# Year in Review: Management of Non-Hodgkin Lymphoma

*A CME/MOC-Accredited Live Webinar*

**Tuesday, April 22, 2025**
**5:00 PM – 6:00 PM ET**

## Faculty

**Stephen M Ansell, MD, PhD**
**Brian T Hill, MD, PhD**

## Moderator

**Neil Love, MD**

RTP Year in Review 2025

# Faculty

**Stephen M Ansell, MD, PhD**
Chair, Division of Hematology
Dorotha W and Grant L Sundquist Professor in Hematologic Malignancies Research
Enterprise Deputy Director, Mayo Clinic Cancer Center
Mayo Clinic in Rochester, Minnesota
Rochester, Minnesota

**Brian T Hill, MD, PhD**
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

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

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# Commercial Support

This activity is supported by educational grants from ADC Therapeutics, AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, and Novartis.

# Dr Love — Disclosures

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# Dr Ansell — Disclosures

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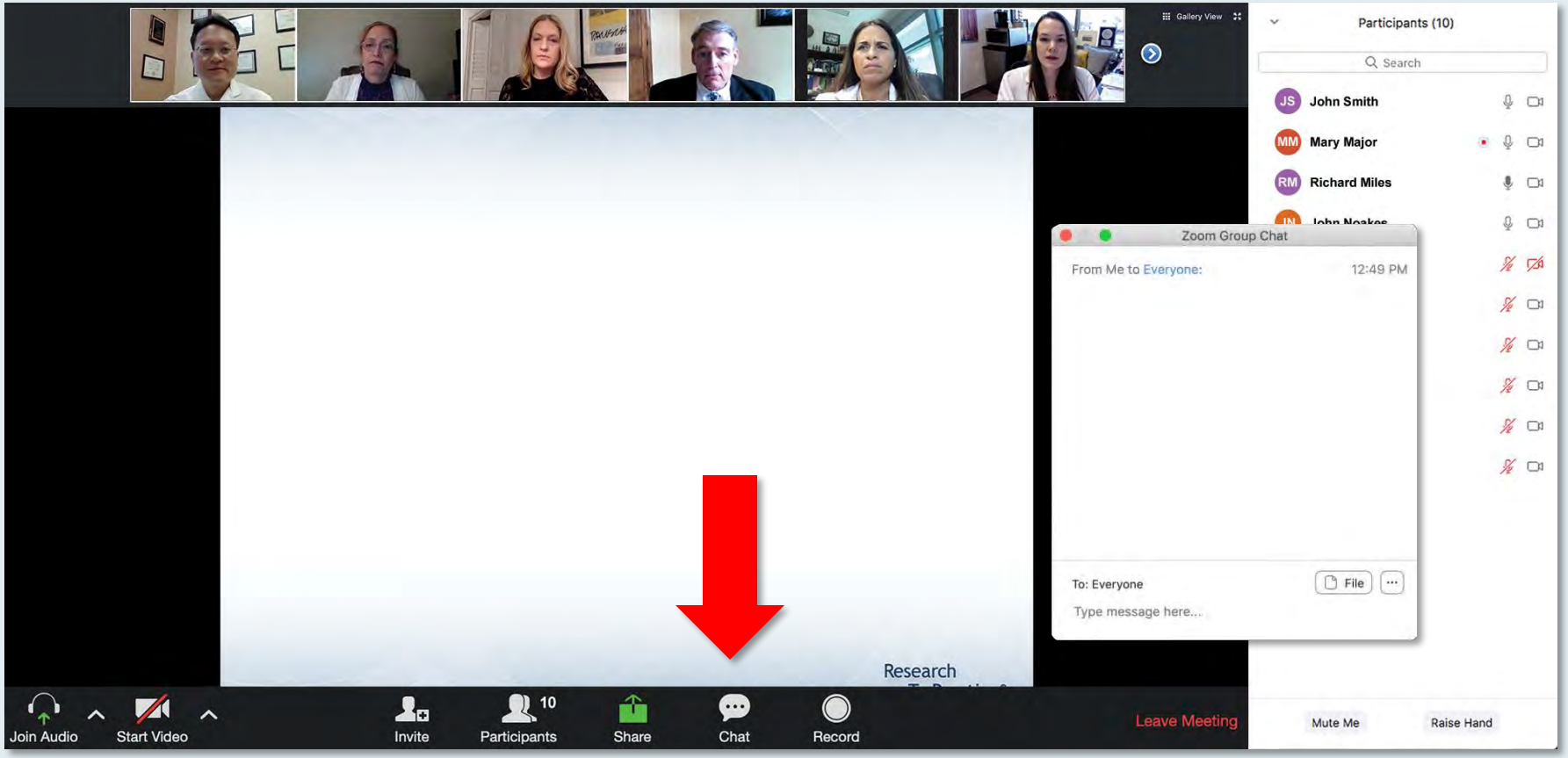


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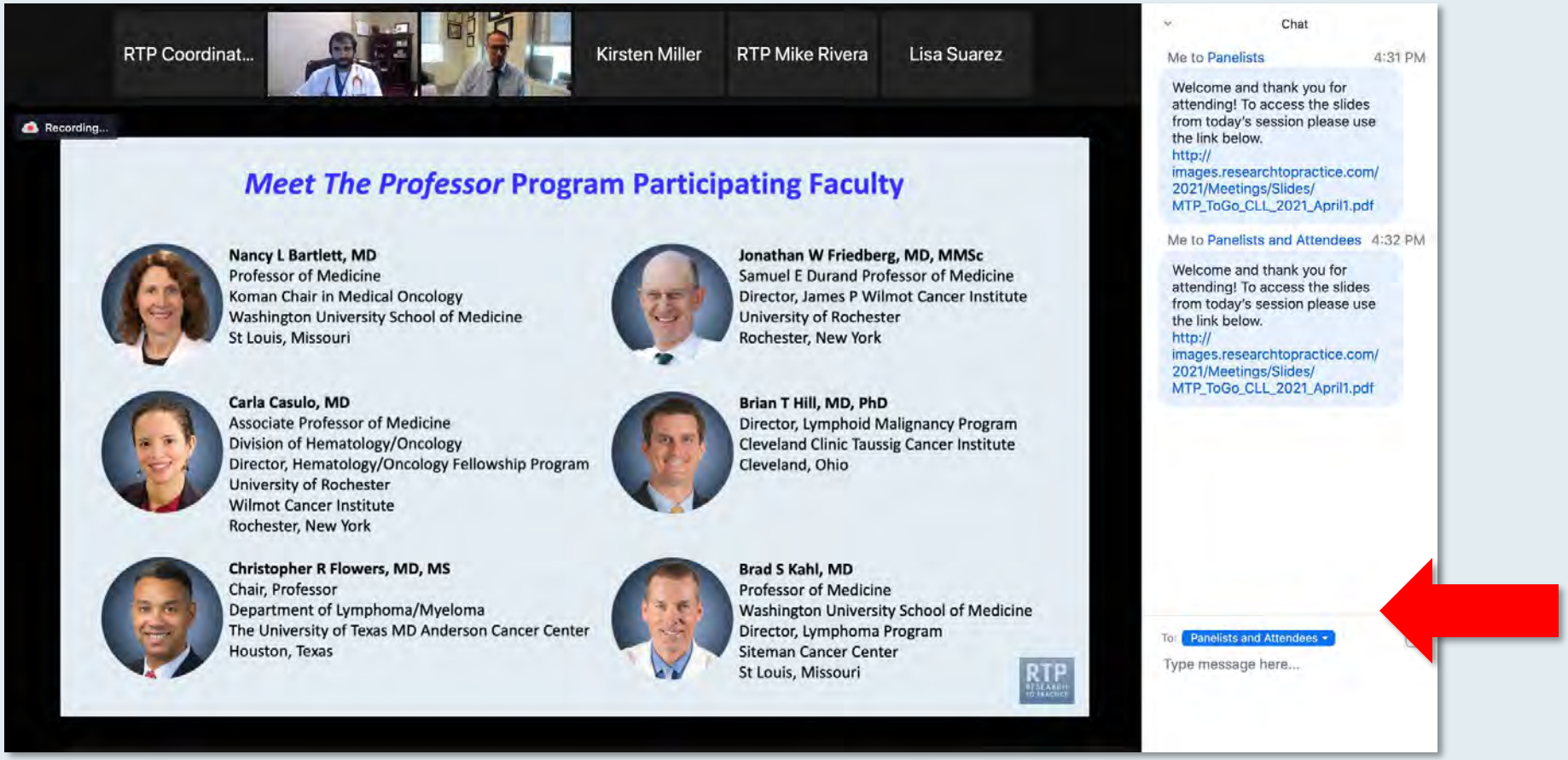


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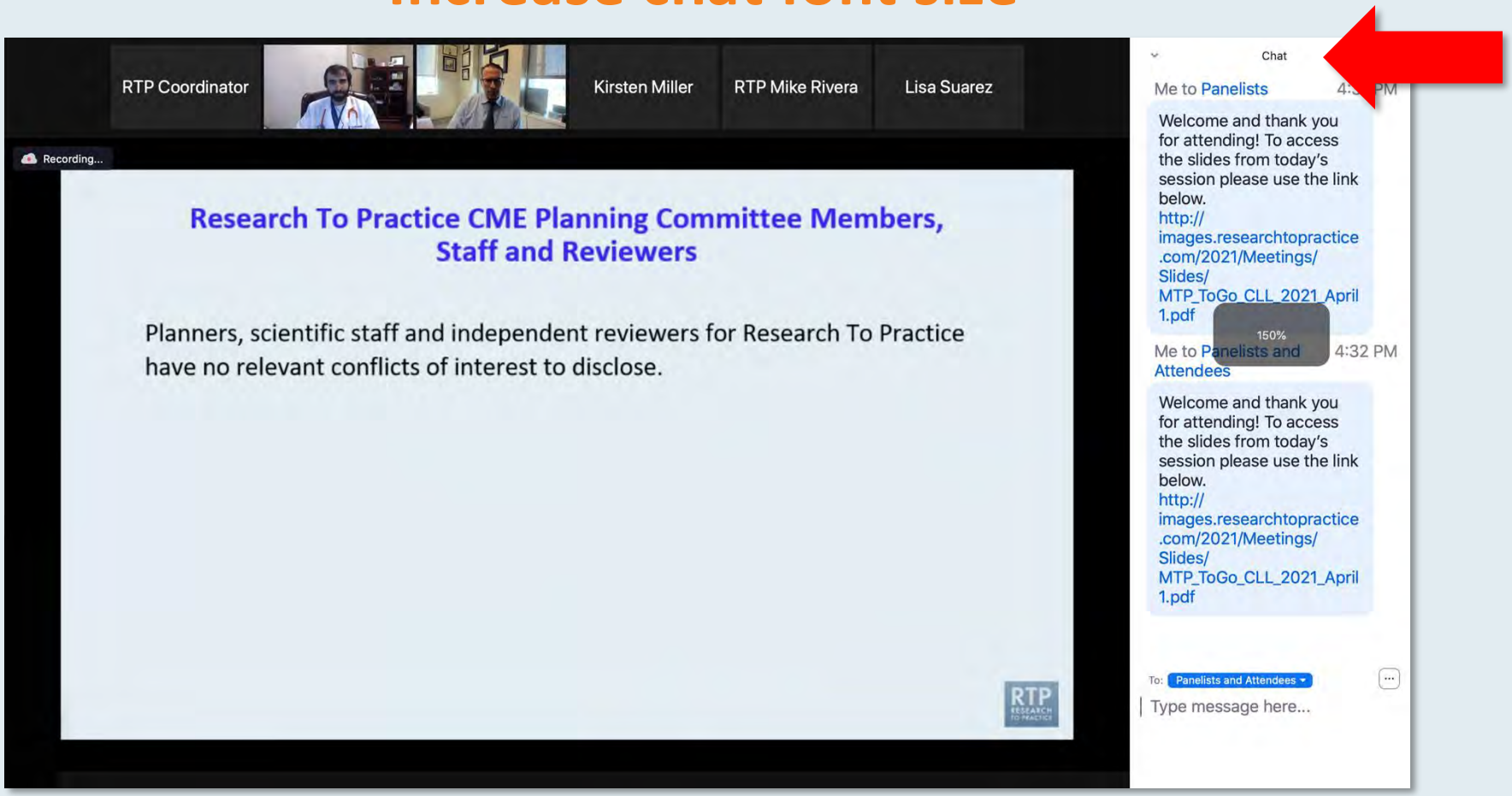


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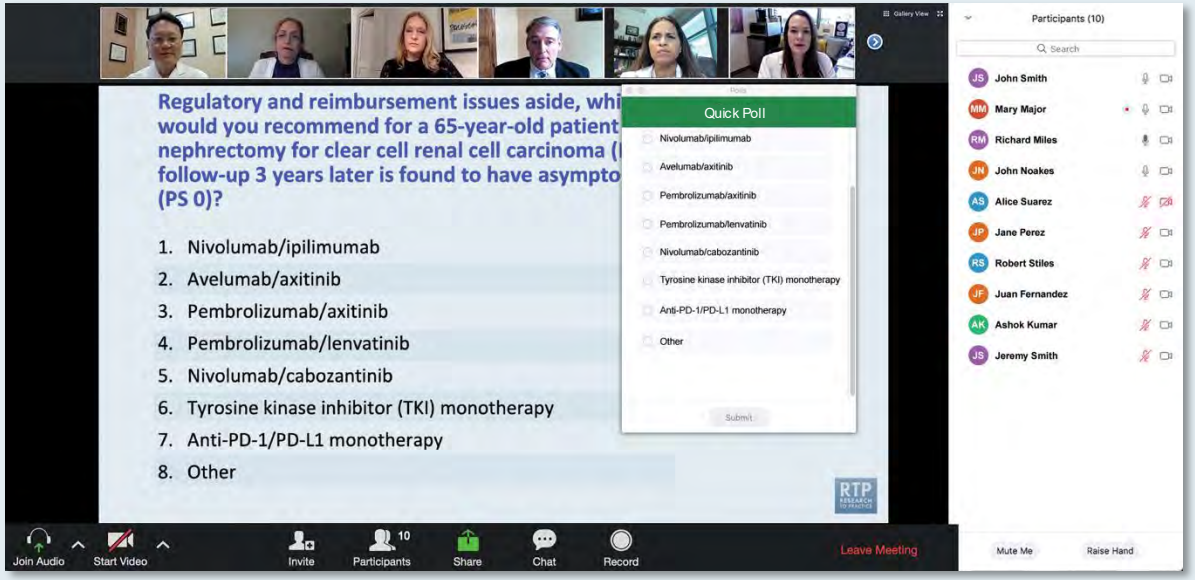
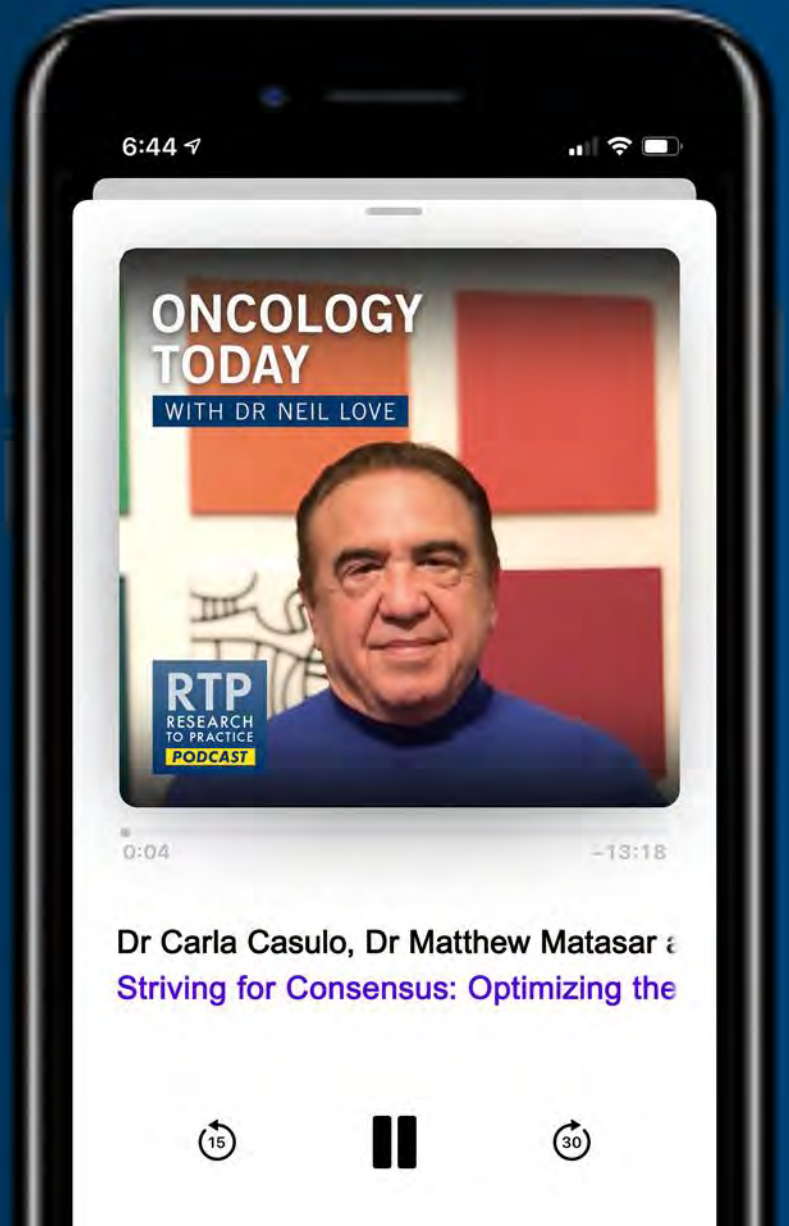


# Striving for Consensus: Optimizing the Selection and Sequencing of Therapy for Patients with Relapsed/Refractory Follicular Lymphoma


DR CARLA CASULO
WILMOT CANCER INSTITUTE

DR MATTHEW MATASAR
RUTGERS CANCER INSTITUTE

DR LAURIE H SEHN
BC CANCER CENTRE FOR LYMPHOID CANCER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# Data + Perspectives: Clinical Investigators Discuss the Emerging Role of AKT Inhibitors in the Care of Patients with Prostate Cancer

*A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2025 (AUA2025)*

**Saturday, April 26, 2025**

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## Faculty

**Leonard G Gomella, MD**

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## Moderator

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RTP RESEARCH TO PRACTICE

# Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

# Management of Myelofibrosis

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**Jessica J Lin, MD**

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**MODULE 1:** Diffuse Large B-Cell Lymphoma

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**MODULE 5:** CAR T-Cell Therapy for Marginal Zone Lymphoma

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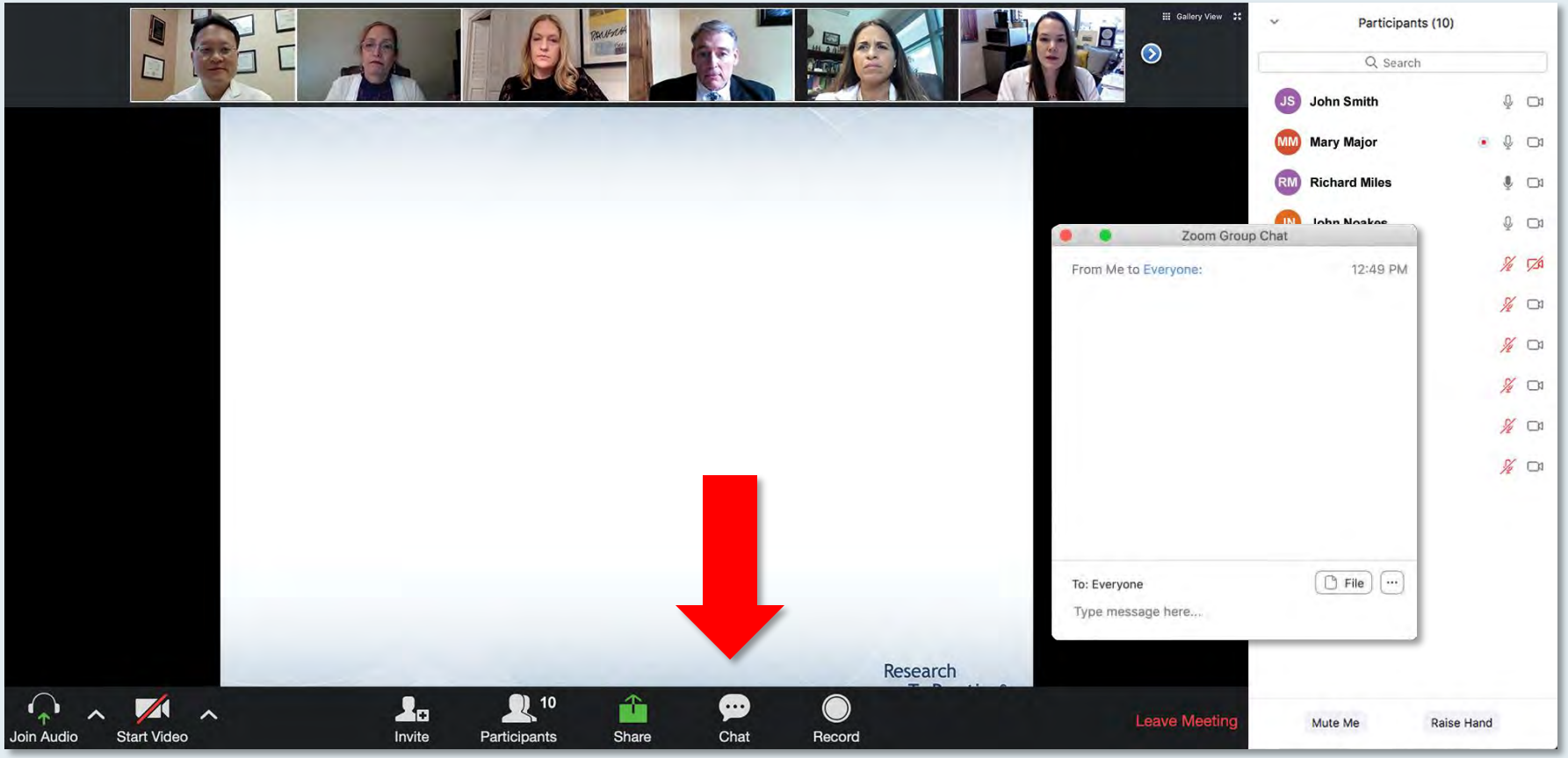


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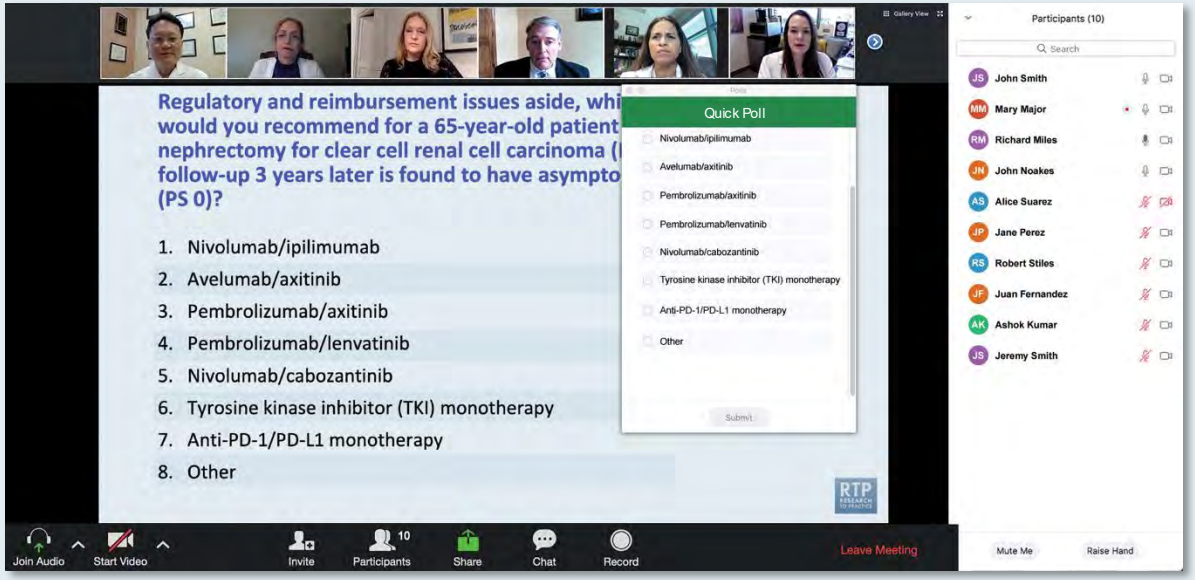

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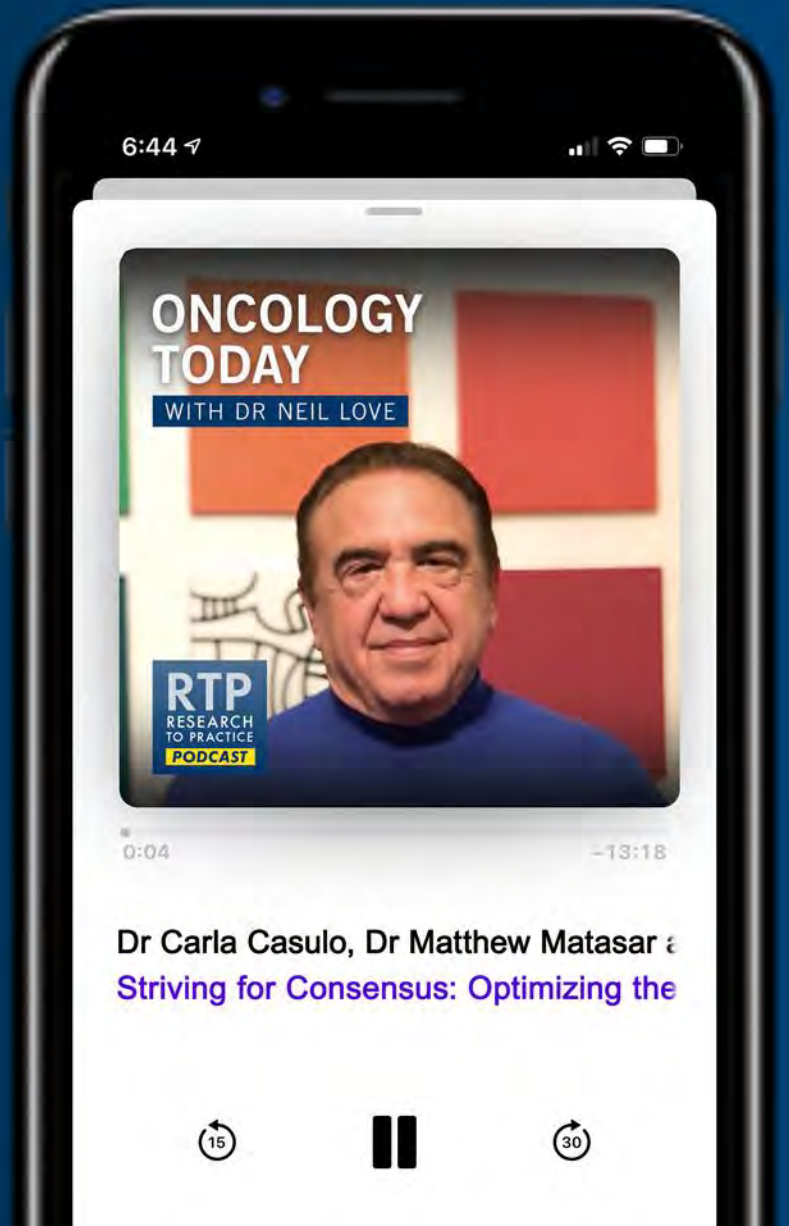


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# Current Role of Chimeric Antigen Receptor (CAR) T-Cell Therapy and Bispecific Antibodies in Various Non-Hodgkin Lymphoma (NHL) Subtypes

**Brian Hill, MD, PhD**
Director, Lymphoid Malignancies Program

Cleveland Clinic
Taussig Cancer Institute

# Other Available and Emerging Novel Therapies for NHL

**Stephen M. Ansell, MD, PhD**
Dorotha W. and Grant L. Sundquist Professor in Hematologic Malignancies Research
Chair, Division of Hematology
Mayo Clinic

# Key Datasets

## Brian T Hill, MD, PhD

- Kamdar MK et al. **Lisocabtagene maraleucel (liso-cel)** vs standard of care (SOC) with salvage chemotherapy (CT) followed by autologous stem cell transplantation (ASCT) as **second-line (2L)** treatment in patients (pt) with **R/R large B-cell lymphoma (LBCL)**: **3-year follow-up (FU)** from the randomized, **phase 3 TRANSFORM study**. ASCO 2024;Abstract 7013.
- Neelapu S et al. **5-year follow-up** analysis from **ZUMA-5**: A phase 2 trial of **axicabtagene ciloleucel (axi-cel)** in patients with **relapsed/refractory indolent non-hodgkin lymphoma**. ASH 2024;Abstract 864.
- Thieblemont C et al. Clinical outcomes of patients with high-risk relapsed/refractory follicular lymphoma treated with **tisagenlecleucel: Phase 2 ELARA 4-year update**. ASH 2024;Abstract 3034.
- Nastoupil L et al. **Lisocabtagene maraleucel (liso-cel)** in patients (pts) with relapsed or refractory (R/R) follicular lymphoma (FL): **Transcend FL 2-year follow-up**. ASH 2024;Abstract 4387.
- Wang M et al. **Lisocabtagene maraleucel (liso-cel)** in patients (pts) with relapsed or refractory (R/R) mantle cell lymphoma (MCL): Results from the **final analysis of the MCL cohort** of the open-label, phase 1, seamless design, multicenter **Transcend NHL 001 (TRANSCEND) study**. *Transplant Cell Ther* 2025;31(Suppl 2):207.

# Key Datasets

## Brian T Hill, MD, PhD (continued)

- **Positive topline results** for **lisocabtagene maraleucel** in adult patients with **relapsed or refractory marginal zone lymphoma** [press release]. February 10, 2025.
- Vose JM et al. **3-year update** from the **Epcore NHL-1 trial: Epcoritamab** leads to deep and durable responses in **relapsed or refractory large B-cell lymphoma**. ASH 2024;Abstract 4480.
- Dickinson M et al. **Fixed-duration glofitamab monotherapy** continues to demonstrate durable responses in patients with **relapsed or refractory large B-cell lymphoma: 3-year follow-up** from a pivotal phase II study. ASH 2024;Abstract 865.
- Gaballa S et al. Evaluation of **AZD0486, a novel CD19xCD3 T-cell engager**, in **relapsed/refractory diffuse large B-cell lymphoma** in an ongoing first-in-human phase 1 study: High complete responses seen in CAR-T-naive and CAR-T-exposed patients. ASH 2024;Abstract 868.
- Abramson JS et al. **Glofitamab plus gemcitabine and oxaliplatin (GemOx)** versus rituximab-GemOx for **relapsed or refractory diffuse large B-cell lymphoma (STARGLO)**: A global phase 3, randomised, open-label trial. *Lancet* 2024;404(10466):1940-54.
- Sehn LH et al. Long-term **3-year follow-up** of **mosunetuzumab** in **relapsed or refractory follicular lymphoma** after ≥2 prior therapies. *Blood* 2025;145(7):708-19.

# Key Datasets

## Brian T Hill, MD, PhD (continued)

- Linton KM et al. **Epcoritamab monotherapy** in patients with **relapsed or refractory follicular lymphoma (EPCORE NHL-1)**: A phase 2 cohort of a single-arm, multicentre study. *Lancet Haematol* 2024;11(8).
- Hou JZ et al. Escalating doses of **AZD0486, a novel CD19xCD3 T-cell engager**, result in high complete remissions with rapid clearance of minimal residual disease in patients with **relapsed/refractory follicular lymphoma**. ASH 2024;Abstract 341.
- Phillips TJ et al. **Glofitamab** in **relapsed/refractory mantle cell lymphoma**: Results from a phase I/II study. *J Clin Oncol* 2025;43(3):318-28.

