10th POSTGRADUATE
Lymphoma
Conference

PRO Bispecifics in Follicular Lymphoma

Martin Hutchings

Rigshospitalet and University of Copenhagen, Denmark

Venice,
March 12-13, 2026

Hotel Monaco & Grand Canal

President:
P.L. Zinzani

Disclosures

- **Advisory boards/consultancy:**
  - AbbVie, AstraZeneca, Genmab, Johnson&Johnson, Merck, Roche, Takeda
- **Research support (institution):**
  - AbbVie, AstraZeneca, Bristol Myers-Squibb, Celgene, Genentech, Genmab, Incyte, Johnson&Johnson, Merck, Novartis, Roche, Takeda

Jeremy Abramson

115K followers • 12 following

Truth teller • Artist • Entrepreneur

📍 Miami & Tel Aviv

Sharing unfiltered conversations on truth!

Digital creator

Message | Follow | Add friend

Phase 2 studies of CARTs in r/r FL versus old and cheap treatment

ELARA[1] – Tisagenlecleucel:

- ORR 86%
- CRR 68% (59% for POD24)
- PFS: 57% at 24 months

TRANSCEND FL[2] – Lisocabtagene maraleucel

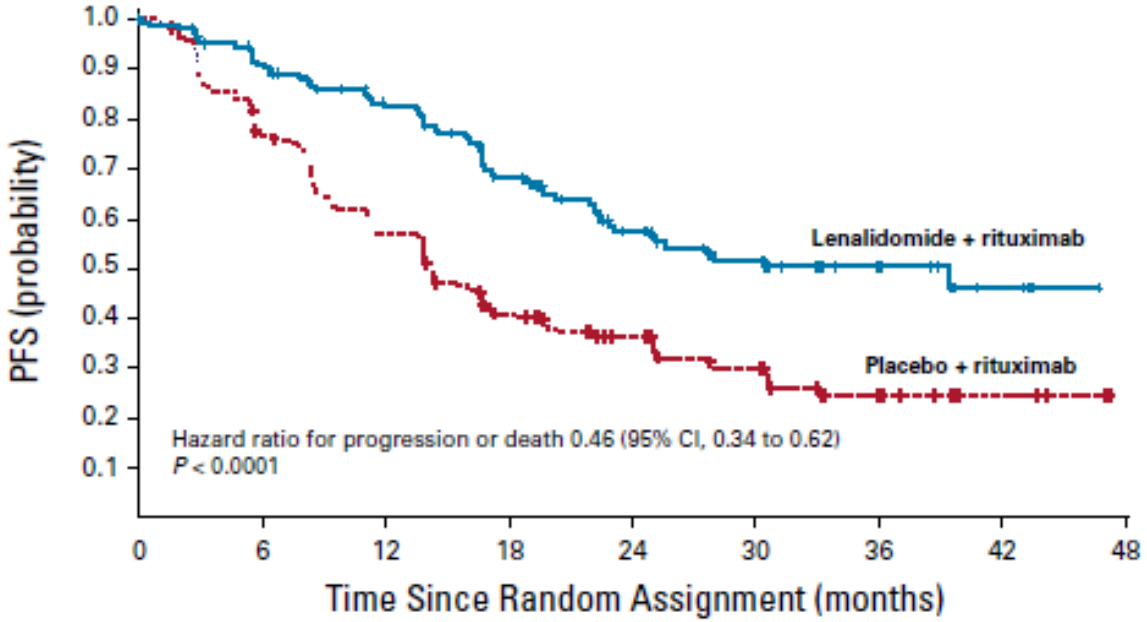
- ORR 93% (ITT)
- CRR 90% (ITT)
- PFS: 72% at 24 months[3]

ZUMA 5[4] – Axicabtagene ciloleucel:

- ORR 94%
- CRR 79%
- PFS: 54% at 36 months

AUGMENT[4] – Rituximab + lenalidomide:

- ORR 78%
- CRR 34% (by CT scan)
- PFS: ~82% at 12 months and 58% at 24 months



1. Dreyling M, et al. Blood 2024; 143 (17): 1713–1725.
2. Morschhauser F, et al. Nature Med 2024; 30(8): 2199-2207.
3. Nastoupil L, et al. ASH 2024, abstract #4387 (poster).
4. Neelapu SS, et al. Blood 2024; 143(6): 496-506.
5. Leonard JP, et al. J Clin Oncol 2019; 37: 1188-1199.

Data from phase 1b-2 studies of mosunetuzumab, odronextamab, epcoritamab, and glofitamab in r/r FL

Pivotal phase 2 study of mosunetuzumab in r/r FL

- **ORR 78%**
- **CRR 60%**

Pivotal, single-arm, Phase II expansion study in patients with R/R FL and ≥2 prior therapies (NCT02500407)

Key inclusion criteria

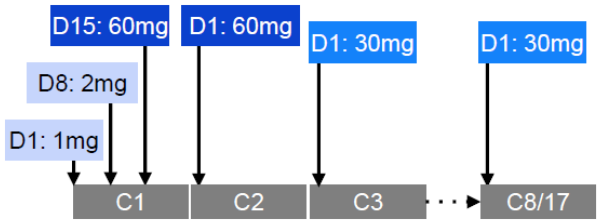
- FL Grade 1–3a
- ECOG PS 0–1
- ≥2 prior therapies including an anti-CD20 antibody and an alkylator

Data analysis

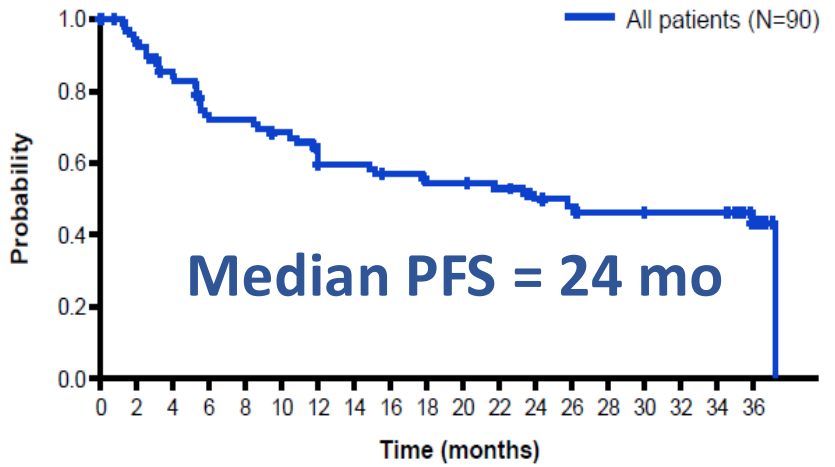
- Study met its primary endpoint: 60% CR rate versus 14% historic control ($p<0.0001$)[1,2]
- Updated efficacy and safety analysis with a median follow-up of 37.4 months

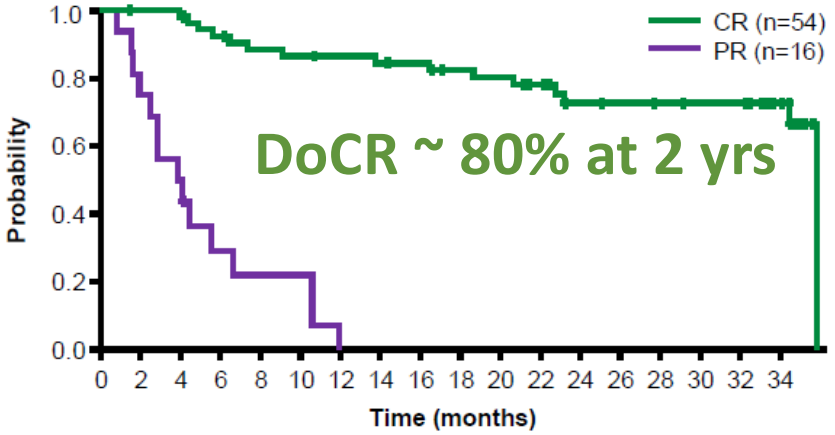
Mosunetuzumab administration

- IV mosunetuzumab administered in 21-day cycles with step-up dosing in C1
- Fixed-duration treatment: 8 cycles if CR after C8; 17 cycles if PR/SD after C8
- Retreatment with mosunetuzumab permitted at relapse for patients who achieved CR
- No mandatory hospitalization



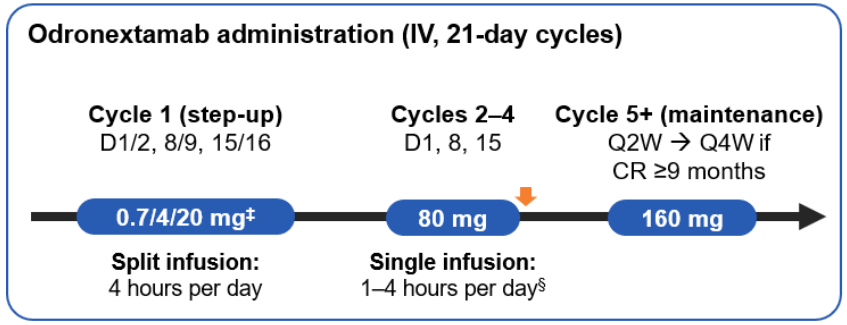
Refractory to last prior therapy	62 (69%)
Refractory to any prior anti-CD20 therapy	71 (79%)
POD24	47 (52%)
Double refractory to prior anti-CD20 and alkylator therapy	48 (53%)





Budde LE, et al. Lancet Oncol 2022;23:1055-65.
Sehn L, et al. Blood 2025, 145(7): 708–719.

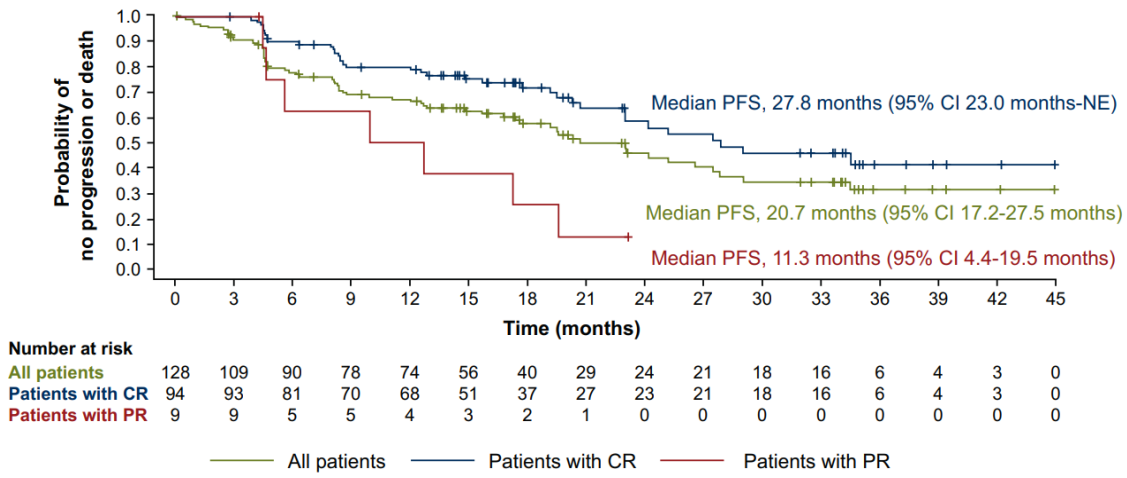
Phase 2 study of odronextamab in r/r FL (ELM-2)

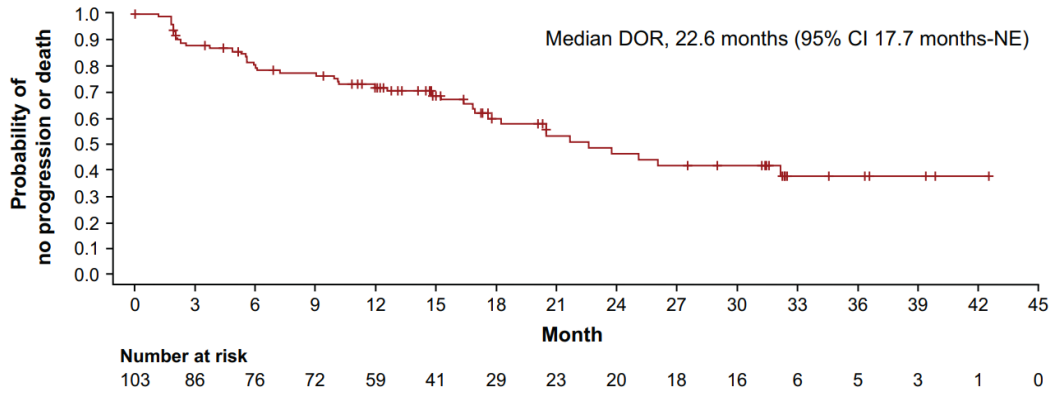


Refractory to last line of therapy, %	**72**
Refractory to anti-CD20 antibody, %	74
Double refractory to alkylator and anti-CD20 antibody, %	41
POD24, %	49

In 128 FL patients, median FU 20 months:

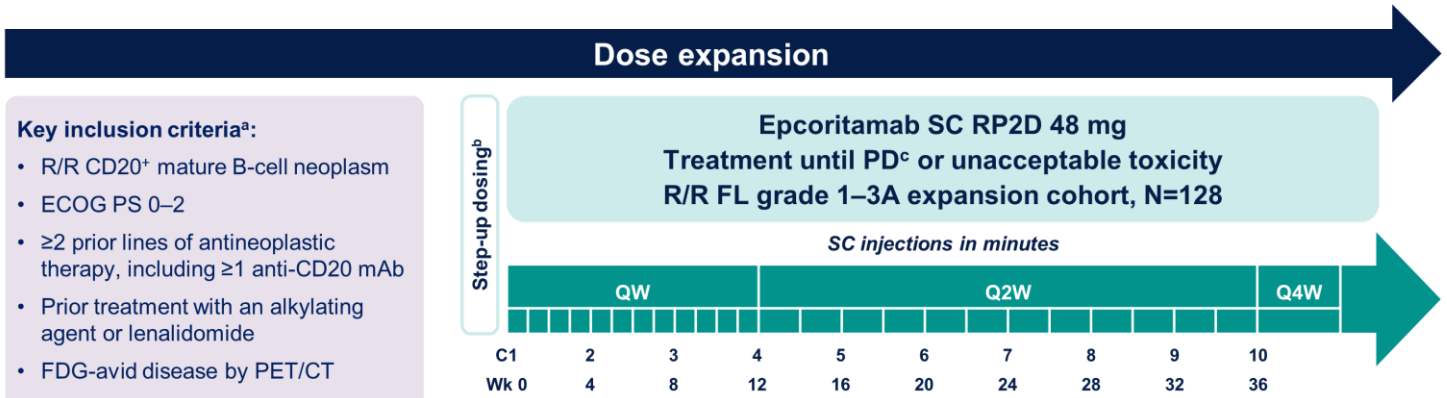
- ORR 80%
- CRR 73%
- Median PFS 21 months
- 2-year PFS rate 46%
- No impact of POD24 on response





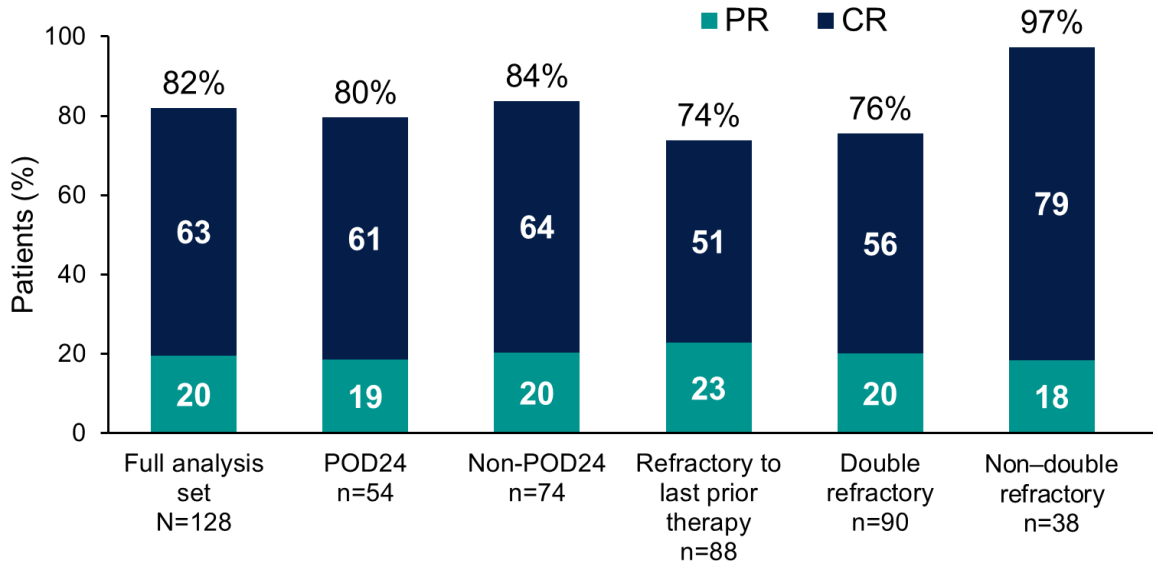
Chong G, et al. AACR 2024, abstract CT243.
Kim TM, et al. Ann Oncol 2024; 35(11): 1039-1047.

