

**What Clinicians Want to Know: Addressing Community  
Oncologists' Questions About the Roles of CAR T-Cell Therapy and  
Bispecific Antibodies in the Management of Non-Hodgkin Lymphoma**

**Sunday, May 31, 2026**

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

**Faculty**

**Joshua Brody, MD**

**Manali Kamdar, MD, MBBS**

**Tycel Phillips, MD, FASCO**

**Jason Westin, MD, MS, FACP, FASCO**

**Moderator**

**Jeremy S Abramson, MD, MMSc**

# Faculty



**Joshua Brody, MD**

Director, Lymphoma Immunotherapy Program  
The Tisch Cancer Institute at Mount Sinai  
Faculty Member, Icahn Genomics Institute  
Icahn School of Medicine at Mount Sinai  
New York, New York



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Lead, Lymphoma and Myeloma Service Line  
Professor, Department of Lymphoma and Myeloma  
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Associate Professor  
Clinical Director of Lymphoma Services  
Morton and Sandra Saffer Endowed Chair in  
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Division of Hematology, Hematologic Malignancies  
University of Colorado Cancer Center  
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**Moderator**

**Jeremy S Abramson, MD, MMSc**

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**Tycel Phillips, MD, FASCO**

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Transplantation  
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# Dr Brody — Disclosures Faculty

No relevant financial relationships to disclose

# Dr Kamdar — Disclosures Faculty

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<b>Data and Safety Monitoring Boards/Committees</b>	Bristol Myers Squibb, Celgene Corporation, Genentech, a member of the Roche Group

# Dr Phillips — Disclosures Faculty

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<b>Advisory Committees</b>	<p>BeOne, Genentech, a member of the Roche Group, Genmab US Inc, Merck</p>
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# Dr Abramson — Disclosures

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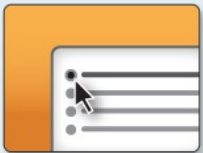
**This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.**

# 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. Survey questions will be discussed throughout the meeting.**



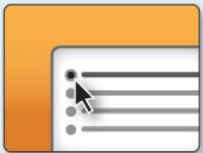
**Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.**

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

# Clinicians Attending via Zoom



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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](http://www.ResearchToPractice.com)



Friday May 29	<b>Gastroesophageal Cancers</b> 11:30 AM – 1:00 PM CT (12:30 PM – 2:00 PM ET)
	<b>Non-Small Cell Lung Cancer</b> 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
	<b>Chronic Lymphocytic Leukemia</b> 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
	<b>Colorectal Cancer</b> 6:30 PM – 8:00 PM CT (7:30 PM – 9:00 PM ET)
Saturday May 30	<b>Ovarian Cancer</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	<b>Prostate Cancer</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	<b>Small Cell Lung Cancer</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Sunday May 31	<b>Oral SERDs and Agents Targeting the PI3K/AKT/mTOR Pathway for Breast Cancer</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	<b>Endometrial Cancer</b> 7:00 PM – 8:30 PM CT (8:00 PM – 9:30 PM ET)
	<b>CAR T-Cell Therapy and Bispecific Antibodies for Non-Hodgkin Lymphoma</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Monday June 1	<b>ADCs for Breast Cancer</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	<b>Novel Therapies for Non-Hodgkin Lymphoma</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	<b>Relapsed/Refractory Multiple Myeloma</b> 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Tuesday June 2	<b>Myelofibrosis (Webinar)</b>

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**What Clinicians Want to Know: Addressing  
Community Oncologists' Questions About the Roles of  
CAR T-Cell Therapy and Bispecific Antibodies in the  
Management of Non-Hodgkin Lymphoma**

**Survey of US-Based General Medical Oncologists  
May 13-26, 2026**

# Agenda

**Module 1:** Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Kamdar

**Module 2:** Bispecific Antibody Therapy for DLBCL — Dr Westin

**Module 3:** CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Abramson

**Module 4:** Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

**Module 5:** Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies — Dr Brody

# Agenda

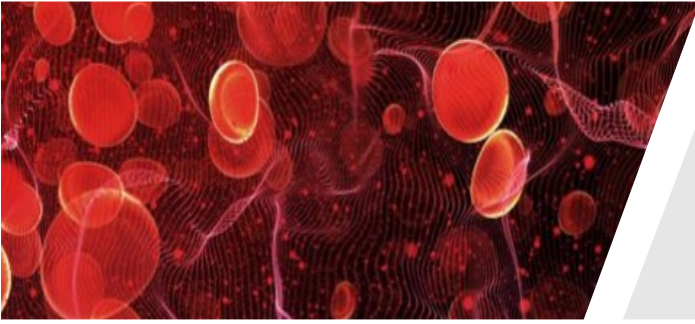
**Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Kamdar**

**Module 2: Bispecific Antibody Therapy for DLBCL — Dr Westin**

**Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Abramson**

**Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips**

**Module 5: Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies — Dr Brody**



# Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL)

**Manali Kamdar, MD, MBBS**

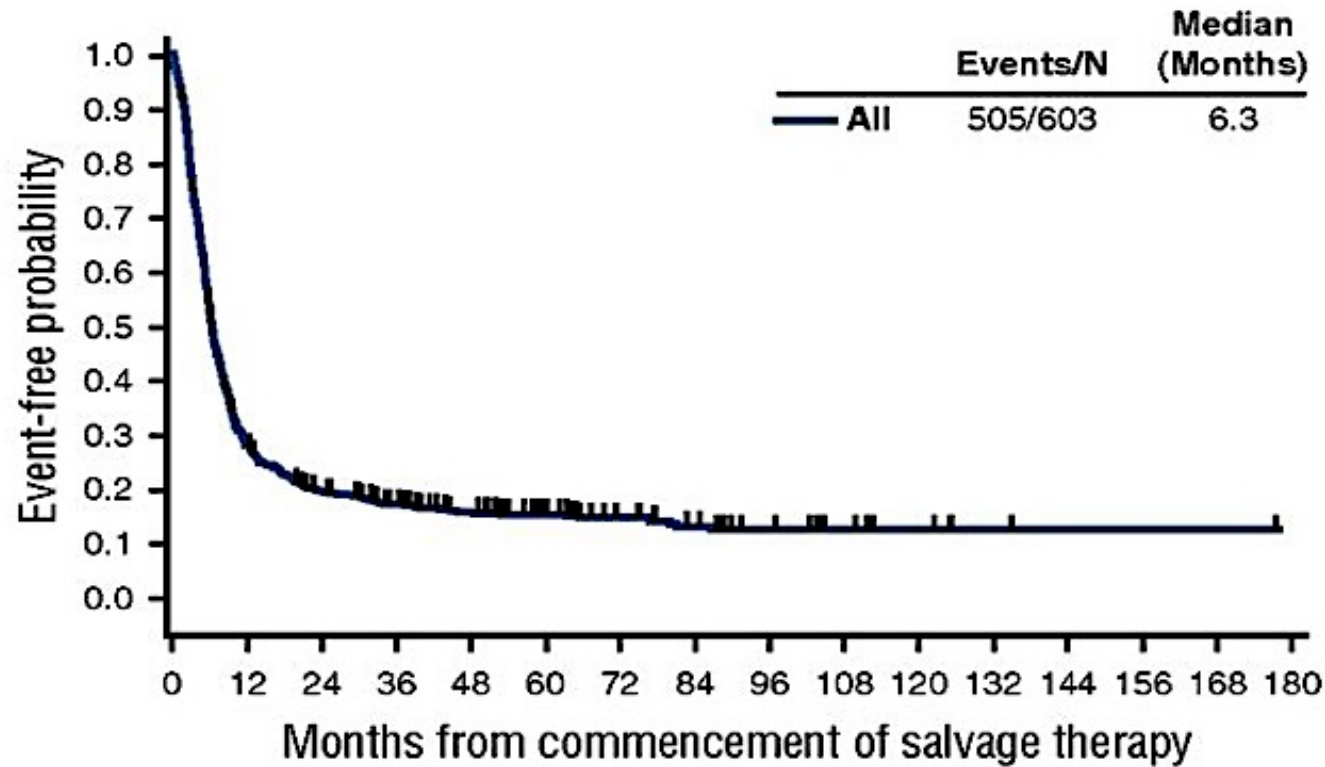
Associate Professor of Medicine, Clinical director of lymphoma services,

Morton and Sandra Saffer Endowed Chair in Hematology Research,  
Division of Hematology,

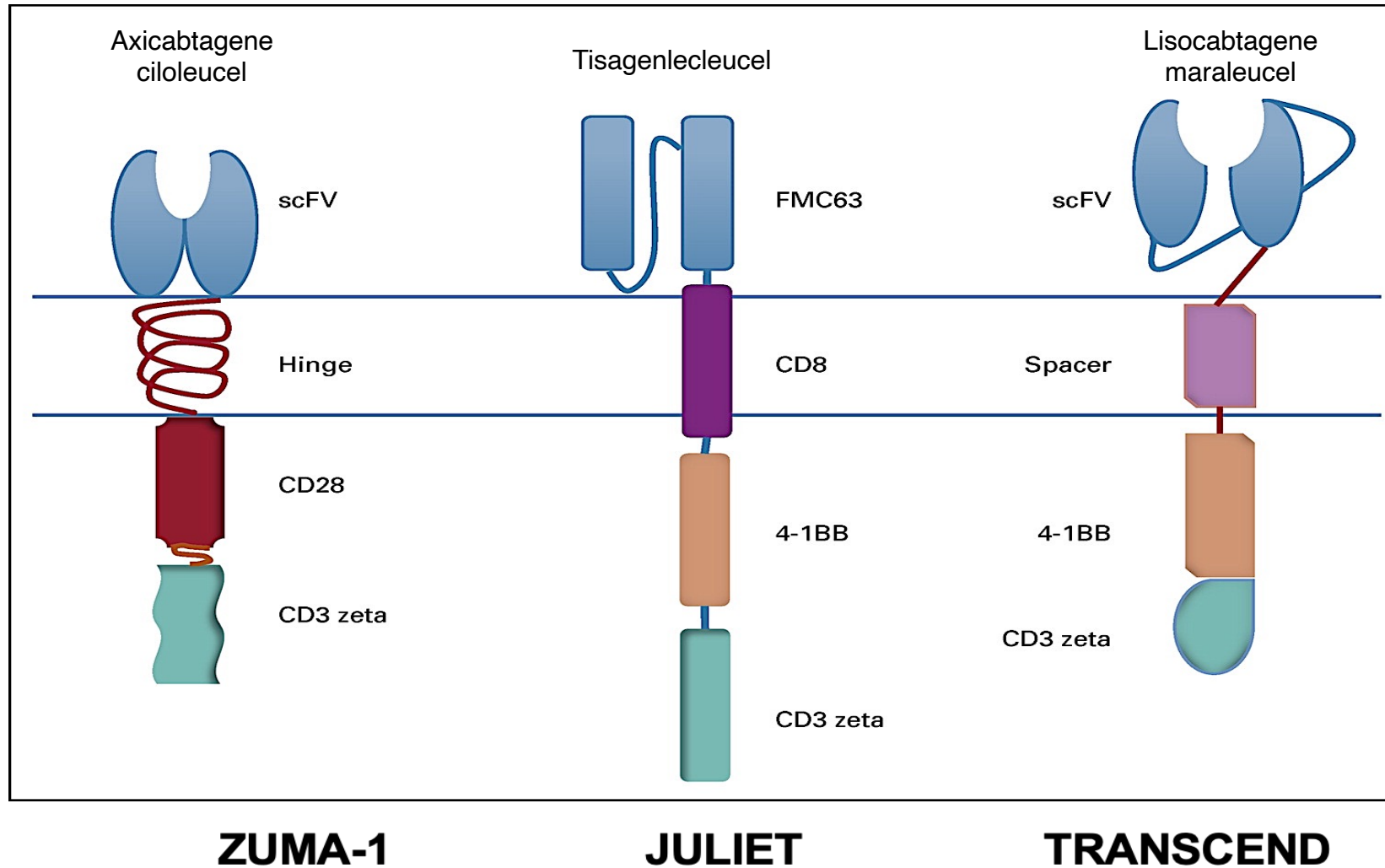
University of Colorado

# Pre-CAR-T ERA

Relapsed/Refractory Chemotherapy-resistant Large B Cell Lymphoma (R/R LBCL) → dismal prognosis



# Anti-CD19 CAR-T cell therapies approved in R/R LBCL after failure of $\geq 2$ lines of treatment



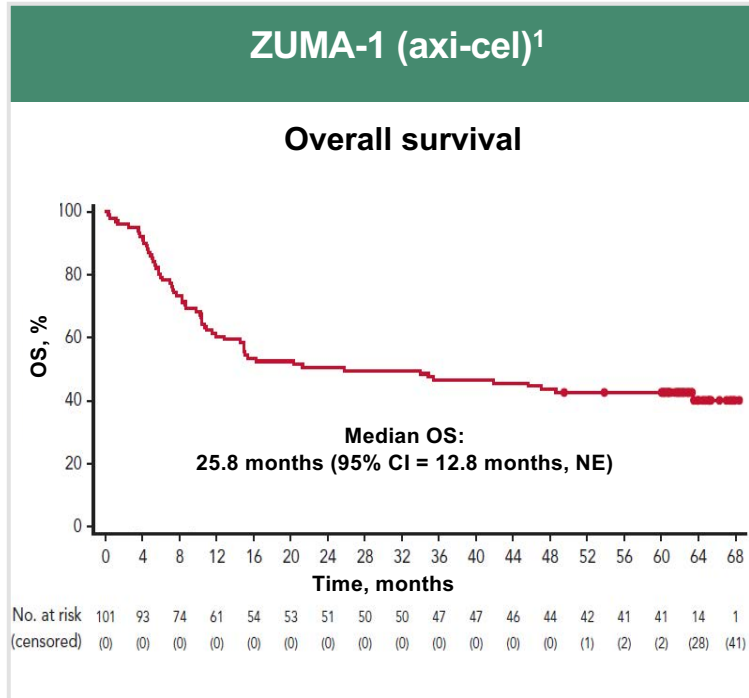
# Baseline Characteristics

	ZUMA-1 Axicabtagene Ciloleucel	TRANSCEND Lisocabtagene Maraleucel	JULIET Tisagenlecleucel
<b>Dose</b>	2 x 10 <sup>6</sup> /kg	100 x 10 <sup>6</sup>	0.6 to 6.0 x 10 <sup>8</sup>
<b>Lymphodepletion x3 days</b>	Flu/Cy 500/30	Flu/Cy 300/30	Flu/Cy 250/25, OR Bendax2
<b># Treated / Enrolled</b>	101/111	269/344	111/165
<b>Bridging Rx (%)</b>	0	59	92
<b>Lymphoma Subtypes</b>	DLBCL, PMBCL, HGBCL, Transformed FL	DLBCL, PMBCL, HGBCL, Transformed FL, Transformed Non-FL, Sec CNS involvement, Prior Allo	DLBCL, Transformed FL
<b>Median Age</b>	58 (23-76)	63 (18-86)	56 (22-76)
<b>Median prior LOT</b>	3	3	2 (44%), 3 (31%)
<b>Refractory/Prior ASCT (%)</b>	100/23	67/35	55/49

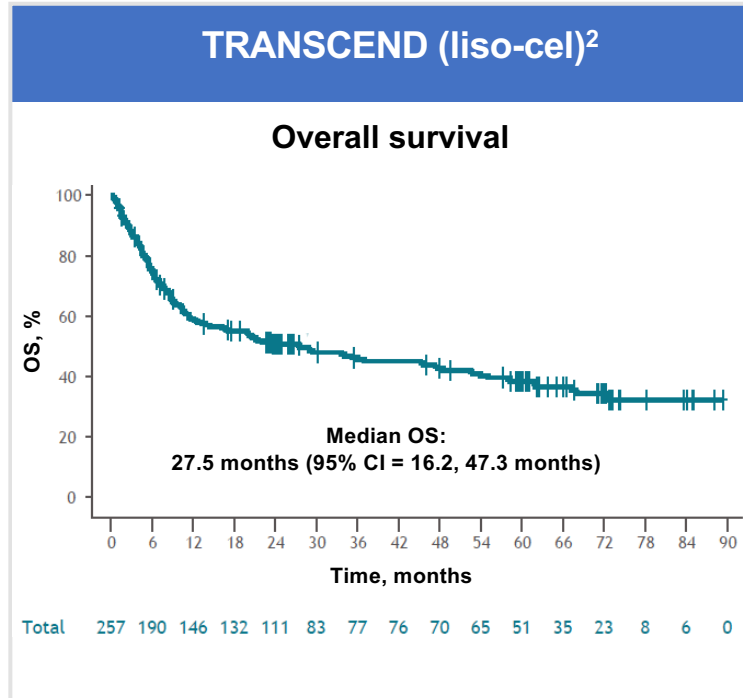
# Efficacy and Safety

	ZUMA-1 Axicabtagene Ciloleucel	TRANSCEND Lisocabtagene Maraleucel	JULIET Tisagenlecleucel
# Treated / Enrolled	101/111	269/344	111/165
<b>ORR/CR (%) by IRC</b>	74/54	73/53	52/40
Construct	antiCD19-CD28-CD3z	antiCD19-41BB-CD3z	antiCD19-41BB-CD3z
Toxicity grading scale	Lee Criteria	Lee Criteria	Penn Criteria
Median time to CRS onset	2 days	5 days	3 days
<b>Any Grade/Gr ≥3 Cytokine release syndrome (CRS)</b>	93% / 11%	42% / 2%	58% / 23%
<b>Any Gr/Gr ≥3 Neurotoxicity</b>	64% / 32%	30% / 10%	21% / 12%
2yr PFS/OS	42% / 51%	41% / 51%	30%/median 11m

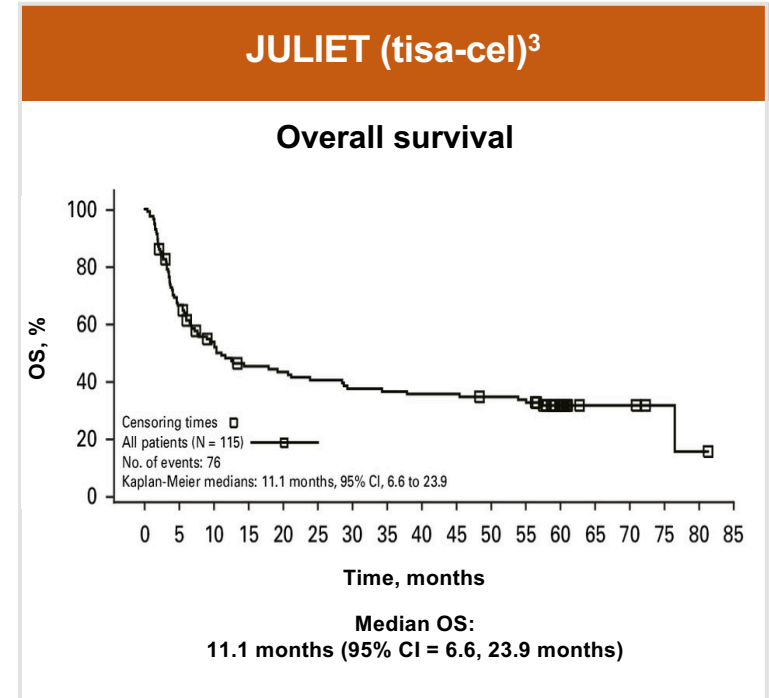
# Long-term follow-up supports the curative potential of CD19 CAR T in R/R 3L+ LBCL



**5-year OS rate: 43%**  
Median follow-up: 63.1 months



**5-year OS rate: 38%**  
Median follow-up: 60.1 months



**5-year OS rate: 32%**  
Median follow-up: 74.3 months

Inter-trial comparisons should not be made due to differences in study design, patient populations, treatment interventions, and durations of follow-up, among others. We cannot make direct comparisons or draw conclusions from one trial to another. For descriptive purposes, efficacy and safety results for each of the studies mentioned are listed.  
3L, third line; axi-cel; axicabtagene ciloleucel; CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; NE, not estimable; OS, overall survival, R/R, relapsed or refractory; tisa-cel, tisagenlecleucel. 1. Neelapu SS, et al. Blood 2023;141:2307—2315. 2. Abramson JS, et al. ASH 2024. Abstract 3125. 3. Maziarz RT et al. J Clin Oncol. 2026 Jan 10;44(2):86-91.

3 Randomized trials of CAR T-cell therapy vs SOC in transplant-eligible DLBCL with early relapse or primary refractory disease

**Primary Analysis of ZUMA-7: a Phase 3 Randomized Trial of Axicabtagene Ciloleucel versus Standard-of-Care Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma**

ASH 2021

Frederick L. Locke, MD<sup>1</sup>; David B. Miklos, MD, PhD<sup>2</sup>; Caron A. Jacobson, MD, MMSc<sup>3</sup>; Miguel-Angel Perales, MD<sup>4</sup>;

**TRANSFORM Study: Lisocabtagene Maraleucel, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy, Versus Standard of Care with Salvage Chemotherapy Followed by Autologous Stem Cell Transplantation as Second-Line Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma: Results from the Randomized Phase 3 TRANSFORM Study**

ASH 2021

Manali Kamdar,<sup>1</sup> Scott R. Solomon,<sup>2</sup> Jon Amason,<sup>3</sup> Patrick B. Johnston,<sup>4</sup> Bertram Glass,<sup>5</sup> Veronika Bachanova,<sup>6</sup> Sami

**Tisagenlecleucel vs Standard of Care as Second-Line Therapy of Primary Refractory or Relapsed Aggressive B-Cell Non-Hodgkin Lymphoma: Analysis of the Phase III BELINDA Study**

ASH 2021

Michael R. Bishop,<sup>1</sup> Michael Dickinson<sup>2</sup>, Duncan Purtil<sup>3</sup>, Pere Barba<sup>4</sup>, Armando Santoro<sup>5</sup>, Nada Hamad<sup>6</sup>, Koji Kato<sup>7</sup>, Anna Sureda<sup>8</sup>, Richard Greif<sup>9</sup>,

Locke, F et al, N Engl J Med. 2022 Feb 17;386(7):640-654. doi: 10.1056/NEJMoa2116133

Kamdar, M et al Lancet. 2022 Jun 18;399(10343):2294-2308. doi: 10.1016/S0140-6736(22)00662-6.

Bishop, M et al N Engl J Med. 2022 Feb 17;386(7):629-639. doi: 10.1056/NEJMoa2116596

	ZUMA 7 (Axi-cel) <sup>1</sup>	TRANSFORM (Liso-cel) <sup>2,4</sup>	BELINDA (Tisa-cel) <sup>3</sup>
<b>N</b>	359	184	322
<b>% pts proceeded in CART vs <u>AutoTx</u></b>	94% vs 36%	97% vs 46%	96% vs 32%
<b>Primary Refractory Double hit lymphoma</b>	75 %/16%	75%/24%	75%/ 19% <u>Tisacel</u> /11% SOC
<b>Median time from registration to CAR</b>	29 days	34 days	52 days
<b>Bridging therapy</b>	Steroids only	1 cycle of salvage chemo allowed (63%)	>1 cycle of salvage chemo allowed (83%)
<b>Crossover</b>	Not allowed	Allowed (51%)	Allowed (51%)
<b>Median follow up</b>	25 months	17.5 months	10 months
<b>Median EFS</b>	8.3 m vs. 2 m	10.1 m vs 2.4 m	3 m vs 3 m
<b>Hazard ratio</b>	0.39 (p<0.0001)	0.34 (p< 0.0001)	1.07 (p=0.69)
<b>ORR</b>	83% vs 50%	87% vs 49%	47% vs 43%
<b>CR rate</b>	65% vs 32%	74% vs 43%	28% vs 28%
<b>Grade <math>\geq</math>3 CRS/NE</b>	6%/21%	1%/4%	5%/3%

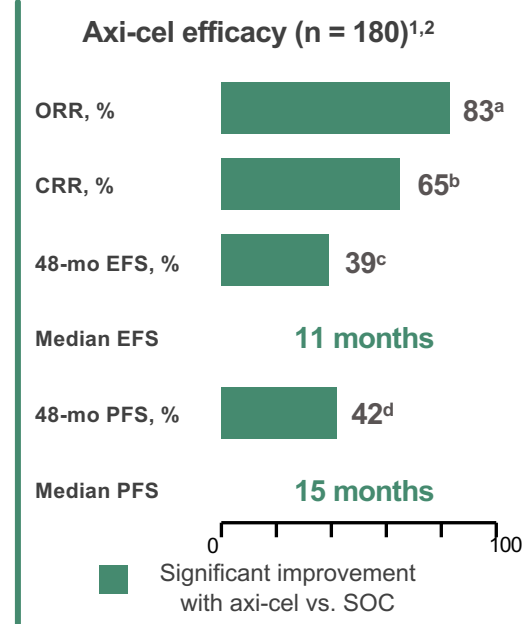
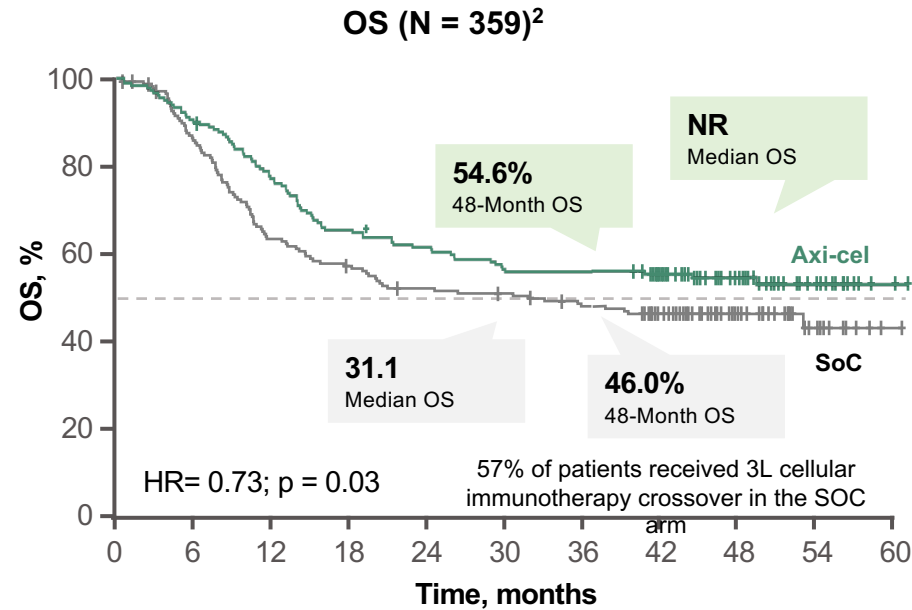
1.Locke, F et al, N Engl J Med. 2022 Feb 17;386(7):640-654. doi: 10.1056/NEJMoa2116133  
2.Kamdar, M et al Lancet. 2022 Jun 18;399(10343):2294-2308. doi: 10.1016/S0140-6736(22)00662-6.  
3.Bishop,M et al N Engl J Med. 2022 Feb 17;386(7):629-639. doi: 10.1056/NEJMoa2116596c  
4.Abramson JS et al Blood 2023 6;141(14):1675-1684

# Axi-cel continued to demonstrate higher rates of survival vs. SOC at ≈ 4 years of follow-up

**ZUMA-7<sup>1,2</sup>**

**mFU: 47.2 months**  
Phase 3, randomized trial of **axi-cel** (n = 180) vs. **SOC** (ASCT, n = 179) as 2L treatment in patients with R/R LBCL (N = 359)

**Axi-cel**  
**Primary refractory: 74%**  
**DHL/THL: 17%**



**Axi-cel provided a 27% reduction in risk of death vs. SOC<sup>2</sup>**

<sup>a</sup> ORR with SOC was 50%; <sup>b</sup> CRR with SOC was 32%; <sup>c</sup> 48-month EFS with SOC was 17%; <sup>d</sup> 48-month PFS with SOC was 24%. 2L, second line; ASCT, autologous stem cell transplant; axi-cel, axicabtagene ciloleucel; CRR, complete response rate; DHL, double-hit lymphoma; EFS, event-free survival; HR, hazard ratio; LBCL, large B-cell lymphoma; mFU, median follow-up; mo, month; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory; SOC, standard of care; THL, triple-hit lymphoma.  
1. Locke FL, et al. N Engl J Med 2022;386:640—654. 2. Westin JR, et al. N Engl J Med 2023;389:148—157.

# Liso-cel continued to demonstrate higher rates of survival at ≈ 3 and 4 years of follow-up

**TRANSFORM<sup>1,2</sup>**

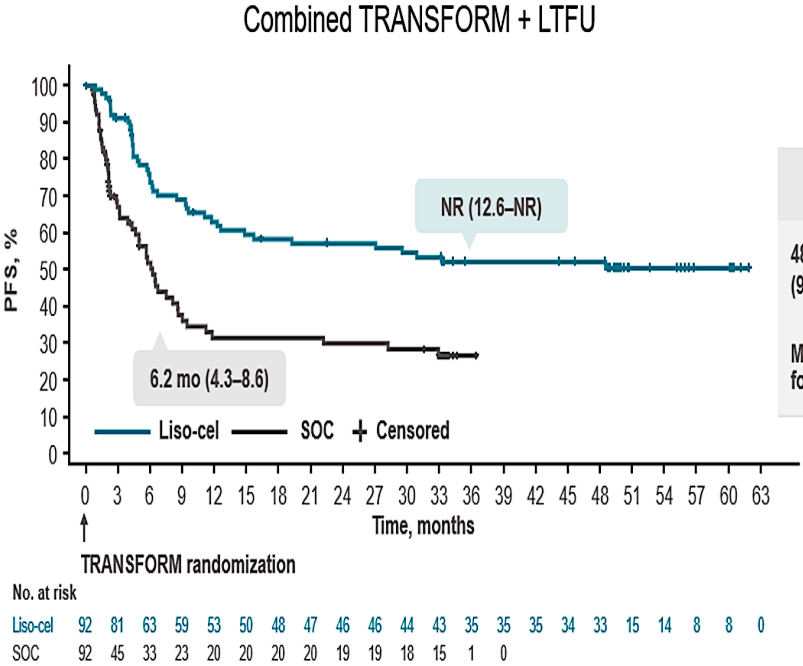
**mFU: 33.9 months**

Phase 3, randomized trial of **liso-cel (n = 92)** vs. **SOC (ASCT, n = 92)** as 2L treatment in patients with R/R LBCL (N = 184)

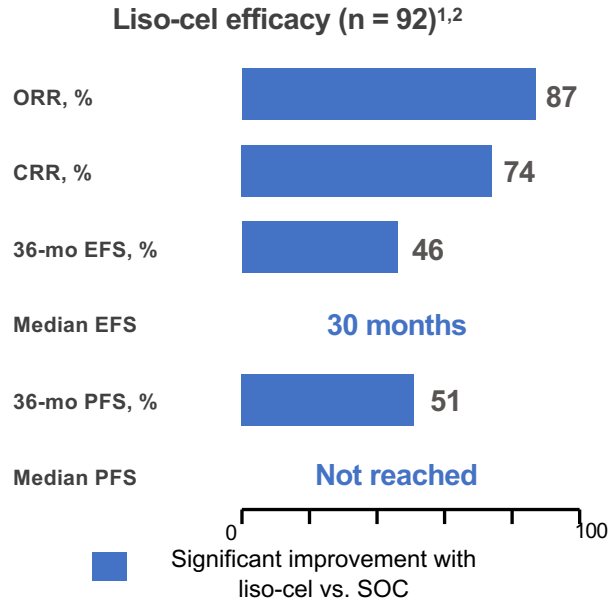
**Liso-cel**

**Primary refractory: 73%**

**DHL/THL: 24%**



	Liso-cel (n = 92)	SOC (n = 92)
48-month rate (95% CI)	<b>52.2%</b> (41.5-62.8)	<b>NA</b> (NA-NA)
Median (95% CI) follow-up	49.4 months (48.7-50.3)	33.2 months (32.9-33.6)

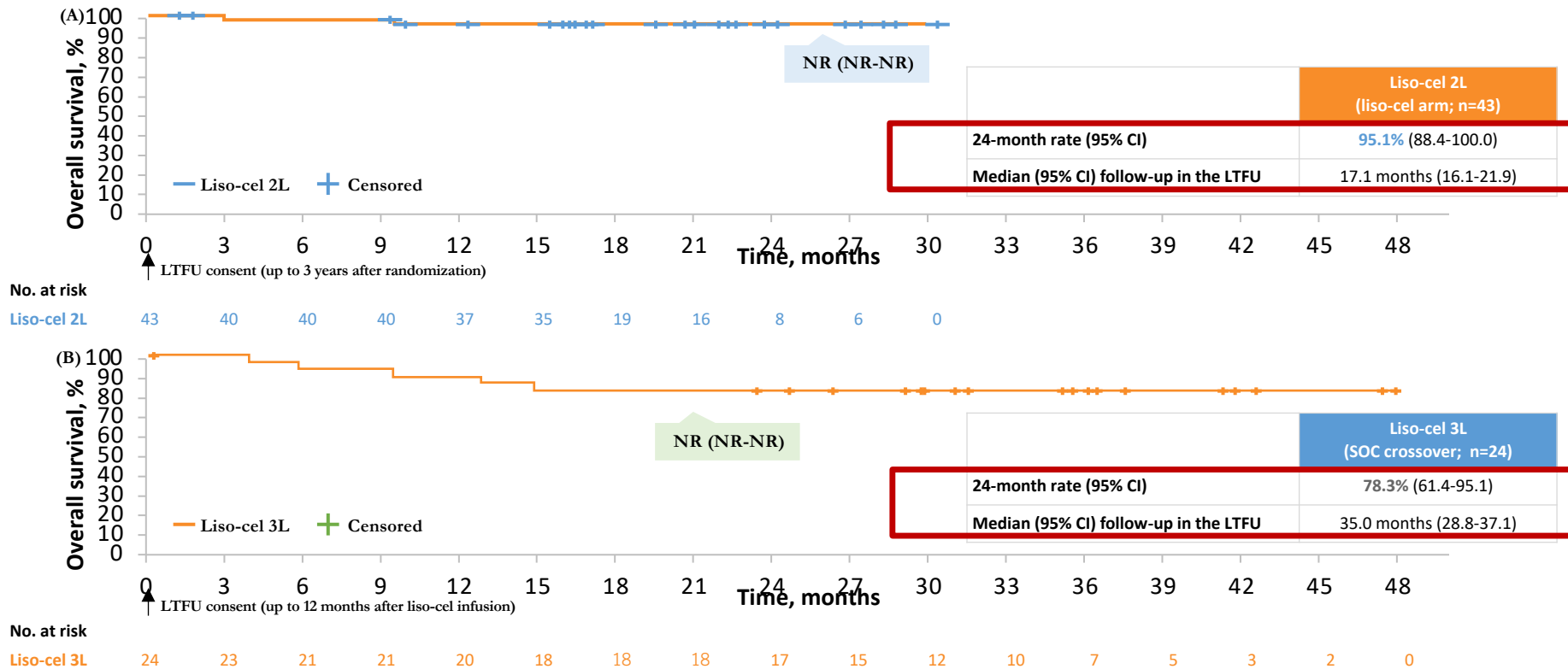


**62% of patients crossed over from the SOC arm to receive liso-cel<sup>1,2</sup>**

**Liso-cel provided a 43% reduction in risk of death vs. SOC in a prespecified analysis adjusted for crossover<sup>1,2,a</sup>**

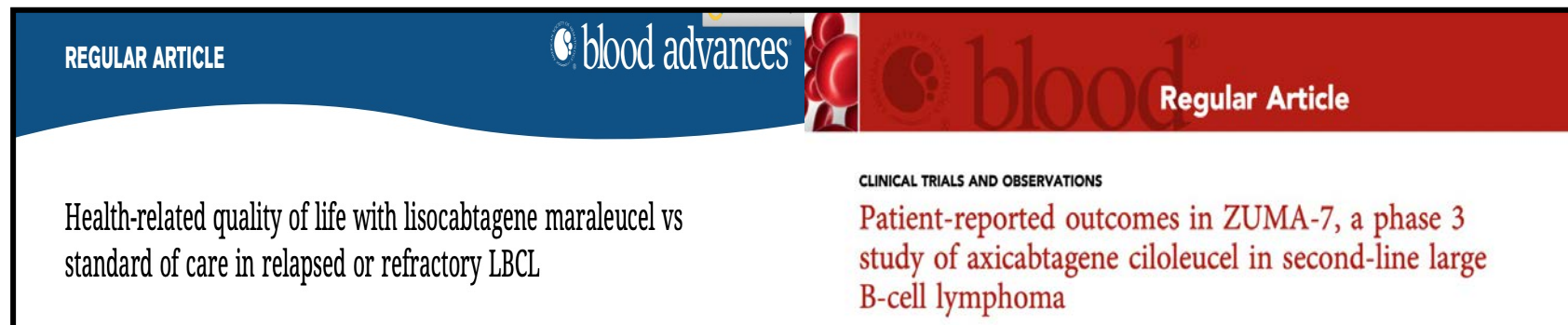
# Receiving CAR-T in 2L versus 3L impacts outcomes

Figure 5. OS in liso-cel 2L (A) and liso-cel 3L (B) patients in the LTFU



Kamdar et. al. ASCO 2024. Oral Presentation

# Patient-reported outcomes



**The TRANSFORM and ZUMA-7 trials showed clinically meaningful improvement in quality of life for patients randomized to CAR T-cell therapy compared with ASCT<sup>1,2</sup>**

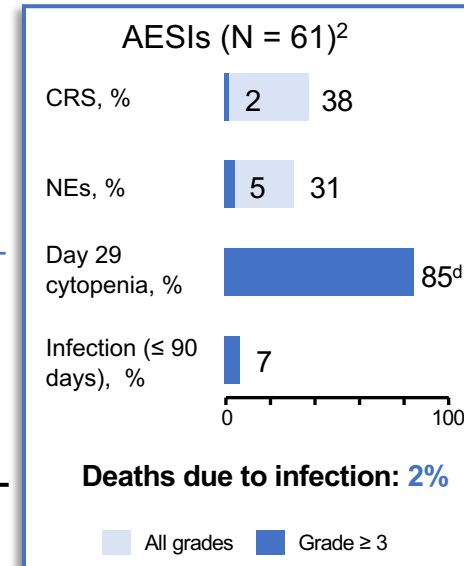
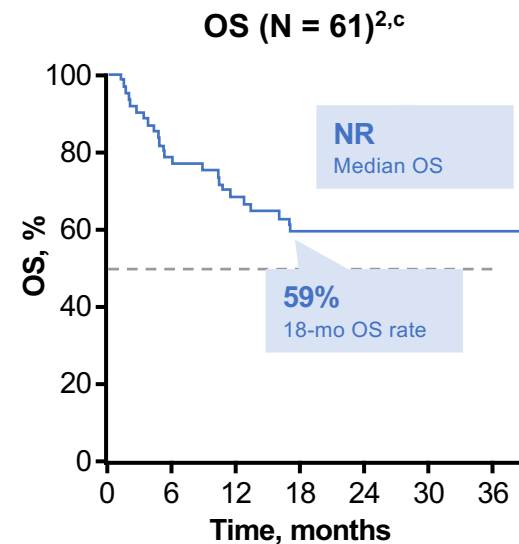
**Liso-cel and axi-cel were approved for transplant-eligible high-risk DLBCL in first relapse<sup>3,4</sup>**

Next question: What about transplant ineligible YET CAR-eligible patients with R/R LBCL?