# Key Datasets

## Stephen M Ansell, MD, PhD

- Salles G et al. **Five-year analysis** of the **POLARIX study**: Prolonged follow-up confirms positive impact of **polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone** (Pola-R-CHP) on outcomes. ASH 2024;Abstract 469.
- Duell J et al. **Tafasitamab** for patients with **relapsed or refractory diffuse large B-cell lymphoma**: final **5-year efficacy and safety findings** in the **phase II L-MIND study**. *Haematologica* 2024;109(2):553-66.
- Caimi PF et al. **Loncastuximab tesirine** in **relapsed/refractory diffuse large B-cell lymphoma**: Long-term efficacy and safety from the **phase II LOTIS-2 study**. *Haematologica* 2024;109(4):1184-93.
- Bartlett NL et al. **Brentuximab vedotin combination** for **relapsed diffuse large B-cell lymphoma**. *J Clin Oncol* 2025;43(9):1061-72.
- Sehn L et al. **Tafasitamab plus lenalidomide and rituximab** for **relapsed or refractory follicular lymphoma**: Results from a **phase 3 study (inMIND)**. ASH 2024;Abstract LBA-1.
- Alderuccio JP et al. **Loncastuximab tesirine with rituximab** in patients with **relapsed or refractory follicular lymphoma**: A single-centre, single-arm, phase 2 trial. *Lancet Haematol* 2025;12(1).

# Key Datasets

## Stephen M Ansell, MD, PhD (continued)

- Dreyling M et al. **Ibrutinib combined with immunochemotherapy with or without autologous stem-cell transplantation** versus immunochemotherapy and autologous stem-cell transplantation in **previously untreated patients with mantle cell lymphoma (TRIANGLE)**: A three-arm, randomised, open-label, phase 3 superiority trial of the European Mantle Cell Lymphoma Network. *Lancet* 2024;403(10441):2293-306.
- Wang M et al. **Acalabrutinib plus bendamustine and rituximab** in **untreated mantle cell lymphoma**: Results from the phase 3, double-blind, placebo-controlled **ECHO trial**. EHA 2024;Abstract LB3439.
- Dreyling M et al. **High-risk subgroups and MRD**: An **updated analysis of the phase 3 ECHO trial** of acalabrutinib with bendamustine/rituximab in previously untreated mantle cell lymphoma. ASH 2024;Abstract 1626.
- Lewis D et al. **Ibrutinib-rituximab** is superior to rituximab-chemotherapy in **previously untreated older mantle cell lymphoma patients**: Results from the international randomised controlled trial, Enrich. ASH 2024;Abstract 235.

# Key Datasets

## Stephen M Ansell, MD, PhD (continued)

- Wang M et al**. Acalabrutinib plus venetoclax and rituximab** in **treatment-naive mantle cell lymphoma**: 2-year safety and efficacy analysis. *Blood Adv* 2024;8(17):4539-48.
- Kumar A et al. **Zanubrutinib, obinutuzumab, and venetoclax** for **first-line** treatment of **mantle cell lymphoma with a *TP53* mutation.** *Blood* 2025;145(5):497-507.
- Wang M et al. **Ibrutinib plus venetoclax** in **relapsed or refractory mantle cell lymphoma (SYMPATICO)**: A multicentre, randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Oncol* 2025;26(2):200-13.

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# Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

*A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress*

# Bispecific T-Cell Engagers for Small Cell Lung Cancer

**Friday, April 11, 2025**

**6:00 AM – 7:30 AM**

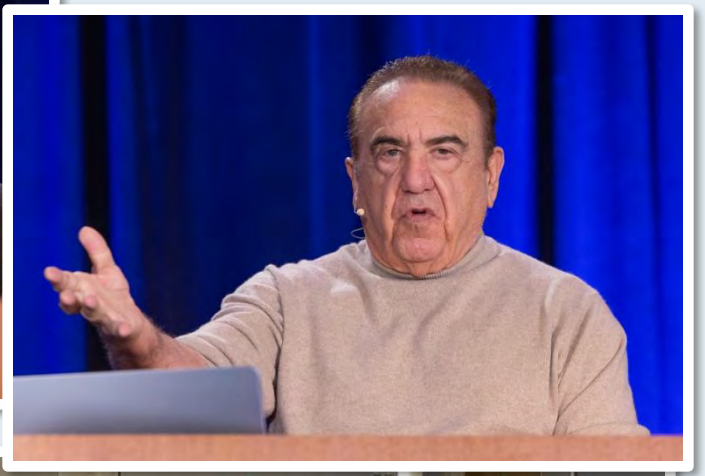
## Faculty

**Anne Chiang, MD, PhD**
**Elizabeth Krueger, NP**
**Beth Sandy, MSN, CRNP, FAPO**
**Erin Schenk, MD, PhD**

## Moderator

**Neil Love, MD**

RTP RESEARCH TO PRACTICE




New and Emerging Targets for SCLC
Antibody-Drug Conjugates
Novel Immune-Based Therapies

**Your patient with follicular lymphoma receives bendamustine/rituximab as first-line treatment followed by lenalidomide/rituximab on relapse. You've decided on mosunetuzumab as the next line of therapy. How will this likely be implemented in your practice?**

1. You will start therapy
2. You will start therapy with input from a tertiary specialist
3. A tertiary specialist will start therapy and then transfer to you
4. A tertiary specialist will administer therapy

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INTRODUCTION: Bispecific Antibodies in Community Practice

**MODULE 1: Diffuse Large B-Cell Lymphoma**

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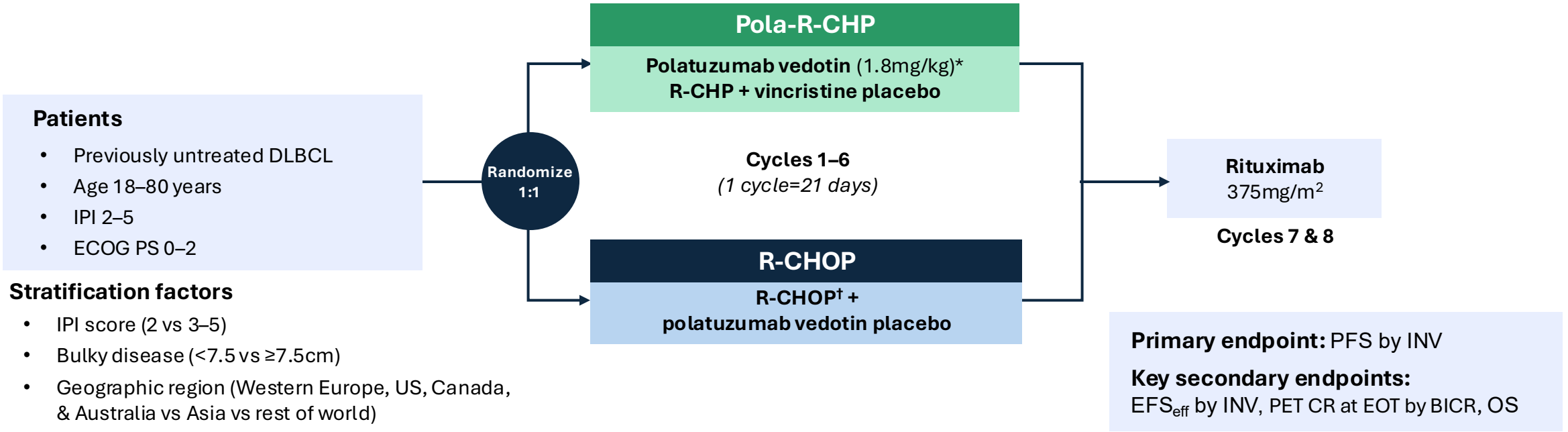
# Five-Year Analysis of the POLARIX study




| | | Pola-R-CHP | R-CHOP | Total | Median PFS follow-up | Median OS follow-up |
|---|---|---|---|---|---|---|
| **Global population** | ITT‡ | 440 | 439 | 879 | 54.9 months | 64.1 months |
| | Safety evaluable§ | 435¶ | 438# | 873 | | |

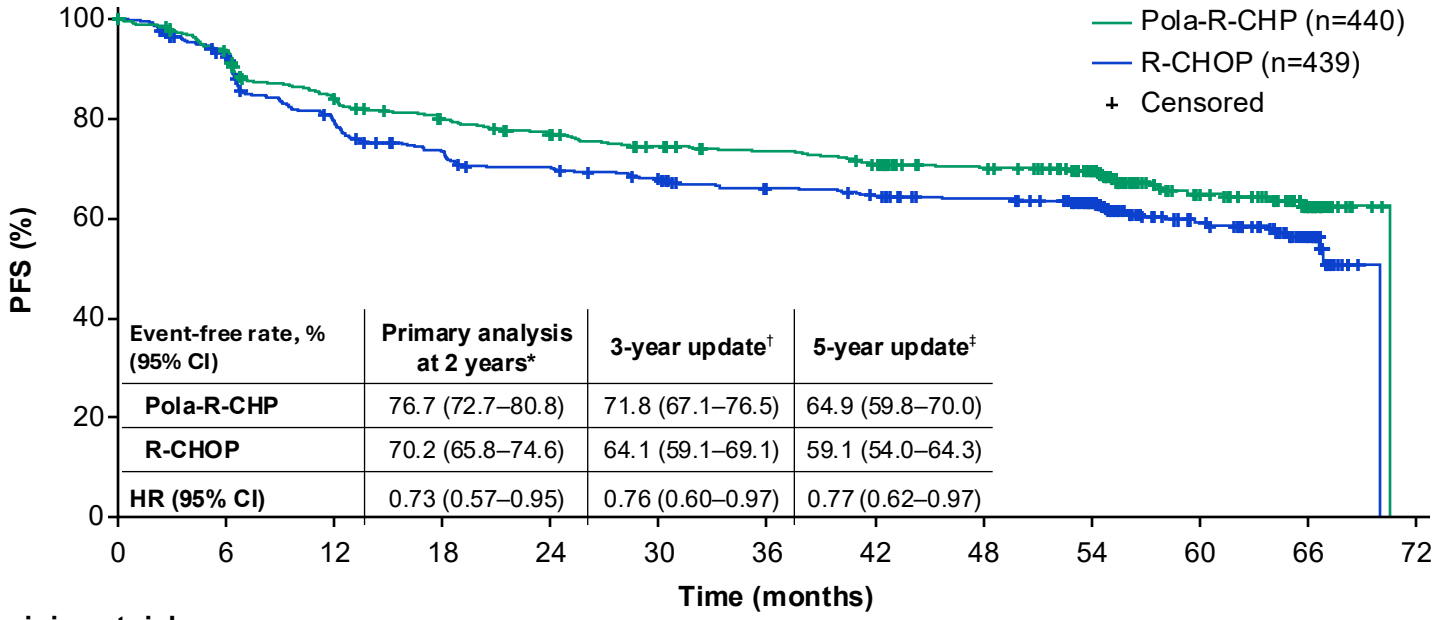
*IV on Day 1; †R-CHOP: IV rituximab 375mg/m$^2$, cyclophosphamide 750mg/m$^2$, doxorubicin 50mg/m$^2$, and vincristine 1.4mg/m$^2$ (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5; ‡As randomized population; §As treated population; ¶One patient was randomized to Pola-R-CHP but did not receive polatuzumab vedotin; #One patient was randomized to R-CHOP but did not receive vincristine.
BICR, blinded independent central review; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS$_{eff}$, event-free survival (efficacy); EOT, end of treatment; INV, investigator; IPI, International Prognostic Index; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; R, randomized; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

Courtesy of Stephen M Ansell, MD, PhD

Salles et al. ASH 2024;Abstract 469.

# Initial PFS benefit of Pola-R-CHP over R-CHOP is maintained at 5 years

## PFS in the global ITT population




| Event-free rate, % (95% CI) | Primary analysis at 2 years* | 3-year update† | 5-year update‡ |
|---|---|---|---|
| Pola-R-CHP | 76.7 (72.7–80.8) | 71.8 (67.1–76.5) | 64.9 (59.8–70.0) |
| R-CHOP | 70.2 (65.8–74.6) | 64.1 (59.1–69.1) | 59.1 (54.0–64.3) |
| HR (95% CI) | 0.73 (0.57–0.95) | 0.76 (0.60–0.97) | 0.77 (0.62–0.97) |

**Patients remaining at risk**

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pola-R-CHP | 440 | 407 | 357 | 335 | 318 | 303 | 292 | 280 | 258 | 213 | 100 | 56 | NE |
| R-CHOP | 439 | 391 | 332 | 302 | 287 | 274 | 258 | 251 | 240 | 192 | 95 | 54 | NE |

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

*Data cut-off: June 28, 2021; †Data cut-off: June 15, 2022; ‡Data cut-off: July 5, 2024.
CI, confidence interval; HR, hazard ratio; NE, not evaluable.

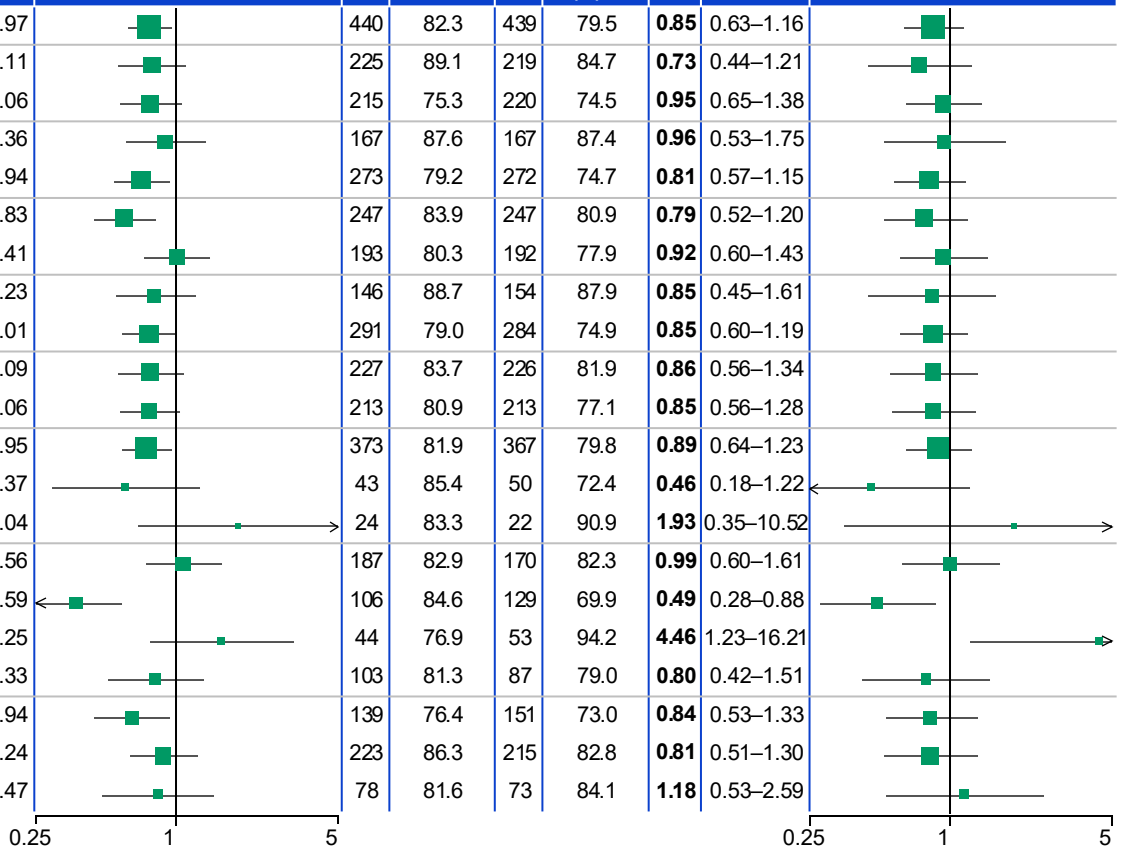

1. Tilly H, et al. N Eng J Med 2022;386:351–63.

Salles et al. ASH 2024;Abstract 469.


Courtesy of Stephen M Ansell, MD, PhD

# 5-year PFS and OS show consistent treatment effect of Pola-R-CHP across subgroups in the global population

| Baseline risk factors | | PFS | | | | | | OS | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Pola-R-CHP (n=440) | | R-CHOP (n=439) | | HR | 95% Wald CI | Pola-R-CHP (n=440) | | R-CHOP (n=439) | | HR | 95% Wald CI |
| | | n | 60-month (%) | n | 60-month (%) | | | n | 60-month (%) | n | 60-month (%) | | |
| **All patients** | | 440 | 64.9 | 439 | 59.1 | **0.78** | 0.62–0.97 | 440 | 82.3 | 439 | 79.5 | **0.85** | 0.63–1.16 |
| **Age group** | ≤65 | 225 | 69.6 | 219 | 64.3 | **0.80** | 0.57–1.11 | 225 | 89.1 | 219 | 84.7 | **0.73** | 0.44–1.21 |
| | >65 | 215 | 60.0 | 220 | 54.5 | **0.78** | 0.58–1.06 | 215 | 75.3 | 220 | 74.5 | **0.95** | 0.65–1.38 |
| **Stratification – IPI score** | 2 | 167 | 67.2 | 167 | 68.3 | **0.91** | 0.61–1.36 | 167 | 87.6 | 167 | 87.4 | **0.96** | 0.53–1.75 |
| | 3–5 | 273 | 63.2 | 272 | 53.5 | **0.72** | 0.55–0.94 | 273 | 79.2 | 272 | 74.7 | **0.81** | 0.57–1.15 |
| **Stratification – bulky disease (≥ 7cm)** | Absent | 247 | 69.9 | 247 | 60.0 | **0.61** | 0.44–0.83 | 247 | 83.9 | 247 | 80.9 | **0.79** | 0.52–1.20 |
| | Present | 193 | 58.5 | 192 | 57.9 | **1.02** | 0.73–1.41 | 193 | 80.3 | 192 | 77.9 | **0.92** | 0.60–1.43 |
| **Baseline LDH** | ≤1xULN | 146 | 65.3 | 154 | 64.8 | **0.83** | 0.55–1.23 | 146 | 88.7 | 154 | 87.9 | **0.85** | 0.45–1.61 |
| | >1xULN | 291 | 64.3 | 284 | 55.7 | **0.77** | 0.59–1.01 | 291 | 79.0 | 284 | 74.9 | **0.85** | 0.60–1.19 |
| **No. of extranodal sites** | 0–1 | 227 | 68.1 | 226 | 64.2 | **0.78** | 0.56–1.09 | 227 | 83.7 | 226 | 81.9 | **0.86** | 0.56–1.34 |
| | ≥2 | 213 | 61.2 | 213 | 53.8 | **0.78** | 0.58–1.06 | 213 | 80.9 | 213 | 77.1 | **0.85** | 0.56–1.28 |
| **NHL subtype** | DLBCL, NOS, ABC, GCB | 373 | 65.7 | 367 | 58.8 | **0.75** | 0.59–0.95 | 373 | 81.9 | 367 | 79.8 | **0.89** | 0.64–1.23 |
| | HGBL, NOS, DHL/THL | 43 | 66.0 | 50 | 57.6 | **0.67** | 0.33–1.37 | 43 | 85.4 | 50 | 72.4 | **0.46** | 0.18–1.22 |
| | Other LBCL | 24 | 49.7 | 22 | 70.3 | **1.86** | 0.69–5.04 | 24 | 83.3 | 22 | 90.9 | **1.93** | 0.35–10.52 |
| **NanoString COO** | NanoString GCB | 187 | 65.9 | 170 | 65.8 | **1.07** | 0.74–1.56 | 187 | 82.9 | 170 | 82.3 | **0.99** | 0.60–1.61 |
| | NanoString ABC | 106 | 72.5 | 129 | 45.8 | **0.38** | 0.24–0.59 | 106 | 84.6 | 129 | 69.9 | **0.49** | 0.28–0.88 |
| | NanoString UNC | 44 | 55.2 | 53 | 70.8 | **1.60** | 0.79–3.25 | 44 | 76.9 | 53 | 94.2 | **4.46** | 1.23–16.21 |
| | Unknown | 103 | 60.2 | 87 | 59.7 | **0.83** | 0.51–1.33 | 103 | 81.3 | 87 | 79.0 | **0.80** | 0.42–1.51 |
| **Double expressor by IHC** | DEL | 139 | 63.1 | 151 | 50.0 | **0.65** | 0.45–0.94 | 139 | 76.4 | 151 | 73.0 | **0.84** | 0.53–1.33 |
| | Non DEL | 223 | 66.6 | 215 | 64.7 | **0.89** | 0.64–1.24 | 223 | 86.3 | 215 | 82.8 | **0.81** | 0.51–1.30 |
| | Unknown | 78 | 63.7 | 73 | 63.5 | **0.84** | 0.48–1.47 | 78 | 81.6 | 73 | 84.1 | **1.18** | 0.53–2.59 |




- PFS and OS by subgroups, including high-risk subgroups, generally favor Pola-R-CHP; however, subgroup analyses are exploratory and generally underpowered (especially for OS).
- Patient characteristics are multidimensional; therefore, translating univariate subgroup results into patient care should be applied with caution.

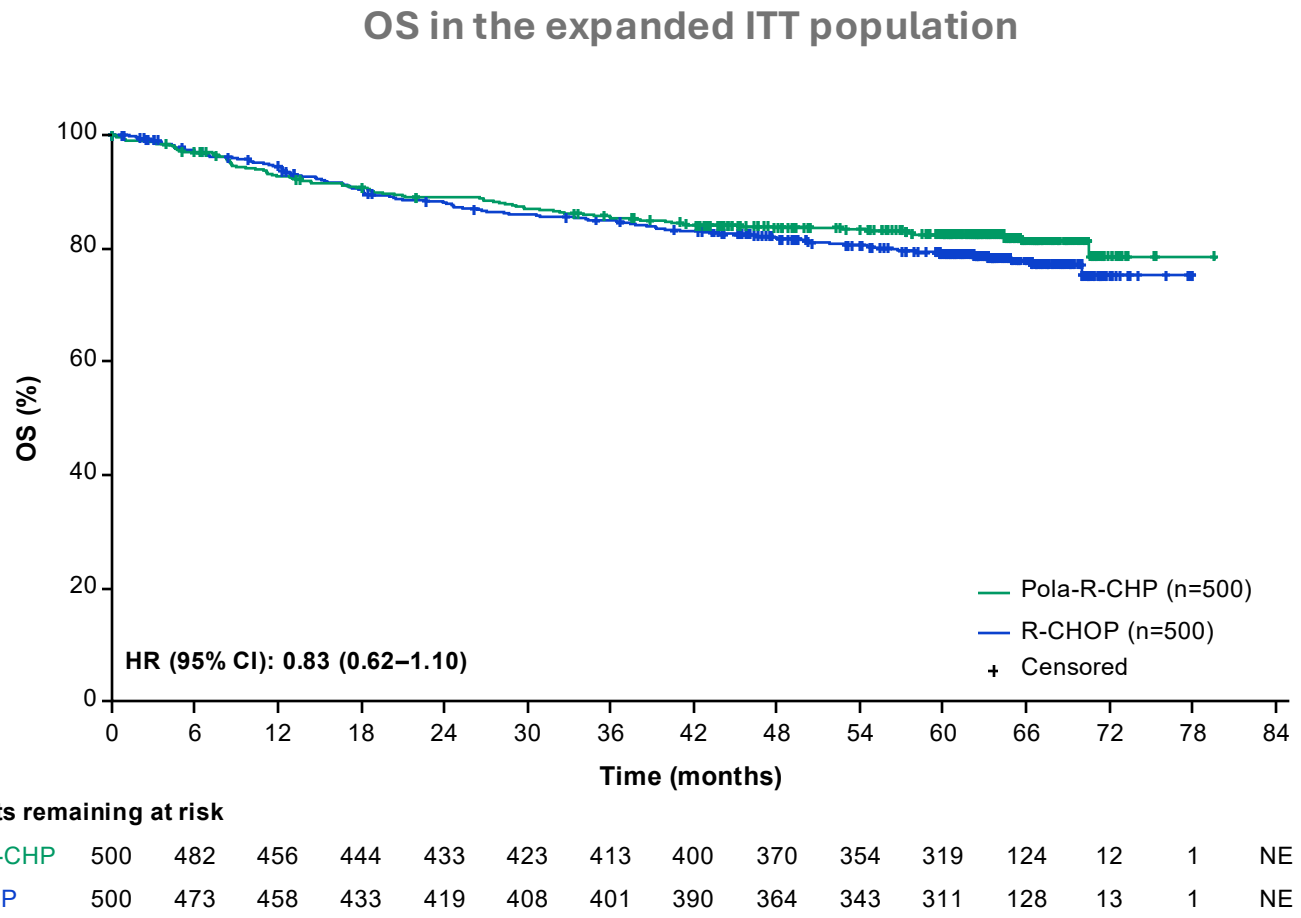
DEL, double-expressor lymphoma; IHC, immunohistochemistry; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; ULN, upper limit of normal; UNC, unclassified.

Courtesy of Stephen M Ansell, MD, PhD

**Salles et al. ASH 2024;Abstract 469.**

# Efficacy outcomes in the expanded population are similar to the global population

| Efficacy analyses | Pola-R-CHP | R-CHOP |
|---|---|---|
| **PFS analysis, n** | 500 | 500 |
| Patients with PFS event, n (%) | 163 (32.6) | 189 (37.8) |
| Stratified HR (95% CI) | **0.80 (0.65–0.98)** | |
| **DFS analysis, n** | 439 | 419 |
| Patients remaining in CR, n (%) | 327 (74.5) | 292 (69.7) |
| Unstratified HR (95% CI) | **0.81 (0.63–1.05)** | |
| **OS analysis, n** | 500 | 500 |
| Patients with OS event, n (%) | 88 (17.6) | 104 (20.8) |
| Stratified HR (95% CI) | **0.83 (0.62–1.10)** | |



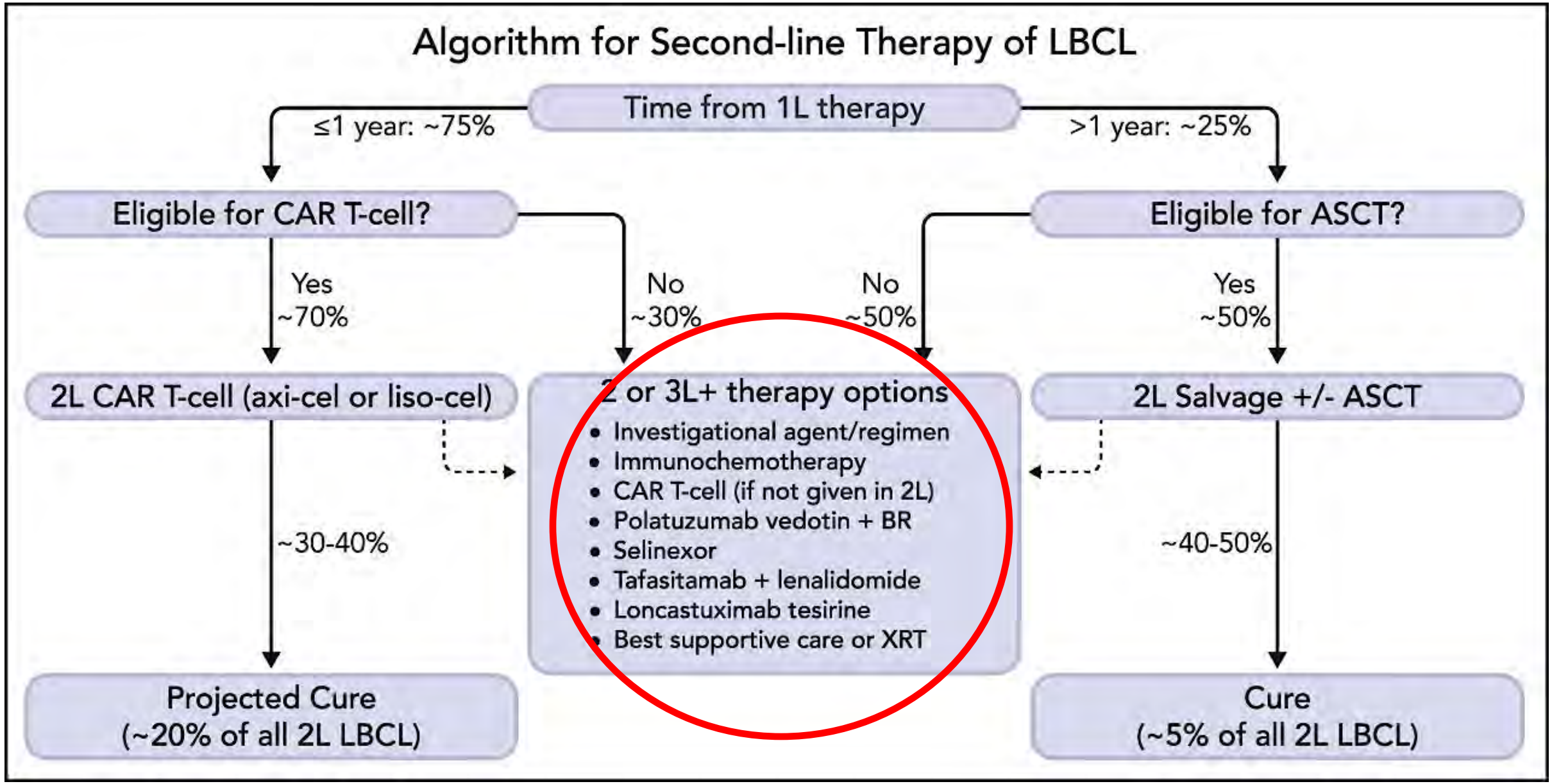

Data cut-off: July 5, 2024.

Courtesy of Stephen M Ansell, MD, PhD

**Salles et al. ASH 2024;Abstract 469.**

# Front-Line Treatment of Diffuse Large B-Cell Lymphoma (DLBCL)

- Pola-R-CHP vs R-CHOP
- R-mini-CHOP




Courtesy of Stephen M Ansell, MD, PhD

Westin J, Sehn LH. Blood. 2022 May 5;139(18):2737-2746.

