▪ CRS | 35 (34.3) |
| ▪ Headache | 32 (31.4) |
| ▪ Nausea | 31 (30.4) |

**Frequency of CRS Events by Cycle and Grade**




**CRS events were mostly grade 1 and all resolved**

| n (%) | N = 102 |
|---|---|
| AE leading to discontinuation | 8 (7.8) |
| Grade 3/4 AE | 41 (40.2) |
| Most common grade 3/4 AE (≥10%) | |
| ▪ Neutrophil count decreased | 12 (11.8) |
| Grade 5 AEs | |
| ▪ COVID-19 pneumonia | 2 (2.0) |
| ▪ Cardiogenic shock | 1 (1.0) |
| ▪ Death (unexplained) | 1 (1.0) |
| Select AEs of interest | |
| ▪ Infections (all) | 75 (73.5) |
| ▪ Grade 3 | 13 (12.7) |
| ▪ Grade 4 | 2 (2.0) |
| ▪ Grade 5 | 2 (2.0) |
| ▪ ICANS, grade 4 | 1 (1.0) |
| Serious AEs | 30 (29.4) |
| Most common serious AEs† | |
| ▪ Infections and infestations | 13 (12.7) |
| ▪ CRS | 11 (10.8) |

†Injection-site reaction, CRS and headache AEs were all grade 1/2; fatigue and nausea AEs were grade 1-3

*After the first mosunetuzumab SC dose, cytokine levels (IL-6, IFN-γ, and TNF-α) increased at C1D2, with a subsequent decrease at later time points. The patients who displayed upregulation of cytokines mainly experienced grade 1/2 CRS.

Flinn. ASCO 2025. Abstr 7014.

# Epcoritamab + Lenalidomide in Previously Untreated FL

- Multicenter, single-arm, open-label phase II study

Adults with histologically confirmed previously untreated FL grade 1-3a; ECOG 0-2 (N = 25)

→

**Lenalidomide** 20 mg PO D1-21 of each cycle
+
**Epcoritamab*** SC D1, D8, D15, D21 of cycles 1-3, D1 of cycles 4-12

→

*Until 12 cycles of therapy, disease progression, or meets off-treatment criteria*

*Doses: 160 µg on Day 1, 800 µg on Day 8, 3 mg on Day 22 of cycle 1; all others = 48 mg.

- **Primary endpoint:** CR rate
- **Key secondary endpoints:** ORR, PFS, DoR, safety

NCT06112847. Thiruvengadam. EHA 2025. Abstr PS1892.

# Glofitamab in R/R MCL: Phase I/II study design

**Study design[1]**

- Multicenter, open-label, dose-escalation and dose-expansion study of glofitamab with Gpt

**Glofitamab IV administration**

- Fixed-duration treatment: maximum 12 cycles

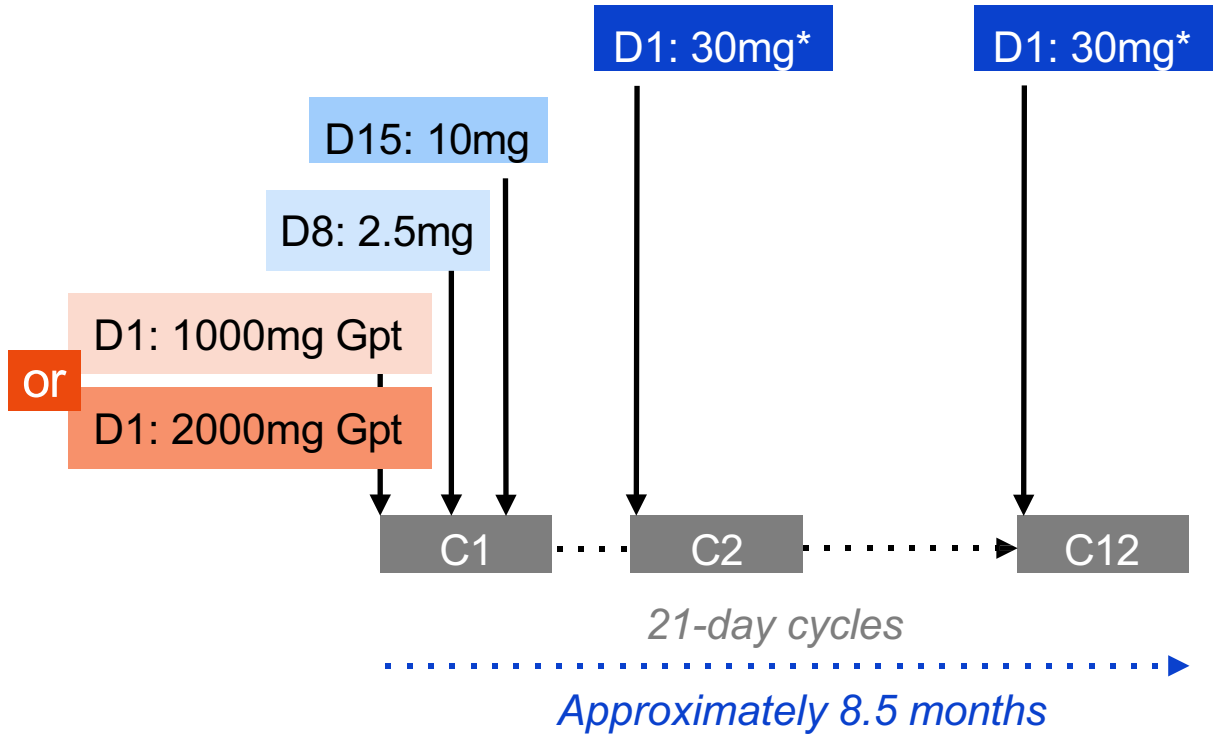
**Population characteristics**

- Age ≥18 years
- ≥1 prior systemic therapy
- ECOG PS 0 or 1

**CRS mitigation**

- Obinutuzumab pretreatment (1000mg or 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

## Dosing schedule

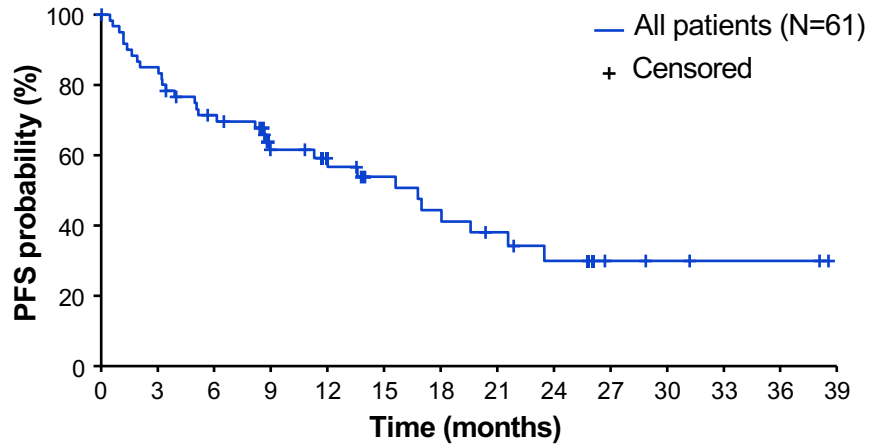



Clinical cut-off date: September 04, 2023.
*In the 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose in the dose escalation phase.
C, cycle; CRS, cytokine release syndrome; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; Gpt, obinutuzumab pretreatment; IV, intravenous.

