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2024 R&D Update and ASH Data Review

December 11, 2024

Forward looking statements

This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding our present and future business strategies and the environment in which we will operate in the future. The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product discovery and development, uncertainties related to the outcome of clinical trials, slower than expected rates of patient recruitment, unforeseen safety issues resulting from the administration of our products in patients, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products obsolete, and other factors. Further, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation. Genmab does not undertake any obligation to update or revise forward looking statements in this presentation nor to confirm such statements to reflect subsequent events or circumstances after the date made or in relation to actual results, unless required by law.

Strategic Partnerships, Collaborations and Licensing Agreements

We will discuss products developed in collaboration with strategic partners or that are the result of product or technology licenses with other companies. This slide is an acknowledgement of those relationships.

- AbbVie Inc: epcoritamab (EPKINLY®, TEPKINLY®)
- Pfizer: tisotumab vedotin (Tivdak®)
- BioNTech SE1: GEN1042 (BNT312, DuoBody®-CD40x4-1BB), GEN1055 (BNT315, HexaBody®-OX40), GEN1059 (BNT314, DuoBody–EpCAMx4-1BB)
- Johnson & Johnson (J&J): HexaBody®-CD38 (GEN3014)[2], daratumumab, daratumumab and hyaluronidase-fihj (DARZALEX®, DARZALEX *FASPRO*®), amivantamab (RYBREVANT®)

1. Partnership is based on 50:50 profit/loss share
2. Genmab is developing HexaBody-CD38 in an exclusive worldwide license and option agreement with J&J

Agenda

11:00 AM	**Welcome & Introduction**	Dr. Jan van de Winkel, President and Chief Executive Officer
11:05 AM	**Building a World-class Pipeline: EPKINLY and Rina-S**	Dr. Tahi Ahmadi, Executive Vice President and Chief Medical Officer, Head of Experimental Medicines
11:10 AM	**Rina-S at ESMO**	Dr. Elizabeth K. Lee, MD Department of Medical Oncology and Division of Gynecologic Oncology Dana-Farber Cancer Institute
11:15 AM	**Epcoritamab at ASH**	Dr. Martin Hutchings, MD, PhD, Sr. Consultant and Professor, Copenhagen University Hospital
11:55 AM	**2025: Strategic Prioritization to Maximize Potential**	Dr. Jan van de Winkel
12:00 PM	**Q&A**	

2024: Investing in Our Successful Future

Bring Our Own Medicines to Patients & Expand Our Markets

- Consistent growth for EPKINLY and Tivdak
- Additional approvals and regulatory submissions
- Two Phase 3 trial starts for EPKINLY

Build World-class Differentiated Pipeline

- Wholly-owned Rina-S and acasunlimab move into Phase 3
- Pipeline prioritization – strategic investments to maximize potential for EPKINLY, Rina-S and acasunlimab

Become a Leading Integrated Biotech Innovation Powerhouse

- First major acquisition – ProfoundBio
- Partner programs receive additional regulatory approvals – further enhancing recurring revenue

Proprietary Technology Platforms and Strategic Investments Enable Us to Build a World-class Pipeline and Bring Medicines to Patients Ourselves

Genmab Platforms


DuoBody technology


HexaBody technology


DuoHexaBody® technology


HexElect ® technology


ADC technology

Genmab ADC Platforms

- **Two proprietary hydrophilic linker-drug platforms with clinical validation:**
  - ─ TOPO1
  - ─ Next-gen MMAE
- Bispecific ADC capability
- Additional novel cytotoxic and immune-stimulating (ISACs) linker-drugs

World-Class Pipeline

epkinly™ epcoritamab-bysp SUBCUTANEOUS INJECTION 4mg/48mg

tivdak® tisotumab vedotin-tftv for injection 40mg

Phase 3 programs: Rina-S and acasunlimab

+

Novel clinical-stage assets

- GEN1042 (BNT312, DuoBody-PD-L1x4-1BB)
- GEN1057 (DuoBody-FAPαxDR4)
- GEN1160 (CD70 - TOPO1)
- GEN1107 (PTK7 - MMAE)
- GEN1286 (EGFRxcMET - TOPO1)
- GEN1055 (BNT315, HexaBody-OX40)
- GEN1059 (BNT314, DuoBody– EpCAMx4-1BB)

Potential for several additional INDs

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Building a World-class Pipeline: EPKINLY and Rina-S

Dr. Tahi Ahmadi
Executive Vice President and Chief Medical Officer, Head of Experimental Medicines

Bringing Our Own Medicines to Patients

EPKINLY: The CORE Therapy across B-cell Malignancies

- ✓ Broad and comprehensive development plan with 5 Phase 3 ongoing, more in planning
- ✓ > 20 abstracts at ASH, 4 oral presentations highlighting epcoritamab as Best-in-Class;
  - ✓ Efficacy and durability
  - ✓ Manageable safety profile
  - ✓ Versatility and combinability
- ✓ U.S.: EPKINLY is the first-and-only BsAb approved for both 3L+ DLBCL and 3L+ FL

B-NHL Type	Indication	Intervention	Phase	Estimated Primary Completion
DLBCL	1L	Epcoritamab + R-CHOP	3	2027
DLBCL	2L	Epcoritamab + lenalidomide	3	2028
DLBCL	2L	Epcoritamab vs SOC	3	2025
FL	1L	Epcoritamab + R2	3	2030
FL	2L	Epcoritamab + R2	3	2030

Expanded Vision for Rina-S
Development Plan for Ovarian Cancer and Beyond

Additional Clinical Data and Clinical Trials in 2025

Planned Rina-S Trials	Phase 1/2 dose escalation / expansion solid tumors (ongoing) 2025: ongoing combination cohorts +carboplatin (PSOC), +bevacizumab (PROC), + PD1 (endometrial cancer)
Ongoing Ovarian Trials	✓Phase 3 trial in 2L+ FRα+ PROC **enrolling** ✓ **All comers**, regardless of FRα expression ✓ Includes patients with **prior exposure to mirvetuximab**

PSOC = platinum-sensitive ovarian cancer; PROC = platinum-resistant ovarian cancer

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Rina-S at ESMO

Presented by Dr. Elizabeth K. Lee, MD, Department of Medical Oncology and Division of Gynecologic Oncology, Dana-Farber Cancer Institute

A Phase 1/2 study of Rinatabart Sesutecan (Rina-S) in Patients With Advanced Ovarian or Endometrial Cancer

Elizabeth K. Lee, Oladapo Yeku, Ira Winer, Erika Hamilton, Debra L. Richardson, Jian Zhang, Gottfried Konecny, Ian Anderson, Xiaohua Wu, Douglas Orr, Sandip P. Patel, Andrea Jewell, Jing Wang, Alexander Spira, Anton Melnyk, Leigh Seamon, Edward Kavalerchik, Zhu Chen, Eric Song, Justin Call

Presented at the ESMO Congress 2024, Barcelona, Spain, 15 September 2024

Declaration of Interests

Elizabeth K. Lee

Research funding (paid to the institution): Merck, OnCusp Therapeutics, Repare Therapeutics, Seagen, KSQ Therapeutics/Roche, ProfoundBio/Genmab, Eli Lilly

Advisory board participation: Aadi Biosciences, OnCusp Therapeutics

Background

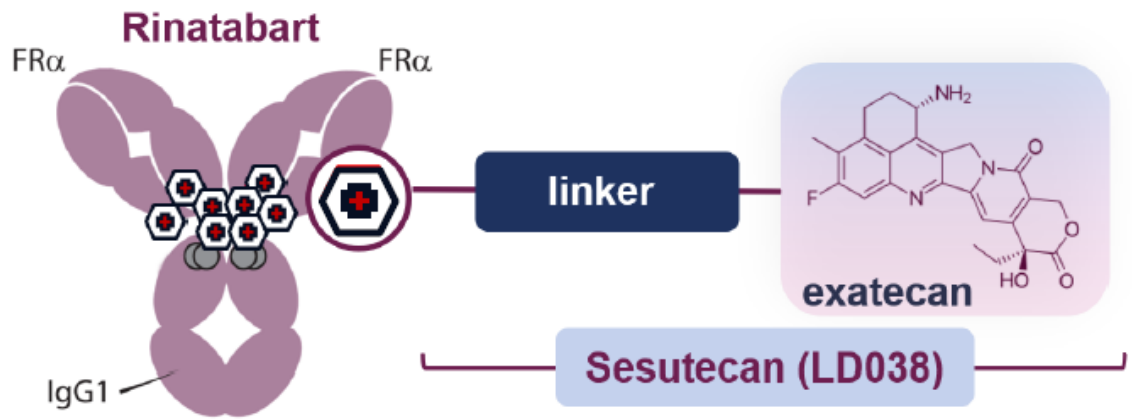
- OC and EC continue to have high unmet needs[1]
- Patients with PROC have a poor prognosis, and treatment options remain limited[2,3]
- Novel, efficacious therapies are needed for patients with EC who have received prior platinum-based chemotherapy and anti-PD-(L)1[4-9]

FRα is overexpressed on multiple solid tumors, including OC and EC[10]

Rinatabart sesutecan (Rina-S) is an investigational, novel ADC composed of[11]:

- A human monoclonal antibody directed at FRα
- A novel hydrophilic protease-cleavable linker
- Exatecan, a topoisomerase I inhibitor

Rina-S features a high, homogenous drug-to-antibody ratio of 8[10]



ADC, antibody-drug conjugate; CT, chemotherapy; EC, endometrial cancer; FRα, folate receptor α; OC, ovarian cancer; PD-(L)1; programmed cell death protein-1/ programmed death-ligand 1; PROC, platinum-resistant ovarian cancer.

1. International Agency for Research on Cancer. 2024. https://gco.iarc.fr/tomorrow/. Accessed: August 9, 2024. 2. Havasi A, et al. *Medicina* 2023;59:544. 3. Atallah GA, et al. *Int J Mol Sci* 2023;24:1-20. 4. Mirza MR, et al. *N Engl J Med* 2023;8;388:2145-2158. 5. Eskander RN, et al. *N Engl J Med* 2023;388:2159-2170. 6. Westin SN, et al. *J Clin Oncol* 2024;42:283-299. 7. Colombo N, et al. *Lancet Oncol* 2024. doi: 10.1016/S1470-2045(24)00334-6. 8. Oaknin A, et al. *Clin Cancer Res* 2023;29:4564-4574. 9. O'Malley DM, et al. *J Clin Oncol* 2022;40:752-761. 10. Ledermann JA, et al. *Ann Oncol* 2015;26(10):2034-2043. 11. Call J, et al. *J Immunother Cancer* 2023;11(Suppl 1):803.