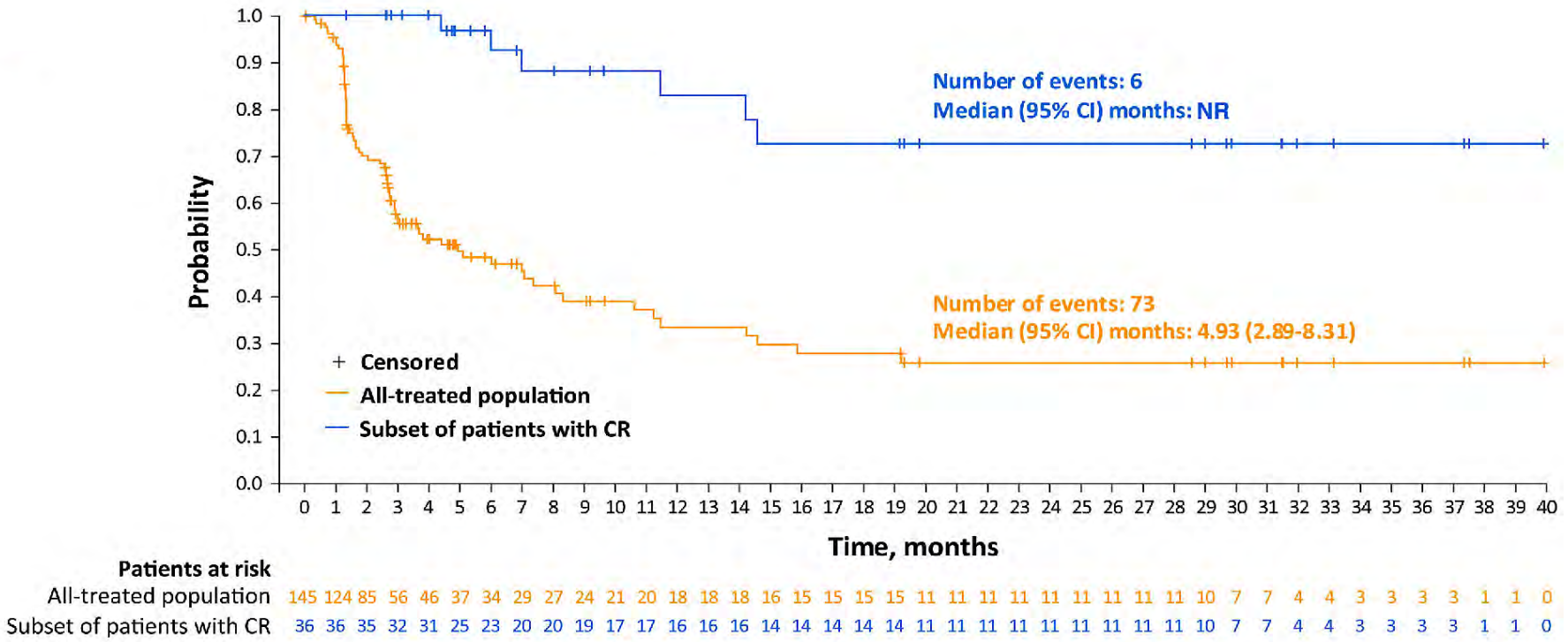
# Tafasitamab for relapsed or refractory diffuse large B-cell lymphoma: final 5-year efficacy


- 80 R/R DLBCL patients
- Received up to 12 cycles of co-administered tafasitamab and lenalidomide, followed by tafasitamab monotherapy until progression
- ORR 57.5%, CR rate 41.3% (n=33).
- Median PFS 11.6 months.
- Median OS 33.5 months.

Courtesy of Stephen M Ansell, MD, PhD

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

# Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy

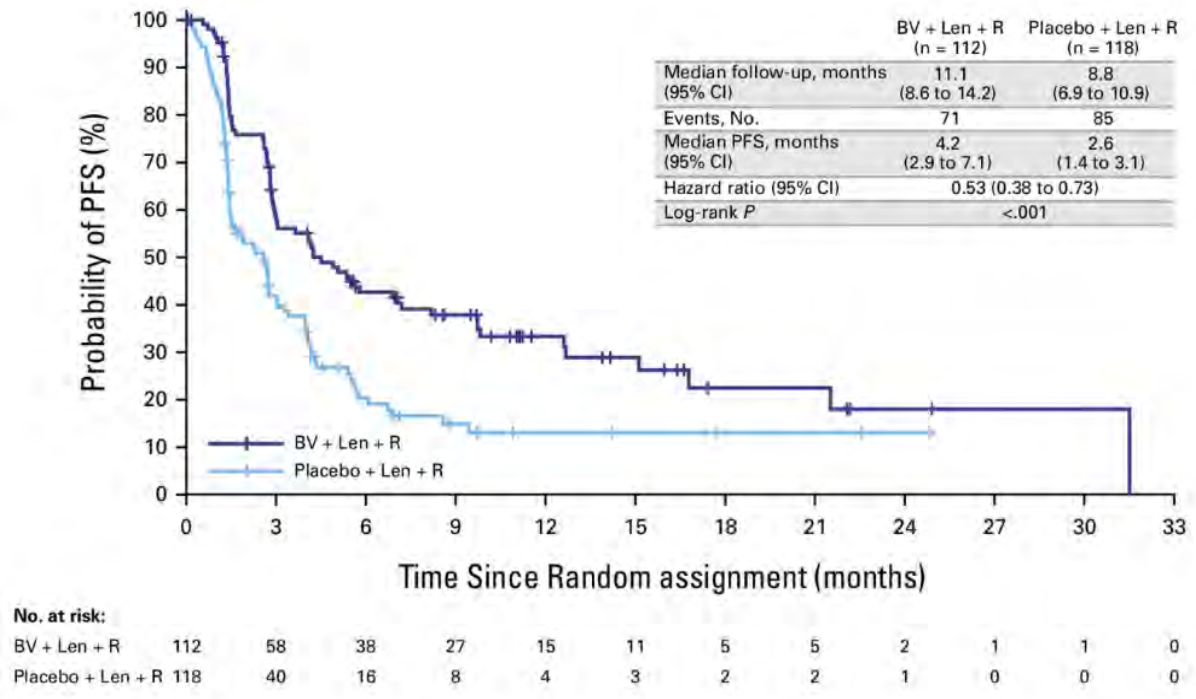



- 145 patients enrolled.
- ORR 48.3%.
- Thirty-six (24.8%) achieved CR, of which 16 (44%) and 11 (31%) were event-free for ≥1 year and ≥2 years, respectively.
- Median OS 9.5 months
- Median PFS 4.9 months.

Courtesy of Stephen M Ansell, MD, PhD

**Caimi PF, et al. Haematologica. 2024 Apr 1;109(4):1184-1193.**

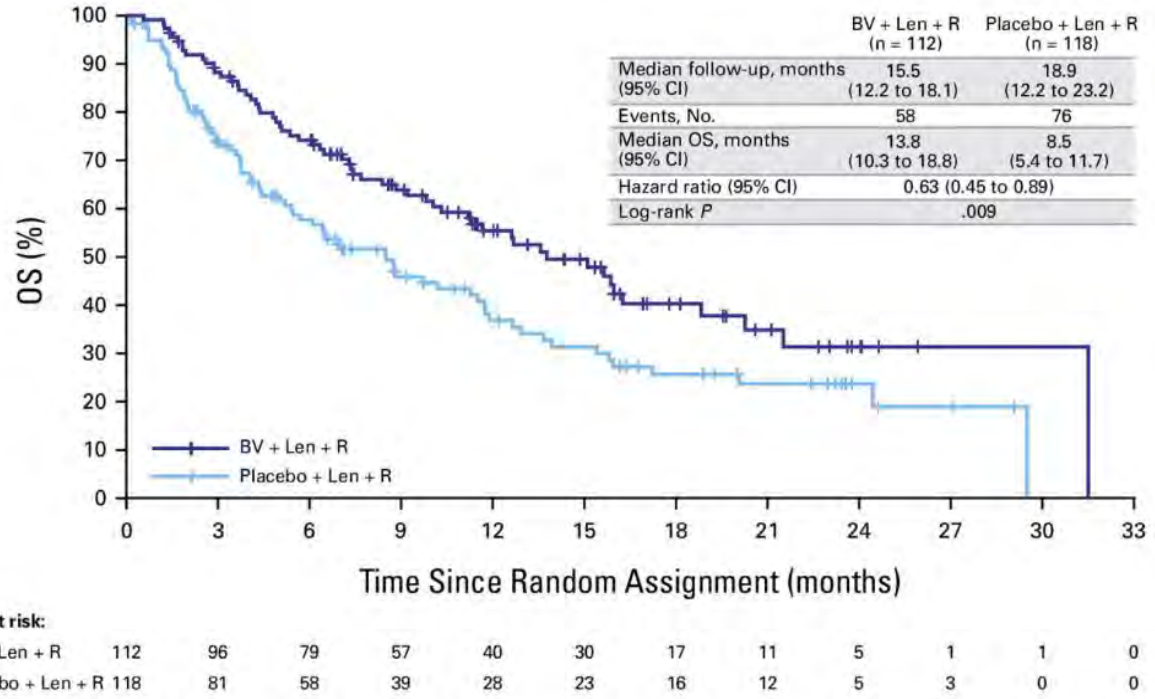
# Brentuximab Vedotin in Combination with R$^2$ for Relapsed Diffuse Large B-Cell Lymphoma (ECHELON-3)




| | BV + Len + R (n = 112) | Placebo + Len + R (n = 118) |
|---|---|---|
| Median follow-up, months (95% CI) | 11.1 (8.6 to 14.2) | 8.8 (6.9 to 10.9) |
| Events, No. | 71 | 85 |
| Median PFS, months (95% CI) | 4.2 (2.9 to 7.1) | 2.6 (1.4 to 3.1) |
| Hazard ratio (95% CI) | 0.53 (0.38 to 0.73) | |
| Log-rank *P* | <.001 | |

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) |
|---|---|---|
| Median follow-up, months (95% CI) | 15.5 (12.2 to 18.1) | 18.9 (12.2 to 23.2) |
| Events, No. | 58 | 76 |
| Median OS, months (95% CI) | 13.8 (10.3 to 18.8) | 8.5 (5.4 to 11.7) |
| Hazard ratio (95% CI) | 0.63 (0.45 to 0.89) | |
| Log-rank *P* | .009 | |

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 |

- 230 patients - BV + Len + R (n = 112) or placebo + Len + R (n = 118).
- Median OS was 13.8 months with BV + Len + R versus 8.5 months with placebo + Len + R (*P* = .009).
- Median PFS was 4.2 months with BV + Len + R versus 2.6 months with placebo + Len + R (*P* < .001).
- ORR was 64% with BV + Len + R and 42% with placebo + Len + R
- CR rates were 40% and 19%, respectively.

Courtesy of Stephen M Ansell, MD, PhD

**Bartlett et al. J Clin Oncol. 2025 Jan 7:JCO2402242.**

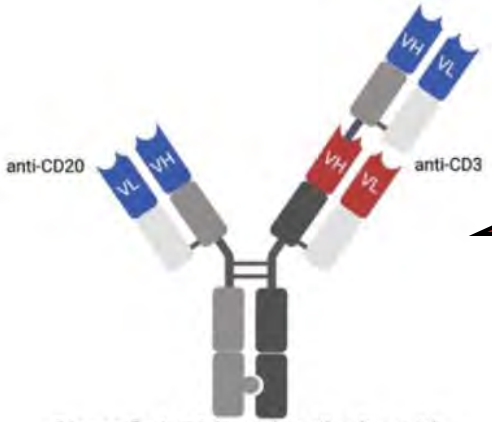
# Considerations for Relapsed DLBCL

- Tafasitamab/lenalidomide
- Loncastuximab tesirine
- Brentuximab vedotin + lenalidomide/rituximab ($R^2$)

# DLBCL: Bispecifics


Bispecific IgG1-based Antibodies
(Epcoritamab, Mosunetuzumab)

Ramp up → Epcoritamab q week until C3, then q14 days until C9, then monthly → NO LIMITS



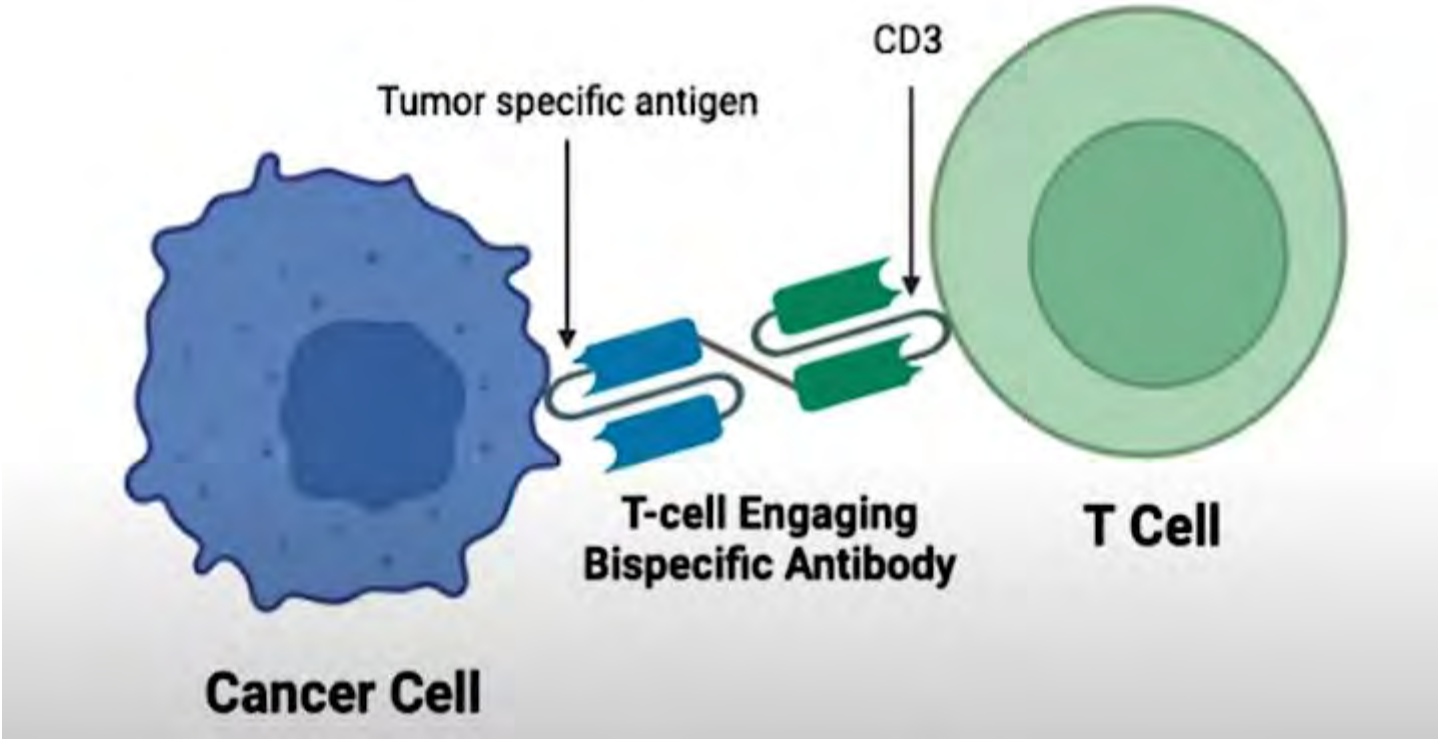

Bispecific IgG1-based Antibodies with additional Ag binding moiety
(Glofitamab)

Ramp up → Glofitamab q21d x 1 year → STOP


Courtesy of Brian T Hill, MD, PhD

# DLBCL: Bispecifics

# Epcoritamab




Courtesy of Brian T Hill, MD, PhD

# 3-Year Update from the EPCORE NHL-1 Trial: Epcoritamab Leads to Deep and Durable Responses in Relapsed or Refractory Large B-Cell Lymphoma

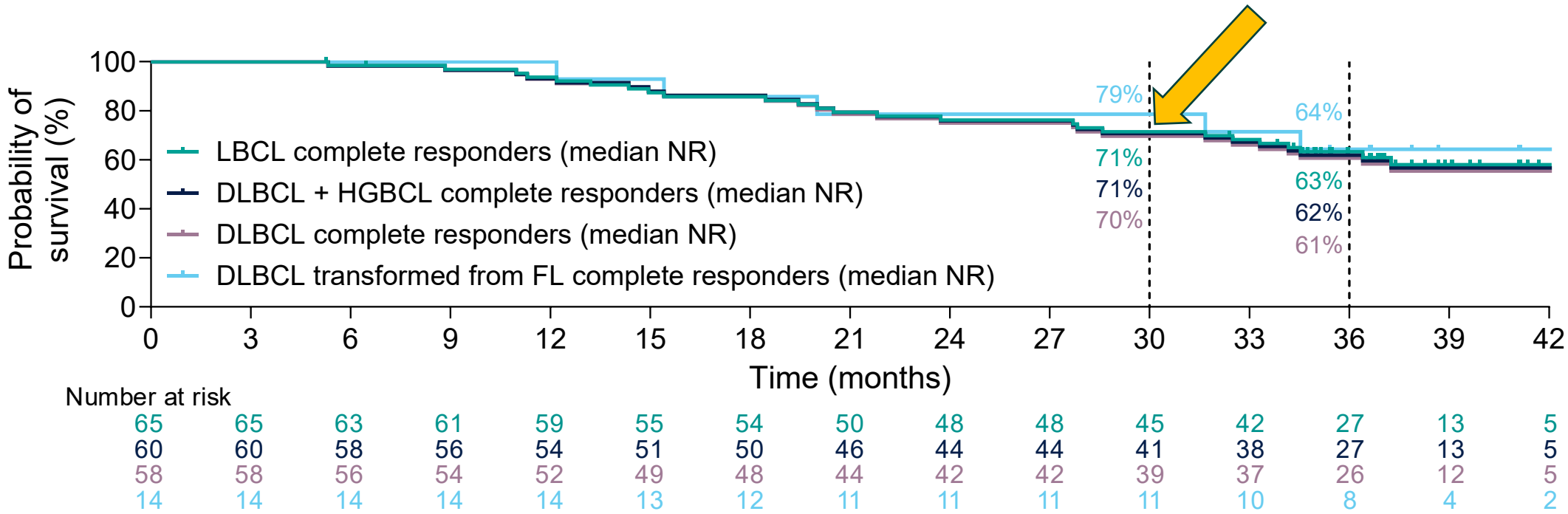
**Julie M. Vose, MD, MBA,[1] Chan Y. Cheah, MBBS, DMSc,[2] Michael Roost Clausen, MD, PhD,[3] David Cunningham, MD, FRCP, FMedSci,[4] Umar Farooq, MD,[5] Tatyana Feldman, MD,[6] Herve Ghesquieres, MD, PhD,[7] Wojciech Jurczak, MD, PhD,[8] Kim M. Linton, MBChB, PhD,[9] Catherine Thieblemont, MD, PhD,[10] Tycel Phillips, MD,[11] Won Seog Kim, MD, PhD,[12] Pegah Jafarinasabian, MD, PhD,[13] Barbara D'Angelo Månsson, PhD,[14] David Soong, PhD,[15] Andrew J. Steele, PhD,[15] Zhu Li, MS,[15] Christian W. Eskelund, MD, PhD,[14] Martin Hutchings, MD, PhD,[16] Yasmin H. Karimi, MD[17]**

[1]University of Nebraska Medical Center, Omaha, NE, USA; [2]Sir Charles Gairdner Hospital and the University of Western Australia, Nedlands, Australia; [3]Vejle Hospital, Vejle, Denmark; [4]The Royal Marsden NHS Foundation Trust, Sutton, UK; [5]University of Iowa, Iowa City, IA, USA; [6]John Theurer Cancer Center at Hackensack Meridian Health, Hackensack Meridian Health School of Medicine, Hackensack, NJ, USA; [7]Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [8]MSC National Research Institute of Oncology, Kraków, Poland; [9]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK; [10]Assistance Publique & Hôpitaux de Paris (APHP), Hôpital Saint-Louis, Hémato-oncologie, Université de Paris, Paris, France; [11]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA (present affiliation: City of Hope, Duarte, CA, USA); [12]Samsung Medical Center, Seoul, Republic of Korea; [13]AbbVie, North Chicago, IL, USA; [14]Genmab, Copenhagen, Denmark; [15]Genmab, Plainsboro, NJ, USA; [16]Rigshospitalet and University of Copenhagen, Copenhagen, Denmark; [17]University of Michigan Division of Hematology/Oncology, Ann Arbor, MI, USA

Presented at the American Society of Hematology Annual Meeting; December 7–10, 2024; San Diego, CA

Courtesy of Brian T Hill, MD, PhD

# Long-Term PFS and OS Benefits With Complete Response



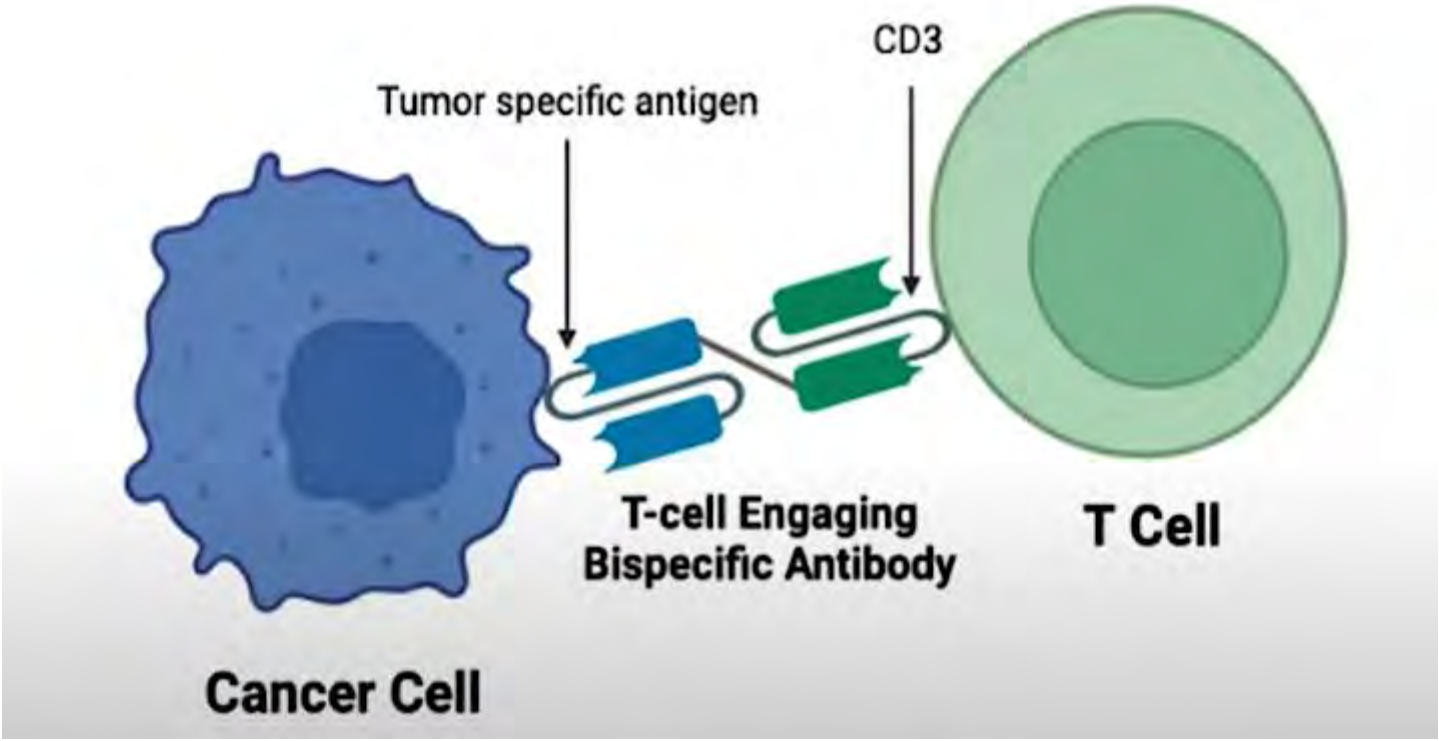

- Median PFS for the overall population (N=157) was 4.2 mo (95% CI, 2.8–5.5)
- Among complete responders (n=65), median PFS was 37.3 mo (95% CI, 26.0–NR)
  - 36-mo PFS estimate was 53%
- Median OS for the overall population (N=157) was 18.5 mo (95% CI, 11.7–27.7); among complete responders, it was NR
- At 36 mo, an estimated 75% of complete responders had not initiated a new antilymphoma therapy

CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; mo, month(s); NR, not reached; OS, overall survival; PFS, progression-free survival.
Vose JM, et al. ASH 2024. Poster 4480.

Courtesy of Brian T Hill, MD, PhD

# DLBCL: Bispecifics

# Glofitamab




Courtesy of Brian T Hill, MD, PhD

# Fixed-duration glofitamab monotherapy continues to demonstrate durable responses in patients with relapsed or refractory large B-cell lymphoma: 3-year follow-up from a pivotal Phase II study

Michael Dickinson,[1] Carmelo Carlo-Stella,[2] Franck Morschhauser,[3] Emmanuel Bachy,[4] Guillaume Cartron,[5] Paolo Corradini,[6] Nancy L. Bartlett,[7] Gloria Iacoboni,[8] Cyrus Khan,[9] Mark Hertzberg,[10] Lorenzo Falchi,[11] Joshua Brody,[12] Marek Trněný,[13] Estefania Mulvihill,[14] Aurelien Berthier,[14] Alessia Bottos,[14] James Relf,[15] Fabiola Bene Tchaleu,[16] Linda Lundberg,[14] Martin Hutchings[17]

*[1]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [2]Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy; [3]Hôpital Claude Huriez and CHU de Lille, Lille, France; [4]Centre Hospitalier Lyon Sud, Lyon, France; [5]CHU de Montpellier, Montpellier, France; [6]University of Milan and Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [7]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]Allegheny Health Network, Pittsburgh, PA, USA; [10]Prince of Wales Hospital and University of New South Wales, Sydney, Australia; [11]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [12]Tisch Cancer Institute, New York, NY, USA; [13]Charles University, Prague, Czech Republic; [14]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Roche Products Ltd, Welwyn Garden City, UK; [16]Genentech, Inc., South San Francisco, CA, USA; [17]Rigshospitalet, Copenhagen, Denmark*

*Presented at the 66th ASH Annual Meeting | December 7–10, 2024*

## Study design

Pivotal single-arm Phase II study in patients with R/R LBCL and ≥2 prior therapies

**Key inclusion criteria**

- DLBCL NOS, HGBCL, transformed FL, or PMBCL
- ECOG PS 0–1
- ≥2 prior therapies, including:
  - Anti-CD20 antibody
  - Anthracycline

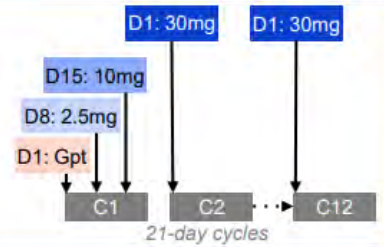
**Glofitamab IV administration**

**Fixed-duration treatment:**

- Q3W
- Up to 12 cycles (8.5 months)

**CRS mitigation:**

- Obinutuzumab IV pre-treatment (1000mg)
- C1 step-up dosing
- Monitoring after first glofitamab dose (2.5mg)




**Endpoints**

- **Primary**: CR rate (as best response) by IRC*
- **Key secondary**: ORR†, DoR†, DoCR†, PFS, OS

**Analyses**

- **Landmark**: PFS and OS by response (CR at EOT)
- **Biomarker:** ctDNA kinetics, immune recovery (B-cell, IgG and IgM)

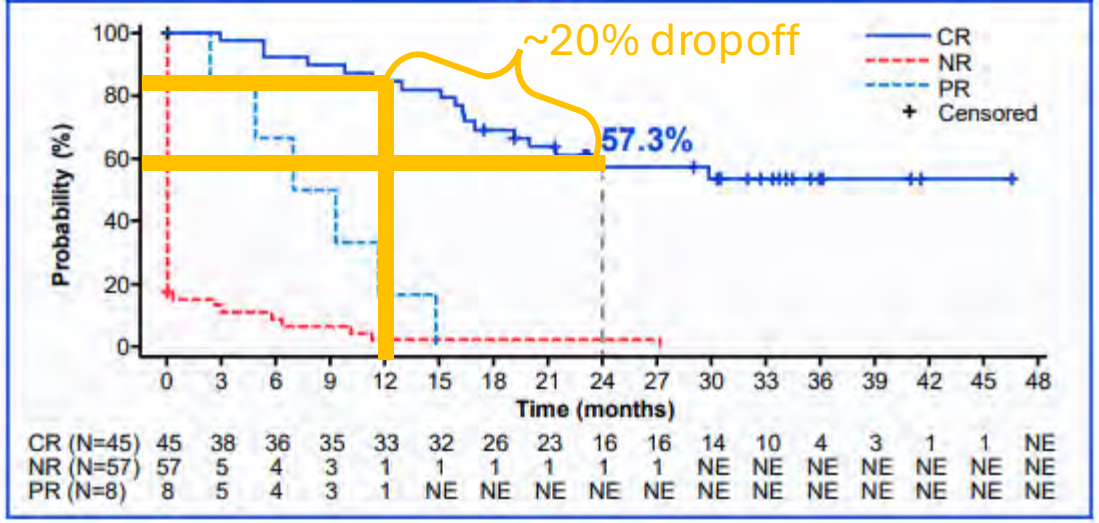
*By PET-CT (Lugano criteria)[1]; †By IRC and investigator.
C, cycle; CRS, cytokine release syndrome; ctDNA, circulating tumor DNA; D, day; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; DoCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; FL, follicular lymphoma; Gpt, obinutuzumab pre-treatment; HGBCL, high-grade B-cell lymphoma; IgG, immunoglobulin G; IgM, immunoglobulin M; IRC, independent review committee; IV, intravenous; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PET-CT, positron emission tomography-computed tomography; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; Q3W, three-weekly.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

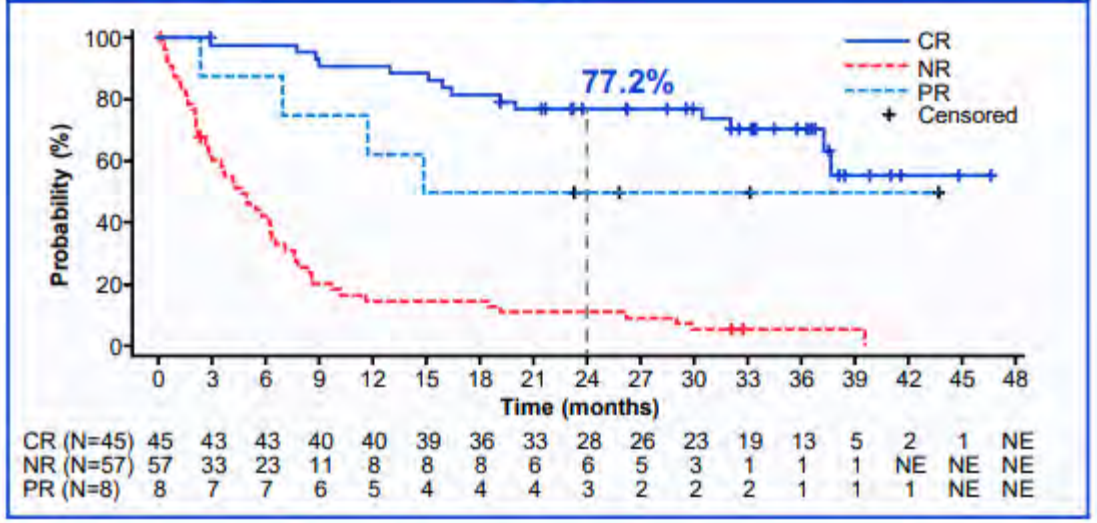
Courtesy of Brian T Hill, MD, PhD

# Landmark analysis by response at end of treatment

## PFS




## OS




| Landmark PFS from EOT in patients with CR at EOT* | N=45 |
|---|---|
| Median PFS, months (95% CI) | NE (20.0–NE) |
| 24-month PFS rate, % (95% CI) | 57.3 (41.2–73.4) |

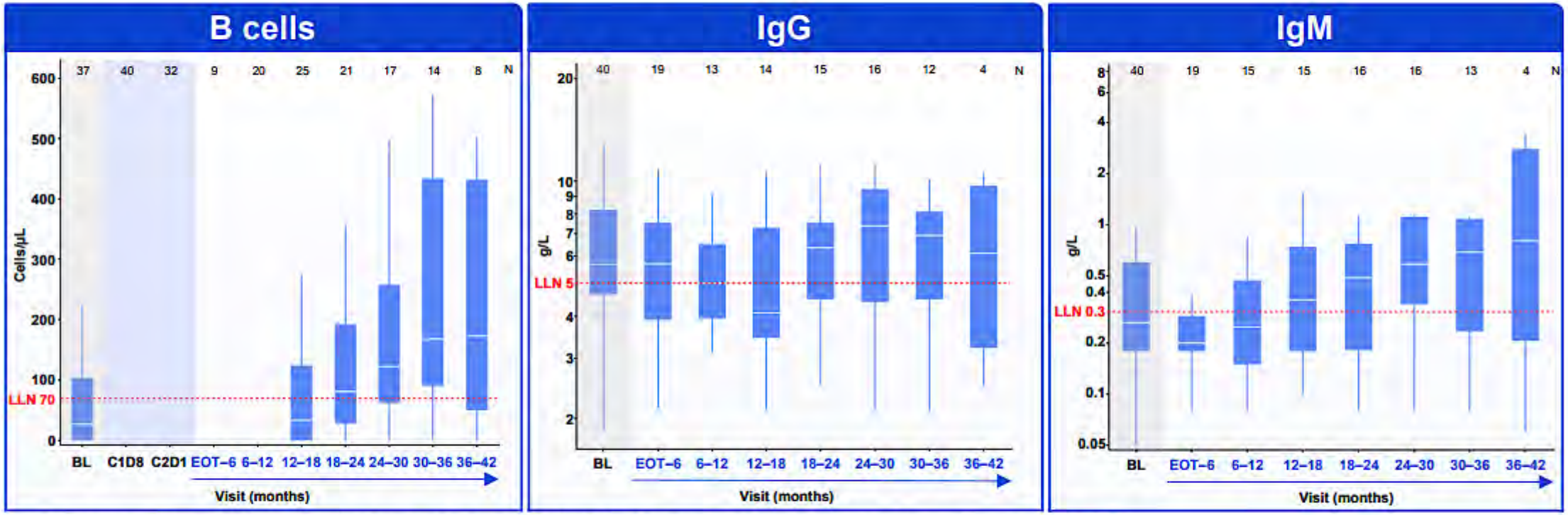
| Landmark OS from EOT in patients with CR at EOT* | N=45 |
|---|---|
| Median OS, months (95% CI) | NE (37.2–NE) |
| 24-month OS rate, % (95% CI) | 77.2 (64.8–89.6) |

**Most patients with a CR at EOT remained progression-free and alive at 24 months after EOT**

*Kaplan-Meier estimates.