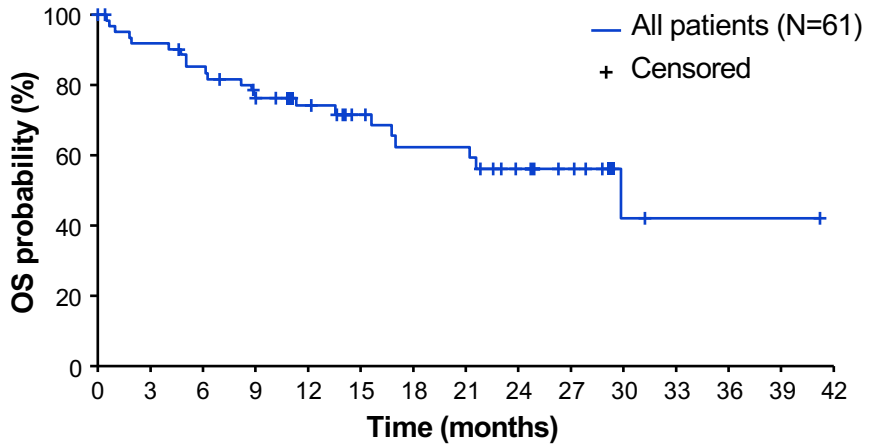
1. NCT03075696. Available at: https:www.clinicaltrials.gov.
Phillips et al EHA 2024.Abstract S231

# Glofitamab in R/R MLC: PFS and OS

## PFS




## OS†




| | Prior BTKi n=32* | All patients N=61* |
|---|---|---|
| **Median PFS follow-up, months (95% CI)** | 26.1 (13.5–31.2) | 19.6 (11.9–26.1) |
| **Median PFS, months (95% CI)** | 8.6 (3.4–15.6) | 16.8 (8.9–21.6) |
| **15-month PFS rate, % (95% CI)** | 33.0 (14.8–51.1) | 54.0 (40.1–67.8) |

| | Prior BTKi n=32* | All patients N=61* |
|---|---|---|
| **Median OS follow-up, months (95% CI)** | 24.7 (13.6–28.8) | 21.8 (14.0–24.9) |
| **Median OS, months (95% CI)** | 21.2 (9.0–NE) | 29.9 (17.0–NE) |
| **15-month OS rate, % (95% CI)** | 55.0 (36.5–73.6) | 71.4 (59.3–83.5) |

**Clinically significant PFS and OS at 15 months were achieved with fixed-duration glofitamab**

Clinical cut-off date: September 04, 2023. *ITT population. †At the time of analysis, 22 patients had died, the majority due to PD (n=7) or COVID-19 (n=7); other causes of death were pneumonia (n=1), septic shock (n=1), cardiac arrest (n=1), and unknown/other (n=5). All patients who died due to COVID-19 had achieved a CR.

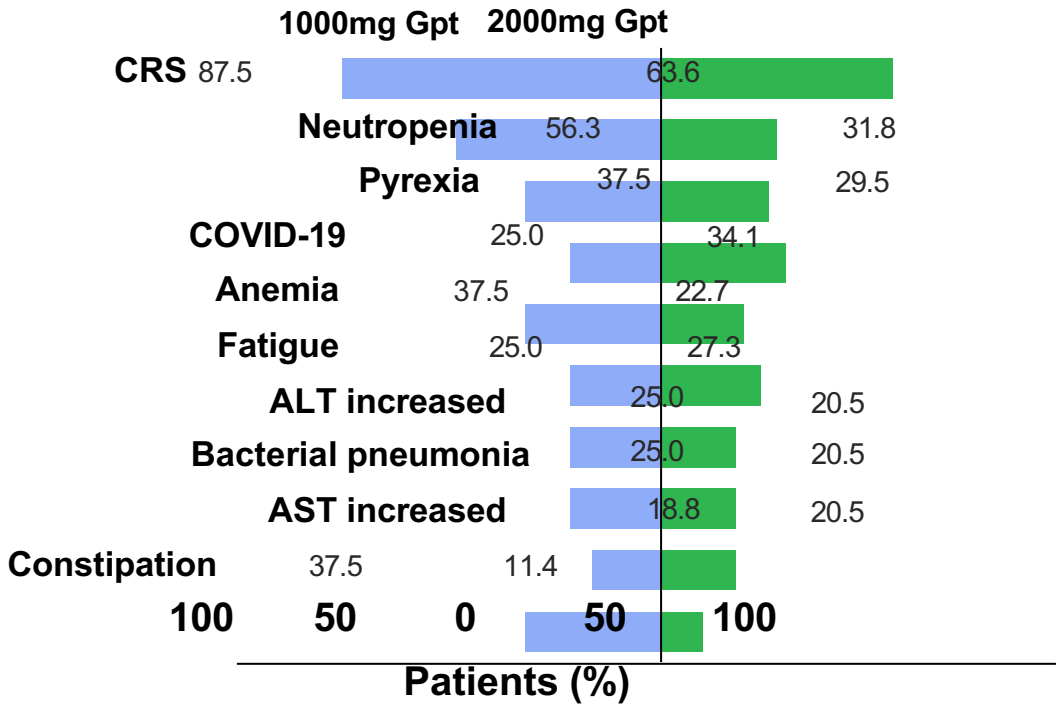
ITT, intention to treat; OS, overall survival; PD, progressive disease; PFS, progression-free survival.