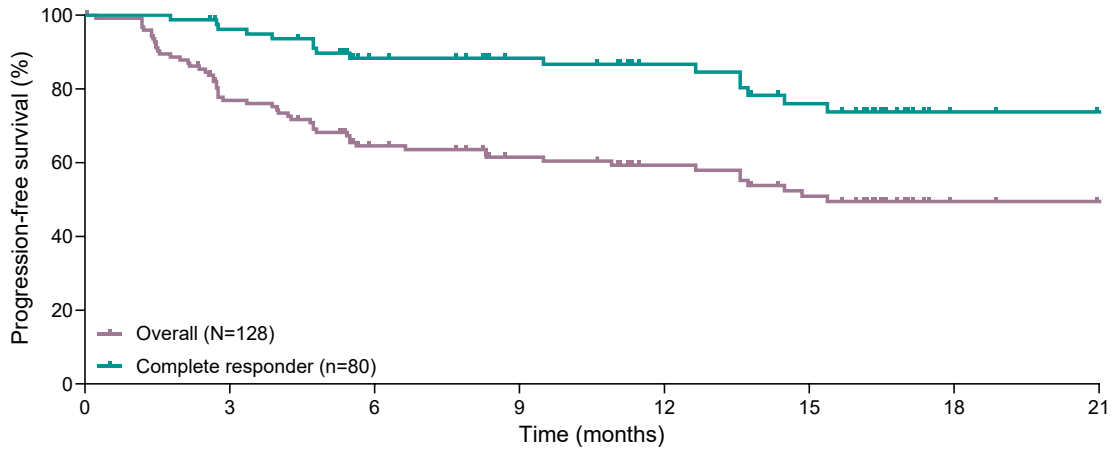
FL expansion cohort from the phase I-II study of epcoritamab in B-NHL (EPCORE NHL-1)



≥4 prior lines, n (%)	40 (31)
POD24,[a] n (%)	54 (42)
Double refractory,[b,c] n (%)	90 (70)
Primary refractory,[b] n (%)	69 (54)
Refractory[b] to last prior systemic therapy, n (%)	88 (69)

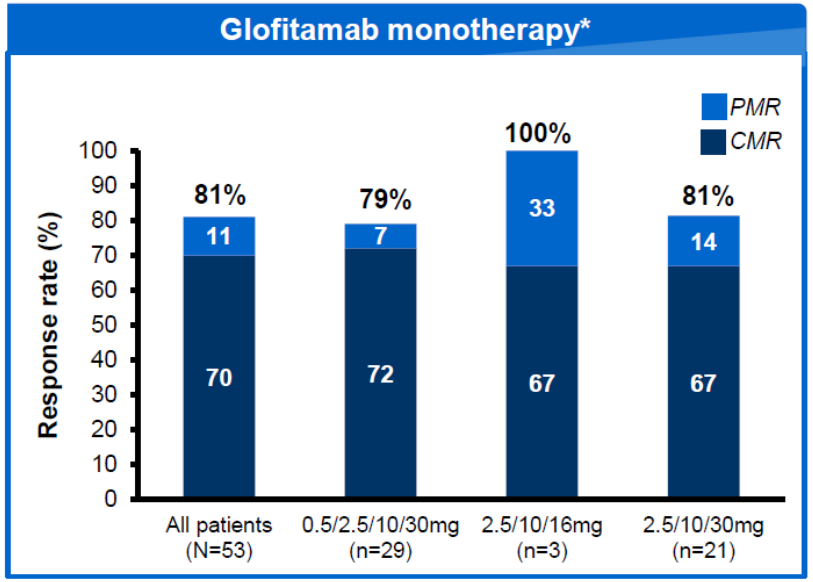
ORR: 82%
CRR: 63%
Median PFS: 15.4 months

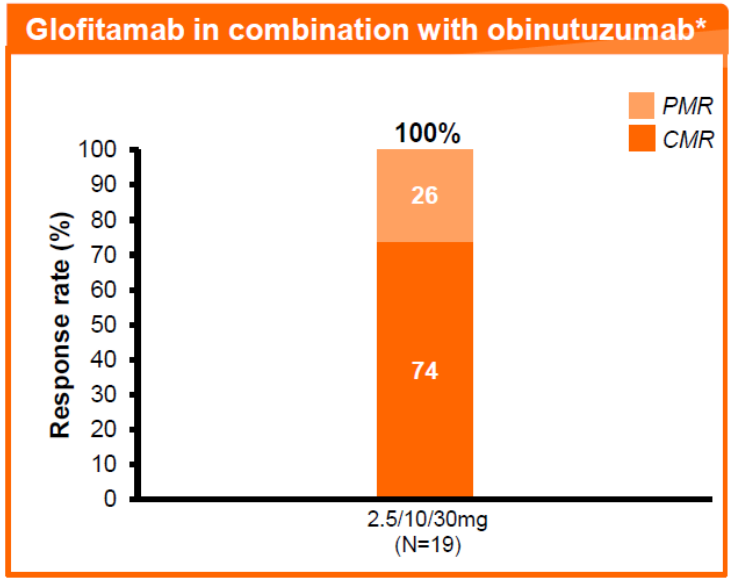


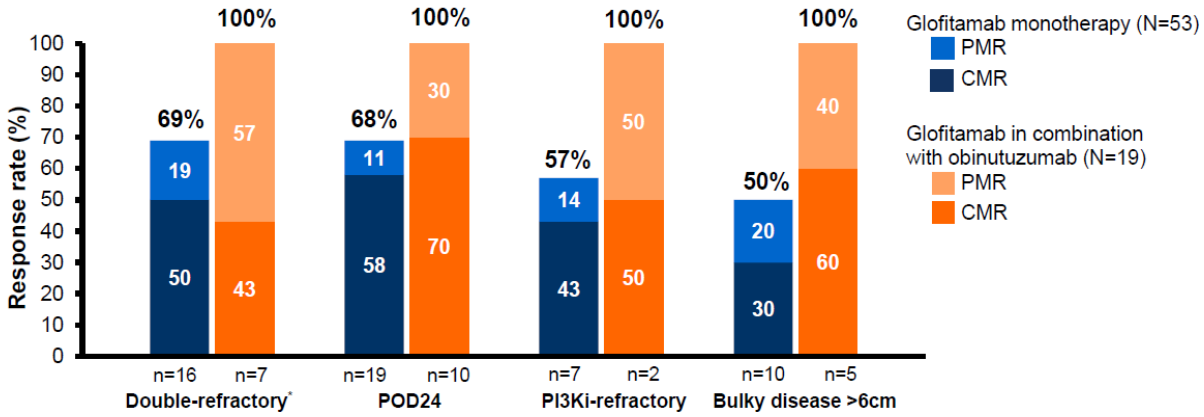


Linton K, et al. Ann Oncol 2024; 11(8): e593-e605.

Glofitamab alone and in combination with obinutuzumab in r/r FL



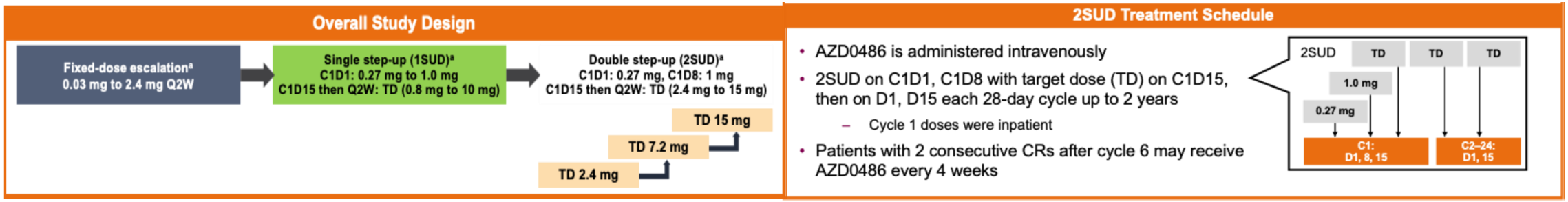


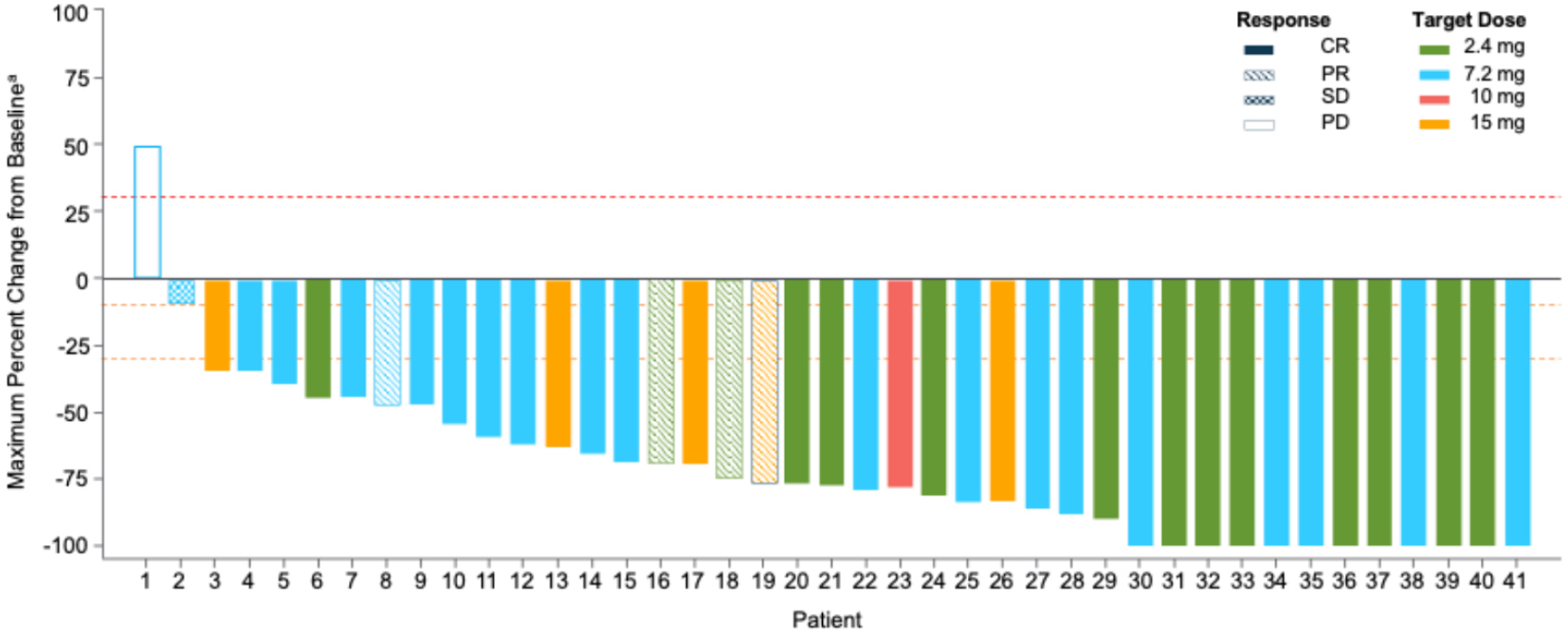


N (%) of patients unless stated	Glofitamab + obinutuzumab cohort (N=19)
Refractory to any prior therapy	13 (68.4)
Refractory to most recent therapy line	8 (42.1)
Refractory to any prior anti-CD20	10 (52.6)
Double-refractory*	7 (36.8)
POD24	10 (52.6)
PI3K inhibitor-refractory	2 (10.5)
Bulky disease >6cm	5 (26.3)

Morschhauser F, et al. ASH 2021, abstract #128.

AZD0486 (surovatamig) in r/r FL (bispecific CD19xCD3 antibody)





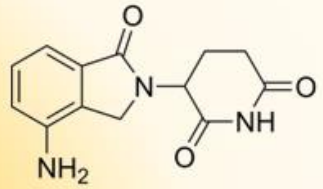
- **ORR was 95% and CR rate 85%** in patients who received AZD0486 ≥2.4 mg (n=41)
- Activity in patients with POD24, prior CD3xCD20 BsAb, or prior CAR-T exposure
- MRD negativity in 96% of patients treated at doses ≥2.4 mg (PhasED-seq)

Hou J-Z, et al. ASH 2024, abstract #341 (oral).

Bispecific antibodies alone or in combination?

Conventional chemotherapy
- Bendamustine
- CHOP

Immunomodulators
- Lenalidomide +/- R
- Golcadomide



Bispecific antibody

Co-stimulatory bispecifics
- Englumafusp alfa (CD19x41-BBL)
- REGN5837 (CD22xCD28)

Antibody-drug conjugates
- Polatuzumab vedotin (CD79b)
- Loncastuximab tesirine (CD19)

Phase Ib study of mosunetuzumab + lenalidomide in R/R FL

Study design

Key inclusion criteria

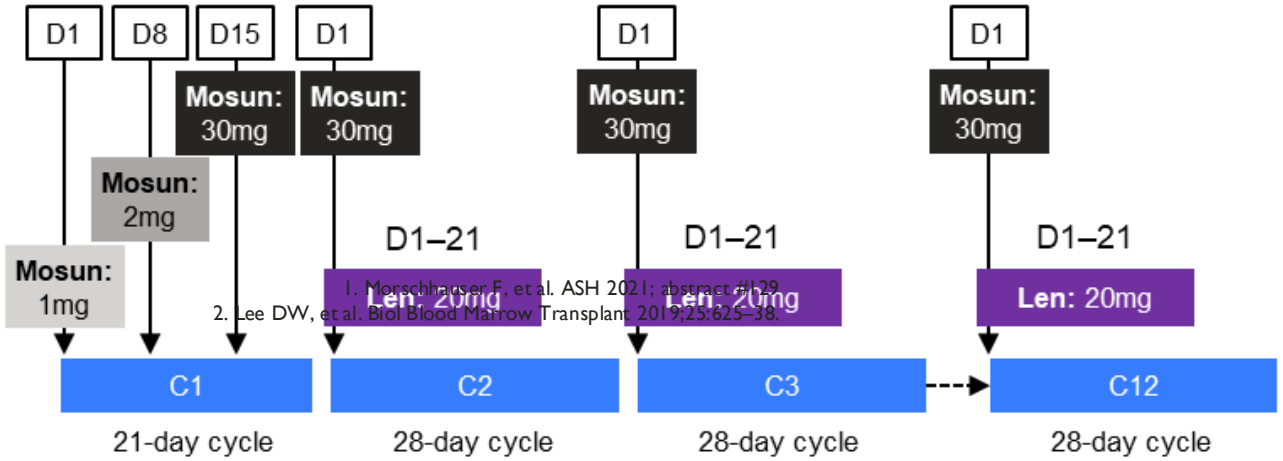
- CD20+ FL Grade 1–3a; ECOG PS 0–2
- R/R to ≥1 prior CIT regimen including an anti-CD20 antibody; prior lenalidomide allowed

Primary objective

- Safety and tolerability of M-Len

Mosunetuzumab IV (up to 12 cycles)

- C1 step-up dosing (CRS mitigation)
- No mandatory hospitalization



1. Morschhauser F, et al. ASH 2021; abstract #129.
2. Lee DW, et al. Biol Blood Marrow Transplant. 2019;25:625–38.

Efficacy

(no = 29)