Courtesy of Brian T Hill, MD, PhD

# Immune recovery after fixed-duration glofitamab monotherapy



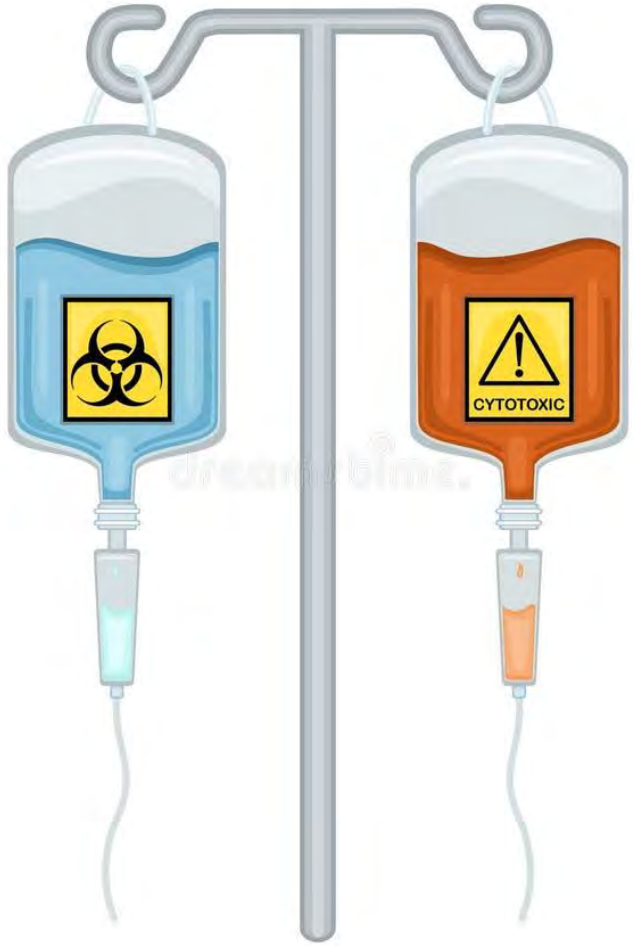

- Between 18–24 months* after EOT, 52% (11/21) of patients showed B cells above LLN, 67% (10/15) of patients showed IgG above LLN and 62% (10/16) patients showed IgM above LLN

**B-cell recovery was observed starting from 12–18 months after EOT in patients completing treatment and in ongoing remission***

*Percentages are based on patients with an available sample at each timepoint;
CD19+B-cells LLN = 70 cell/µL; IgG LLN = 5 g/L; IgM LLN = 0.3g/L. LLN, lower limit of normal.

Courtesy of Brian T Hill, MD, PhD

# DLBCL: Bispecifics + Chemotherapy



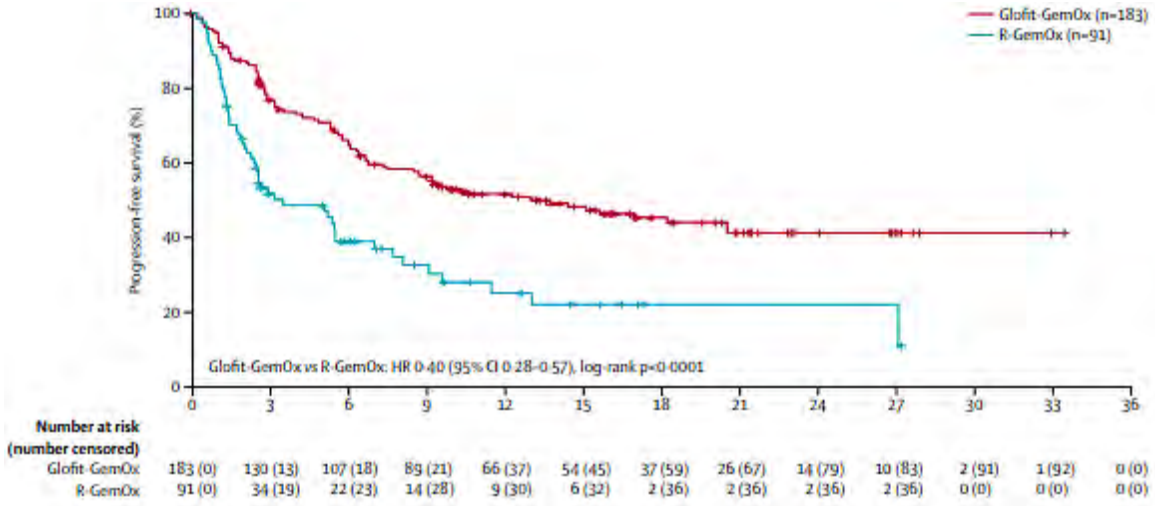

Courtesy of Brian T Hill, MD, PhD

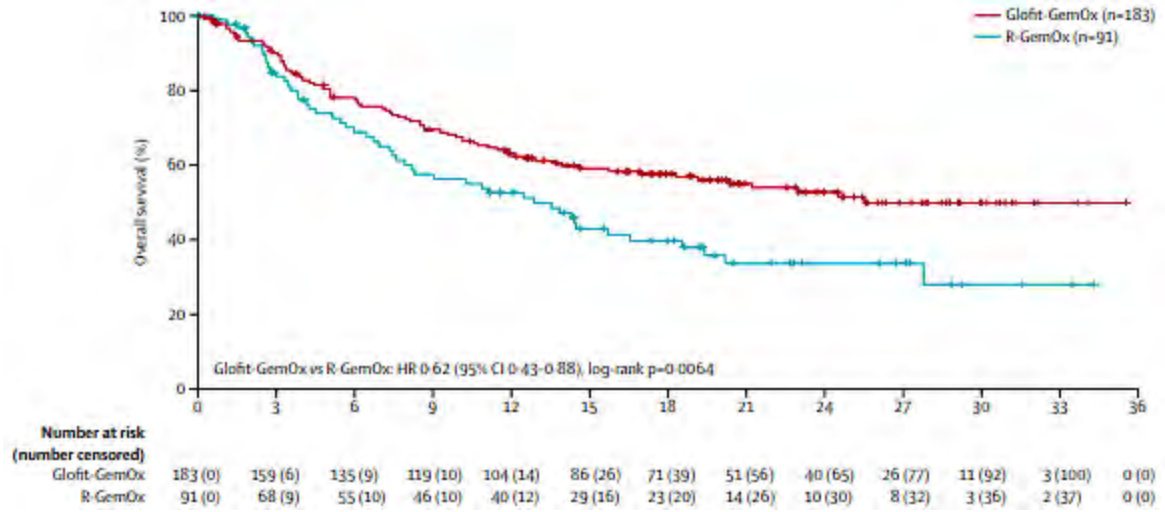
Lancet 2024; 404: 1940–54

# Glofitamab plus gemcitabine and oxaliplatin (GemOx) versus rituximab-GemOx for relapsed or refractory diffuse large B-cell lymphoma (STARGLO): a global phase 3, randomised, open-label trial

*Jeremy S Abramson, Matthew Ku, Mark Hertzberg, Hui-Qiang Huang, Christopher P Fox, Huilai Zhang, Dok Hyun Yoon, Won-Seog Kim, Haifaa Abdulhaq, William Townsend, Charles Herbaux, Jan M Zaucha, Qing-Yuan Zhang, Hung Chang, Yanyan Liu, Chan Yoon Cheah, Herve Ghesquieres, Stephen Simko, Victor Orellana-Noia, Richard Ta, James Relf, Mark Dixon, Martine Kallemeijn, Estefania Mulvihill, Huang Huang, Linda Lundberg, Gareth P Gregory**

- Global, randomized Phase 3:  GemOx ± Glofitamab
- Transplant ineligible r/r DLBCL
- Median prior line of therapy = 1




Courtesy of Brian T Hill, MD, PhD

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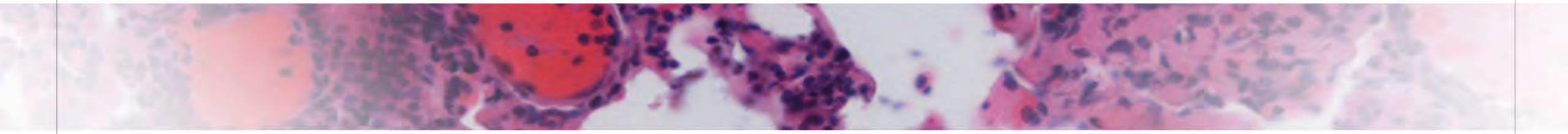
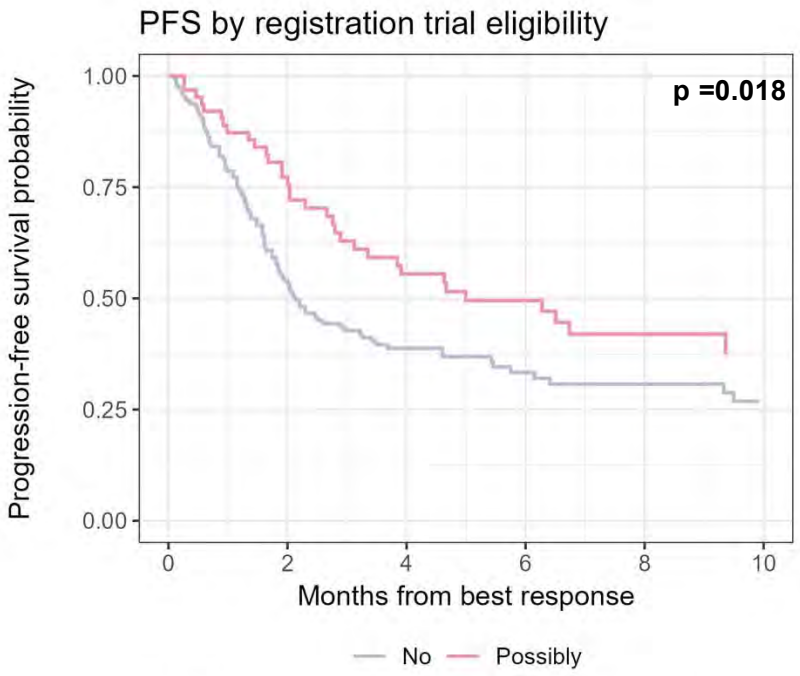


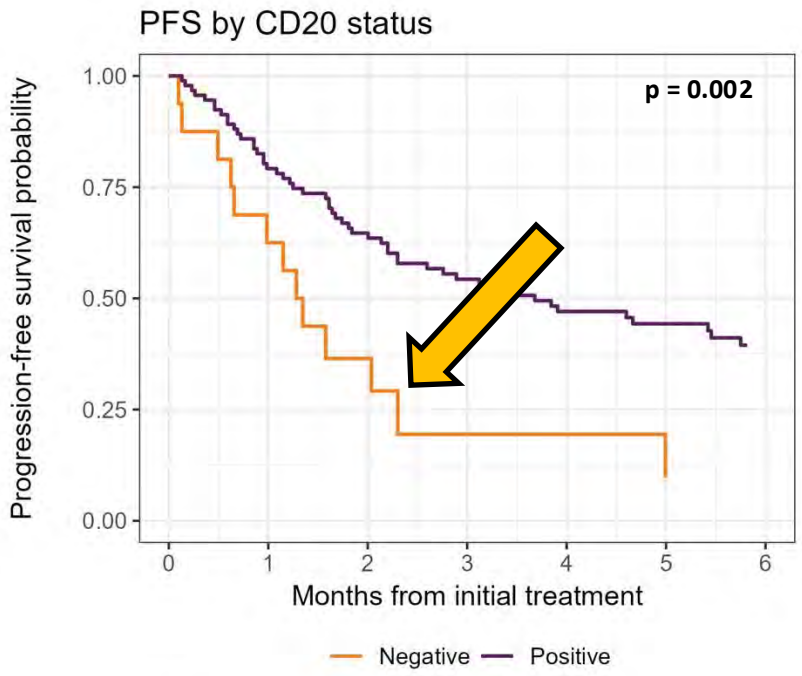
# Real-World Outcomes with Bispecific T-Cell Engagers (REALBiTE) for Relapsed or Refractory Large B-Cell Lymphoma: A Multi-Center, Retrospective Cohort Study

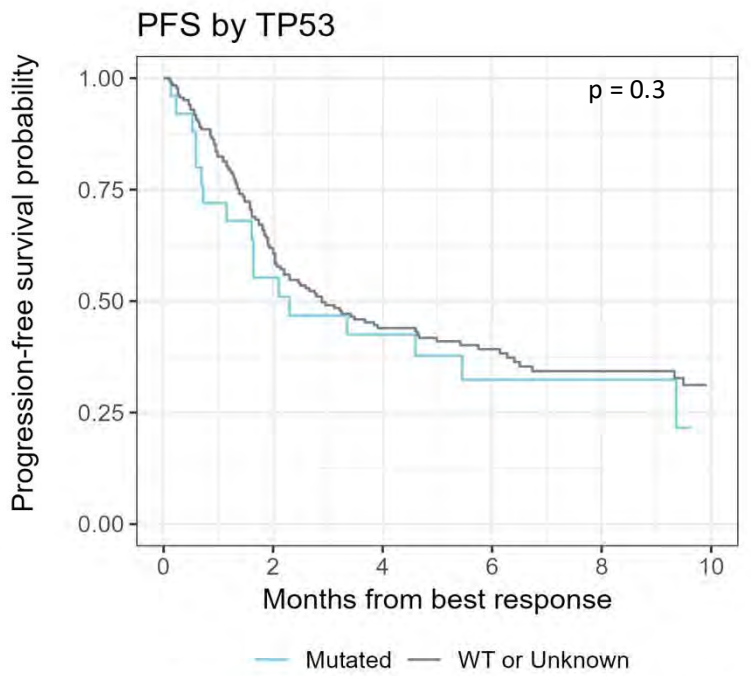
**Taylor R. Brooks, MD**, Emily C. Zabor, DrPH, Yohanna B. Bedelu, MPH, Nikita Dave, MD, Daniel J. Landsburg, MD, Adrienne N. Nedved, PharmD, RPh, Yucai Wang, MD, PhD, Catherine Reinert, RN, BSN, OCN, MBA, Ajay Major, MD, MBA, Megan Sears-Smith, DO, Nilanjan Ghosh, MD, PhD, Kiarash Salafian, MD, Emily Ayers, MD, Jordan Miller, PharmD, Natalie Grover, MD, Chelsea Peterson, DO, Cyrus Khan, MD, Sean P. Bliven, MD, Mayur Narkhede, MD, Carrie I. Ho, MD, Stephen D. Smith, MD, Alyssa Gibson, Justin Kline, MD, Suchitra Sundaram, MBBS, Joshua Brody, MD Kelsey Baron, MD, Boyu Hu, MD, Daniel C. Trotier, MD, Priyanka A Pophali, MBBS, Xi Yang, MD, Yasmin H. Karimi, MD, Marshall McKenna, MD, Claire Yun Kyoung Ryu Tiger, MD, PhD, Alex Niu, MD, Francisco Hernandez-Ilizaliturri, MD, Javier Munoz, MD, MBA, Rodolfo Garza-Morales, MD, Fadzai Chinyengetere, MD, Sandeep Dave, MD, Nayef Abdel-Razeq, MD, Muhamad Alhaj Moustafa, MD, MS, Paolo F. Caimi, MD, MBA, Brian T. Hill MD, PhD

Courtesy of Brian T Hill, MD, PhD

# Progression-Free Survival of Subgroups



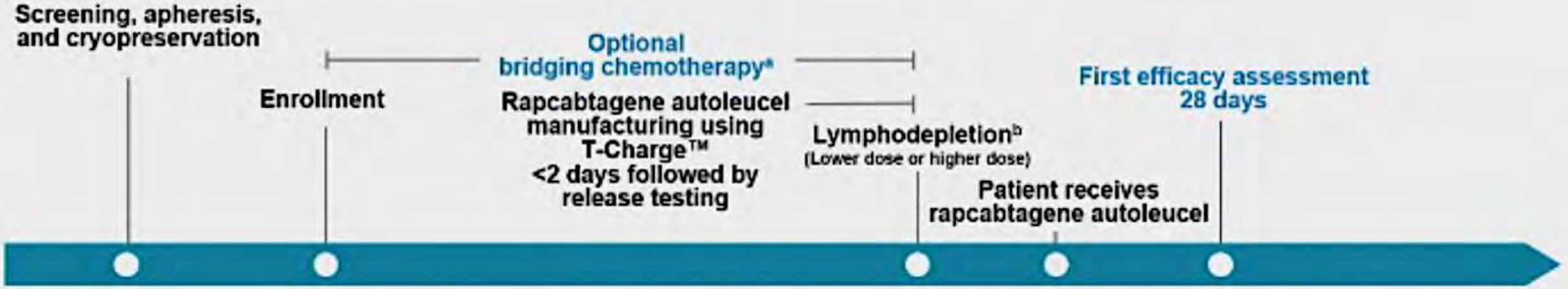




Courtesy of Brian T Hill, MD, PhD

# Bispecific Antibodies for Relapsed DLBCL

- Epcoritamab
- Glofitamab

# Rapcabtagene Autoleucel for Relapsed/Refractory DLBCL: Phase II Study Design



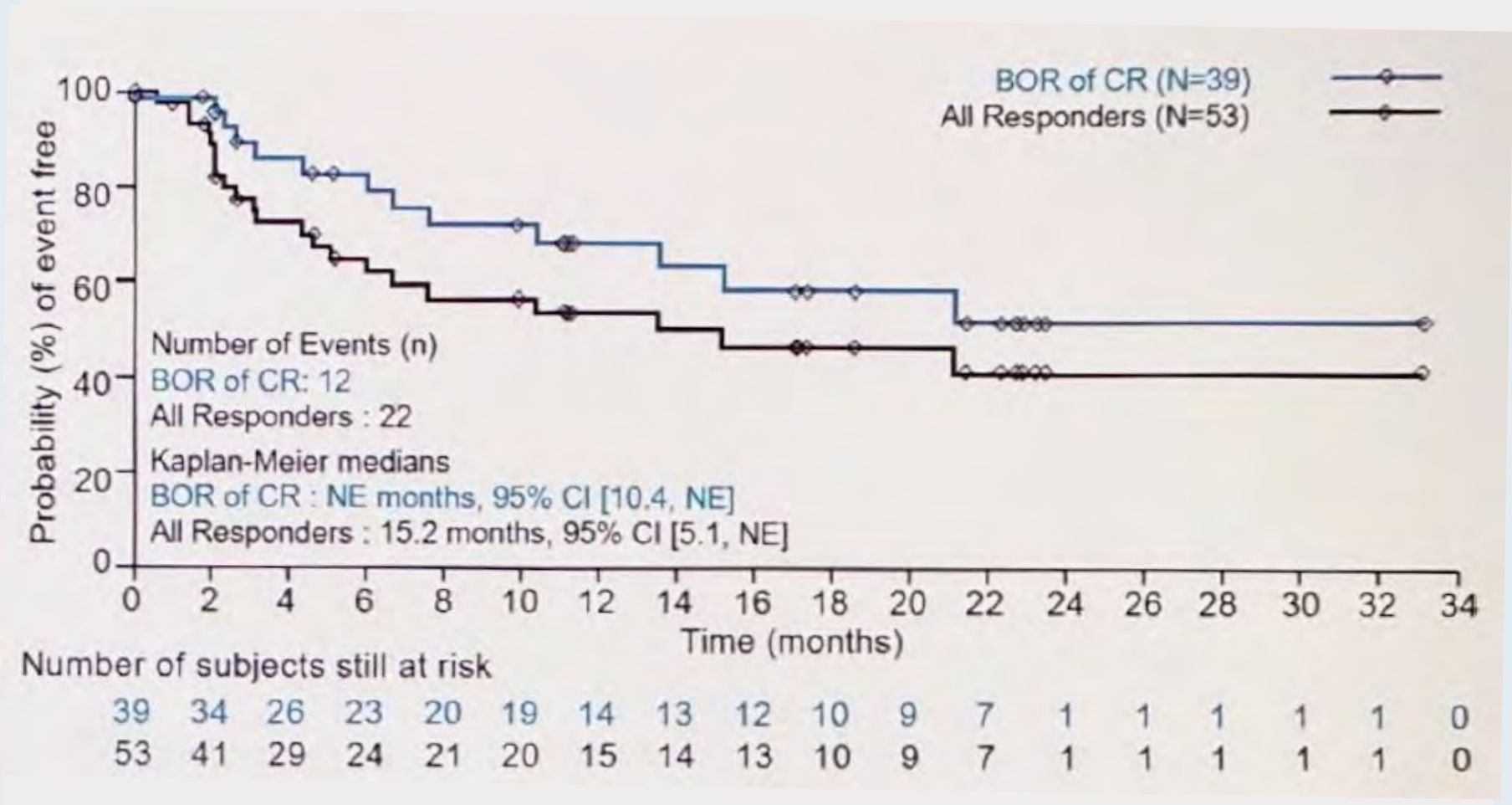

| Key eligibility criteria | Study treatment | End points |
|---|---|---|
| • ≥18 years of age<br>• Measurable disease at enrollment<br>• ECOG PS 0-1<br>• Relapsed/refractory disease[c] | • Rapcabtagene autoleucel single IV dose at $12.5\times10^6$ CAR+ cells | **Primary:** CRR (BOR of CR)<br><br>**Secondary:** ORR, PFS, DOR, OS, cellular kinetics, and safety |

CRR = complete response rate; BOR = best observed response; CR = complete response; ORR = overall response rate; PFS = progression-free survival; DOR = duration of response; OS = overall survival

Riedell P et al. ASH 2024;Abstract 67.

# Rapcabtagene Autoleucel: Overall Response (N = 60)

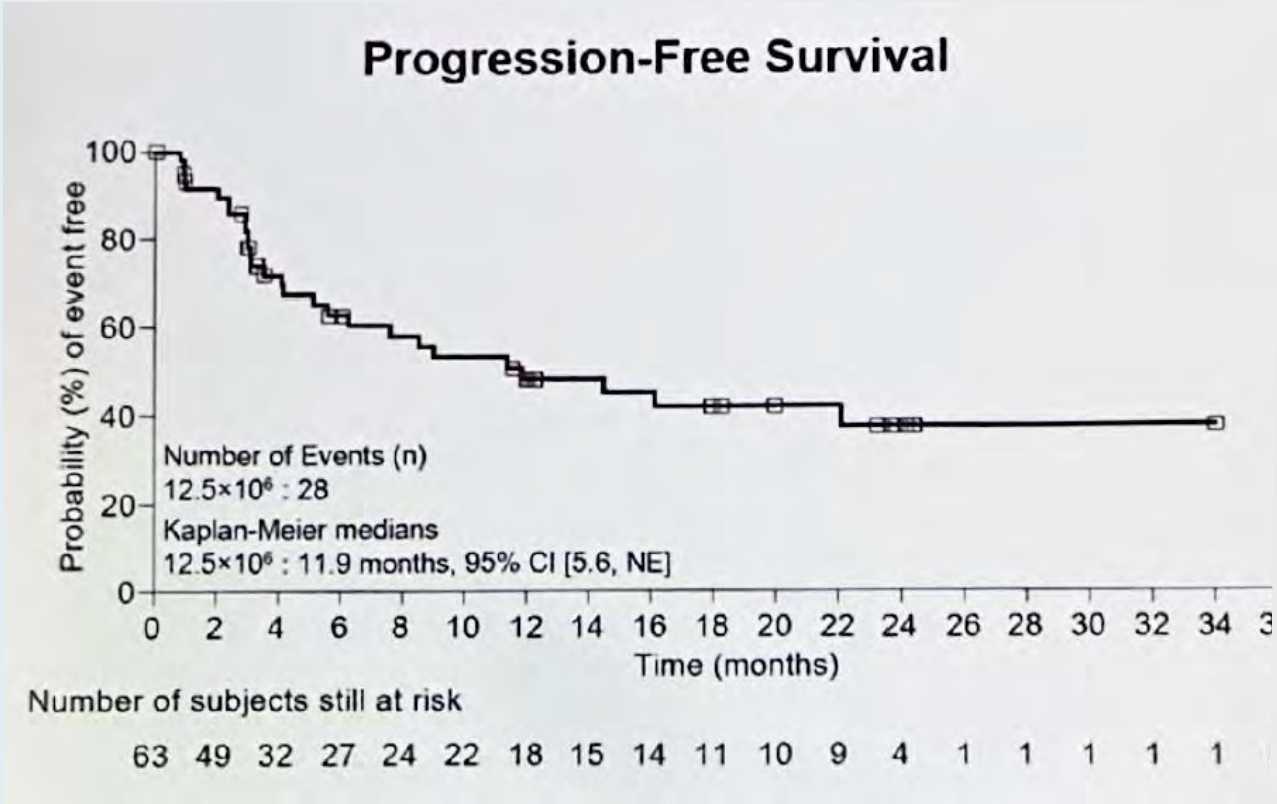
ORR: 88.3% (95% CI, 77.4%-95.2%)
CR: 65.0% (95% CI, 51.6%-76.9%)

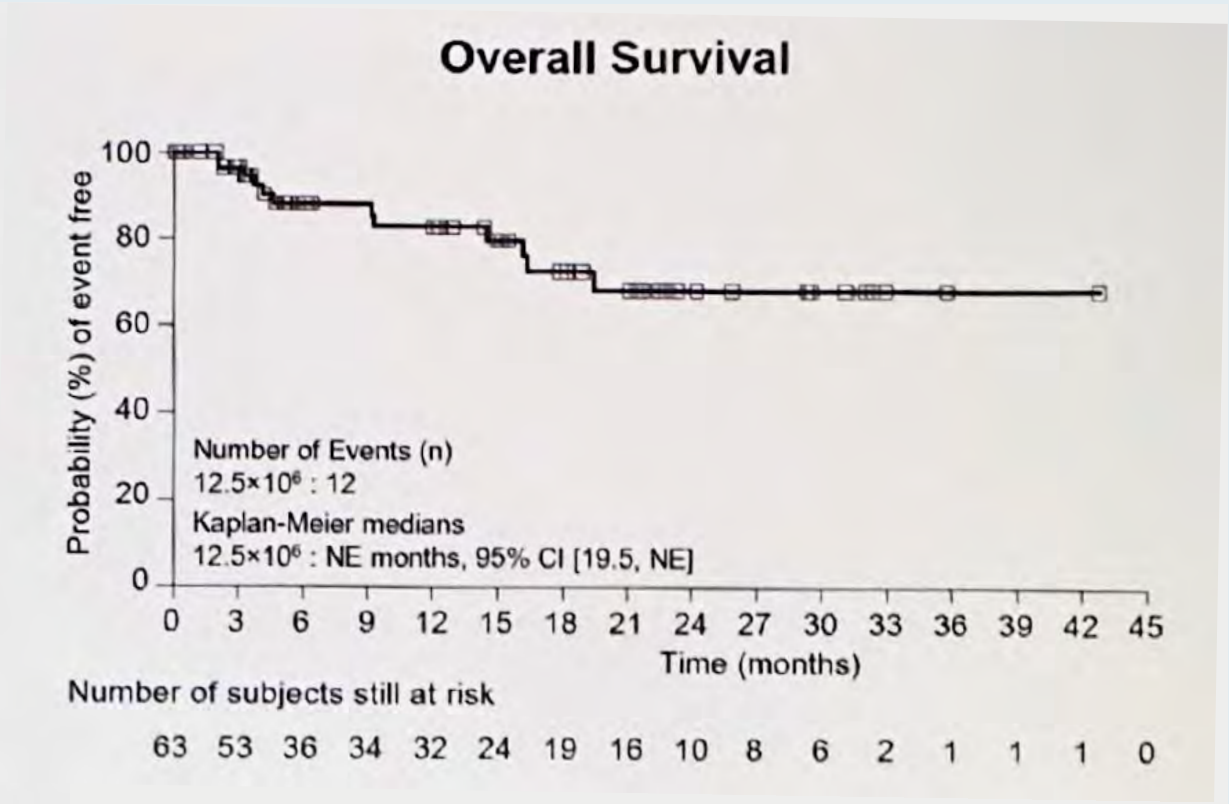



NE = not estimable

Riedell P et al. ASH 2024;Abstract 67.

# Rapcabtagene Autoleucel: Survival Outcomes (N = 63)




Median PFS: 11.9 months (95% CI, 5.6-NE)
12-month PFS: 48.2%

Median OS: NE (95% CI, 19.5-NE)
12-month OS: 83.0%

Riedell P et al. ASH 2024;Abstract 67.

# Rapcabtagene Autoleucel: Safety Outcomes

| | Rapcabtagene autoleucel $12.5\times10^6$ (N = 63) n (%) |
|---|---|
| Adverse events[a] | |
| Any grade | 62 (98.4) |
| Grade ≥3 | 53 (84.1) |
| Grade 5 | 6 (9.5) |
| Serious AE | 33 (52.4) |
| Deaths | 12 (19.0) |
| Disease progression | 6 (9.5) |
| Adverse event[b] | 6 (9.5) |
| Nonrelapse mortality[c] | 4 (6.3) |

| | Rapcabtagene autoleucel (N = 63) |
|---|---|
| ICANS, n (%) | |
| - Grade 1 | 2 (3.2%) |
| - Grade 2 | 0 |
| - Grade 3 | 2 (3.2%) |
| - Grade 4 | 1 (1.6%) |
| Median time to onset (range) | 13 days (10-28) |
| Median time from onset to resolution (range) | 17 days (11-24) |

AE = adverse event; ICANS = immune effector cell-associated neurotoxicity syndrome

Riedell P et al. ASH 2024;Abstract 67.