Phillips EHA 2024. Abstract S231

# Glofitamab in R/R MCL: Safety Summary

| AEs, n (%) | 1000mg Gpt cohort (n=16) | 2000mg Gpt cohort (n=44) | All patients (N=60) |
|---|---|---|---|
| **Any grade AE** | 16 (100) | 44 (100) | 60 (100) |
| Glofitamab related | 16 (100) | 39 (88.6) | 55 (91.7) |
| **Serious AE** | 15 (93.8) | 32 (72.7) | 47 (78.3) |
| Glofitamab related | 12 (75.0) | 24 (54.5) | 36 (60.0) |
| **Grade 3/4 AE** | 13 (81.3) | 26 (59.1) | 39 (65.0) |
| Glofitamab related | 13 (81.3) | 22 (50.0) | 35 (58.3) |
| **Grade 5 AE** | 2 (12.5) | 7 (15.9) | 9 (15.0) |
| Glofitamab related | 0 | 0 | 0 |

## AEs with an incidence of ≥15% in all patients (N=60)




The incidence and severity of AEs were consistent with the known safety profile of glofitamab[1]

Clinical cut-off date: September 04, 2023.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate transaminase.


1. Dickinson MJ, et al. N Engl J Med 2022;387:2220–31
Phillips EHA 2024; Abstract S231

# Mosun+Polatuzumab in R/R MCL Study Schema

## Key inclusion criteria

- R/R MCL
- ECOG PS 0–2
- ≥2 prior therapies (including an anti-CD20 antibody, anthracycline or bendamustine therapy, and BTKi)

## Objectives

- Primary: efficacy of mosun-pola (best ORR by IRC)
- Secondary: efficacy by INV, durability of response, and safety

## Mosun-pola fixed duration administration (NCT03671018)

**Mosun**

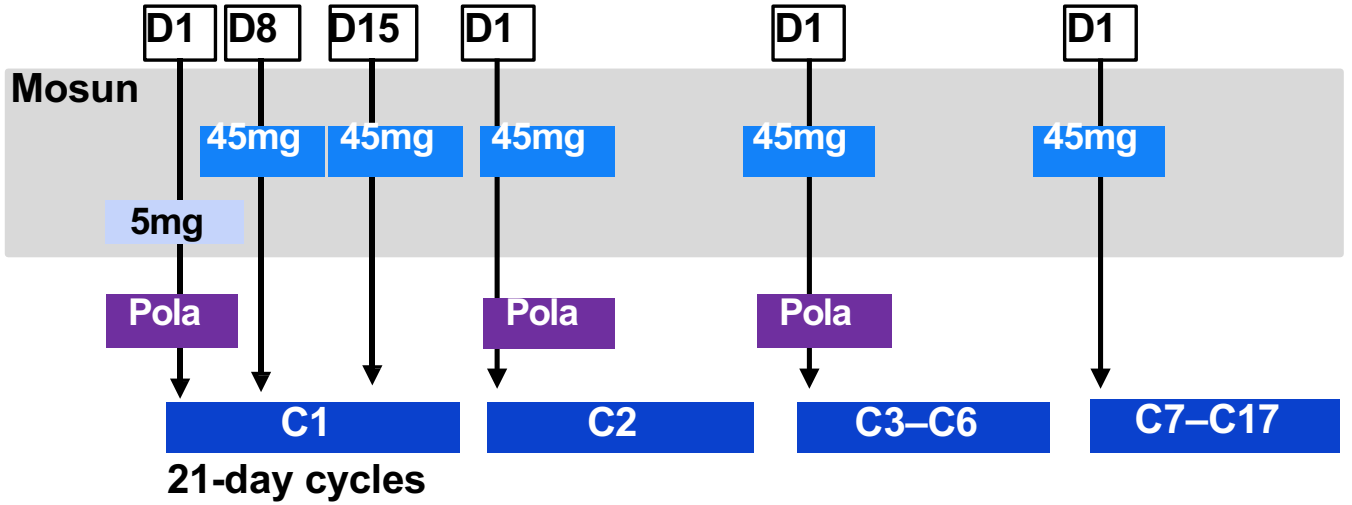
- SC administered in 21-day cycles with step-up dosing in Cycle (C) 1; total of 17 cycles