ASCT, autologous stem cell transplant; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; R/R, relapsed or refractory.  
1. Abramson J, et al. Blood Adv 2022;6:23:5969—5979. 2. Elsayw M, et al. Blood 2022;140:2248—2260. 3. Lisocabtagene maraleucel PI 2026. Axicabtagene ciloleucel PI. 2026.  
4. Axicabtagene ciloleucel. Summary of product characteristics. Gilead Sciences; 2024.

# PILOT study : Liso-cel demonstrated outcomes comparable to those in TRANSFORM in an ASCT-ineligible population

PILOT	ASCT ineligibility criteria	Liso-cel, % (N = 61)
<b>mFU: 24.3 months</b>		
Phase 2, single-arm analysis assessing <b>liso-cel</b> as 2L treatment in patients with R/R LBCL who were deemed ineligible for ASCT <sup>a</sup> (N = 61) <sup>1,2</sup>	Age ≥ 70 years	79
	ECOG PS 2	26
	CrCl < 60 mL/min	25
	DL <sub>CO</sub> ≤ 60%	7
	LVEF < 50%	2
<b>ORR: 80%<sup>2,b</sup></b>		

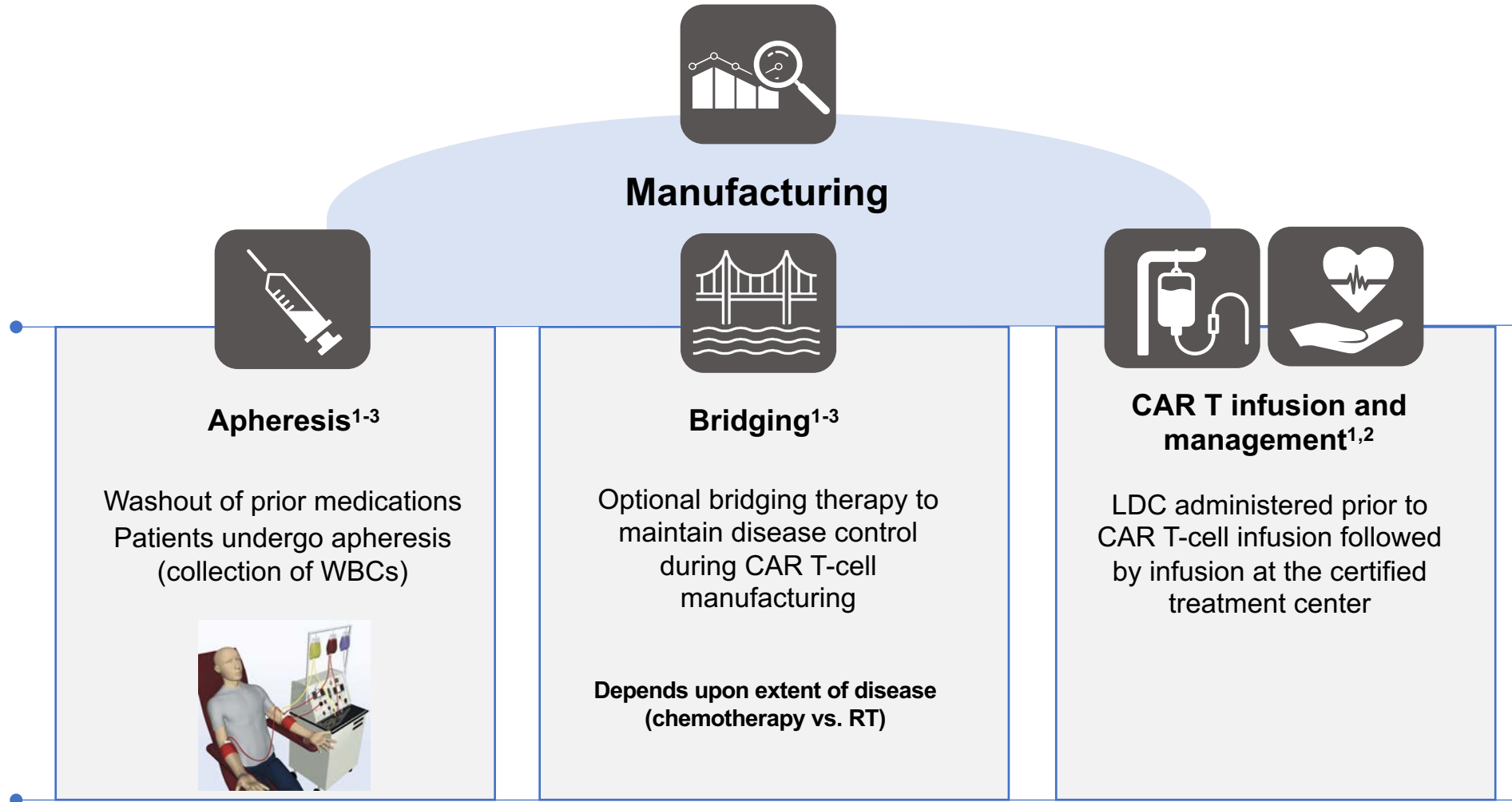


**Median OS was not reached with liso-cel at ≈ 2-year median follow-up<sup>2</sup>**

**Liso-cel is not approved in Europe for the 2L treatment of DLBCL in patients who experienced relapse more than 12 months after completion of 1L therapy.**

<sup>a</sup> Patients must have also met at least one transplant-not-intended criterion as determined by the investigator: age ≥ 70 years, ECOG PS of 2, DLCO ≤ 60%, LVEF < 50%, CrCl < 60 mL/min, ALT/AST > 2 × ULN; <sup>b</sup> Median follow-up of 12.3 months; <sup>c</sup> OS data include data from the LTFU study; <sup>d</sup> Prolonged cytopenia is defined as Grade ≥ 3 decreased hemoglobin level, neutrophil count or platelet count at the Day 29 visit as confirmed by laboratory results. 1L, first line; 2L, second line; AESI, adverse event of special interest; ALT, alanine transaminase; ASCT, autologous stem cell transplant; AST, aspartate aminotransferase; CrCl, creatinine clearance; CRS, cytokine release syndrome; DL<sub>CO</sub>, diffusing capacity of the lungs for carbon monoxide; ECOG PS, Eastern Cooperative Oncology Group performance status; LBCL, large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; LTFU, long-term follow up; LVEF, left ventricular ejection fraction; mFU, median follow-up; mo, month; NE, neurologic events; NR, not reached; ORR, overall response rate; OS, overall survival; R/R, relapsed or refractory, ULN, upper limit of normal. 1. Sehgal A, et al. Lancet Oncol 2022;23:1066—1077. 2. Sehgal A, et al. ASH 2023 Oral presentation 105.

# Logistics: THE PROCESS



The biggest barrier to CAR-T is often not biology, it is delayed recognition and delayed referral.

## Why Early Referral Matters

Referral should occur ASAP  
“**BRAIN**” to “**VEIN**” time (*courtesy*  
Dr Lunning)

**Real-world analyses show substantial attrition before CAR-T access-** Many patients are never referred despite eligibility (2/10 based on claims data)

**Early Referral**  
improves access and planning  
allows insurance approval, caregiver planning,  
and leukapheresis coordination

Telehealth and early specialist input can  
reduce delays

## Bridging Therapy

### Therapy Considerations
















Steroids  
Radiation  
Bispecific antibodies/T-cell engagers  
Selected chemotherapy approaches  
**AVOID BENDAMUSTINE**

Consult CAR-T specialists **BEFORE**  
bridging whenever possible

# Determination of CAR-T eligibility

- Several real-world studies<sup>1</sup> have shown that chronological age, comorbidities, or cognitive and/or functional impairments do not affect post-CAR T outcomes.
- Automatic exclusion of patients based on age/comorbidities is not advised
- Transplant eligibility  $\neq$  CAR-T eligibility

2

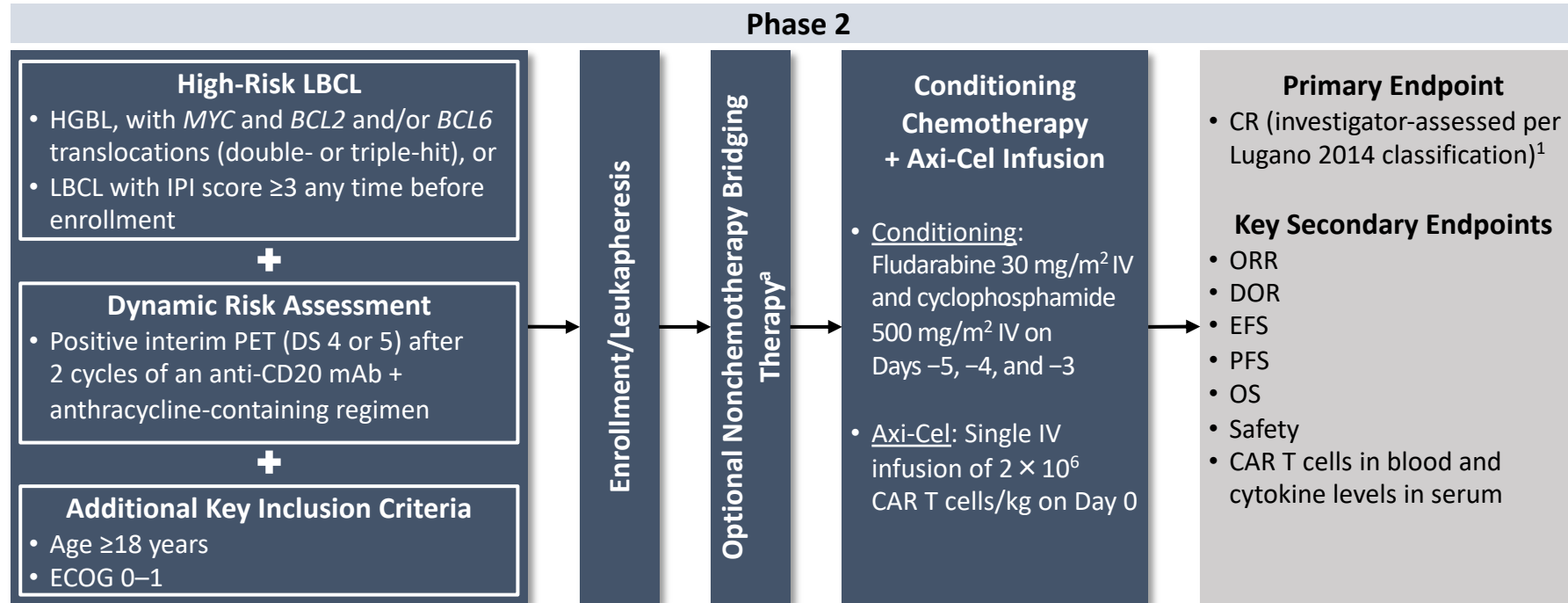
Who Is Eligible for CAR T-Cell Therapy? Expert Perspectives on Overcoming Referral Barriers		
Shadman M, et al.		
Characteristic 	CAR T-cell therapy 	ASCT (for comparison) 
 Advanced age		Age $\leq$ 70 years or refer
 Poor performance status		ECOG PS $\leq$ 2   Karnofsky PS $\geq$ 60
 Lack of response to chemotherapy	No response requirement	Require response to salvage chemotherapy
 Impaired cardiovascular function		NYHA class I or II   LVEF $\geq$ 40 and no uncontrolled CVD or arrhythmia
 Impaired pulmonary function		DLCO $\geq$ 50%
 Impaired renal function	 and 	Serum creatinine $<$ 2 mg/dL   CrCl $>$ 50 mL/min
 Impaired hepatic function		No cirrhosis
 Unresolved, active infections		No unresolved, active infections
 Other considerations	Not restricted: autoimmune disease, obesity, SOT, or sCNS	Not restricted: obesity, sCNS involvement, and SOT   Restricted: CHIP or MDS

**Before considering implementing these recommendations, please make appropriate adaptations to clinical practice based on the most recent regulations, policy requirements, and institutional guidelines.**

ASCT, autologous stem cell transplantation; CAR, chimeric antigen receptor; CHIP, clonal hematopoiesis of indeterminate potential; CNS, central nervous system; CrCl, creatinine clearance; DLCO, diffusing capacity of the lungs for carbon monoxide; CVD, cardiovascular disease; ECOG, Eastern Cooperative Oncology Group; LVEF, left ventricular ejection fraction; MDS, myelodysplastic syndromes; NYHA, New York Heart Association; PS, performance status; sCNS, secondary central nervous system; SOT, solid organ transplantation.

**“If a patient can tolerate lymphoma-directed therapy, they deserve CAR-T evaluation”**

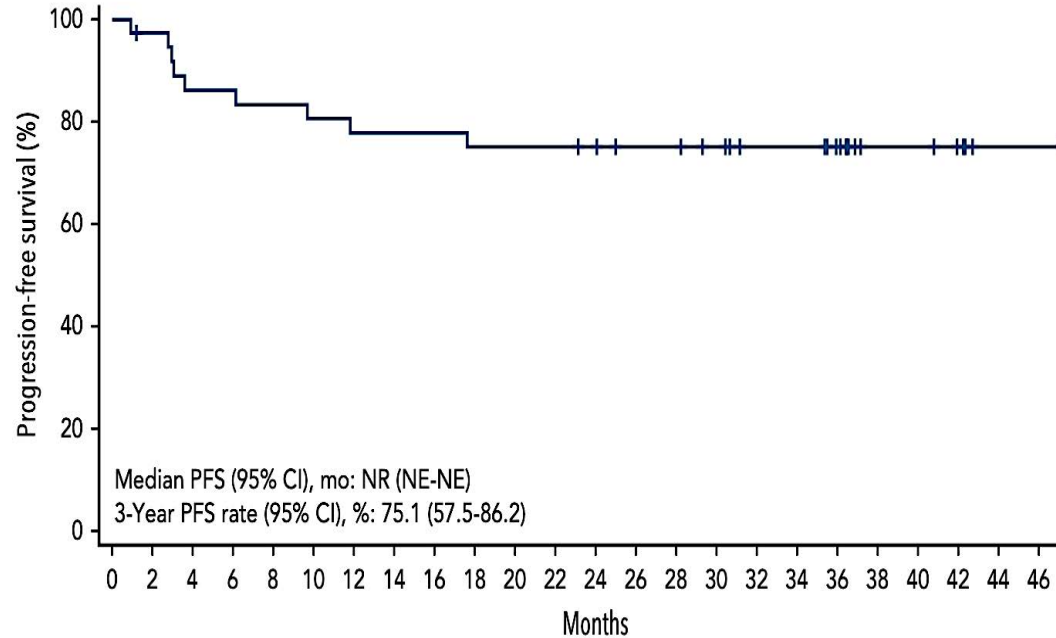
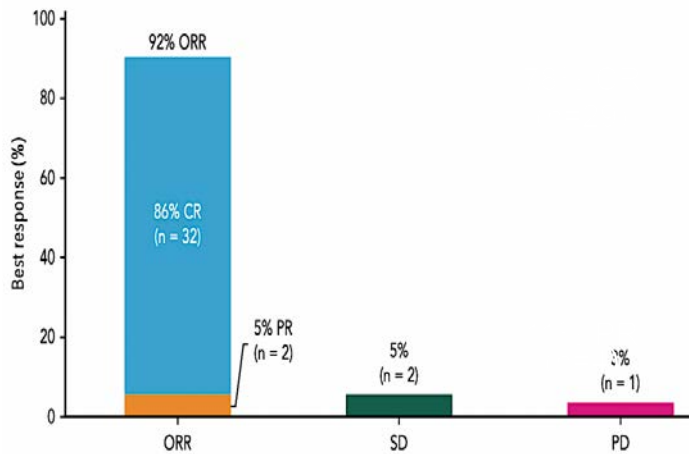
# CARs in the front-line setting: ZUMA-12 Study Design



N= 40, Median age 61 (23-86); DHL/THL: 25%, IPI score of  $\geq 3$  78%, DS 4: 48%, DS 5 53%

# ZUMA-12 : Efficacy/Safety

ORR 89% and  
CR Rate 78%



The most common axi-cel-related Grade  $\geq 3$  AEs were neutropenia (53%), anemia (30%), encephalopathy (15%) and thrombocytopenia (15%)

**CRS** : Any Grade: 100%,  
Grade 3/> 8%  
No Grade 4 and 5 CRS  
occurred

**NE**: Any Grade 73%, Grade  
3/>23%, 5% Grade 4  
No Grade 5 NE occurred

3 yr PFS 75%; 3 yr OS 81%

# Early results with other CAR T-cell platforms in DLBCL

## Rapcabtagene Autoleucel (YTB323) in Patients with Relapsed/Refractory Diffuse Large B-cell Lymphoma: Phase II Trial Clinical Update

CD19-directed CAR-T cell therapy utilizes the T-Charge™ platform-preserve T-cell stemness + 2 day manufacturing time followed by release testing.

Phase II study;  $12.5 \times 10^6$  CAR+ viable T-cell dose;

Primary Endpoint: Complete response rate (CR)

N=63, Median age 64, HGBCL -25% Refractory – 58%; mLOT- 2, BT- 60%

### RESULTS

Median follow up 16 months

Primary Endpoint met- ORR 88% CR 62%

### SAFETY

Most common cytopenias

CRS (44%)

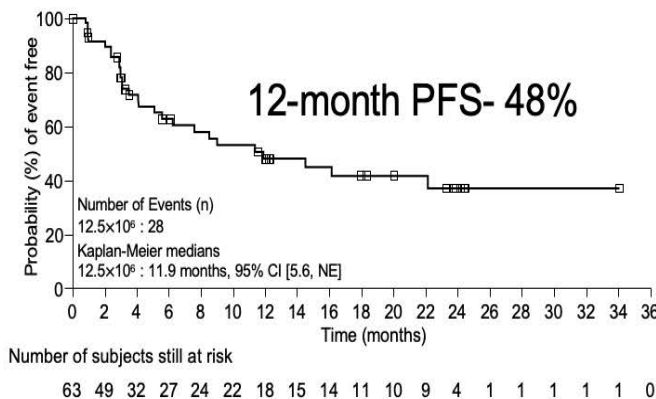
Grade  $\geq 3$  CRS (6%) and ICANS (5%)

1 Grade 3 HLH,

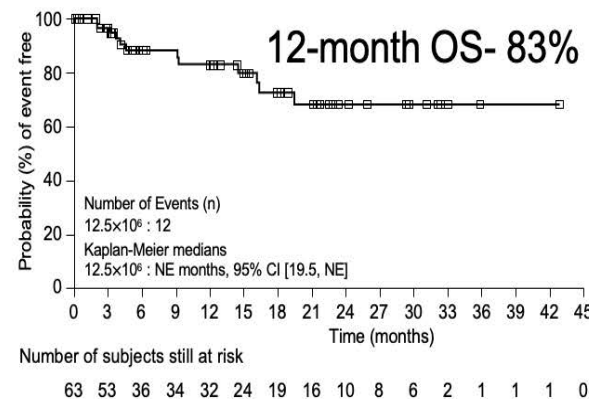
Grade  $\geq 3$  infection 27%

Grade 5 – 6 patients ( 2 with PD)

Progression-Free Survival



Overall Survival



### 2 doses of LD chemo tested

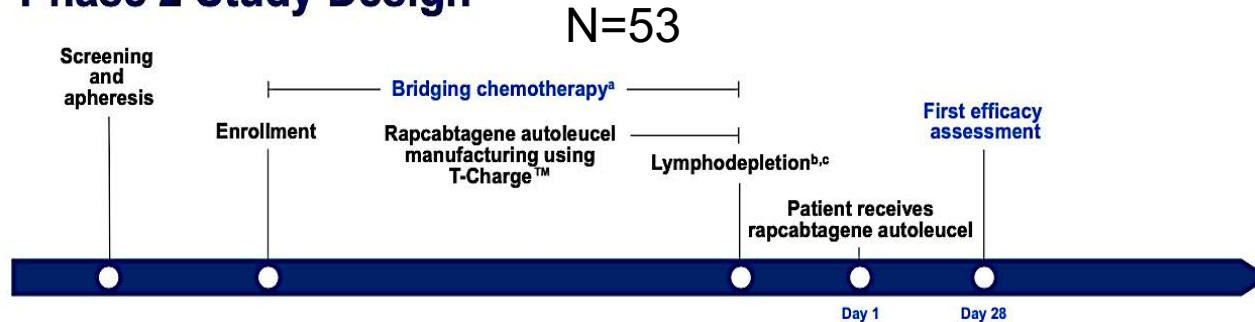
Lower dose n=28 Fly/Cy 25/250

Higher dose n=33 Flu/Cy 30/500

Risk-benefit analyses support lower-dose

# Rapcabtagene Autoleucel (YTB323) for Patients With First Line High-Risk Large B-Cell Lymphoma: Phase 2 Interim Results

## Phase 2 Study Design



Key eligibility criteria	Study treatment	End points
<ul style="list-style-type: none"> <li>• ≥18 years of age</li> <li>• IPI score 3-5 and/or double-hit lymphoma</li> <li>• Deauville PET score of 4-5 and PR/SD after two cycles of 1L chemoimmunotherapy</li> </ul>	<ul style="list-style-type: none"> <li>• Rapcabtagene autoleucel single IV dose at <math>12.5 \times 10^6</math> CAR+ cells</li> </ul>	<p><b>Primary:</b> CRR (BOR of CR)</p> <p><b>Secondary:</b> ORR, DOR, PFS, EFS, OS, cellular kinetics, and safety</p> <p><b>Exploratory:</b> Immunophenotyping data</p>

## SAFETY

Most common cytopenias  
 38% low grade CRS  
 No grade ≥3 CRS events  
 Median time to onset of CRS  
 10 days  
 8% ICANS, 2% Grade 3  
 Median time to onset 17 days

## Response Rate

	Full analysis set (N = 53)
Median follow-up, months (range)	8.5 (2-24)
ORR (95% CI) <sup>a</sup>	89% (77-96)
BOR	
CR (95% CI) <sup>a</sup>	74% (60-85)
PR <sup>b</sup>	15%

	All patients (N = 53)	Patients with CR at month 3 (N = 29)
Median PFS, <sup>a</sup> months	NR <sup>b</sup>	NR <sup>b</sup>
6-month PFS, <sup>c</sup> %	76	96

# Beyond CD19: Early Clinical Signals with CD19/CD20 CAR-T Constructs

Trial (NCT)	Phase	N	Method (regimen/duration)	Primary Endpoint	Median Follow-Up	ORR	CR	Median PFS	Key ≥G3 toxicities / safety notes
<b>LYL314 / IMPT-314</b> (NCT05826535)	1/2	45, 31 eval	Dual CD19×CD20 CAR-T; CD62L+ enriched product; single infusion	Safety/ tolerability	9 mos.	<b>94%</b>	<b>74%</b>	NR	CRS 62% (mostly low grade), ICANS ≥G3 13%, infections 13%
<b>KITE-363</b> (NCT04989803)	1	34	Bicistronic CD19/CD20 CAR-T; single infusion	Toxicities and ORR	7.3 mos.	<b>87%</b>	<b>78%</b>	NR	CRS ≥G3 3%, ICANS ≥G3 8%; no grade 4/5 CRS/ICANS
<b>JNJ90014496 / CCAR039</b> (NCT05421663)	1b	42	Bispecific anti-CD19/CD20 CAR-T; RP2D 75M CAR+ cells	Safety/ tolerability	12 mos.	<b>90%</b>	<b>76%</b>	NR	No ≥G3 CRS/ICANS; ≥G3 neutropenia 68%

**Next Wave of Trials – ENROLLING NOW!**

**Phase III RCTs comparing SOC CD19 CARs VERSUS CD19/20 CARs in 2L DBCL**

# Conclusion

## The Path Forward

- Move from *center-based excellence* → *system-wide capability*
- Measure success by **who receives CAR-T**, not just **who can deliver it**
- Align stakeholders—clinicians, payers, industry, and regulators—around **access as a quality metric**
  
- **The future of CAR-T is not just innovation it is implementation, scalability, and access.**
  
- **Relapse should trigger referral because access to CAR-T may be access to cure.**

# Discussion Questions

**80 y/o man with stage IV DLBCL, non-GCB subtype**

**PMH: coronary artery disease, stage 3 chronic kidney disease, atrial fibrillation on anticoagulation**

**R-CHOP as initial therapy with CR for 3 years; relapsed with nodal and extranodal disease**

**Tafasitamab/lenalidomide as second-line treatment with good response for 2 years; now with multifocal progressive disease**

**Would you recommend CAR T-cell therapy, a bispecific antibody or something else at this point? Which specific platform or agent/regimen would you select?**

## Discussion Questions (Questions)

80 y/o man with stage IV DLBCL, non-GCB subtype

PMH: coronary artery disease, stage 3 chronic kidney disease, atrial fibrillation on anticoagulation

R-CHOP as initial therapy with CR for 3 years; relapsed with nodal and extranodal disease

Tafasitamab/lenalidomide as second-line treatment with good response for 2 years; now with multifocal progressive disease

**How does prior use of a CD19-directed approach influence your sequencing of available therapies, and do you conduct CD19 expression testing to assist in decision-making?**

**Would you consider palliative radiation or bridging therapy before instituting CAR-T or a bispecific?**

# Discussion Questions

**65 y/o woman with stage 2 DLBCL**

**R-CHOP as initial therapy; recurrent disease at 13 months**

**Would you offer CAR-T over SCT in this situation? In general, what factors do you consider when making this decision? Has your enthusiasm for SCT waned at all given the effectiveness of CAR-T?**

**What are the advantages and disadvantages of the available CAR-T products? Would you have any preference for one platform versus the others for this patient?**

**53 y/o man with double-hit DLBCL**

**R-EPOCH as initial therapy; recurrent disease at 18 months**

**Although this patient is transplant eligible, is CAR-T a consideration?**

# Discussion Questions

**67 y/o man with DLBCL**

**R-CHOP as initial therapy with rapid relapse**

**Poor performance status and logistics prevented CAR-T**

**GemOx + epcoritamab as second-line treatment**

**The patient would now be eligible for CAR-T — would you offer it if/when he progresses? Is the efficacy of CAR-T diminished after progression on a bispecific-based approach?**

# Agenda

**Module 1:** Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Kamdar

**Module 2:** Bispecific Antibody Therapy for DLBCL — Dr Westin

**Module 3:** CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Abramson

**Module 4:** Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

**Module 5:** Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies — Dr Brody

# **Bispecific Antibody Therapy for DLBCL**

**Jason Westin, MD, MS**

Director, Lymphoma Clinical Research

Section Chief, Aggressive Lymphoma

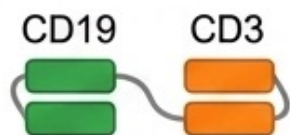
Professor, Department of Lymphoma and Myeloma

The University of Texas MD Anderson Cancer Center

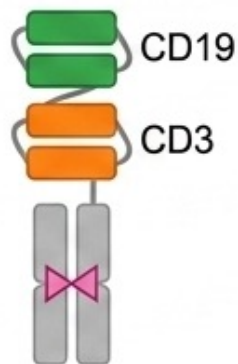
Houston, Texas

# Bispecific CD3/CD20 Antibodies in B-NHL

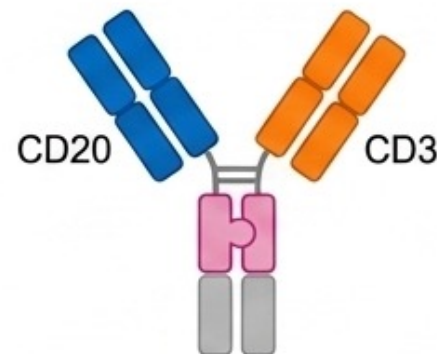
**Blinatumomab**



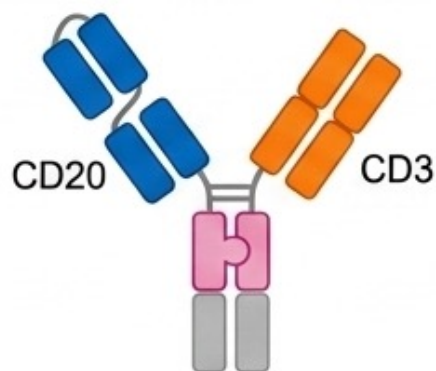
**CD3xCD19 HLE-BiTE**



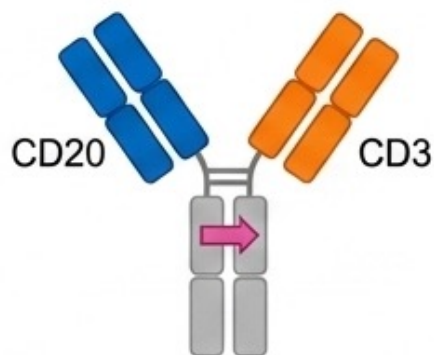
**Mosunetuzumab**



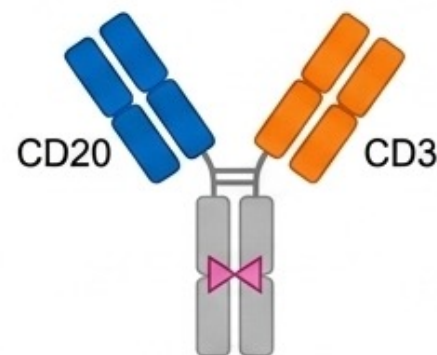
**Glofitamab**



**Odronextamab**



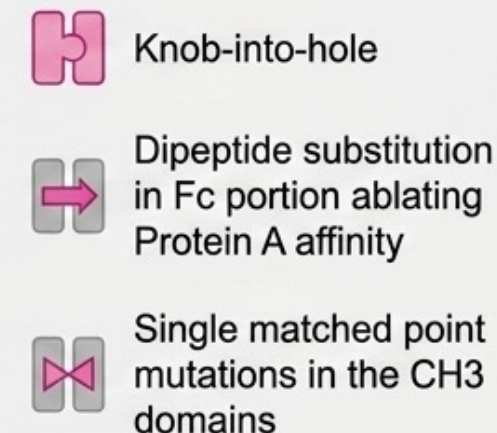
**Epcoritamab**



## Target Domains



## Structural Engineering Markers



Adapted from Lussana et al, J Clin Oncol. 2021 Feb 10;39(5):444-455

\*Design of odronextamab exploits differences in the affinities of the immunoglobulin isotypes for Protein A coupled with the use of common light chain, allowing efficient large-scale purification.

B-NHL, B-cell non-Hodgkin lymphoma; Fc, fragment crystallisable; HLE-BiTE, half-life-extended-bispecific T-cell engager.

# Glofitamab Monotherapy: Efficacy and Safety in Relapsed/Refractory Large B-Cell Lymphoma (LBCL)

Data from a pivotal Phase II study (**NCT03075696**) evaluating fixed-duration glofitamab monotherapy in heavily pretreated patients. **Glofitamab** is a CD20xCD3 bispecific antibody that redirects T cells to eliminate malignant B cells.

## CLINICAL EFFICACY OUTCOMES

### 52% Objective Response Rate (ORR)

Over half of the heavily pretreated patients achieved a clinical response.



### 40% Complete Response Rate (CRR)

Data from a 3-year follow-up confirms high rates of total cancer disappearance.



### 4.9 Months Median Progression-Free Survival (PFS)

Represents the median time patients remained alive without disease progression.



## TOXICITY AND CYTOKINE RELEASE SYNDROME (CRS)



### 63% Overall CRS Incidence

Cytokine Release Syndrome occurred in nearly two-thirds of patients, primarily during early doses.



### 4% Grade 3 or Higher CRS

Severe or life-threatening CRS events were uncommon with step-up dosing and pretreatment.

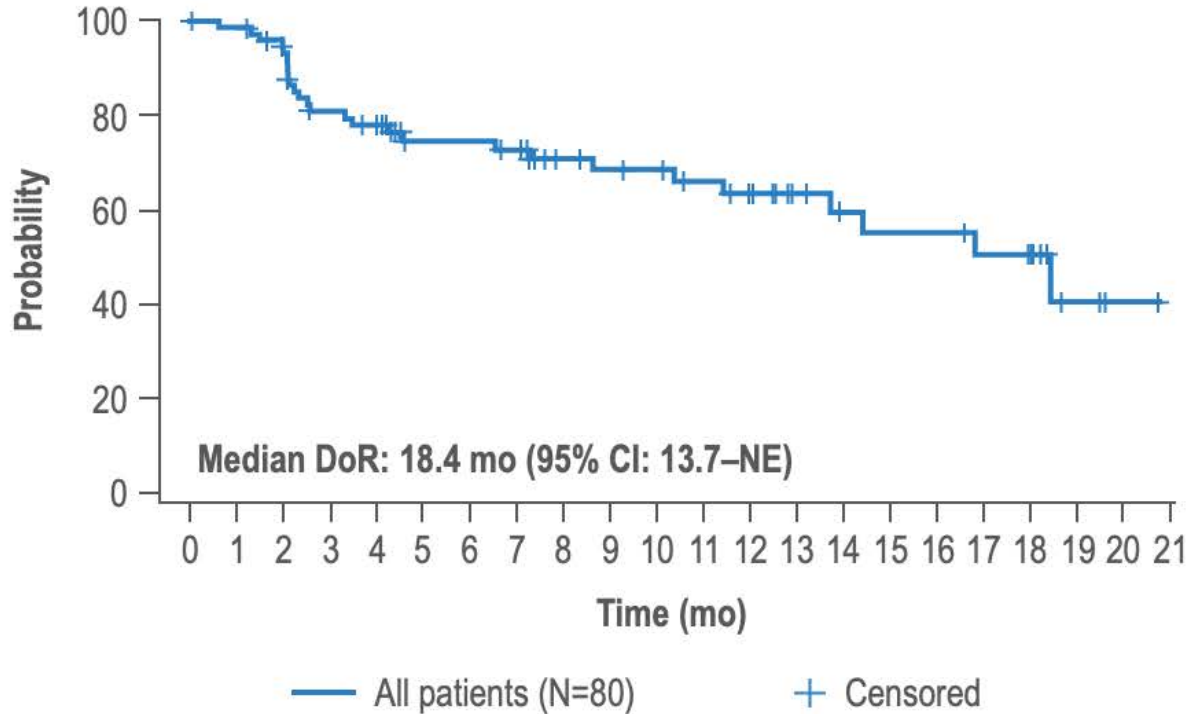


### Predictable Safety Profile

Most CRS events were low-grade (Grade 1-2) and manageable with standard protocols.

# Durable Responses Maintained After Cessation of Therapy

## DoR by IRC



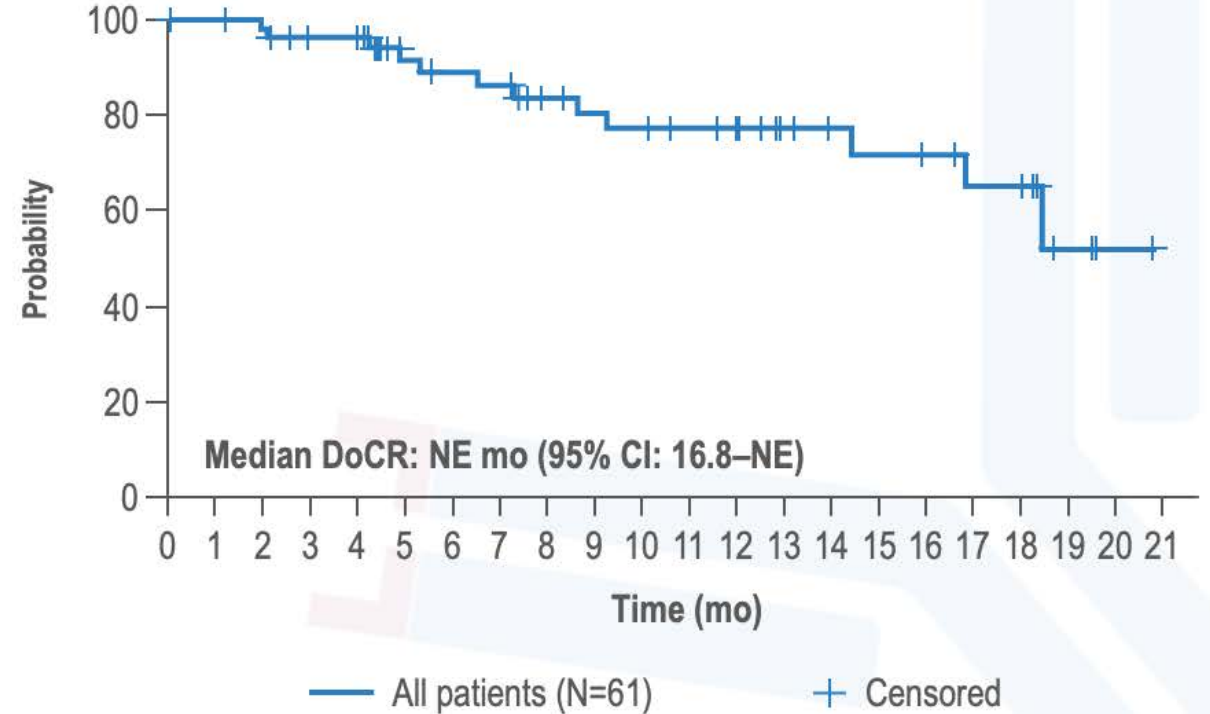
**(N=80)**

Median DoR follow-up, mo (range)      10.6 (0–21)

**12-mo DoR, % (95% CI)**      **63.6 (51.1–76.2)**

ORs ongoing at CCOD, n (%)      53 (66.3)

## DoCR by IRC



**(N=61)**

Median DoCR follow-up, mo (range)      10.6 (0–21)

**12-mo DoCR, % (95% CI)**      **77.6 (64.3–90.8)**

CRs ongoing at CCOD, n (%)      49 (80.3)

# Epcoritamab Monotherapy: Efficacy and Safety in Relapsed/Refractory Large B-Cell Lymphoma (LBCL)

Data from the pivotal Phase I/II EPCORE NHL-1 study (NCT03625037) evaluating subcutaneous epcoritamab monotherapy in heavily pretreated patients. Epcoritamab is a CD3×CD20 bispecific antibody that directs T cells to eliminate malignant B cells.