# Unique Approach to CAR T-Cell Therapy for DLBCL

- Rapcabtagene autoleucel
- T-Charge™ platform

# AGENDA

## Year in Review: Management of Non-Hodgkin Lymphoma

**INTRODUCTION:** Bispecific Antibodies in Community Practice

**MODULE 1:** Diffuse Large B-Cell Lymphoma

**MODULE 2: CD19, CD20 or Both? AZD0486 Bispecific Antibody**

**MODULE 3:** Mantle Cell Lymphoma

**MODULE 4:** Follicular Lymphoma

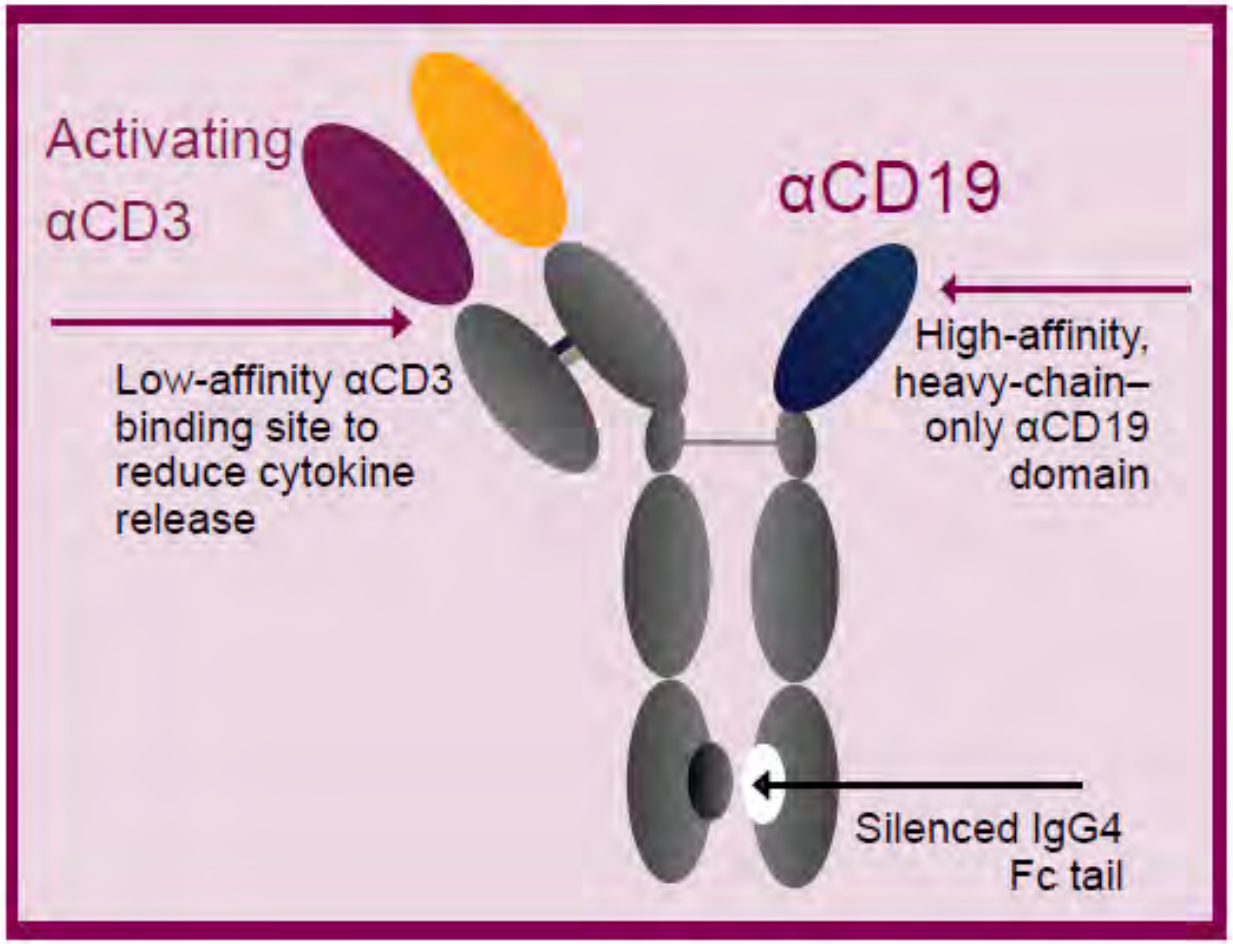
**MODULE 5:** CAR T-Cell Therapy for Marginal Zone Lymphoma

RTP Year in Review 2025

# Introduction

- AZD0486 is an IgG4 fully human CD19xCD3 bispecific T-cell engager (TCE), with half-life of 8–12 days[1-3]
- Two step-up dosing (C1D1: 0.27 mg, C1D8: 1 mg, C1D15: target dose) enabled administration of the drug to achieve therapeutic target dose[4,5]
- Here, we present safety and efficacy of an ongoing Phase 1 study of AZD0486 in the cohort of patients with R/R DLBCL

## AZD0486 Structure

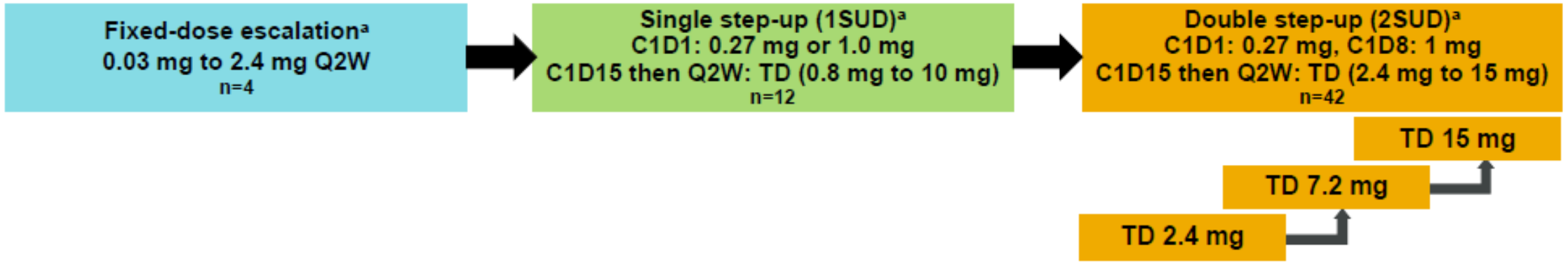



**1.** Malik-Chaudhry HK, et al. *MAbs*. 2021;313:1890411. **2.** Trinklein ND, et al. *MAbs*. 2019;11:639-52. **3.** Hou JZ, et al. *Blood*. 2022;140(Suppl 1):1474-5. **4.** Gaballa S, et al. *Blood*. 2023(suppl 1):1662. **5.** Devata S, et al. *HemaSphere*. 2024;8(Suppl 1):2059-2060.

Courtesy of Brian T Hill, MD, PhD

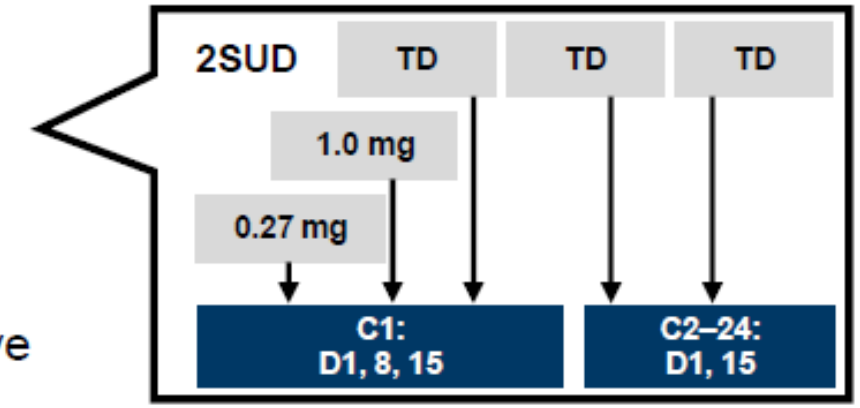
# AZD0486 in a First-in-Human Phase 1 Study

## Overall Study Design




## 2SUD Treatment Schedule

- AZD0486 is administered intravenously
- 2SUD on C1D1, C1D8 with target dose (TD) on C1D15, then on D1, D15 each 28-day cycle up to 2 years
  - Cycle 1 doses were inpatient
- Patients with 2 consecutive CRs after Cycle 6 may receive AZD0486 every 4 weeks



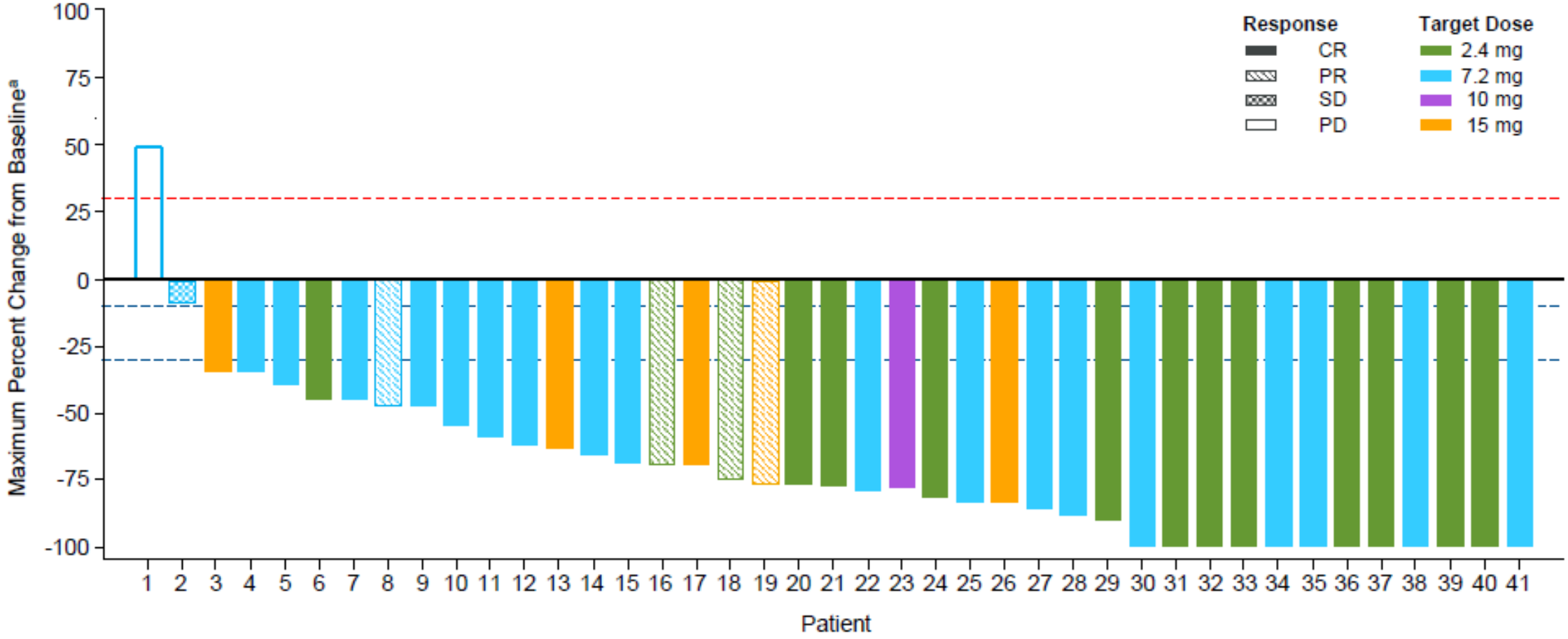

NCT04594642; data cutoff: 18 June 2024

[a]In the DLBCL cohort (N=58), 4 (7%) patients received a fixed dose, 12 (21%) received 1SUD, and 42 (72%) received 2SUD.

Courtesy of Brian T Hill, MD, PhD

# Tumor Regression

- ORR was 95% and CR rate was 85% in patients who received AZD0486 ≥2.4 mg (n=41)




[a]Waterfall chart indicates tumor shrinkage in evaluable patients as assessed by RECIL (change in sum of longest diameters).

Courtesy of Brian T Hill, MD, PhD

# AGENDA

## Year in Review: Management of Non-Hodgkin Lymphoma

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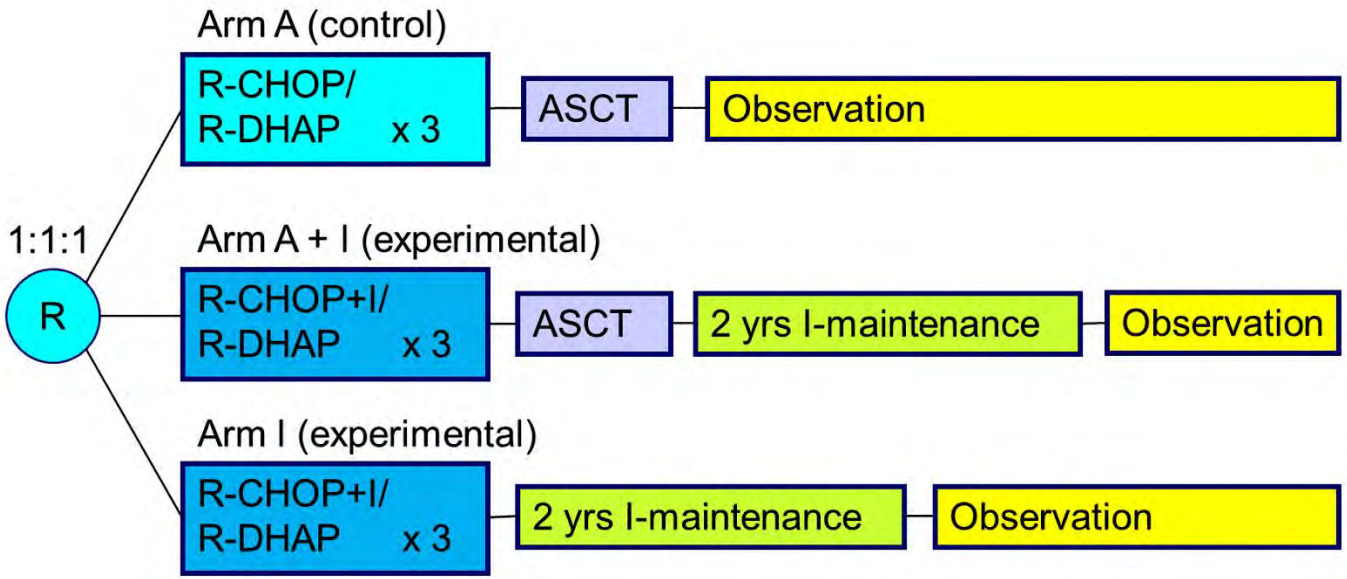
RTP Year in Review 2025

# Ibrutinib +/- immunochemotherapy with or without autologous stem-cell transplantation in previously untreated patients with mantle cell lymphoma (TRIANGLE)

- MCL patients
- previously untreated
- stage II-IV
- younger than 66 years
- suitable for HA and ASCT
- ECOG 0-2

- Primary outcome: FFS

- Secondary outcomes:
  - Response rates
  - PFS, RD
  - OS
  - Safety

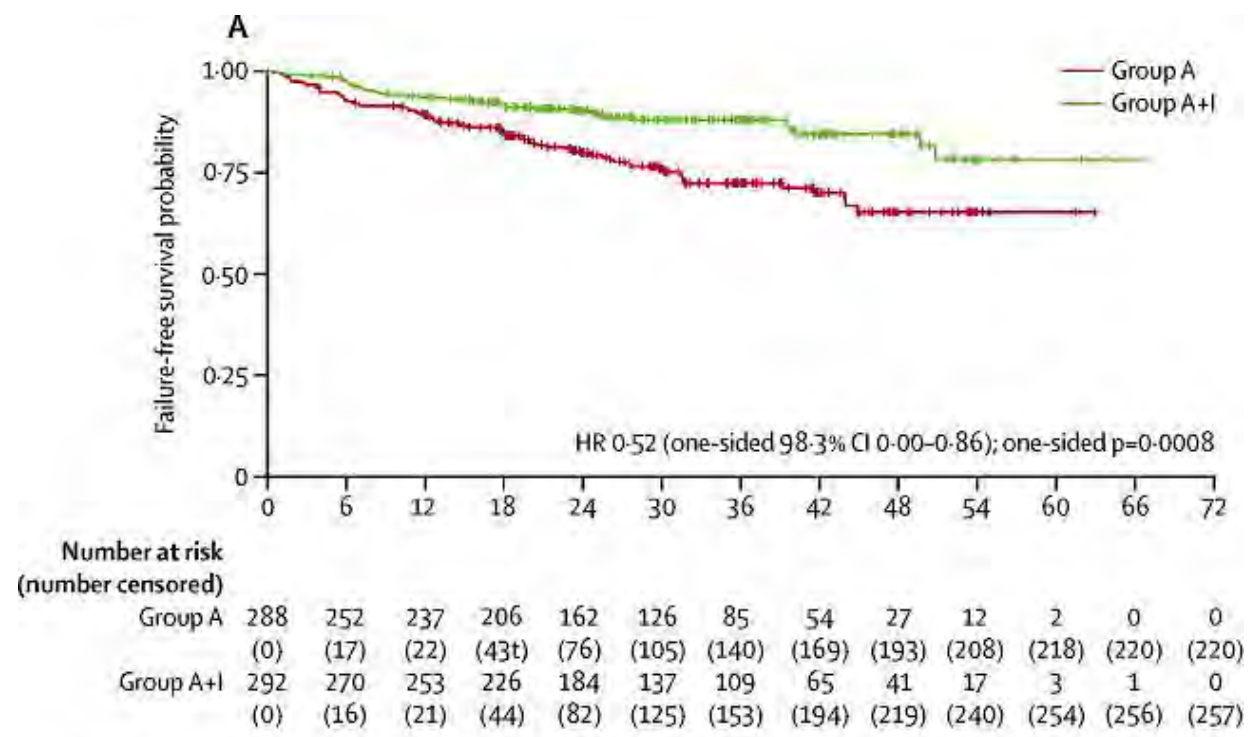


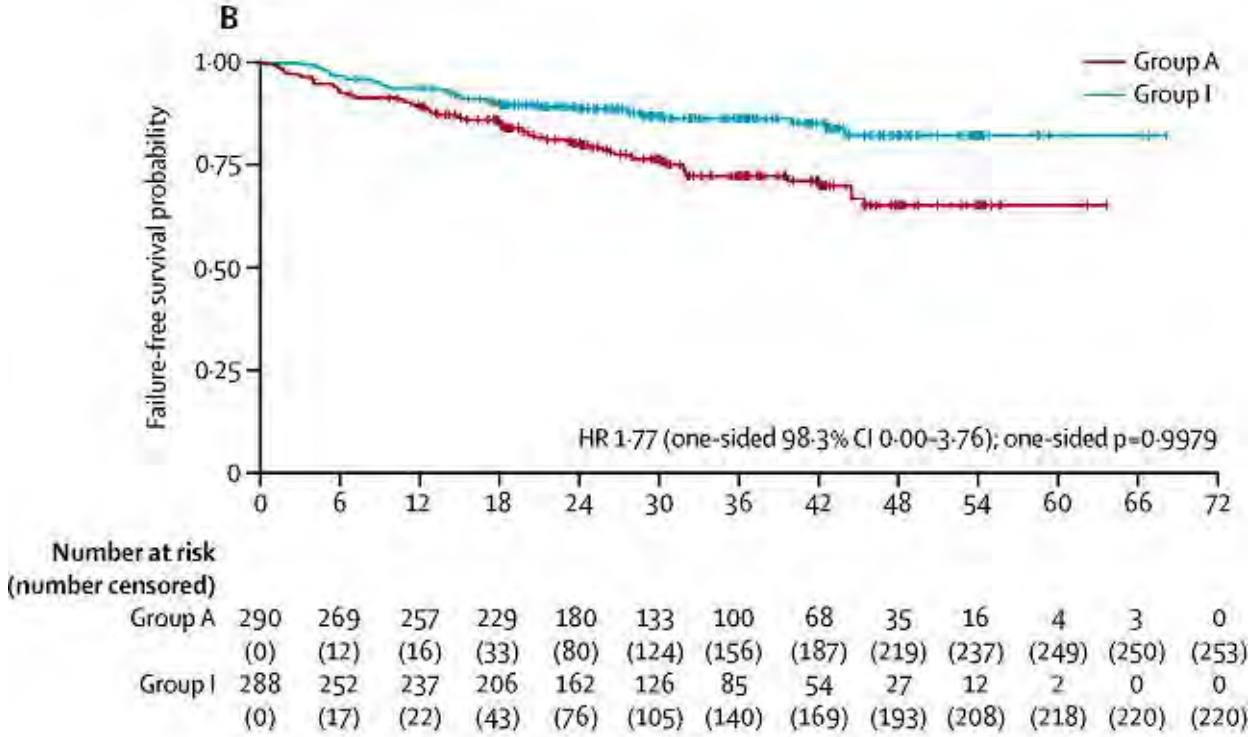

- R maintenance was added following national guidelines in all 3 trial arms
- Rituximab maintenance (without or with Ibrutinib) was started in 168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients.

Courtesy of Stephen M Ansell, MD, PhD

Dreyling et al. Lancet. 2024 May 25;403(10441):2293-2306.

# Ibrutinib +/- immunochemotherapy with or without autologous stem-cell transplantation in previously untreated patients with mantle cell lymphoma (TRIANGLE)



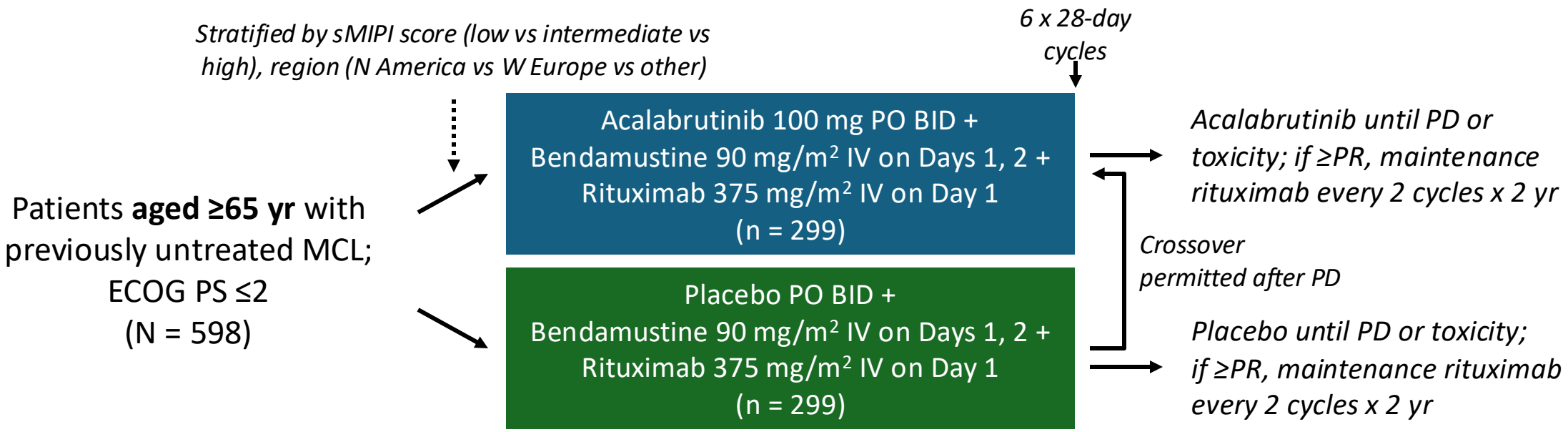




Courtesy of Stephen M Ansell, MD, PhD

Dreyling et al. Lancet. 2024 May 25;403(10441):2293-2306.

# Acalabrutinib plus bendamustine and rituximab in untreated elderly patients with mantle cell lymphoma (ECHO)

- International, randomized, double-blind phase III trial



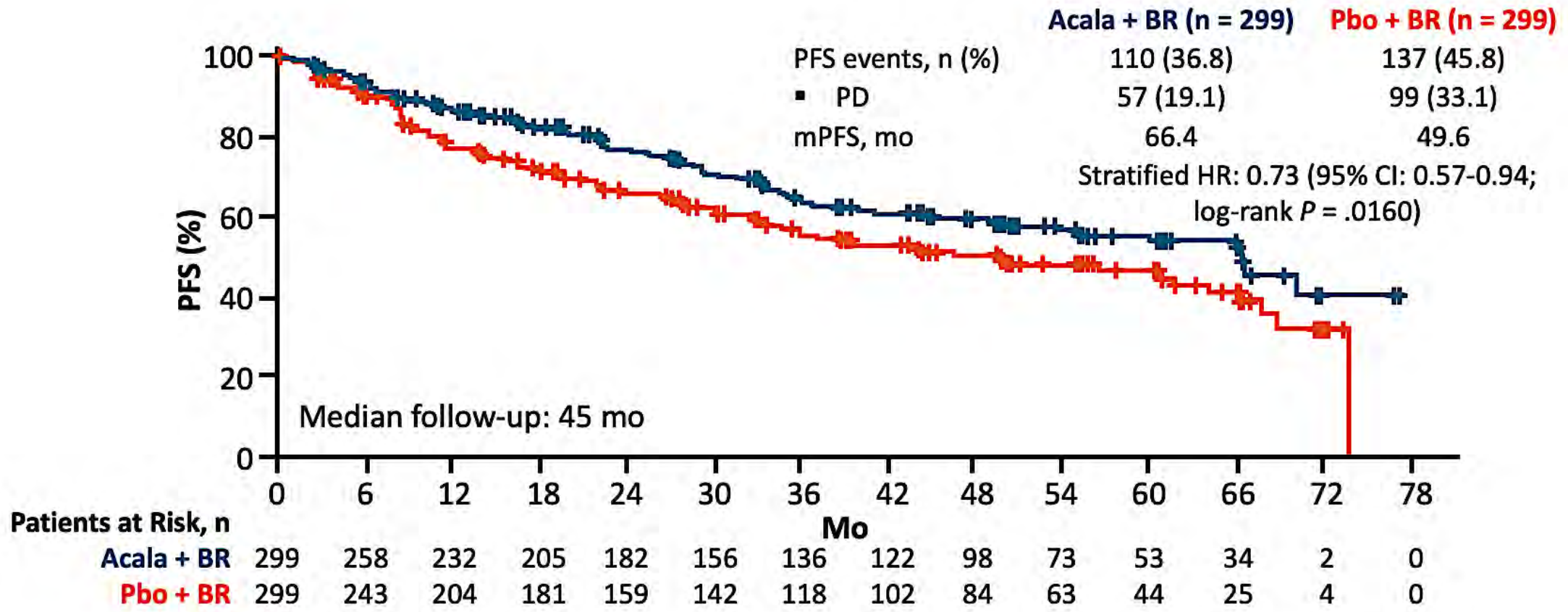

**Primary endpoint:**
PFS per IRC

**Key secondary endpoints:**
ORR per IRC, OS, safety

Courtesy of Stephen M Ansell, MD, PhD

**Wang et al. EHA 2024. Abstr LB3439.**

# Acalabrutinib plus bendamustine and rituximab in untreated elderly patients with mantle cell lymphoma (ECHO)

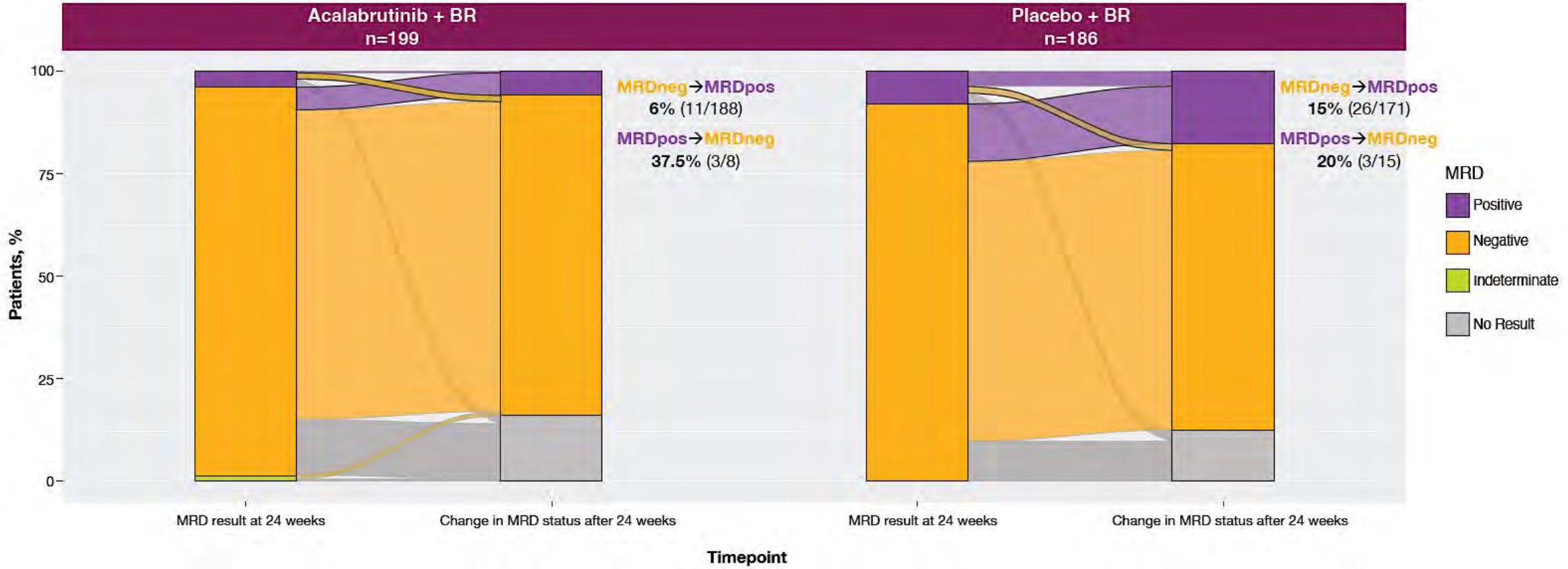



- ORR 91% vs 88%; CR rate 67% vs 54%
- Of the 99 patients with PD on Pbo + BR, 69% subsequently received a BTK inhibitor

Courtesy of Stephen M Ansell, MD, PhD

Wang et al. EHA 2024. Abstr LB3439.