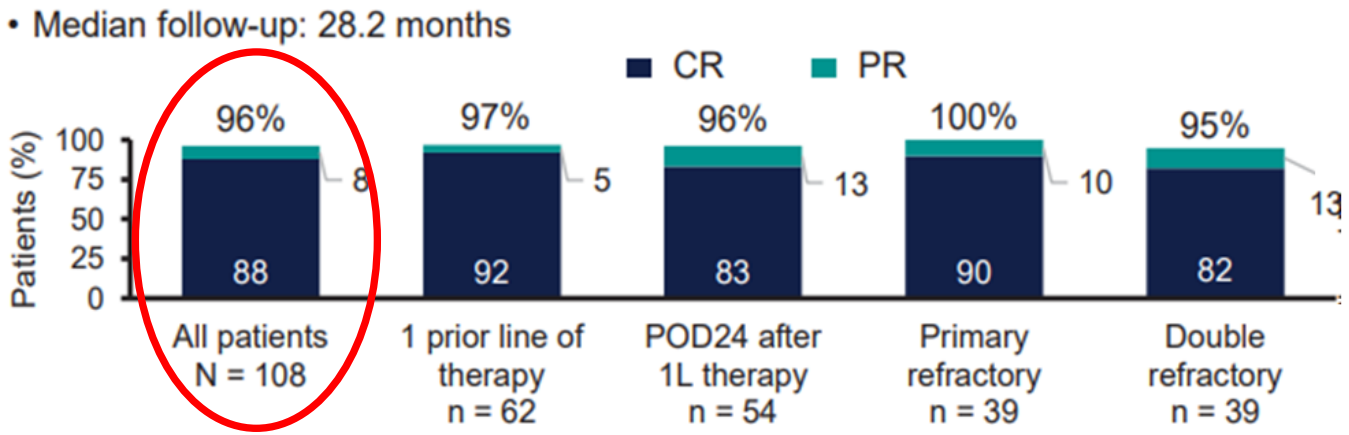
- ORR: 89.7%; CMR rate: 65.5%
- CMR rates by subgroup: POD24 (n=3), 66.7%; anti-CD20 refractory (n=9), 55.6%; double refractory (n=7), 42.9%

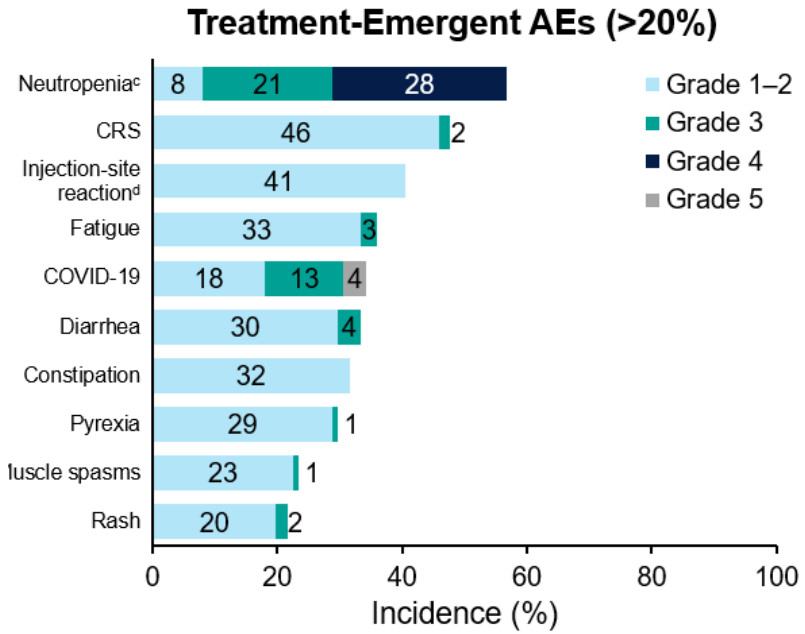
Safety

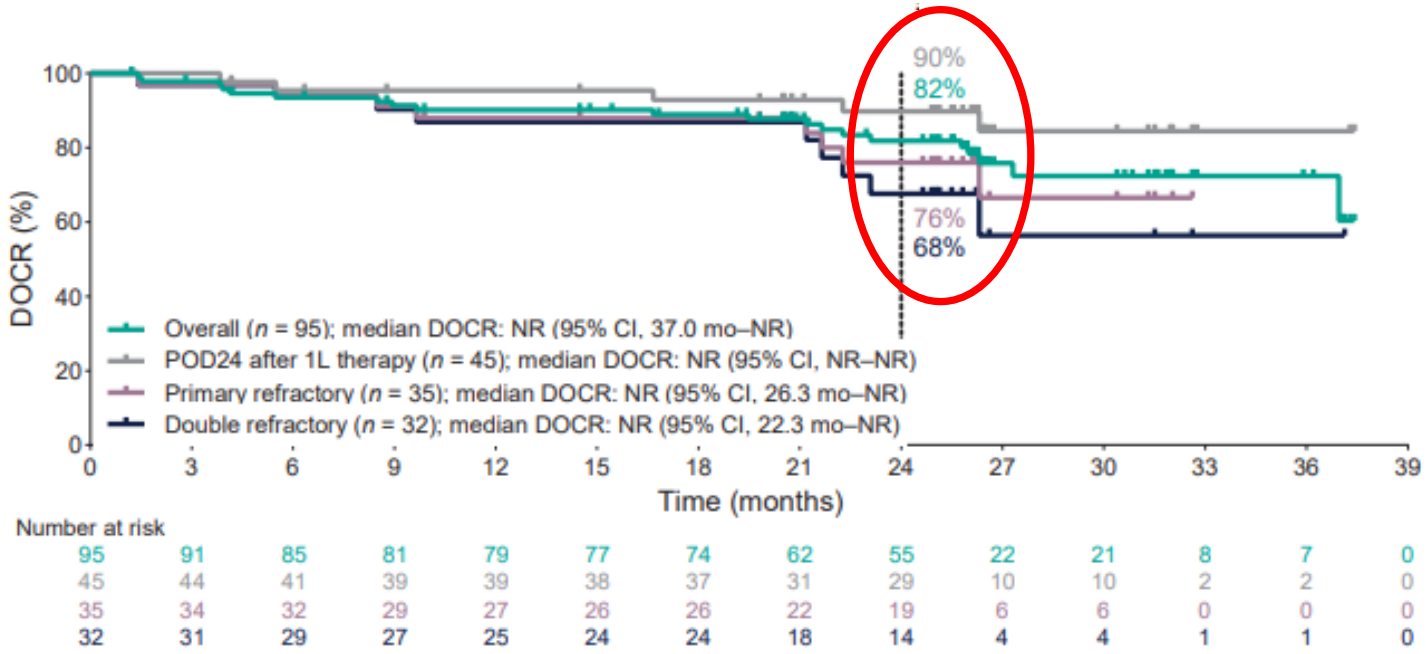
- No Grade 5 AEs or AEs leading to mosunetuzumab discontinuation
- CRS:* 27.6% (any grade), all resolved; no Grade ≥3 events

Morschhauser F, et al. ASH 2021; abstract #129

Phase Ib/II study of fixed-duration epcoritamab + R^2 in patients with R/R FL







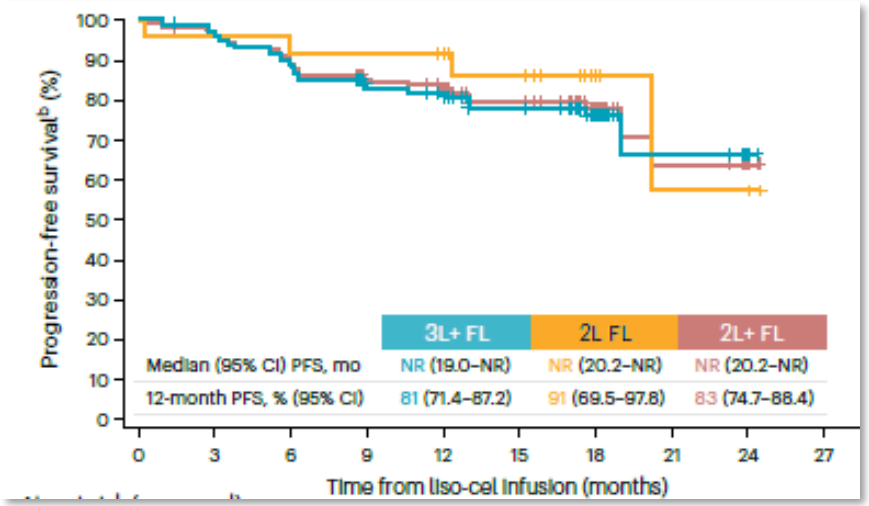
Falchi L, et al. Blood 2025, Sep 8: doi: 10.1182/blood.2025029909. Online ahead of print.

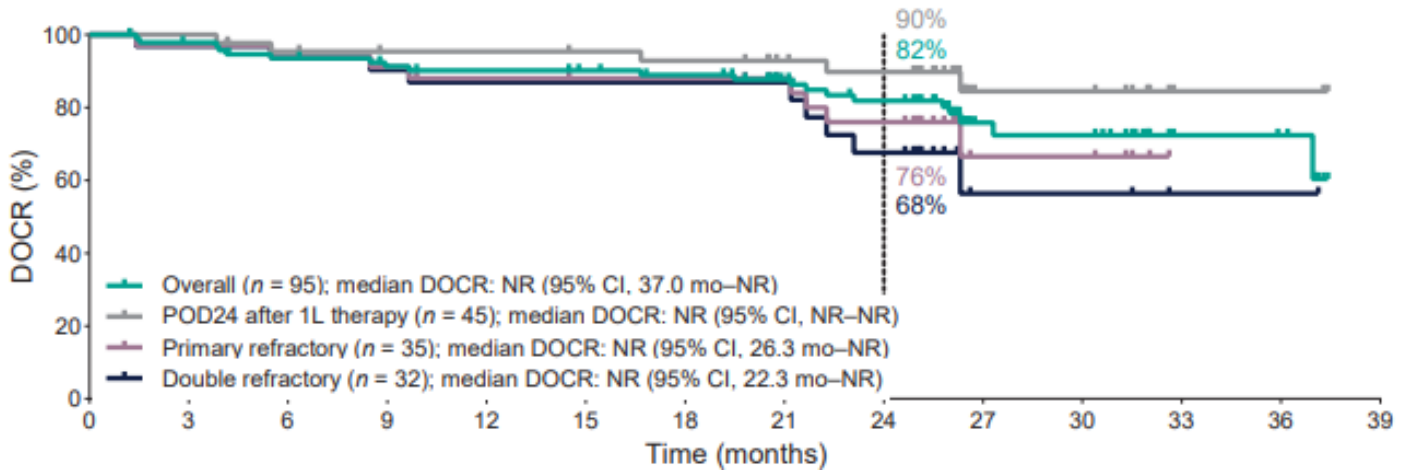
TRANSCEND FL (Liso-cel)

- 139 patients
- CRS: 59%, mainly grade 1-2
- ICANS: **15%**
- MAS/HLH in one patient
- Second primary malignancies in 4 patients
- ORR 93%
- CRR 90%
- PFS: 72% at 24 months

EPCORE NHL-2 arm 2 (Epco + R^2)

- 111 patients
- CRS: 48%, mainly grade 1-2
- ICANS: **2%**
- MAS/HLH not observed
- Second primary malignancies not observed
- ORR 96%
- CRR 88%
- PFS: 82% at 24 months (90% for POD24)





Morschhauser F, et al. Nature Med 2024; 30(8): 2199-2207.
Nastoupil L, et al. ASH 2024, abstract #4387 (poster).
Falchi L, et al. Blood 2025;

Ongoing phase 3 studies of bispecific antibodies in combination with lenalidomide in R/R FL

Regimen	Trial (Phase)	Patients (R/R FL cohorts)	Treatment duration and administration	Primary endpoint	Study status
Mosunetuzumab-Len versus R-Len	**CELESTIMO** (Phase III)[1]	478[1]	**Mosunetuzumab** (IV) 12 cycles **Len** (oral) 12 cycles[1]	PFS (by IRC)[1]	Active, not recruiting[1]
Odronextamab-Len versus R-Len	**OLYMPIA-5** (Phase III)[2]	~352[2]	**Odronextamab** (IV) 12 cycles **Len** (oral) 12 cycles[2]	Safety and PFS (by IRC)[2]	Recruiting[2]
Epcoritamab *+ R-Len versus R-Len*	***EPCORE FL-1*** *(Phase III)[3]*	*549[3]*	***Epcoritamab*** *(SC) 12 cycles* ***Len*** *(oral) 12 cycles[3]*	*ORR and PFS (by IRC)[3]*	*Results available[4]*

1. NCT04712097. Available at: https://clinicaltrials.gov/study/NCT04712097
2. NCT06149286. Available at: https://clinicaltrials.gov/study/NCT06149286
3. NCT05409066. Available at: https://clinicaltrials.gov/study/NCT05409066
4. Falchi L, et al. ASH 2025 and Lancet 2026; 407(10524): 161-173.

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

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^2

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

R^2

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

Stratification factors

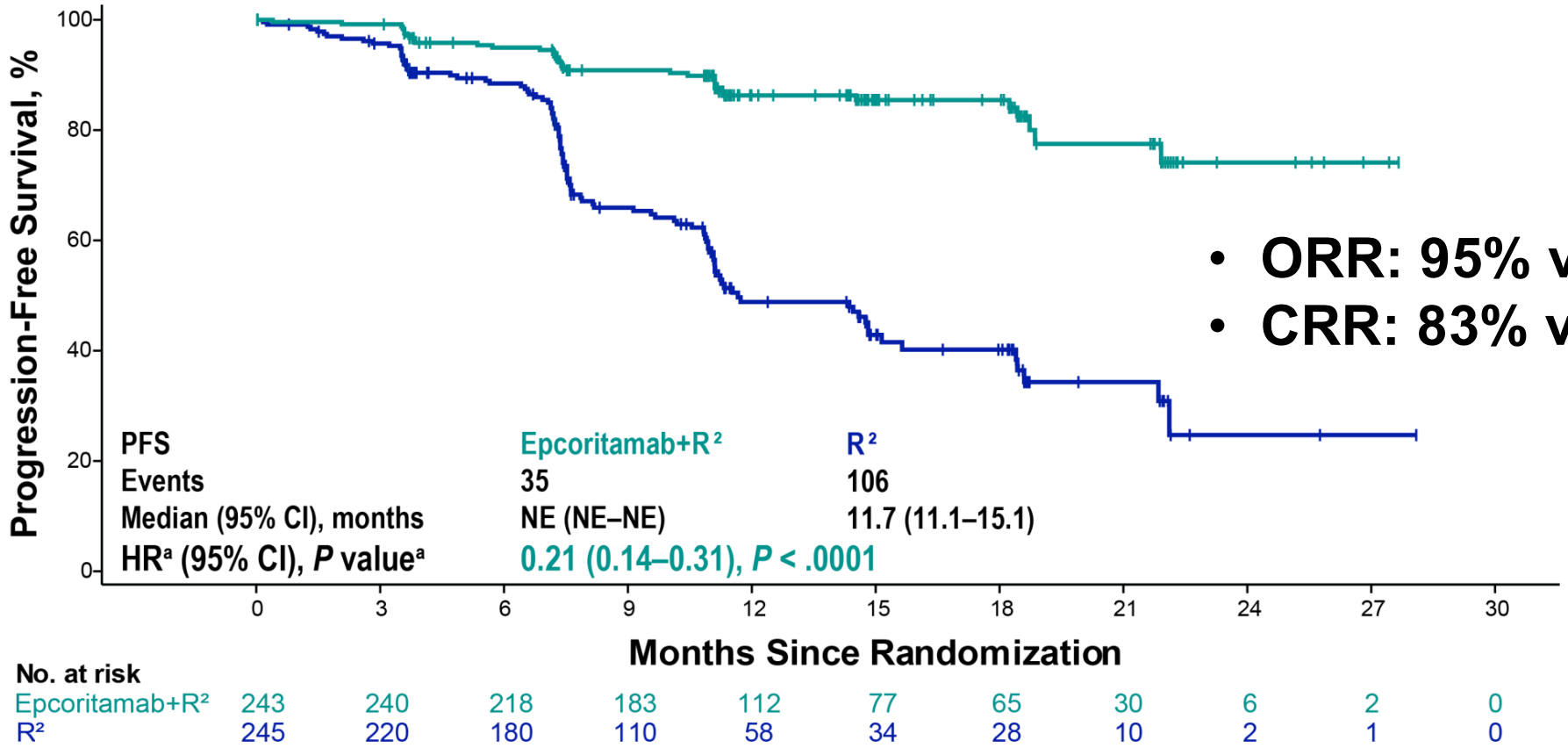
- Disease status:
  - 2L: > or ≤ 2 years since last therapy
  - 3L+: > or < 6 months since last therapy
- Region: US/EU vs Rest of World

- **Dual primary endpoints: ORR per IRC and PFS per IRC**
- Key secondary endpoints: CR rate per IRC, OS, and MRD[c]
- Additional secondary endpoints: DOR, DOCR, TTNLT, safety, and PRO assessments

Data cutoff: May 24, 2025; median follow-up: 14.8 months[d]
Enrollment period: October 2022 - January 2025

Falchi L, et al. ASH 2025 and Lancet 2026; 407(10524): 161-173.