**Pola**

- 1.8mg/kg IV on Day [D],1 of C1–6

**No mandatory hospitalization**

All patients received corticosteroid premedication prior to each dose in C1*



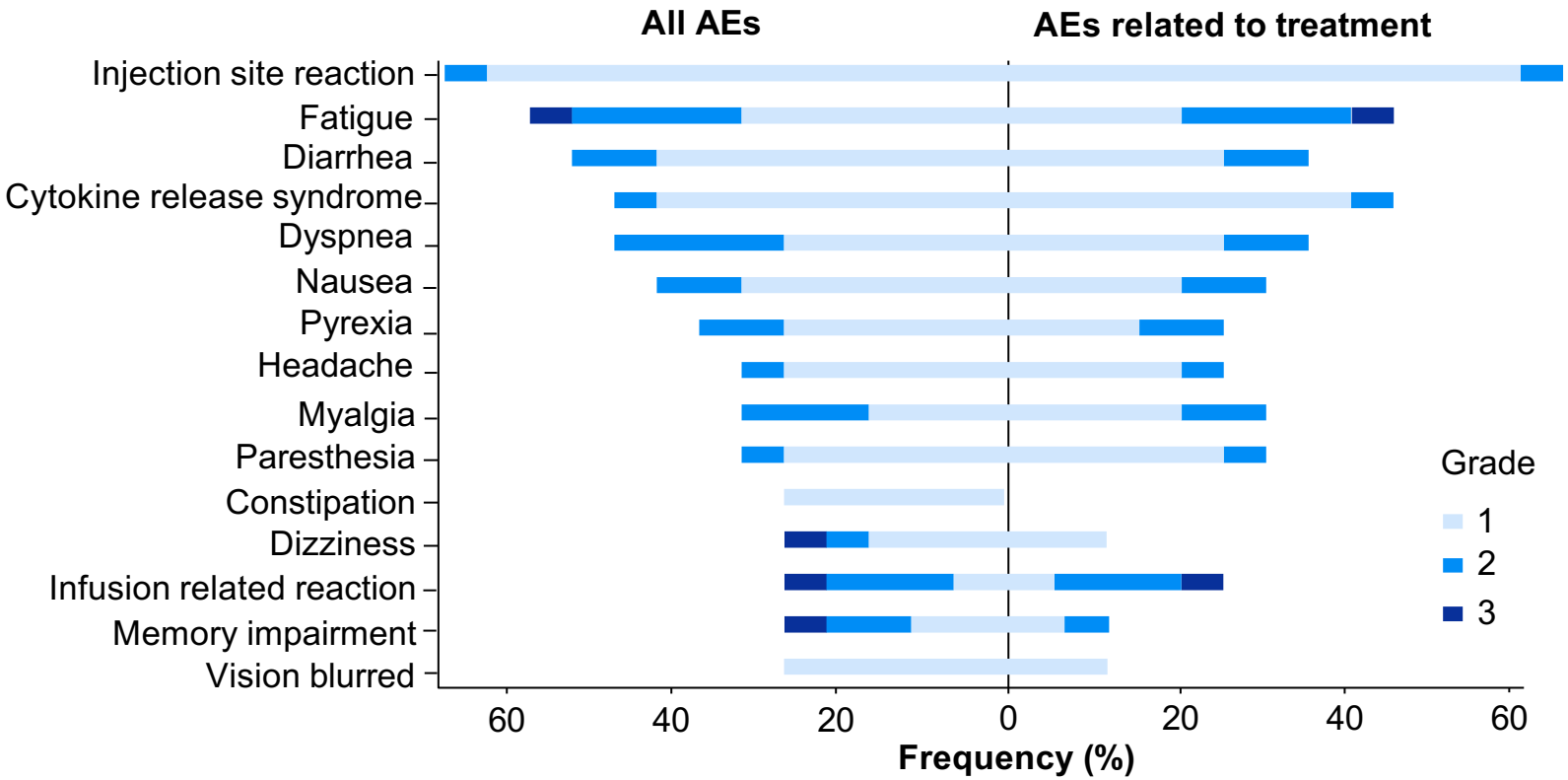

*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally.

Wang ML, et al. Blood. 2023;142(1_ Suppl):734.

# Mosun+Pola in R/R MCL: Safety profile

| AE summary, n (%) | N=20 |
|---|---|
| **AE** | 20 (100) |
| Treatment-related | 18 (90) |
| **Grade 3/4 AE** | 12 (60) |
| Treatment-related | 9 (45) |
| **Serious AE** | 13 (65) |
| Treatment-related | 9 (45) |
| **Grade 5 (fatal) AE** | 3 (15)* |
| Treatment-related | 0 |
| **AE leading to treatment discontinuation** | 4 (20)† |
| Treatment-related | 2 (10) |

**AEs (≥20%) by grade**




**No new safety signals observed; SC injection site reaction (all grade 1–2) was the most common AE**

Clinical cut-off date: July 6, 2023. *Includes COVID-19 pneumonia (n=2) and COVID-19 (n=1).
†Includes Grade 5 COVID-19 pneumonia (n=2; not treatment related), Grade 3 uveitis (n=1; mosun- and pola-related), Grade 3 pneumonitis (n=1; mosun- and pola-related; pola-discontinuation) and *Clostridioides difficile* (n=1; mosun-related; mosun-discontinuation).

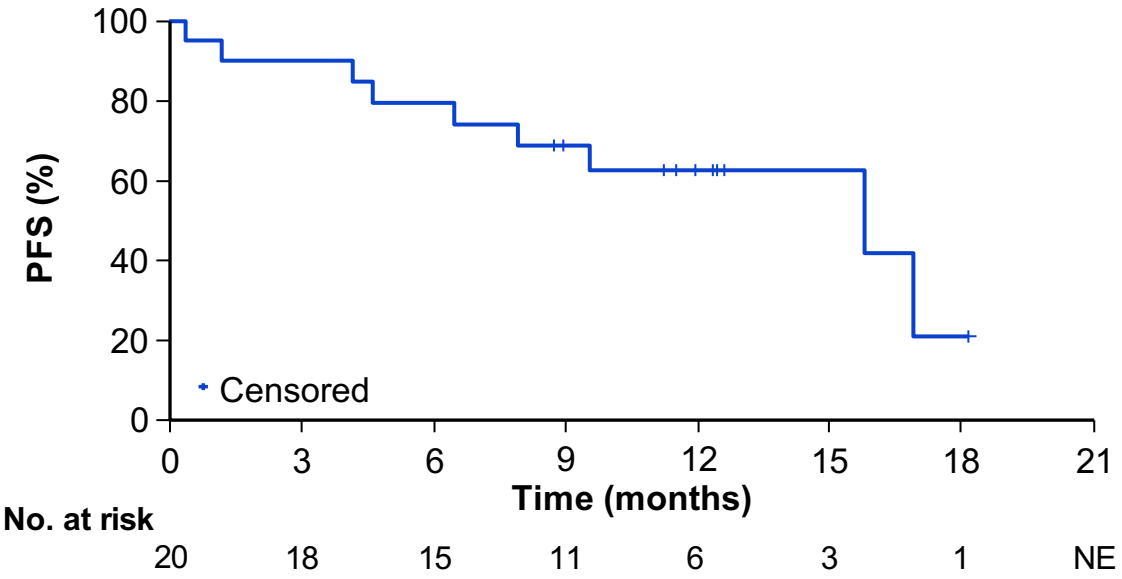
Wang ML, et al. Blood. 2023;142(1_ Suppl):734.

Sunday, 12/7/25, 6:00-8:00PM, West Hall B3-B4, Presentation ID 3735

# Mosun+Pola in R/R MCL: PFS and OS

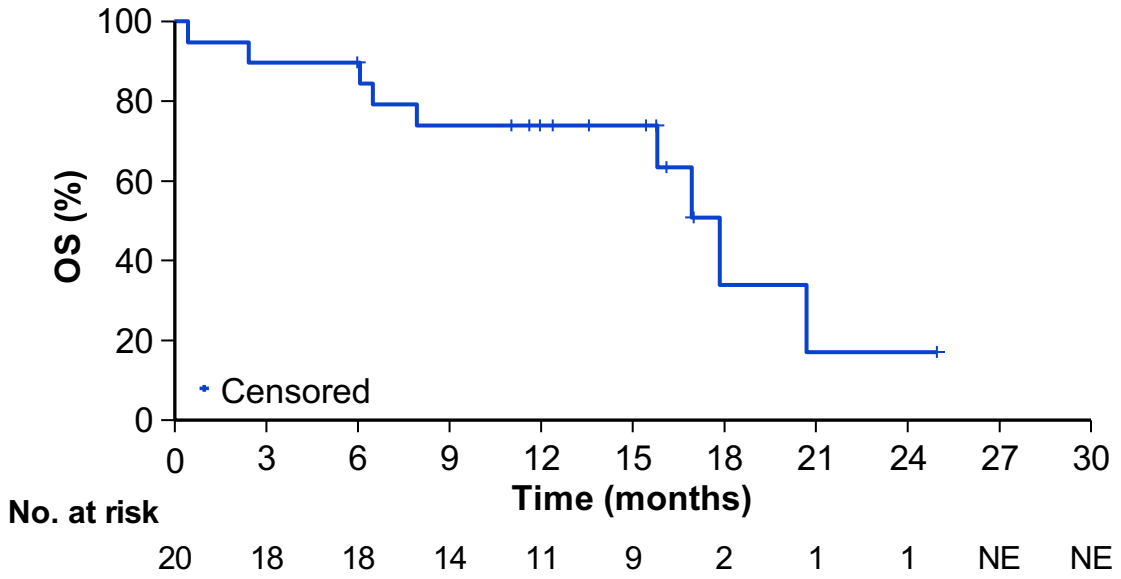
**Median follow-up: 15.8 months (95% CI: 12.4–NE)**