# High-risk Subgroups and MRD: An Updated Analysis of the Phase 3 ECHO Trial




- PFS benefit was consistent across subgroups with high-risk disease characteristics (TP53 mutation, high Ki-67 index, and blastoid/ pleomorphic histology)
- Among patients who were MRD-negative after induction, fewer acalabrutinib-treated patients converted to MRD-positive during maintenance

Courtesy of Stephen M Ansell, MD, PhD

**Dreyling et al. ASH 2024;Abstract 1626**

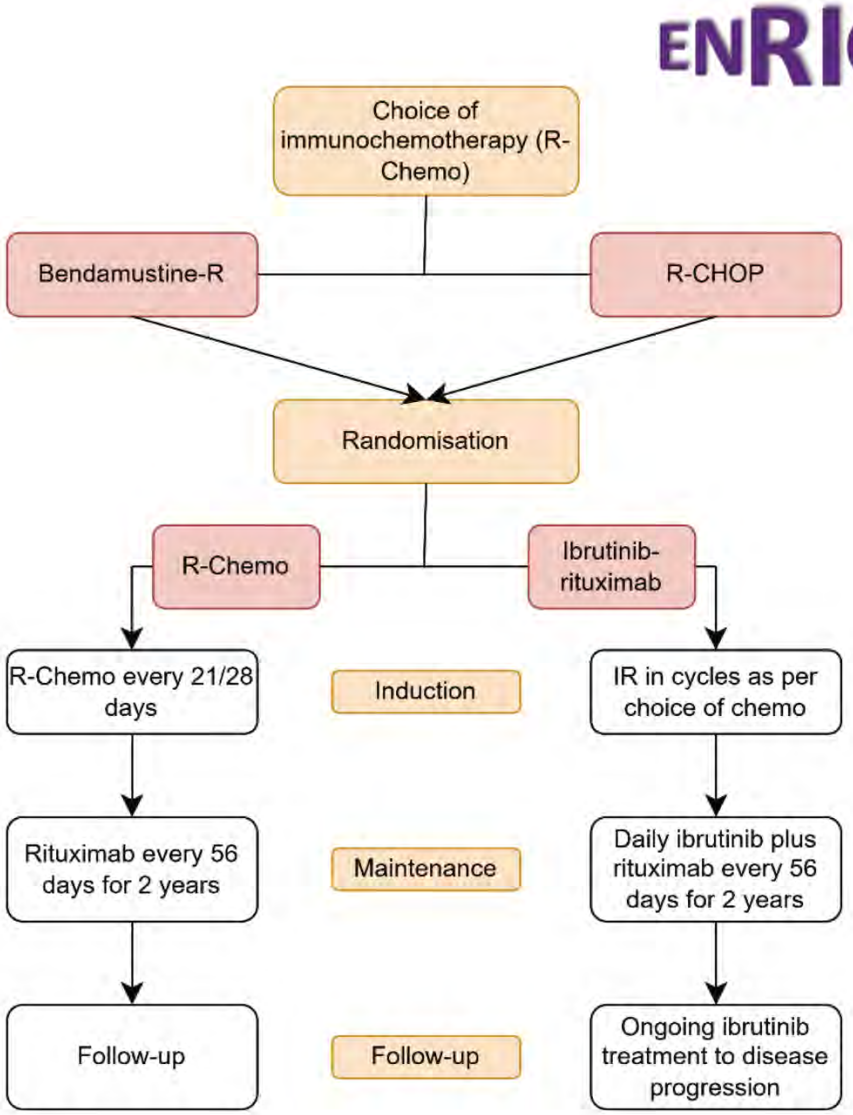
# Ibrutinib-Rituximab Is Superior to Rituximab-Chemotherapy in Previously Untreated Older Mantle Cell Lymphoma Patients

## Trial design

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

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

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




Courtesy of Stephen M Ansell, MD, PhD

Lewis et al. ASH 2024;Abstract 235.

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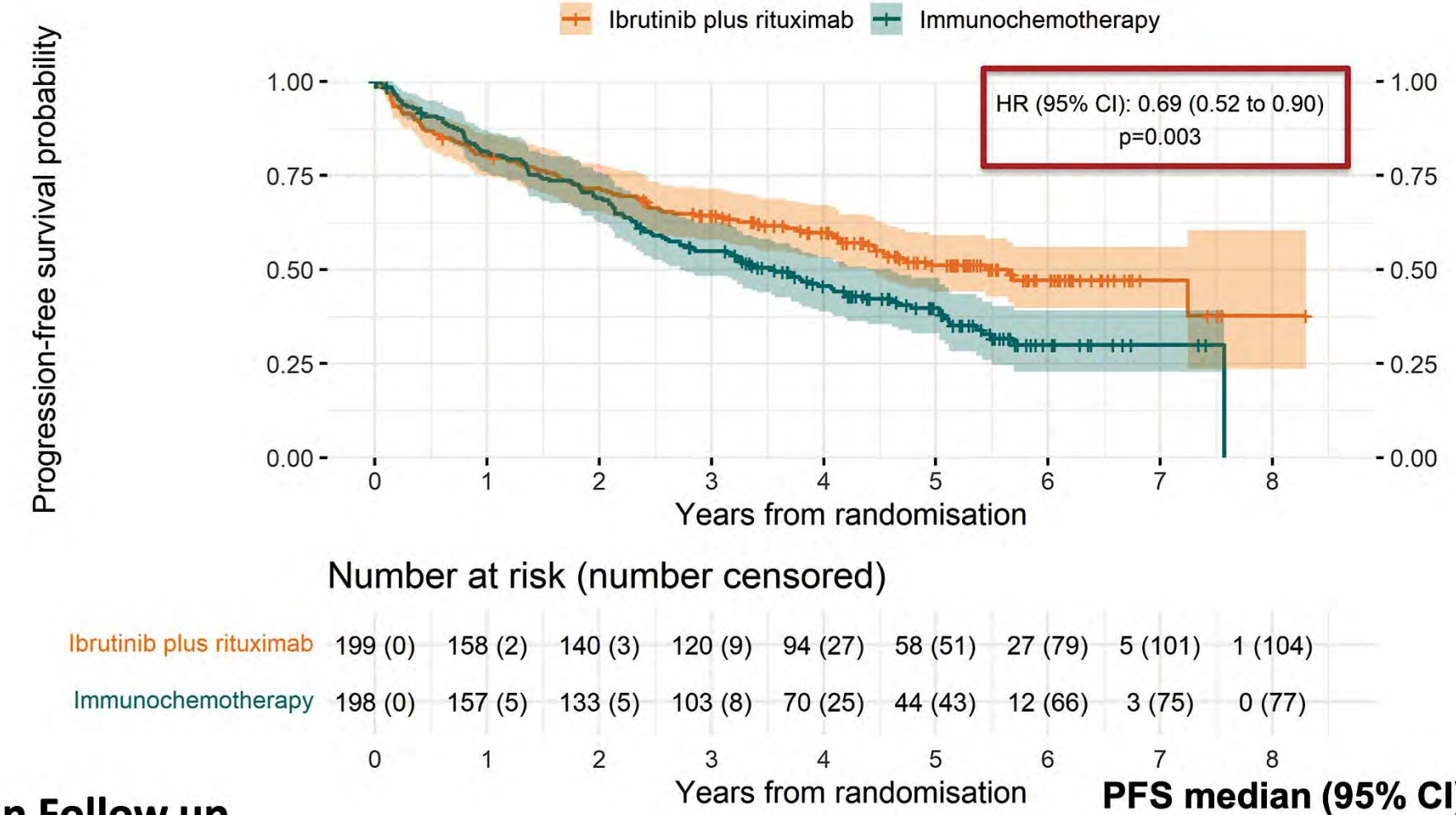


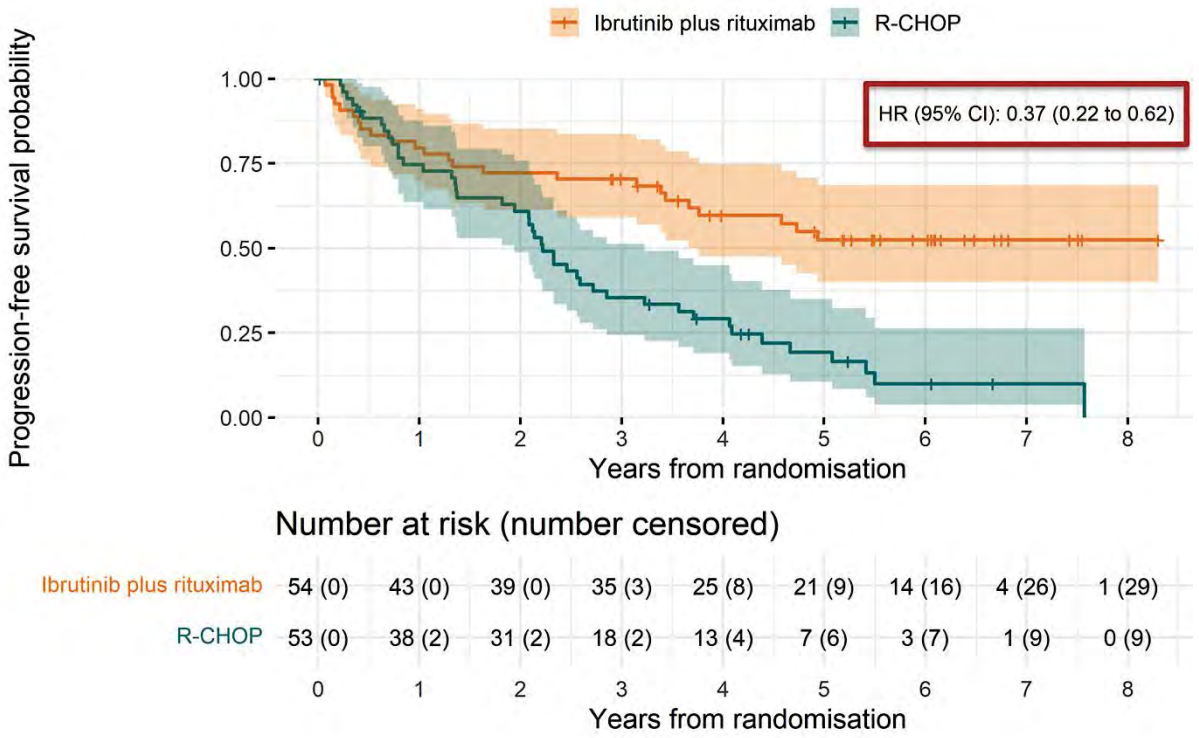

**Median Follow up**
**47.9 months**

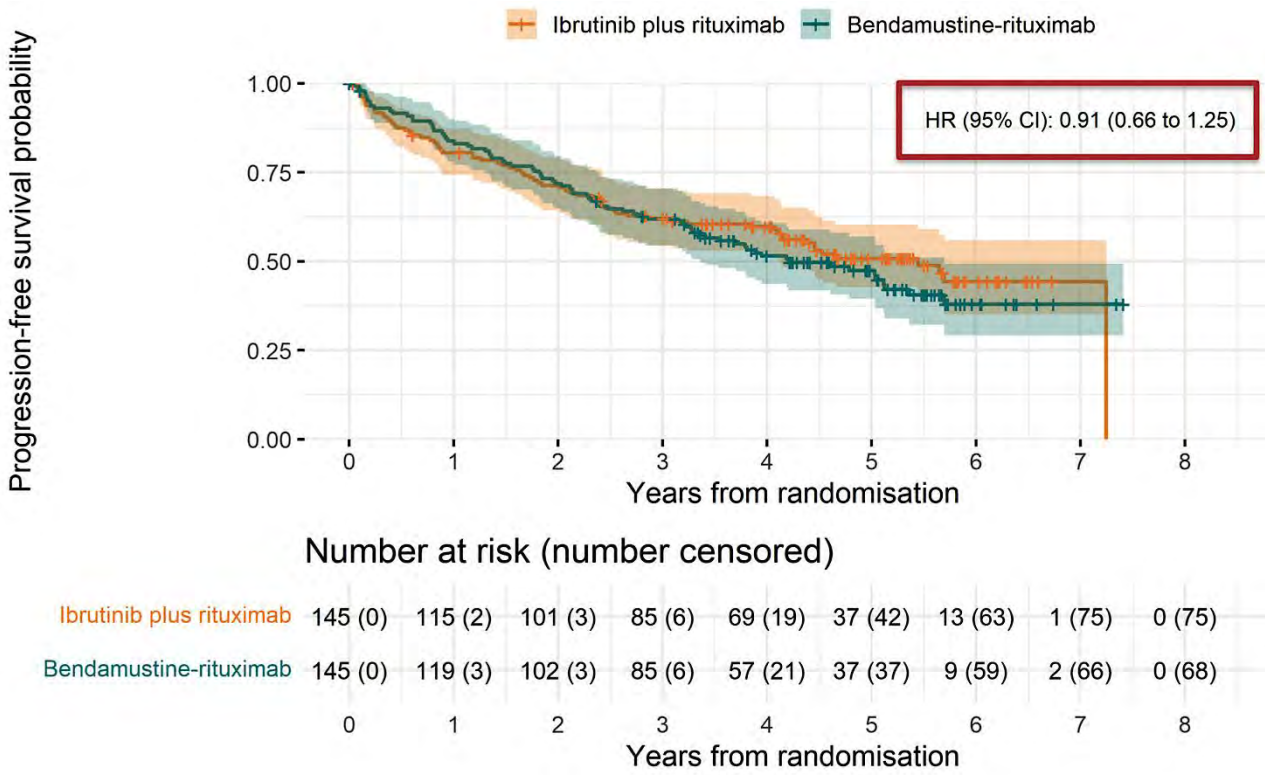
**PFS median (95% CI)**
**IR: 65.3 mo (52.7 to not evaluable**
**R-chemo: 42.4 mo (32.7 to 55.3)**

Courtesy of Stephen M Ansell, MD, PhD

**Lewis et al. ASH 2024;Abstract 235.**

# Ibrutinib-Rituximab Is Superior to Rituximab-Chemotherapy in Previously Untreated Older Mantle Cell Lymphoma Patients




**5-year PFS (95% CI)**
**IR: 52.4% (40.0% to 68.6%)**
**R-CHOP: 19.2% (10.6% to 35.1%)**

**5-year PFS (95% CI)**
**IR: 50.8% (42.8% to 60.4%)**
**BR: 47.4% (39.5% to 56.9%)**

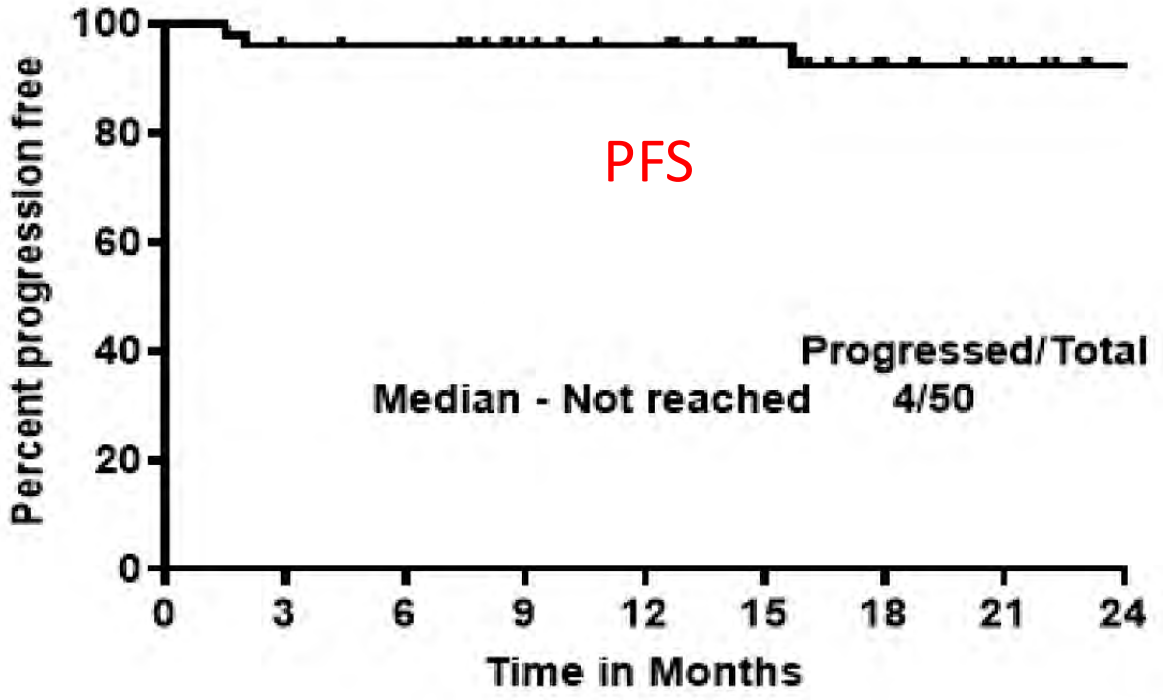
Courtesy of Stephen M Ansell, MD, PhD

**Lewis et al. ASH 2024;Abstract 235.**

# Phase II Study of Acalabrutinib with Rituximab as First-Line Therapy for Older Patients with Mantle Cell Lymphoma (MCL)

**Frontline AR in elderly MCL-Responses**

| Response (ITT) | All patients |
|---|---|
| Week 12 Best response | N (%) |
| Evaluable patients | 49 |
| ORR | 46/50 (92) |
| CR | 37/50 (74) |
| PR | 9/50 (18) |
| Best response | |
| Evaluable patients | 49 |
| ORR | 46/50 (92) |
| CR | 46/50 (92) |
| MRD at LFU (n=32) | 19/32 (60%) MRD negative |
| Median number of AR cycles to reach CR (range) | 3(2-7) |




MRD = minimal residual disease

With median follow-up of 28 months,
median PFS and OS were not reached.

2-year PFS: 94%
2-year OS: 96%

Jain P et al. ASH 2024;Abstract 3038.

# Acalabrutinib plus venetoclax and rituximab in treatment-naive mantle cell lymphoma

Patients
Treatment-naive
MCL (N = 21)

Acalabrutinib: From cycle 1, day 1: 100 mg BID until PD or treatment discontinuation
Venetoclax: From cycle 2, day 1 after ramp-up: 400 mg daily, through cycle 25
Rituximab: 375 mg/m$^2$ (day 1, 6 cycles); maintenance every other cycle for pts with CR or PR through cycle 24

- Primary end point: Safety
- Secondary end points per Lugano criteria: ORR, DOR, PFS
- Exploratory end point: MRD

## Results

| Median age | Ann Arbor stage IV | Bone marrow involvement | High-risk sMIPI | Blastoid histology[a] | Bulky disease >5 cm | Ki-67 proliferation index ≥30% |
|---|---|---|---|---|---|---|
| 66 y | 90% | 71% | 19% | 5% | 33% | 48% |

Median follow-up = 27.8 mo
57% remained on study at DCO (June 15, 2022)

### Safety – Events of clinical interest grade ≥3

14 (66%) pts had infections – 7 were from COVID-19

8 (38%) pts had neutropenia

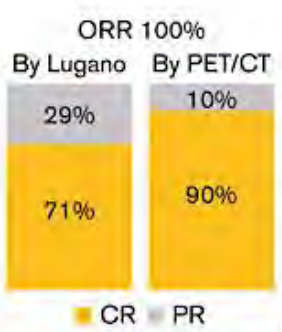
1 (5%) pt had hypertension

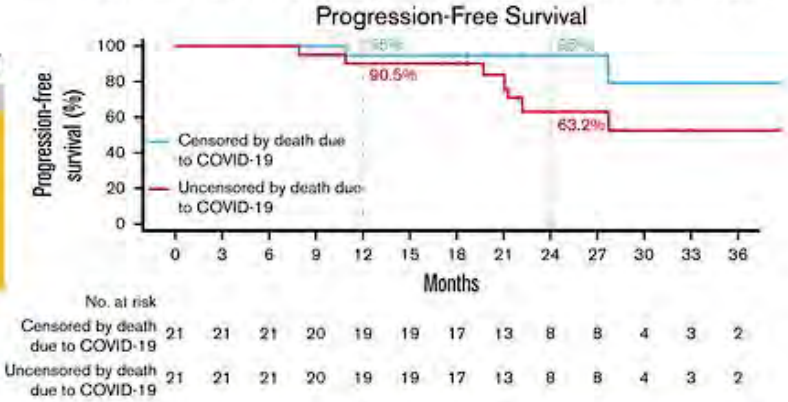
There were NO CASES of grade ≥3 hemorrhage, cardiac events, or atrial fibrillation

6 pts died; 5 due to COVID-19, 1 due to PD

### Efficacy

- Median TTIR was 2.8 mo
- Median DOR: not reached
- Without censoring for 5 COVID-19 deaths, 1-y and 2-y OS rates were 95% and 75%, respectively
- After censoring for 5 COVID-19 deaths, 1-y and 2-y OS rates were 100%




### MRD

- 16 pts had available MRD data
- 14 of those 16 pts (87.5%) achieved MRD negativity ($10^{-6}$) at least once during treatment

[a]No patient had the pleomorphic variant.

AVR, acalabrutinib plus venetoclax plus rituximab; BID, twice daily; CR, complete response; CT, computed tomography; DCO, data cutoff; DOR, duration of response; MCL, mantle cell lymphoma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; PR, partial response; pt, patient; sMIPI, simplified MCL International Prognostic Index; TN, treatment-naive; TTIR, time to initial response

**Conclusions**

- Treatment with AVR is well tolerated and safe for pts with TN MCL
- 100% of pts responded to AVR; 90% achieved CR by PET/CT and 71% by Lugano
- Treatment with AVR resulted in a high rate of complete molecular responses

Courtesy of Stephen M Ansell, MD, PhD

**Wang et al. Blood Adv, 2024 Sep 10;8(17):4539-4548.**

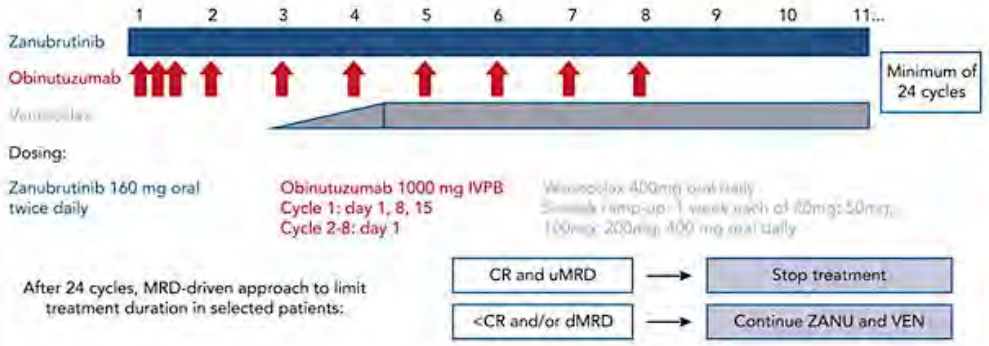
# Zanubrutinib, obinutuzumab, and venetoclax for first-line treatment of MCL with TP53 mutations (BOVen)

## Context of Research

- *TP53*-mutant MCL is associated with poor survival outcomes with standard chemoimmunotherapy.
- We tested dual BTK and BCL2-inhibition with anti-CD20 monoclonal antibody therapy in *TP53*-mutant MCL

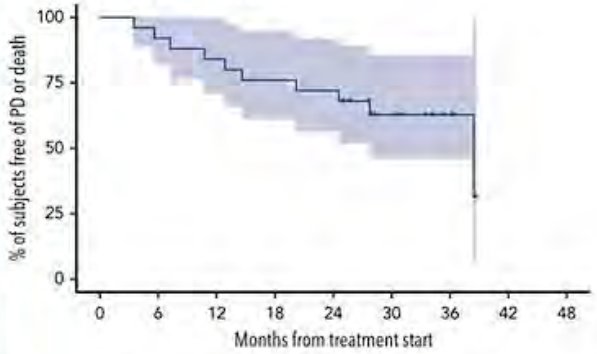
## Patients and Methods

- Phase 2 clinical trial of zanubrutinib, obinutuzumab, and venetoclax (NCT03824483). Primary outcome measure: 2-year progression-free survival
- Enrolled 25 MCL patients with *TP53* mutation. Treatment schema (BOVen):

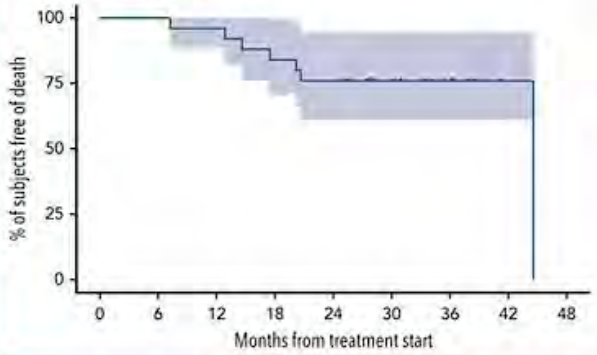



## Main Outcomes

- Best Overall Response Rate 96% (24/25) and Complete Response Rate 88% (22/25).
- Toxicity was manageable. 32% (8/25) w/neutropenia, no febrile neutropenia, 20% (5/25) received growth factor support.
- 2-year PFS: 72% (56, 92)



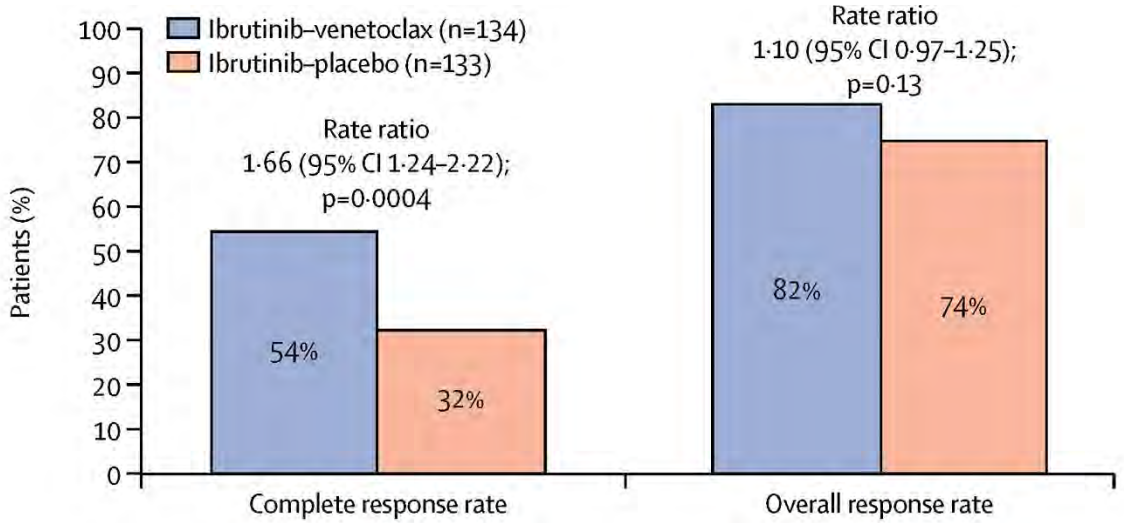

- 2-year OS: 76% (61, 95)



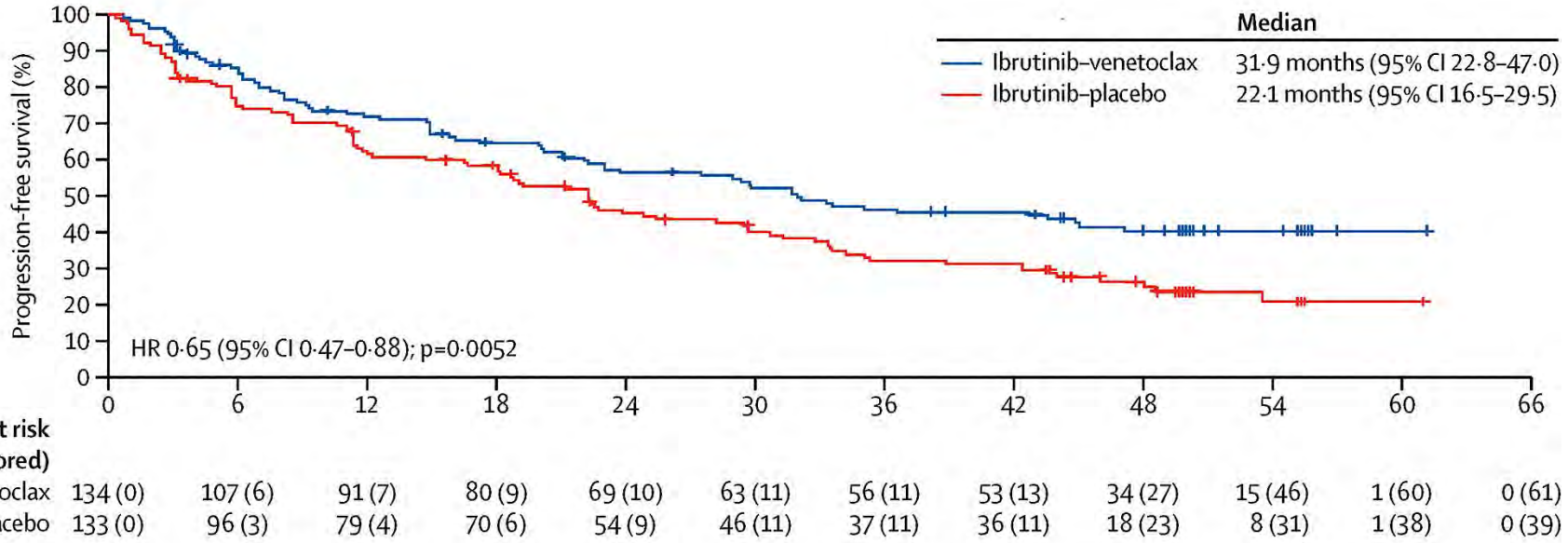

Kumar et al. Blood. 2025 Jan 30;145(5):497-507.

Courtesy of Stephen M Ansell, MD, PhD

# Ibrutinib plus venetoclax in relapsed or refractory mantle cell lymphoma (SYMPATICO)




267 patients were enrolled -
134 to ibrutinib-venetoclax and
133 to ibrutinib-placebo




Courtesy of Stephen M Ansell, MD, PhD

Wang et al. Lancet Oncol. 2025 Feb;26(2):200-213.

# Take away messages

- The addition of a BTK inhibitor to chemotherapy or immunotherapy in newly diagnosed mantle cell lymphoma improves outcomes – and makes intensive chemotherapy and an autologous stem cell transplant unnecessary.
- Venetoclax added to a BTK inhibitor and an anti-CD20 antibody is effective as initial therapy for mantle cell lymphoma – particularly in p53 mutated disease.
- Venetoclax added to ibrutinib is superior to ibrutinib alone in relapsed mantle cell lymphoma patients.

Courtesy of Stephen M Ansell, MD, PhD

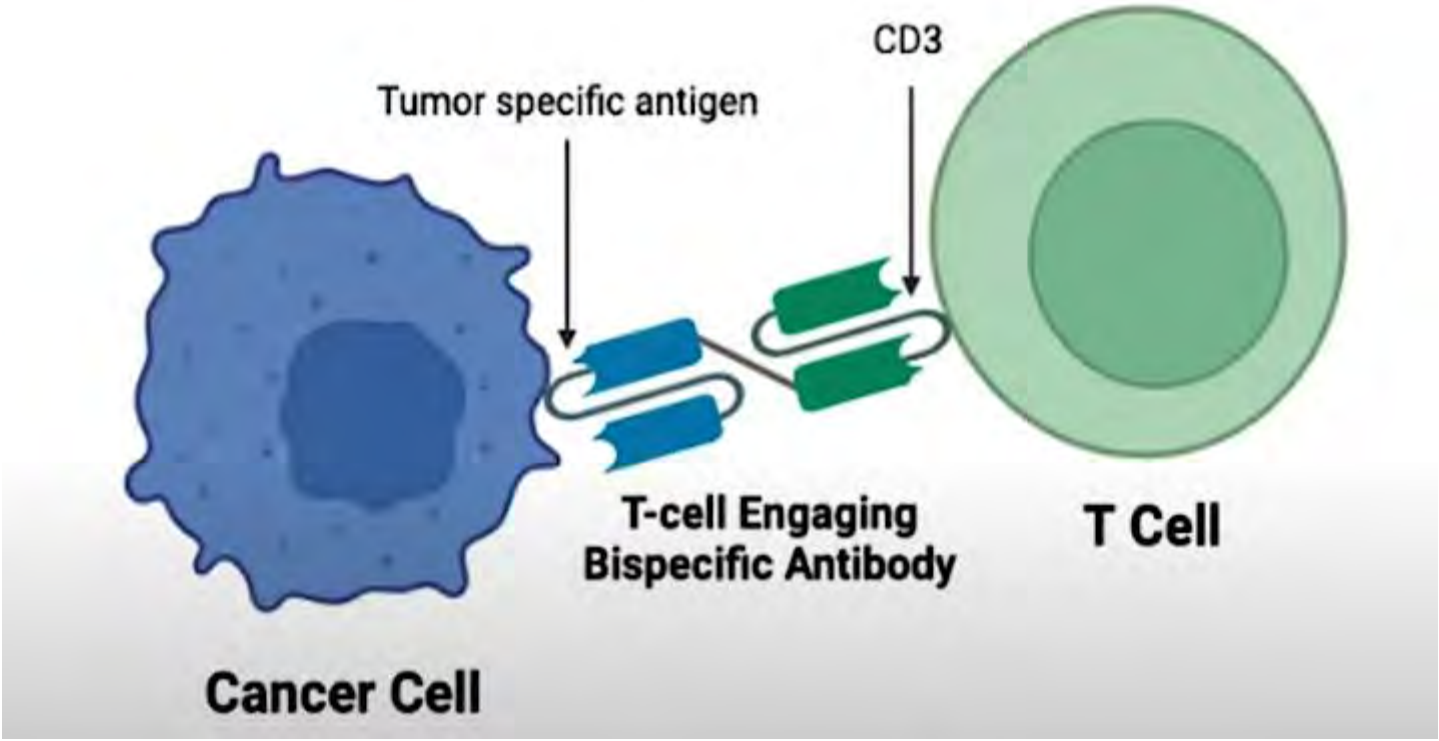

CANCER
CANCER

# First-Line Treatment of Mantle Cell Lymphoma

- Older versus younger patients
- TP53 mutation, high Ki-67, blastoid histology?