EPCORE FL-1: Superior PFS of epco+R with 79% risk reduction

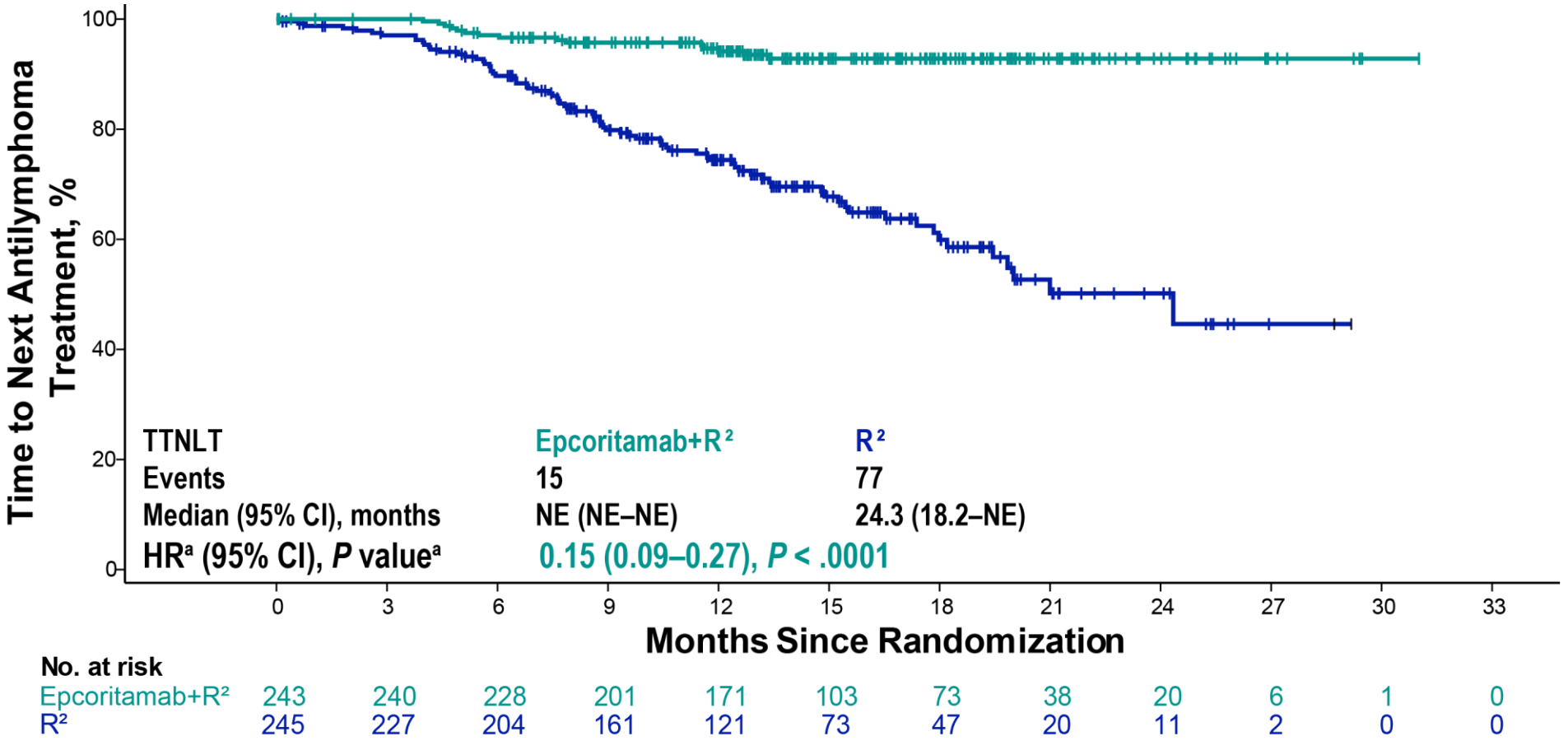


- **ORR: 95% vs. 79%**
- **CRR: 83% vs. 50%**

- 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^2 and 40.2% (95% CI: 31.8, 48.4) for R^2
- Median FU 14.4 months

Falchi L, et al. ASH 2025 and Lancet 2026; 407(10524): 161-173.

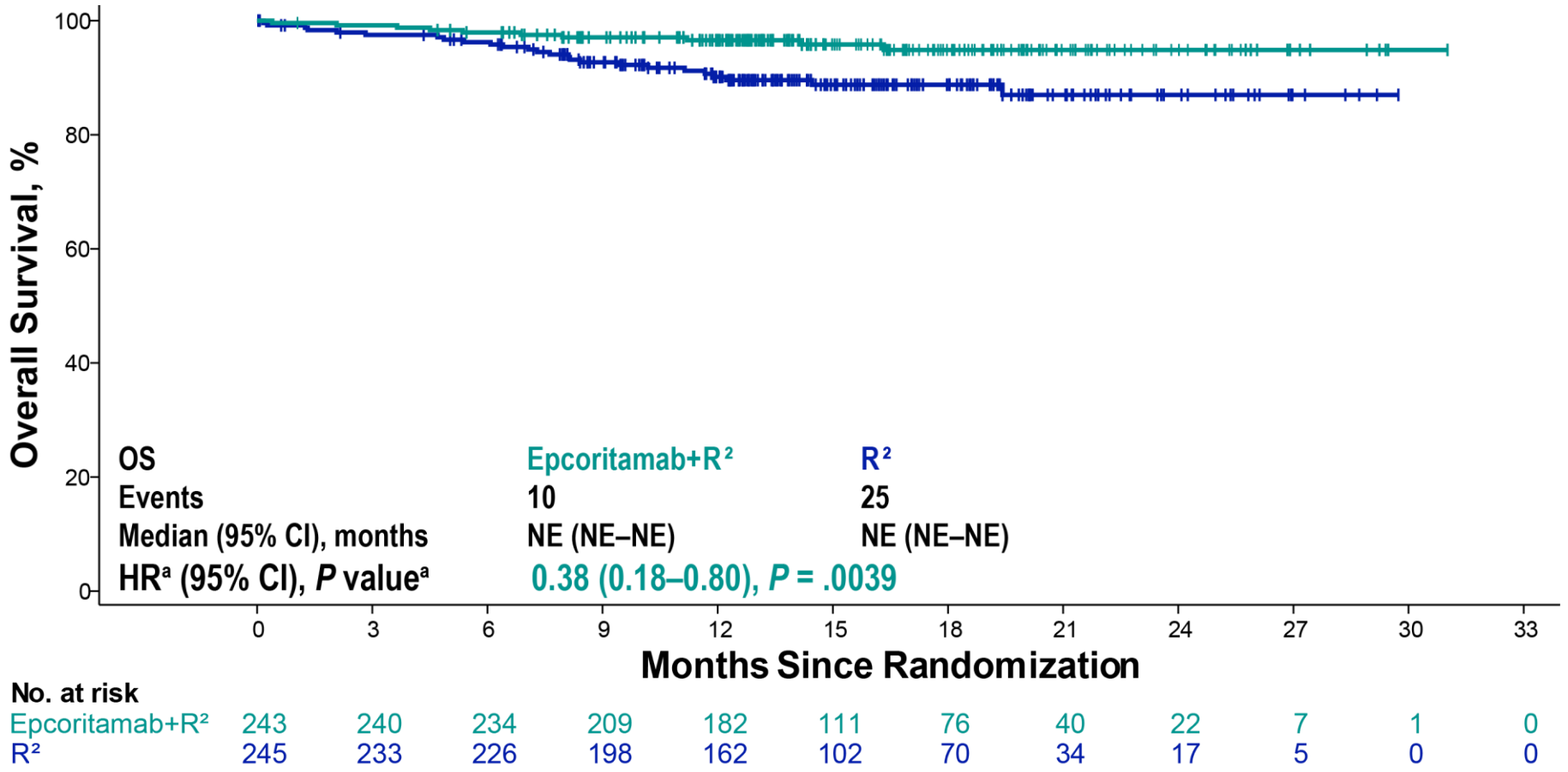
EPCORE FL-1: Time to next treatment



- At 16 months, 92.8% of patients treated with epcoritamab+R^2 remained free from new anti-lymphoma treatment compared with 64.9% of patients treated with R^2

Falchi L, et al. ASH 2025 and Lancet 2026; 407(10524): 161-173.

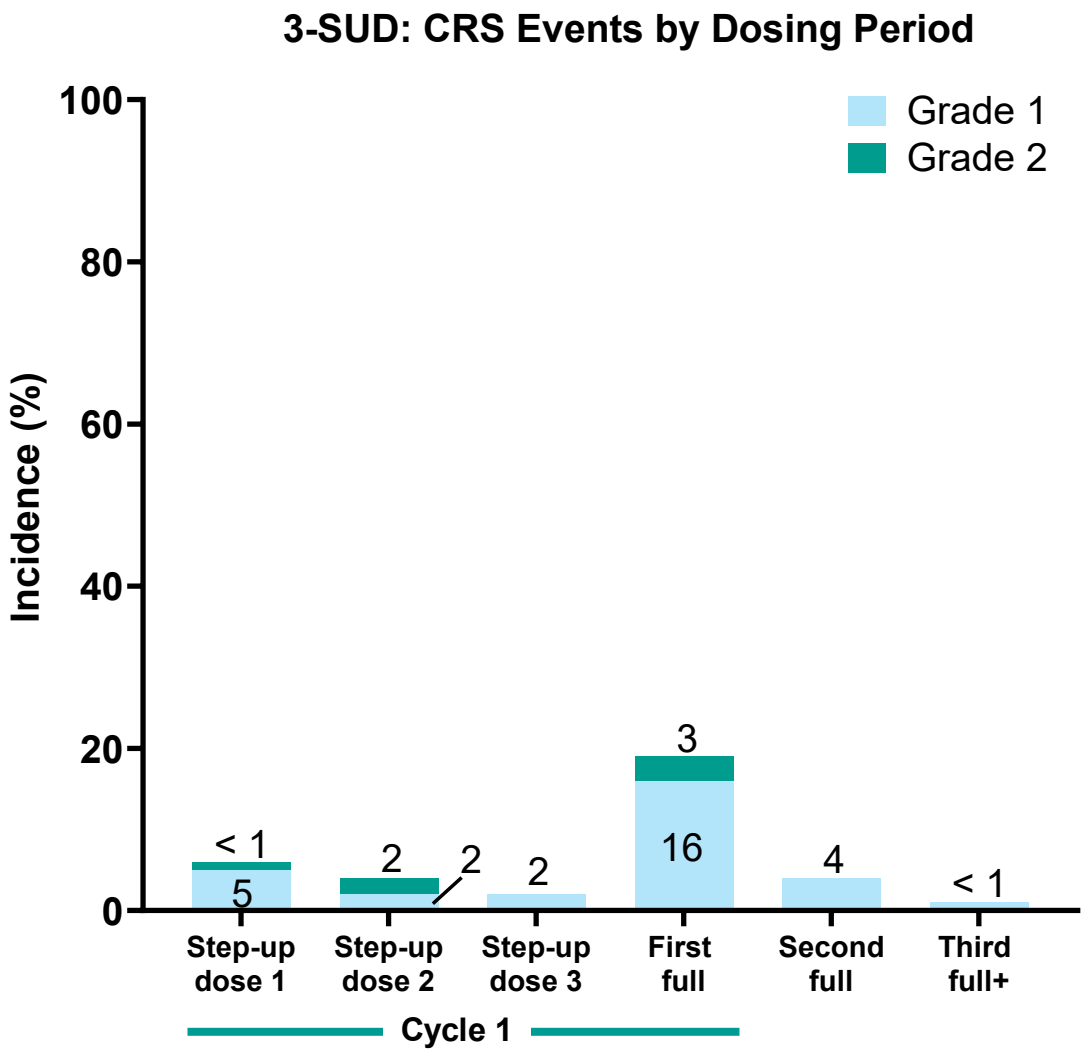
EPCORE FL-1: Overall survival



- The 16-month estimate for OS was 95.8% with epcoritamab+R^2 and 88.8% with R^2

Falchi L, et al. ASH 2025 and Lancet 2026; 407(10524): 161-173.

EPCORE FL-1: Cytokine release syndrome and ICANS



	Epcoritamab+R^2 2-SUD N = 110	Epcoritamab+R^2 3-SUD[a] 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 (%)*		
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 (%)*		
Treated with tocilizumab	12 (24)	9 (26)
Treated with corticosteroid	23 (46)	13 (37)

*Of patients who had CRS

- One event of ICANS was observed and was grade 1
- No discontinuations due to CRS and ICANS. All events resolved.

Falchi L, et al. ASH 2025 and Lancet 2026; 407(10524): 161-173.

Why bispecific antibodies in r/r FL?

- Single-agent activity
  - Mosun: ORR 78% and CRR 60%, mPFS 24mo
  - Epco: ORR 82% and CRR 63%, mPFS 15 mo
  - Glofitamab: ORR 81%, CRR 70%
  - Odronextamab ORR 80%, CRR 73%
  - (Mosunetuzumab and Epcoritamab are FDA and EMA approved for treatment of r/r FL with ≥ 2 prior treatment lines)
- Toxicity profile
  - Very little CRS > grade 2
  - Very little treatment-related CNS toxicity
- Simplicity
  - Off-the-shelf and easy to deliver
- Price
  - Not as expensive as CARTs
  - You can stop treatment if no CR, as only complete responses are durable
- Combinability
  - Epco + R^2: ORR 96%, CRR 88%, 24-m PFS 82%
  - Glofit + Obinutuzumab: ORR 100%, CRR 74%
  - Mosun + lenalidomide: ORR 90%, CRR 66%
- Randomised evidence
  - Epco + R^2 is superior to R^2 and recently FDA approved for the treatment of r/r FL with ≥ prior treatment lines

UNIVERSITY OF COPENHAGEN

Trial Nation
Clinical Trials Denmark

Phase 1 Unit, Haematology translational research team:

Simon Husby
Emil Kyvsgaard
Chiara Bancone

Phase 1 team, Clinical research unit, Department of Haematology, Rigshospitalet:

Tina Bjerg, Claudia Jensen, Karina Juhls, Maria Lind, Chris Mathiasen, Sissel Brendes Olsen, Nikoline Rykind-Eriksen

Phase 1 Unit, Departments of Oncology and Haematology, Rigshospitalet:

Haematology consultants:
Caroline Riley
Claudia Schöllkopf

Oncology consultants:
Martin Højgaard
Kristoffer Rohrberg
Lise Høj Omland
Ulrik Lassen

Lymphoma and CLL team, Department of Haematology, Rigshospitalet:

Fazila Asmar
Mads Emil Bjørn
Peter de Nully Brown
Caspar da Cunha-Bang
Lisbert Enggaard
Anne Ortved Gang
Jette Gørløv
Troels Hammer
Pär Josefsson
Carsten Niemann
Jindrich Mourek
Michael Pedersen
Caroline Riley
Dorte Tholstrup

Backup slides:
Bispecifics in 1st line treatment of FL

MITHIC-FL1 Trial: Mosunetuzumab monotherapy in untreated FL

Endpoints:

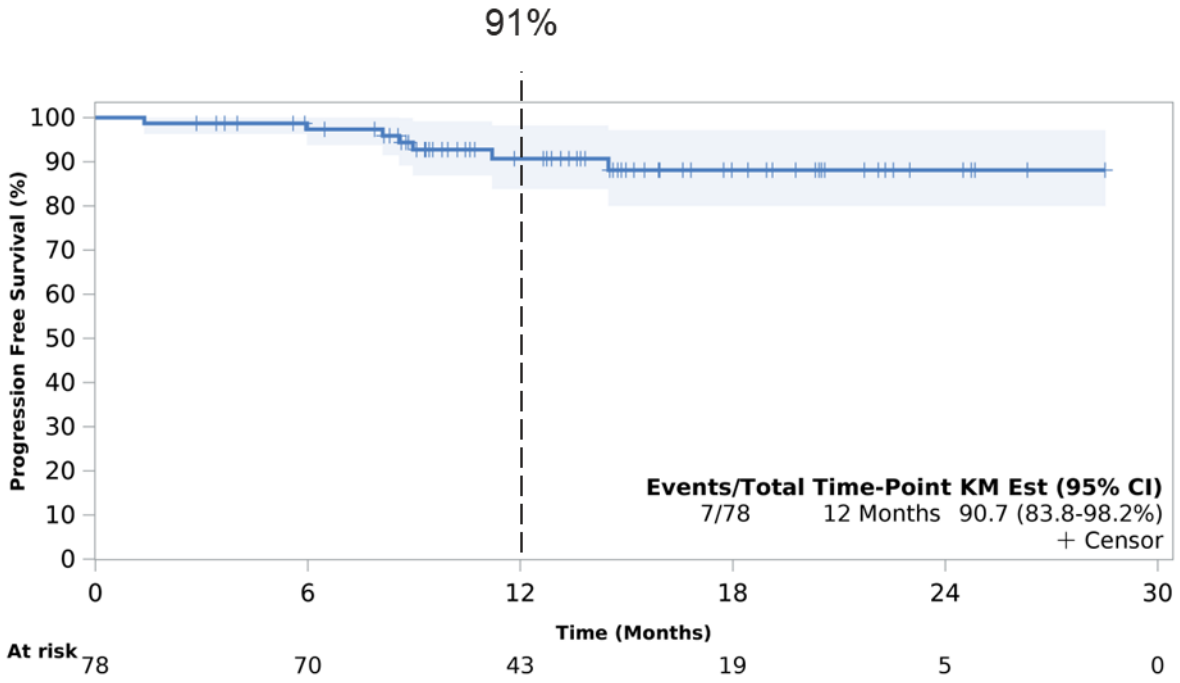
- **Primary:** CR rate per Lugano
- **Secondary:** ORR, safety, PFS, DOR, TTNT, OS
- **Exploratory:** PD, ctDNA monitoring

Eligibility:

- ≥18 years; PS 0-2
- CD2+0 previously untreated FL,
- G1-3A, stage II–IV
- **Need of therapy per GELF criteria**

- **91% of patients remained progression-free at 1 year**
- 7 patients progressed:
  - 3 patients had CD20- POD with FL histology
  - 3 patients had transformation to CD20+ DLBCL (one 6 weeks after study entry); after chemoimmunotherapy all achieved CR

Response type	**Response evaluable (N=76)**	Intention-to-treat (N=78)
Overall response	**96%**	94%
Complete response	**80%**	78%
Partial response	16%	15%
Stable disease	3%	3%
Progressive disease	1%	1%
Non-evaluable	n/a	3%



Falchi et al. ICML 2025, abstract #27.

Epcoritamab-R2 in 1L FL (EPCORE NHL-2, Arm 6)

Key inclusion criteria
- 1L CD20+ FL, G1-3a
- ECOG PS 0–2
- Measurable disease
- Adequate organ function

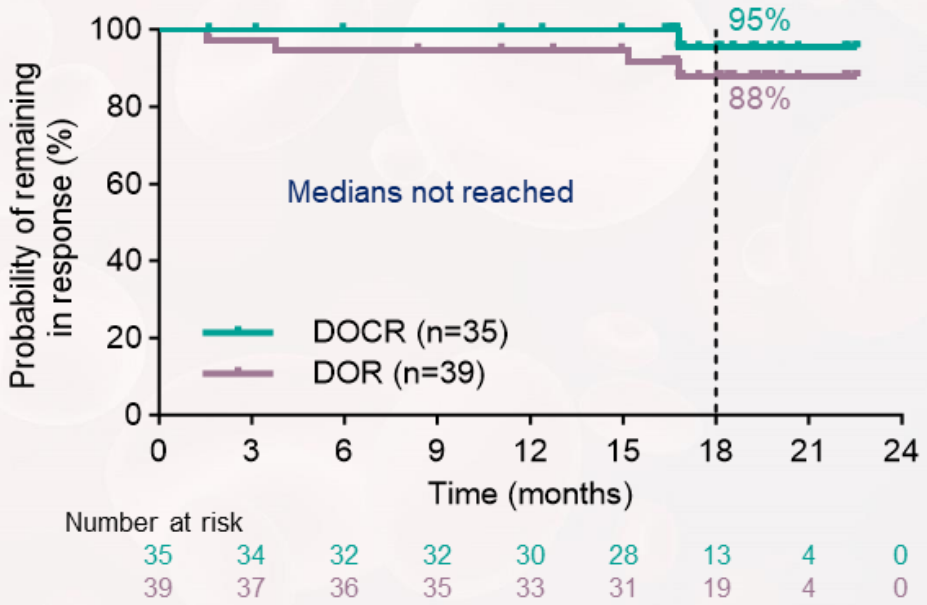
Arm 6 (1L FL) expansion, N=41

Epcoritamab (SC)	Rituximab (IV)	Lenalidomide (oral)
48 mg	375 mg/m²	20 mg
QW C1–2, Q4W C3+ (28 d/C)	QW C1, Q4W C2–6	QD for 21 d in C1–12
Treatment up to 2 y		

Median follow-up: 22.8 mo
Primary objective: Antitumor activity (ORR)
Key secondary endpoints: Safety, DOR, DOCR, PFS, OS

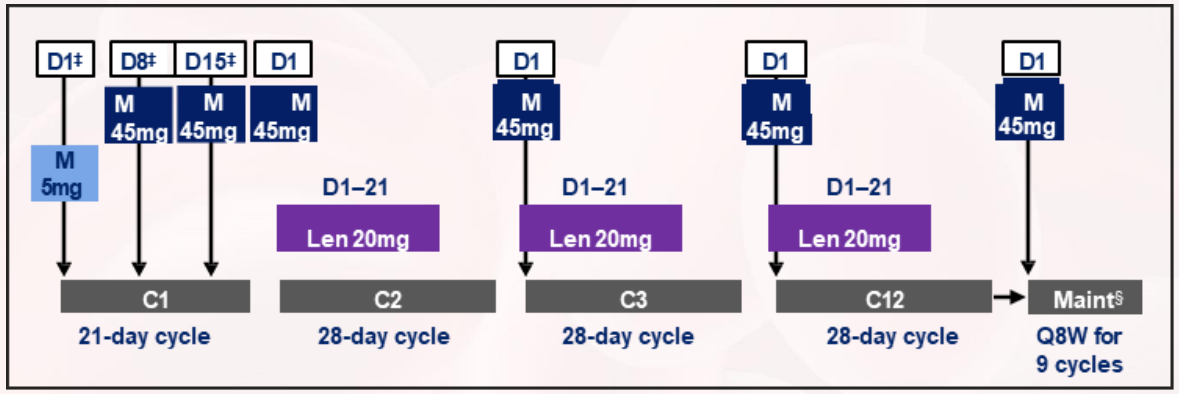
	N=41[a]
Overall response, n (%)	**39 (95)**
Complete response, n (%)	**35 (85)**
Partial response, n (%)	4 (10)
Progressive disease, n	0
Median time to response, mo (range)	2.7 (1.2–5.5)
Median time to CR, mo (range)	2.8 (1.4–11.4)

1L, previously untreated; DOCR, duration of complete response; DOR, duration of response; FL, follicular lymphoma; mo, month(s); R², rituximab + lenalidomide. Kaplan–Meier estimates of DOR and DOCR assessed by investigator. [a]A total of 2 patients were not evaluable.

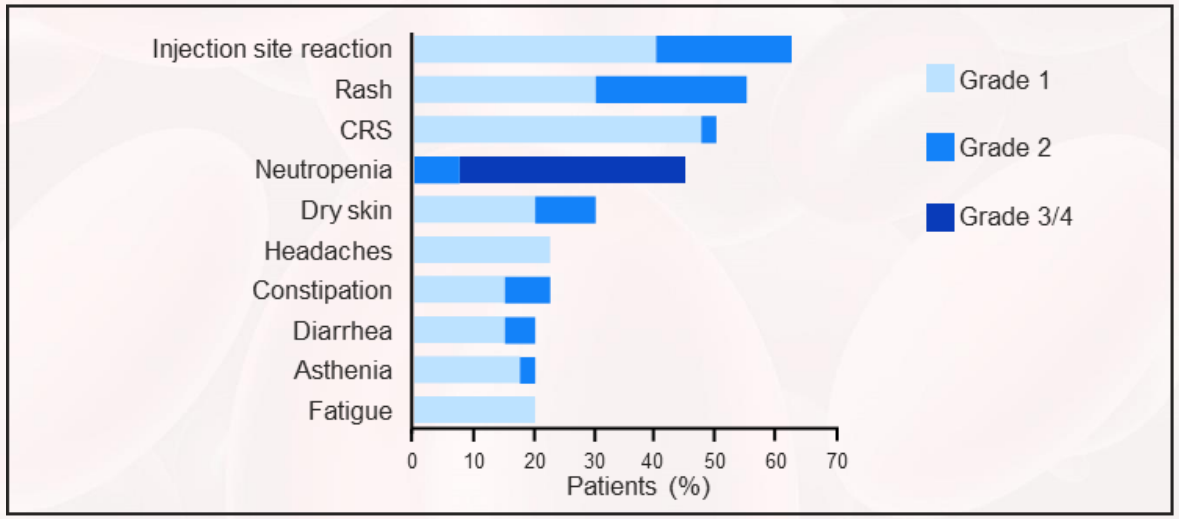


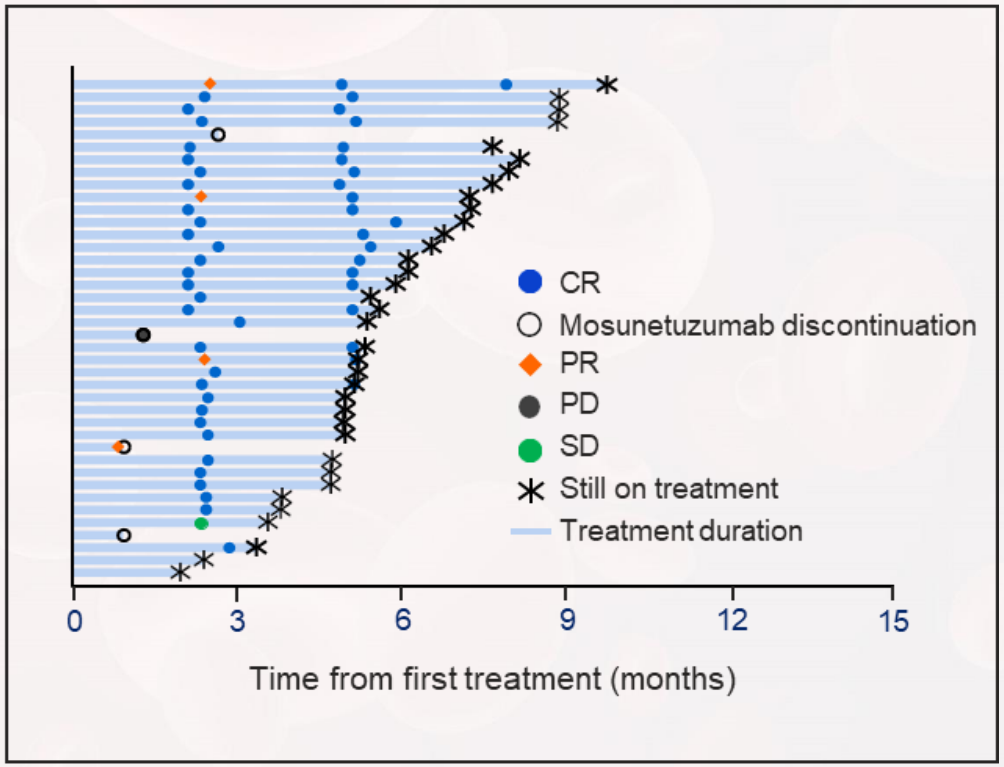
Leslie LA, et al. ASCO 2024, abstract #7014.

Mosunetuzumab and lenalidomide in 1L FL: Phase 2 results (N=40)



- Median duration of follow-up: 5.2 months (range: 1–10)
- **Best ORR 92%; best CR 89%**





Morschhauser et al. Blood (2023) 142 (Supplement 1): 605

Phase 3 studies of bispecifics in untreated FL

Name (NCT#)	N.	Experimental arm	Control arm	Duration of therapy	Primary endpoint
EPCORE FL-2 (NCT04663347)	1095	Epcoritamab R-lenalidomide	• G/R-CHOP • G/R-benda • R^2	2.5 y	CR30, PFS
MorningLyte (NCT06284122)	790	Mosunetuzumab-lenalidomide	• G/R-CHOP • G/R-benda	1.5 y	PFS
OLYMPIA-1 (NCT06091254)	478	Odronextamab	• R-CHOP • R-CVP • R-benda	2 y	CR30
OLYMPIA-2 (NCT06097364)	733	Odronextamab-CHOP/ CVP +/- O-maintenance	• R-CHOP/CVP + R-maintenance	6 m vs 2.5 y	CR30
SOUNDTRACK-F1 (NCT06549595)	1015	AZD0486-rituximab +/- AZD0486 maintenance	• R-CHOP/CVP + R-maintenance • R-benda	6-12 m vs. up to 2.5 y	PFS

Data per Clinicaltrials.gov; last accessed Aug 17, 2025

Backup slides:
EPCORE FL-1: ASH 2025

Primary Phase 3 Results From the EPCORE FL-1 Trial of Epcoritamab With Rituximab and Lenalidomide (R^2) Versus R^2 for Relapsed or Refractory Follicular Lymphoma

Lorenzo Falchi,[1*] Marcel Nijland,[2] Huiqiang Huang,[3] Kim M. Linton,[4] John F. Seymour,[5] Rong Tao,[6] Michal Kwiatek,[7] Abel Costa,[8] Theodoros P. Vassilakopoulos,[9] Richard Greil,[10] Ana Jiménez-Ubieto,[11] Shane Gangatharan,[12] Ohad Benjamini,[13] Catherine Thieblemont,[14] Alessandra Tucci,[15] Anna Elinder-Camburn,[16] Arpad Illes,[17] Jan Novak,[18] Miguel Pavlovsky,[19] Andrew McDonald,[20] Dok Hyun Yoon,[21] Yuko Mishima,[22] Gauri Sunkersett,[23] JP Mei,[23] Nabanita Mukherjee,[23] Feng Zhu,[23] Elena Favaro,[24] Franck Morschhauser[25]

*Presenting author

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]University Medical Center Groningen, University of Groningen, Groningen, Netherlands; [3]Sun Yat-sen University, Guangzhou, China; [4]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK; [5]Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Melbourne, Australia; [6]Fudan University Cancer Hospital, Shanghai, China; [7]Aidport Clinical Trials Hospital, Skorzewo (Poznan), Poland; [8]Instituto D'Or de Pesquisa e Ensino, São Paulo, Brazil; [9]Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [10]Paracelsus Medical University Salzburg; Salzburg Cancer Research Institute-Center for Clinical Cancer and Immunology Trials; Cancer Cluster Salzburg, Salzburg, Austria; [11]Hospital Universitario 12 de Octubre, Madrid, Spain; [12]Fiona Stanley Hospital, Murdoch, Australia; [13]The Chaim Sheba Medical Center, Ramat Gan, Israel; [14]Hôpital Saint-Louis, Paris, France; [15]ASST degli Spedali Civili di Brescia, Brescia, Italy; [16]North Shore Hospital, Auckland, New Zealand; [17]Debreceni Egyetem-Klinikai Kozpont, Debrecen, Hungary; [18]Fakultni nemocnice Kralovske Vinohrady, Prague, Czechia; [19]FUNDALEU, Buenos Aires, Argentina; [20]Alberts Cellular Therapy, Gauteng, South Africa; [21]Asan Medical Center, University of Ulsan, College of Medicine, Seoul, South Korea; [22]Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; [23]AbbVie, North Chicago, IL, USA; [24]Genmab, Copenhagen, Denmark; [25]Hôpital Claude Huriez, Lille, France.