## PFS




| | N=20 |
|---|---|
| Median PFS, months (95% CI) | 15.8 (8.0–NE) |
| 9-month event-free rate, % (95% CI) | 68.8% (48.1–89.6) |

## OS



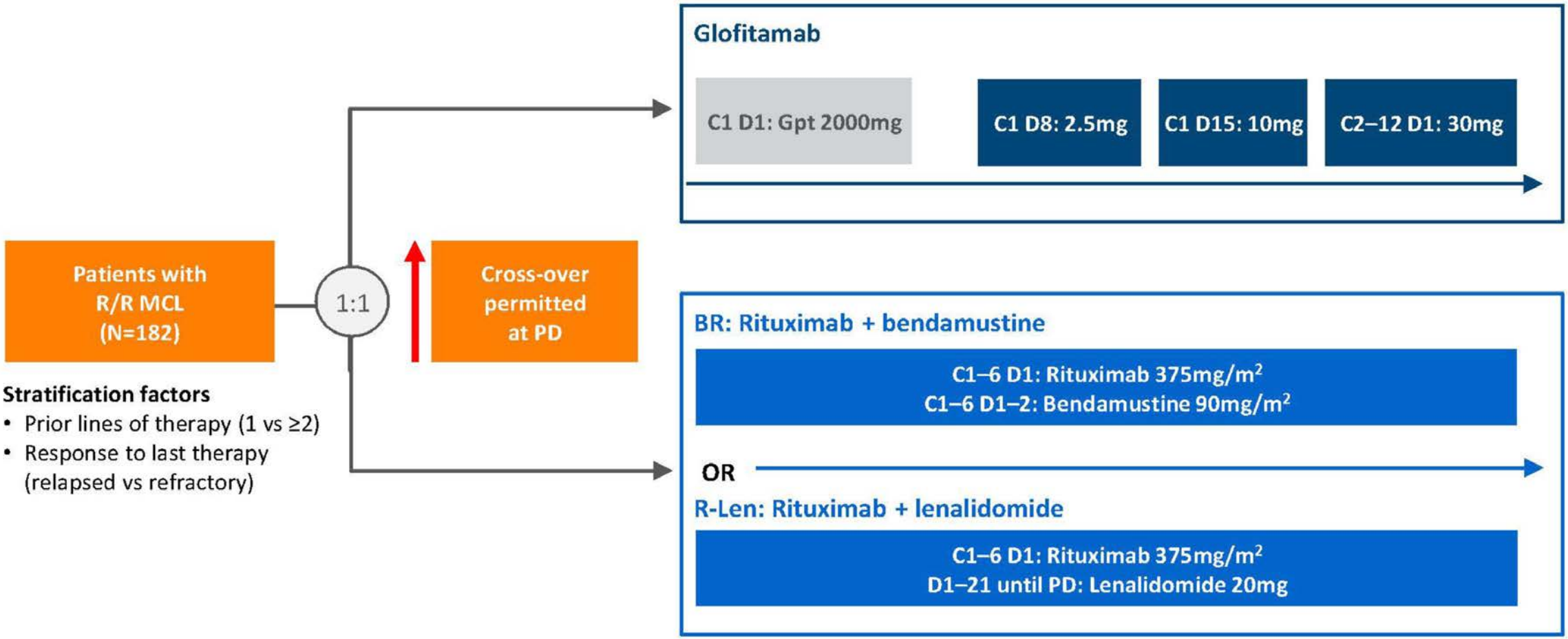

| | N=20 |
|---|---|
| Median OS, months (95% CI) | 17.9 (15.8–20.7) |
| 9-month event-free rate, % (95% CI) | 74.1% (54.5–93.7) |

**Promising PFS and OS benefits from longer follow up**

Clinical cut-off date: July 6, 2023.

Wang ML, et al. Blood. 2023;142(1_ Suppl):734.

# GLOBRYTE: Phase III, Open-label, Randomized Trial in R/R MCL




Phillips TJ et al. *Blood.* 2023;142(1_Suppl):3052.

# ELM-2 study design: R/R MZL cohort

Monday, 12/8/25, 6:00-8:00PM, West Hall B3-B4, Presentation ID 3588

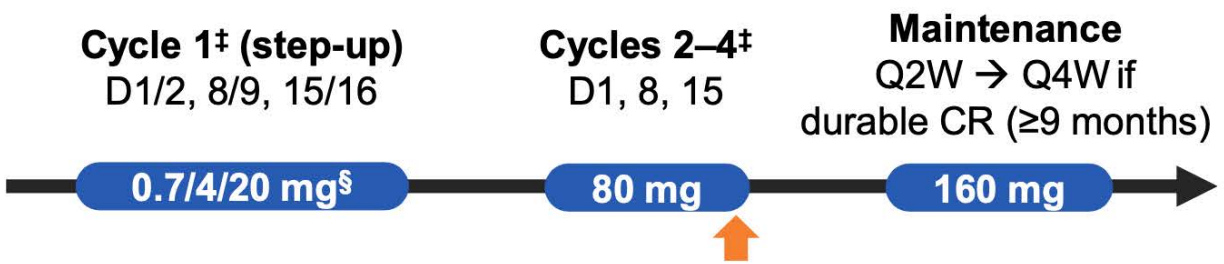
- Phase 2, open-label, multicohort, multicenter study of odronextamab monotherapy in patients with R/R B-NHL (NCT03888105)

**Key eligibility criteria**
- ≥18 years old
- MZL (extranodal, splenic, or nodal subtype)*
- ECOG PS 0 or 1
- Refractory to, or relapsed after, ≥2 prior lines of systemic therapy

**Primary endpoint**
- ORR† by ICR

**Secondary endpoints**
- ORR† by local investigator
- DOR,† PFS,† and OS
- Safety and tolerability
- Patient-reported outcomes