## CLINICAL EFFICACY OUTCOMES

### 63.1% Overall Response Rate (ORR)

Deep and rapid responses achieved in highly refractory, heavily pretreated patients.



### 38.9% Complete Response Rate (CRR)

Represents the proportion of patients achieving total cancer disappearance.



### 4.4 Months Median Progression-Free Survival (PFS)

Represents the median time patients remained alive without disease progression.



## TOXICITY AND CYTOKINE RELEASE SYNDROME (CRS)



### 49.7% Overall CRS Incidence

Cytokine Release Syndrome occurred in roughly half of patients, primarily low-grade and during early cycle step-up dosing.



### 2.5% Grade 3 or Higher CRS

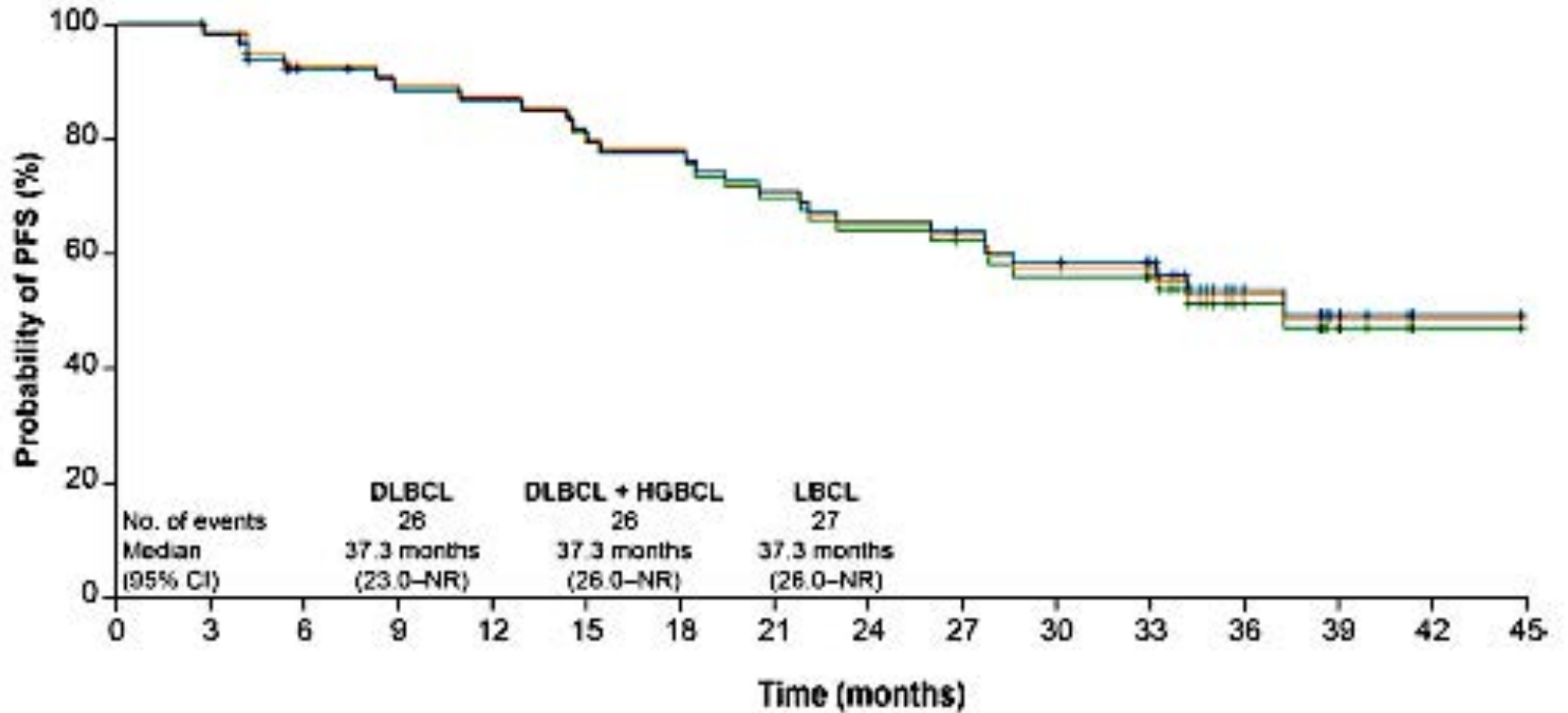
Severe or life-threatening CRS events were uncommon, with no Grade 4 or 5 events reported.



### Predictable Safety Profile

Most adverse events were manageable with standard protocols, allowing patients to remain on treatment.

# Durability of response to Epcoritamab



## Patients at risk

	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
LBCL	65	62	53	50	49	45	44	40	37	35	32	29	13	7	1	0
DLBCL+HGBCL	60	57	50	48	47	43	42	38	35	33	30	27	13	7	1	0
DLBCL	58	55	48	46	45	41	40	36	33	31	28	26	12	7	1	0

# EPCORE DLBCL-1: Epcoritamab Monotherapy vs. Chemoimmunotherapy (CIT)

R/R DLBCL | ASCT-ineligible | ≥1 prior line of therapy (73% had ≥2 prior lines)

1:1 Randomisation (N=483). Epcoritamab vs. CIT (R-GemOx or BR)

## Efficacy Profile (Primary & Secondary Endpoints)

	Epcoritamab	CIT	
Progression-Free Survival (PFS)	30% (24-mo PFS)	13% (24-mo PFS)	<b>HR: 0.74</b> <b>(P=0.0059)</b>
Complete Response Rate (CRR)	38%	26%	<b>Nominal</b> <b>P=0.0032</b>
Duration of Response (DOR)	37 months (Median)	6 months (Median)	
Overall Survival (OS)	38% (24-mo OS)	33% (24-mo OS)	HR 0.96

**Clinical Context:** OS was confounded by COVID-19 mortality and subsequent novel treatments (26% of CIT arm received subsequent CAR-T/bsAb/SCT vs. only 6% in Epcoritamab arm).

**Adjusted OS HR: 0.76** (95% CI, 0.59–0.99).

## Safety Profile

### Immune Effector Toxicities

CRS: **53%** Overall | Grade 3: **3%**

ICANS: **4%** Overall | Grade 3–4: **1%**

### Infections & COVID-19 Impact

67% of patients randomised during the Omicron wave (2022 or later).

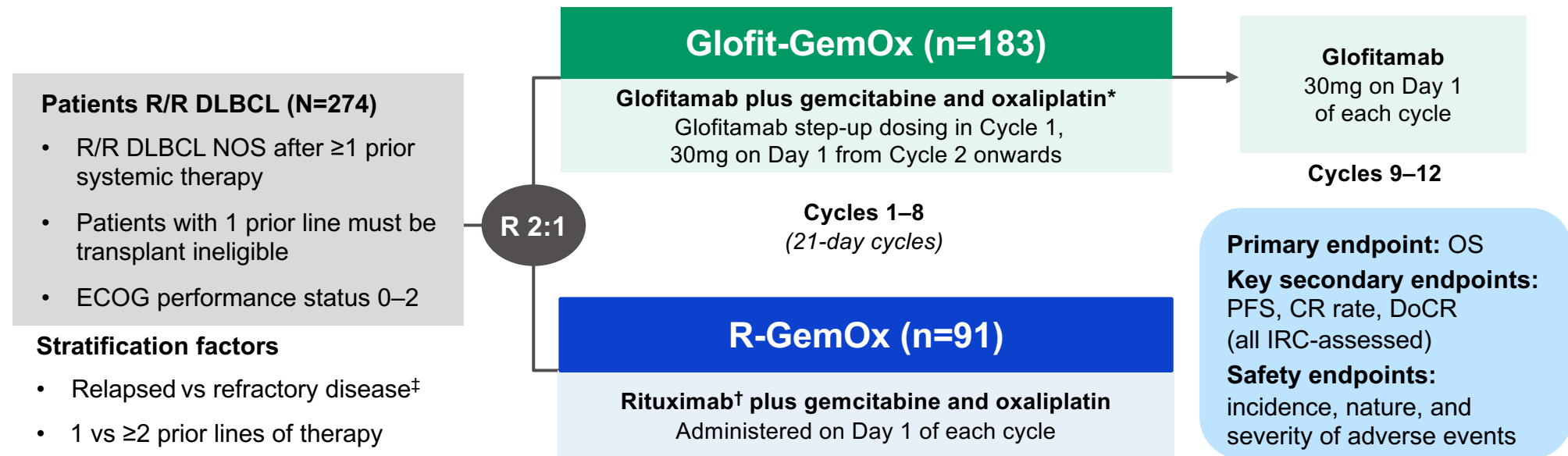
**Grade 3–4 Infections:** 30% (Epcoritamab) vs. 12% (CIT)

**Grade 5 TEAEs:** 17% (Epcoritamab) vs. 6% (CIT)

Largely attributable to Grade 5 COVID-19 mortality (9% Epcoritamab vs. 2% CIT).

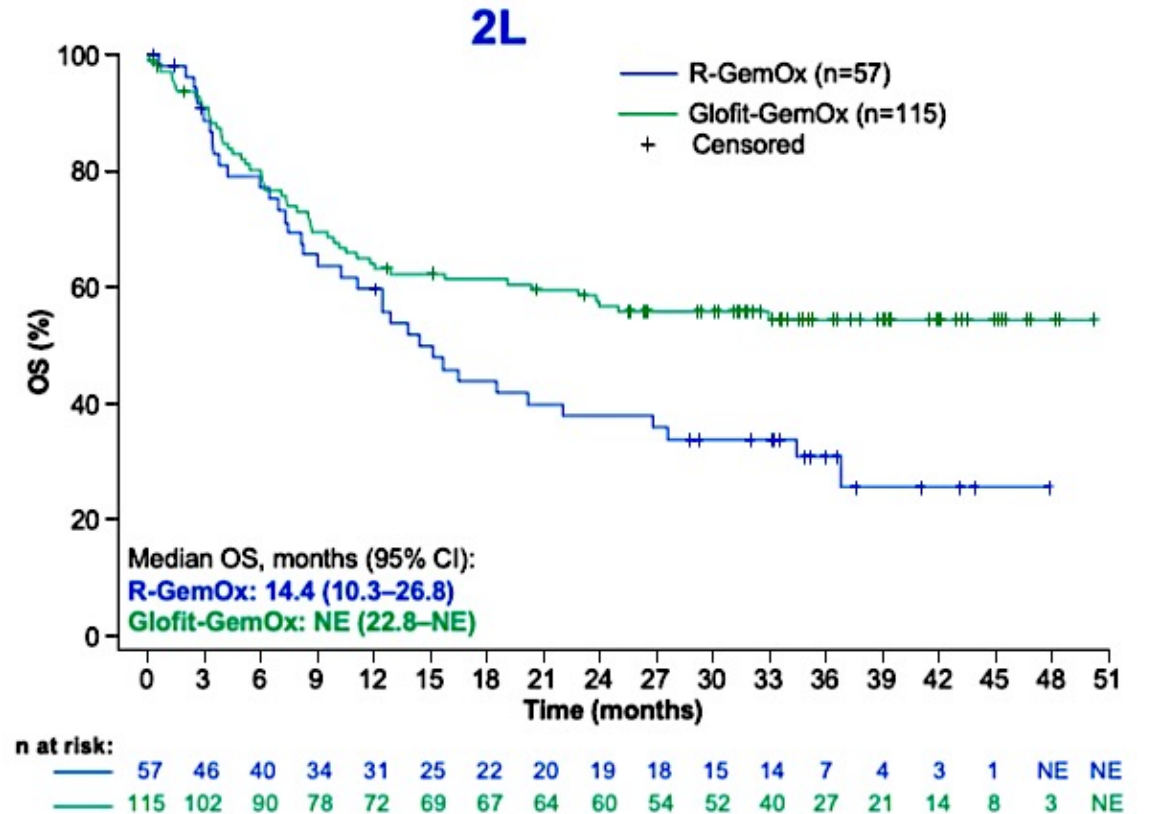
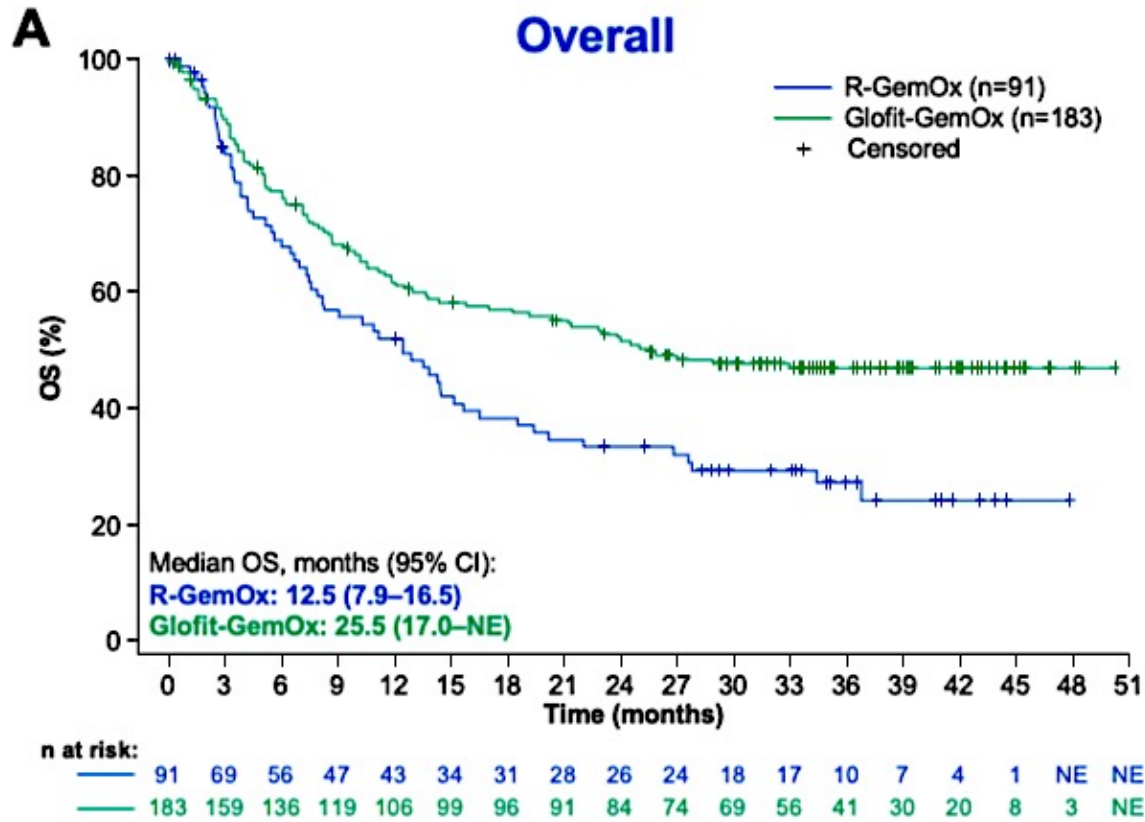
# STARGLO (NCT04408638): A randomized, global, Phase III trial

- Glofit-GemOx has shown clinically meaningful and statistically significant benefits in OS, PFS, and CR rate compared with R-GemOx in patients with ASCT-ineligible R/R DLBCL in the STARGLO trial<sup>1</sup>

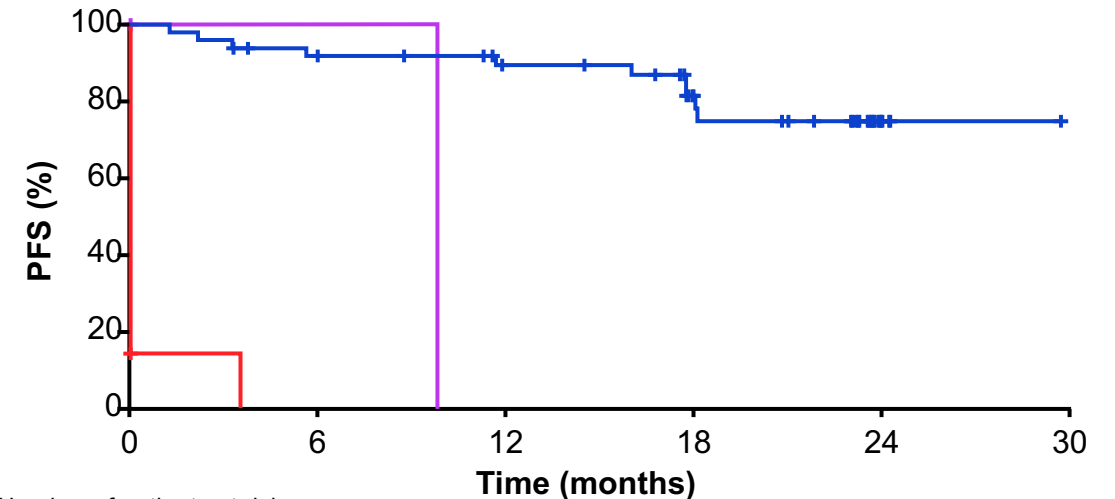
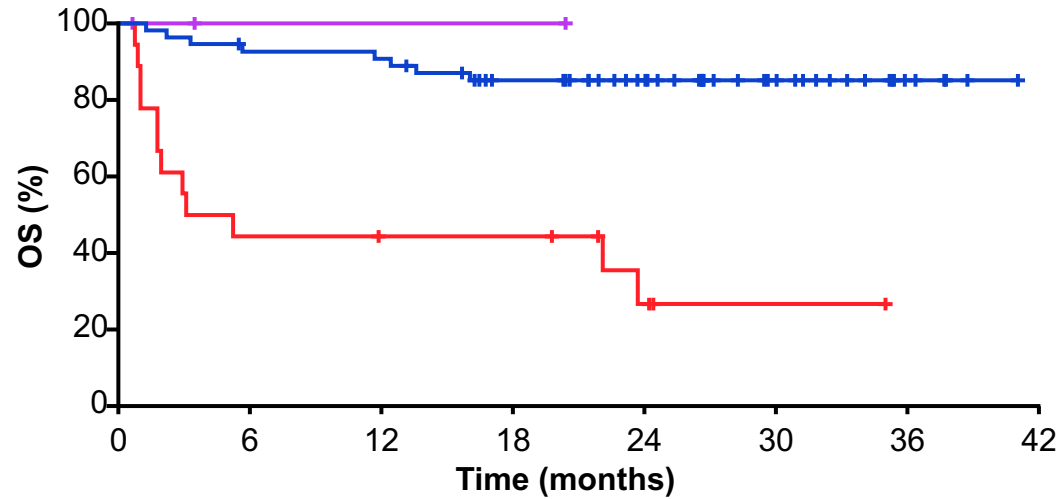


\*Gemcitabine 1000mg/m<sup>2</sup>, oxaliplatin 100mg/m<sup>2</sup>. In Cycle 1, obinutuzumab pretreatment administered on Day 1, GemOx on Day 2, Glofit 2.5mg on Day 8, Glofit 10mg on Day 15; in Cycles 2–8, Glofit 30mg and GemOx administered on Day 1. <sup>†</sup>Rituximab 375mg/m<sup>2</sup>. <sup>‡</sup>Relapsed disease: recurrence after a response that lasted ≥6 months after completion of last line of therapy; refractory disease: disease that did not respond to, or that progressed <6 months after completion of last line of therapy. ASCT, autologous stem cell transplant; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoCR, duration of complete response; ECOG, Eastern Cooperative Oncology Group; IRC, independent review committee; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; R 2:1, randomized in a 2:1 ratio.

# STARGLO OS at 3y



# Landmark analysis by response at EOT in 2L patients treated with Glofit-GemOx



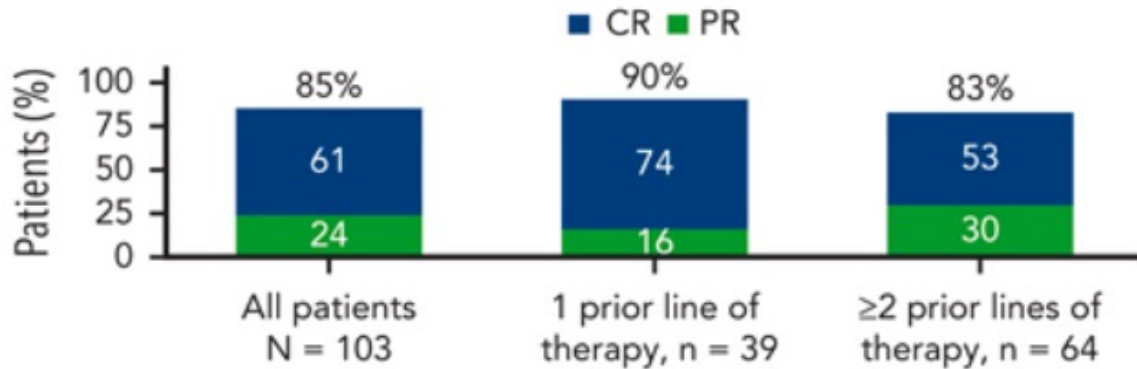
Landmark OS from EOT in 2L patients with CR at EOT		n=55	
Median OS, months (95% CI)		NR (NE)	
24-month OS, % (95% CI)		85.2 (75.7–94.7)	

Landmark PFS from EOT in patients with CR at EOT		n=55	
Median PFS, months (95% CI)		NR (NE)	
24-month PFS, % (95% CI)		74.8 (60.9–88.7)	

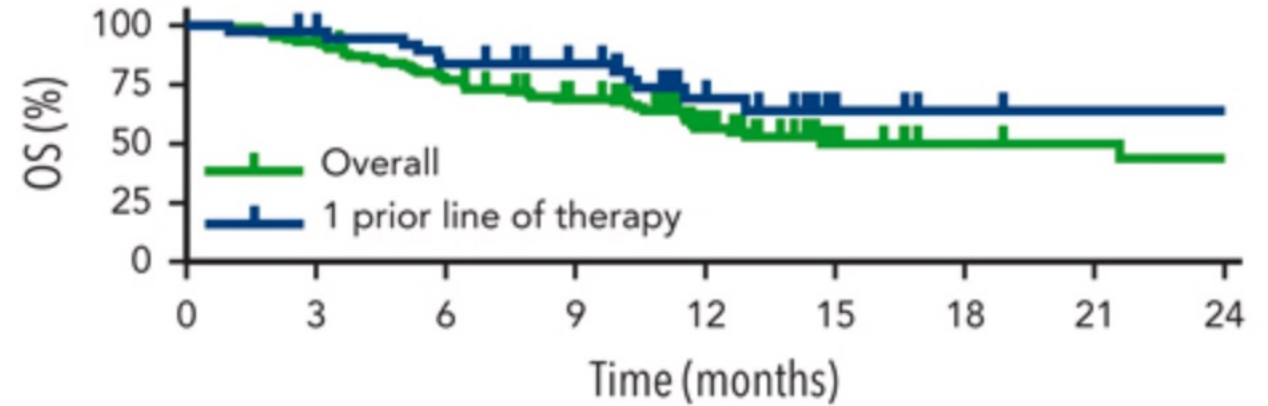
The majority of 2L patients who reached CR at EOT remained alive and progression free 2 years after EOT

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

## Response and Overall Survival



- Median DOCR was 23.6 months



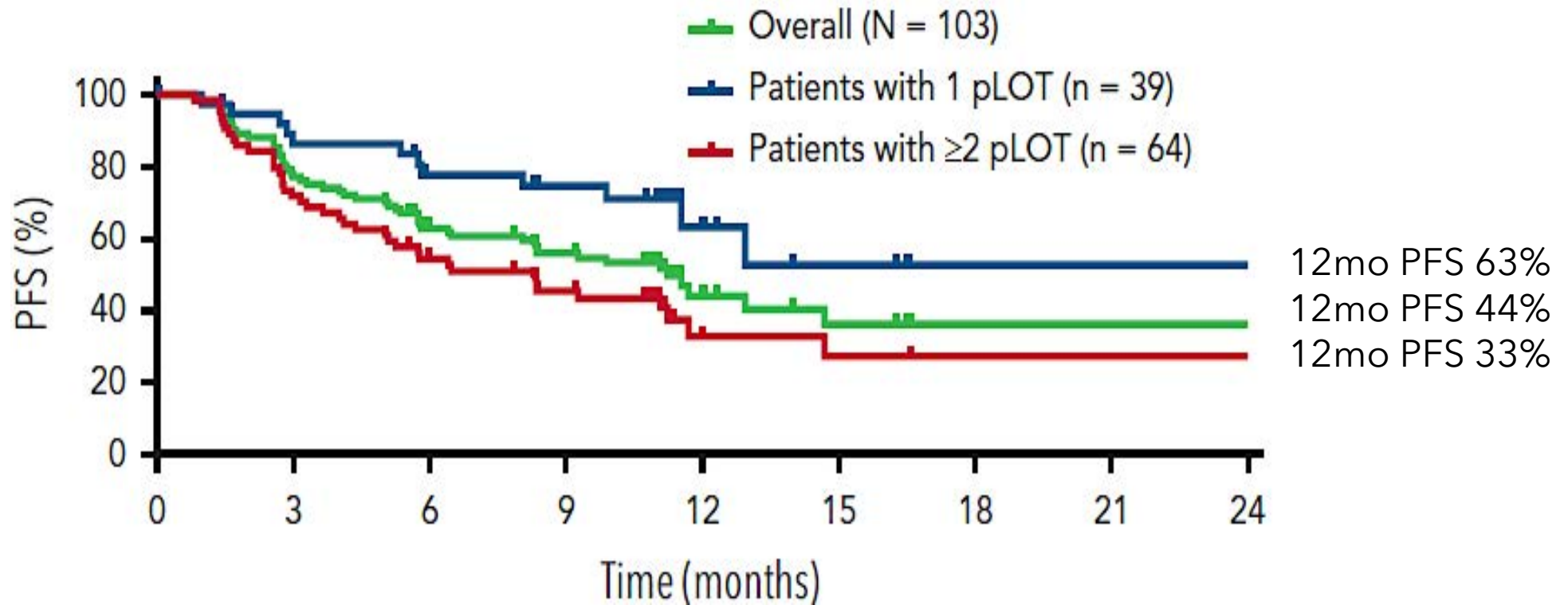
Number at risk

Time (months)	0	3	6	9	12	15	18	21	24
Overall	103	95	77	62	36	15	9	8	7
1 prior line of therapy	39	37	31	27	15	6	3	2	2

- Median OS was 21.6 months overall and not reached in patients with CR
  - 12-month OS estimate in patients with 1 prior line of therapy was 69%

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

## 2<sup>nd</sup> vs later line of therapy significantly affected outcomes



# SUNMO Study design

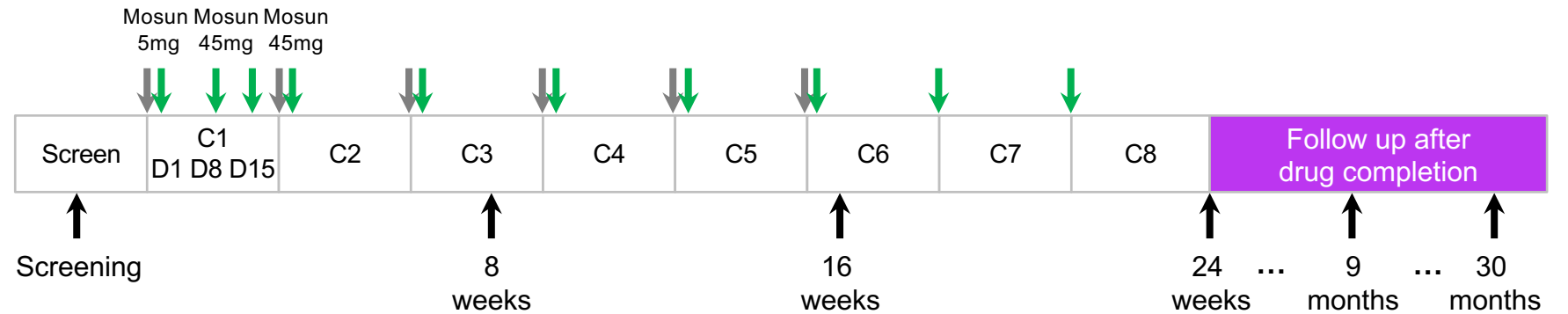
## Key eligibility

R/R LBCL with  
 $\geq 1$  prior therapy and  
 ASCT-ineligible:

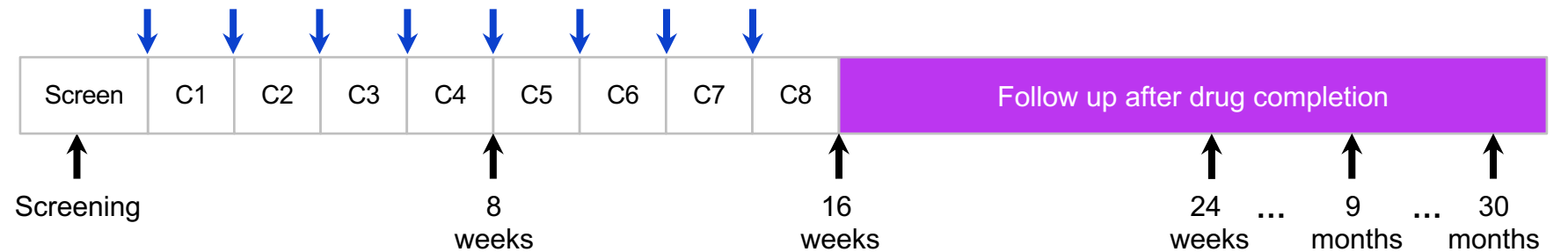
- DLBCL NOS
- Transformed FL
- HGBCL
- Grade 3B FL

2:1

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



**R-GemOx IV (8 x 14–21-day cycles\*)**



## Stratification factors

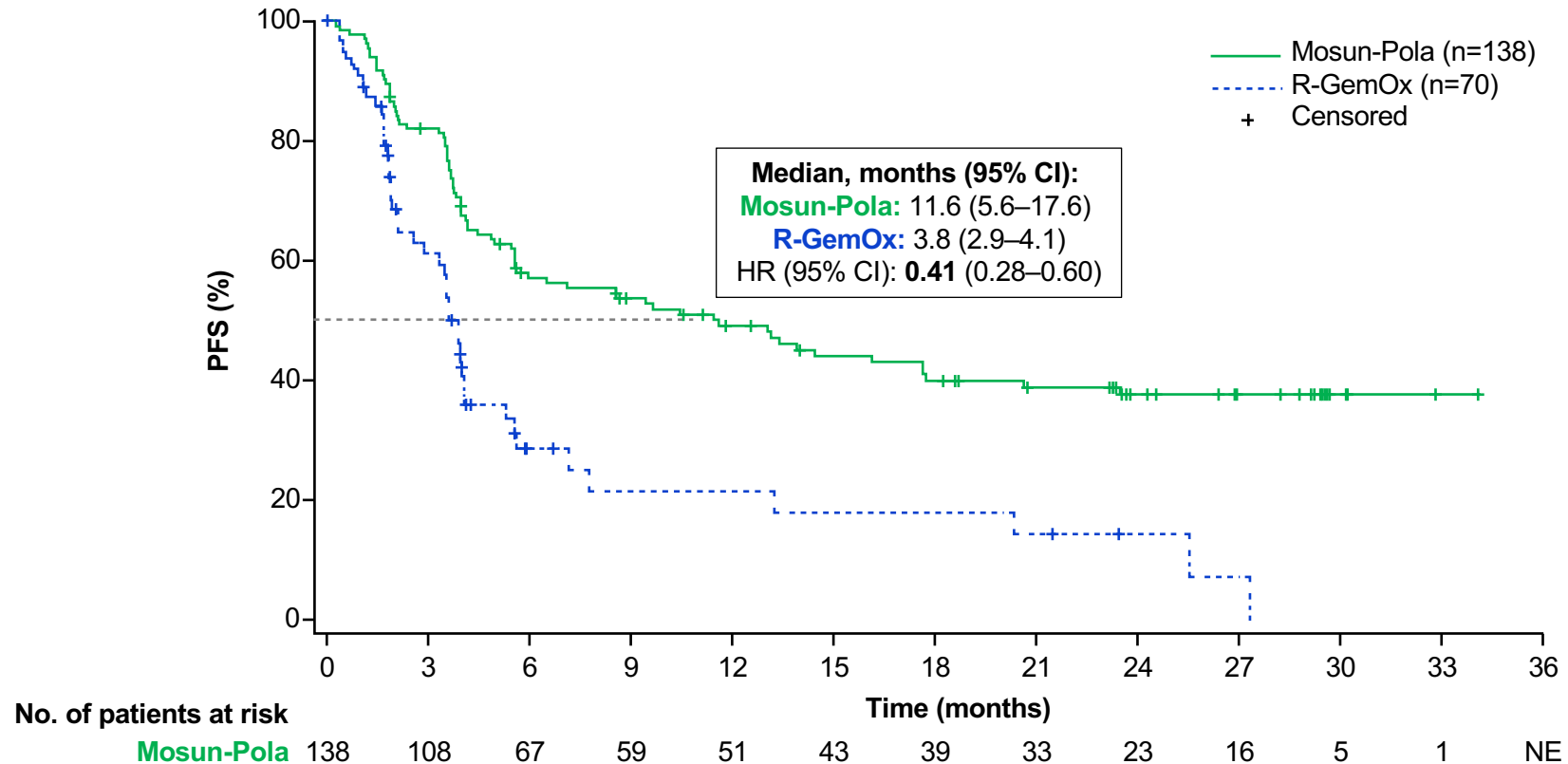
- 1 vs  $\geq 2$  prior lines of systemic therapy
- Relapsed vs refractory disease

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



# Mosun-Pola continued to demonstrate a durable PFS benefit after a median follow-up of 28.3 months

Primary endpoint: PFS by IRC in ITT



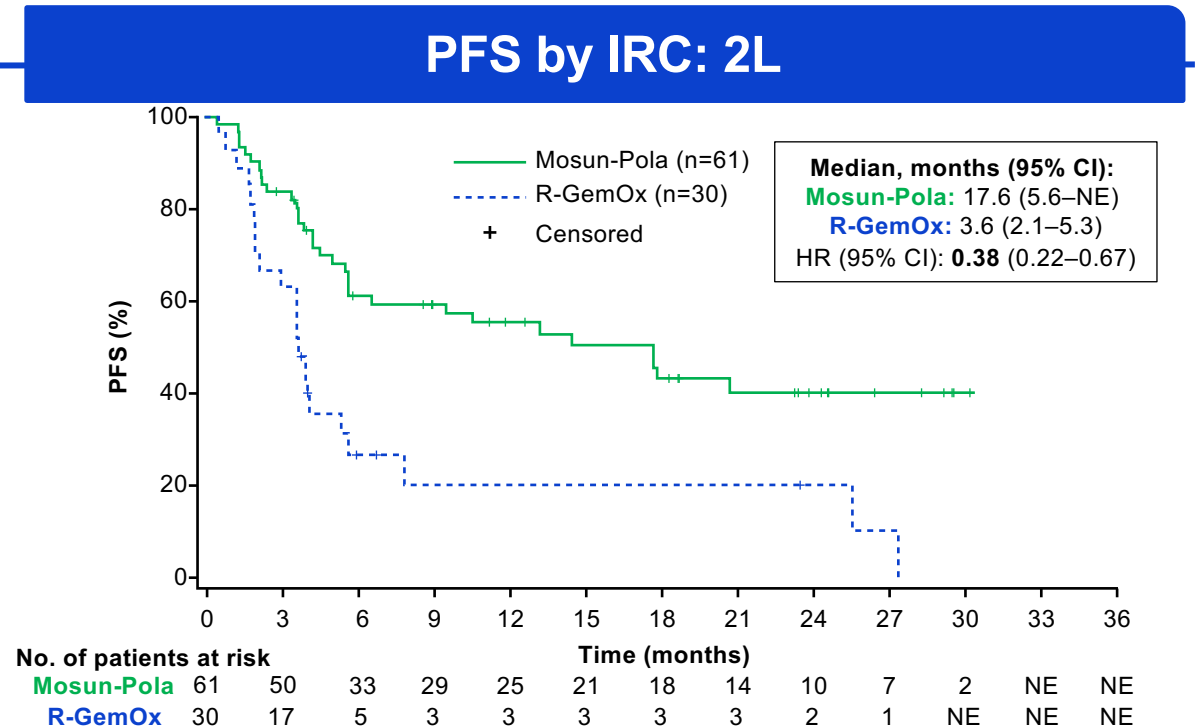
Clinical cut-off date: August 8, 2025.

PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first.

CI, confidence interval; HR, hazard ratio; NALT, new anti-lymphoma therapy; NE, not evaluable.