Presented at the American Society of Hematology; December 6–9, 2025; Orlando, FL, USA; DV-017521

Background

- Most patients with follicular lymphoma (FL) experience disease relapse and the duration of remission is shorter with each subsequent line of therapy[1], underscoring the need for more effective therapies in earlier lines
- The combination of lenalidomide plus rituximab (R^2) is a chemotherapy-free standard of care in relapsed/refractory (R/R) FL; however, outcomes remain suboptimal for many patients[2]
- Epcoritamab is a CD3×CD20 bispecific antibody, approved as monotherapy for R/R FL after ≥ 2 prior lines of treatment,[3–5] which when combined with lenalidomide and rituximab may augment antilymphoma activity and lead to improved clinical outcomes in patients with R/R FL[6–8]
  - Unique among CD3xCD20 T-cell engagers, preclinical studies have demonstrated minimal interference between epcoritamab and rituximab antitumor activity when combined[9]
- Early data from the phase 1b/2 EPCORE® NHL-2 trial (NCT04663347) with fixed-duration epcoritamab plus R^2 for R/R FL showed deep and durable responses with encouraging clinical outcomes and manageable safety[10]

We present pivotal efficacy and safety data from the phase 3 EPCORE FL-1 trial (NCT05409066) of fixed-duration epcoritamab+R^2 versus R^2 alone for R/R FL

1. Rivas-Delgado A, et al. *Br J Haematol*. 2019;184(5):753–9. **2.** Leonard JP, et al. *J Clin Oncol*. 2019;37(14):JCO.19.00010. **3.** FDA. EPKINLY (Epcoritamab) [Prescribing Information] Plainsboro, NJ. 2025. **4.** EMA. Tepkinly: Annex I Summary of Product Characteristics. **5.** Epkinly [Japan package insert]. AbbVie GK, Genmab KK. 2025. **6.** Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. **7.** Golay J, et al. *Antibodies*. 2020;9(4):58. **8.** Gribben JG, et al. *J Clin Oncol*. 2015;33(25):2803–11. **9.** Dandamudi DB, et al. *Leuk Lymphoma* 2025; 66: 1688–99. **10.** Falchi L, et al. *Blood*. 2024;144(Supplement 1):342–342.

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

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 R²

- **Epcoritamab** (3-SUD cycle 1: QW;[a,b] cycles 2–3, QW; cycles 4–12, Q4W)
- **Rituximab** (375 mg/m²), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- **Lenalidomide** (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

R²

- **Rituximab** (375 mg/m²), 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

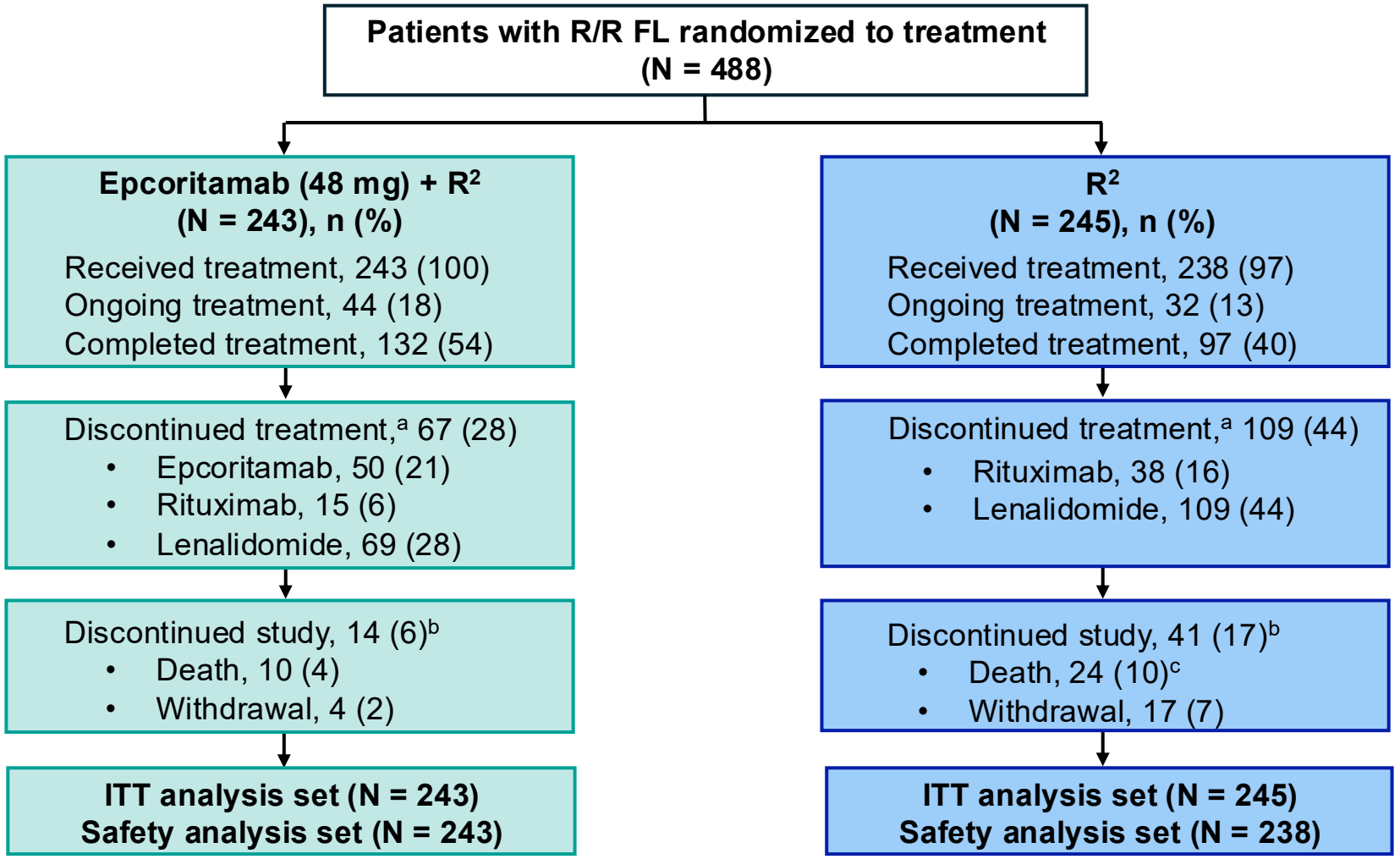
- **Dual primary endpoints: ORR per IRC and PFS per IRC**
- Key secondary endpoints: CR rate per IRC, OS, and MRD[c]
- Additional secondary endpoints: DOR, DOCR, TTNLT, safety, and PRO assessments

Data cutoff: May 24, 2025; median follow-up: 14.8 months[d]
Enrollment period: October 2022 - January 2025

[a]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).[1] [b]The 24 mg epcoritamab plus R² arm was closed to enrollment based on the superior efficacy for the 48 mg dose from EPCORE NHL-2.[2] Only the data for the optimal dose explored (48 mg) are presented here. [c]Minimal residual disease data are forthcoming in a future analysis. [d]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.

Patient Disposition



[a]Discontinued study treatment means: 1) discontinuation of all study drugs; 2) at least one study drug discontinued, and rest completed. [b]Ongoing study, 229 patients for epcoritamab+R², 204 patients for R². [c]One additional patient died in the R² arm with reason as 'withdrawal'.

Baseline Demographics and Disease Characteristics Were Generally Balanced

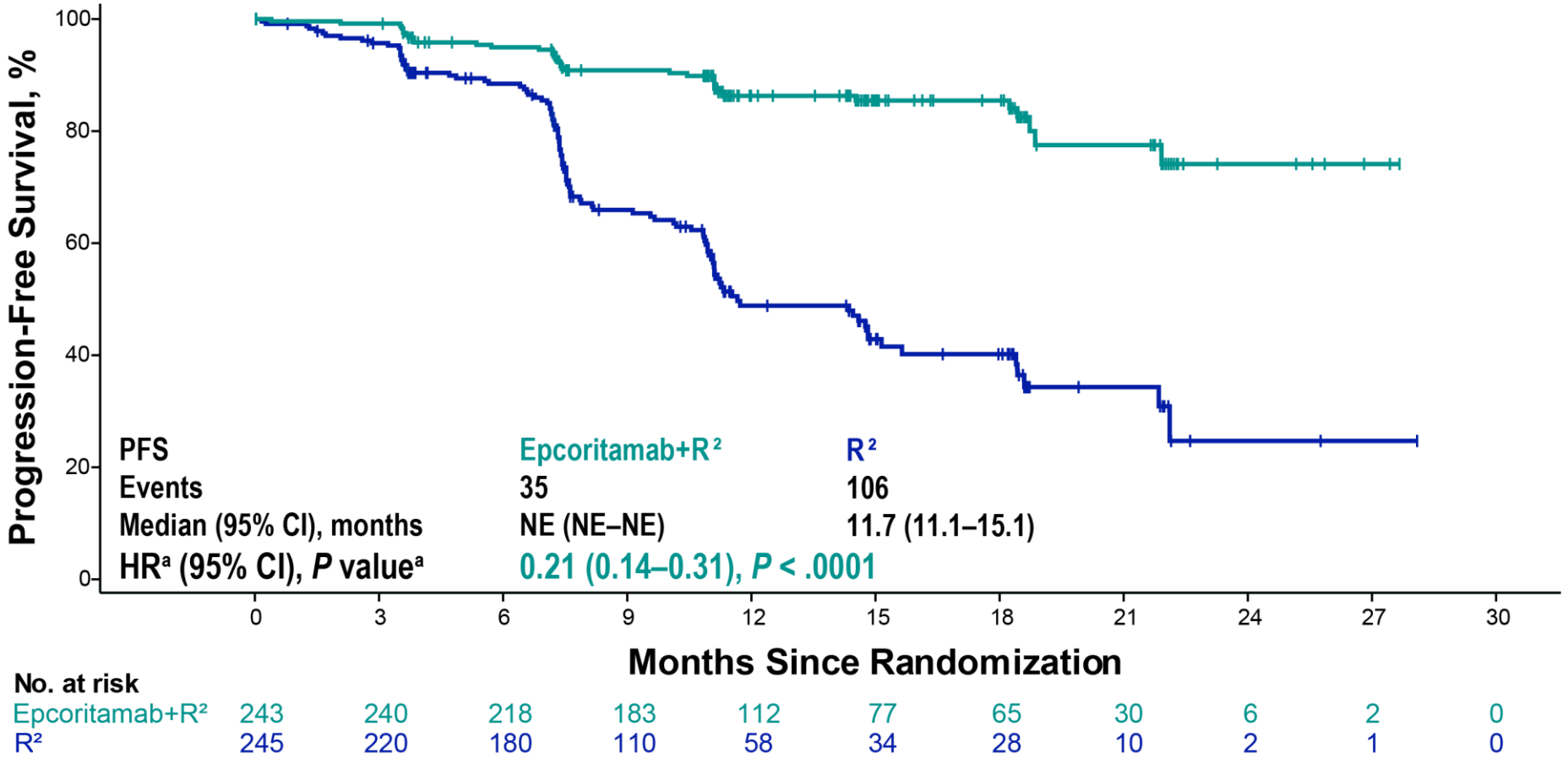
Characteristic	Epcoritamab+R² (N = 243)	R² (N = 245)	Overall (N = 488)
Median age, y (range)	60 (30, 84)	63 (24, 89)	61 (24, 89)
≥ 65, n (%)	88 (36)	106 (43)	194 (40)
Male, n (%)	139 (57)	138 (56)	277 (57)
Race, n (%)			
Asian	63 (26)	54 (22)	117 (24)
Black	6 (2)	2 (< 1)	8 (2)
White	168 (69)	184 (75)	352 (72)
Ethnicity, n (%)			
Hispanic	29 (12)	28 (11)	57 (12)
ECOG, n (%)			
0	166 (68)	170 (69)	336 (69)
1-2	77 (32)	75 (31)	152 (31)
Ann Arbor stage, n (%)			
II	37 (15)	44 (18)	81 (17)
III-IV	206 (85)	201 (82)	407 (83)
FLIPI score, n (%)			
0–1	63 (26)	56 (23)	119 (24)
2	79 (33)	76 (31)	155 (32)
3–5	100 (41)	113 (46)	213 (44)
Bulky disease (≥ 7 cm), n (%)	47 (19)	61 (25)	108 (22)

Treatment History Was Generally Balanced Across Epcoritamab+R² and R²

	Epcoritamab+R² (N = 243)	R² (N = 245)	Overall (N = 488)
Median time from initial diagnosis to randomization, years (range)	4.5 (0.2, 30.3)	5.3 (0.1, 43.0)	5.0 (0.1, 43.0)
Number of prior lines of therapy, median (range)	1 (1, 7)	1 (1, 6)	1 (1, 7)
1, n (%)	145 (60)	141 (58)	286 (59)
2, n (%)	58 (24)	61 (25)	119 (24)
≥ 3, n (%)	40 (16)	43 (18)	83 (17)
Prior anti-CD20 antibody, n (%)	243 (100)	245 (100)	488 (100)
Prior anti-CD20 antibody containing chemotherapy, n (%)	239 (98)	240 (98)	479 (98)
Prior bendamustine in last line, n (%)	53 (22)	47 (19)	100 (20)
Prior R², n (%)	8 (3)	9 (4)	17 (3)
POD24,[a] n (%)	106 (44)	93 (38)	199 (41)
Refractory to 1L therapy, n (%)	86 (35)	81 (33)	167 (34)
Refractory to anti-CD20 antibody, n (%)	104 (43)	103 (42)	207 (42)
Refractory to last line of therapy, n (%)	84 (35)	82 (33)	166 (34)
Double refractory[b]	91 (37)	91 (37)	182 (37)

[a]POD24 is defined as progression of disease ≤ 2 years from the date of initiation of frontline therapy. [b]Double refractory is refractory to prior anti-CD20 therapy and prior alkylator therapy.

Epcoritamab+R² Resulted in Superior PFS per IRC With 79% Risk Reduction



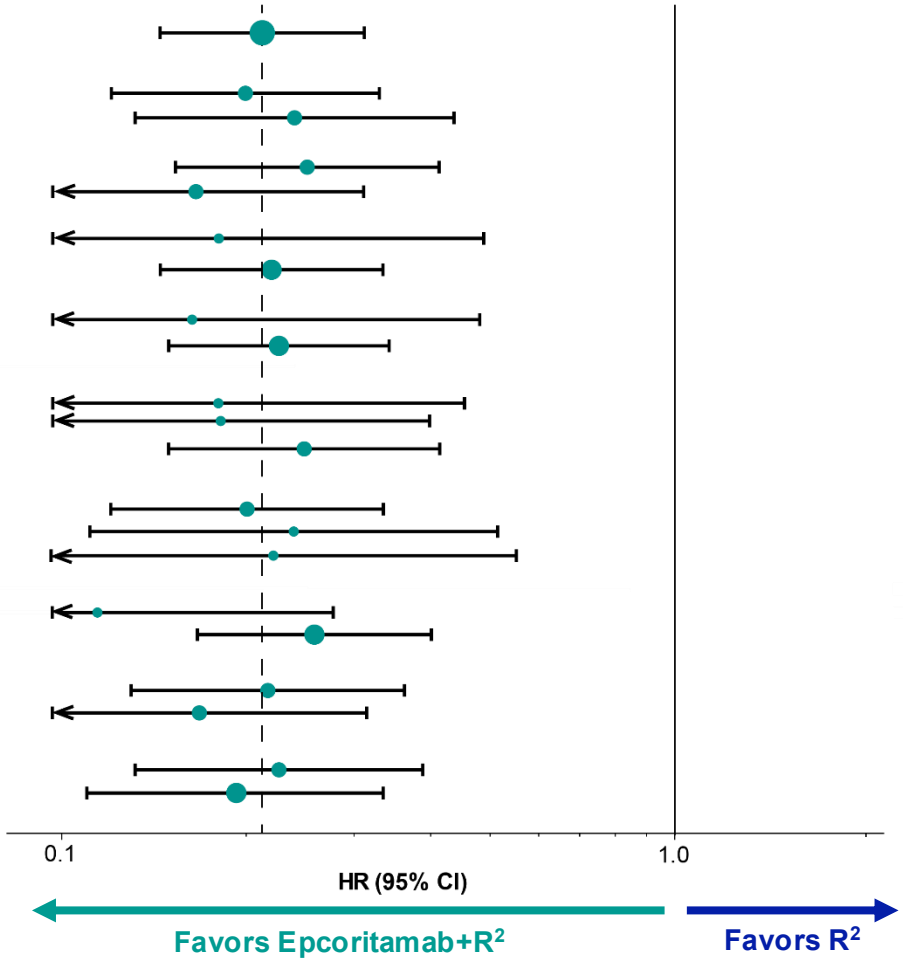
- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for epcoritamab+R² and 40.2% (95% CI: 31.8, 48.4) for R²

Median follow-up for PFS: epcoritamab+R² (14.4m), R² (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.