# Mantle Cell Lymphoma: Bispecifics

# Glofitamab

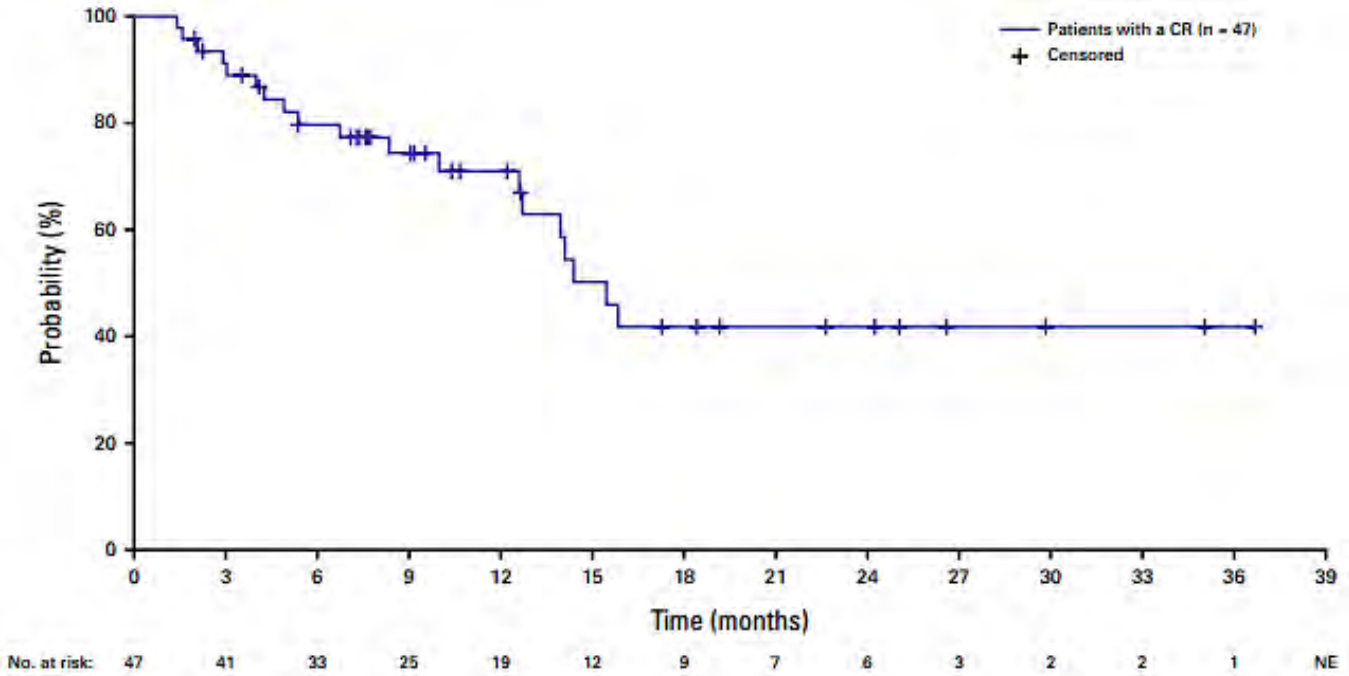



Courtesy of Brian T Hill, MD, PhD

Original Reports | Hematologic Malignancy

# Glofitamab in Relapsed/Refractory Mantle Cell Lymphoma: Results From a Phase I/II Study

Tycel Jovelle Phillips, MD[1,2]; Carmelo Carlo-Stella, MD[3]; Franck Morschhauser, MD, PhD[4]; Emmanuel Bachy, MD, PhD[5]; Michael Crump, MD, FRCPC[6]; Marek Trněný, MD[7]; Nancy L. Bartlett, MD[8]; Jan Zaucha, MD, PhD[9]; Tomasz Wrobel, PhD[10]; Fritz Offner, MD, PhD[11]; Kathryn Humphrey, BSc[12]; James Relf, MD[12]; Audrey Filézac de L'Etang, PhD[13]; David J. Carlile, PhD[12]; Ben Byrne, MSc[12]; Naseer Qayum, MBChB, DPhil[12]; Linda Lundberg, PhD[13]; and Michael Dickinson, MBBS, DMedSc[14]




Phillips TJ et al. Glofitamab in Relapsed/Refractory Mantle Cell Lymphoma: Results From a Phase I/II Study. J Clin Oncol 2025;43(3):318-28.

Courtesy of Brian T Hill, MD, PhD

# AGENDA

## Year in Review: Management of Non-Hodgkin Lymphoma

**INTRODUCTION:** Bispecific Antibodies in Community Practice

**MODULE 1:** Diffuse Large B-Cell Lymphoma

**MODULE 2:** CD19, CD20 or Both? AZD0486 Bispecific Antibody

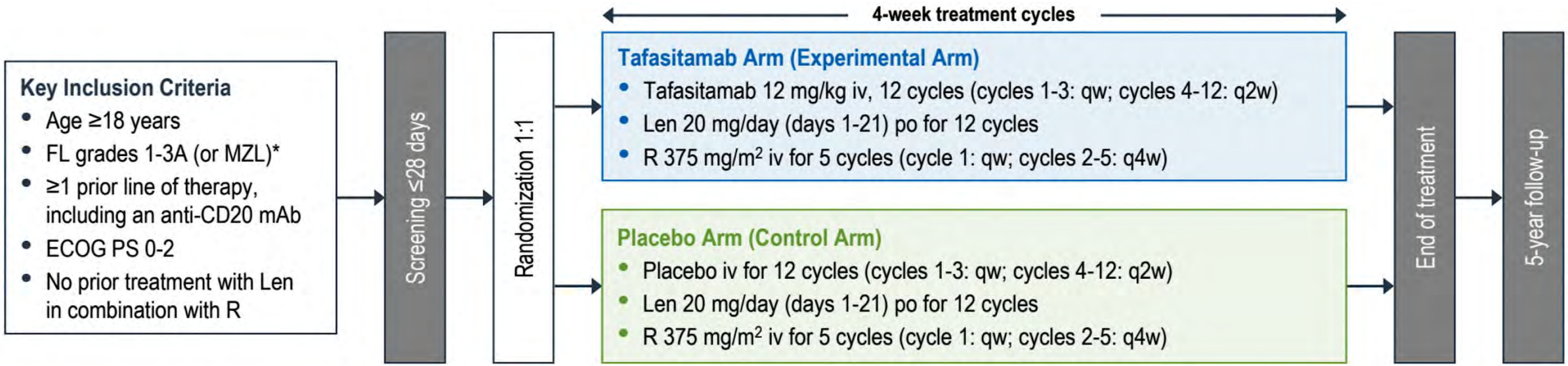
**MODULE 3:** Mantle Cell Lymphoma

**MODULE 4: Follicular Lymphoma**

**MODULE 5:** CAR T-Cell Therapy for Marginal Zone Lymphoma

RTP Year in Review 2025

# Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Phase 3 Study (inMIND).




**Stratification Factors (Patients With FL)**

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

**Study Endpoints in FL Population (Investigator Assessed Unless Specified)**

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

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

Courtesy of Stephen M Ansell, MD, PhD

Sehn et al. ASH 2024;Abstract LBA-1.

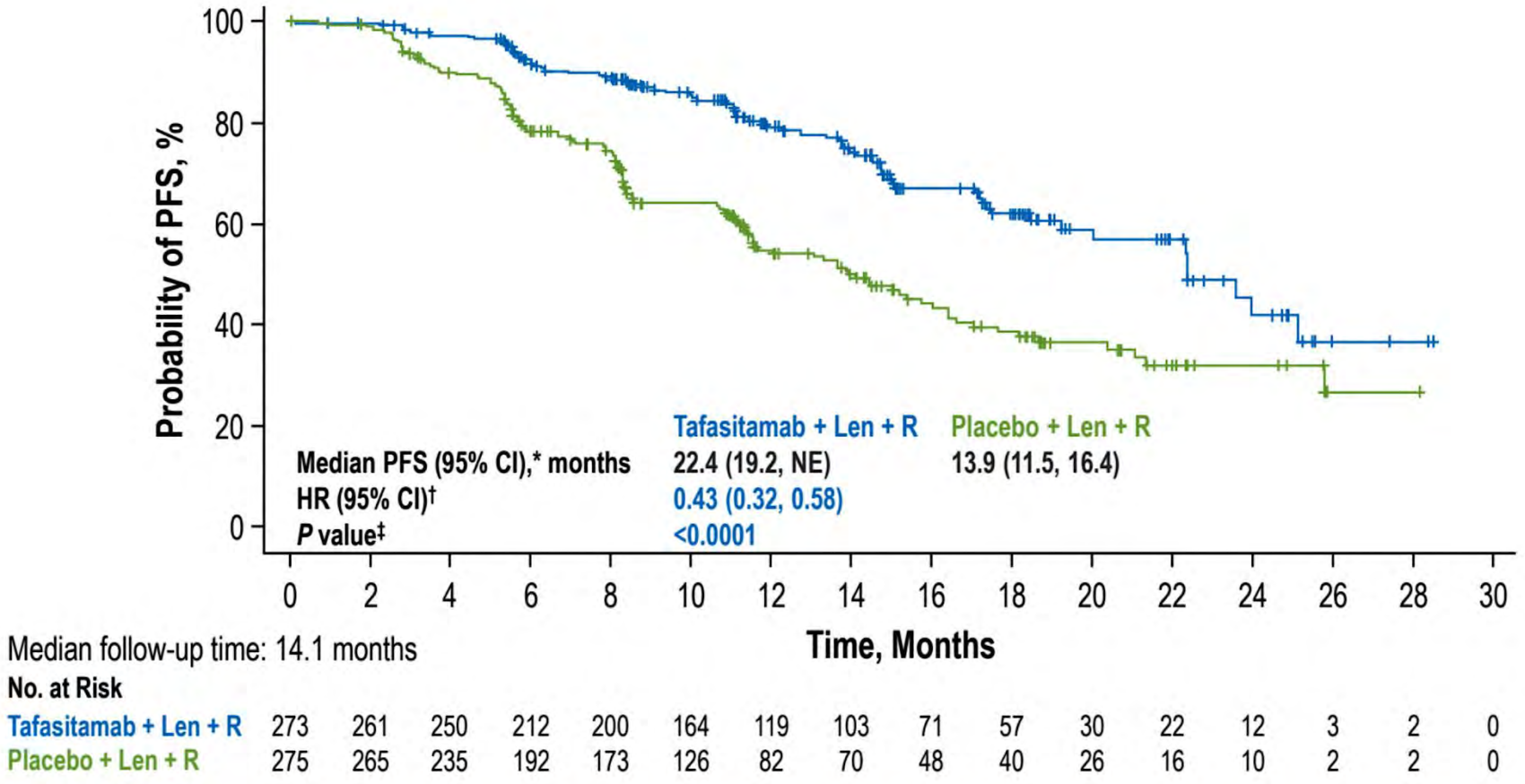
# Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Phase 3 Study (inMIND).

| 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** | |

Courtesy of Stephen M Ansell, MD, PhD

**Sehn et al. ASH 2024;Abstract LBA-1.**

# Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Phase 3 Study (inMIND).

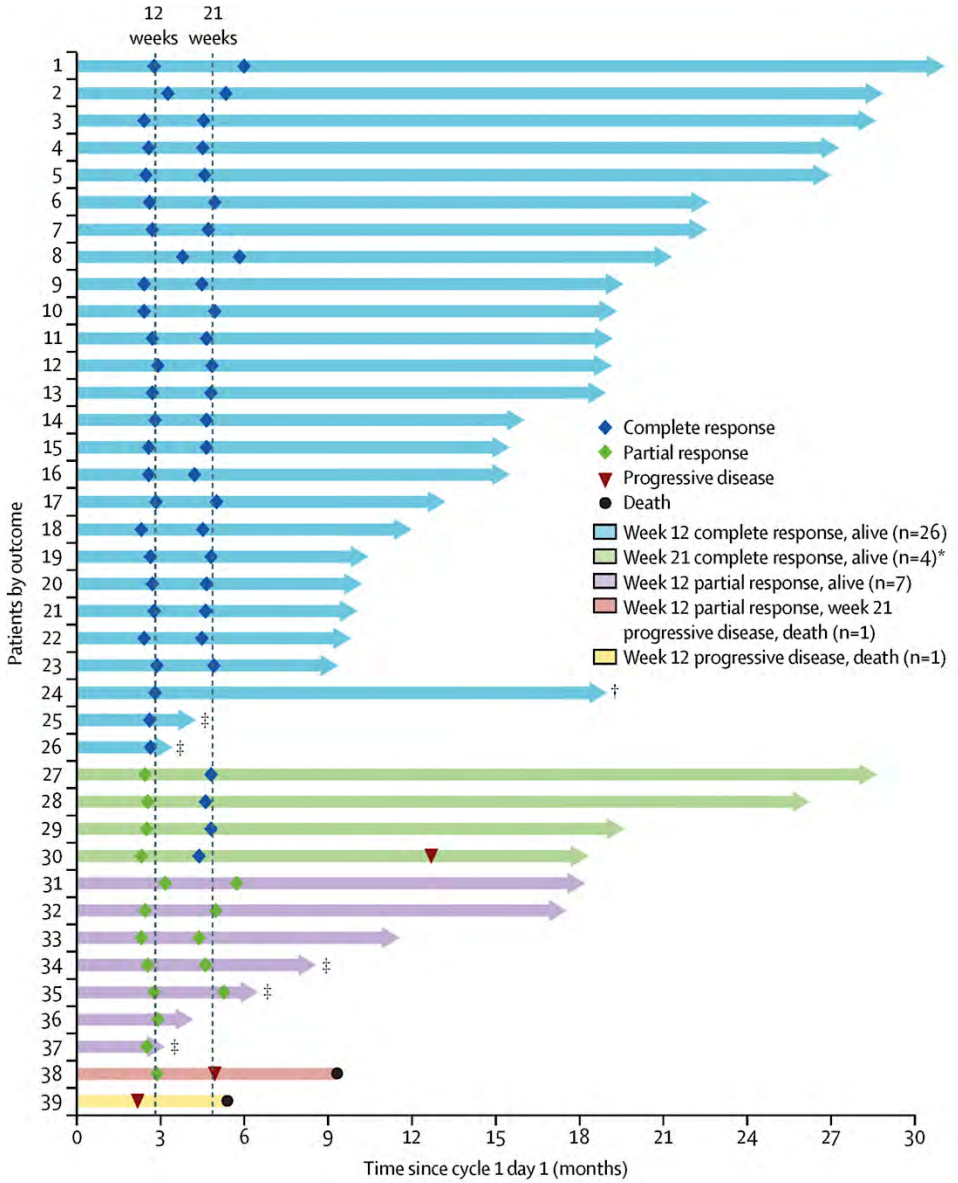



**Significant improvement in PFS was observed with tafasitamab**

Courtesy of Stephen M Ansell, MD, PhD

**Sehn et al. ASH 2024;Abstract LBA-1.**

# Loncastuximab tesirine with rituximab in patients with relapsed or refractory follicular lymphoma

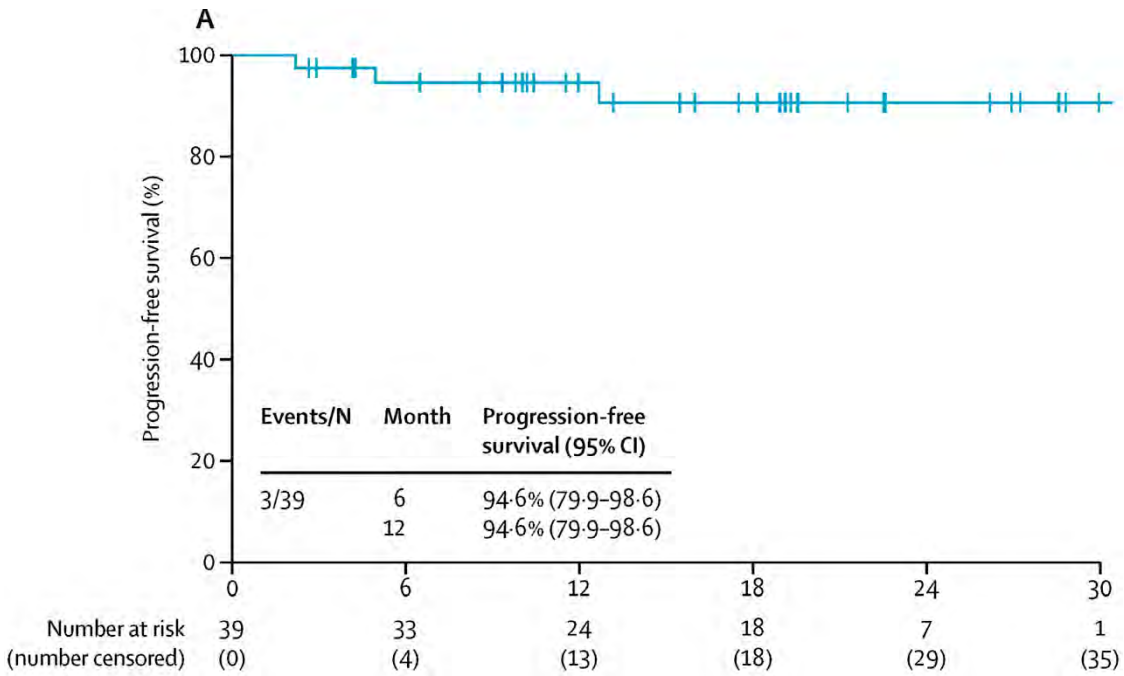


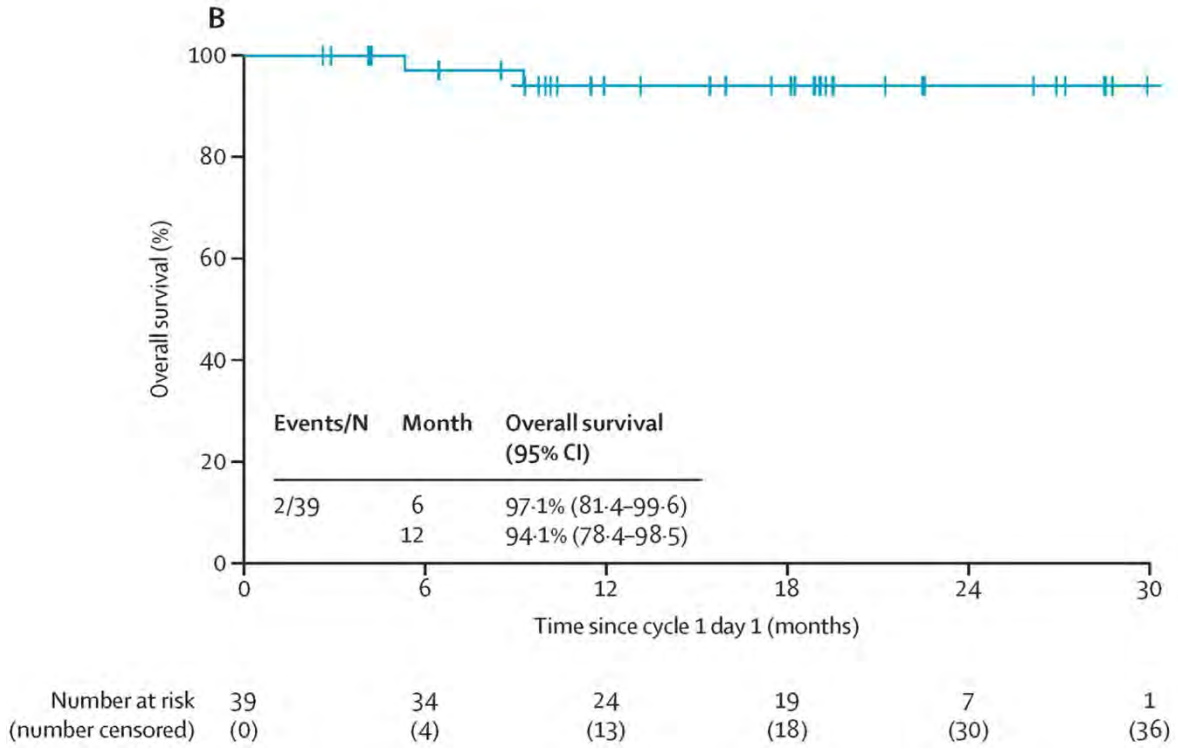

- 39 patients
- Primary endpoint of week 12 CR rate was 67% (n=26 of 39).
- Secondary endpoint of week 12 ORR was 97% (n=38 of 39).
- 23 of 26 patients with a week 12 CR maintained a CR at the week 21

**Alderuccio et al. Lancet Haematol 2025;12(1):e23-e34.**

Courtesy of Stephen M Ansell, MD, PhD

# Loncastuximab tesirine with rituximab in patients with relapsed or refractory follicular lymphoma



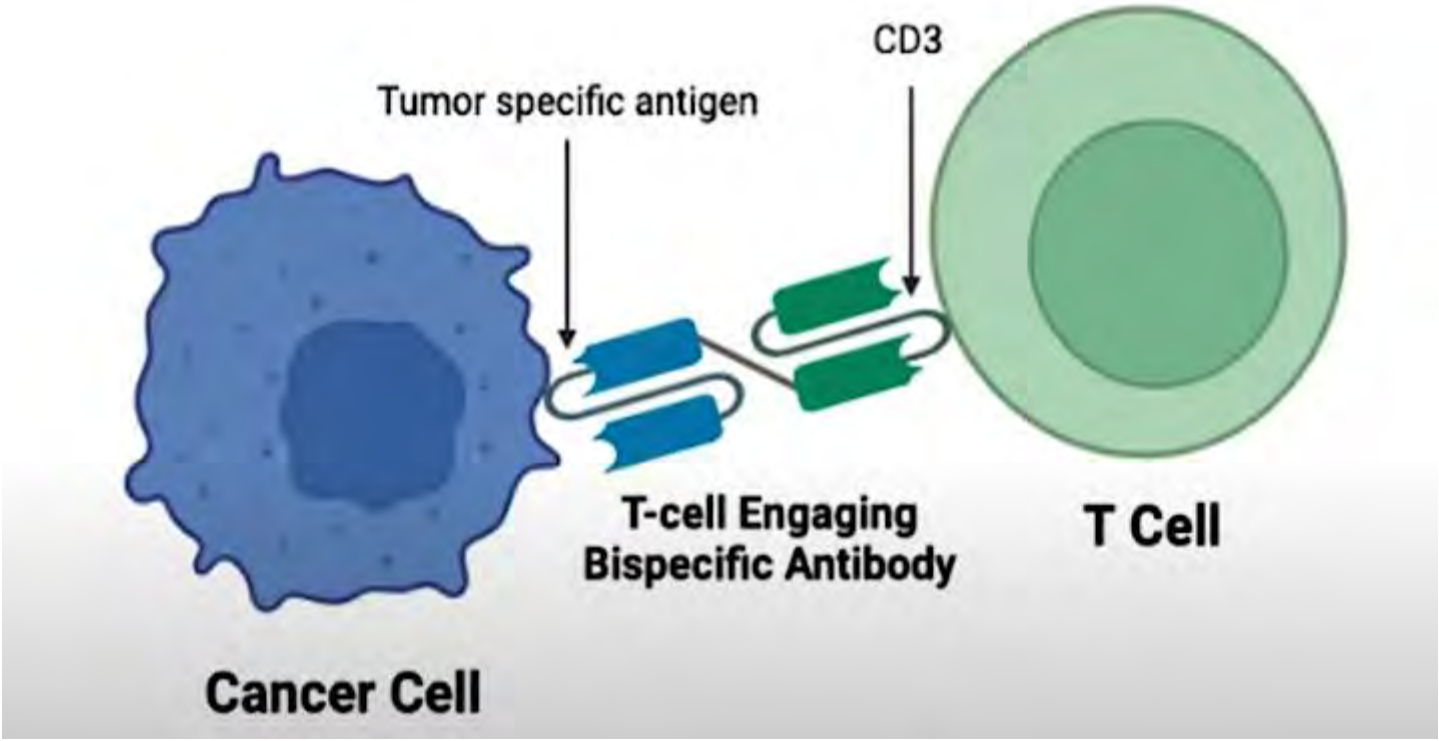




Courtesy of Stephen M Ansell, MD, PhD

**Alderuccio et al. Lancet Haematol 2025;12(1):e23-e34.**

# Follicular Lymphoma: Bispecifics

# Mosunetuzumab



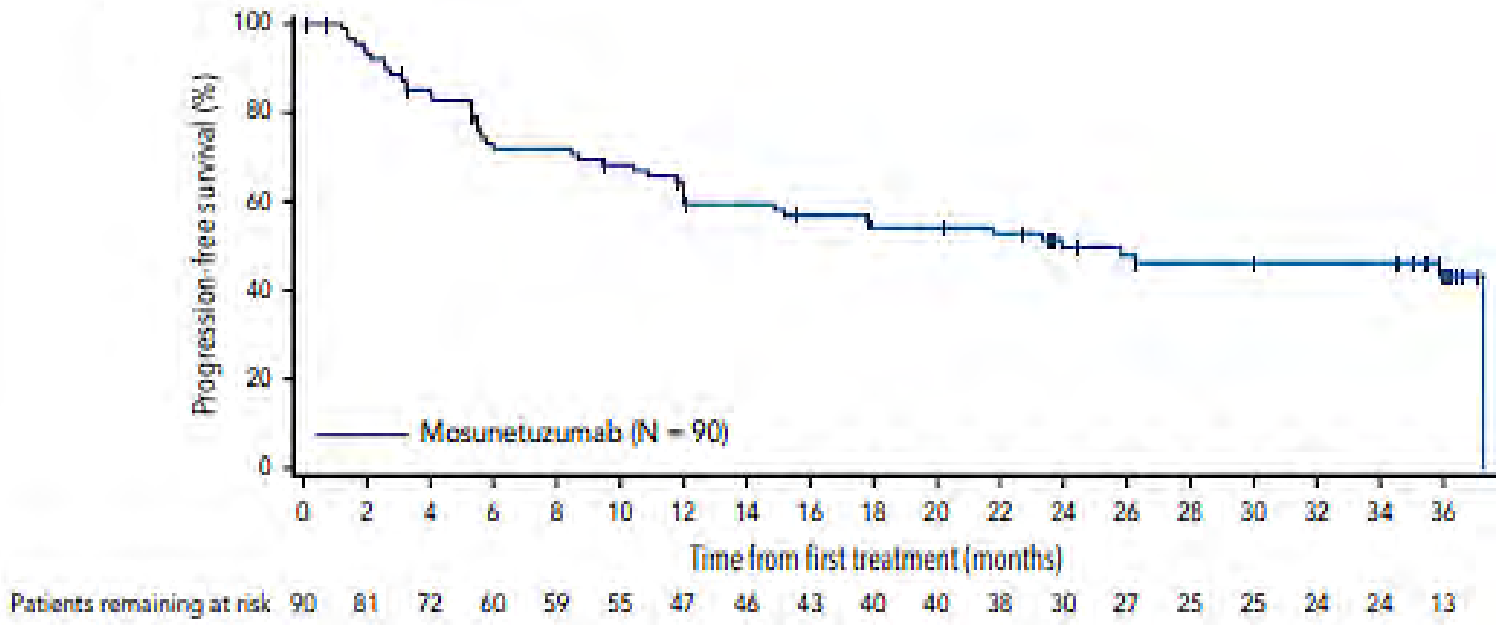

Courtesy of Brian T Hill, MD, PhD

blood
Regular Article

CLINICAL TRIALS AND OBSERVATIONS

# Long-term 3-year follow-up of mosunetuzumab in relapsed or refractory follicular lymphoma after ≥2 prior therapies

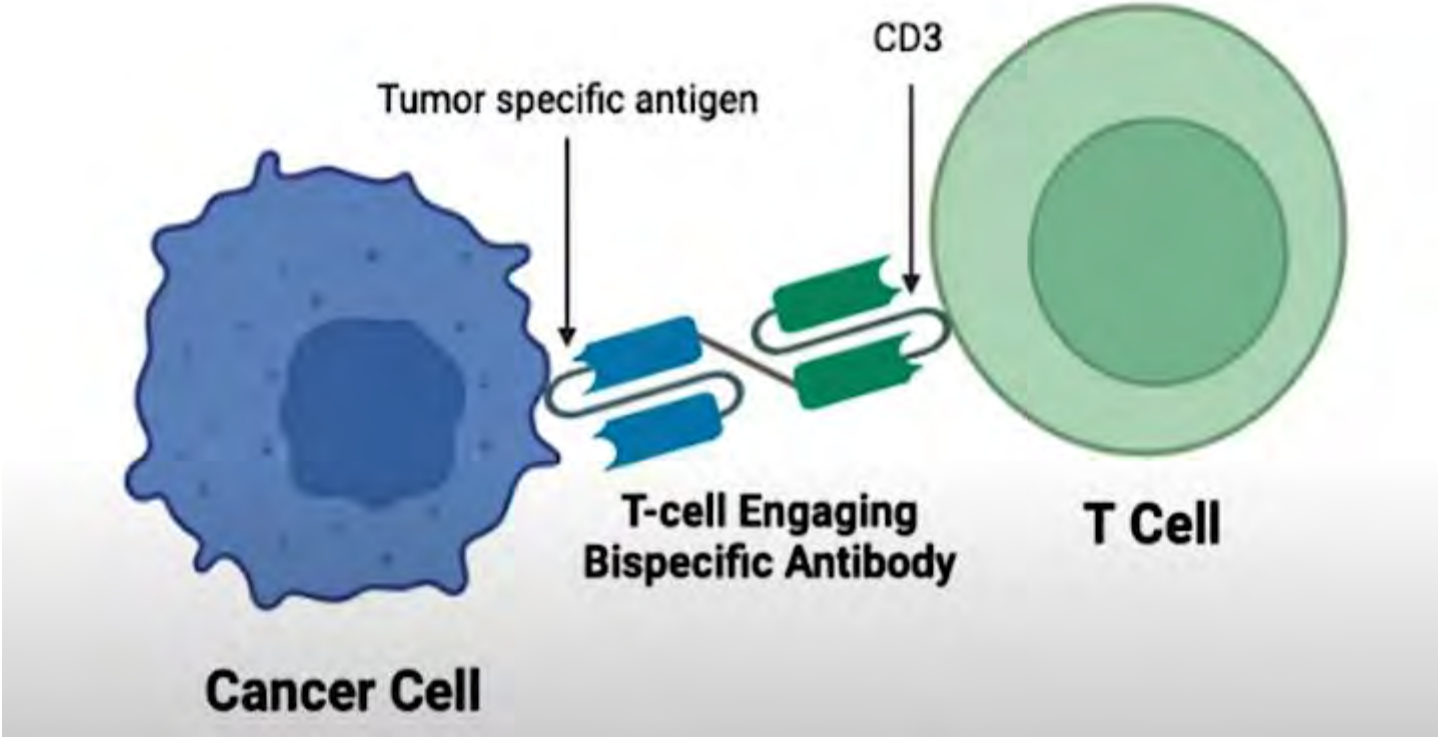
Laurie H. Sehn,[1] Nancy L. Bartlett,[2] Matthew J. Matasar,[3] Stephen J. Schuster,[4] Sarit E. Assouline,[5] Pratyush Giri,[6] John Kuruvilla,[7] Mazyar Shadman,[8] Chan Yoon Cheah,[9] Sascha Dietrich,[10] Keith Fay,[11] Matthew Ku,[12] Loretta J. Nastoupil,[13] Michael C. Wei,[14] Shen Yin,[14] Iris To,[14] Derrick Kaufman,[14] Antonia Kwan,[14] Elicia Penuel,[14] Christopher R. Bolen,[14] and Lihua E. Budde[15]