**Odronextamab IV administration**



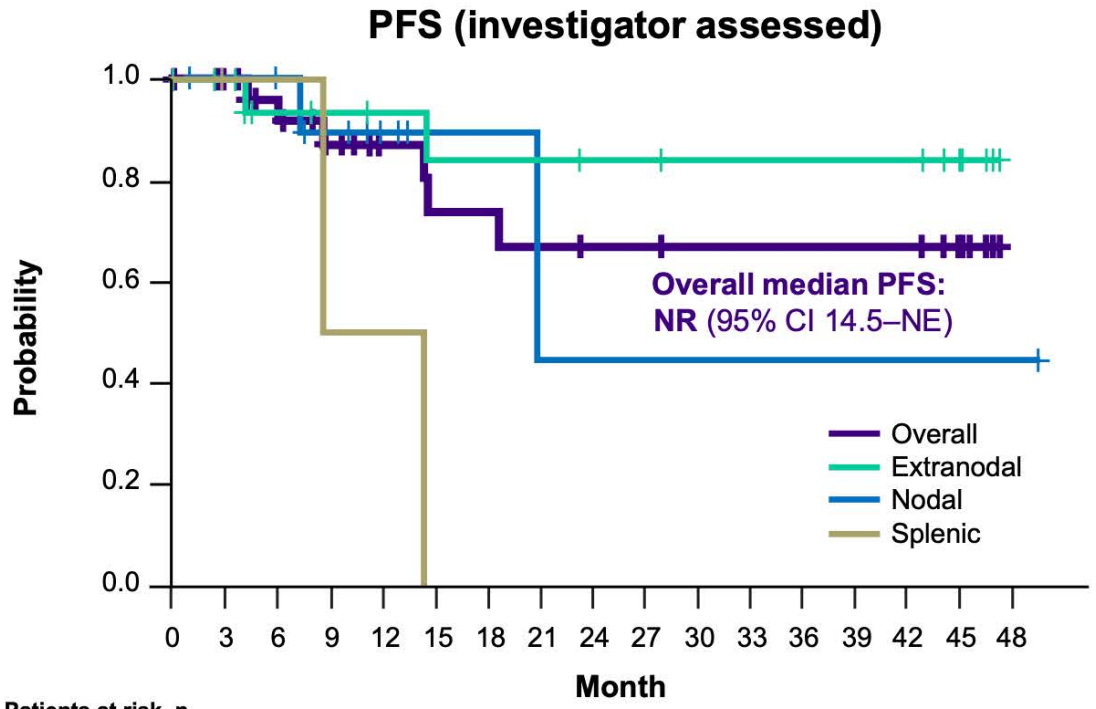

Measures taken to facilitate diverse, inclusive enrollment:
- Diverse trial sites
- Translated consents
- Extended screening windows
- Broad eligibility criteria
- Investigator training

Anti-infection prophylaxis including IVIg supplementation and antivirals was recommended, and PJP prophylaxis was mandated

*Per World Health Organization 2017 classification;[1] †According to Lugano criteria;[2] ‡Each cycle = 21 days; §The study initiated with a Cycle 1 step-up regimen of 1/20 mg. This was modified to 0.7/4/20 mg to further mitigate the risk of CRS. Premedication administered during Cycle 1 step-up included dexamethasone, diphenhydramine, and acetaminophen.
B-NHL, B-cell non-Hodgkin lymphoma; CR, complete response; CRS, cytokine release syndrome; D, day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICR, independent central review; IVIg, intravenous immunoglobulin; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PJP, *Pneumocystis jirovecii* pneumonia; QXW, once every X weeks; R/R, relapsed/refractory.

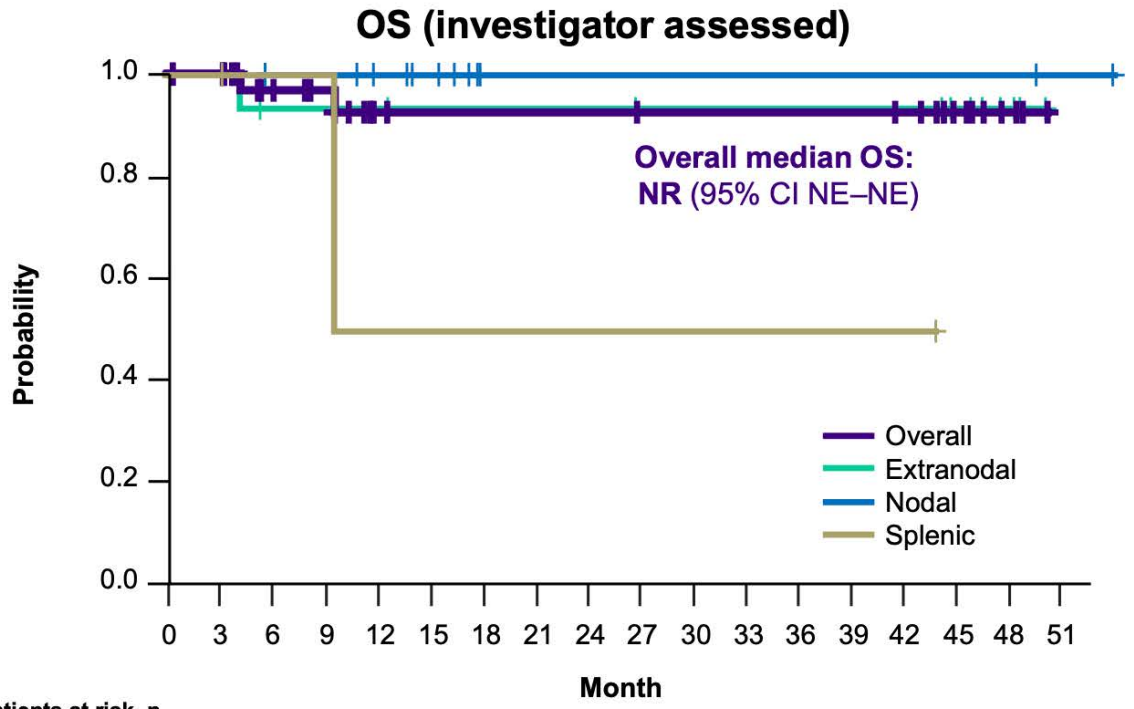
1. Beham-Schmid C. *Memo* 2017;10(4):248–54; 2. Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68.