[a]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.

Epcoritamab+R² Demonstrated Favorable PFS Across a Broad R/R FL Population

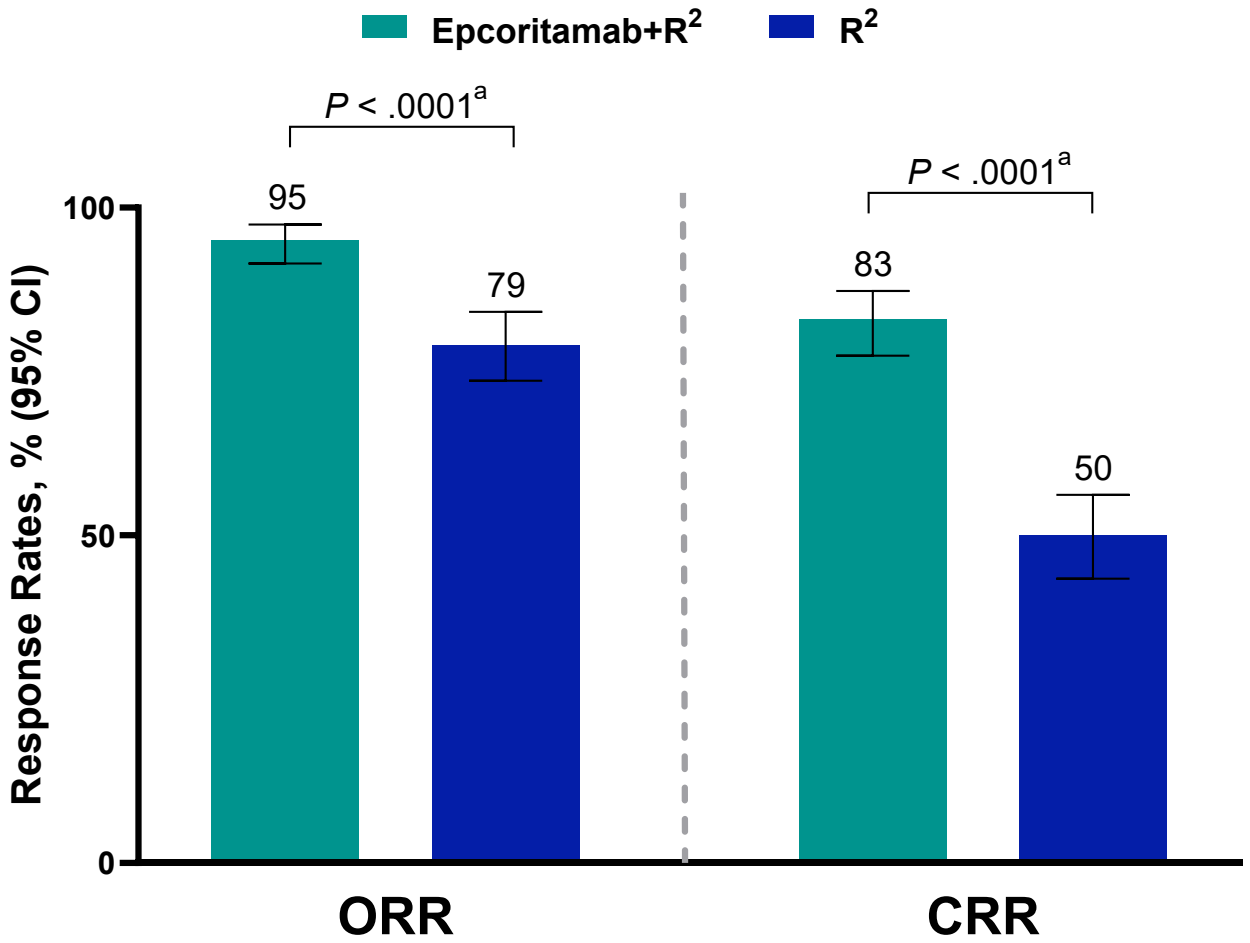
Prespecified Subgroups	Epcoritamab+R² Event/N (%)	R² Event/N (%)	HR (95% CI)
All patients	35/243 (14)	106/245 (43)	0.22 (0.15, 0.32)
Age (years)			
< 65	21/155 (13)	58/139 (42)	0.20 (0.12, 0.33)
≥ 65	14/88 (16)	48/106 (45)	0.24 (0.13, 0.44)
Sex			
Male	23/139 (17)	54/138 (39)	0.25 (0.15, 0.42)
Female	12/104 (12)	52/107 (49)	0.17 (0.09, 0.31)
Region			
US/Western Europe	5/58 (9)	18/60 (30)	0.18 (0.07, 0.49)
Rest of World	30/185 (16)	88/185 (48)	0.22 (0.15, 0.34)
Ann Arbor stage			
II	4/37 (11)	21/44 (48)	0.16 (0.06, 0.49)
III+IV	31/206 (15)	85/201 (42)	0.23 (0.15, 0.35)
FLIPI score at baseline			
0-1	6/63 (10)	19/56 (34)	0.18 (0.07, 0.46)
2	8/79 (10)	30/76 (39)	0.18 (0.08, 0.40)
3-5	21/100 (21)	57/113 (50)	0.25 (0.15, 0.42)
Number of prior lines			
1	20/145 (14)	58/141 (41)	0.20 (0.12, 0.34)
2	9/58 (16)	26/61 (43)	0.24 (0.11, 0.52)
≥ 3	6/40 (15)	22/43 (51)	0.23 (0.09, 0.56)
Bulky disease (≥ 7 cm)			
Yes	6/47 (13)	31/61 (51)	0.12 (0.05, 0.28)
No	28/191 (15)	71/176 (40)	0.26 (0.17, 0.41)
POD24			
Yes	22/106 (21)	47/93 (51)	0.22 (0.13, 0.37)
No	12/131 (9)	54/144 (38)	0.17 (0.09, 0.32)
Double refractory			
Yes	19/91 (21)	47/91 (52)	0.23 (0.13, 0.39)
No	16/152 (11)	59/154 (38)	0.19 (0.11, 0.34)



- Trends in favor of epcoritamab+R² were shown for all prespecified subgroups and ORR, CR, and DOR endpoints

N represents the total number of patients within each category in each arm. Arrows indicate that the confidence interval is extended more than current range. 95% CI is by unstratified Cox proportional hazard model.

Epcoritamab+R² Resulted in Higher Response Rates Versus R²

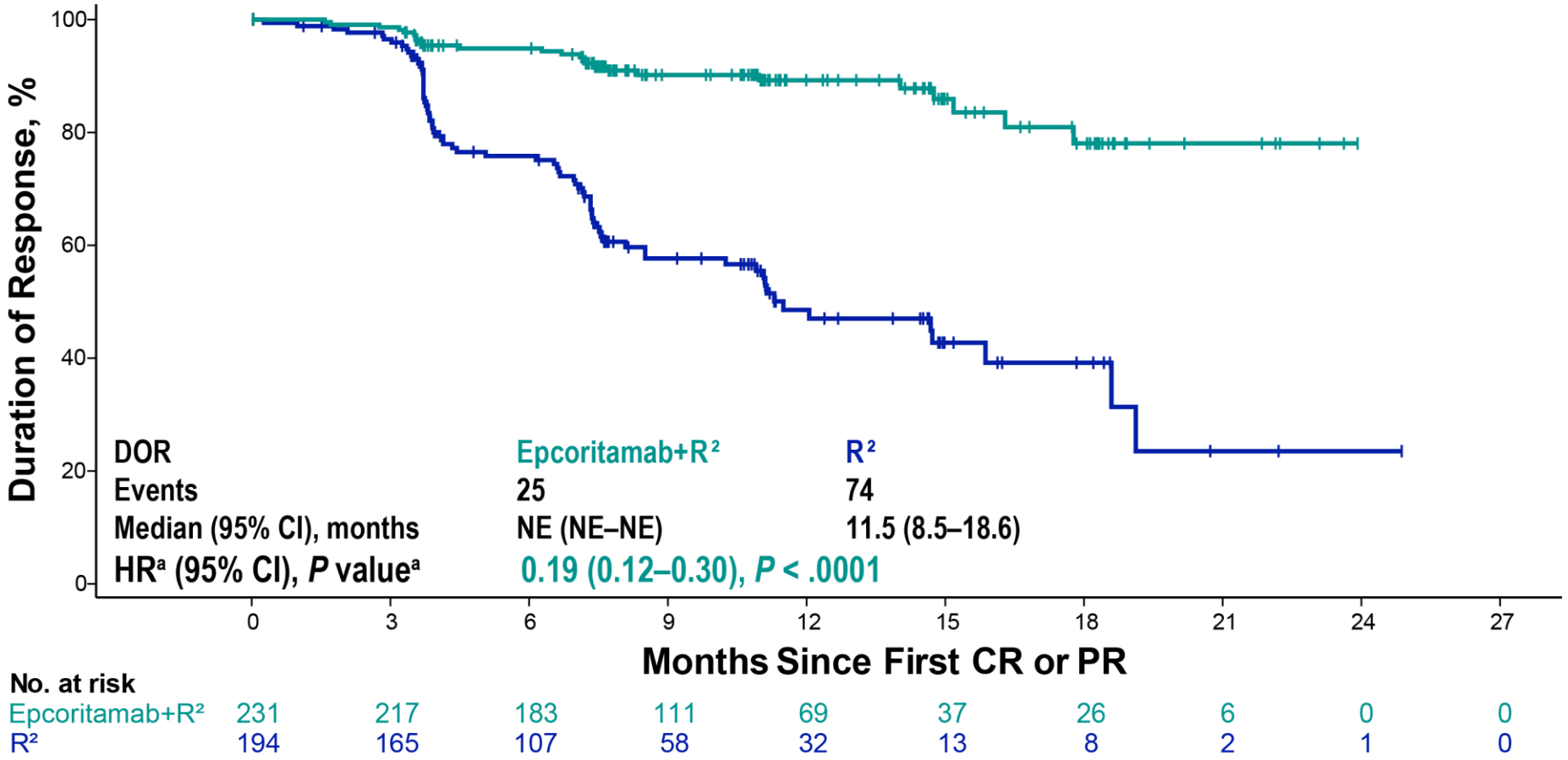


	Epcoritamab+R² (N = 243)	R² (N = 245)
ORR, n (%)	231 (95)	194 (79)
CRR, n (%)	201 (83)	122 (50)
PR, n (%)	30 (12)	72 (29)
SD, n (%)	1 (< 1)	17 (7)
PD, n (%)	7 (3)	16 (7)
NE,[b] n (%)	4 (2)	18 (7)

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).

[a]Nominal *P* value by stratified Cochran-Mantel-Haenszel method. [b]Patients with no post-baseline disease assessment were also included.

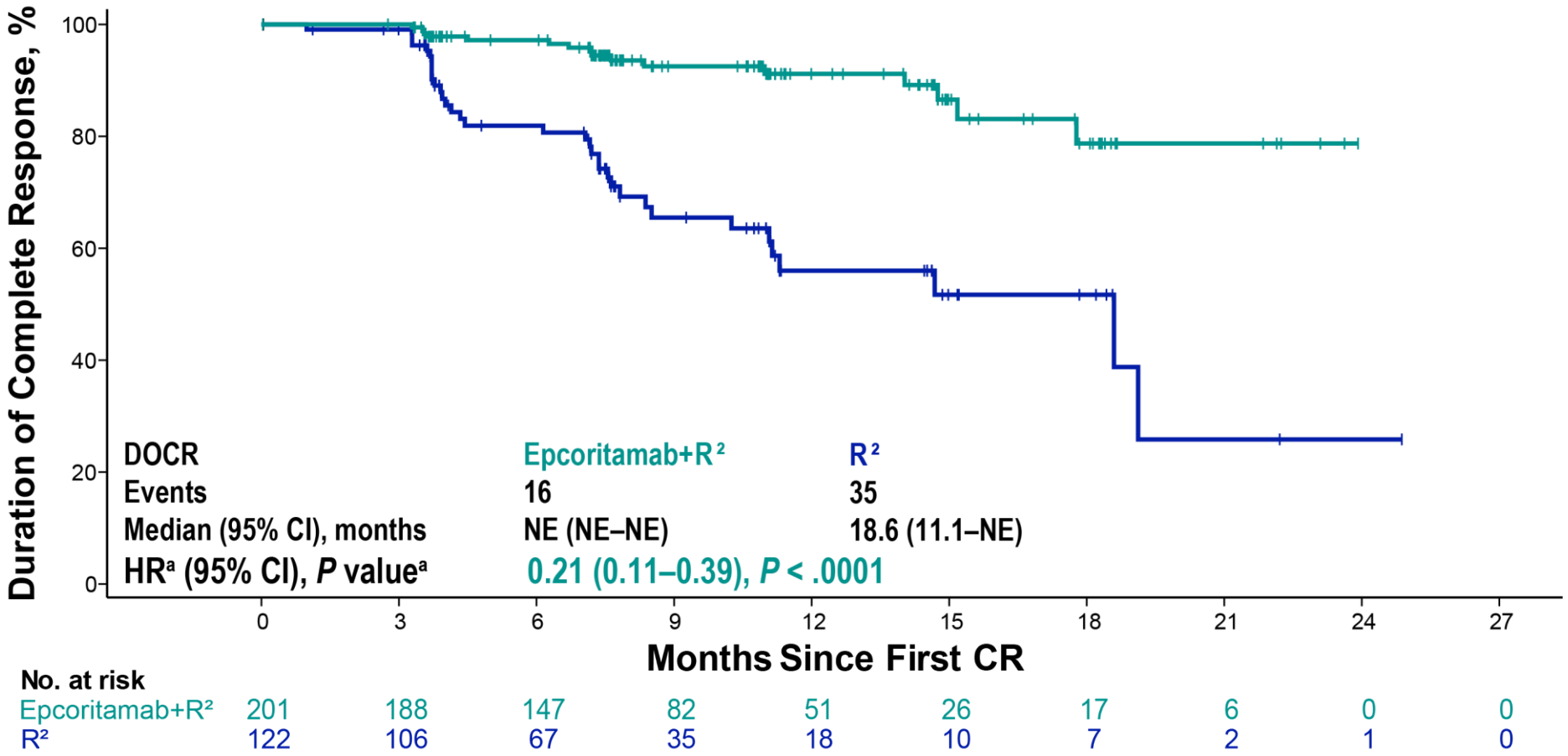
Epcoritamab+R² Resulted in Durable Responses



- Improvement in DOR was seen with epcoritamab+R²

Median follow-up for DOR: epcoritamab+R² (10.6m), R² (10.6m). DOR results are for descriptive purposes only.
[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