Courtesy of Brian T Hill, MD, PhD

# Follicular Lymphoma: Bispecifics

# Epcoritamab

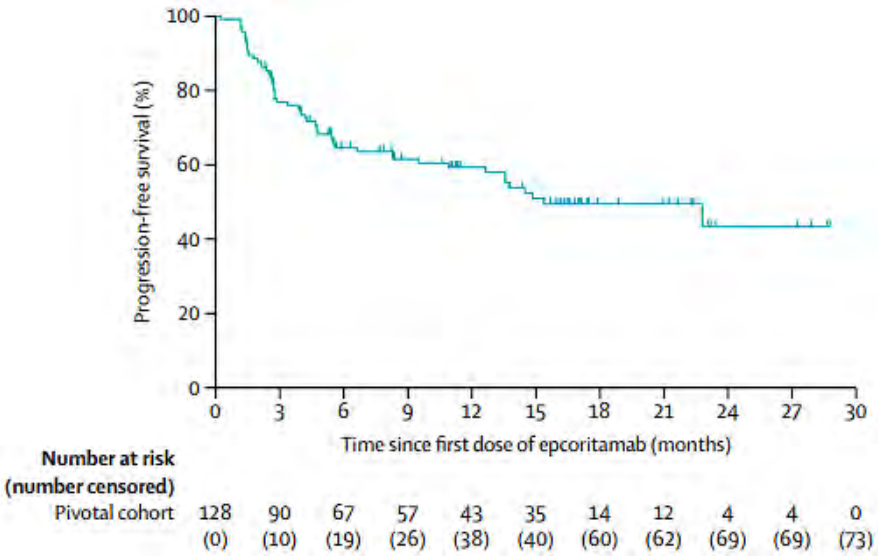


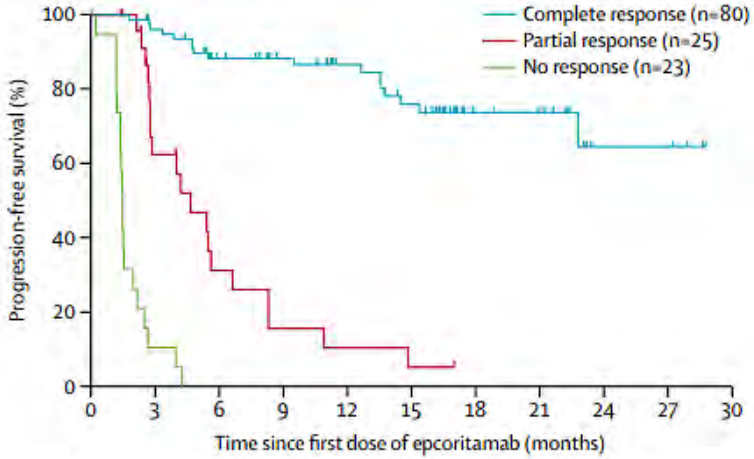

Courtesy of Brian T Hill, MD, PhD

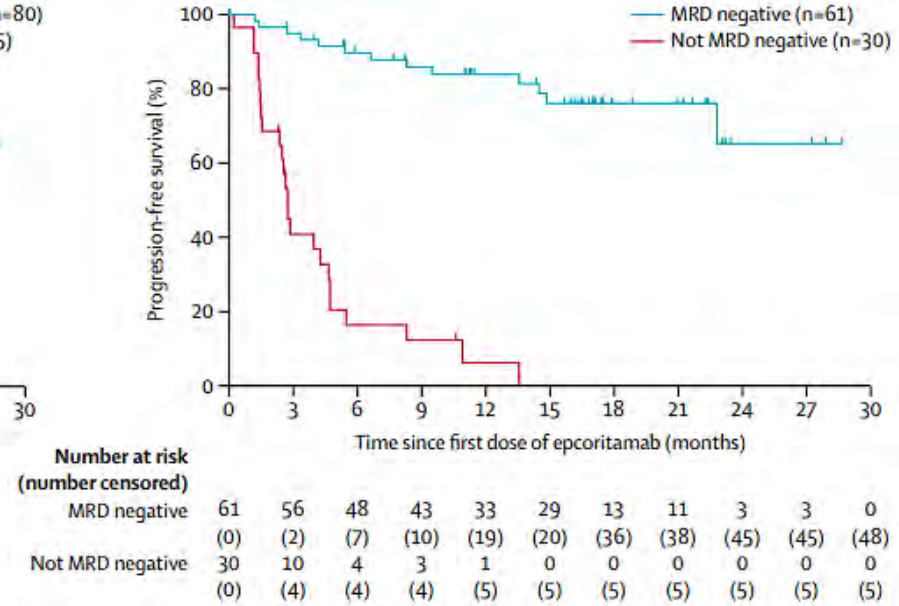
Lancet Haematol 2024;
11: e593–605

# Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma (EPCORE NHL-1): a phase 2 cohort of a single-arm, multicentre study

*Kim M Linton, Umberto Vitolo, Wojciech Jurczak, Pieternella J Lugtenburg, Emmanuel Gyan, Anna Sureda, Jacob Haaber Christensen, Brian Hess, Hervé Tilly, Raul Cordoba, David John Lewis, Craig Okada, Martin Hutchings, Michael Roost Clausen, Juan-Manuel Sancho, Tara Cochrane, Sirpa Leppä, Martine E D Chamuleau, Diana Gernhardt, Işıl Altıntaş, Yan Liu, Tahamtan Ahmadi, Minh H Dinh, Daniela Hoehn, Elena Favaro, Brian Elliott, Catherine Thieblemont, Julie M Vose*



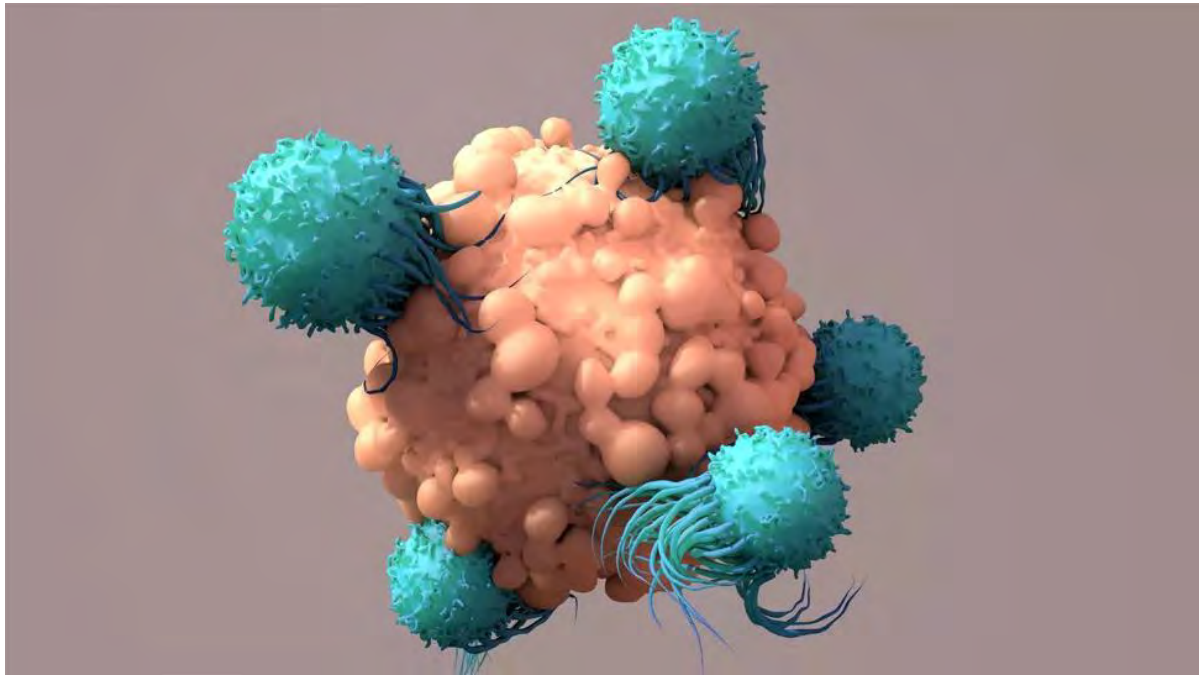




Courtesy of Brian T Hill, MD, PhD

# Follicular Lymphoma: CAR-T

## *Liso-Cel*



Courtesy of Brian T Hill, MD, PhD

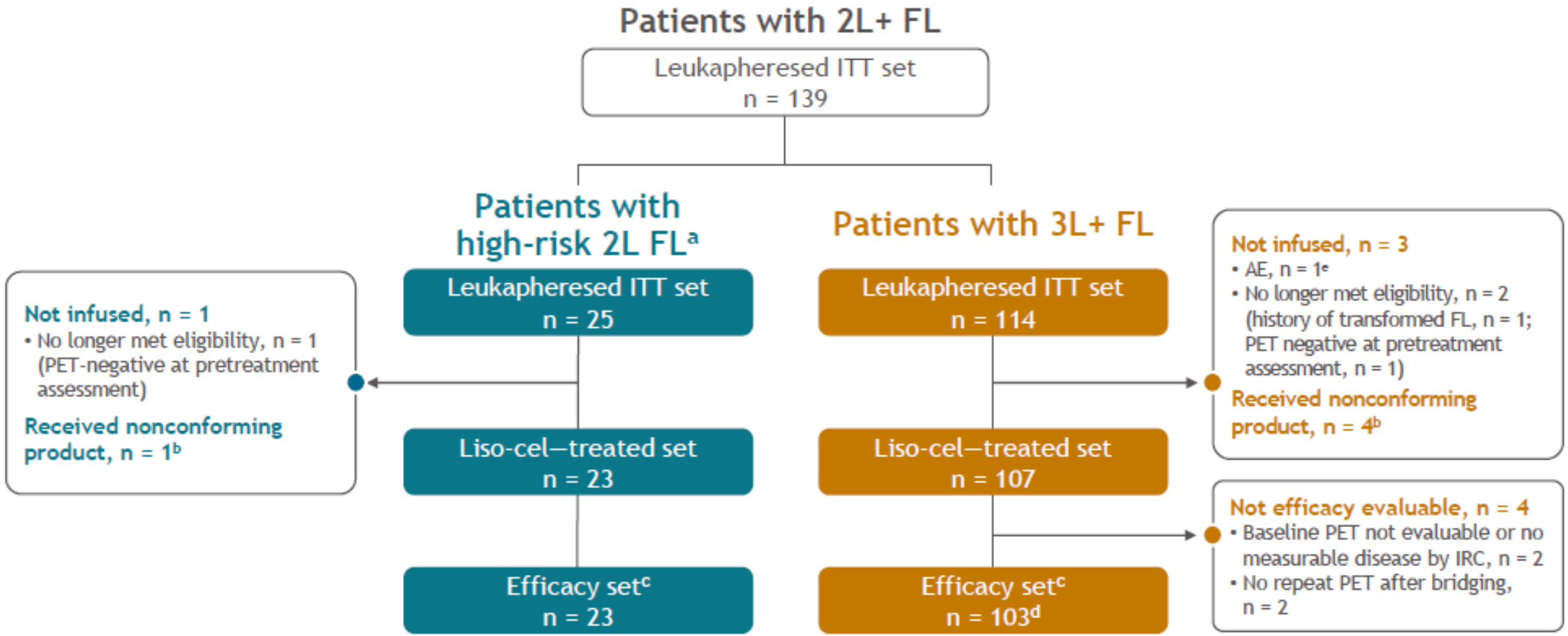
# Lisocabtagene maraleucel in patients with relapsed or refractory follicular lymphoma: TRANSCEND FL 2-year follow-up

Loretta J. Nastoupil, MD,[1] Saurabh Dahiya, MD, FACP,[2] M. Lia Palomba, MD,[3] Alejandro Martin Garcia-Sancho, MD, PhD,[4] Juan Luis Reguera Ortega, MD,[5] John Kuruvilla, MD, FRCPC,[6] Ulrich Jäger, MD,[7] Guillaume Cartron, MD, PhD,[8] Koji Izutsu, MD, PhD,[9] Martin Dreyling, MD,[10] Brad Kahl, MD,[11] Hervé Ghesquieres, MD, PhD,[12] Kirit Ardeshna, MD, MA, FRCP,[13] Hideki Goto, MD, PhD,[14] Anna Maria Barbui, MD,[15] Jeremy S. Abramson, MD, MMSC,[16] Peter Borchmann, MD,[17] Isabelle Fleury, MD, MSc, FRCPC,[18] Stephan Mielke, MD,[19] Alan Skarbnik, MD,[20] Manali Kamdar, MD, MBBS,[21] Reem Karmali, MD,[22] Andreas Viardot, MD,[23] Thalia Farazi, MD, PhD,[24] Grace Shih Hui Kao, MD,[25] Min Vedal, PhD,[26] Rina Nishii, PhD,[27] Jessica Papuga, PhD,[26] Jinender Kumar, MS,[27] Franck Morschhauser, MD, PhD[28]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Stanford University School of Medicine, Stanford, CA, USA, and University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD, USA; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Hospital Universitario de Salamanca, IBSAL, CIBERONC, Universidad de Salamanca, Salamanca, Spain; [5]Hospital Universitario Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBIS)/CSIC, Universidad de Sevilla, Seville, Spain; [6]Princess Margaret Cancer Centre, Toronto, ON, Canada; [7]Medical University of Vienna, Vienna, Austria; [8]Montpellier University Hospital Center, UMR CNRS 5535, Montpellier, France; [9]National Cancer Center Hospital, Tokyo, Japan; [10]Medizinische Klinik III, Klinikum der Universität, LMU München, München, Germany; [11]Washington University School of Medicine in St. Louis, St. Louis, MO, USA; [12]Hôpital Lyon Sud, Lyon, France; [13]University College London Hospitals NHS Foundation Trust, London, UK; [14]Hokkaido University Hospital, Sapporo, Japan; [15]Azienda Socio Sanitaria Terriroriale Papa Giovanni XXIII, Bergamo, Italy; [16]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; [17]Universität zu Köln, Köln, Germany; [18]Hôpital Maisonneuve – Rosemont, Montreal, QC, Canada; [19]Karolinska Institutet and University Hospital; Karolinska Comprehensive Cancer Center, Karolinska ATMP Center, Stockholm, Sweden; [20]Novant Health Cancer Institute, Charlotte, NC, USA; [21]University of Colorado Cancer Center, Aurora, CO, USA; [22]Northwestern University Feinberg School of Medicine, Robert H. Lurie Comprehensive Cancer Center, Chicago, IL, USA; [23]University Hospital, Ulm, Germany; [24]Bristol Myers Squibb, San Francisco, CA, USA; [25]Bristol Myers Squibb, Cambridge, MA, USA; [26]Bristol Myers Squibb, Boudry, Switzerland; [27]Bristol Myers Squibb, Princeton, NJ, USA; [28]Centre Hospitalier Universitaire de Lille, Groupe de Recherche sur les formes Injectables et les Technologies Associées, Lille, France

Courtesy of Brian T Hill, MD, PhD

# Figure 2. Patient disposition and analysis groups



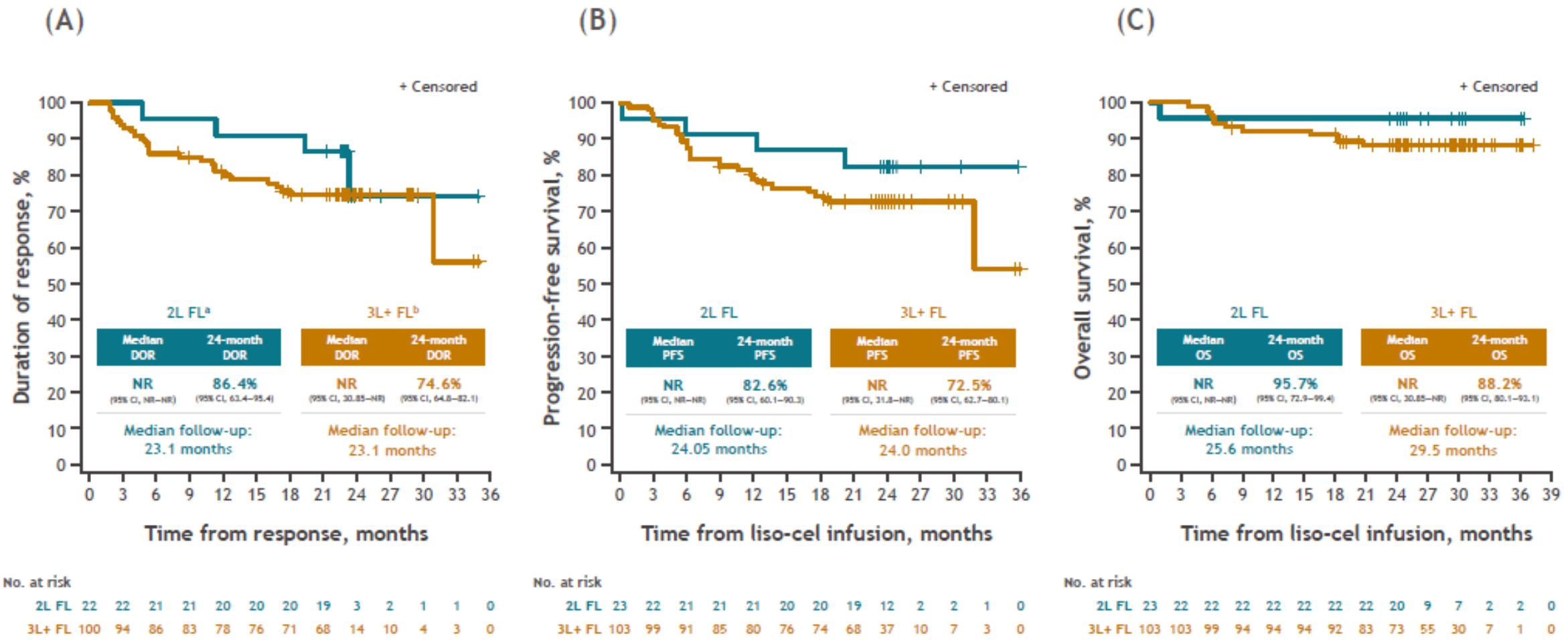

- At data cutoff (January 10, 2024), 107 3L+ and 23 2L FL high-risk patients had received liso-cel and were evaluable for safety; 103 3L+ FL and 23 2L FL patients were efficacy evaluable (**Figure 2**)

[a]The high-risk 2L FL cohort included patients with POD24 from diagnosis and/or mGELF; [b]Nonconforming product was defined as any product wherein one of the CD8 or CD4 cell components did not meet one of the requirements to be considered liso-cel but could be considered appropriate for infusion; [c]Liso-cel–treated patients with PET/CT-positive disease per IRC before infusion; [d]Compared with the primary analysis, this 2-year follow-up analysis includes 2 additional patients as images confirming PET-positive disease at pretreatment were received after the primary analysis; [e]Acute respiratory failure (enterovirus/rhinovirus pneumonia).
ITT, intent to treat.

Courtesy of Brian T Hill, MD, PhD

# Figure 3. TRANSCEND FL efficacy outcomes after 2 years of follow-up (A) DOR per IRC, (B) PFS per IRC, and (C) OS



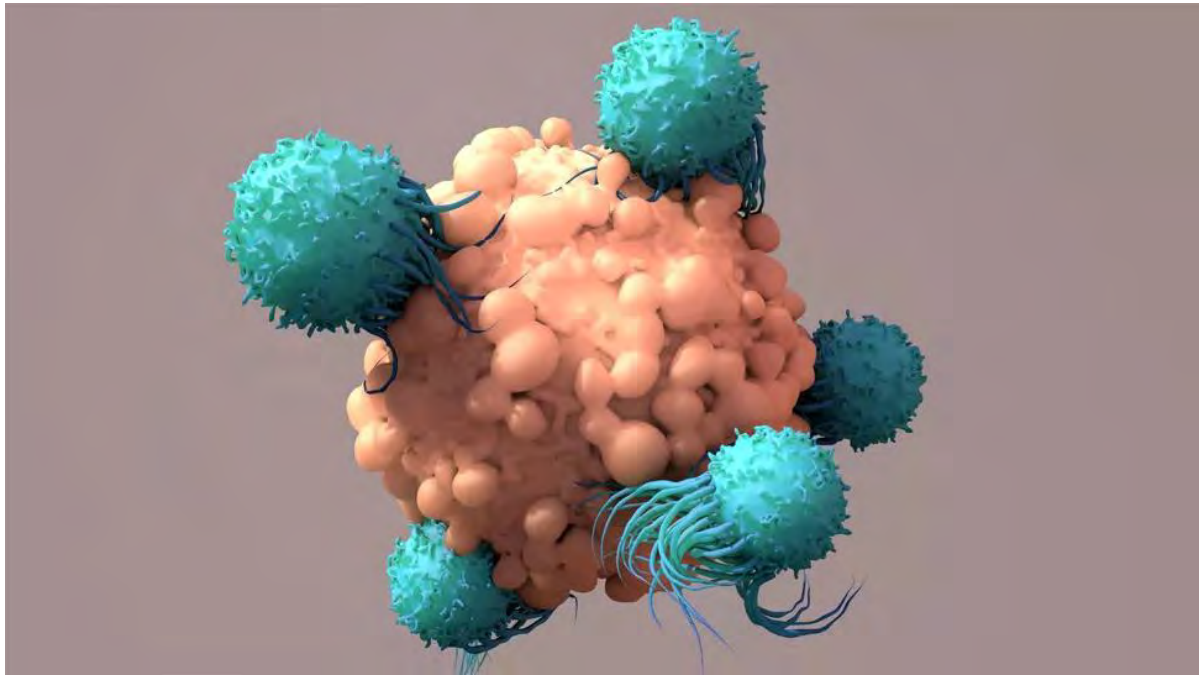



[a]Twenty-two of the 23 patients with 2L FL were responders; [b]One hundred of the 103 patients with 3L+ FL were responders.
NR, not reached.

Courtesy of Brian T Hill, MD, PhD

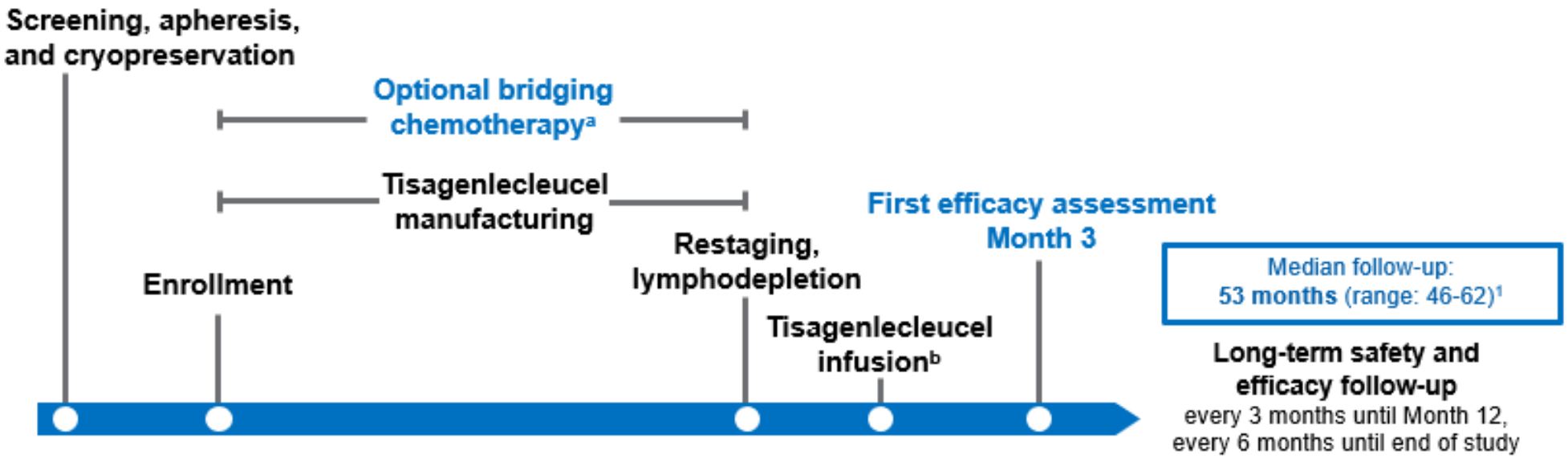
# Follicular Lymphoma: CAR-T

## *Tisa-Cel*



Courtesy of Brian T Hill, MD, PhD

# ELARA: Phase II, Single-Arm, Multicenter, Open-Label Trial in Adults With r/r FL




- Bridging therapy was allowed and was followed by disease re-evaluation before tisagenlecleucel infusion[2,3]
- 18% (17/97) of patients received tisagenlecleucel in the outpatient setting[2,3]

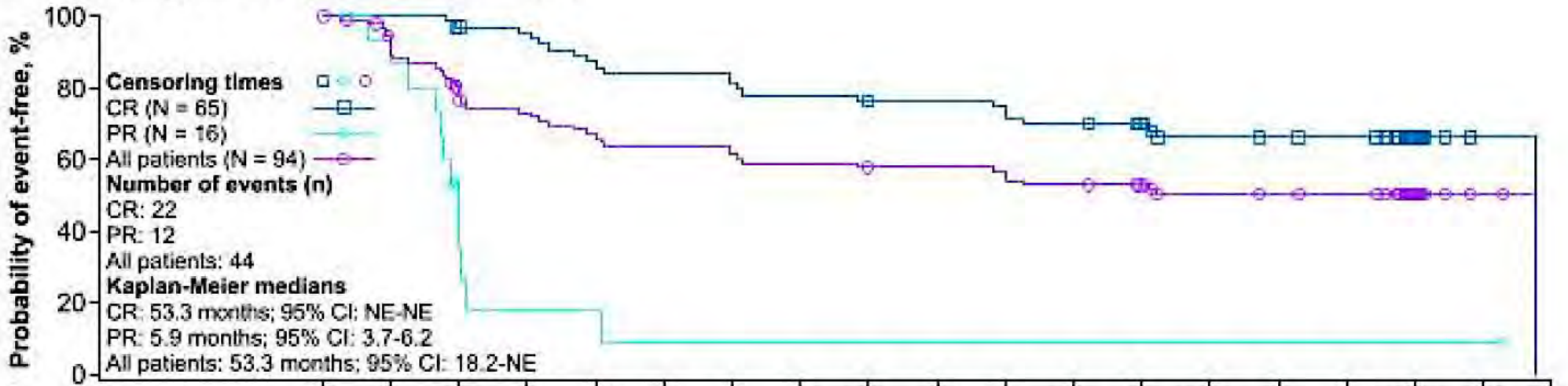
FL, follicular lymphoma; r/r, relapsed or refractory.
[a]Disease was reassessed prior to infusion for all patients requiring bridging therapy. [b]Infusion was conducted on an in- or outpatient basis according to local policy and at investigator's discretion.

**References: 1.** Thieblemont C et al. Poster presented at: ASH 2024; December 7-10, 2024; San Diego, CA. Poster presentation 3034.
From Clinical outcomes of patients with high-risk relapsed/refractory follicular lymphoma treated with tisagenlecleucel: phase 2 ELARA 4-year update, presented by Thieblemont C et al at the 2024 ASH Annual Meeting. Reproduced with permission from the American Society of Hematology.
**2.** Dreyling M, et al. Oral presented at: ASH 2022; December 10-13, 2022; New Orleans, LA. Oral presentation 608; **3.** Fowler NH, et al. *Nat Med.* 2022;28(2):325-332. doi: 10.1038/s41591-021-01622-0.

Courtesy of Brian T Hill, MD, PhD

# ELARA: Progression-Free Survival

**Figure 3. Progression-Free Survival**




| Number of patients still at risk | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CR | 65 | 65 | 62 | 60 | 55 | 53 | 51 | 49 | 47 | 47 | 45 | 43 | 40 | 35 | 34 | 33 | 14 | 1 | 0 |
| PR | 16 | 13 | 4 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| All patients | 94 | 80 | 67 | 62 | 57 | 54 | 52 | 50 | 48 | 48 | 46 | 44 | 41 | 36 | 35 | 34 | 15 | 2 | 0 |

CR, complete response; NE, not estimable; PR, partial response.

Courtesy of Brian T Hill, MD, PhD

Thieblemont C et al. ASH 2024;Abstract 3034.

# Considerations for Relapsed/Refractory Follicular Lymphoma

- Tafasitamab/lenalidomide
- Loncastuximab tesirine
- Bispecific antibodies
- CAR T-cell therapy

# AGENDA

## Year in Review: Management of Non-Hodgkin Lymphoma

**INTRODUCTION:** Bispecific Antibodies in Community Practice

**MODULE 1:** Diffuse Large B-Cell Lymphoma

**MODULE 2:** CD19, CD20 or Both? AZD0486 Bispecific Antibody

**MODULE 3:** Mantle Cell Lymphoma

**MODULE 4:** Follicular Lymphoma

**MODULE 5: CAR T-Cell Therapy for Marginal Zone Lymphoma**

RTP Year in Review 2025

# Positive Topline Results for Lisocabtagene Maraleucel (Liso-cel) in Adult Patients with Relapsed or Refractory Marginal Zone Lymphoma

## Press Release: February 10, 2025

"The Phase 2 TRANSCEND FL trial evaluating lisocabtagene maraleucel in adult patients with relapsed or refractory indolent B-cell non-Hodgkin lymphoma met its primary endpoint in the marginal zone lymphoma (MZL) cohort. Results showed lisocabtagene maraleucel demonstrated a statistically significant and clinically meaningful overall response rate (ORR) in these patients.

The study also met the key secondary endpoint of complete response rate (CRR). In the topline analysis, lisocabtagene maraleucel continued to demonstrate durable responses and a consistent safety profile with no new safety signals observed."

https://news.bms.com/news/corporate-financial/2025/Bristol-Myers-Squibb-Announces-Positive-Topline-Results-for-Breyanzi-lisocabtagene-maraleucel-in-Adult-Patients-with-Relapsed-or-Refractory-Marginal-Zone-Lymphoma/default.aspx

# Data + Perspectives: Clinical Investigators Discuss the Emerging Role of AKT Inhibitors in the Care of Patients with Prostate Cancer

*A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2025 (AUA2025)*

**Saturday, April 26, 2025**

**8:00 AM – 9:30 AM PT (11:00 AM – 12:30 PM ET)**

## Faculty

**Leonard G Gomella, MD**

**Evan Y Yu, MD**

## Moderator

**Daniel J George, MD**

RTP RESEARCH TO PRACTICE

*Thank you for joining us!*

*Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.*

*Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.*

RTP Year in Review 2025