# Mosun-Pola demonstrated high efficacy in the 2L setting

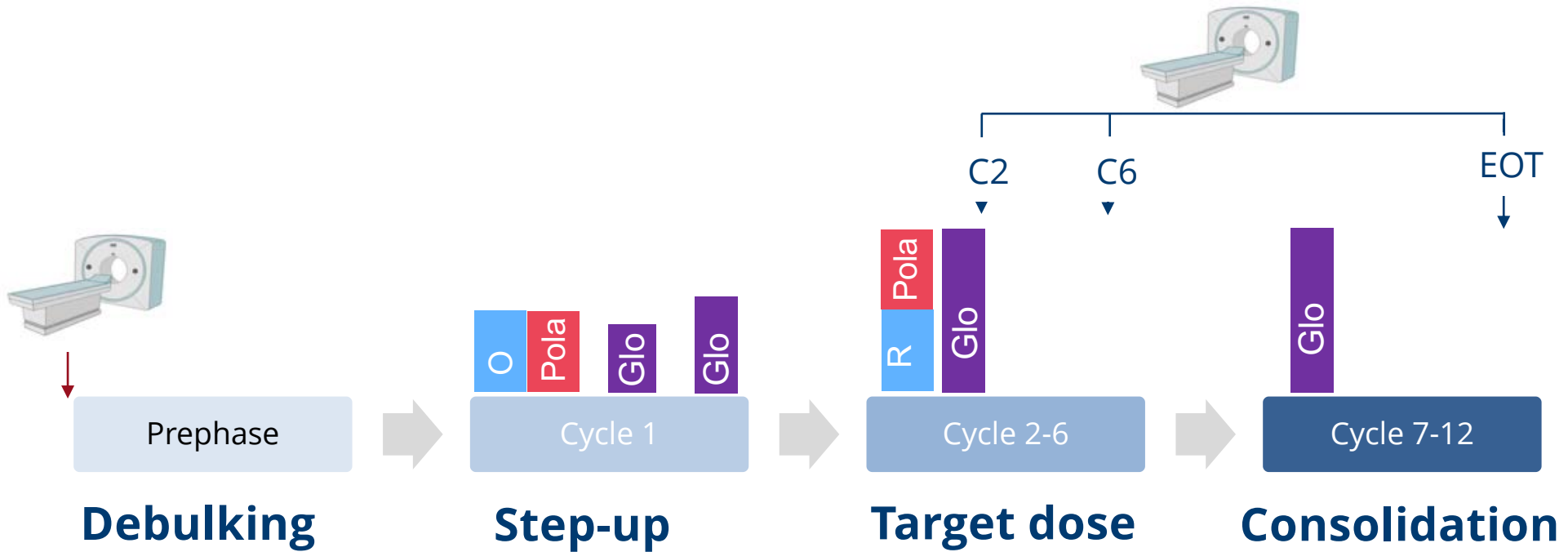
IRC-assessed efficacy % (95% CI), unless otherwise stated	2L Mosun-Pola (n=61)	2L R-GemOx (n=30)
<b>Median PFS, months (95% CI)</b>	17.6 (5.6–NE)	3.6 (2.1–5.3)
<b>ORR</b>	75.4 (62.7–85.5)	36.7 (19.9–56.1)
<b>CR</b>	60.7 (47.3–72.9)	20.0 (7.7–38.6)
<b>Median DOR, months (95% CI)</b>	18.8 (11.3–NE)	6.0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



- A PFS HR of 0.38 was demonstrated in the 2L population
  - The 2-year PFS rate was doubled with Mosun-Pola versus R-GemOx: 40.3% vs 20.1%
  - Median DOCR was not reached with Mosun-Pola

Clinical cut-off date: August 8, 2025.

# R-Pola-Glo – Study Design



## Indication

- **Untreated** patients >60 yo with LBCL
- Non-eligible for full dose R-CHOP

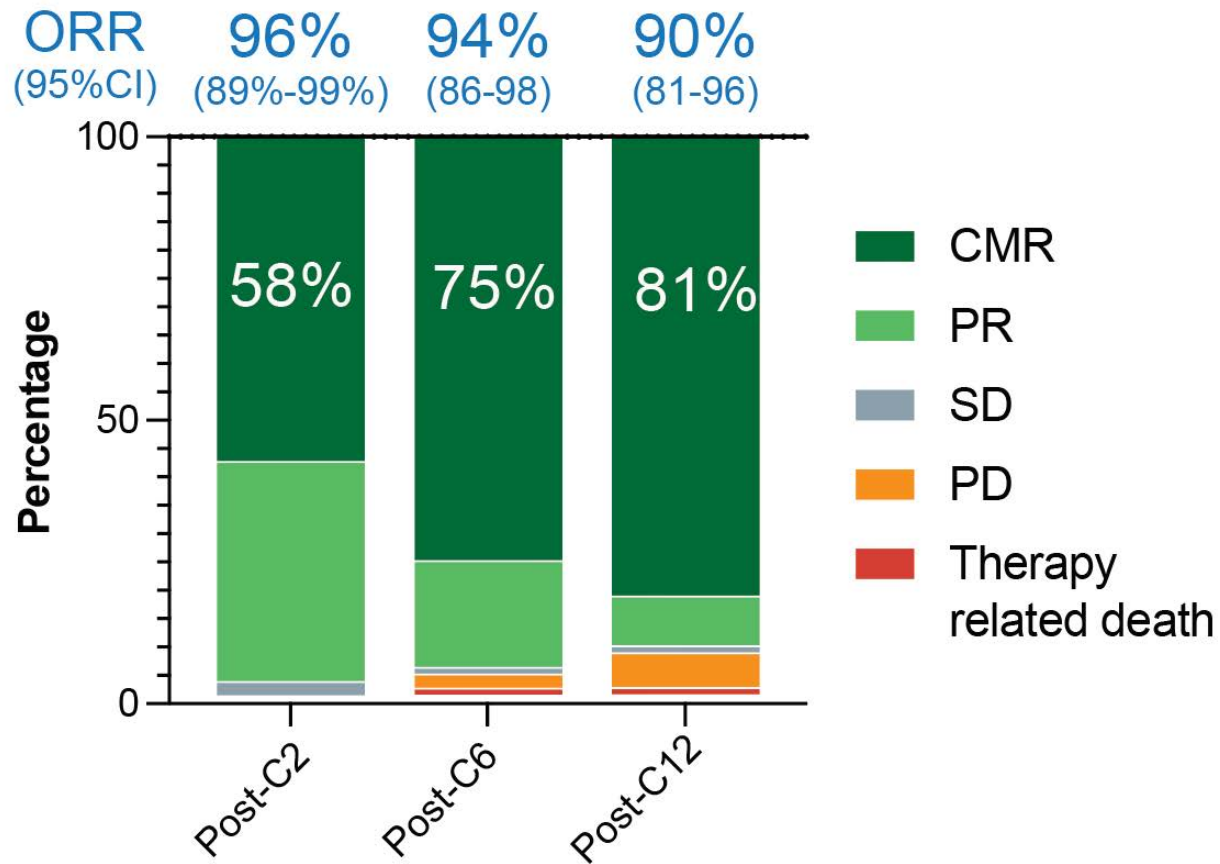
## Study Design

- One-arm, multicenter phase II
- 30 centers in Germany and Austria
- **80 pts** (C1-6 mandatory inpatient)
- Mandatory prophylaxis

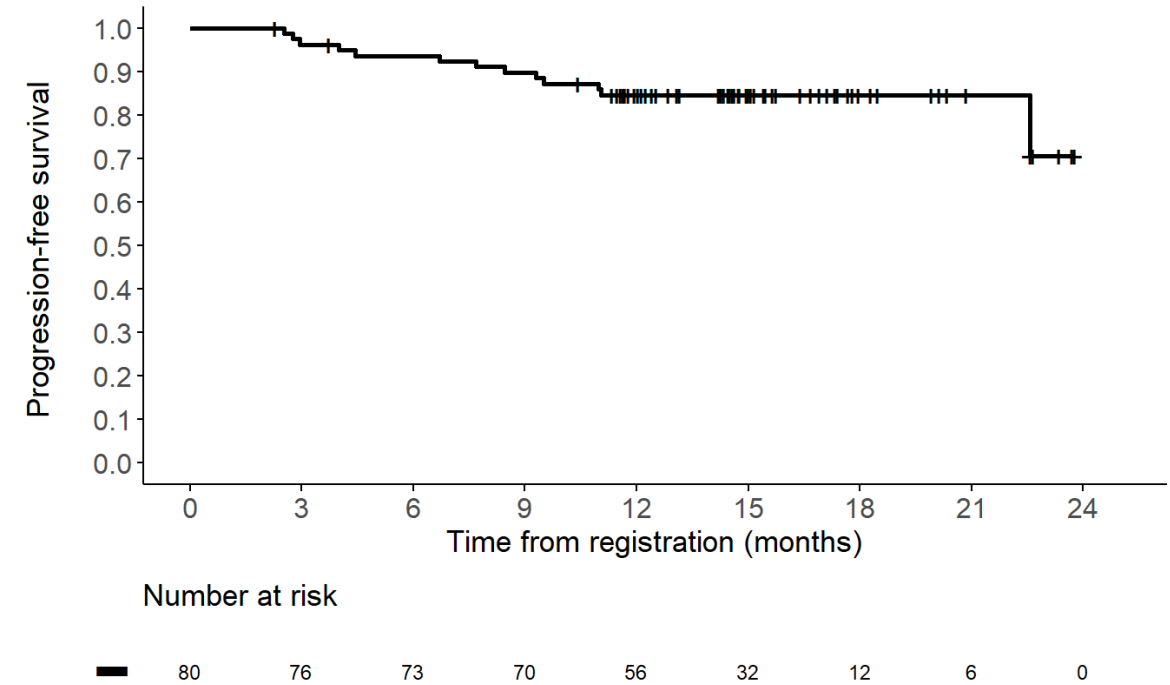
## Endpoints

- **Primary: 1y-PFS rate**
- **Secondary:**
  - Efficacy (OS, EFS)
  - Feasibility/Toxicity

# R-Pola-Glo – Outcome



## 1-year Progression-free Survival (PFS)



# NCCN Suggested Treatment Regimens

<b>SECOND-LINE THERAPY<sup>e,j,k</sup></b> (relapsed disease >12 mo)	
Intention to Proceed to Transplant	No Intention to Proceed to Transplant
<p><b>Preferred (in alphabetical order)</b></p> <ul style="list-style-type: none"> <li>• DHA + platinum (Carboplatin, Cisplatin, or Oxaliplatin) ± Rituximab</li> <li>• GDP ± Rituximab</li> <li>• ICE ± Rituximab</li> </ul> <p><b>Other recommended (in alphabetical order)</b></p> <ul style="list-style-type: none"> <li>• ESHAP ± Rituximab</li> <li>• GEMOX ± Rituximab</li> </ul>	<p><b>Preferred (in alphabetical order by category)</b></p> <ul style="list-style-type: none"> <li>• CAR T-cell therapy (CD19-directed)<sup>l</sup> (with pre/postpheresis therapy as needed; <a href="#">BCEL-C 2 of 7</a>) (if eligible)               <ul style="list-style-type: none"> <li>▶ Lisocabtagene maraleucel</li> </ul> </li> <li>• GEMOX + Epcoritamab-bysp<sup>n,o</sup></li> <li>• GEMOX + Glofitamab-gxbm<sup>n,o</sup></li> <li>• GEMOX<sup>n</sup> + Polatuzumab vedotin-piiq + Rituximab</li> <li>• Lenalidomide + Tafasitamab-cxix<sup>p</sup></li> <li>• Polatuzumab vedotin-piiq ± Bendamustine<sup>m</sup> ± Rituximab</li> <li>• Mosunetuzumab-axgb (IV or SC)<sup>n,o,q</sup> + Polatuzumab vedotin-piiq</li> <li>• Glofitamab-gxbm<sup>n,o</sup> + Polatuzumab vedotin-piiq (category 2B)</li> </ul> <p><b>Other recommended (in alphabetical order)</b></p> <ul style="list-style-type: none"> <li>• CEOP ± Rituximab</li> <li>• GDP ± Rituximab</li> <li>• GEMOX ± Rituximab (if unable to receive epcoritamab-bysp, glofitamab-gxbm, or polatuzumab vedotin-piiq)</li> <li>• Rituximab</li> </ul> <p><b>Useful in certain circumstances</b></p> <ul style="list-style-type: none"> <li>• Brentuximab vedotin</li> <li>• Ibrutinib<sup>n</sup> (non-GCB DLBCL)</li> <li>• Lenalidomide ± Rituximab (non-GCB DLBCL)</li> </ul>

# Epcor-R-mini CVP: Study Design



Biopsy ↑

Blood ↑

↑↑↑↑

↑↑↑↑

↑

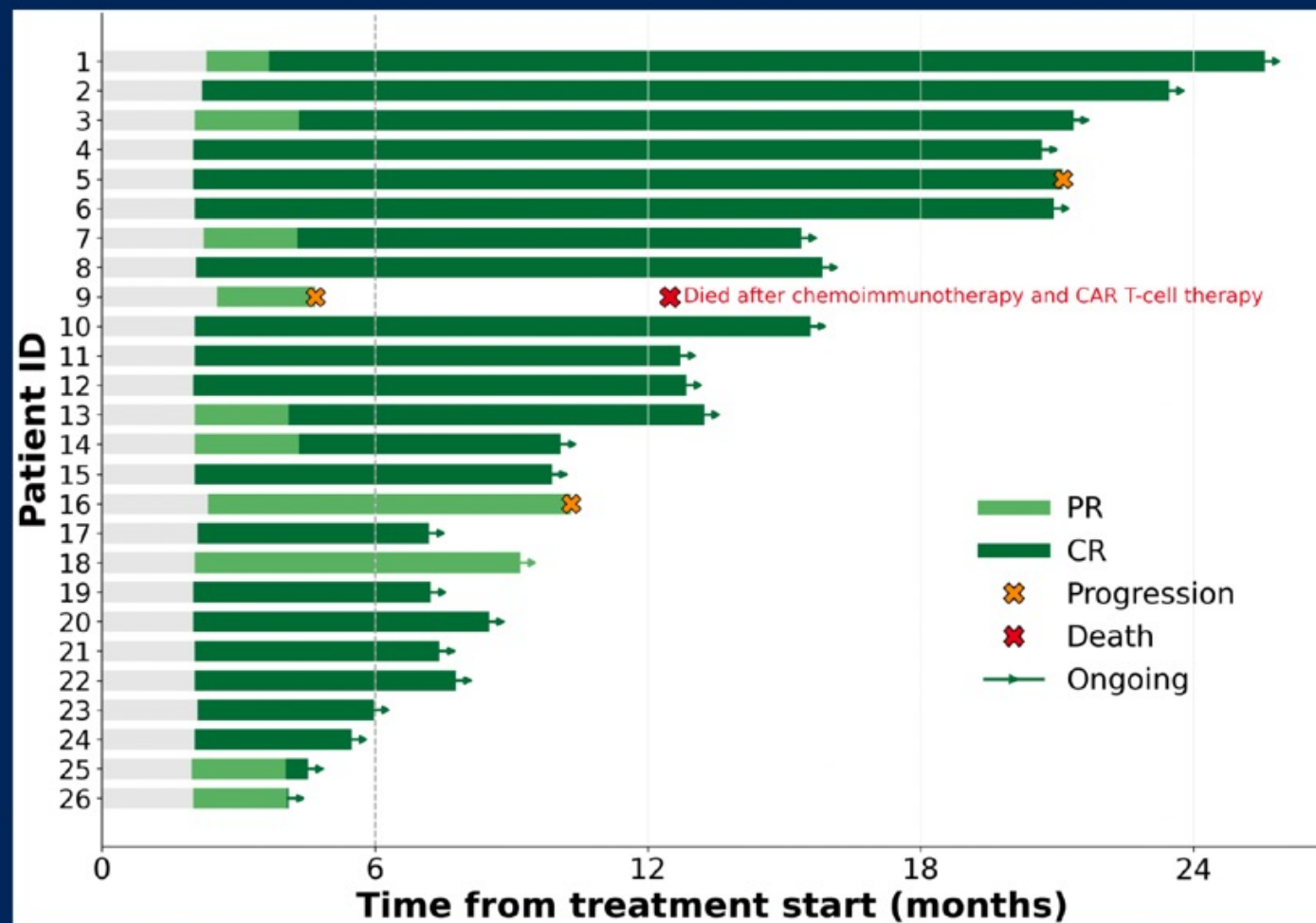
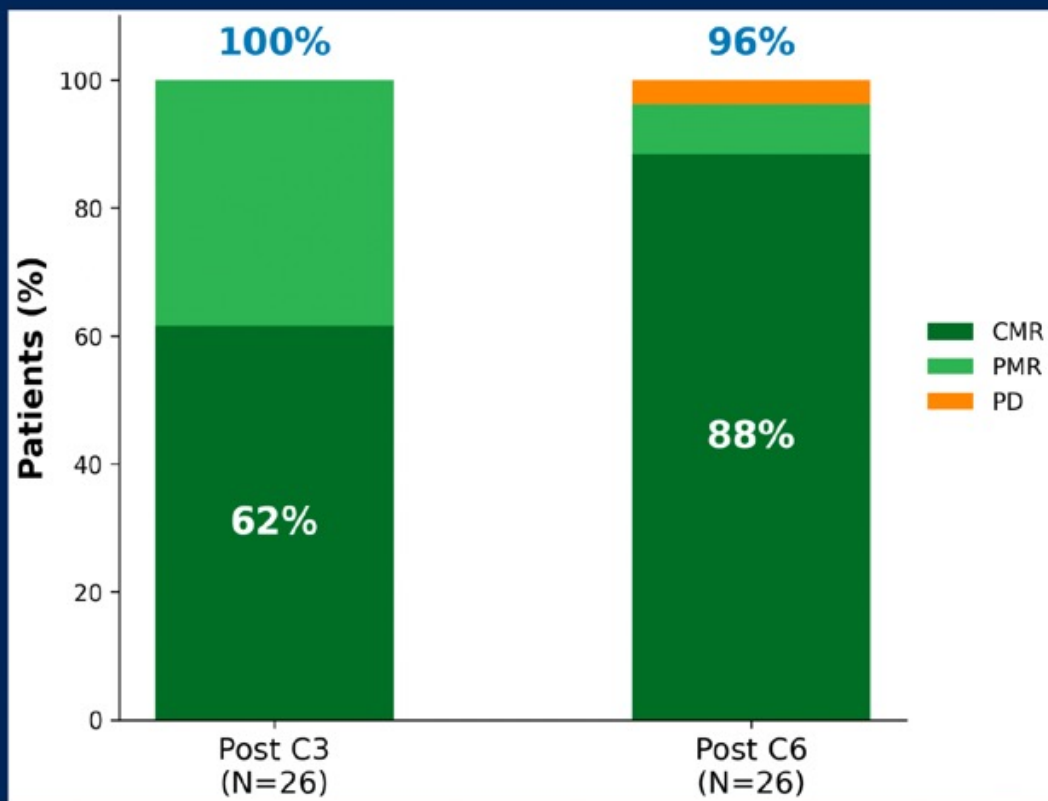
↑

- Epcoritamab maintenance for those who are in PR after C6

## Mini CVP

Cyclophosphamide: 400mg/m<sup>2</sup>  
Vincristine: 1mg  
Prednisone: 40mg/m<sup>2</sup>

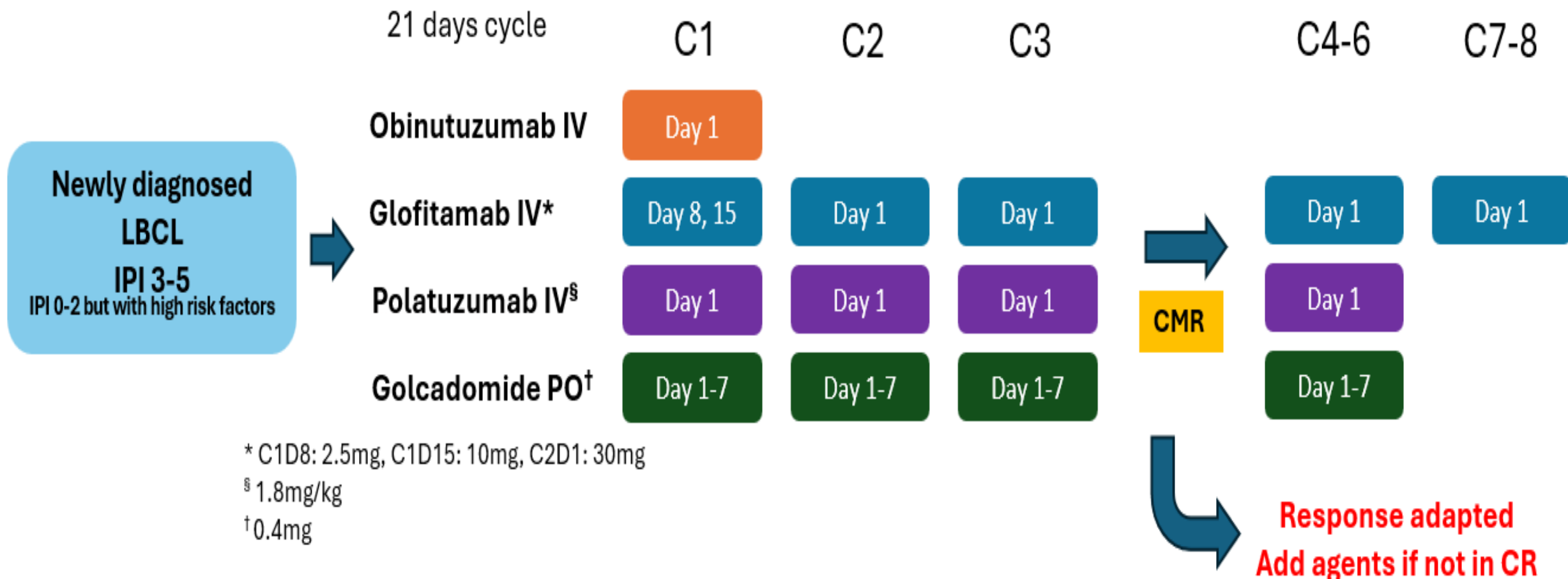
# Epco-R-mini CVP: Response



## Select Ongoing Phase III Trials of Bispecific Antibody Combination Regimens in LBCL

Trial Identifier	Setting	Treatment Arms	Primary Endpoint
SKYGLO (NCT06047080)	Newly Diagnosed	<ul style="list-style-type: none"> <li>Glofitamab + Pola-R-CHP</li> <li>Pola-R-CHP</li> </ul>	PFS
EPCORE-DLBCL-2 (NCT05578976)	Newly Diagnosed	<ul style="list-style-type: none"> <li>Epcoritamab + R-CHOP</li> <li>R-CHOP</li> </ul>	PFS with IPI 3-5
Olympia-3 (NCT06091865)	Newly Diagnosed	<ul style="list-style-type: none"> <li>Odronextamab + CHOP</li> <li>R-CHOP</li> </ul>	PFS
EPCORE-DLBCL-4 (NCT06508658)	Relapsed/Refractory	<ul style="list-style-type: none"> <li><u>Arm A</u>: Epcoritamab (subcutaneous) + Lenalidomide</li> <li><u>Arm B</u>: R-GemOx</li> <li><u>Arm C</u>: Epcoritamab (subcutaneous)</li> </ul>	PFS

# Smart 3



# Conclusion:

## Bispecific Antibody Therapy for DLBCL

- Highly effective as single agents in R/R LBCCL
  - Glofit CRR: 40%, EpcO CRR 39%
- Highly effective compared with GemOx
  - Glofit-GemOx improved OS
  - EpcO improved PFS
  - Mosun-Pola improved PFS
- Frontline trials are eagerly anticipated

# Discussion Questions

**58 y/o man with stage IV DLBCL, non-GCB subtype**

**R-CHOP as initial therapy with only partial response followed by progression within 6 months**

**Salvage polatuzumab vedotin/BR with transient response but rapid progression**

**CD19-directed CAR T-cell therapy with initial metabolic complete response on PET imaging**

**Recurrent adenopathy and biopsy-confirmed relapse less than 6 months later**

**How would you treat this patient? How are you thinking about bispecific antibody combinations for DLBCL? Are you prioritizing combinations over monotherapy for most patients?**

# Discussion Questions (Continued)

58 y/o man with stage IV DLBCL, non-GCB subtype

R-CHOP as initial therapy with only partial response followed by progression within 6 months

Salvage polatuzumab vedotin/BR with transient response but rapid progression

CD19-directed CAR T-cell therapy with initial metabolic complete response on PET imaging

Recurrent adenopathy and biopsy-confirmed relapse less than 6 months later

**Would you consider allogeneic stem cell transplantation in a younger, fit patient who achieves a response after bispecific antibody therapy?**

**How do you approach CRS and infection-risk monitoring in heavily pretreated patients receiving sequential immune-engaging therapies?**

# Discussion Questions

**81 y/o woman with stage IV DLBCL, non-GCB subtype**

**The patient is frail with a history of Parkinson's disease**

**R-mini-CHOP as initial therapy with CR but symptomatic relapse at 13 months**

**What treatment would you recommend?**

**Is there an age at which you will no longer consider CAR-T, or is the decision solely based on performance status/patient fitness?**

## Discussion Questions (Continued)

81 y/o woman with stage IV DLBCL, non-GCB subtype

The patient is frail with a history of Parkinson's disease

R-mini-CHOP as initial therapy with CR but symptomatic relapse at 13 months

**For a patient in whom you are going to use bispecific antibody monotherapy, how do you choose between epcoritamab and glofitamab? Do you view them as equivalent options? Are there any advantages or disadvantages to either approach?**

## Discussion Questions

**56 y/o man with DLBCL and bulky right neck LN  
Primary refractory to Pola-R-CHP as initial therapy  
CAR-T as second-line therapy; recurrence in the right neck 6  
months later**

**What treatment would you offer next? Are there any promising  
investigational approaches in this space? Do CD19 bispecifics have  
any potential advantages over those directed at CD20?**

**If you were going to use a bispecific antibody combination, which  
one would you use?**

## Discussion Questions (Continued)

56 y/o man with DLBCL and bulky right neck LN

Primary refractory to Pola-R-CHP as initial therapy

CAR-T as second-line therapy; recurrence in the right neck 6 months later

**For patients who receive polatuzumab as part of induction therapy, will you use it in later lines as part of a bispecific-based combination?**

# Agenda

**Module 1:** Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Kamdar

**Module 2:** Bispecific Antibody Therapy for DLBCL — Dr Westin

**Module 3:** CAR T-Cell Therapy for Other Lymphoma Subtypes —  
Dr Abramson

**Module 4:** Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips

**Module 5:** Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies — Dr Brody

# CAR T-cell Therapy in Other Lymphoma Subtypes (FL, MZL, MCL)

**Jeremy S. Abramson, MD, MMSc**

Professor of Medicine, Harvard Medical School

Director, Center for Lymphoma, Mass General Brigham Cancer Institute



# Follicular and Marginal Zone lymphomas

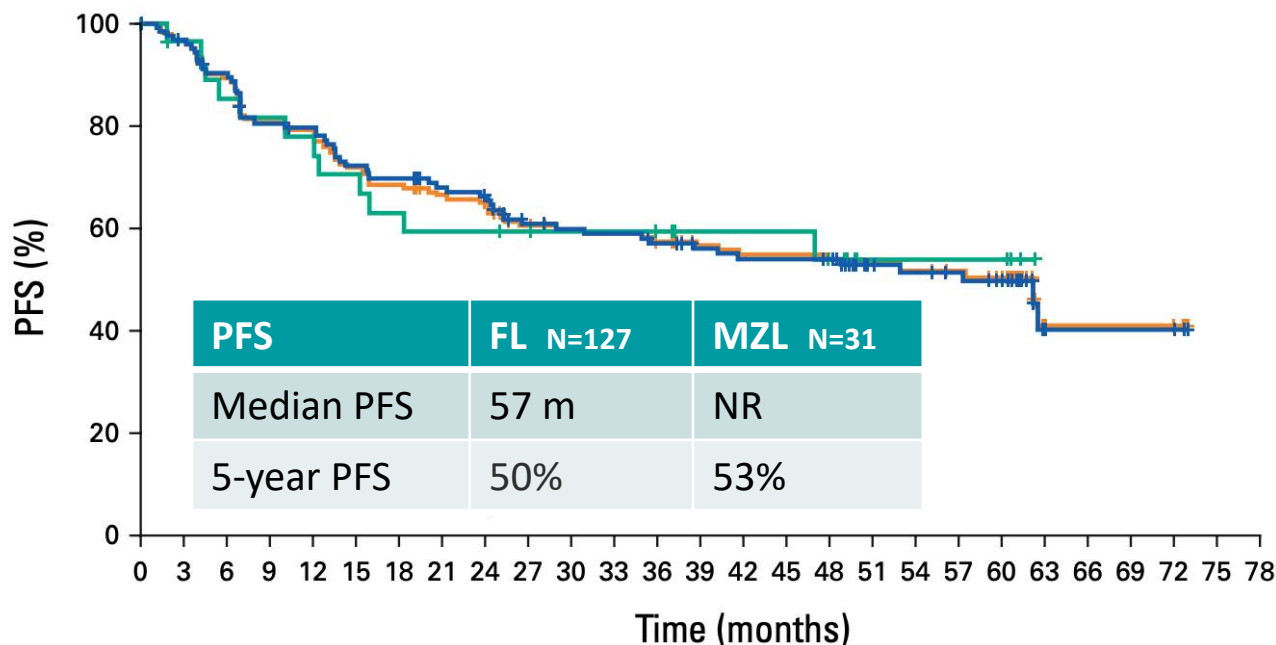


# Three CAR T-cell products for 3<sup>rd</sup> line + follicular lymphoma

	Lisocabtagene Maraleucel TRANSCEND-FL	Tisagenlecleucel ELARA	Axicabtagene Ciloleucel ZUMA-5
n	107	94	124
Median # prior lines	3	4	3
Chemorefractory	67%	78%	68%
POD24	54%	60%	55%
OR rate	97%	86%	94%
CR rate	94%	69%	79%
CRS, any grade %	58	49	82
CRS, severe %	1	0	7
Neurotox, any grade %	15	4	59
Neurotox, severe %	2	1	15
References	Morschhauser, et al. Nature Med 2024 Ahmed, et al. Proc ASH 2025	Fowler, et al. Nat Med 2022. Schuster, et al. Proc ASH 2025	Jacobson, et al. Lancet Onc 2022 Neelapu, et al. JCO 2025

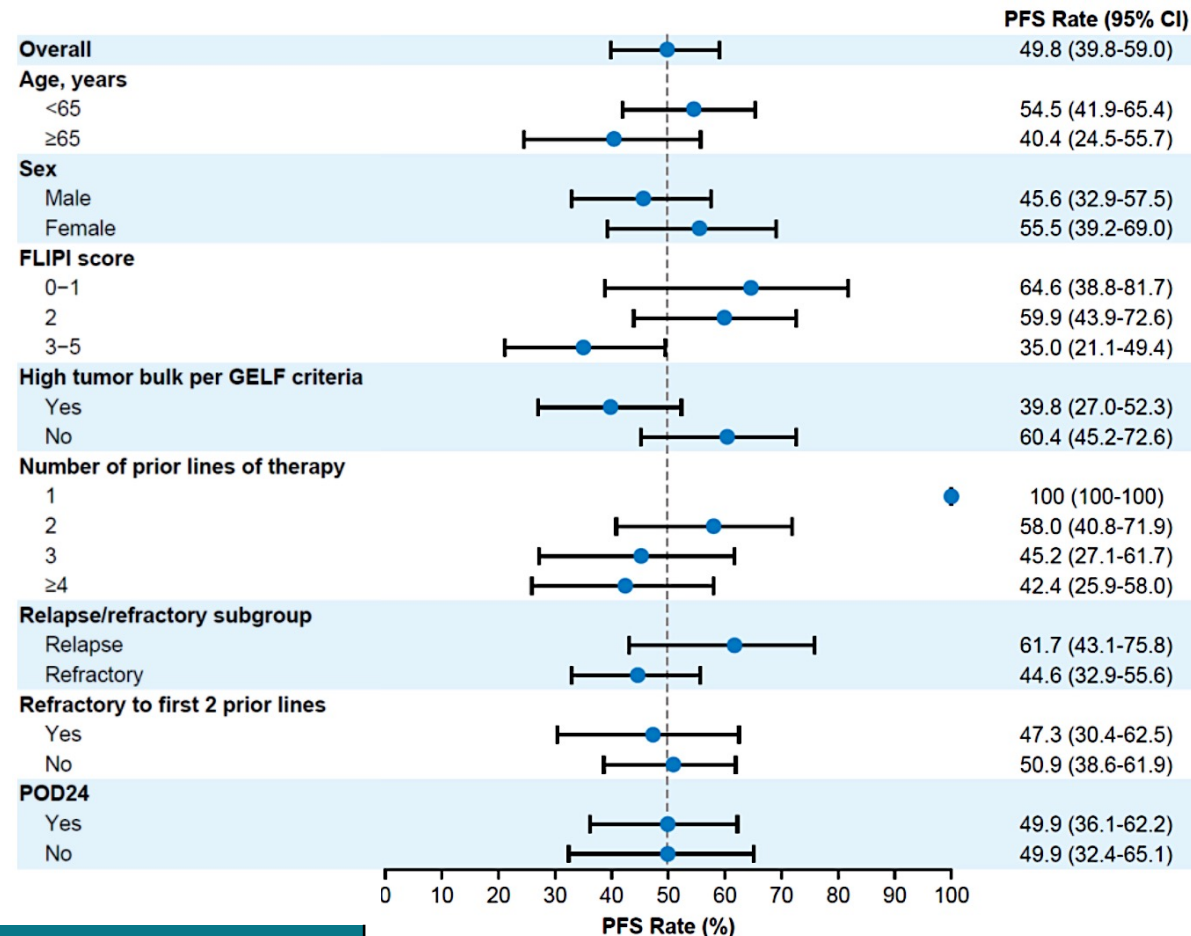


# ZUMA-5: Sustained PFS at 5 years in FL and MZL



**Number at risk:**

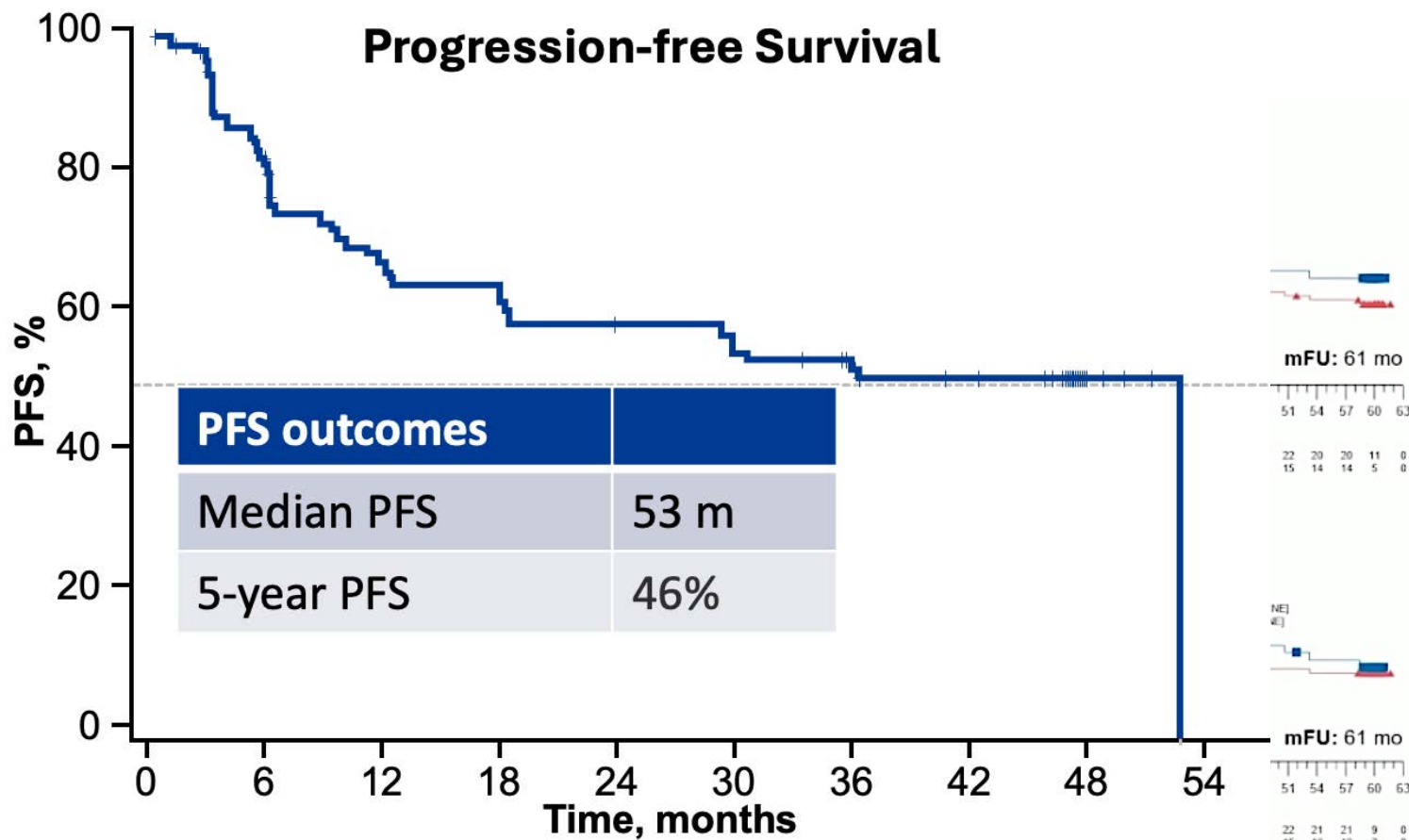
	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78
<b>FL</b>	127	120	111	98	96	87	84	78	75	65	63	62	59	55	53	53	52	36	34	32	29	7	6	6	6	0	
<b>MZL</b>	31	26	23	22	21	19	17	16	16	15	14	14	13	11	11	11	9	4	4	4	4	0					
<b>All patients</b>	159	146	134	120	117	106	101	94	91	80	77	76	72	66	64	64	61	40	38	36	33	7	6	6	6	0	