Study Design and Patient Demographics

Objective: Report safety and efficacy of single-agent Rina-S Q3W from dose escalation (OC and EC) and dose expansion (OC) of an open-label, multicenter phase 1/2 study (NCT05579366)[1]

Study Design

Part A – Dose Escalation

- Solid tumors[a] dose escalation (n = 53) included patients regardless of FRα expression with previously treated OC (n = 32; 23 received Rina-S 100-120 mg/m² Q3W) and EC (n = 11; 5 received Rina-S 100-120 mg/m² Q3W)

Part B – Dose Expansion

- Planned tumor-specific dose expansion includes OC, EC, and *EGFR*-mutant NSCLC regardless of FRα expression[b]
- **Cohort B1 - OC Dose Expansion**
  - Inclusion criteria
    - Histologically or cytologically confirmed OC (must have epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer)
    - Prior treatment (1-3 prior lines for PROC or 4 prior lines regardless of platinum-sensitivity status)
    - ECOG PS 0-1
    - Measurable disease per RECIST v1.1
    - Adequate hematologic, hepatic, renal, and cardiac function
  - Randomized 1:1 to receive Rina-S 100 mg/m² or Rina-S 120 mg/m² Q3W

Patient Demographics and Disease Characteristics in OC Dose Expansion

OC Dose Expansion	Rina-S 100 mg/m² n = 22	Rina-S 120 mg/m² n = 20
Age, median (range), years	62.5 (42-82)	64.5 (37-83)
Prior lines of therapy, median (range)	3 (1-5)	3 (1-4)
Bevacizumab, n (%)	20 (90.9)	18 (90.0)
PARPi, n (%)	15 (68.2)	13 (65.0)
Mirvetuximab soravtansine, n (%)	4 (18.2)	4 (20.0)
Platinum sensitivity status, n (%)		
Resistant	20 (90.9)	19 (95.0)
Sensitive	2 (9.1)	1 (5.0)

DCO: July 28, 2024

[a]Patient populations included patients with epithelial OC, EC, HER2- BC, NSCLC, and mesothelioma. [b]FRα levels retrospectively assessed.
BC, breast cancer; DCO, data cutoff; EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FRα, folate receptor α; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; OC, ovarian cancer; PARPi, poly-ADP ribose polymerase inhibitor; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; Rina-S, rinatabart sesutecan.

1. National Library of Medicine. https://www.clinicaltrials.gov/study/NCT05579366. Accessed: August 7, 2024.

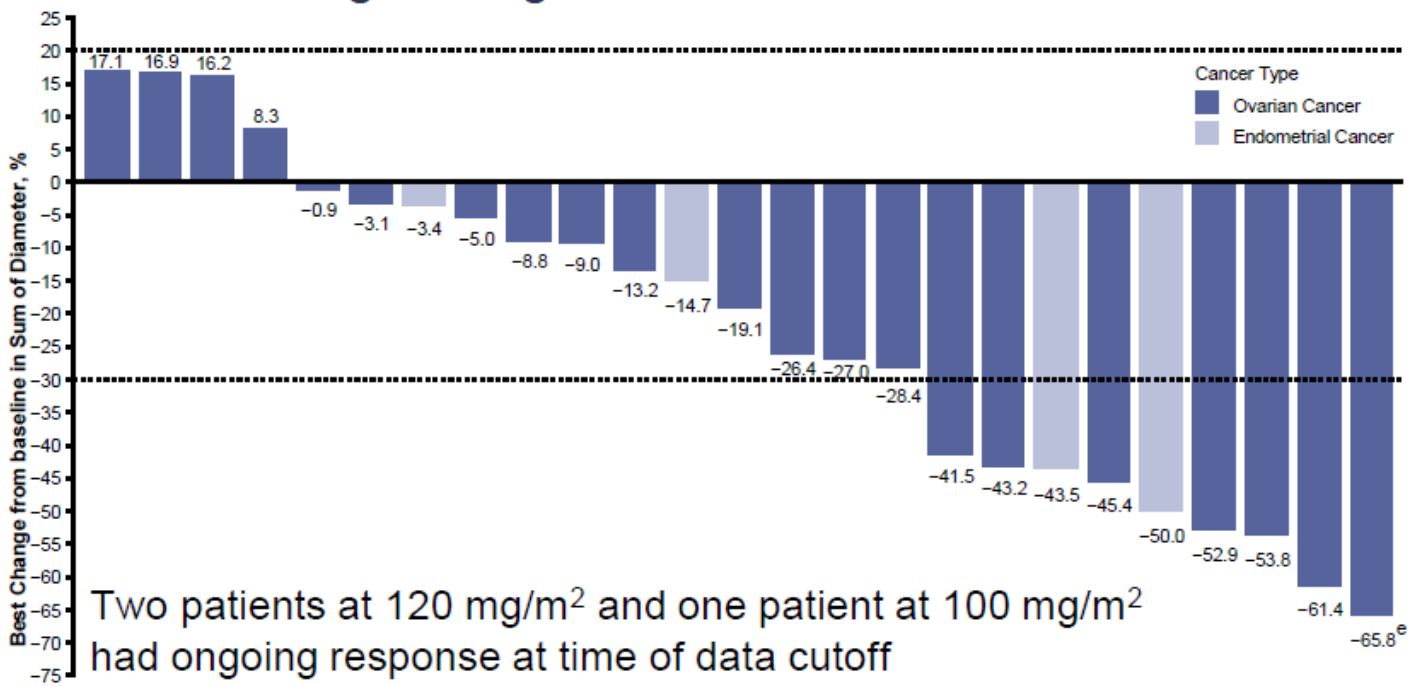
Antitumor Activity | OC, EC – Dose Escalation

Rina-S Q3W showed encouraging antitumor activity in patients with heavily pretreated OC and EC

OC and EC Dose Escalation	Rina-S 100 and 120 mg/m² n = 26[a]
Confirmed ORR,[b] % (95% CI)	30.8 (14.3-51.8)
Best overall response,[b] n (%)	
PR	8 (30.8)
SD	15 (57.7)
PD	3 (11.5)
DCR, % (95% CI)	88.5 (69.8-97.6)
Median DOR, weeks (95% CI)	35.3 (20.14-NE)

Median prior lines treatment, n (range): 4 (1-13)[c]
Treatment duration, range: 0.6-57.7+ weeks[c]
Median on-study follow-up, n: 34.6 weeks[d]

Best Change in Target Lesion in OC and EC Dose Escalation



Two patients at 120 mg/m² and one patient at 100 mg/m² had ongoing response at time of data cutoff

Median no. of cycles: 5.0+

[a]Response-evaluable population; includes all treated patients who had a baseline and at least 1 evaluable postbaseline tumor assessment, or who had documented PD any time after their first dose of Rina-S. Response assessment per RECIST v1.1. [b]Based on investigator assessment. [c]For all patients who received Rina-S 100 mg/m² or 120 mg/m². [d]For patients with OC and EC who received Rina-S 100 mg/m² or 120 mg/m². [e]Per RECIST v1.1 patient had a best response of SD; patient had PR at week 6 followed by PD at week 12.
CI confidence interval; DCR, disease control rate; DOR, duration of response; EC, endometrial cancer; OC, ovarian cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; Rina-S, rinatabart sesutecan; SD, stable disease.

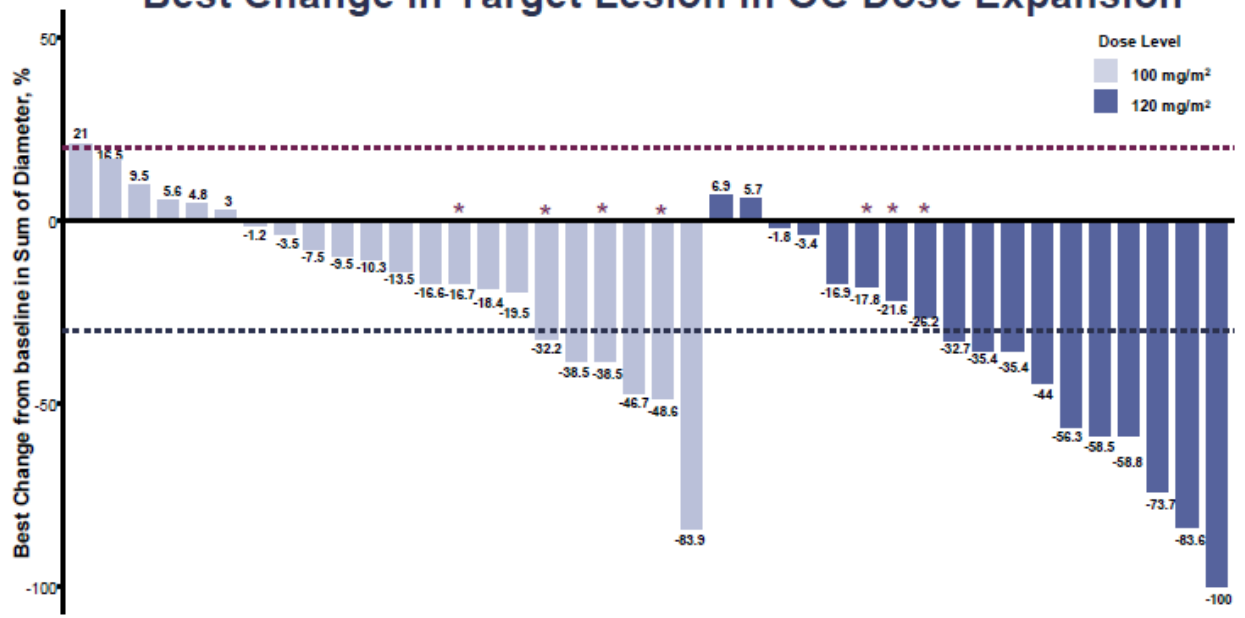
Antitumor Activity | OC – Dose Expansion

Rina-S showed encouraging antitumor activity at 120 mg/m² Q3W, including a complete response, in patients with heavily pretreated OC

OC Dose Expansion	Rina-S 100 mg/m² n = 22[b]	Rina-S 120 mg/m² n = 18[b]
Confirmed ORR,[a,b] % (95% CI)	18.2 (5.2-40.3)	50.0 (26.0-74.0)
Best overall response,[b] n (%)		
CR	0	1 (5.6)
PR	4 (18.2)	8 (44.4)
SD	15 (68.2)	7 (38.9)
PD	3 (13.6)	1 (5.6)
Not evaluable	0	1 (5.6)
DCR, % (95% CI)	86.4 (65.1-97.1)	88.9 (65.3-98.6)
Median DOR (95% CI)	NR (NR-NR)	