# Odronextamab in R/R MZL: PFS and OS




Patients at risk, n

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Overall | 35 | 28 | 23 | 18 | 13 | 11 | 11 | 10 | 9 | 9 | 8 | 8 | 8 | 8 | 8 | 5 | 0 |
| Extranodal | 19 | 16 | 12 | 11 | 10 | 9 | 9 | 9 | 8 | 8 | 7 | 7 | 7 | 7 | 7 | 4 | 0 |
| Nodal | 12 | 10 | 9 | 6 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| Splenic | 3 | 2 | 2 | 1 | 1 | 0 | | | | | | | | | | | |




Patients at risk, n

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Overall | 35 | 34 | 25 | 22 | 15 | 14 | 14 | 14 | 14 | 13 | 13 | 13 | 13 | 13 | 12 | 8 | 3 | 0 |
| Extranodal | 19 | 19 | 12 | 12 | 11 | 10 | 10 | 10 | 10 | 9 | 9 | 9 | 9 | 9 | 9 | 7 | 3 | 0 |
| Nodal | 12 | 11 | 10 | 7 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 0 | |
| Splenic | 3 | 3 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | |

**12-month PFS rate (95% CI):**

| Overall | Extranodal | Nodal | Splenic |
|---|---|---|---|
| 87.5 (65.9–95.8) | 93.3 (61.3–99.0) | 88.9 (43.3–98.4) | 50.0 (0.6–91.0) |

**12-month OS rate (95% CI):**

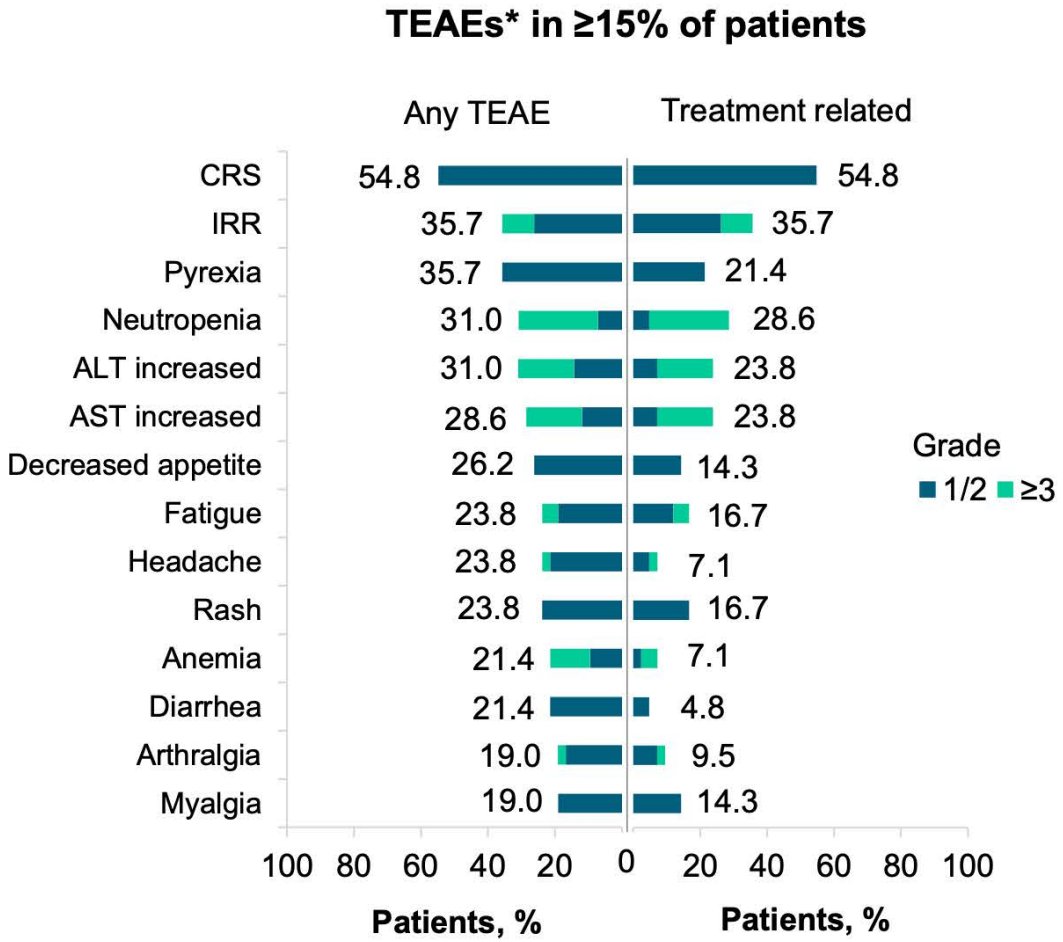
| Overall | Extranodal | Nodal | Splenic |
|---|---|---|---|
| 92.2 (71.8–98.0) | 93.3 (61.3–99.0) | 100 (100–100) | 50.0 (0.6–91.0) |

Data cut-off date: August 15, 2024. Efficacy per local investigator assessment.
CI, confidence interval; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

# Odronextamab demonstrated generally manageable safety consistent with that reported in 3L+ R/R FL

| n (%) | Overall (n=42) | |
|---|---|---|
| | Any event | Treatment related |
| Any TEAE | 42 (100.0) | 42 (100.0) |
| Grade ≥3 TEAE | 35 (83.3) | 31 (73.8) |
| Serious TEAE | 27 (64.3) | 17 (40.5) |
| TEAE leading to dose interruption/delay | 35 (83.3) | 33 (78.6) |
| TEAE leading to dose reduction | 4 (9.5) | 3 (7.1) |
| TEAE leading to discontinuation | 4 (9.5) | 1 (2.4) |
| TEAE leading to death | 0 | 0 |

- Safety profile was generally consistent across MZL subtypes, with CRS, IRR, and pyrexia among the most frequent TEAEs
- Treatment-related TEAEs leading to discontinuation: CRS (n=1)
- Overall safety consistent with that in 3L+ R/R FL in ELM-2[2]