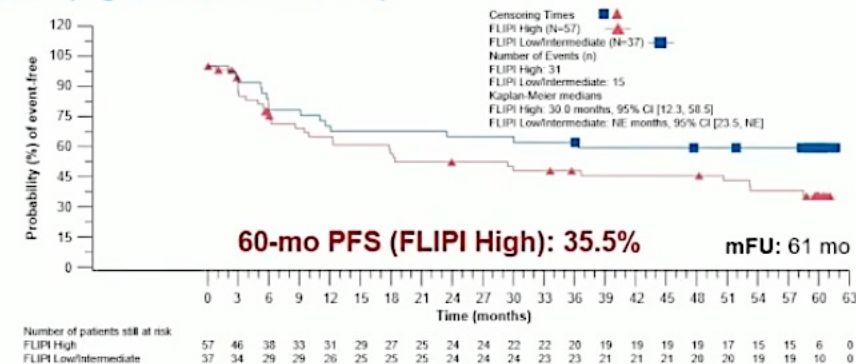
	Prior bendamustine exposure			
	None (n = 39)	≤ 6 mo (n = 8)	6-12 mo (n = 10)	> 12 mo (n = 70)
<b>24-month DOR, %</b>	70	40	56	52
<b>24-month PFS, %</b>	70	25	70	50



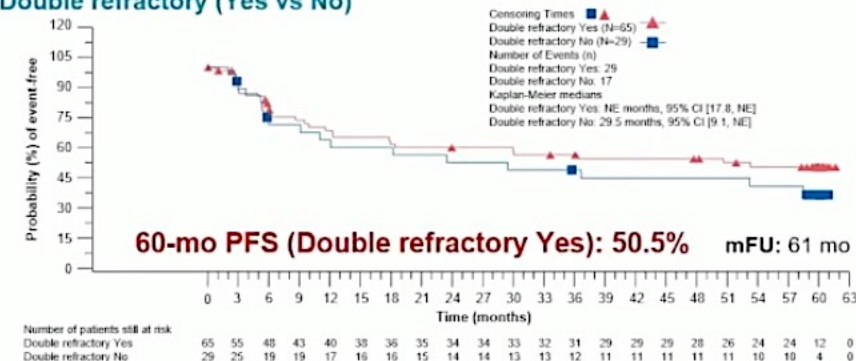
# Long term follow up of Tisa-cel: 5-year results from ELARA



## FLIPI (High vs Low/Intermediate)

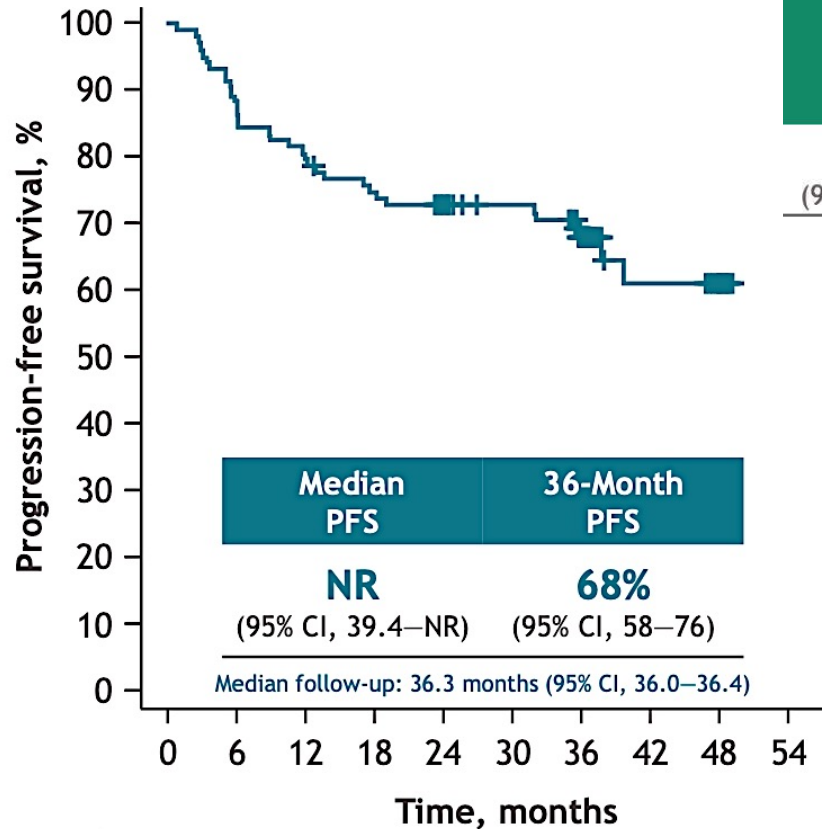


## Double refractory (Yes vs No)



# Long term follow up of TRANSCEND FL: Liso-cel at 3 years

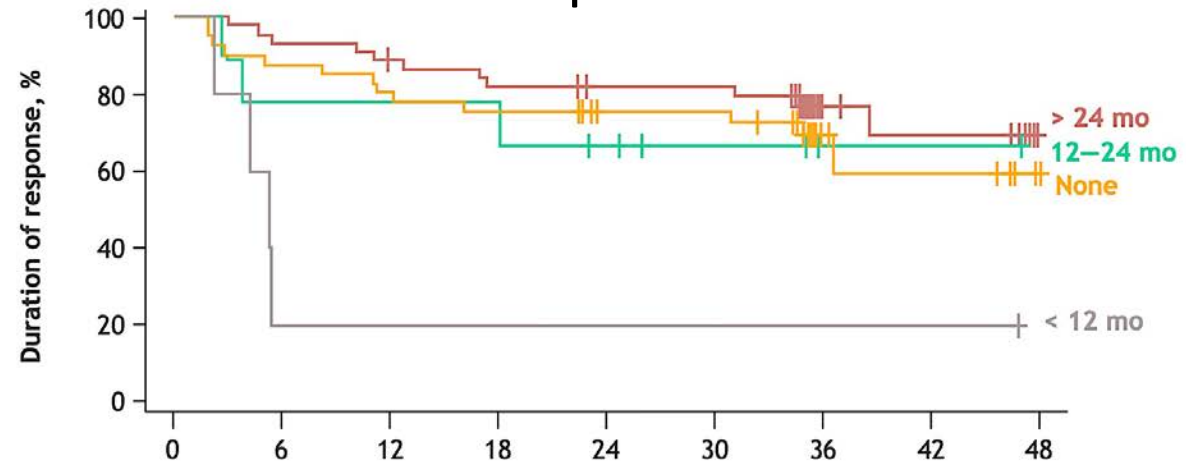
## PFS



## 3-year PFS in high-risk subsets

POD24 (n = 57)	No POD24 (n = 46)	Bulky disease (n = 31)	No bulky disease (n = 72)	Double refractory (n = 67)	Not double refractory (n = 36)
<b>58%</b> (95% CI, 43–70)	<b>80%</b> (95% CI, 65–89)	<b>61%</b> (95% CI, 41–75)	<b>71%</b> (95% CI, 58–80)	<b>60%</b> (95% CI, 47–71)	<b>83%</b> (95% CI, 66–92)

## DOR based on prior bendamustine

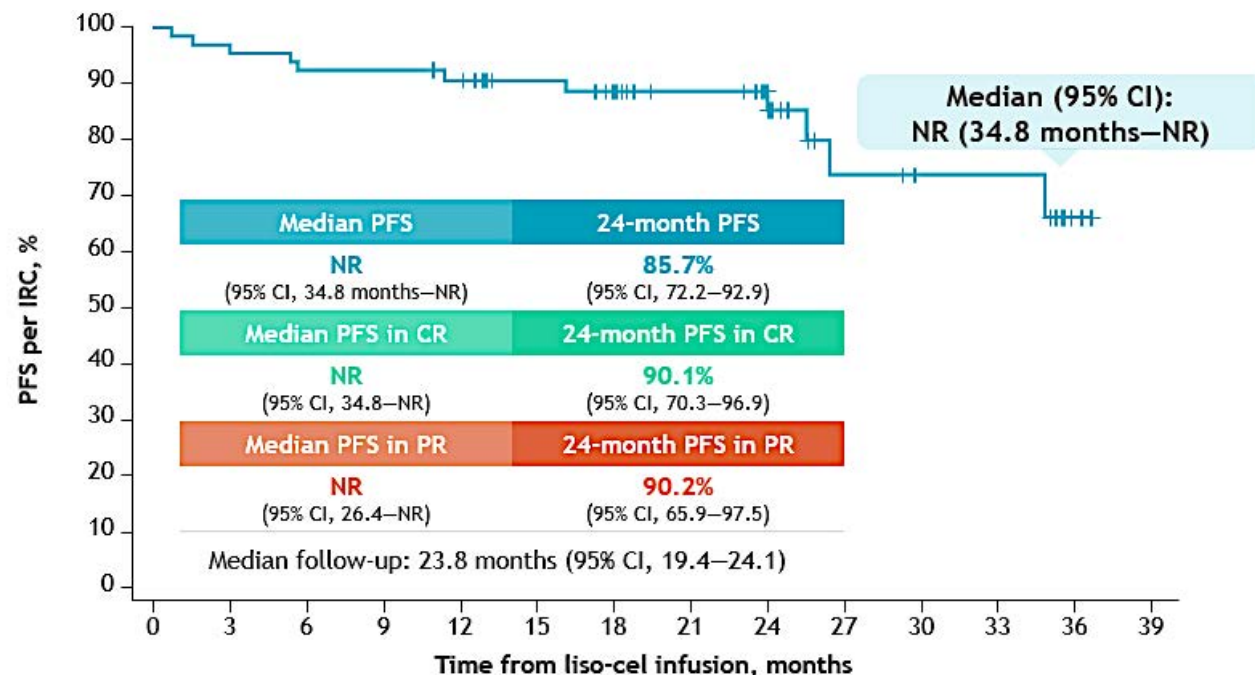
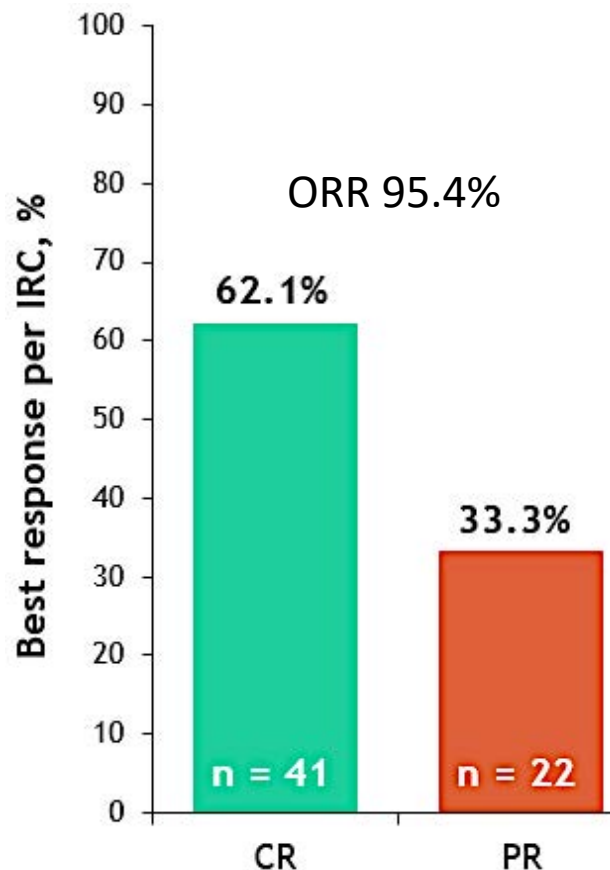


No. at risk	0	6	12	18	24	30	36	42	48
< 12 mo	5	1	1	1	1	1	1	1	0
12–24 mo	9	7	7	7	5	3	1	1	0
> 24 mo	45	42	39	36	34	34	11	9	0
None	41	36	33	31	27	27	9	6	0

No. at risk	0	6	12	18	24	30	36	42	48	54
3L+ FL	103	91	82	76	69	65	44	17	9	0

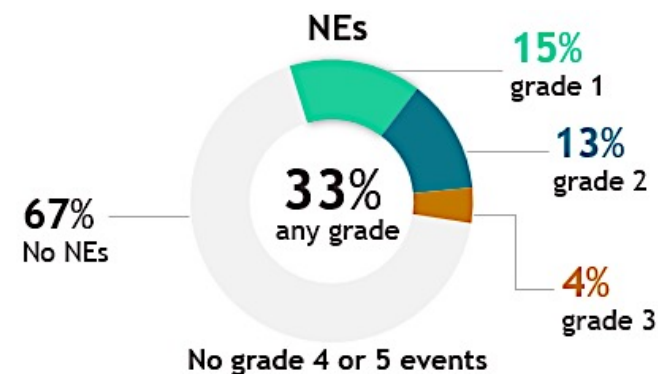
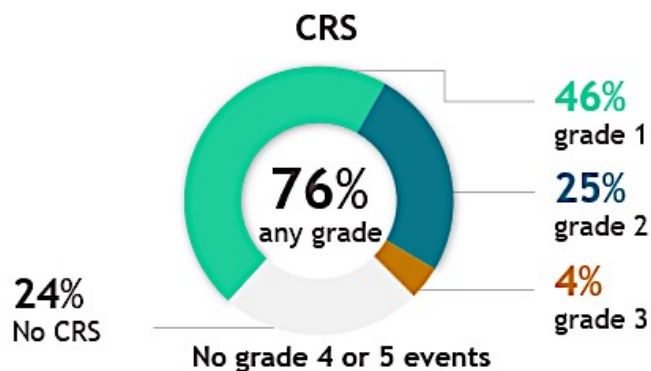


# Sustained efficacy and safety for liso-cel in relapsed/refractory marginal zone lymphomas



No. at risk

3L+ MZL	0	3	6	9	12	15	18	21	24	27	30	33	36	39
3L+ MZL	66	63	61	61	59	51	45	37	23	12	10	10	3	0



# Future directions in FL: randomized trials

## ZUMA-22

Randomized phase III trial of axi-cel vs. SOC in relapsed/refractory follicular lymphoma

- Grade 1-3A FL
- 1 prior line of tx and POD, *or*  $\geq 2$  prior lines
- SOC: investigators choice of R-CHOP, R-Benda, or R-Len
- Primary endpoint PFS

NCT05371093

## LEDA

Randomized phase III trial of tisa-cel vs. SOC in relapsed/refractory follicular lymphoma

- Grade 1-3A FL
- $\geq 2$  prior lines of tx
- SOC: investigators choice of R-CHOP or R-Len
- Primary endpoint PFS

NCT05888493



# Mantle cell lymphoma



# Brexu-cel for 3L+ MCL post cBTK inhibition: ZUMA-2

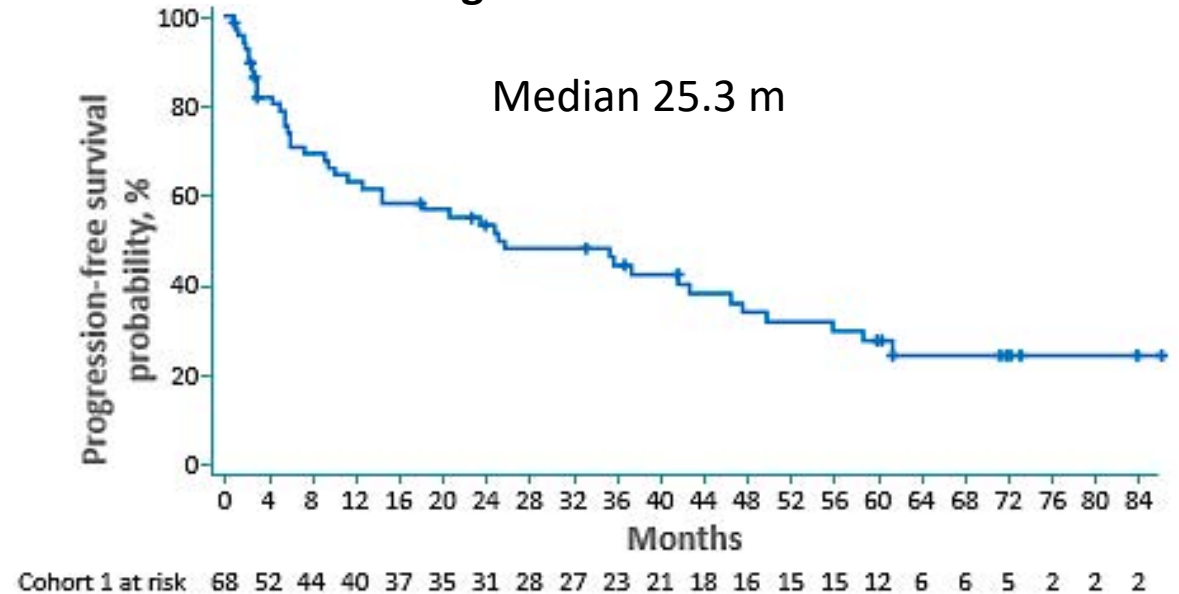
## Baseline Characteristics

n	68
Median # prior lines	3 (1-5)
BTKI refractory	62%
TP53 mut	17%
Blastoid	31%
KI67 ≥ 30%	82%

## Endpoint n=68

ORR	93%
CRR	67%
Median DOR	36.5 m
Median DOCR	46.7 m

## Progression-free survival



## Toxicity

Any-grade CRS	91%
Grade ≥ 3 CRS	15%
Any-grade ICANS	63%
Grade ≥ 3 ICANS	31%

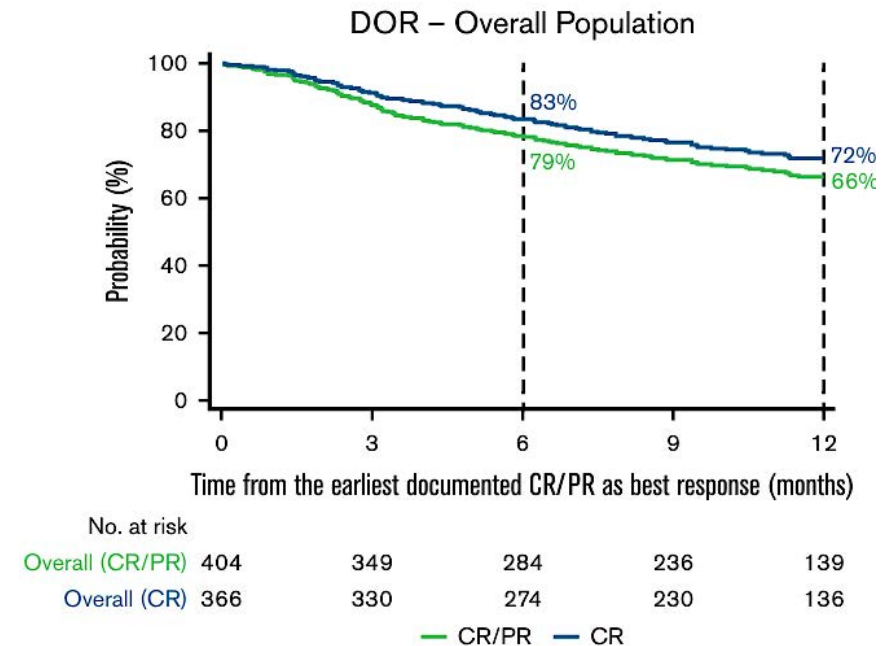
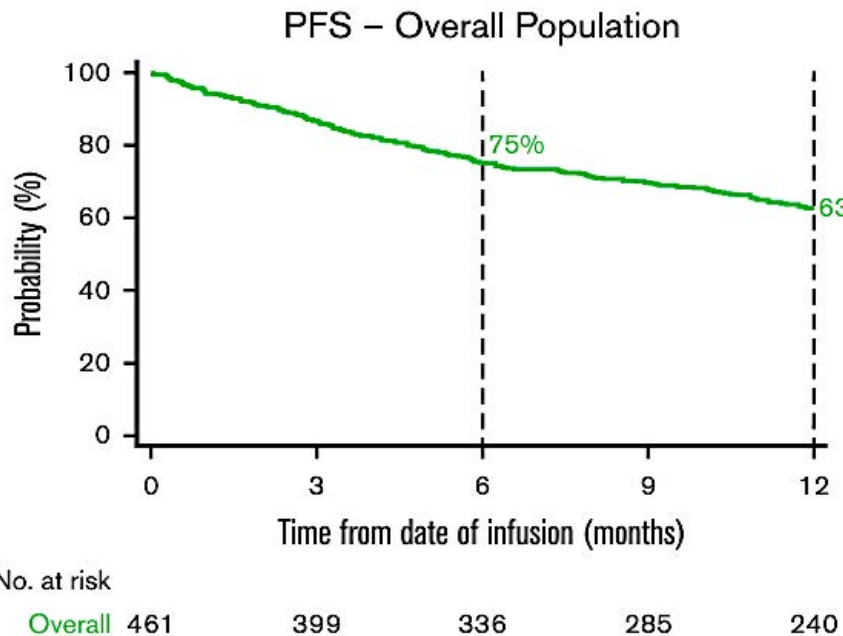


# Real world evidence for Brexu-cel in MCL from CIBMTR

Characteristics	n = 476
Median age	67 (34-85)
TP53 mutated	19%
KI67 ≥ 30%	68%
Median no. of prior treatments	4 (1-12)
Prior BTKi	88%
Prior ASCT	30%

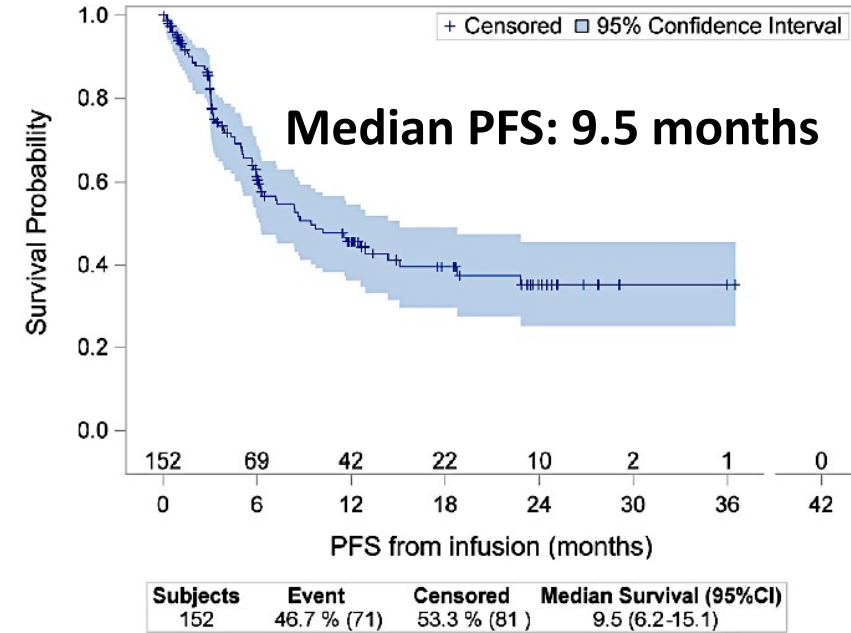
Endpoint	
ORR	91%
CRR	82%
12m DOR	79%

Toxicity	
Any-grade CRS	89%
Grade ≥ 3 CRS	11%
Any-grade ICANS	62%
Grade ≥ 3 ICANS	30%
12m NRM	8%



# Real world evidence for Brexu-cel in MCL from DESCAR-T

Characteristics	n = 152 (of 178)
Median age	69 (39-83)
TP53 mutated	30%
KI67 ≥ 30%	79%
Median no. of prior treatments	3 (1-9)
Prior BTKi	100%
Prior ASCT	40%



Endpoint	
ORR	85%
CRR	72%

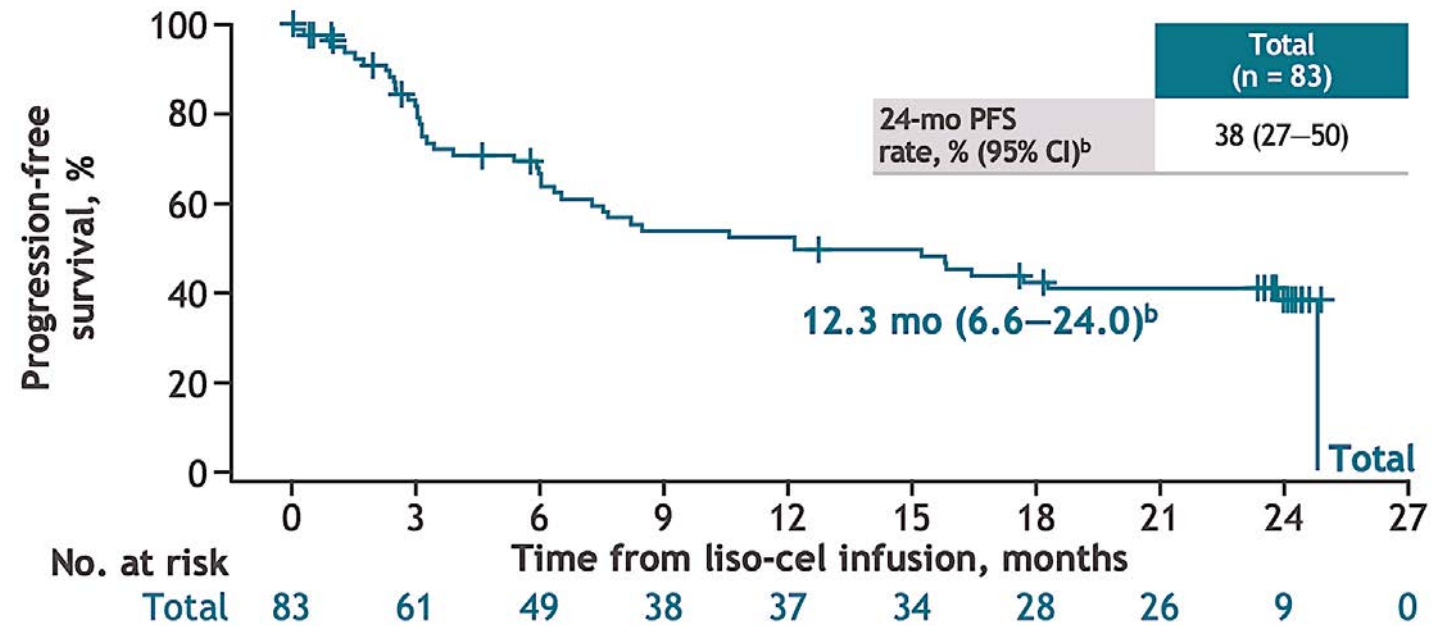
Toxicity	
Any-grade CRS	88%
Grade ≥ 3 CRS	12%
Any-grade ICANS	55%
Grade ≥ 3 ICANS	15%
ICU	34%
NRM	11%



# Liso-cel for 3L+ MCL post cBTK inhibition: TRANSCEND

Baseline Characteristics	
n	88
Median # prior lines	3 (1-11)
BTKI refractory	53%
TP53 mut	23%
Blastoid	31%

Endpoint	n=83
ORR	83%
CRR	72%
Median DOR	14.5 m
Median DOCR	15.7 m



Toxicity	
Any-grade CRS	61%
Grade ≥ 3 CRS	1%
Any-grade ICANS	31%
Grade ≥ 3 ICANS	9%
ICU	6%



# Discussion Questions

**68 y/o man with Stage IV FL, grade 2, FLIPI 4 with widespread LAN and bone marrow involvement without B symptoms, ECOG 1**

**PMH: HTN, type 2 diabetes, AMI with preserved EF**

**BR as initial therapy with partial response; progression at 18 months**

**R<sup>2</sup> with CR; progression 14 months later with axillary and inguinal LAN and cytopenias**

**Obinutuzumab + chemo with PR; progression after 9 months**

**In FL, are you typically using CAR-T or bispecific antibodies first? What would you recommend for this patient?**

**Given this patient has already received R<sup>2</sup>, is there any role for bispecific combinations?**

# Discussion Questions

**59 y/o man with FL**

**R-CHOP followed by R maintenance as initial therapy**

**Epcoritamab + R<sup>2</sup> as second-line therapy; currently in remission**

**At disease progression, what would you offer as third-line therapy?**

**Would the length of remission influence your decision-making in any way?**

# Discussion Questions

**70 y/o man, a retired physician, with extensive, symptomatic MCL  
BR as initial therapy with response; progression within 2 years  
Ibrutinib with response but now with extensive, symptomatic GI and nodal  
progression**

**What therapy would you use next? If CAR-T, would you have a preference for one platform versus the others?**

**For patients with MCL going to CAR-T, what bridging therapy, if any, do you typically employ?**

**How, if at all, does the recent approval of sonrotoclax impact your sequencing of therapy for MCL?**

**Is there any role for bispecifics in MCL at the current time?**

# Agenda

**Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Kamdar**

**Module 2: Bispecific Antibody Therapy for DLBCL — Dr Westin**

**Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Abramson**

**Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips**

**Module 5: Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies — Dr Brody**

Tycel Phillips, MD

Associate Professor

City of Hope

# **Evolving Role of Bispecific Antibodies in Low and Intermediate Grade Lymphoma**

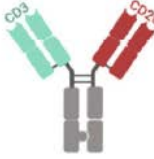

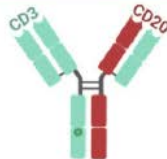

# Follicular Lymphoma

- R/R FL has unmet need for improved survival
- approval of several new therapies
- CAR-T
  - Approval of axicabtagene autemcelt (Yescarta)
- Small Molecule
  - Zanubrutinib
    - Roseburto (MAK)
  - Tazemetostat
    - RIP



in the

# Bispecific Antibodies

Bi-Specific Antibody	Targets	Design	Ig Fragment Formats	Ref.
mosunetuzumab	CD20 x CD3		<ul style="list-style-type: none"> <li>humanized mouse heterodimeric IgG1-based antibody</li> <li>monovalent CD20 and monovalent CD3ε binding</li> <li>modified Fc devoid of FcγR and complement binding</li> </ul>	4
glofitamab	(CD20) <sub>2</sub> x CD3		<ul style="list-style-type: none"> <li>humanized mouse IgG1-based antibody</li> <li>bivalent CD20 and monovalent CD3ε binding</li> <li>modified Fc devoid of FcγR and complement binding</li> </ul>	5
odronextamab	CD20 x CD3		<ul style="list-style-type: none"> <li>fully human IgG4-based heterodimeric antibody</li> <li>monovalent CD20 and monovalent CD3ε binding</li> <li>Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding</li> <li>common κ light chain from anti-CD3ε mAb</li> </ul>	6
epcoritamab	CD20 x CD3		<ul style="list-style-type: none"> <li>humanized mouse IgG1-based heterodimeric antibody</li> <li>monovalent CD20 and monovalent CD3 binding</li> <li>IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield</li> </ul>	7

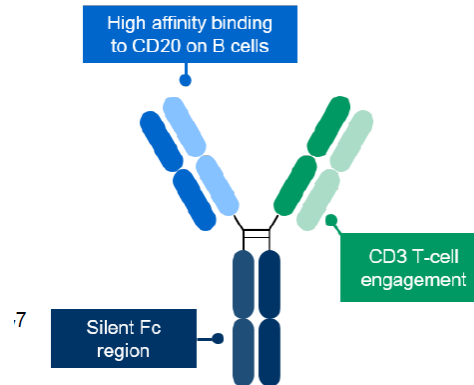
Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

<sup>1</sup>Dufner V, et al. Blood Adv (2019) 3:2491; <sup>2</sup>Goebeler ME, et al. J Clin Oncol (2016) 34:1104; <sup>3</sup>Viardot et al. Blood (2016) 127(11):1410; <sup>4</sup>Schuster SJ, et al. ASH 2019, Plenary Abstract 6;

<sup>5</sup>Hutchings M, et al. ASH 2020, Abstract 403; <sup>6</sup>Bannerji R, et al. ASH 2020, Abstract 400; <sup>7</sup>Hutchings M, et al. ASH 2020, Abstract 406

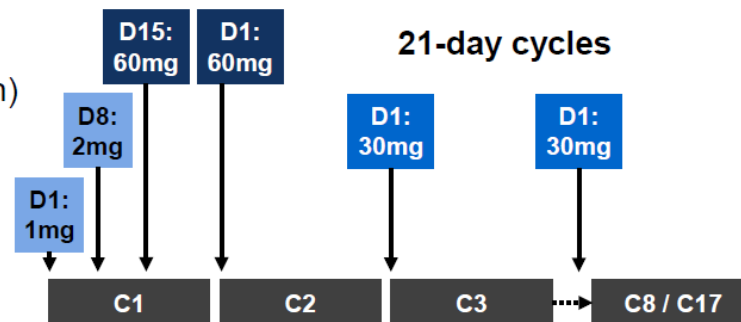
# Mosunetuzumab

## Mosunetuzumab: CD20xCD3 bispecific antibody<sup>4</sup>



### Mosunetuzumab administration

- Q3W intravenous administration
- C1 step-up dosing (CRS mitigation)
- **Fixed-duration treatment**
  - 8 cycles if CR after C8
  - 17 cycles if PR/SD after C8
- **No mandatory hospitalization**



Budde LE et al. Lancet Oncol 2022;23(8):1055-1065.

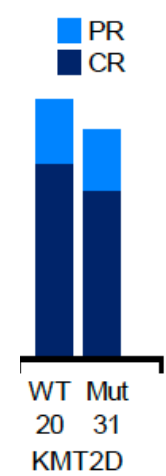
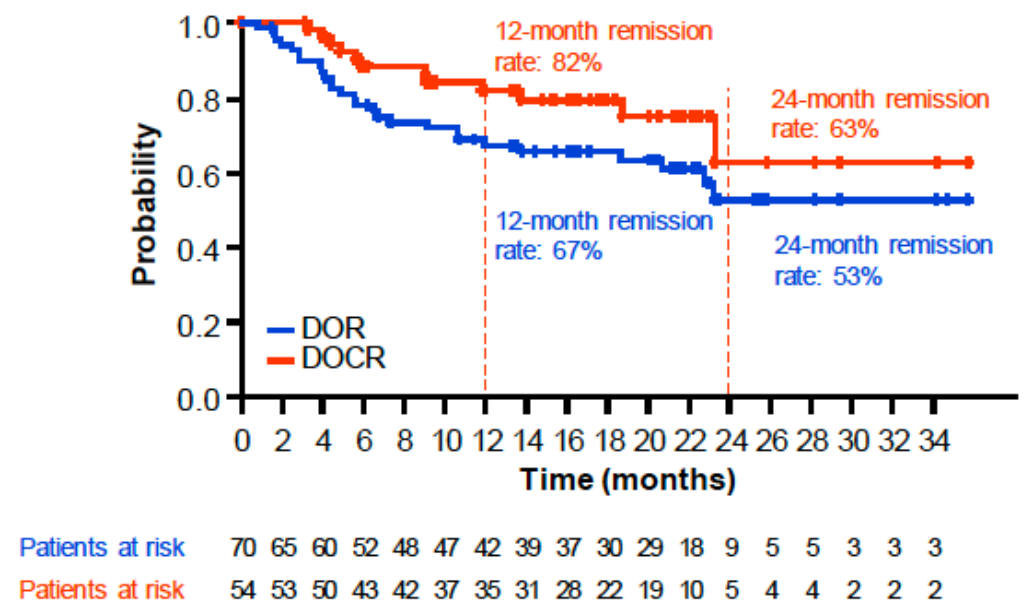
SQ dosing 5 mg (C1D1), 45 mg (C1D8), 45 mg C1D15 until EOT

# Mosunetuzumab Response (FL)

## Durability of responses

Efficacy endpoint by investigator assessment	N=90
Median DOR, months (range), n=70 24-month DOR (95% CI)	NR (21–NR) 53% (38–68)
Median DOCR, months (range), n=54 24-month DOCR (95% CI)	NR (23–NR) 63% (38–88)
Median PFS, months (range) 24-month PFS (95% CI)	24 (12–NR) 48% (36–60)
Median TTNT, months (range) 24-month TTNT (95% CI)	NR (18–NR) 56% (45–67)
Median OS, months (range) 24-month OS (95% CI)	NR (NR–NR) 87% (80–94)

### DOR and DOCR



**Durable responses: majority of patients in remission after 2 years**

DOCR, duration of complete response; TTNT, time-to-next therapy.