Treatment duration, range: 3.0-42.0+ weeks
Median on-study follow-up: 24 weeks

Best Change in Target Lesion in OC Dose Expansion



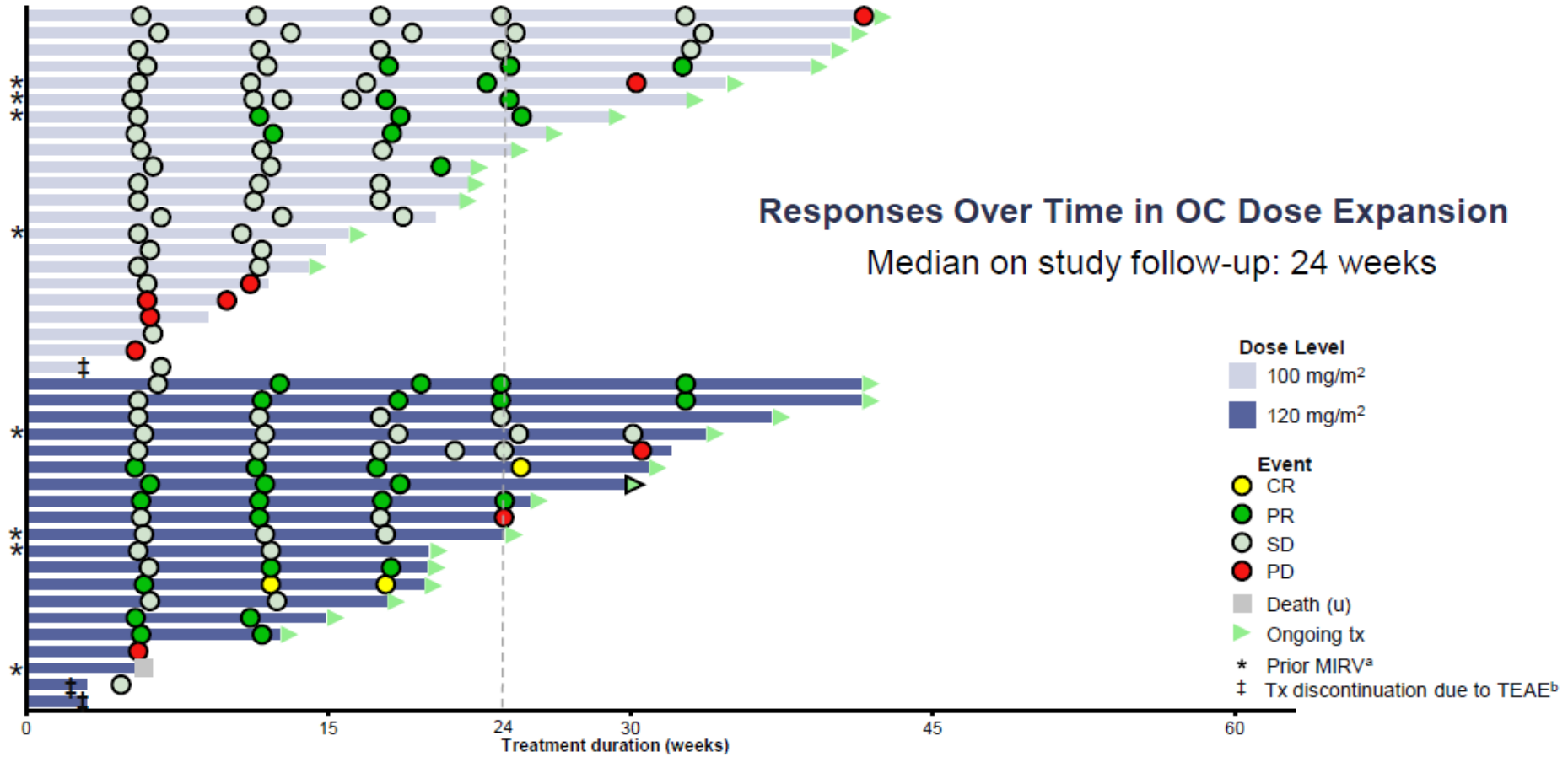
*Prior mirvetuximab soravtansine treatment[c]

Median no. of cycles: 6.5 (100 mg/m²) and 7.0+ (120 mg/m²)

[a]Based on investigator assessment. [b]Response-evaluable population. [c]One patient in the 120 mg/m² cohort with prior mirvetuximab soravtansine was not response-evaluable.
CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; NR, not reached; OC, ovarian cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; Rina-S, rinatabart sesutecan; SD stable disease.

Antitumor Activity | OC – Dose Expansion

Most responses with Rina-S 120 mg/m^2 Q3W were observed early (at week 6) and all confirmed responses with 120 mg/m^2 were ongoing at the time of data cutoff in patients with heavily pretreated OC

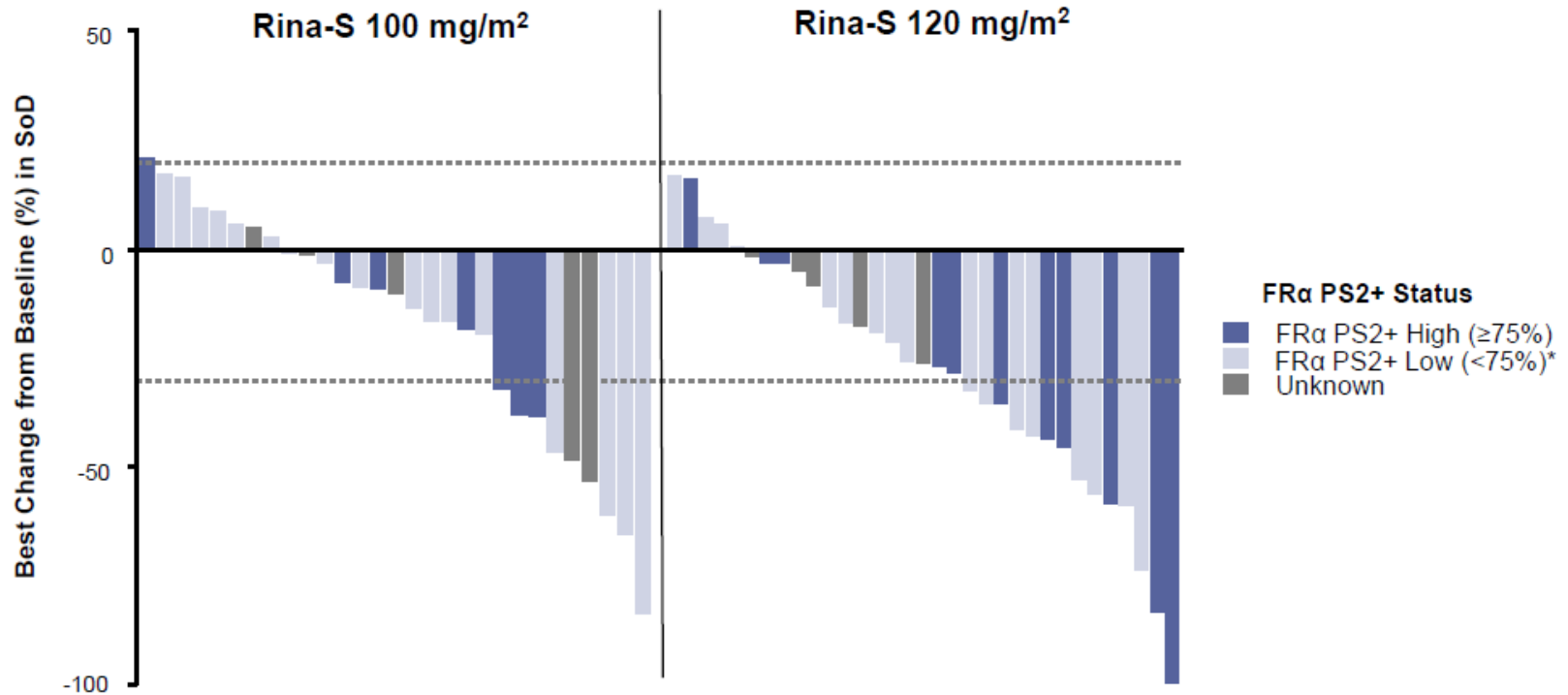


[a]One patient in 120 mg/m^2 cohort with prior mirvetuximab was not response-evaluable. [b]Reasons for discontinuation included alanine aminotransferase increased (n = 1; related to treatment), neutrophil count decreased (n = 1; related to treatment), and a small intestinal perforation and rectal hemorrhage (n = 1; not related to treatment; same patient).
CR, complete response; MIRV, mirvetuximab soravtansine; OC, ovarian cancer; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; Rina-S, rinatabart sesutecan; SD, stable disease; tx, treatment.

Response by FRα Expression | OC – Dose Escalation & Expansion

Responses in patients with OC were observed regardless of FRα expression levels

Best Change in Target Lesion SoD by FRα PS2+ Status in OC Dose Escalation and Expansion

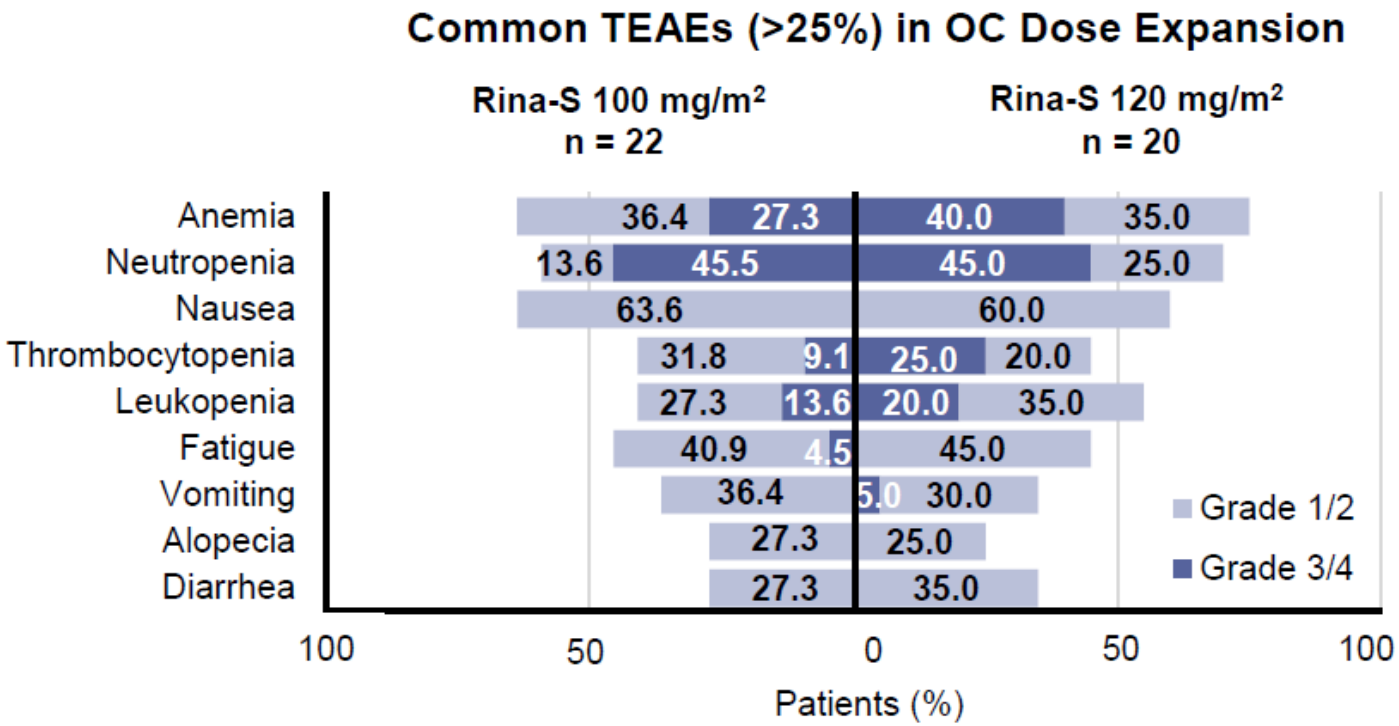


*Clinical activity was observed at lower cutoffs (FRα PS1+ <25%).
FRα, folate receptor α; OC, ovarian cancer; PS, positive staining; SoD, sum of diameter; Rina-S, rinatabart sesutecan

Overall Safety

- In dose escalation at 100 - 120 mg/m^2 (n = 35), the most common any grade TEAEs were cytopenias[a] (34.3% - 60.0%)
- No signals of ocular toxicities, neuropathy, or ILD were observed

OC Dose Expansion	Rina-S 100 mg/m^2 n = 22	Rina-S 120 mg/m^2 n = 20
Any-grade TEAE, %	100.0	100.0
Grade 3/4	63.6	60.0[b]
TEAEs leading to dose reductions, %	18.2	20.0
TEAEs leading to treatment discontinuation[c], %	4.5	10.0
GCSF use[d], %	31.8	50.0



[a]Events included neutropenias, anemia, leukopenias, and thrombocytopenias. [b]One Grade 5 acute respiratory failure was unrelated to the study treatment. [c]Reasons for discontinuation included alanine aminotransferase increased (n = 1; related to treatment), neutrophil count decreased (n = 1; related to treatment), and a small intestinal perforation and rectal hemorrhage (n = 1; not related to treatment; same patient). [d]GCSF-prophylaxis was not permitted in cycle 1.
GCSF, granulocyte colony-stimulating factor; ILD, interstitial lung disease; OC, ovarian cancer; Rina-S, rinatabart sesutecan; TEAE, treatment-emergent adverse event