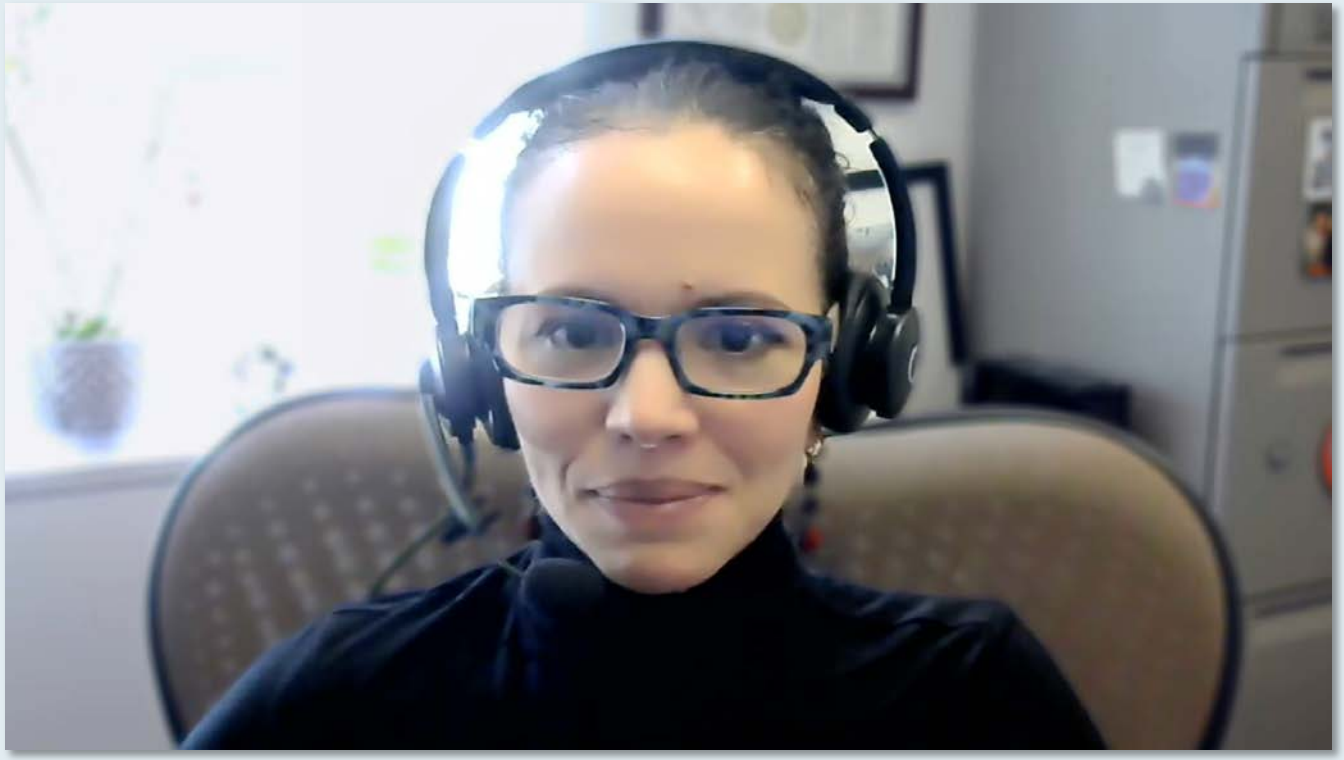



Data cut-off date: August 15, 2024.
*Preferred Term description of AEs per NCI-CTCAE v5.0. CRS per Lee DW, et al. 2019 criteria.[1]
3L+, third line of treatment and beyond; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; FL, follicular lymphoma; IRR, infusion-related reaction; MZL, marginal zone lymphoma; NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event.
1. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38; 2. Kim TM, et al. *Ann Oncol* 2024;35(11):1039–47.

# Bispecifics in FL, MZL, and MCL

- Bispecific antibodies demonstrate promising efficacy as single agents after 2 or more lines of therapy in FL
- Bispecific antibodies are associated with manageable safety profile in FL and lend themselves to combination strategies
- Epcoritamab has a full FDA approval in 2L+ in combination with R2 or as monotherapy in 3L+
- Novel agents and combination studies are underway including with a CD19xCD3 bispecific antibody, surovatamig
- These agents are under investigation in 1L FL, if the trials are positive, we will need large scale efforts to ensure access to these therapies in community settings
- Bispecific antibodies have demonstrated promising safety and efficacy in MCL and MZL in phase I/II trials

# Case Presentation: 54-year-old woman with multiregimen-recurrent FL receives mosunetuzumab



Dr Carla Casulo (Rochester, New York)

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**How do you compare the efficacy, tolerability and convenience of the available BSAbs for FL?**

**In general, how are you incorporating BSAbs for R/R FL into your practice? For patients with R/R FL to whom you plan to administer a BSAb, how do you choose between mosunetuzumab and epcoritamab?**

**How do you choose between CAR T-cell therapy and a BSAb for a patient with R/R FL who is eligible for both?**

# Case Presentation: 78-year-old man with multiregimen-refractory FL receives mosunetuzumab with ongoing CR

**Dr Laurie Sehn (Vancouver, British Columbia)**

RTP
RESEARCH
TO PRACTICE

# Discussion Questions

**Do you have any predictions on the outcomes that will be observed from the SWOG-2308 trial evaluating rituximab versus BSAb (mosunetuzumab) as first-line therapy for patients with low tumor-burden FL?**

**What is required to initiate treatment with a BSAb in a community-based oncology setting?**

**Where do you see BSAb "landing" in the next 5 years in the management of FL?**

# Discussion Questions

**Based on available data and your personal clinical experience, what is the incidence and spectrum of CRS symptoms associated with BSAbs in patients with R/R FL?**

**What long-term infection issues are seen with BSAbs, and how can these be minimized?**

**For which other B-cell lymphomas (eg, MCL, MZL) do BSAbs look promising? What do the available data suggest in these settings?**

# CASES FROM THE COMMUNITY
# Investigators Discuss the Role of Antibody-Drug Conjugates in the Management of Triple-Negative and HR-Positive Metastatic Breast Cancer

*Part 1 of a 3-Part CME Satellite Symposium Series*

**Tuesday, December 9, 2025**

**7:00 PM – 8:30 PM CT (8:00 PM – 9:30 PM ET)**

## Faculty

**Javier Cortés, MD, PhD**

**Professor Peter Schmid, FRCP, MD, PhD**

**Rita Nanda, MD**

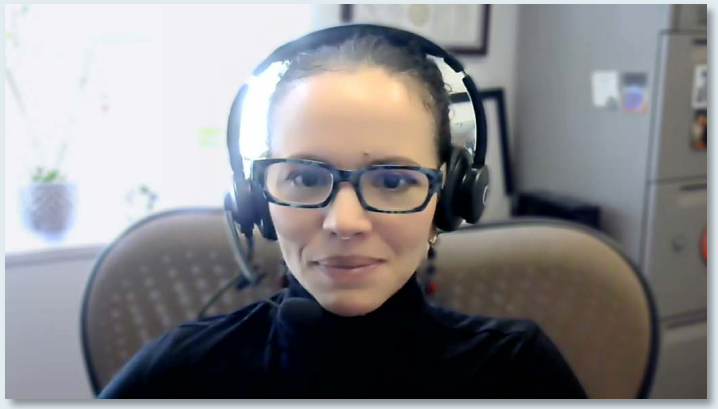
**Priyanka Sharma, MD**

## Moderator

**Neil Love, MD**

RTP RESEARCH TO PRACTICE

# Consulting Faculty



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