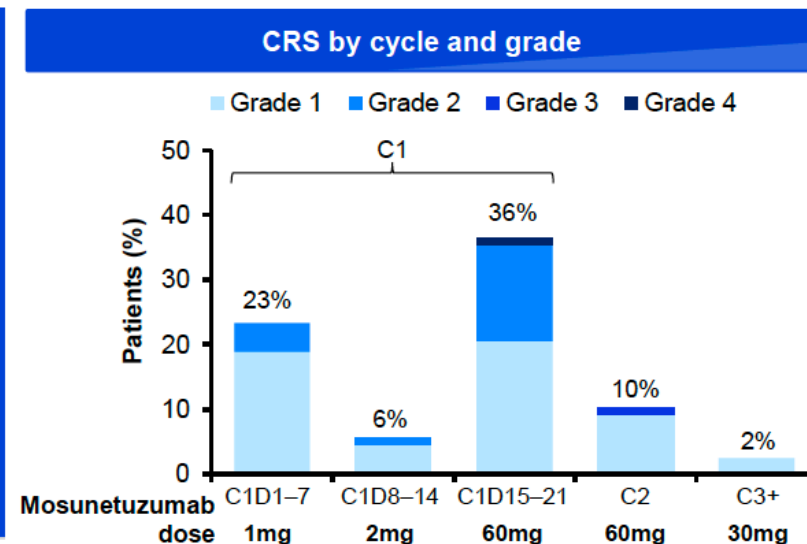
# Mosunetuzumab Safety (FL)

## Safety profile

Adverse events (AEs)	N=90
<b>AE</b>	100%
Mosunetuzumab related	92%
<b>Grade 3/4 AE</b>	70%
Mosunetuzumab related	51%
<b>Serious AE</b>	47%
Mosunetuzumab related	33%
<b>Grade 5 (fatal) AE</b>	2%*
Mosunetuzumab related	0
<b>AE leading to treatment discontinuation</b>	4%†
Mosunetuzumab related	2%

## CRS summary

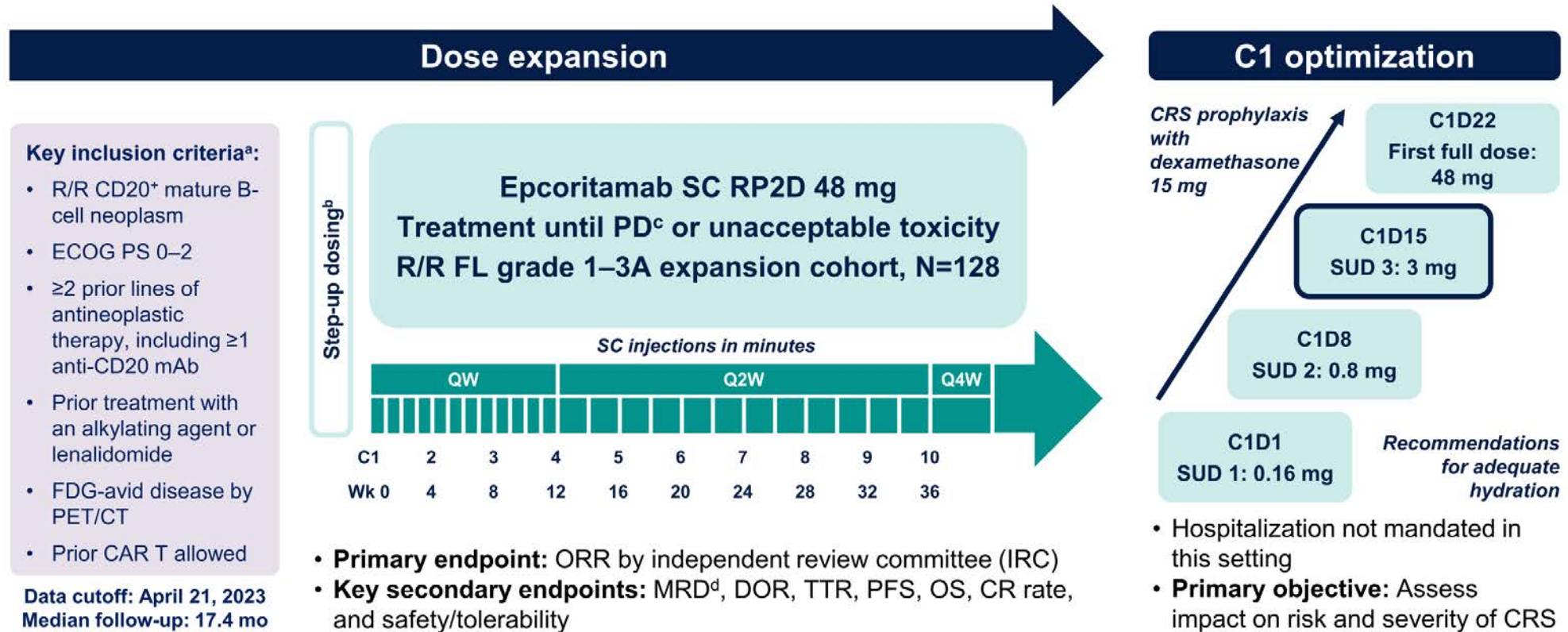
CRS by ASTCT criteria <sup>1</sup>	N=90
CRS (any grade)	44%
Grade 1	26%
Grade 2	17%
Grade 3	1%
Grade 4	1%
Median time to CRS onset, hours (range)	
C1D1	5.2 (1.2–24)
C1D15	27 (0.1–391)
Median CRS duration, days (range)	3 (1–29)
Corticosteroids for CRS management	11%
Tocilizumab for CRS management	8%
Events resolved	100%



**CRS was predominantly low grade and during Cycle 1**  
**All CRS events resolved; no new events were reported with 10 months of additional follow-up**

# Epcoritamab

## Trial Design: Pivotal EPCORE™ NHL-1 Study

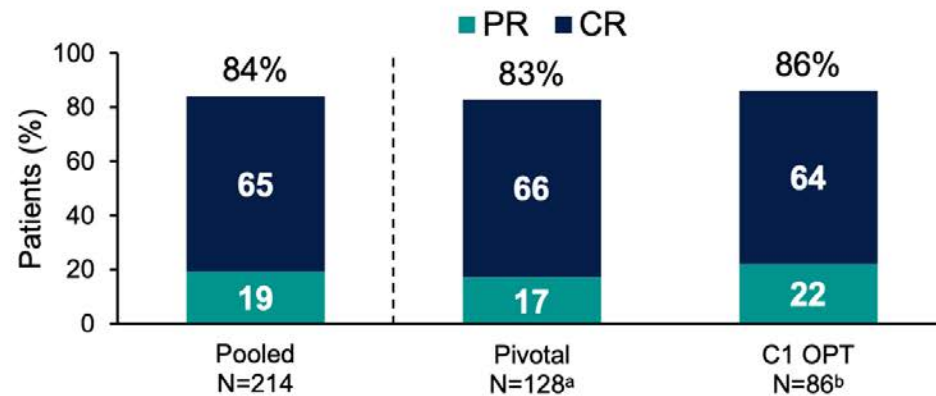


Phase 1/2 trial. <sup>a</sup>Patients enrolled in this trial (and excluded from trials of other T-cell–engaging therapies) included those with worse anemia, lymphopenia, and/or renal function. <sup>b</sup>Step-up dosing (SUD; priming [SUD 1] 0.16 mg and intermediate [SUD 2] 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. <sup>c</sup>≥2 measurable (by CT/MRI) and FDG PET–positive lesions; radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. <sup>d</sup>MRD was assessed in peripheral blood using the clonoSEQ<sup>®</sup> (Adaptive Biotechnologies, Seattle, WA) next-generation sequencing assay. ClinicalTrials.gov: NCT03625037; EudraCT: 2017-001748-36.

# Epcoritamab Response (R/R FL)

Epcoritamab in R/R FL

## High Rates of Complete Response and MRD Negativity



MRD-Negativity Rate	n (%)
Pooled (n=135)	89 (66)
Pivotal (n=91)	61 (67)
C1 OPT (n=44)	28 (64)

Based on MRD-evaluable population per clonoSEQ<sup>®</sup> PBMC assay with 10<sup>-6</sup> cutoff.

- At 6 mo in C1 OPT, an estimated 86% of patients with CR remained in CR
- No impact on time to response in C1 OPT
  - Median time to response was 1.4 mo in both cohorts<sup>c</sup>
  - Median time to complete response was 1.5 mo in both cohorts<sup>d</sup>

CR was complete metabolic response (ie, PET negativity). CR, complete response; PBMC, peripheral blood mononuclear cell; PR, partial response. <sup>a</sup>Three patients (2%) were not evaluable. <sup>b</sup>Five patients (6%) were not evaluable. <sup>c</sup>Range: 1.2–4.4 in C1 OPT, 1.0–3.0 in pivotal. <sup>d</sup>Range: 1.2–4.7 in C1 OPT, 1.2–11.1 in pivotal.

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# Epcoritamab Safety (R/R FL)

## C1 Optimization Reduced Risk and Severity of CRS

	Pivotal Cohort N=128	C1 Optimization Cohort <sup>a</sup> N=50
CRS, n (%) <sup>b</sup>	85 (66)	24 (48)
Grade 1	51 (40)	20 (40)
Grade 2	32 (25)	4 (8)
Grade 3	2 (2)	0
Treated with tocilizumab, n/n (%)	31/85 (36)	6/24 (25)
<b>Leading to epcoritamab discontinuation, n (%)</b>	<b>0</b>	<b>0</b>
<b>CRS resolution, n/n (%)</b>	<b>85/85 (100)</b>	<b>24/24 (100)</b>
Median time to resolution, d (range)	2 (1–54)	3 (1–14)

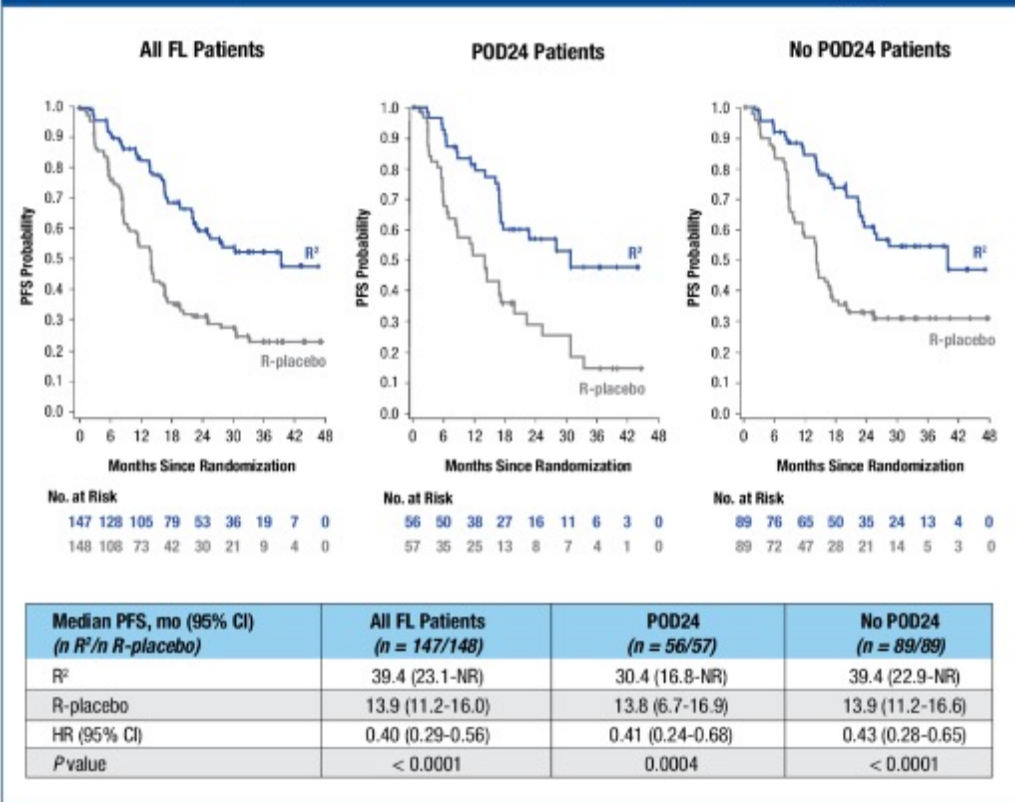
- Patient baseline characteristics were consistent between cohorts
- C1 optimization substantially reduced rate and severity of CRS
- In both cohorts, CRS was mostly confined to C1
- Similar response rates were observed in the C1 optimization cohort
- There were no cases of ICANS in the C1 optimization cohort; 8 cases were observed in the pivotal cohort (all grade 1–2 and resolved; none led to discontinuation)

<sup>a</sup>Data cutoff: September 21, 2023. Median follow-up: 3.8 mo (range, 1.9–8.7). <sup>b</sup>Graded by Lee et al 2019 criteria.<sup>1</sup> 1. Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-38.

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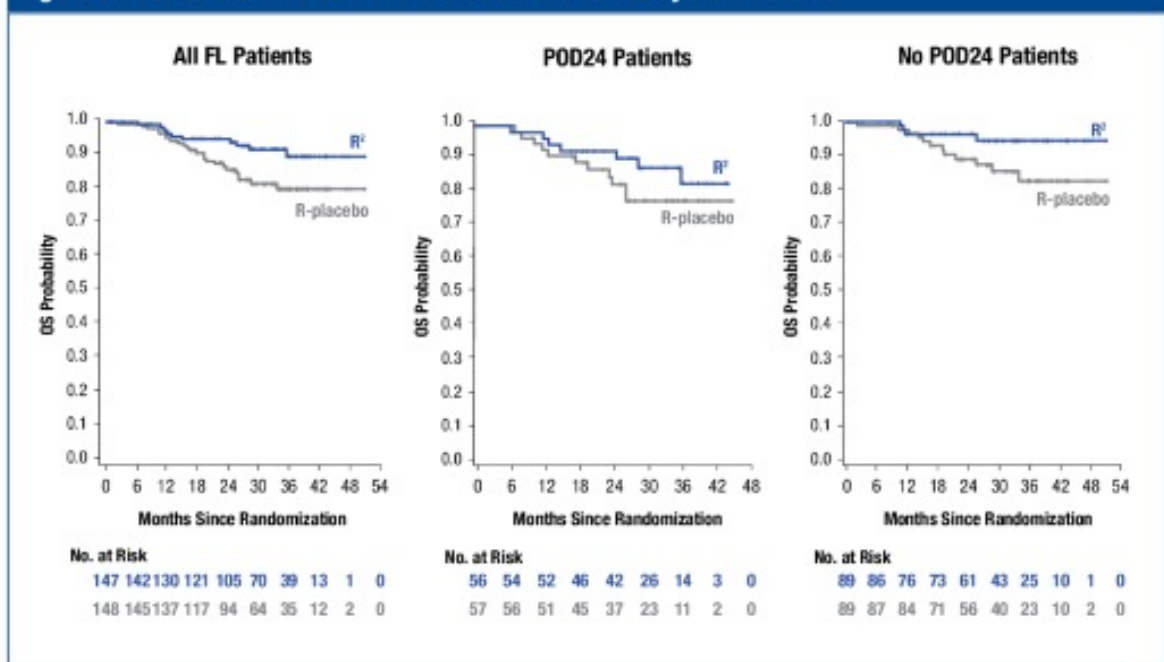
# 2L FL: AUGMENT

Figure 2. AUGMENT: Progression-Free Survival for All FL Patients and by POD24 Status (ITT)



Data cutoff June 22, 2018. PFS, progression-free survival. Note: Censoring rules were based on FDA guidance.

Figure 4. AUGMENT: Overall Survival for All FL Patients and by POD24 Status



Data cutoff June 22, 2018. OS, overall survival.

- At a median follow-up of 28.6 mo (range, 0.5-50.9), OS was not reached in all patients or according to POD24 status (Figure 4)

# EPCORE FL-1

Epcoritamab+R<sup>2</sup> in R/R FL

## EPCORE FL-1: Phase 3, Global, Randomized, Open-Label Study

Page Content

Fixed-Duration: 12 Cycles (28-Day Cycles)

### Key eligibility criteria

- Histologically confirmed CD20+ FL
- Grade 1-3a, Stage II-IV
- ≥ 1 prior treatment including anti-CD20 mAb plus an alkylating agent
- Met ≥ 1 GELF criterion

Randomization 1:1

### Epcoritamab (48 mg) plus R<sup>2</sup>

- Epcoritamab (3-SUD cycle 1: QW;<sup>a,b</sup> cycles 2–3, QW; cycles 4–12, Q4W)
- Rituximab (375 mg/m<sup>2</sup>), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- Lenalidomide (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

### R<sup>2</sup>

- Rituximab (375 mg/m<sup>2</sup>), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- Lenalidomide (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

### Stratification factors

- Disease status:
  - 2L: > or ≤ 2 years since last therapy
  - 3L+: > or < 6 months since last therapy
- Region: US/EU vs Rest of World

### Dual primary endpoints: ORR per IRC and PFS per IRC

- Secondary endpoints: CR rate per IRC, OS, and MRD<sup>c</sup>
- Additional secondary endpoints: DOR, DOCR, TTNLT, safety, and PRO assessments

Data cutoff: May 24, 2025; median follow-up: 14.8 months<sup>d</sup>

Enrollment period: October 2022 - January 2025

<sup>a</sup>Two step-up dosing (SUD) regimens during cycle 1 to mitigate the risk of cytokine release syndrome: either a 2-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8), or 3-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8, 3 mg on cycle 1 day 15) regimen, followed by full dose 48 mg. The 3-SUD regimen was implemented after reduced CRS severity and incidence had been observed in the EPCORE NHL-1 FL trial (NCT03625037).<sup>1</sup> <sup>b</sup>The 24 mg epcoritamab plus R<sup>2</sup> arm was closed to enrollment based on the superior efficacy for the 48 mg dose from EPCORE NHL-2.<sup>2</sup> Only the data for the optimal dose explored (48 mg) are presented here. <sup>c</sup>Minimal residual disease data are forthcoming in a future analysis. <sup>d</sup>The data presented here are from the second planned interim analysis (May 24, 2025) after 78% Information Fraction for PFS had occurred.

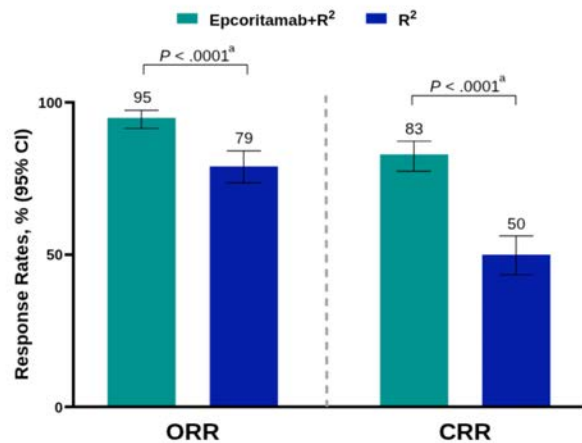
1. Vose J, et al. *J Clin Oncol*. 2024;42(16\_suppl):7015–7015. 2. Falchi L, et al. *Blood*. 2024;144(Supplement 1):342–342.

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# EPCORE FL-1: Response

## Epcoritamab+R<sup>2</sup> Resulted in Higher Response Rates Versus R<sup>2</sup>

Epcoritamab+R<sup>2</sup> in R/R FL



	Epcoritamab+R <sup>2</sup> (N = 243)	R <sup>2</sup> (N = 245)
ORR, n (%)	231 (95)	194 (79)
CRR, n (%)	201 (83)	122 (50)
PR, n (%)	30 (12)	72 (29)
SD, n (%)	1 (< 1)	17 (7)
PD, n (%)	7 (3)	16 (7)
NE, <sup>b</sup> n (%)	4 (2)	18 (7)

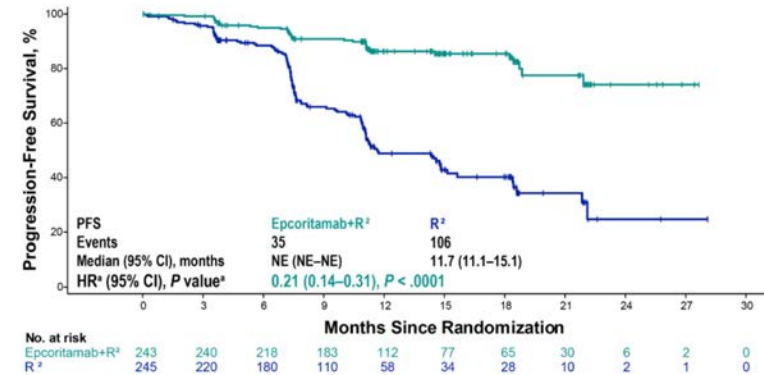
The first planned interim analysis (January 10, 2025) achieved statistical significance for ORR (N = 232; 95.7% vs 81.0%;  $P < 0.0001$ , with a 1-sided significance level of 0.005) and CR (74.5% vs 43.3%;  $P < 0.0001$ , with a 1-sided significance level of 0.025).

<sup>a</sup>Nominal P value by stratified Cochran-Mantel-Haenszel method. <sup>b</sup>Patients with no post-baseline disease assessment were also included.

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## Epcoritamab+R<sup>2</sup> Resulted in Superior PFS per IRC With 79% Risk Reduction

Epcoritamab+R<sup>2</sup> in R/R FL



- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for epcoritamab+R<sup>2</sup> and 40.2% (95% CI: 31.8, 48.4) for R<sup>2</sup>

Median follow-up for PFS: epcoritamab+R<sup>2</sup> (14.4m), R<sup>2</sup> (11.5m). The first planned interim analysis (January 10, 2025) achieved statistical significance on PFS, HR 0.21 (95% CI 0.13, 0.33)  $P < 0.0001$ , with a 1-sided significance level of 0.0023.

<sup>a</sup>Nominal P value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model. This analysis was performed on the 78% information fraction.

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# EPCORE FL-1: Safety

Epcoritamab+R<sup>2</sup> in R/R FL

## Manageable AEs With No New Safety Signals

Adverse Event, n (%)	Epcoritamab+R <sup>2</sup> (N = 243)		R <sup>2</sup> (N = 238)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any adverse event	242 (100)	219 (90)	235 (99)	161 (68)
Serious adverse event	135 (56)	-	69 (29)	-
Adverse event leading to treatment discontinuation	46 (19)	-	29 (12)	-
Epcoritamab	21 (9)	-	-	-
Rituximab	7 (3)	-	12 (5)	-
Lenalidomide	45 (19)	-	29 (12)	-
Adverse event of clinical interest > 20% <sup>a,b</sup>				
Infections <sup>c</sup>	188 (77)	81 (33)	125 (53)	37 (16)
Neutropenia	180 (74)	167 (69)	123 (52)	100 (42)
Cytokine release syndrome	85 (35)	-	1 (< 1)	-
Anemia	68 (28)	19 (8)	41 (17)	11 (5)
Thrombocytopenia	67 (28)	23 (9)	44 (18)	15 (6)
Pyrexia	58 (24)	1 (< 1)	33 (14)	3 (1)
Rash	58 (24)	19 (8)	53 (22)	9 (4)
COVID-19	54 (22)	7 (3)	32 (13)	4 (2)

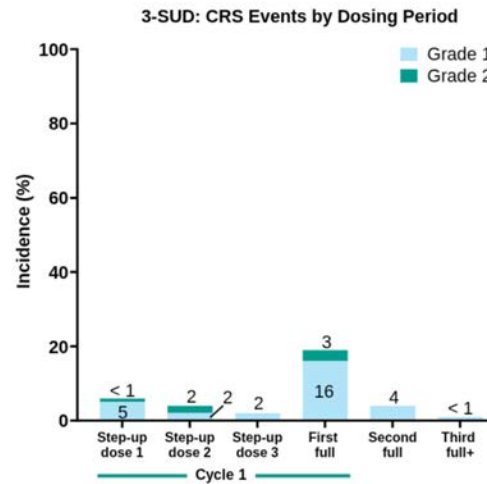
- Neutropenia was manageable and few patients discontinued any study drug (epcoritamab+R<sup>2</sup>, 3%; R<sup>2</sup>, 2%)
  - Incidence of febrile neutropenia: epcoritamab+R<sup>2</sup>, 6%; R<sup>2</sup>, 3%
- Infections were manageable and few patients discontinued any study drug (epcoritamab+R<sup>2</sup>, 6%; R<sup>2</sup>, 1%)
- Fatal adverse events were rare (epcoritamab+R<sup>2</sup>, 2%; R<sup>2</sup>, 4%)
- Despite higher rates of AEs in the epcoritamab+R<sup>2</sup> arm, most patients completed the prescribed regimen (median relative dose intensity ≥ 90% for epcoritamab+R<sup>2</sup>)

<sup>a</sup>Neutropenia, anemia, pyrexia, rash and COVID-19 are grouped terms comprising multiple clinically related Preferred Terms. <sup>b</sup>This includes the AESI of CRS. <sup>c</sup>Events were in the MedDRA system organ class "Infections and Infestations." No grade 5 infections were reported.

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Epcoritamab+R<sup>2</sup> in R/R FL

## CRS Was Low-Grade and Predictable With Epcoritamab+R<sup>2</sup>



	Epcoritamab+R <sup>2</sup> 2-SUD N = 110	Epcoritamab+R <sup>2</sup> 3-SUD <sup>a</sup> N = 133
CRS, n (%)	50 (45)	35 (26)
CRS grade, n (%)		
1	40 (36)	28 (21)
2	10 (9)	7 (5)
CRS signs and symptoms, n (%) <sup>*</sup>		
Fever	49 (98)	33 (94)
Hypotension	9 (18)	6 (17)
Hypoxia	1 (2)	2 (6)
Time to first CRS onset from first full dose, days, median (range)	1 (< 1, 6)	1.5 (< 1, 10)
Time to CRS resolution, days, median (range)	1 (< 1, 12)	1 (< 1, 26)
CRS interventions, n (%) <sup>*</sup>		
Treated with tocilizumab	12 (24)	9 (26)
Treated with corticosteroid	23 (46)	13 (37)

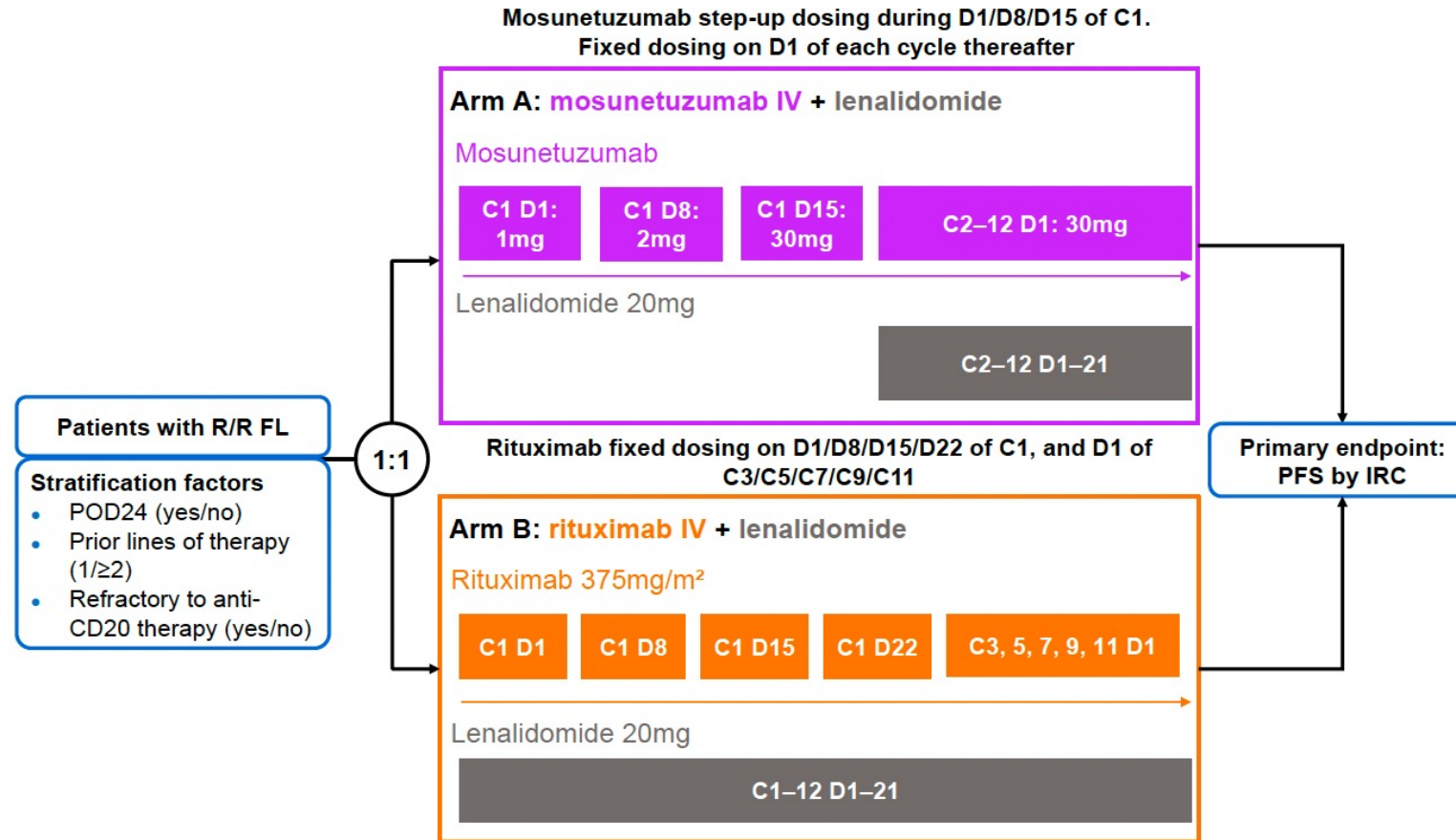
<sup>\*</sup>Of patients who had CRS

- Hydration and dexamethasone were utilized for CRS prophylaxis
- One event of ICANS was observed and was grade 1
- No discontinuations due to CRS and ICANS. All events resolved.
- No events of CTLs were reported

<sup>a</sup>The 3-SUD regimen was implemented based off the EPCORE NHL-1 FL trial (NCT03625037).<sup>1</sup>  
<sup>1</sup>Vose J, et al. J Clin Oncol 2024; 42 (suppl 16): 7015.

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# CELESTIMO Trial of Mosunetuzumab-Lenalidomide versus R<sup>2</sup> in 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.

# CELESTIMO US Cohort: Baseline Characteristics

## Non-randomized single arm US extension of CELESTIMO

Key inclusion criteria	Endpoints	
<ul style="list-style-type: none"> <li>CD20+ FL Grade 1–3a</li> </ul>	<ul style="list-style-type: none"> <li>Preliminary efficacy of Mosun-Len: INV-assessed ORR and CR</li> </ul>	
Refractory to previous therapy		
Refractory to first-line therapy	86 (35%)	81 (33%)
Progression of disease within 24 months*	106 (44%)	93 (38%)
Double refractory disease†	91 (37%)	91 (37%)
Refractory to previous anti-CD20 antibody	104 (43%)	103 (42%)
Refractory to last line of therapy	84 (35%)	82 (33%)

AE, adverse event; U, day; ELOG PS, Eastern Oncology Group performance status; INV, investigator; IV, intravenous; M, mosunetuzumab; ORR, objective response rate; QW, weekly.

1. Grieson DU, et al. J Clin Oncol 2014;32:3059–68; 2. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

n (%)		2L+ FL US cohort (n=54)
FLIPI score	0/1	n=52† 13 (25.0)
	2	18 (34.6)
	3	17 (32.7)
	4	3 (5.8)
	5	1 (1.9)
FL grade	1/2	n=47† 28 (59.6)
	3a	19 (40.4)
POD24	Yes	16 (29.6)
Number of prior lines of therapy	1	30 (55.6)
	≥2	24 (44.4)
Refractory to prior CD20 therapy	Yes	n=48† 19 (39.6)
Relapsed after prior CD20 therapy	Yes	n=48† 17 (35.4)
Double refractory	Yes	n=53† 9 (17.0)

# CELESTIMO US Cohort: Safety/Response

## Mosun-Len had manageable safety

n (%)	2L+ FL US cohort (n=54)	n (%)	2L+ FL US cohort (n=54)
<b>Any grade AE</b>	54 (100)	<b>CRS by ASTCT grading</b>	15 (27.8)
Mosunetuzumab related	48 (88.9)	Grade 1	12 (22.2)
Lenalidomide related	50 (92.6)	Grade 2	2 (3.7)
AE leading to discontinuation of mosunetuzumab	6 (11.1)	Grade 3	1 (1.9)
AE leading to discontinuation of lenalidomide	10 (18.5)	<b>Infections<sup>†</sup></b>	31 (57.4)
<b>Grade 3/4 AE</b>	31 (57.4)	Grade 1	2 (3.7)
<b>Grade 5*</b>	1 (1.9)	Grade 2	24 (44.4)
<b>Serious AE</b>	15 (27.8)	Grade 3	3 (5.6)
Mosunetuzumab related	9 (16.7)	Grade 4	1 (1.9)
Lenalidomide related	4 (7.4)	Grade 5	1 (1.9)
		<b>Neutropenia/neutrophil count decreased</b>	22 (40.7)
		Grade 3/4	18 (33.3)
		<b>Febrile neutropenia (Grade 3)</b>	2 (3.7)

CRS events were mainly low grade and all resolved

- Median duration of CRS: 4.0 days (range: 1.0–23.0)
- Median time to onset of first CRS event: 2.0 days (range: 1.0–27.0)

The most common AEs (any grade, by preferred term) were fatigue (57.4%), maculo-papular rash (42.6%), and constipation (42.6%)

Data cut-off: June 9, 2025. \*Pneumonia, considered to be mosunetuzumab related. <sup>†</sup>The most common infections were: COVID-19, 20.4%; sinusitis, 18.5%; and upper respiratory tract infection, 16.7%; which were mainly Grade 2 (44.4%) in severity.

## Mosun-Len achieved high response rates in patients with R/R FL

n (%)	2L+ FL US cohort (n=54)
<b>ORR</b>	52 (96.3)
CR	47 (87.0)
PR	5 (9.3)
<b>Stable disease</b>	0
<b>Progressive disease</b>	2 (3.7)

The median duration of follow-up was 12.7 months (range: 5–20)

Data cut-off: June 9, 2025. PR, partial response.

# Ongoing Studies

Phase	Line	Drug	Comparator	Study	Primary Endpoint	Global	Sites
3	2L	Mosunetuzumab + lenalidomide	CIT	MorningLyte	PFS	N	France Germany Portugal Spain
3	1L	Mosunetuzumab	Rituximab	S2308	PFS	N	USA
3	1L	Odronextamab	CIT	OLYMPIA-1	CR30	Y	
3	2L	Odronextamab + R <sup>2</sup>	R <sup>2</sup>	OLYMPIA-5*	PFS	Y	
3	1L	Epcoritamab + R <sup>2</sup>	CIT	EPCORE – FL -2	CR30 PFS	Y	
3	2L	Mosunetuzumab + lenalidomide	CIT or R <sup>2</sup>	MARSUN	PFS	N	France Germany Portugal Belgium Italy

\*includes MZL

# R/R MCL – Glofitamab updated data after a 3.5-year follow-up

- Remains a difficult space despite approval of
  - CAR-T (long term follow up w/ very few patients still in remission (cure unlikely)).
  - Pirtobrutinib (likely best served as a bridge for most patients).
  - Sonrotoclax (response rates similar to pirtob)
- As such other options are still needed.
  - Mosun/Pola – Impressive early response, and safety but lacks long term data to support durability

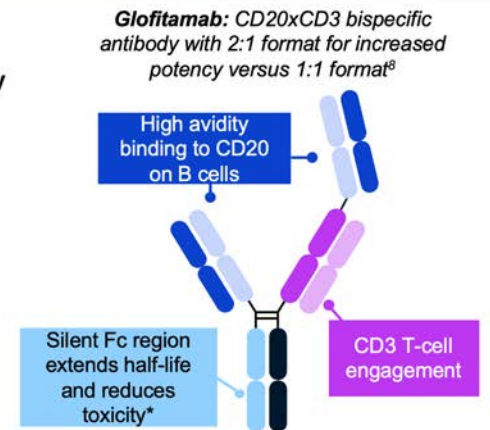
## Background

### MCL unmet medical need

- Treatment of R/R MCL remains **challenging**, with **limited durability of response** for many patients outside of **CAR T-cell therapy**<sup>1</sup>
- Increasing use of **covalent BTKi therapy**, including in the **1L setting**, highlights the need for **effective non-BTKi treatment options following progression**<sup>2-4</sup>

### Glofitamab

- **Glofitamab** is an **off-the-shelf, fixed-duration CD20xCD3 bispecific antibody approved in the US** for 3L+ DLBCL<sup>5</sup>
- In heavily pretreated R/R MCL, including post-BTKi, glofitamab demonstrated **high CR rates and durable responses** in the **Phase I/II NP30179 study (NCT03075696)**<sup>6,7</sup>

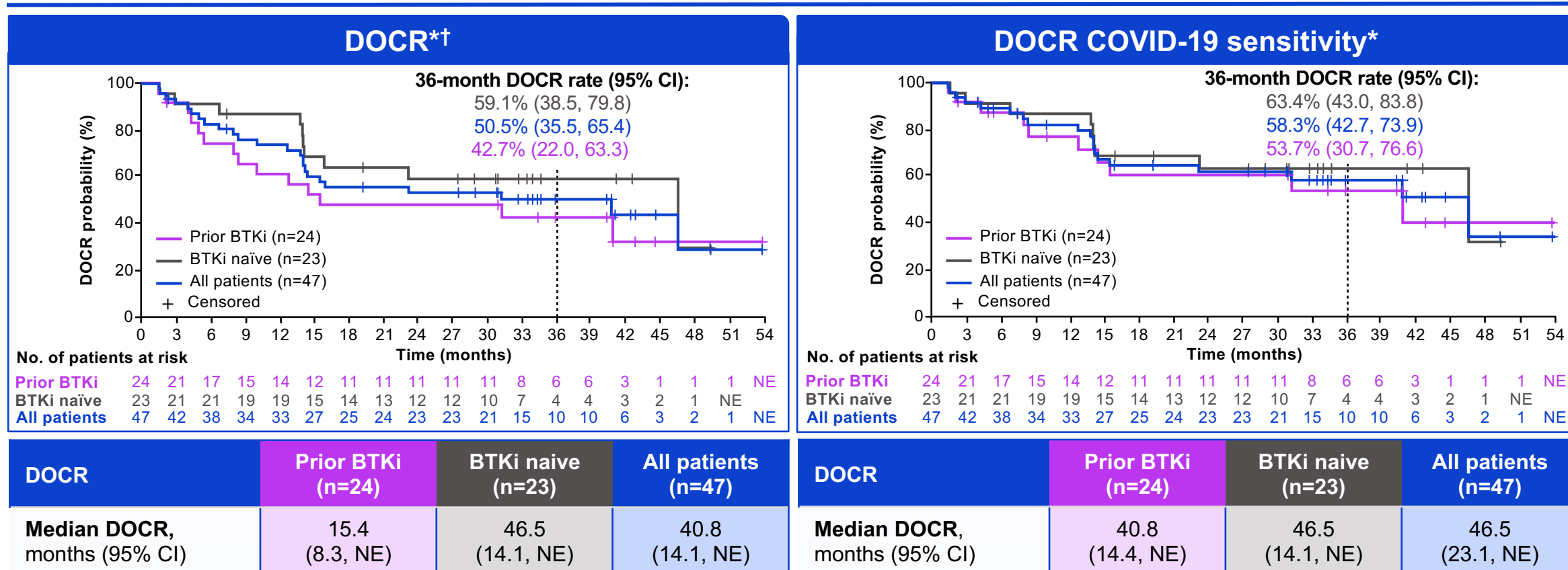


We report the efficacy and safety of glofitamab monotherapy in patients with R/R MCL, including those previously exposed to BTKi therapy, after a median follow-up of 41.5 months

\*Compared with non-Fc bearing T-cell engaging bispecific antibodies.  
1L, first line; 3L+, third-line and later; CAR, chimeric antigen receptor;  
CR, complete response; DLBCL, diffuse large B-cell lymphoma;  
Fc, fragment crystallizable; US, United States of America.