Conclusions

- Rina-S, an investigational, novel ADC directed at FRα, showed encouraging antitumor activity as a single agent given Q3W in patients with heavily pretreated OC and EC in dose escalation
- Treatment with Rina-S at 120 mg/m^2 Q3W resulted in a confirmed ORR of 50.0%, including one complete response, in patients with heavily-pretreated OC in dose expansion; all responses were ongoing at data cutoff
  - Based on these results 120 mg/m^2 has been selected for further evaluation
- Responses with Rina-S were observed regardless of FRα expression levels and in patients with prior MIRV exposure
- Treatment with Rina-S was well tolerated, with manageable TEAEs
  - Hematologic AEs were manageable without significant dose reductions and with low rates of treatment discontinuation
  - No signals of ocular toxicities, neuropathy, or ILD were observed
- Based on these findings, further evaluation of Rina-S is ongoing as a single-agent and in combination[a]
  - EC dose expansion (Cohort B2, fully-enrolled): single agent Rina-S in patients with EC after ≥1 prior lines of therapy including with prior platinum and ICI
  - PROC dose expansion (Part C, enrolling): single agent Rina-S in patients with PROC after 1-3 prior lines of therapy

[a]Part D is evaluating Rina-S in combination with carboplatin in patients with PSOC (cohort D1), in combination with bevacizumab in patients with PROC (cohort D2), and in combination with pembrolizumab in patients with EC (cohort D3).
ADC, antibody-drug conjugate; AE, adverse event; EC, endometrial cancer; FRα, folate receptor α; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; MIRV, mirvetuximab soravtansine; OC, ovarian cancer; PROC, platinum-resistant ovarian cancer. Rina-S, rinatabart sesutecan; TEAEs, treatment-emergent adverse events

Acknowledgments

- On behalf of all the authors, we thank the patients, study investigators, and site personnel for their participation in this study
- This study was funded by Genmab A/S
- Medical writing and editorial support were provided by Charlene Rivera, PhD, CMPP, of MEDiSTRAVA and funded by Genmab

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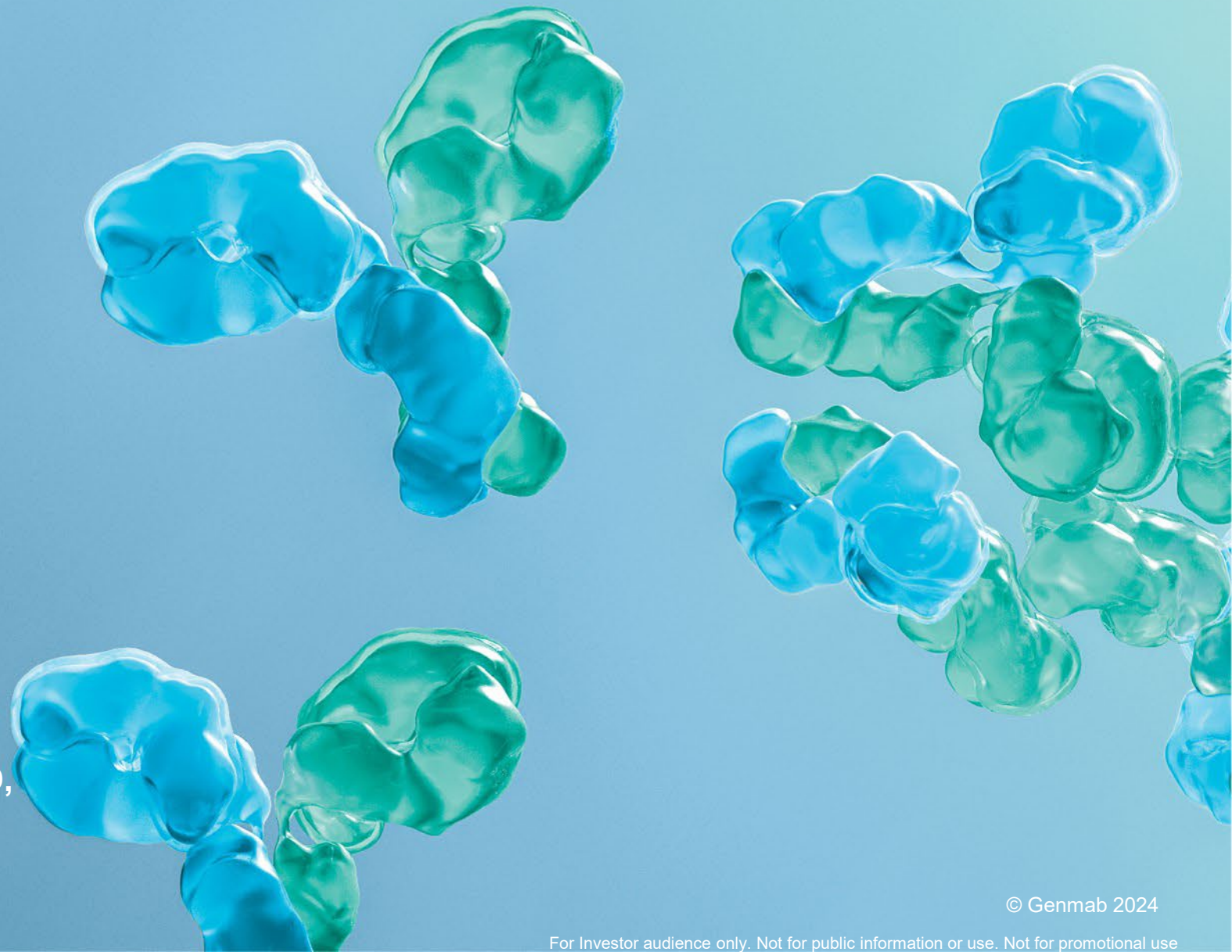
Epcoritamab at ASH



Presented by Dr. Martin Hutchings, MD, PhD, Sr. Consultant and Professor, Copenhagen University Hospital

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

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

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

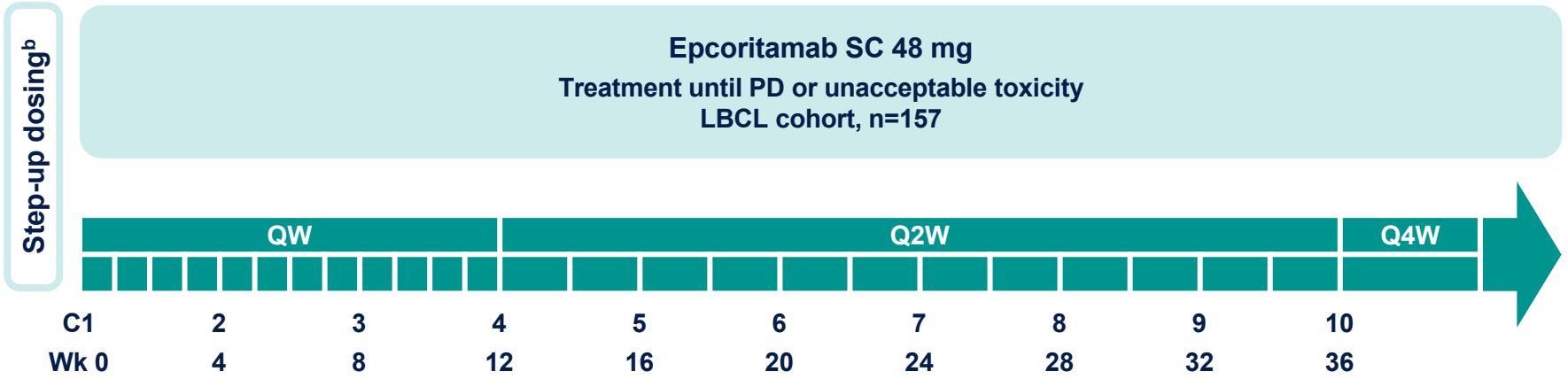
Study Design: Pivotal EPCORE® NHL-1 Trial

Dose expansion

Key inclusion criteria:

- R/R CD20+ LBCL
  - DLBCL (*de novo* or transformed)
  - "Double-" or "triple-hit" DLBCL[a]
  - PMBCL
  - HGBCL
  - FL G3B
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, incl ≥1 anti-CD20 mAb
- Measurable disease by CT/MRI
- Prior CAR T therapy allowed

Median follow-up: 37.1 mo



- **Primary endpoint:** ORR per Lugano criteria[1]
- **Key secondary endpoints:** CR, DOR, DOCR, PFS, OS, TTNT, MRD- rate, and safety/tolerability
- Exploratory MRD analyses of ctDNA were performed using the clonoSEQ® NGS assay[c]

We present 3-year follow-up results, including long-term efficacy and safety, in patients with R/R LBCL treated with epcoritamab monotherapy in the pivotal EPCORE NHL-1 trial

[a]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [b]SUD 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. Corticosteroid prophylaxis was used in C1 to mitigate CRS. To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 h; this requirement has since been removed in the C1 optimization cohort. [c]Samples collected on D1 of Cs 3, 5, 7, 10, and 13, then every 6 mo (±1 mo) for up to 3 y from C1D1. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36. **1.** Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-68.

No New Safety Findings

- The overall safety profile was consistent with previous reports[1-3]
- 73% of patients on treatment ≥2 y did not experience a G≥3 infection
- Incidence of G≥3 cytopenias was highest (27%) during the first 8 wk of treatment, but were lowered (0%–13%) in subsequent 12-wk time periods up to wk 144

Long-term safety consistent with previous reports

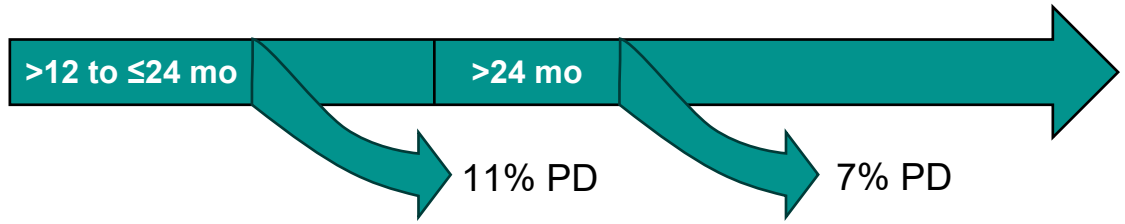
[*a]An additional patient died due to COVID-19 pneumonia prior to the data cutoff (not considered related to epcoritamab), but the AE was upgraded to G5 after the data cutoff (May 3, 2024).

1. Thieblemont C, et al. *J Clin Oncol*. 2023;41:2238-47. **2.** Thieblemont C, et al. *Leukemia*. 2024;DOI:10.1038/s41375-024-02410-8. **3.** Karimi YH, et al. ASCO 2024. Abstract 7039.