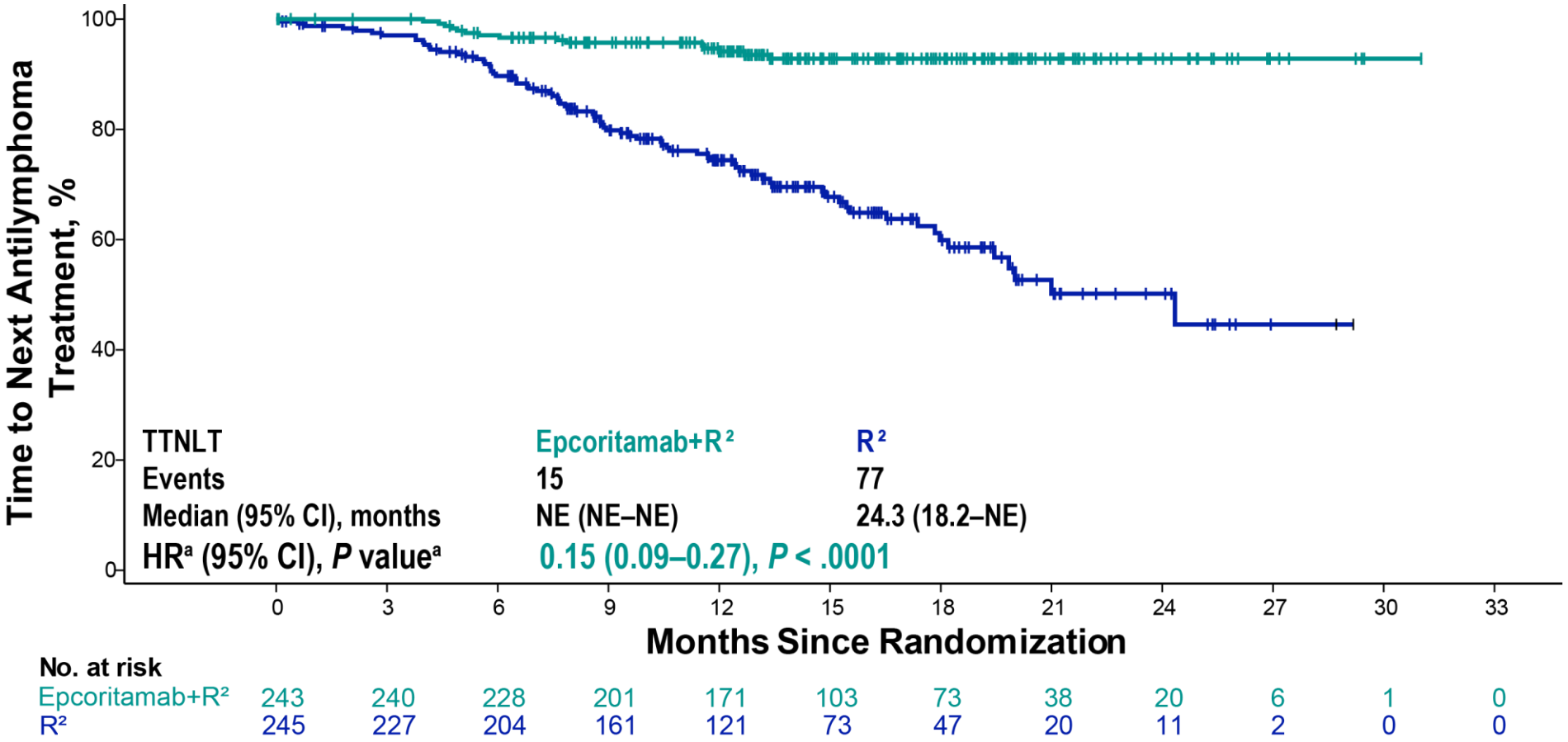
Epcoritamab+R² Resulted in Deep and Durable Complete Responses



- Improvement in DOCR was seen with epcoritamab+R²

Median follow-up for DOCR: epcoritamab+R² (7.9m), R² (7.6m). DOCR results are for descriptive purposes only.
[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

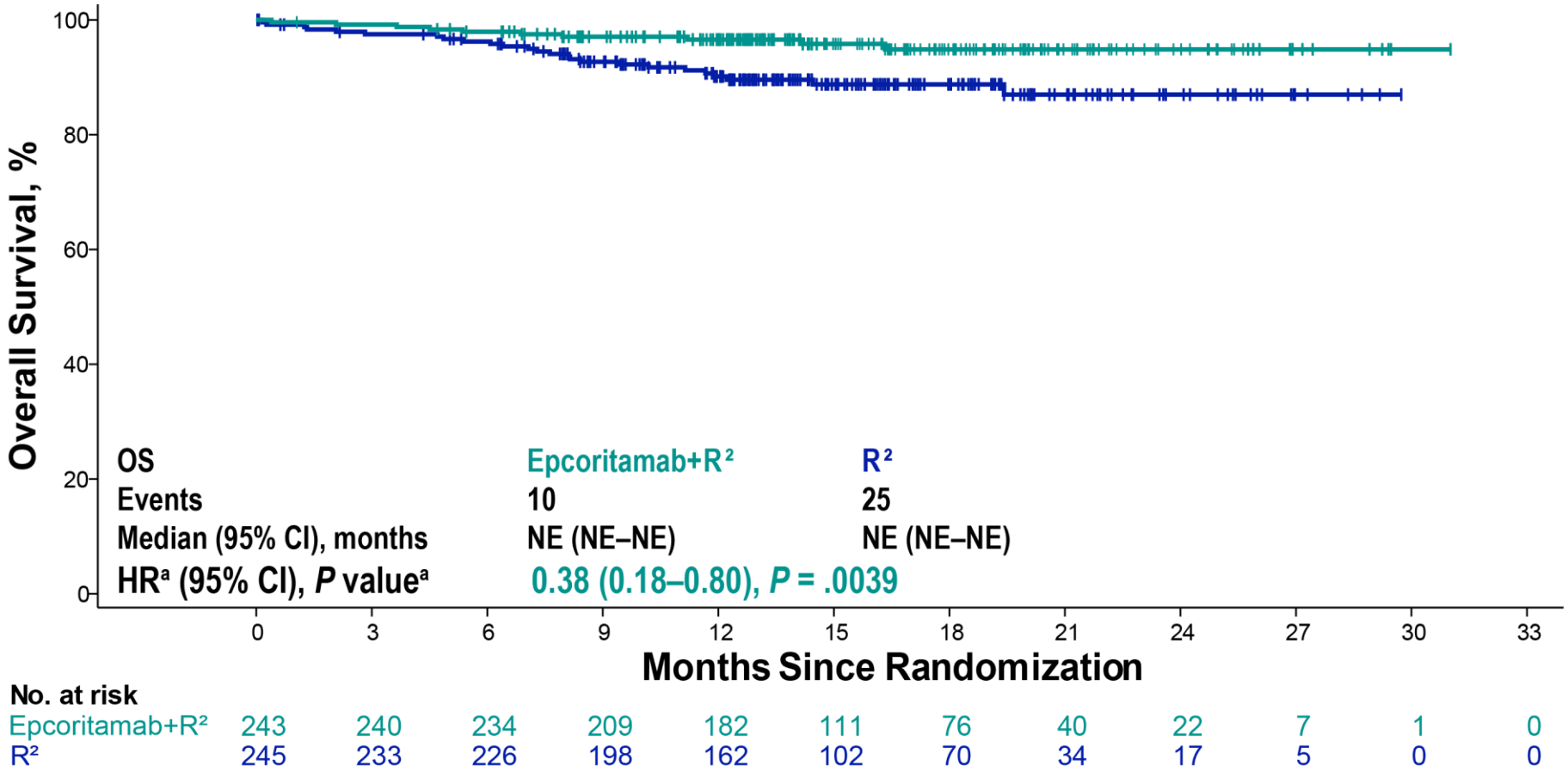
Epcoritamab+R² Extended Time to Next Treatment



- At 16 months, 92.8% of patients treated with epcoritamab+R² remained free from new antilymphoma treatment compared with 64.9% of patients treated with R²

Median follow-up for TTNLT: epcoritamab+R² (14.6m), R² (14.1m). TTNLT results are for descriptive purposes only.
[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

Positive Trend for Overall Survival With Epcoritamab+R²



- The 16-month estimate for OS was 95.8% with epcoritamab+R² and 88.8% with R²

Median follow-up for OS: epcoritamab+R² (14.8m), R² (14.6m). The OS data is based on the 24% (35/146 events) information fraction and has not yet reached statistical significance; additional analyses are forthcoming.
[a]*P* value is based on stratified log-rank test with 1-sided significance level of 0.000005. Hazard ratio is estimated using stratified Cox proportional hazards model.

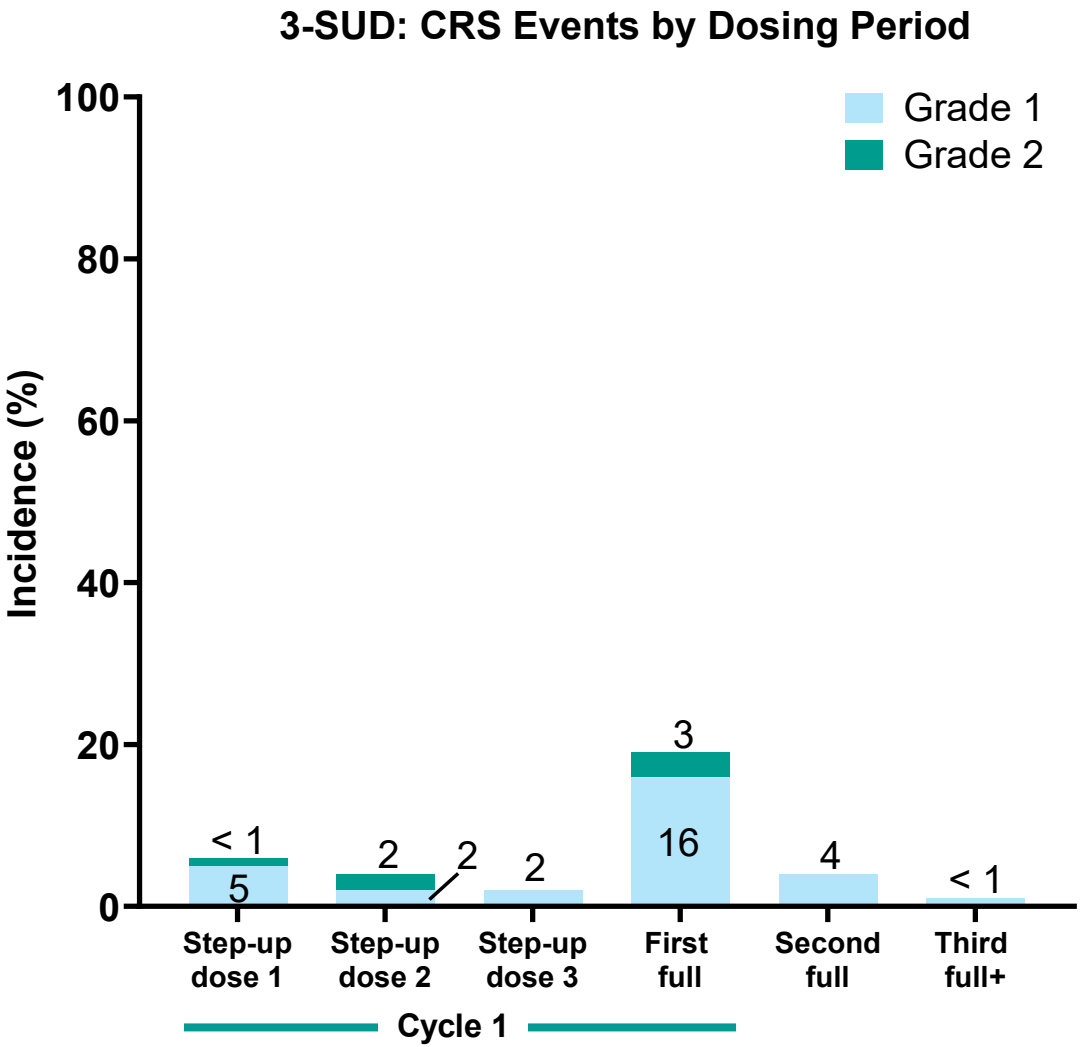
Manageable AEs With No New Safety Signals

Adverse Event, n (%)	Epcoritamab+R² (N = 243)		R² (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%[a,b]				
Infections[c]	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+R², 3%; R², 2%)
  - Incidence of febrile neutropenia: epcoritamab+R², 6%; R², 3%
- Infections were manageable and few patients discontinued any study drug (epcoritamab+R², 6%; R², 1%)
- Fatal adverse events were rare (epcoritamab+R², 2%; R², 4%)
- Despite higher rates of AEs in the epcoritamab+R² arm, most patients completed the prescribed regimen (median relative dose intensity ≥ 90% for epcoritamab+R²)

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

CRS Was Low Grade and Predictable With Epcoritamab+R²



	Epcoritamab+R² 2-SUD N = 110	Epcoritamab+R² 3-SUD[a] 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 (%)*		
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 (%)*		
Treated with tocilizumab	12 (24)	9 (26)
Treated with corticosteroid	23 (46)	13 (37)

*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

[a]The 3-SUD regimen was implemented based off the EPCORE NHL-1 FL trial (NCT03625037).[1]

[1]Vose J, et al. *J Clin Oncol* 2024; 42 (suppl 16): 7015.

Conclusions

- In this phase 3 trial in patients with 2L+ FL, fixed-duration epcoritamab plus R^2 was superior to R^2
  - 79% reduction in the risk of disease progression or death
  - Higher rates and durable deep responses (CRR: 83% for epcoritamab+R^2, 50% for R^2; DOCR: not reached for epcoritamab+R^2, 18.6 months for R^2)
  - Benefit was consistent across broad patient subgroups, including both low- and high-risk populations
  - Superior TTNLT and positive trend in OS for epcoritamab+R^2
- The safety profile was manageable in the outpatient setting and remained consistent with the known toxicities of the individual components
- **Epcoritamab+R^2 is a novel chemotherapy-free, fixed-duration therapy suitable for outpatient administration, and this regimen sets a new benchmark as standard of care in 2L+ FL**

Supporting Poster Presentations at ASH

- **Exposure-response/-safety analysis support epcoritamab 48 mg plus R^2 regimen**
  - Presentation ID 1820
  - Optimal dose regimen of epcoritamab in combination with lenalidomide and rituximab in relapsed or refractory follicular lymphoma – analyses of pharmacokinetics and exposure-response relationships of EPCORE FL-1 phase 3 study
  - Saturday, December 6, 05:30 PM – 07:30 PM EST

- **High baseline health-related quality of life was preserved for both epcoritamab+R^2 and R^2**
  - Presentation ID 5370
  - Health-related quality of life (HRQoL) in patients with relapsed/refractory follicular lymphoma treated with epcoritamab in combination with rituximab plus lenalidomide (E+R2): primary results of the EPCORE FL-1 trial
  - Monday, December 8, 06:00 PM – 08:00 PM EST

FDA Approval and Publication in *The Lancet*

- This pivotal Phase 3 study resulted in FDA full approval of epcoritamab with lenalidomide and rituximab in R/R FL on November 18, 2025
  - This is the first bispecific-based treatment regimen approved in the 2L+ setting
  - This is the third disease indication for epcoritamab approved by the FDA in addition to 3L+ FL and 3L+ DLBCL

Now Live!

Epcoritamab, lenalidomide, and rituximab versus lenalidomide and rituximab for relapsed or refractory follicular lymphoma (EPCORE FL-1): a global, open-label, randomised, phase 3 trial

THE LANCET

Lorenzo Falchi, Marcel Nijland, Huiqiang Huang, Kim M Linton, John F Seymour, Rong Tao, Michal Kwiatek, Abel Costa, Theodoros P Vassilakopoulos, Richard Greil, Ana Jiménez-Ubieto, Shane A Gangatharan, Ohad Benjamini, Catherine Thieblemont, Alessandra Tucci, Anna Elinder-Camburn, Arpad Illes, Jan Novak, Miguel A Pavlovsky, Andrew McDonald, Dok Hyun Yoon, Dai Maruyama, Gauri Sunkersett, Jian P Mei, Nabanita Mukherjee, Feng Zhu, Abualbishr Alshreef, Elena Favaro, Franck Morschhauser, on behalf of the EPCORE FL-1 Investigators

Published online December 7, 2025 https://doi.org/10.1016/S0140-6736(25)02360-8

Acknowledgments

- We thank the patients, their families and caregivers, study investigators, and site personnel for their participation in this study.
- This study was funded by AbbVie and Genmab A/S.
- All authors had access to relevant data and participated in the drafting, review, and approval of this presentation. No honoraria or payments were made for authorship.
- We also wish to thank Alena Vajikova, MS, of AbbVie for study management, Yukun Li, PhD, of AbbVie for statistical analyses, and Ruiling Zhang, MS, of AbbVie for statistical programming. Medical writing support was provided by Kristina Y. Aguilera, PhD, and was funded by AbbVie.