1. Kumar A, et al. Blood Cancer J 2019;9:50–60; 2. Martin P, et al. Blood 2016;127:1559–63;  
3. Dreyling M, et al. Lancet 2024;403:2293–306; 4. McCulloch R, Br J Haematol 2023;202:718–19;  
5. Dickinson MJ, et al. N Engl J Med 2022;387:2220–31; 6. NCT03075696. Available at: <https://clinicaltrials.gov/>;  
7. Phillips TJ, et al. J Clin Oncol 2024;43:318–28; 8. Bacac M, et al. Clin Cancer Res 2018;24:4785–97.

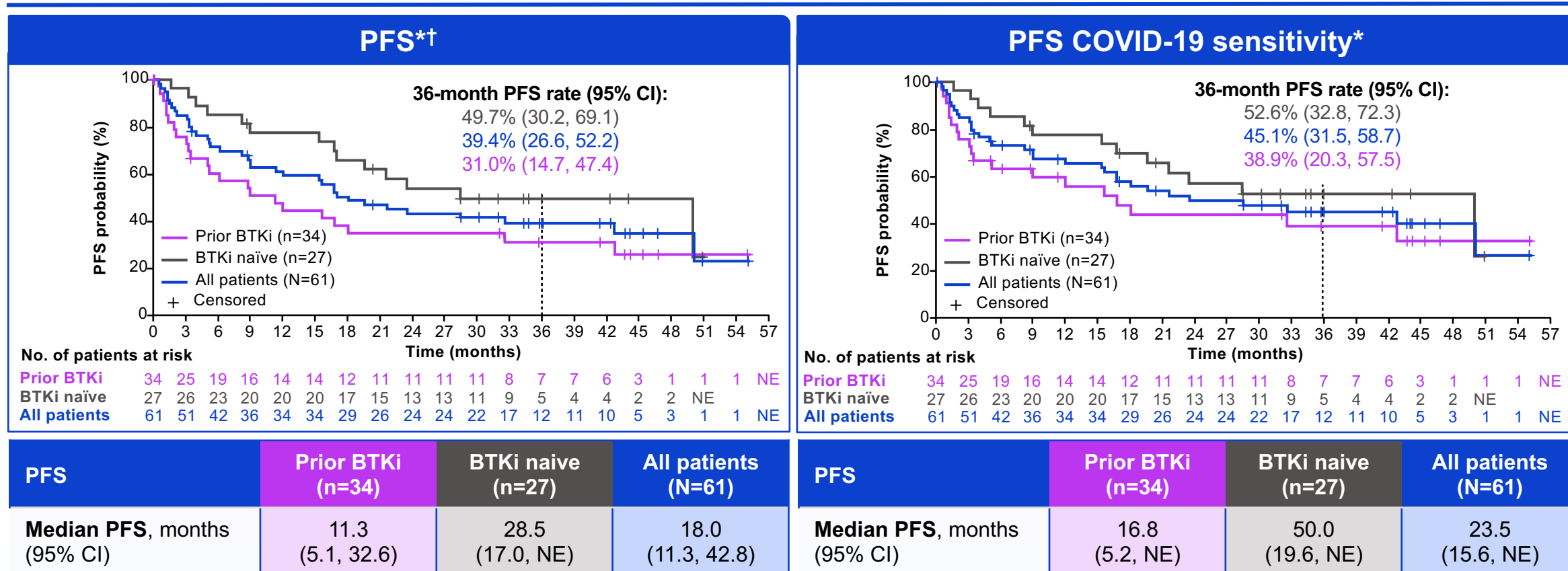
# Duration of complete response



Fixed-duration glofitamab monotherapy achieved durable CRs in patients with prior BTKi and those who were BTKi naïve; COVID-19 censoring further extended the median DOCR

\*INV-assessed. †Median DOCR follow-up was 34.6 months (range: 1–54) overall, and 40.3 months (range: 1–54) and 33.4 months (range: 2–49) in the prior-BTKi and BTKi-naïve cohorts, respectively. CI, confidence interval; NE, not estimable.

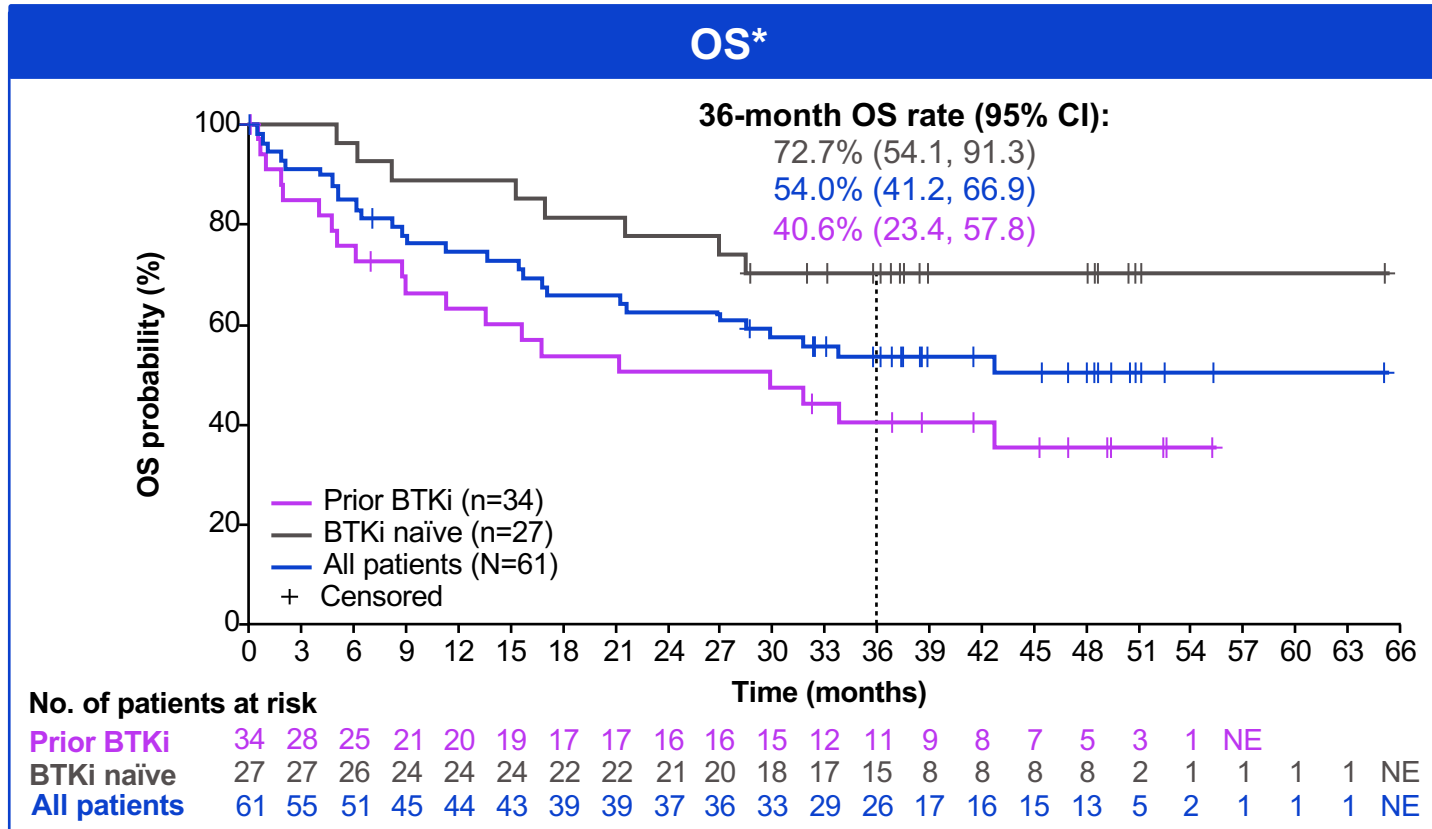
# Progression-free survival



Clinically meaningful PFS was achieved with glofitamab monotherapy after 3.5 years of follow-up; COVID-19 censoring further extended the median PFS from 18.0 to 23.5 months

\*INV-assessed. †Median PFS follow-up was 36.0 months (range: 0–55) overall, and 43.7 months (range: 0–55) and 35.9 months (range: 2–51) in the prior-BTKi and BTKi-naïve cohorts, respectively.

# Overall survival

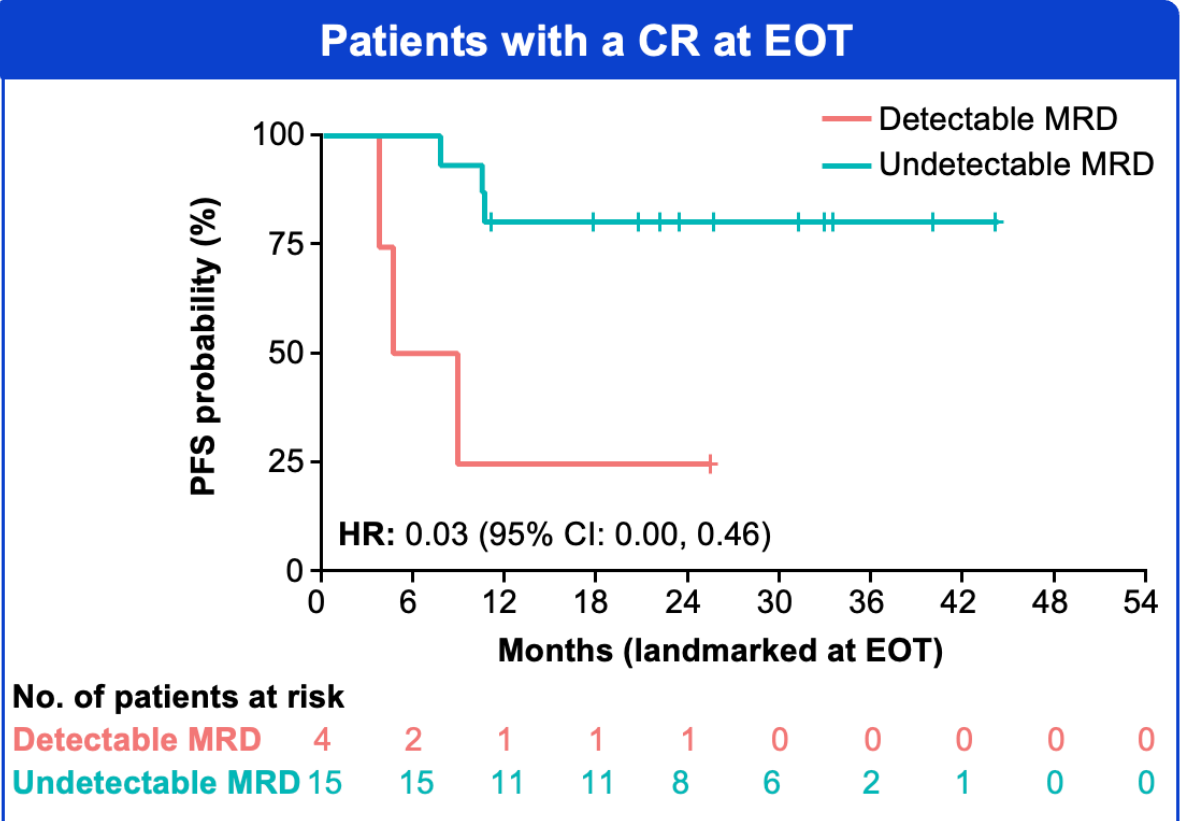
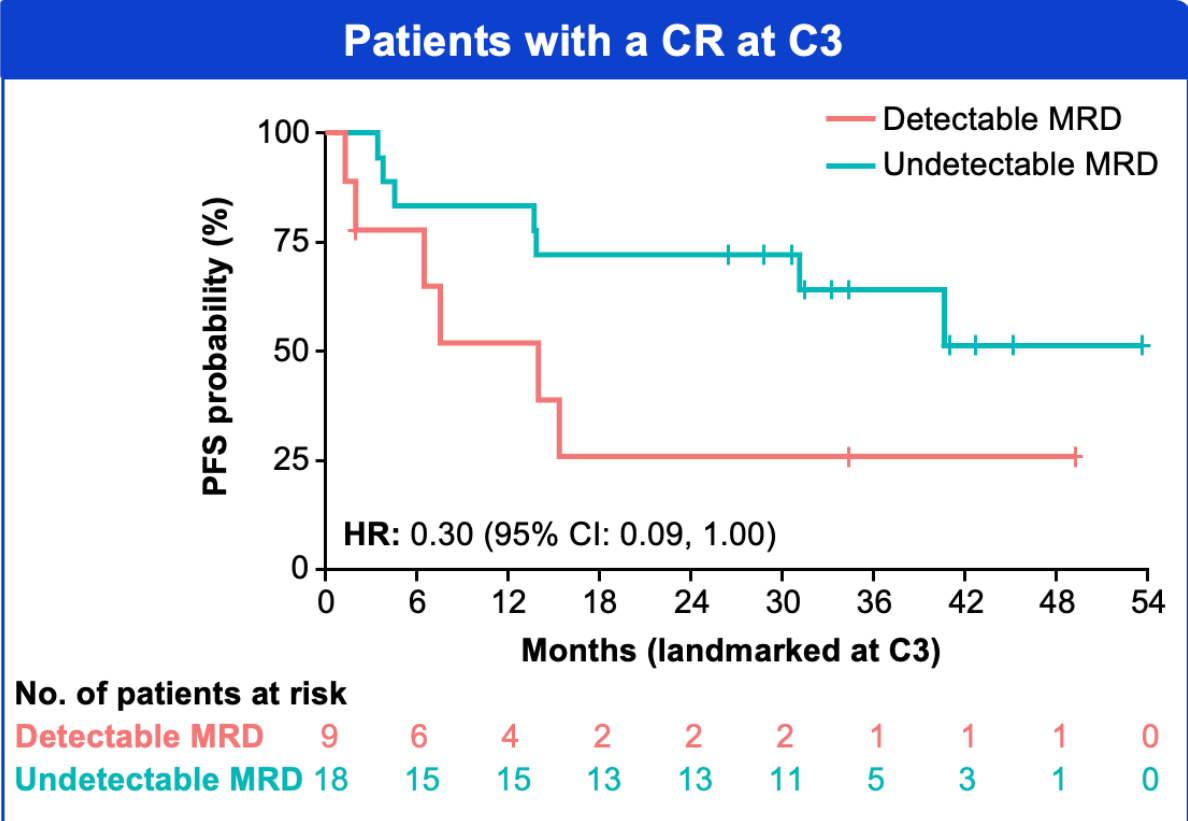


OS	Prior BTKi (n=34)	BTKi naïve (n=27)	All patients (N=61)
<b>Median OS, months (95% CI)</b>	29.9 (11.3, NE)	NE (NE, NE)	NE (26.9, NE)

Durable OS was achieved with fixed-duration glofitamab monotherapy in patients with prior BTKi and those who were BTKi naïve

\*Median OS follow-up was 41.5 months (range: 0–65) overall, and 45.4 months (range: 0–55) and 38.4 months (range: 5–65) in the prior-BTKi and BTKi-naïve cohorts, respectively; at the time of analysis, 22 patients had died, the majority due to progressive disease (n=7) or COVID-19 (n=7). All patients who died due to COVID-19 had achieved a CR, and six remained in remission at the time of death.

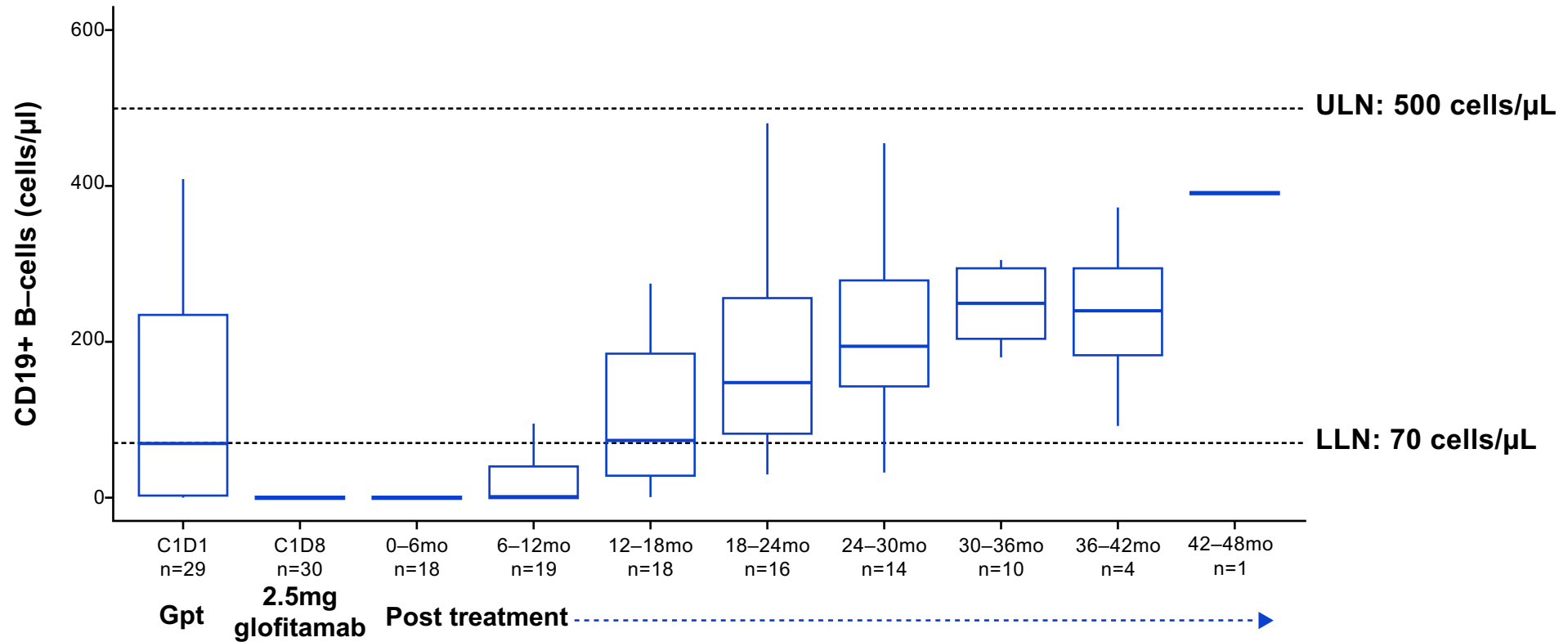
# Landmark analysis of PFS by MRD status



The majority of patients with a CR with undetectable MRD at C3 (66.7%) and EOT (78.9%) achieved durable PFS

MRD performed using Clonoseq assay. HRs were calculated using Cox regression and adjusted for MIPI score (<6, ≥6) and age (≤65 vs >65 years). HRs are calculated in a biomarker evaluable population and are exploratory in nature. HR, hazard ratio; MRD, minimal residual disease; PET-CT, positron emission tomography-computed tomography.

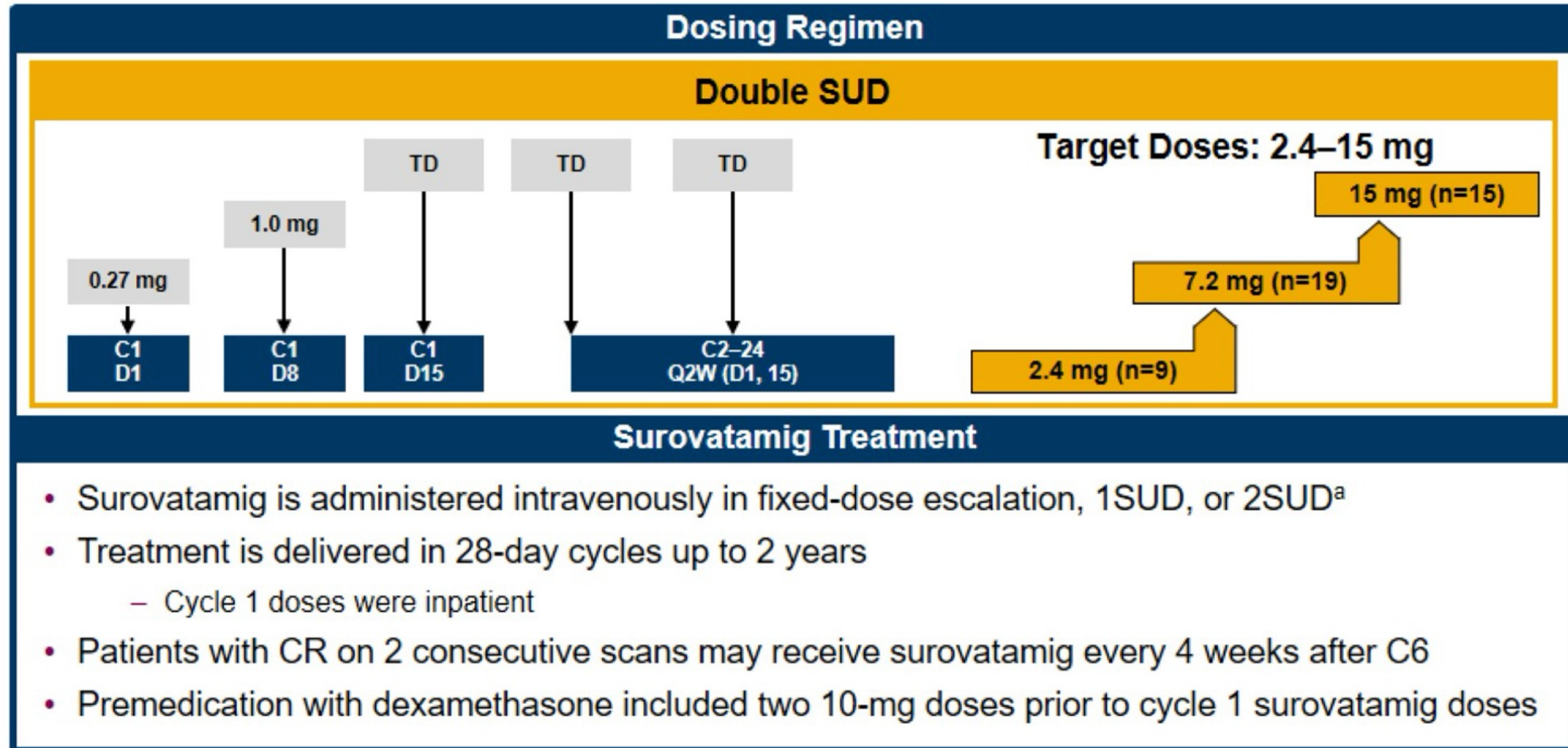
# B-cell depletion and recovery



Peripheral B-cell depletion was rapid and sustained after treatment initiation.  
Recovery above the lower limit of normal was observed 12–18 months post EOT

Patients who completed 12 cycles of treatment and did not have progressive metabolic disease at EOT were included in this analysis. Samples occurring within 45 days of a progression event were excluded. Only serious infections were systematically collected beyond the 90-day AE reporting period. LLN, lower limit of normal; mo, months; ULN, upper limit of normal.

# Surovatamig Phase I Study: FL Cohort

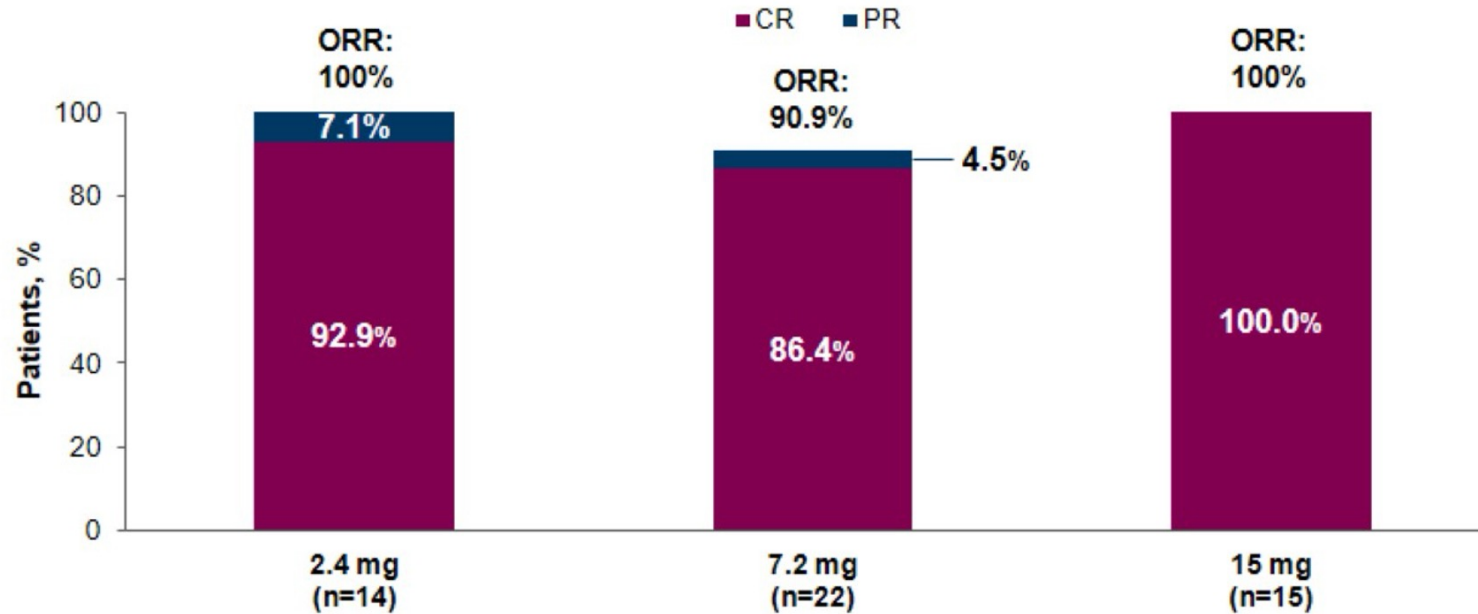


5

NCT04594642; data cutoff: 19 May 2025

<sup>a</sup> Fixed-dose escalation (n=6), 1SUD (n=12), 2SUD (n=43)

# Surovatamig Phase I Study: Response Rates in FL Cohort



- ORR/CR rate for patients who received  $\geq 2.4$  mg was 96%/92%

Responses were noted in various patient subgroups examined, including those with prior exposure to CD19 CAR T and CD20 T-cell engagers

95% of MRD-evaluable patients with CR achieved undetectable MRD

# Phase III SOUNDTRACK-F1 study

## Global, Randomized, Phase 3, Multicenter, Open-label Study of Surovatamig Plus Rituximab in Patients With Previously Untreated High Tumor Burden FL

SOUNDTRACK-F1 Consists of a SRI Followed by a Phase 3 Portion

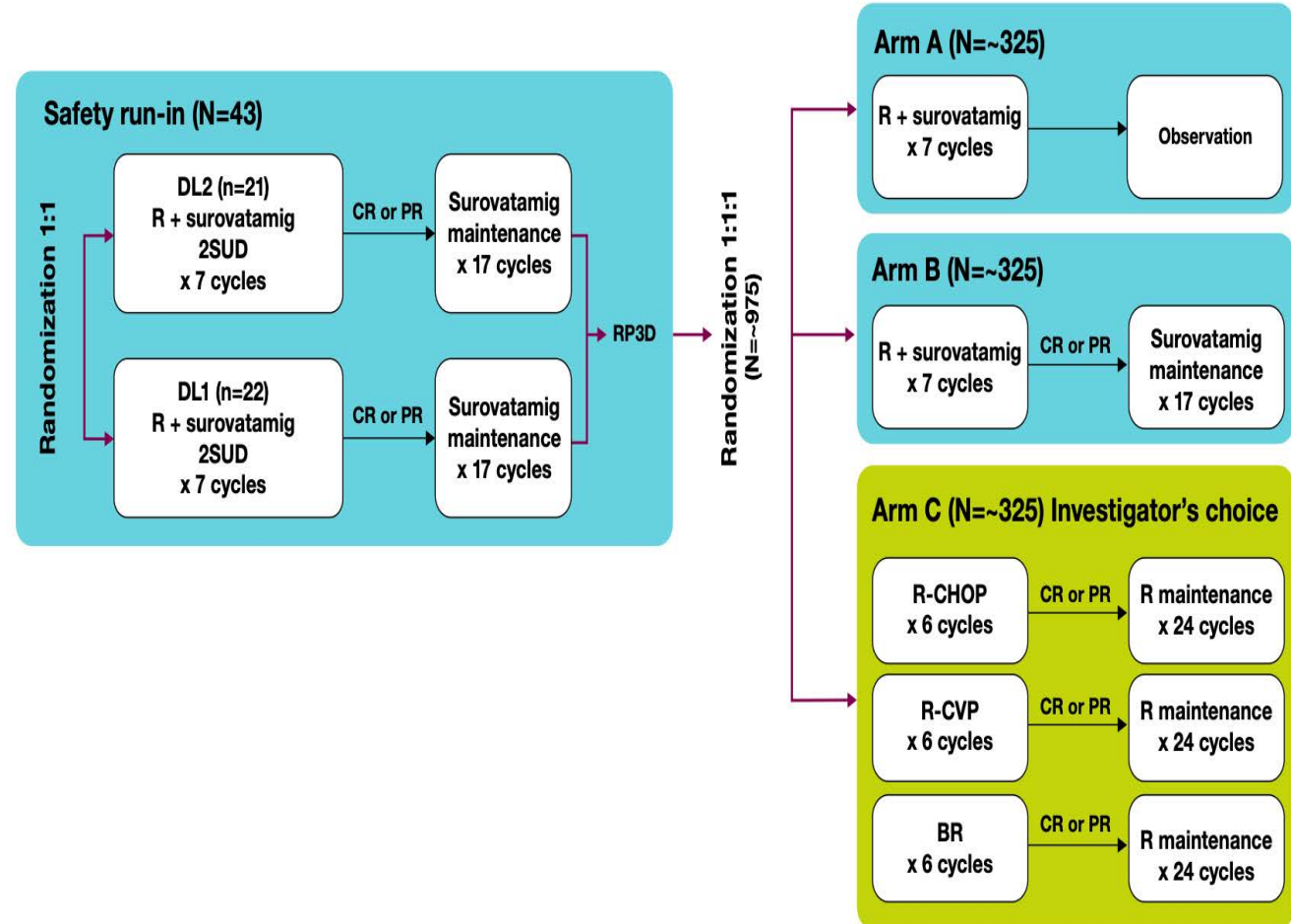


### Study Design

- The SRI will identify the RP3D of surovatamig in combination with rituximab (**Figure 3**)
  - Dose 1:** surovatamig 2.4 mg (monotherapy RP2D minus 1 dose level for R/R FL)
  - Dose 2:** surovatamig 7.2 mg (monotherapy RP2D for R/R FL)
- The phase 3 portion consists of 3 randomization arms (**Figure 3**); patients will be randomized 1:1:1 to:
  - Arm A:** surovatamig + rituximab without maintenance therapy
  - Arm B:** surovatamig + rituximab with maintenance therapy
  - Arm C:** rituximab-based CIT<sup>a</sup> with rituximab maintenance therapy

### Phase 3 Study Endpoints

- Dual primary:** PFS; ORR at EOI
- Key secondary:** OS



# Conclusion

- Bispecific antibodies w/ excellent response rate and safety as single agents in FL.
- Combination w/ lenalidomide has helped to improve DOR, ORR, PFS, and TTNT.
  - Impressive data in 2L FL and pending studies in 1L setting vs. rituximab (asymptomatic patients) and CIT (symptomatic by GELF).
- Additional options need in R/R MCL.
  - Time limited glofitamab w/ durable responses in patients who obtain a complete response
    - Especially notable in those who maintain a CR at EOT.
    - Improvement in rates/severity of CRS is needed.

# Discussion Questions

60 y/o man with FL

BR as initial therapy; progression 6 month into R maintenance

Switched to temporizing R<sup>2</sup>

Rebiopsy shows no transformation to DLBCL

**Would you add epcoritamab to R<sup>2</sup> at the current time? In general, how are you using that regimen in your practice? Are you prioritizing it over R<sup>2</sup> alone and tafasitamab/R<sup>2</sup> for most patients with FL?**

# Discussion Questions

**80 y/o woman with FL**

**BR as initial therapy; progression**

**Tafasitamab/R<sup>2</sup> as second-line therapy; ECOG 2 and frail**

**What is the optimal third-line therapy for R/R FL in elderly, frail patients, given the withdrawal of tazemetostat? Is a bispecific a reasonable consideration? If so, would you have a preference for mosunetuzumab or epcoritamab?**

# Discussion Questions

**78 y/o woman with FL and excellent performance status**

**Past treatments include weekly rituximab, BR and R<sup>2</sup>**

**Would you offer either tafasitamab/R<sup>2</sup> or epcoritamab/R<sup>2</sup> to this patient?**

**If so, what is the minimum interval for these treatments after prior exposure to R<sup>2</sup>?**

# Agenda

**Module 1: Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) — Dr Kamdar**

**Module 2: Bispecific Antibody Therapy for DLBCL — Dr Westin**

**Module 3: CAR T-Cell Therapy for Other Lymphoma Subtypes — Dr Abramson**

**Module 4: Bispecific Antibody Therapy for Follicular Lymphoma and Other Lymphoma Subtypes — Dr Phillips**

**Module 5: Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies — Dr Brody**

# Tolerability Considerations with CAR T-Cell Therapy and Bispecific Antibodies

Joshua Brody MD  
Professor of Hematology and Medical Oncology  
Director, Lymphoma Immunotherapy Program  
Mount Sinai School of Medicine, New York, NY



# Comparative CRS and ICANS with αCD19 CAR-T in NHL

<u>subtype</u>	<u>construct</u>	<u>trial</u>	<u>pub year</u>	<u>N</u>	<u>CRS any</u>	<u>CRS ≥3</u>	<u>ICANS any</u>	<u>ICANS ≥3</u>
LBCL	axi-cel	ZUMA-1	2017	111	93%	<b>13%</b>	64%	<b>28%</b>
LBCL	tisa-cel	JULIET	2019	93	58%	<b>22%</b>	21%	<b>12%</b>
LBCL	liso-cel	TRANSCEND	2020	256	42%	<b>2%</b>	30%	<b>10%</b>
MCL	brexu-cel	ZUMA-2	2020	60	91%	<b>15%</b>	63%	<b>31%</b>
FL	axi-cel	ZUMA-5	2021	104	82%	<b>7%</b>	59%	<b>19%</b>
LBCL (2L)	axi-cel	ZUMA-7	2022	180	92%	<b>6%</b>	60%	<b>21%</b>
LBCL (2L)	tisa-cel	BELINDA	2022	162	61%	<b>5%</b>	10%	<b>2%</b>
LBCL (2L)	liso-cel	TRANSFORM	2022	92	49%	<b>1%</b>	11%	<b>4%</b>
FL	tisa-cel	ELARA	2022	97	49%	<b>0%</b>	37%	<b>3%</b>

# Guidelines for mitigation, monitoring, management of CRS and ICANS

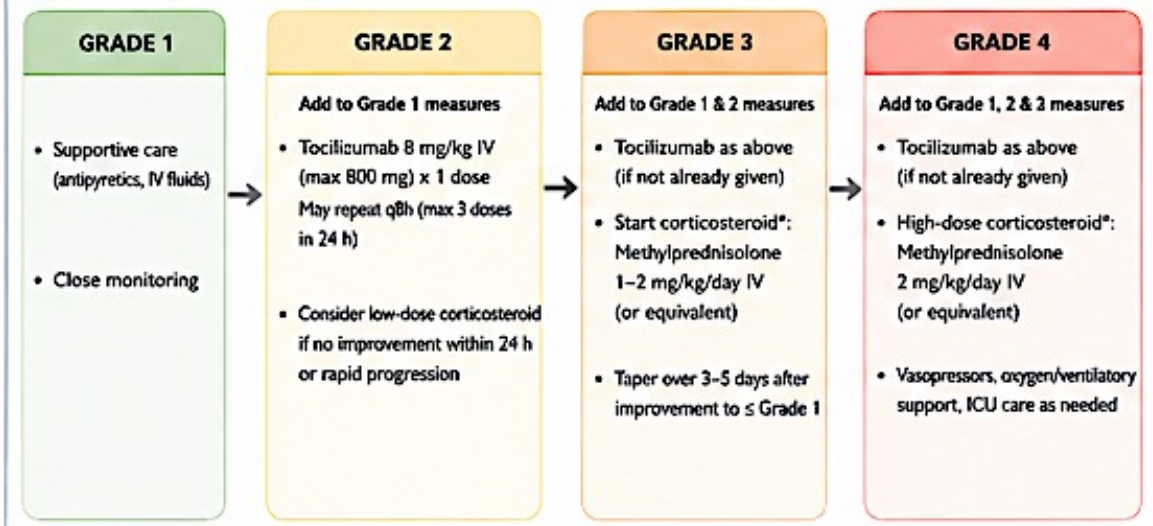


## CYTOKINE RELEASE SYNDROME (CRS)

Systemic inflammatory response due to cytokine release.