Long-Term Efficacy Outcomes

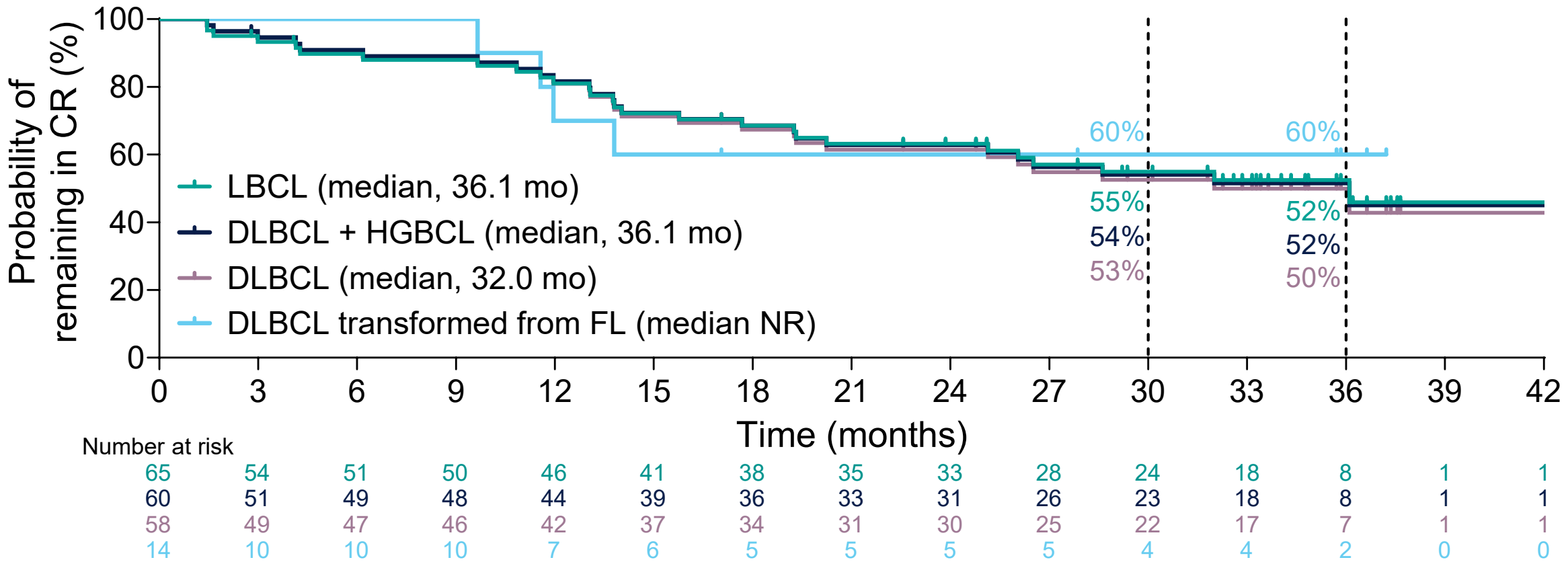
	LBCL N=157
ORR, n (%)	92 (59)
CR	65 (41)
PR	27 (17)

- Notably, few patients progressed after remaining on epcoritamab treatment beyond 1 year:
  - 5 of 47 patients (11%) from >12 to ≤24 mo
  - 2 of 29 patients (7%) beyond 24 mo



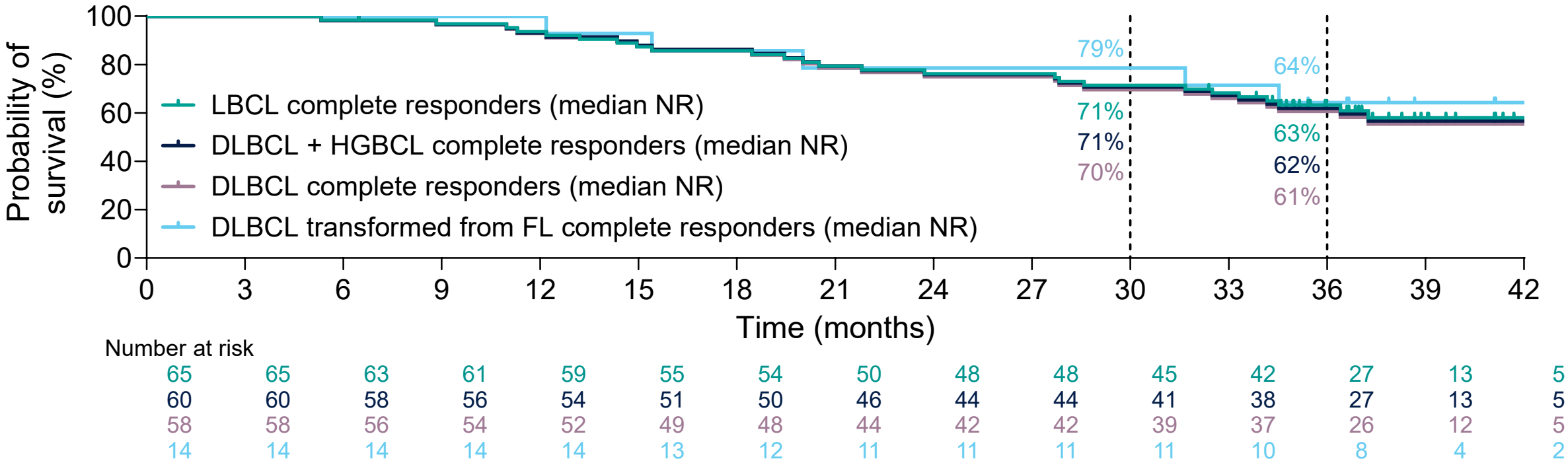
Response rates were high, with few progressions beyond 12 months

Durable Complete Responses beyond 3 years



Durable Complete Responses > 2 years indicate the curative potential of epcoritamab

Overall Survival



Among CR patients mOS was NR

At 3 years, 75% of complete responders had not initiated a new antilymphoma therapy

Conclusions: 3 years Follow Up

- Long-term safety was consistent with previous reports and the established safety profile of epcoritamab[1-3]
- Complete Responses were durable beyond 3 years
- Among complete responders:
  - mDoCR 36.1 mo
  - mPFS 37.3 mo
  - mOS NR
- Long-term remissions support a treat-to-progression approach in this 3L+ patient population and suggests curative potential

1. Thieblemont C, et al. *J Clin Oncol*. 2023;41:2238-47. **2.** Thieblemont C, et al. *Leukemia*. 2024;DOI:10.1038/s41375-024-02410-8. **3.** Karimi YH, et al. ASCO 2024. Abstract 7039.

Fixed-Duration Epcoritamab + R-CHOP Induces High Complete Response Rates in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma with High-Risk Features: Long-Term Results from the EPCORE NHL-2 Trial

Lorenzo Falchi, MD,[1] Fritz Offner, MD, PhD,[2] Sven de Vos, MD, PhD,[3] Joshua D. Brody, MD,[4] Raul Cordoba, MD, PhD,[5] Kim M. Linton, MBChB, PhD,[6] Sylvia Snauwaert, MD, PhD,[7] Michael Roost Clausen, MD, PhD,[8] Toshihiko Oki, MD, PhD,[9] Andrew J. Steele, PhD,[10] Yi Hao, DrPH,[10] Kimberly G. Archer,[10] Ali Rana, MD, PhD,[10] David Belada, MD, PhD[11]

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

Background

- R-CHOP is an accepted standard treatment for 1L DLBCL; however, approximately one-third of patients experience relapse, mostly within 2 years[1-3]
  - No regimens since R-CHOP have shown improved overall survival in 1L DLBCL[1,2]

- Initial data for epcor+ R-CHOP showed combinability and encouraging efficacy when given for a fixed duration of 1 year with R-CHOP for the treatment of 1L DLBCL[3]

We present long-term outcomes (>2 years) with epcoritamab + R-CHOP for patients with high-risk 1L DLBCL

1. Sehn LH, Salles G. *N Engl J Med*. 2021;384:842-58. **2.** Tilly H, et al. *N Engl J Med*. 2022;386:351-63.. **.** Clausen MR, et al. EHA 2023. Abstract P1116.

Study Design: EPCORE® NHL-2 Arm 1 (NCT04663347)

Key inclusion criteria

- Newly diagnosed CD20+ DLBCL[a]
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - Double-hit or triple-hit DLBCL
  - FL grade 3B
- **IPI score 3-5**
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: May 15, 2024

Median follow-up: 27.4 mo

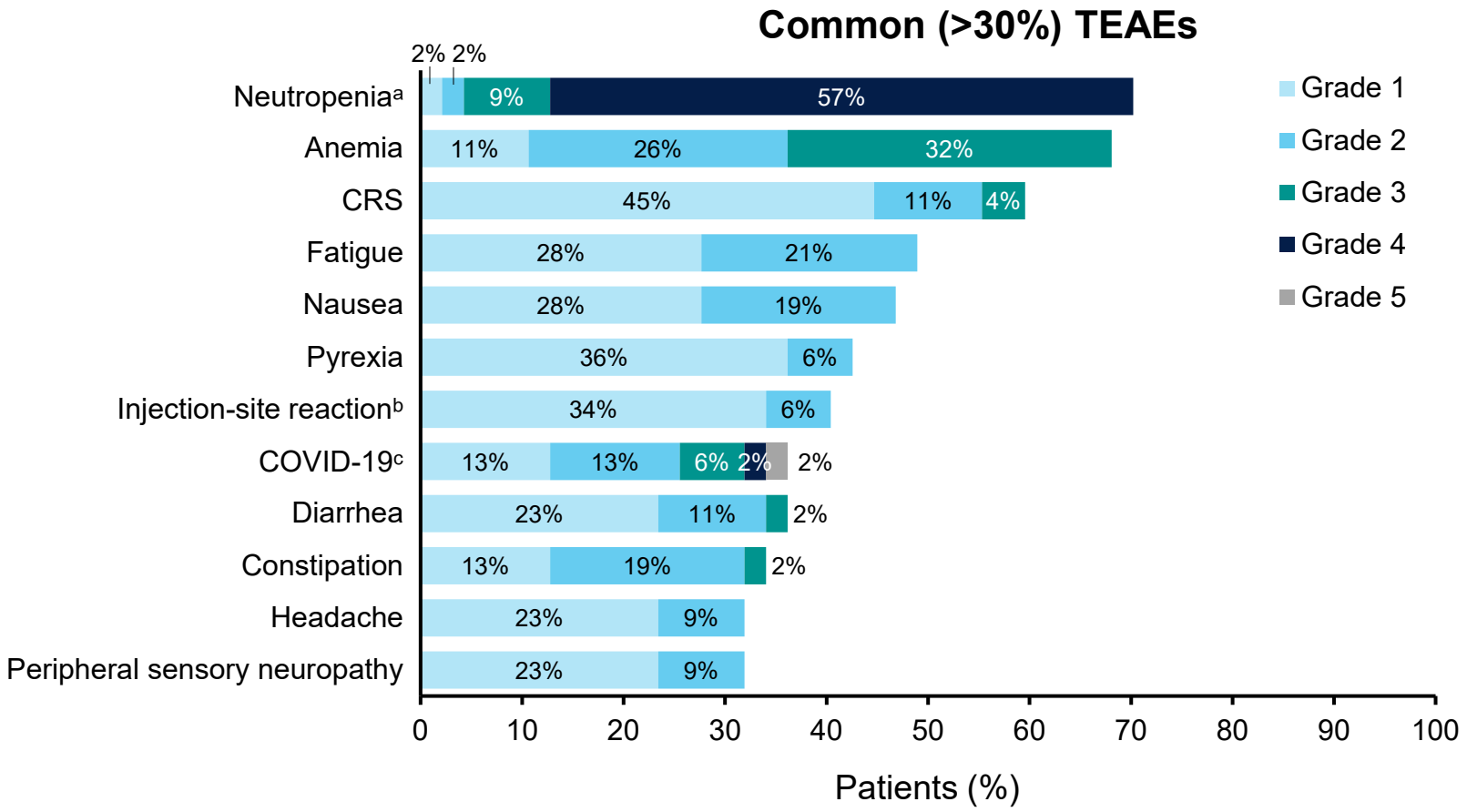
Treatment regimen: concomitant fixed-duration epcoritamab SC 48 mg + R-CHOP[b]

	Agent	C1–4	C5–6	C7+
	Epcoritamab SC 48 mg	QW	Q3W	Q4W Up to 1 year per protocol
R-CHOP	Rituximab IV 375 mg/m^2	Q3W		
R-CHOP	Cyclophosphamide IV 750 mg/m^2			
R-CHOP	Doxorubicin IV 50 mg/m^2			
R-CHOP	Vincristine IV 1.4 mg/m^2			
R-CHOP	Prednisone IV or oral 100 mg/d	D1–5 of each cycle		

- **Primary objective:** Antitumor activity based on best overall response (at any time point)[c]
- MRD negativity was assessed as a secondary endpoint using AVENIO ctDNA

[a]De novo or histologically transformed from FL or nodal marginal zone lymphoma. [b]Patients received SC epcoritamab with 2 SUDs (0.16 mg and 0.8 mg) before the first full dose and corticosteroid prophylaxis to mitigate CRS. R-CHOP was given in 21-d cycles. Subsequent cycles of epcoritamab were 28 d.. [c]Tumor response was evaluated by PET-CT

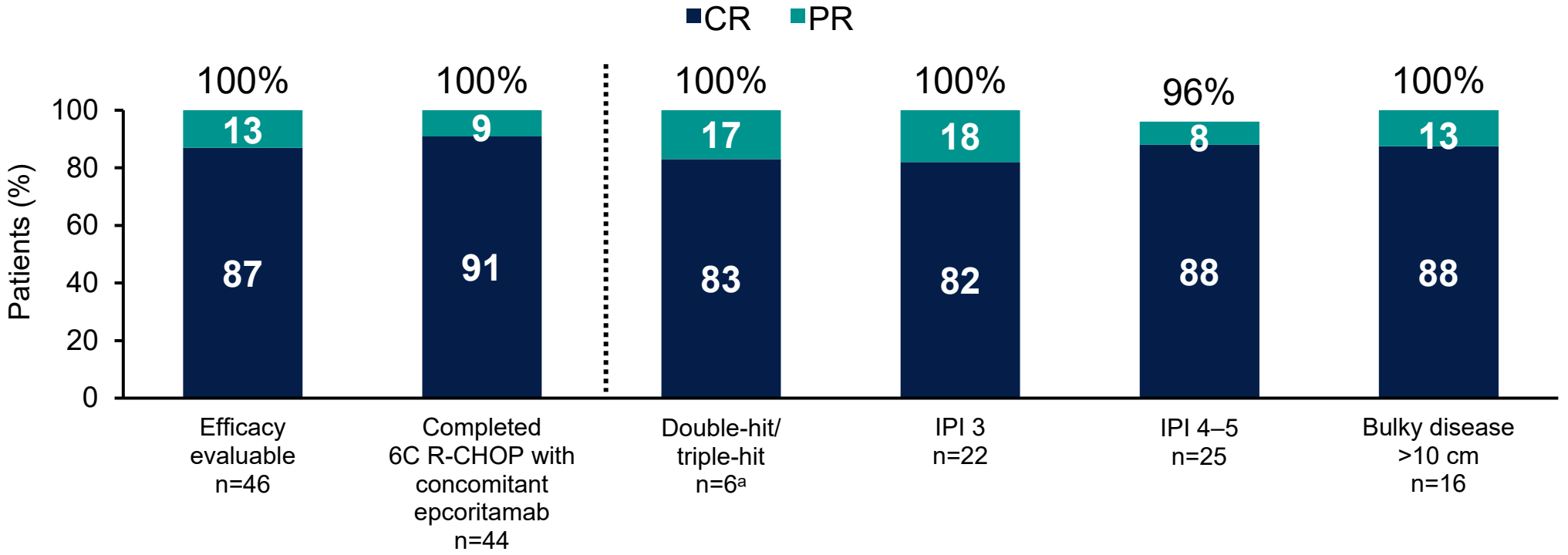
Safety Profile Was Manageable, With No New Safety Signals



- The safety profile was consistent with previous reports
- CRS was low grade and did not lead to discontinuation
- There were two grade 5 TEAEs (COVID-19 and septic shock)
- Two low-grade ICANS events resolved rapidly and did not lead to treatment discontinuation

[a]Combined term includes neutropenia and neutrophil count decreased. [b]Combined term includes injection-site reaction, pruritus, rash, discoloration, erythema, hematoma, and pain. [c]Combined term includes COVID-19 and COVID-19 pneumonia.

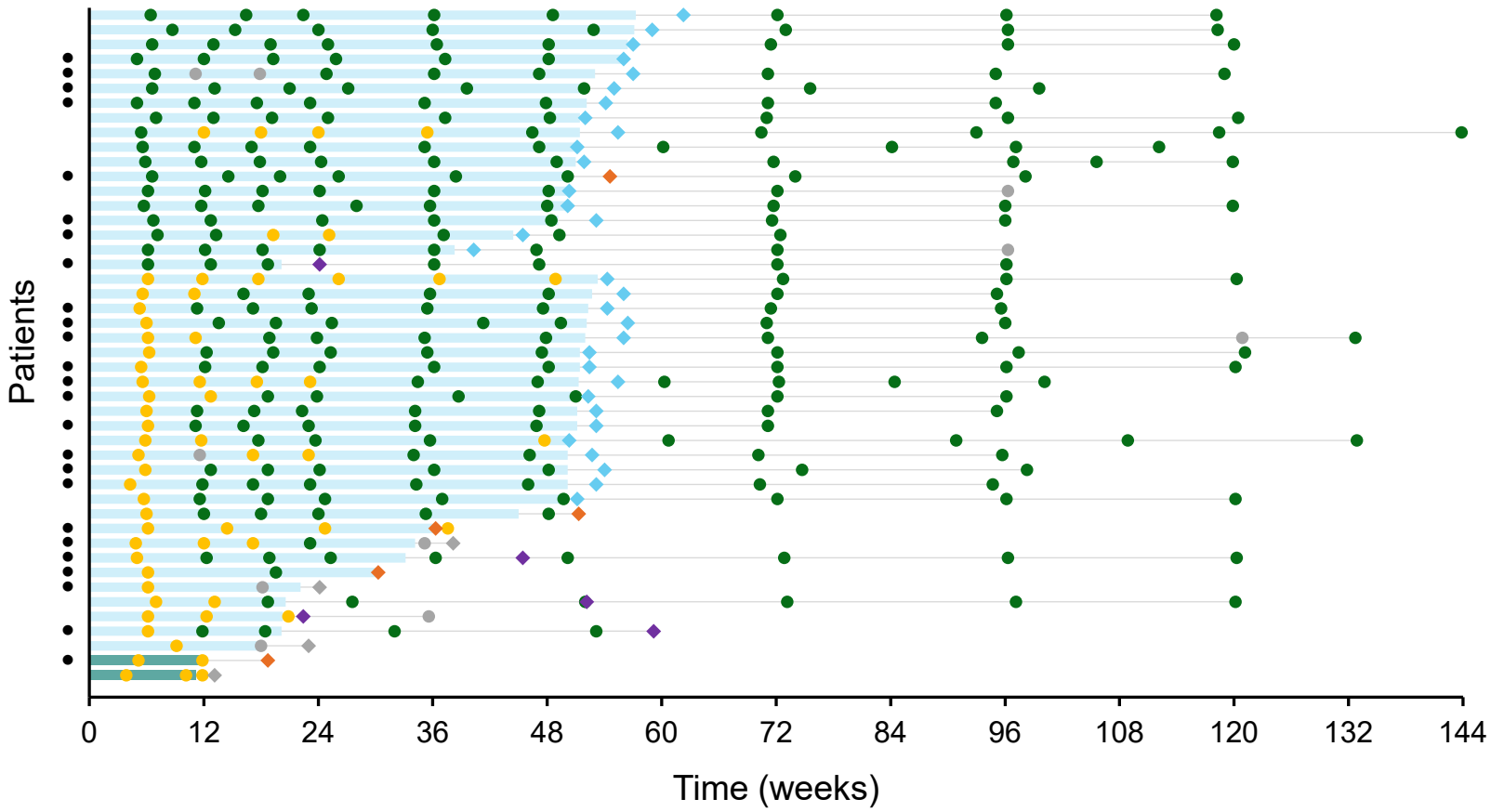
High Complete Response Rates Including Across High-Risk Subgroups



- Median relative dose intensity of R-CHOP 95%–98% was for all individual components

Median follow-up: 27.4 mo. Response rates based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and who had ≥1 postbaseline response evaluation or died within 60 d of first trial treatment. [a]Double-hit/triple-hit status by central lab was not evaluable in 19 patients.

Complete Responses Sustained After End of Treatment



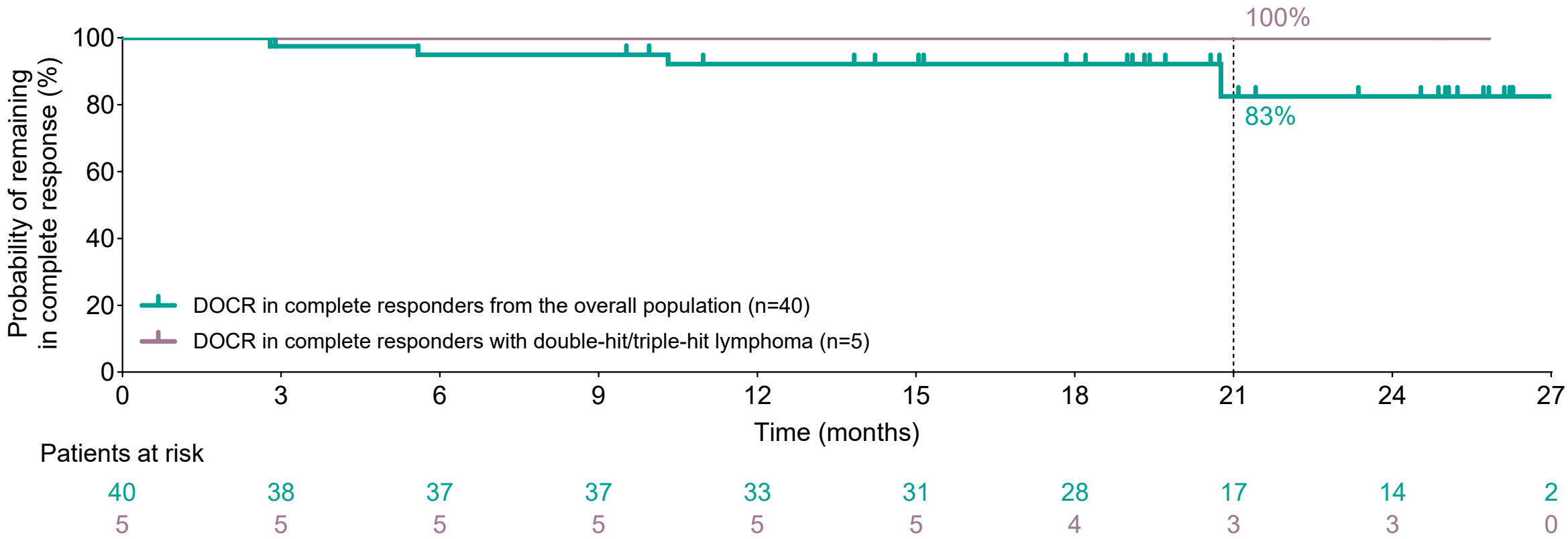
Of 32 patients who completed treatment per protocol, 94% remained in CR at data cutoff

n=46

- Time on treatment, completed 6C R-CHOP
- Time on treatment, did not complete 6C R-CHOP[b]
- CR PR PD
- Completed treatment
- Discontinued due to PD
- Discontinued due to AE
- Discontinued due to other reasons
- Patients with MRD negativity by C3D1[c]