GRADE	FEVER	HYPOTENSION	HYPOXIA	MONITORING
1	≥38°C	None	None	<ul style="list-style-type: none"> <li>• Monitor at least every 4–6 h during high-risk period (first 7–14 days)</li> <li>• Vital signs, oxygen saturation</li> <li>• Daily labs: CBC, CMP, CRP, ferritin, IL-6 (if available), coags</li> <li>• Assess for organ dysfunction</li> </ul>
2	≥38°C	Responds to fluids or low dose vasopressor	Requiring low flow oxygen	
3	≥38°C	Requiring high dose vasopressor ± vasopressin	Requiring high flow oxygen	
4	≥38°C	Life-threatening consequences	Requiring positive pressure (ventilation)	

### MANAGEMENT ALGORITHM



# Rationale for and implications: 7/2025 elimination of CAR-T REMS

FDA: *“accumulated physician experience, improved toxicity-recognition algorithms, standardized management pathways for CRS and ICANS, and extensive safety data now make formal REMS programs unnecessary”*

## Rationale:

### **1. Clinical familiarity and standardization**

- extensive experience managing CRS and ICANS
- consensus grading systems, standardized steroid/toci algorithms, and earlier intervention reduced high-grade AEs

### **2. Real-world evidence demonstrating manageable risk**

- 100s of centers and 10,000s of patients => large post-marketing datasets showing that toxicities are predictable and treatable. - boxed warnings and product labeling alone are now sufficient to communicate these risks.

## Implications:

### **1. Access barriers created by REMS**

- REMS significantly constrained geographic availability of CAR-T
- for small hospitals: certification, staffing requirements, reporting obligations, and pharmacy prep were resource-intensive

### **2. Operational inefficiency and delays**

- CAR-T patients may have rapidly progressive dx =>
- administrative delays with REMS certification and transfer to specialized centers prevents timely treatment.
- eliminating REMS is expected to shorten referral-to-infusion timelines, box warnings remain in place

### **3. Updated label requirements**

- Duration to stay near site **reduced** to 2 weeks
- Driving restrictions **reduced** to 2 weeks
- Boxed warnings remain

# CAR T-Cells: Late toxicities - cytopenias

Platelet Count

Absolute Neutrophil Count (ANC)

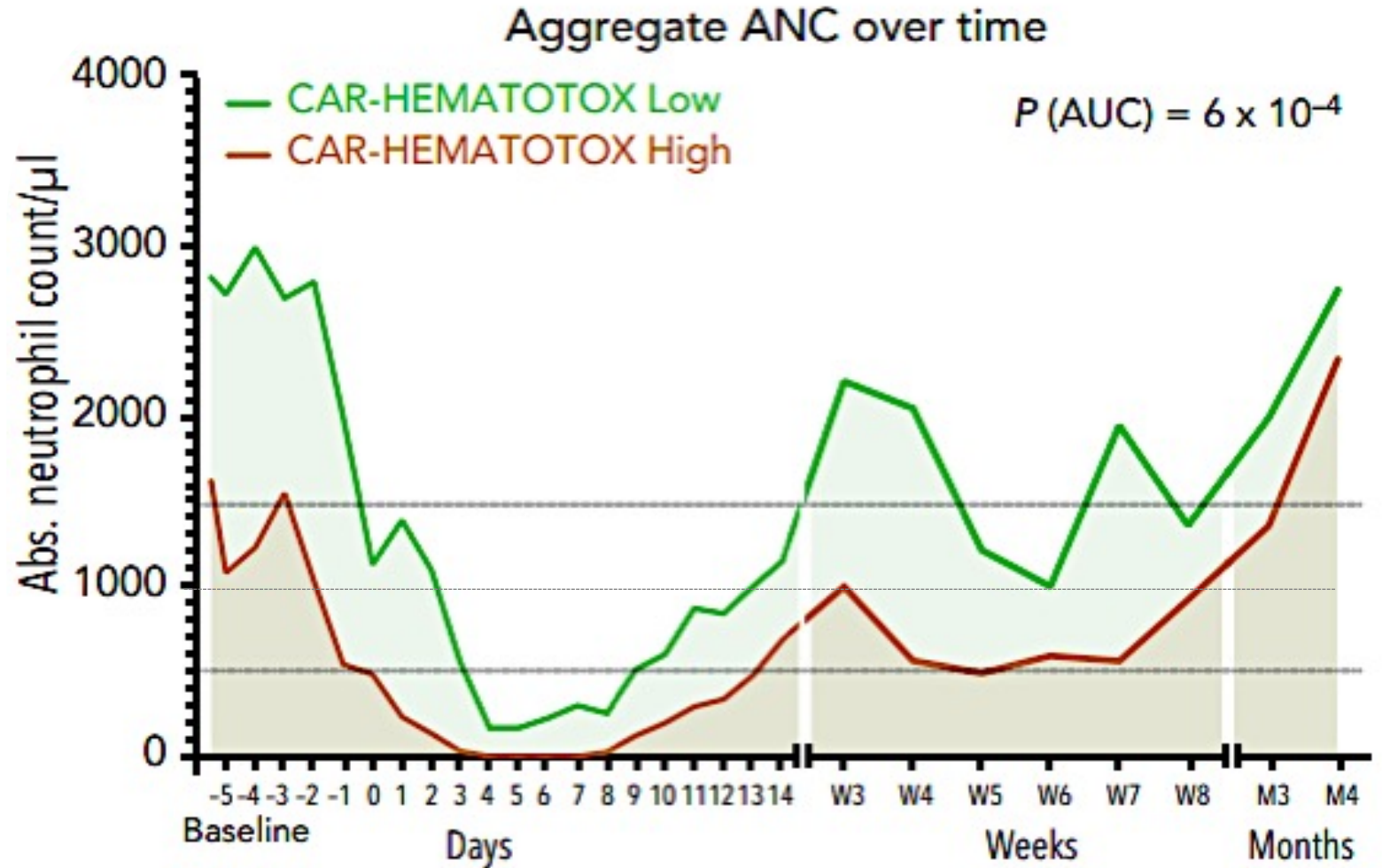
Hemoglobin

C-reactive protein (CRP)

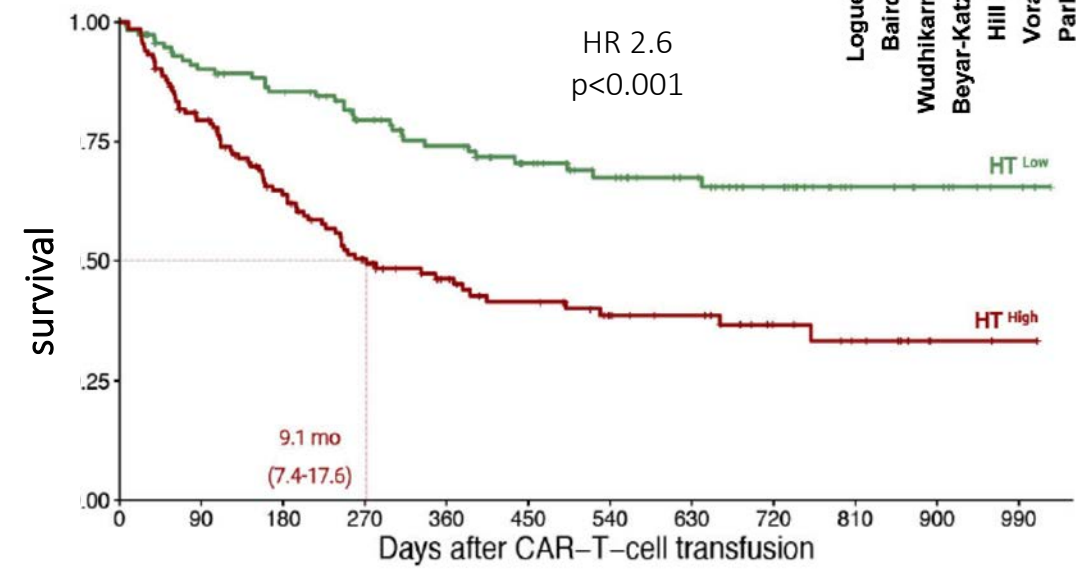
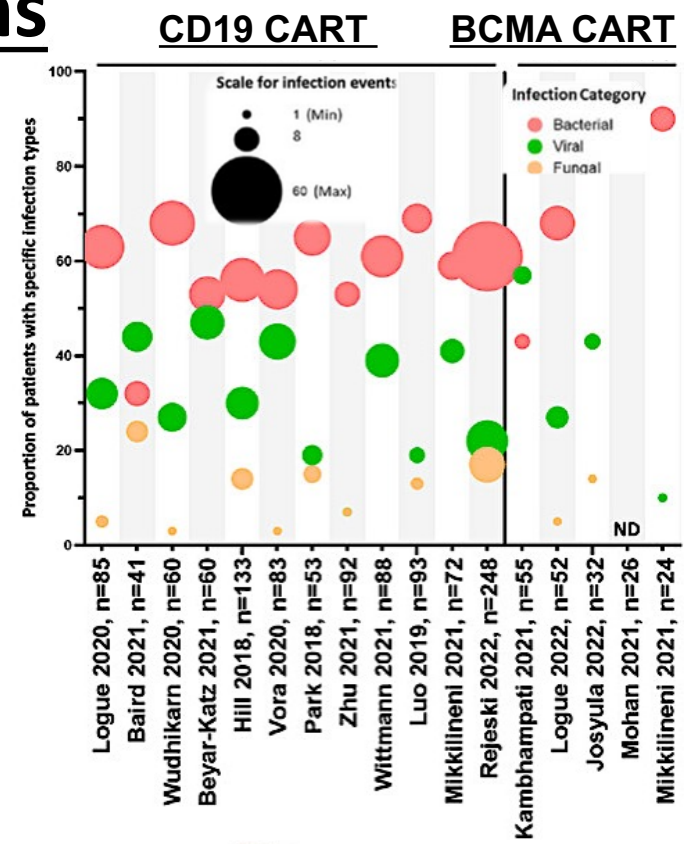
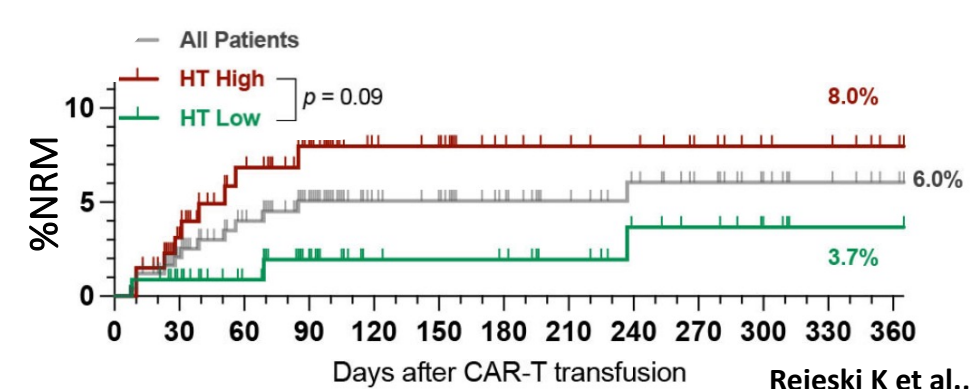
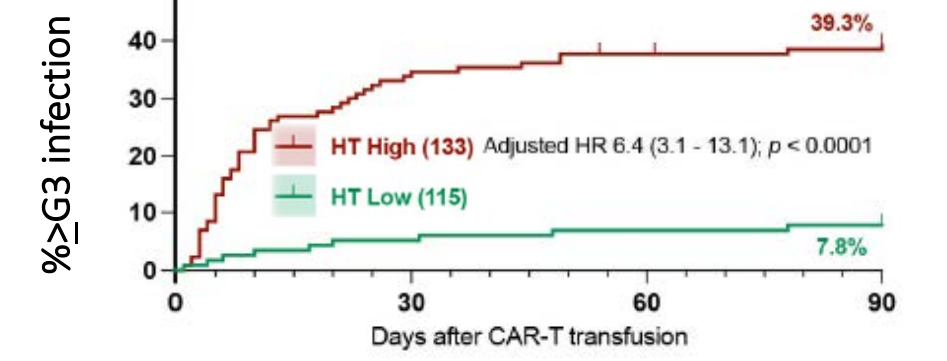
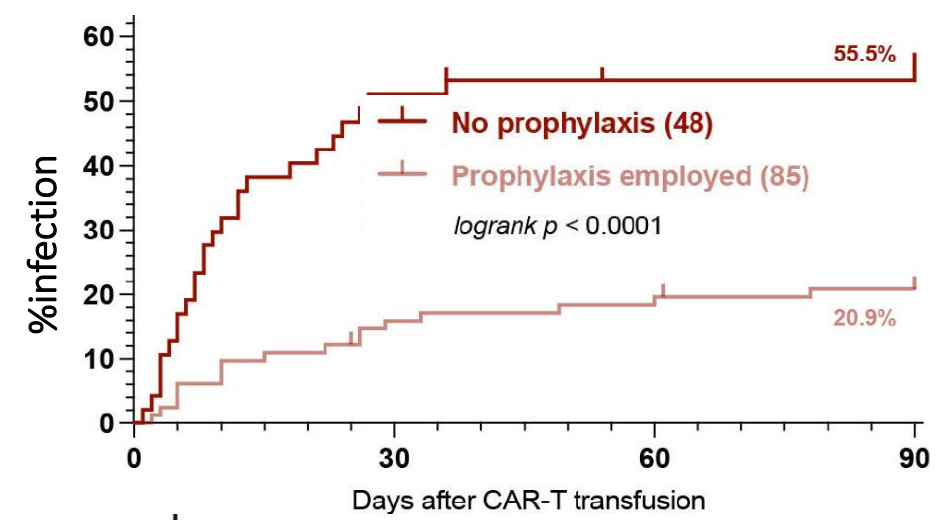
Ferritin

CAR-HEMATOTOX score 6

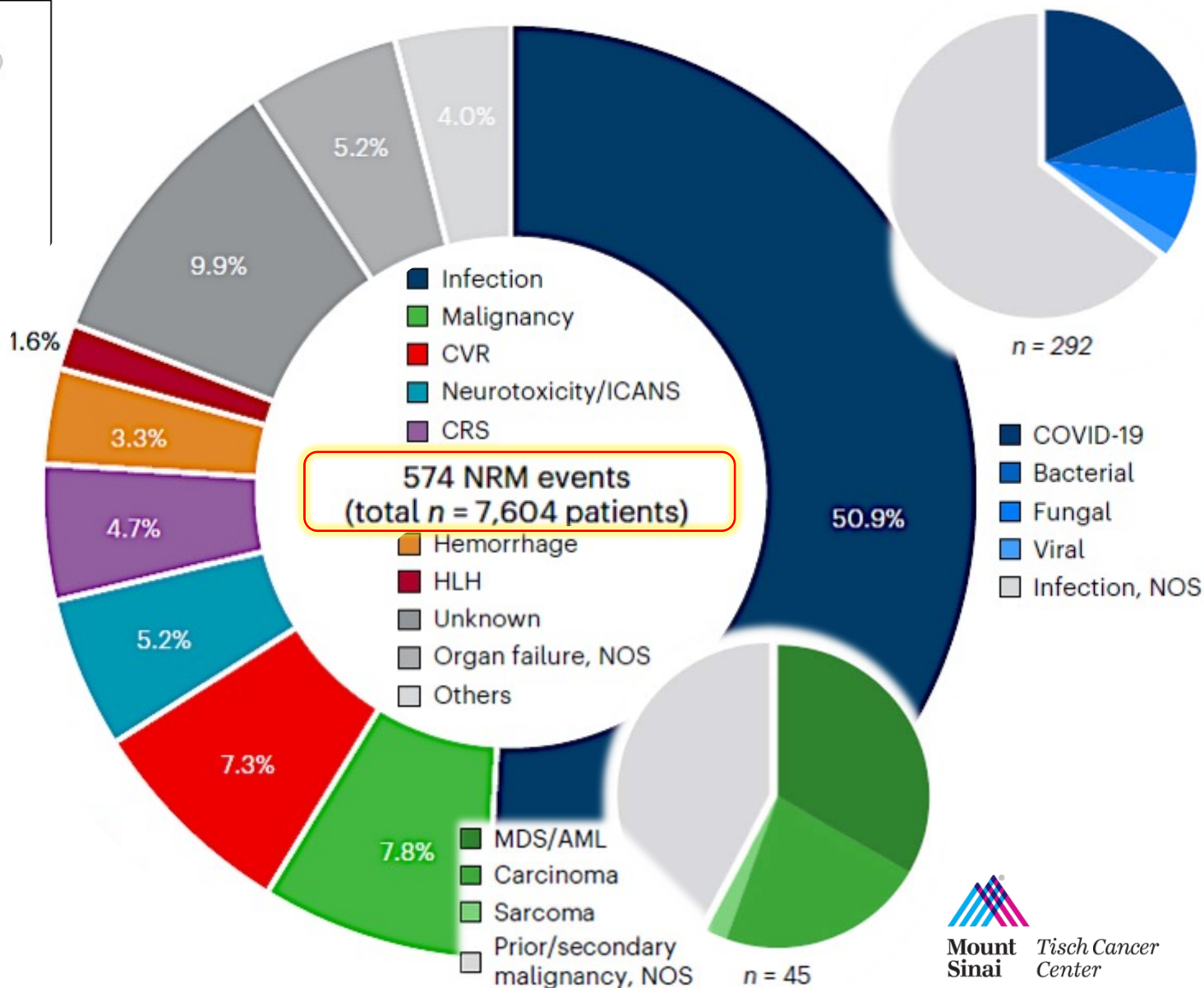
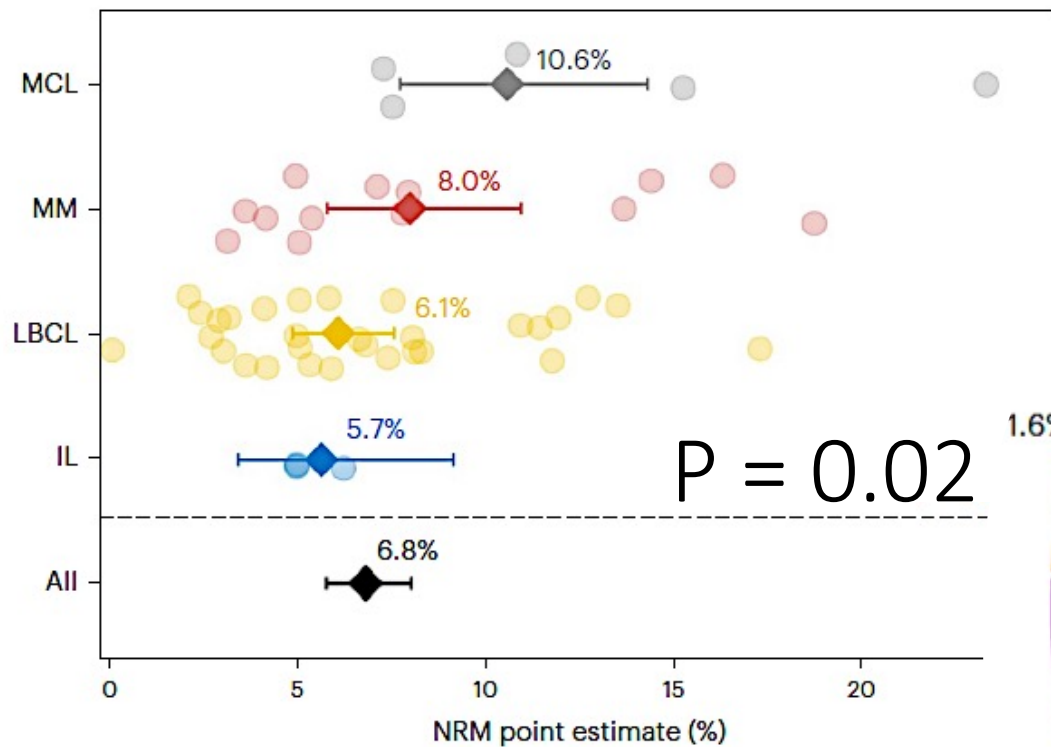
**Patient belongs to CAR-HEMATOTOX *high* risk group.**



# CAR T-Cells: Late toxicities - infections



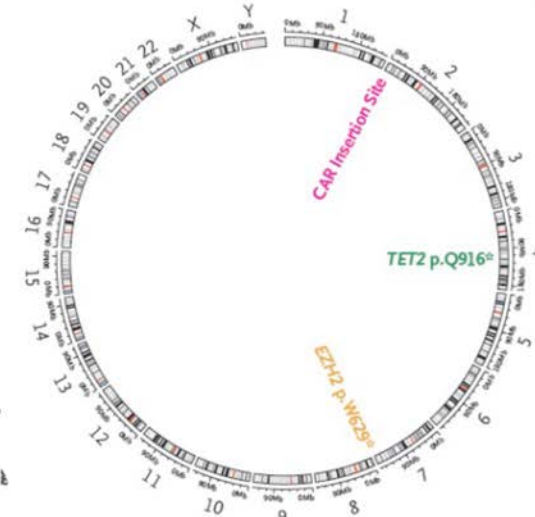
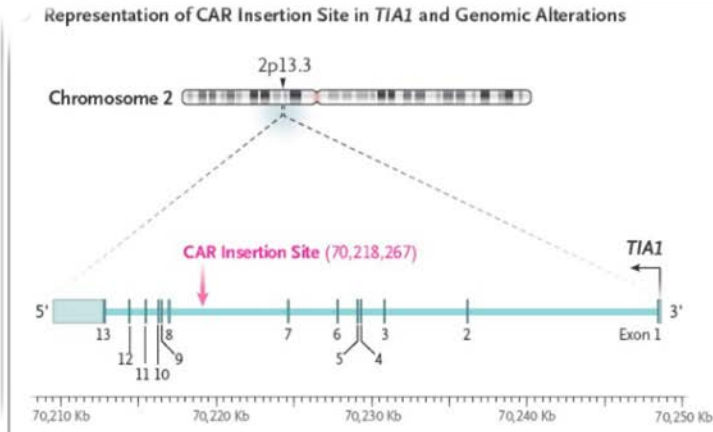
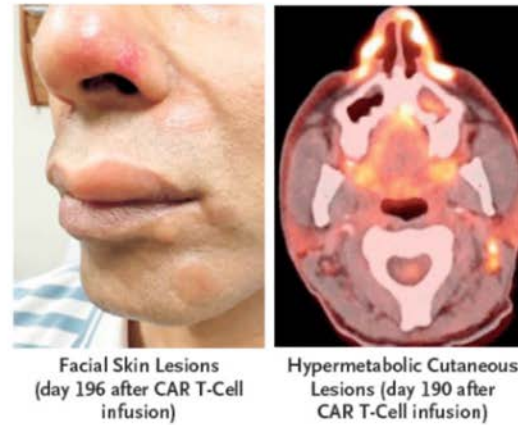
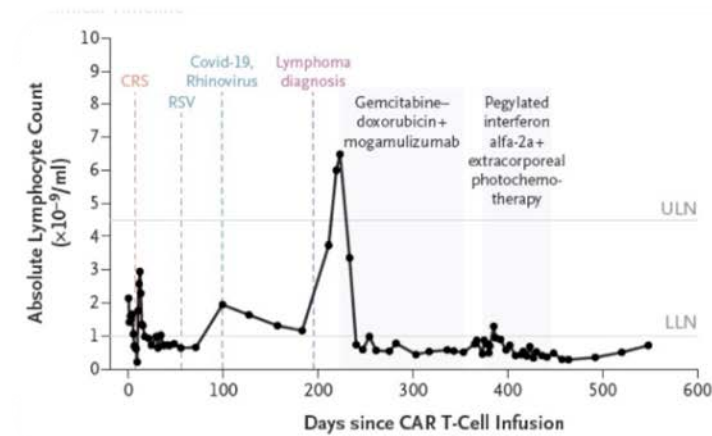
# CAR T-Cells: Late toxicities - infections



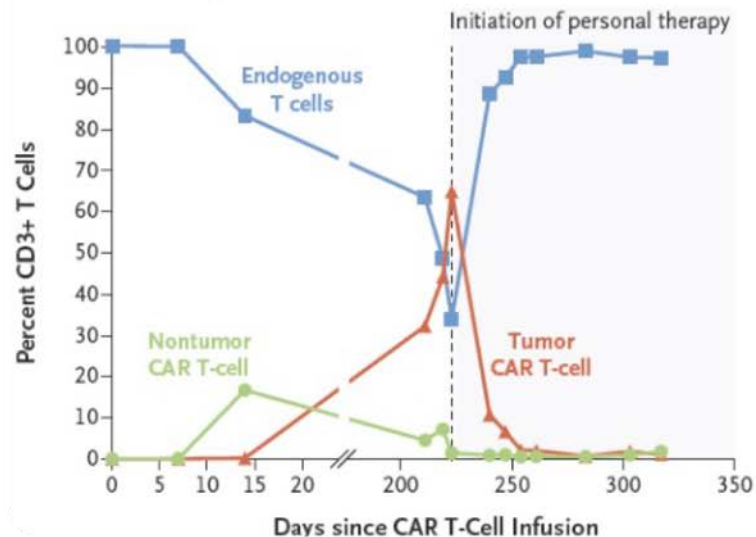
# Long-term tolerability/toxicity: secondary malignancy

## Targeted Therapy of CAR+ T-Cell Lymphoma after Anti-BCMA CAR T-Cell Therapy

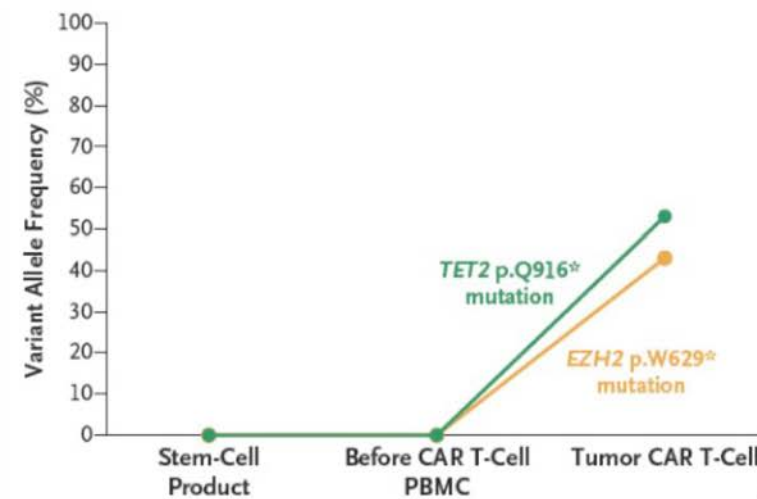
Published August 20, 2025 | N Engl J Med 2025;393:823-825 | DOI: 10.1056/NEJMc2504588 | VOL. 393 NO. 8



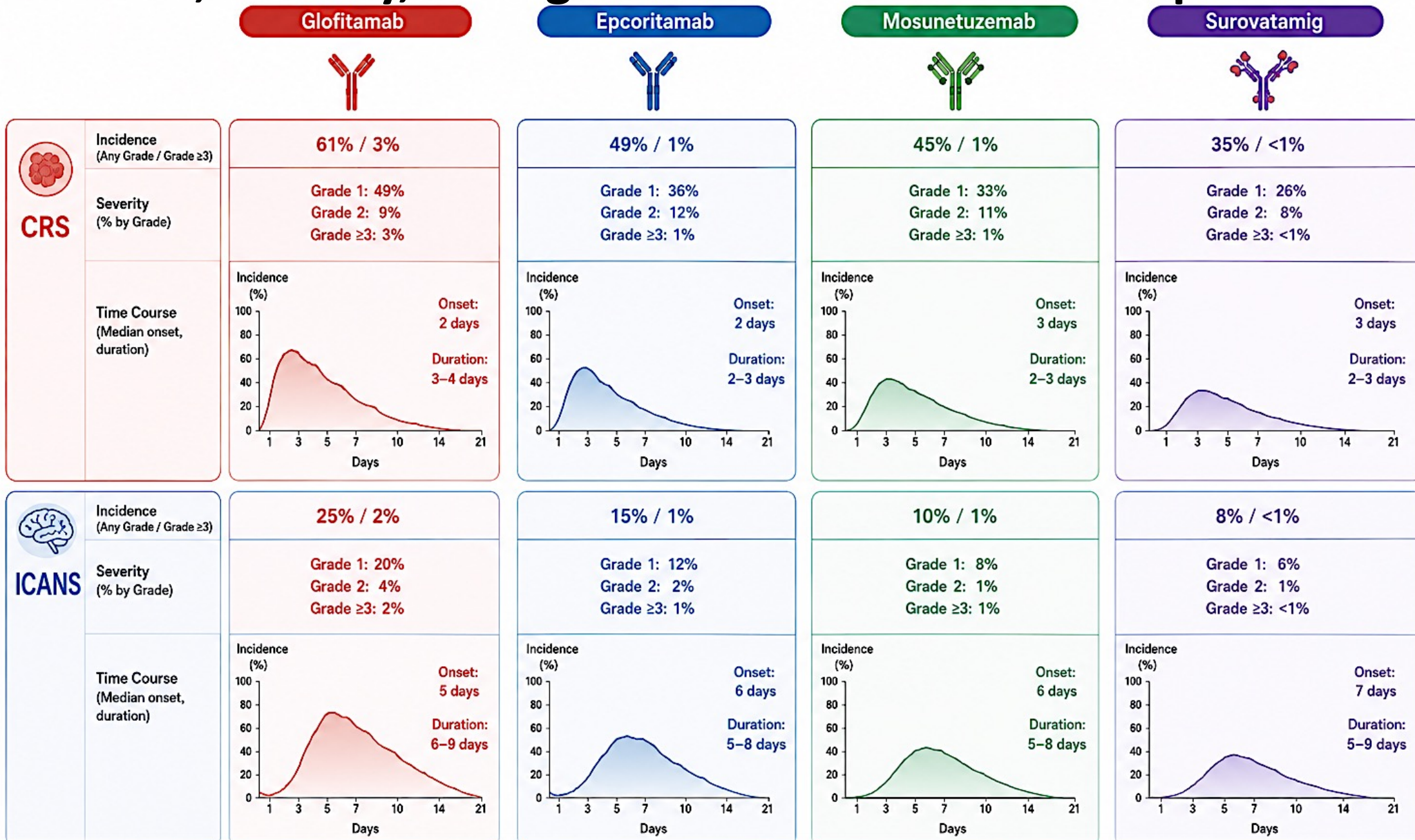
### B CD3+ T-Cell Composition after CAR T-Cell Infusion



### C Longitudinal Variant Allele Frequency by Whole Genome Sequencing



# Incidence, severity, timing of CRS and ICANS with bispecifics in B-NHL



## Fewer Infections with *Lymphoma* vs Myeloma Bispecifics

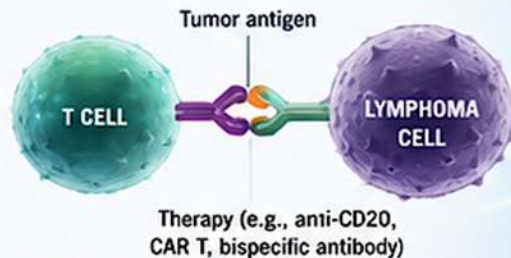
Agent		Grade ≥ 3 Infections	Grade 5 Infections	Grade ≥ 3 CRS	Grade ≥ 3 Neutropenia
Multiple Myeloma	BCMA target <sup>[1]</sup>				
	Linvoseltamab	29%	4%	1%	23%
	Elranatamab	32%	5%	0	48%
	Teclistamab	45%	12%	1%	64%
Multiple Myeloma	Non-BCMA target <sup>[1]</sup> (talquetamab)	18%	0	3%	37%
<b>Lymphoma</b>	<b>Mosunetuzumab<sup>[2]</sup></b>	<b>14%</b>	<b>–</b>	<b>1%</b>	<b>27%</b>
<b>Lymphoma</b>	<b>Epcoritamab<sup>[3]</sup></b>	<b>14%</b>	<b>–</b>	<b>2.5%</b>	<b>14.6%</b>

# Lymphoma Immunotherapy 2026: miraculous advances since 2000

## HOW IT WORKS: IMMUNOTHERAPY IN ACTION

### 1 RECOGNIZE

Immunotherapies help T cells recognize lymphoma cells as abnormal.



### 2 ACTIVATE

Therapies remove the brakes or provide a boost, activating T cells.



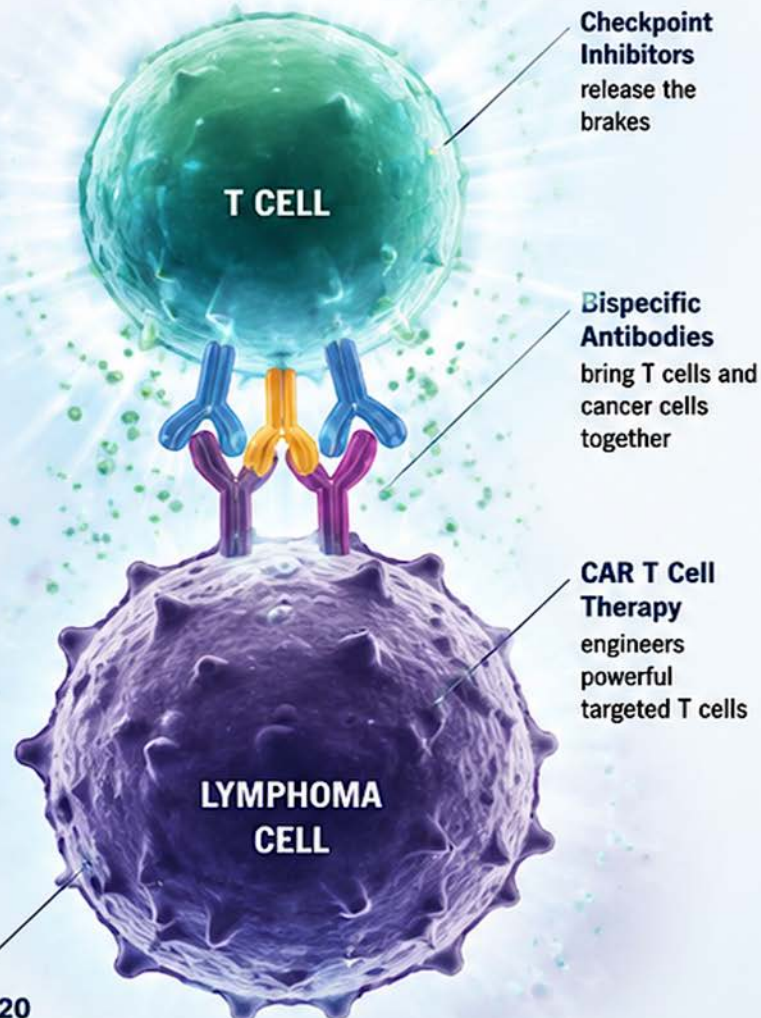
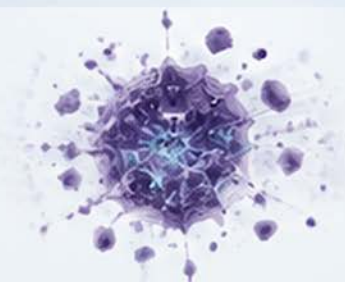
### 3 ATTACK

Activated T cells multiply and attack lymphoma cells.



### 4 ELIMINATE

Cancer cells are destroyed, leading to remission and longer, healthier lives.



Checkpoint Inhibitors release the brakes

Bispecific Antibodies bring T cells and cancer cells together

CAR T Cell Therapy engineers powerful targeted T cells

Anti-CD20 Antibodies mark cancer cells for destruction

# Discussion Questions

**71 y/o woman with FL with bulky symptomatic nodal disease**

**PMH: COPD, recurrent respiratory infections**

**Past treatments include weekly BR and R<sup>2</sup>**

**Currently receiving a bispecific antibody with good clinical response**

**What are the current best practices regarding infection prophylaxis, IVIG replacement and long-term monitoring for patients receiving bispecifics for FL?**

**For patients with NHL receiving bispecific antibodies, are you recommending prophylactic tocilizumab as is commonly done in multiple myeloma?**

# Discussion Questions

**72 y/o man with blastoid variant MCL with TP53 mutation  
R-CHOP/acalabrutinib as initial therapy with almost no response  
Treated with emergent fractionated cyclophosphamide/rituximab/  
radiotherapy followed by CAR-T; dramatic CR on PET  
Patient had grade 2 CRS and grade 1 ICANS**

**Is there more CRS and/or ICANS with CAR-T in MCL versus DLBCL or FL?  
If so, why?**

**How should we be monitoring patients with ongoing responses to CAR-T?  
Is there a time point after which toxicities are highly unlikely to occur?**

**Would the experts recommend any type of maintenance therapy post  
CAR-T, and if so what?**

# Discussion Questions

**50 y/o woman with stage 4, grade 2 FL diagnosed in 2012**

**BR as initial treatment; disease progression at 2 years**

**R-CHOP followed by 2 years of R maintenance as second-line therapy;**

**long-term remission with symptomatic progression in 2023**

**Mosunetuzumab as third-line therapy**

**Recurrent admissions for hematuria; cystoscopy shows hemorrhagic cystitis**

**Is hemorrhagic cystitis associated with mosunetuzumab?**

**Are there any uncommon toxicities with bispecific antibodies that community-based clinicians should know about?**

**What Clinicians Want to Know: Addressing Community  
Oncologists' Questions About the Current and Future Role of  
Antibody-Drug Conjugates in the Management of Breast Cancer**  
*A CME Symposium Held Adjunct with the 2026 ASCO® Annual Meeting*

**Monday, June 1, 2026**

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

**Faculty**

**Professor Giuseppe Curigliano, MD, PhD**

**Rebecca A Dent, MD, MSc**

**Erika Hamilton, MD**

**Nadia Harbeck, MD, PhD**

**Moderator**

**Hope S Rugo, MD**

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

*A CME Symposium Held Adjunct with the 2026 ASCO® Annual Meeting*

**Monday, June 1, 2026**

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

## **Faculty**

**Christopher Flowers, MD, MS, FASCO**

**Matthew Lunning, DO**

**Sonali M Smith, MD**

## **Moderator**

**Brad S Kahl, MD**

**Consensus or Controversy? Documenting  
and Discussing Investigators' Approaches to the  
Management of Relapsed/Refractory Multiple Myeloma**

*A CME Symposium Held Adjunct with the 2026 ASCO® Annual Meeting*

**Monday, June 1, 2026**

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

**Faculty**

**Melissa Alsina, MD**

**Hans Lee, MD**

**Paul G Richardson, MD**

**Moderator**

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

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

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

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