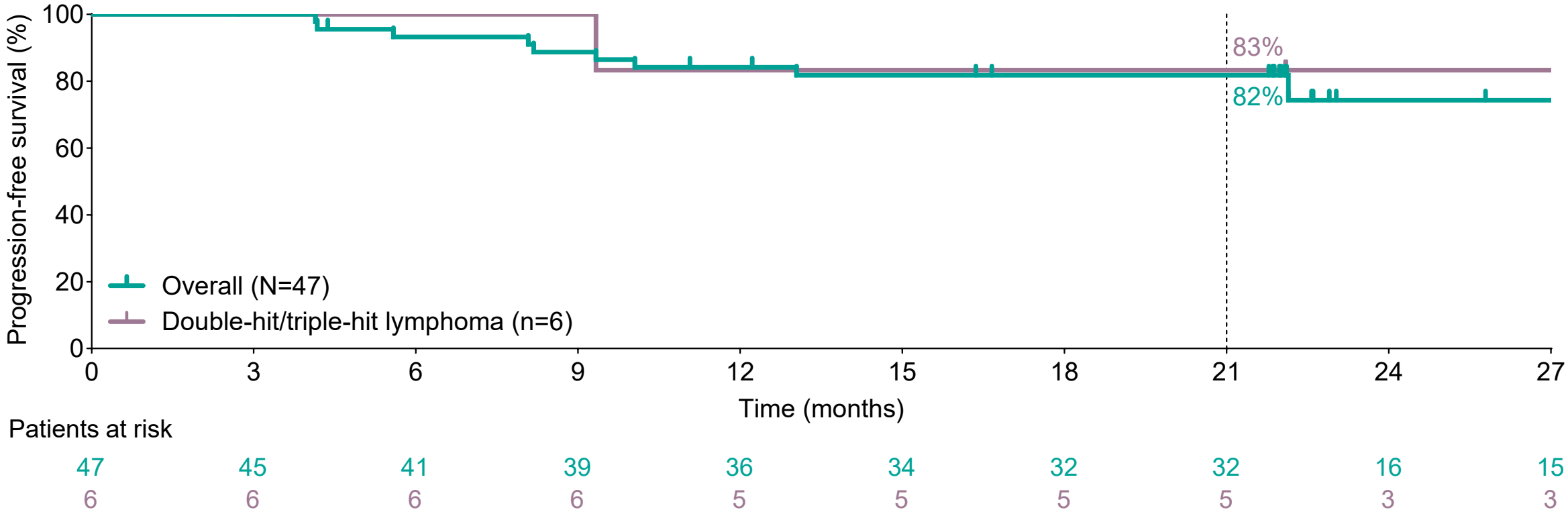
[a]Median follow-up from end of treatment to survival at data cutoff was 15.2 mo. [b]Three patients, including 2 responders shown here, did not complete 6C R-CHOP due to withdrawal of consent, PD, and an AE (n=1 each). [c]MRD negativity was assessed among patients with ≥1 baseline or on-treatment MRD result and MRD not negative at baseline.

Durable Complete Responses



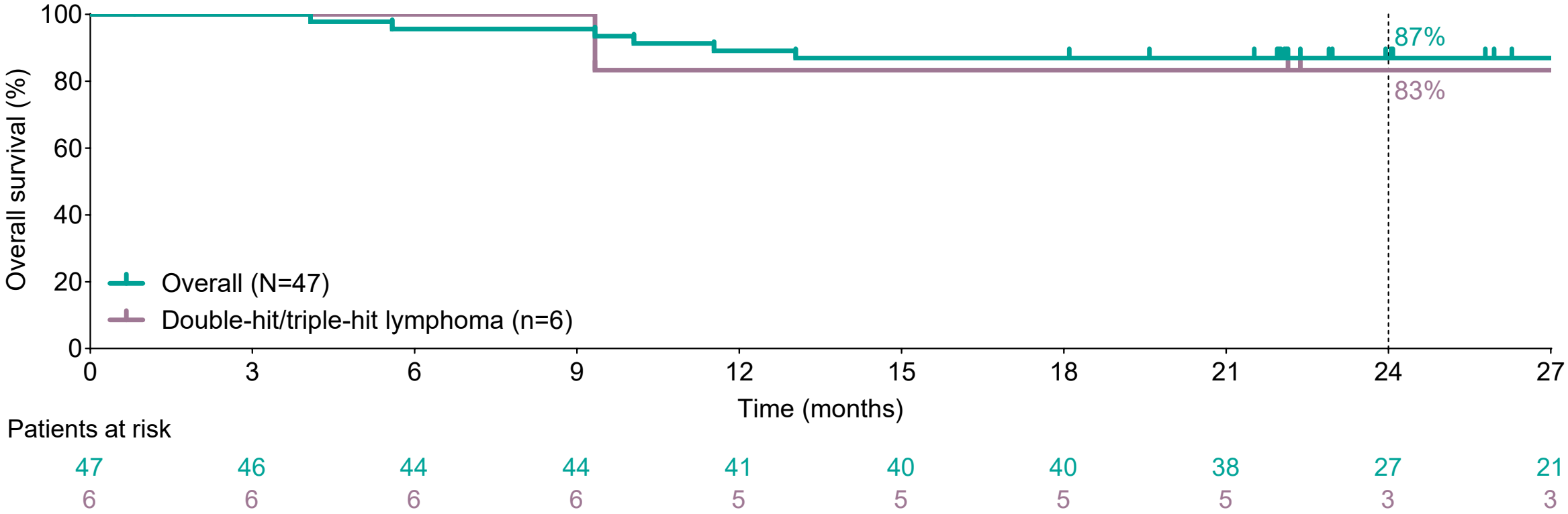
Median follow-up for DOCR: 21.1 months. Kaplan–Meier estimated probability of remaining in complete response.

High Rates of Progression-Free Survival



Median follow-up for PFS: 22.9 months. Kaplan–Meier estimated probability of remaining progression free.

Encouraging 2-Year Overall Survival



Median follow-up for OS: 27.4 months. Kaplan–Meier estimated probability of remaining alive.

Conclusions

- Fixed-duration epcoritamab + R-CHOP induced remissions of >2 years in 94% of patients with 1L DLBCL suggesting a high curative potential for this regimen
- High rates of durable complete responses and MRD negativity were observed, including those with high-risk disease features (double-hit/triple-hit lymphoma)
- No new safety signals were detected
- These findings compare favorably with R-CHOP alone and support the ongoing Phase 3 trial of epcoritamab + R-CHOP in 1L DLBCL (NCT05578976)

EPCORE DLBCL-3 First Disclosure: Fixed-Duration Epcoritamab Monotherapy in Older (≥75 y), Anthracycline-Ineligible Patients with Previously Untreated Large B-Cell Lymphoma

Franck Morschhauser, MD, PhD,[1] David Belada, MD, PhD,[2] Johannes Duell, MD,[3] Wojciech Jurczak, MD, PhD,[4] Tae Min Kim, MD, PhD,[5] Won Seog Kim, MD, PhD,[6] Takahiro Kumode, MD, PhD,[7] Javier López Jiménez, MD,[8] Caressa Meert, MD,[9] Sergio Ortegon Alcaide, MD,[10] Catherine Thieblemont, MD, PhD,[11] Tony Jiang, MD, PhD,[12] Mina Khoshdeli, PhD,[13] Yanli Wang, MS,[13] Evelyn Guo,[13] Daniela Hoehn, MD, PhD,[13]* Sherida Woei-A-Jin, MD, PhD[14]*

[1]University of Lille, CHU Lille, Lille, France; [2]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [3]Medizinische Klinik und Poliklinik II, Universitätsklinikum Würzburg, Würzburg, Germany; [4]MSC National Research Institute of Oncology, Kraków, Poland; [5]Seoul National University Hospital, Seoul, Republic of Korea; [6]Samsung Medical Center, Seoul, Republic of Korea; [7]Department of Hematology and Rheumatology, Kindai University, Osaka, Japan; [8]Servicio de Hematología y Hemoterapia, Hospital Universitario Ramón y Cajal, Madrid, Spain; [9]Algemeen Ziekenhuis Delta, Roeselare, Belgium; [10]Hospital Universitario Virgen Macarena, Sevilla, Spain; [11]Assistance Publique & Hôpitaux de Paris (APHP), Hôpital Saint-Louis, Hémato-oncologie, Université de Paris, Paris, France; [12]AbbVie, North Chicago, IL, USA; [13]Genmab, Plainsboro, NJ, USA; [14]University Hospitals Leuven, Leuven, Belgium

*Authors contributed equally.

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First Data-Disclosure in Anthracycline-Ineligible in 1L DLBCL

- Anthracycline-containing regimens, including R-CHOP and R-mini-CHOP, are standards of care for newly diagnosed patients with DLBCL[1]
  - However, ~10% of newly diagnosed patients are ineligible for anthracycline treatment due to advanced age and/or underlying comorbidities[2,3] and a very poor prognosis[4]

We report initial results from the EPCORE DLBCL-3 trial of epcoritamab monotherapy in older (≥75 y), anthracycline-ineligible patients with newly diagnosed LBCL

1. Sehn LH, Salles G. *N Engl J Med*. 2021;384:842-58. **2.** Hershman DL, et al. *J Clin Oncol*. 2008;26:3159-65. **3.** Moccia AA, et al. *Blood Adv*. 2021;5:1483-9. **4.** Lugtenburg PJ, Mutsaers PGNJ. *Blood*. 2023;141: 2566-75. **5.** Thieblemont C, et al. *Leukemia*. 2024;38:2653-62. **6.** Linton KM, et al. *Lancet Haematol*. 2024;11:e593-e605. **7.** Vermaat JSP, et al. ASH 2023. Abstract 4457. **8.** Brody JD, et al. ASCO 2024. Abstract 7037. **9.** Falchi L, et al. ASH 2024. Abstract 581.

Study Design: EPCORE® DLBCL-3

A phase 2, open-label trial evaluating the efficacy and safety of fixed-duration epcoritamab in older, anthracycline-ineligible adults with newly diagnosed LBCL

Key inclusion criteria

- Newly diagnosed CD20+ LBCL
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - Double-hit or triple-hit DLBCL
  - FL grade 3B
- ICE score ≥8[a]
- ECOG PS 0–2
- Ineligible for anthracycline-based therapy/cytotoxic chemotherapy due to:
  - Age ≥80 y, or
  - Age ≥75 y with a comorbid condition[b]
- Measurable disease by CT or MRI

1:1 RANDOMIZATION

Agent	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W

Agent	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W
Lenalidomide PO 10–20 mg	QD D1–21	QD D1–21

Data cutoff: September 21, 2024

Median follow-up: 9.5 mo (range, 0.4–17.7+)

- **Primary endpoint:** CR rate per Lugano criteria
- **Key secondary endpoints:** ORR, TTR, DOR, DOCR, PFS, OS, MRD negativity,[d] and safety

ClinicalTrials.gov: NCT05660967. Tumor response evaluated by PET-CT. [a]ICE score per the Immune Effector Cell–Associated Encephalopathy assessment tool [2] [b]Comorbid conditions: impaired cardiac function; moderate to severe valvular heart disease; previous cardiotoxic cancer treatment; elevated baseline troponin and/or elevated baseline BNP or NT-proBNP; and pulmonary, hepatic, renal, or other comorbidities that made the patient ineligible for cytotoxic drug treatment. [c]2 step-up doses of epcoritamab administered before the first full dose. [d]MRD negativity was assessed by ctDNA using the AVENIO assay.

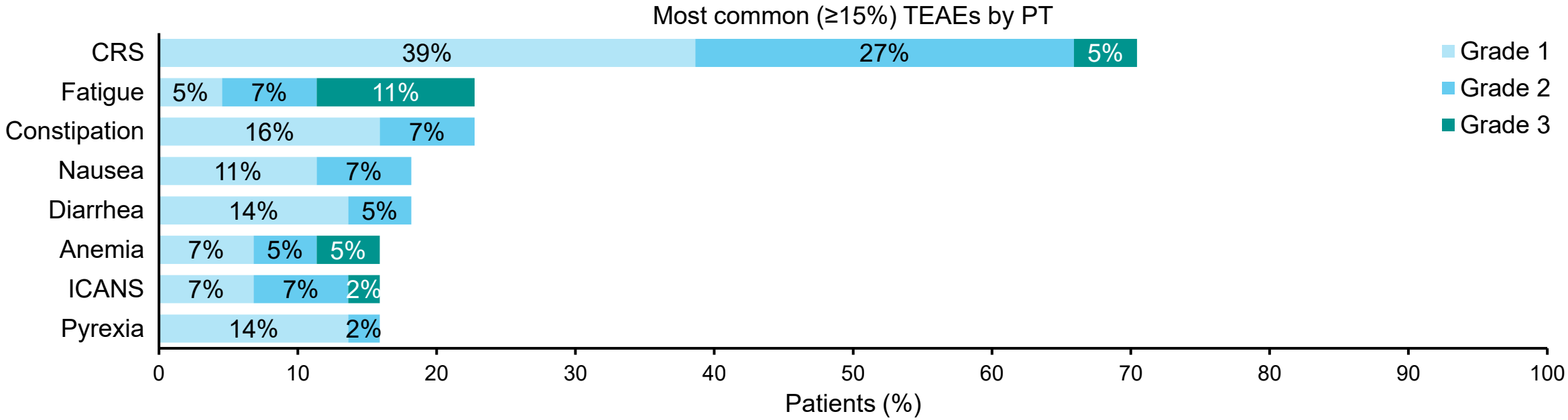
Patients Had Cardiovascular Comorbidities and Risk Factors

n (%)	N=45
Hypertension	35 (78)
Elevated cardiac enzymes[a]	32 (71)
Atrial fibrillation	7 (16)
Coronary artery disease/prior myocardial infarction	7 (16)
Moderate to severe valvular heart disease	6 (13)
Diabetes	5 (11)
Previous cardiotoxic therapy	3 (7)
Thrombosis	3 (7)
Cerebral small vessel ischemic disease	3 (7)
Reduced LVEF (<50%)	2 (4)
Carotid artery stenosis	2 (4)
Arteriosclerosis	2 (4)

- 87% had cardiac and/or cardiovascular disorders
- 40% had other comorbidities that made the patient ineligible for cytotoxic drug treatment

[a]Above institutional norm.

Epcoritamab Was Generally Well Tolerated

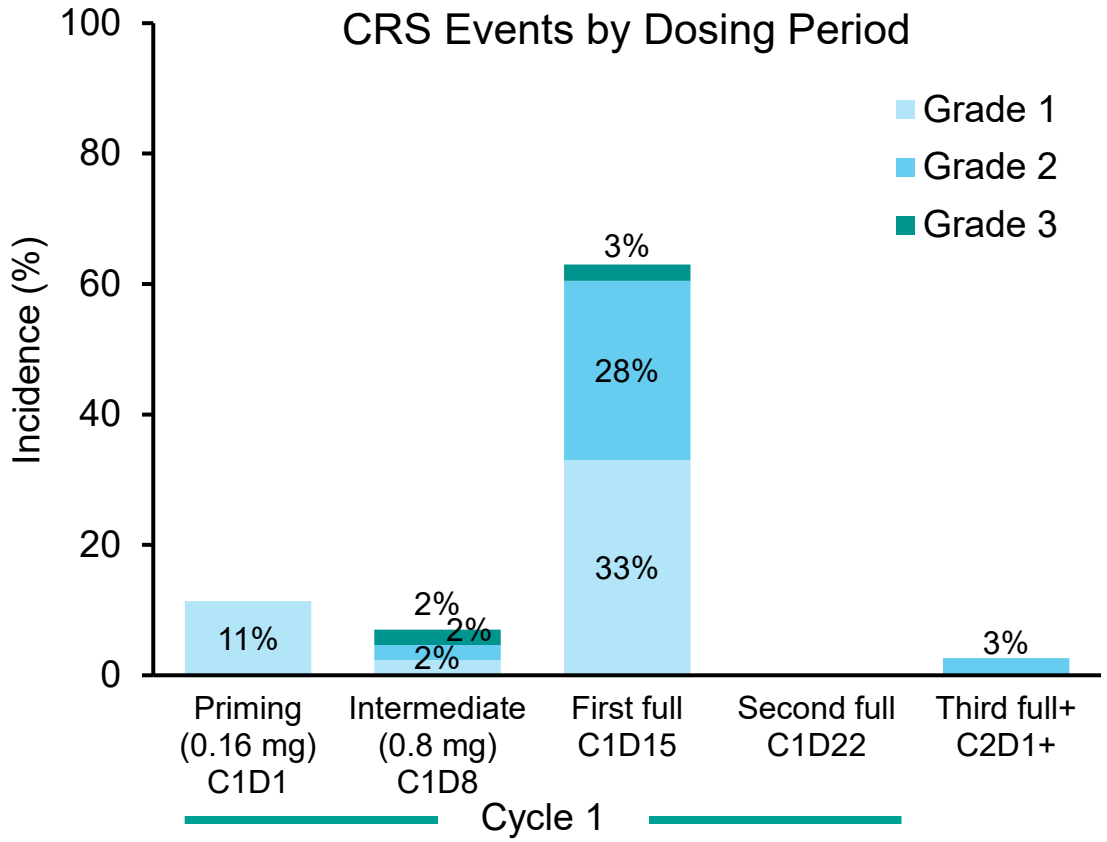


- 8 patients (18%) experienced a serious infection, including 4 (9%) with serious COVID-19 infections
- Neutropenia was observed in only 4 patients (9%), with no cases of febrile neutropenia
- 8 patients (18%) experienced TEAEs that led to epcoritamab discontinuation
- 5 patients had fatal TEAEs (COVID-19 [n=2], CMV reactivation, tumor hemorrhage, TLS)
- ICANS was reported in 7 patients (16%); all ICANS events resolved

Data are from the safety analysis set, defined as patients who received ≥1 dose of epcoritamab..

CRS Was Mostly Low Grade and Primarily Occurred in Cycle 1

	n=44
CRS,[a] n (%)	31 (71)
Grade 1	17 (39)
Grade 2	12 (27)
Grade 3	2 (5)
Median time to onset from first full dose, h (range)	15 (9–26)
Treated with tocilizumab, n (%)	14 (32)
Treated with corticosteroids, n (%)	10 (23)
CRS resolution,[b] n/n (%)	30/31 (97)
Median time to resolution, d (range)	2 (1–5)
Leading to treatment discontinuation, n (%)	0

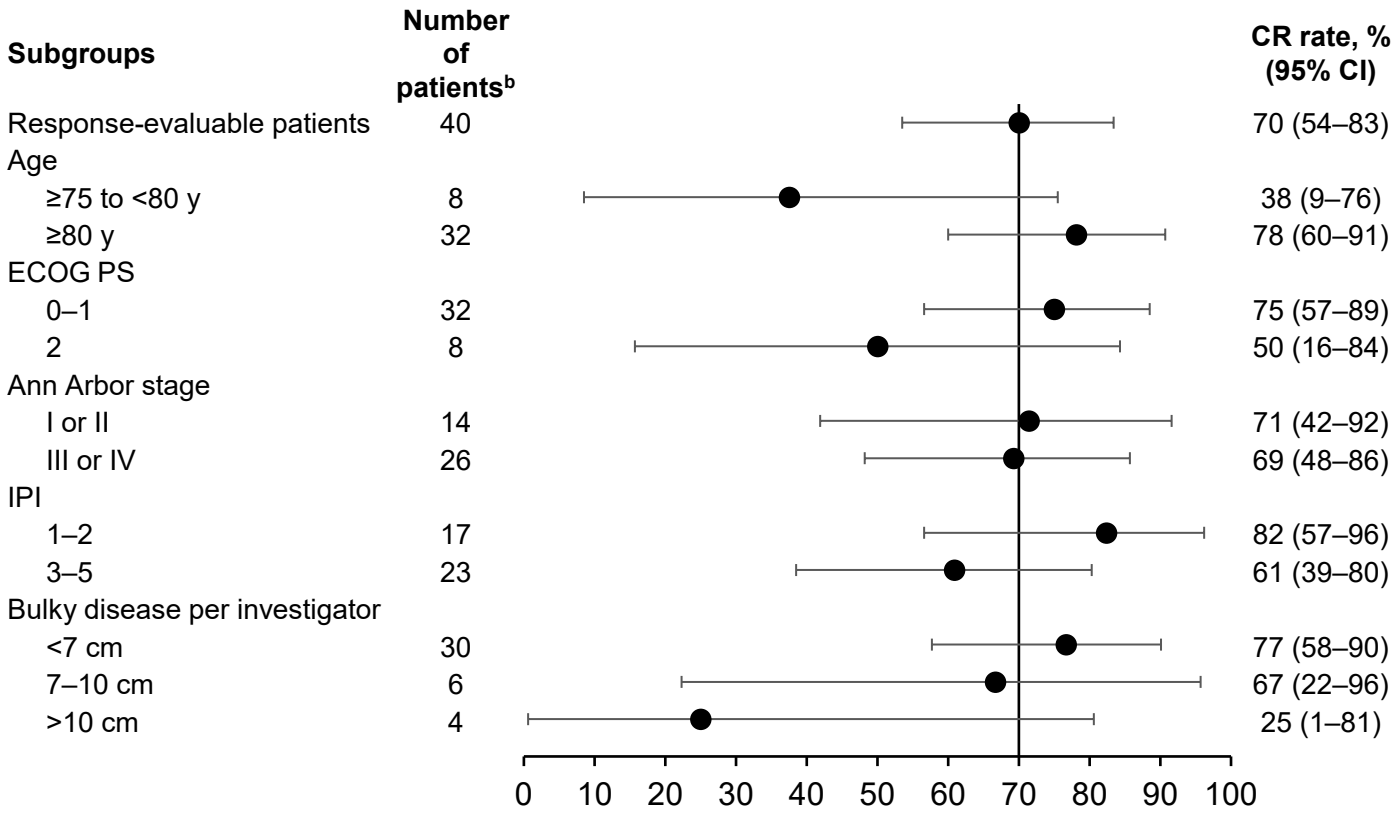


- 97% of CRS events occurred in cycle 1

[a]Lee et al 2019 criteria.[1] [b]One patient died with ongoing (unresolved) CRS.

CR Rates Were High Across Most Subgroups

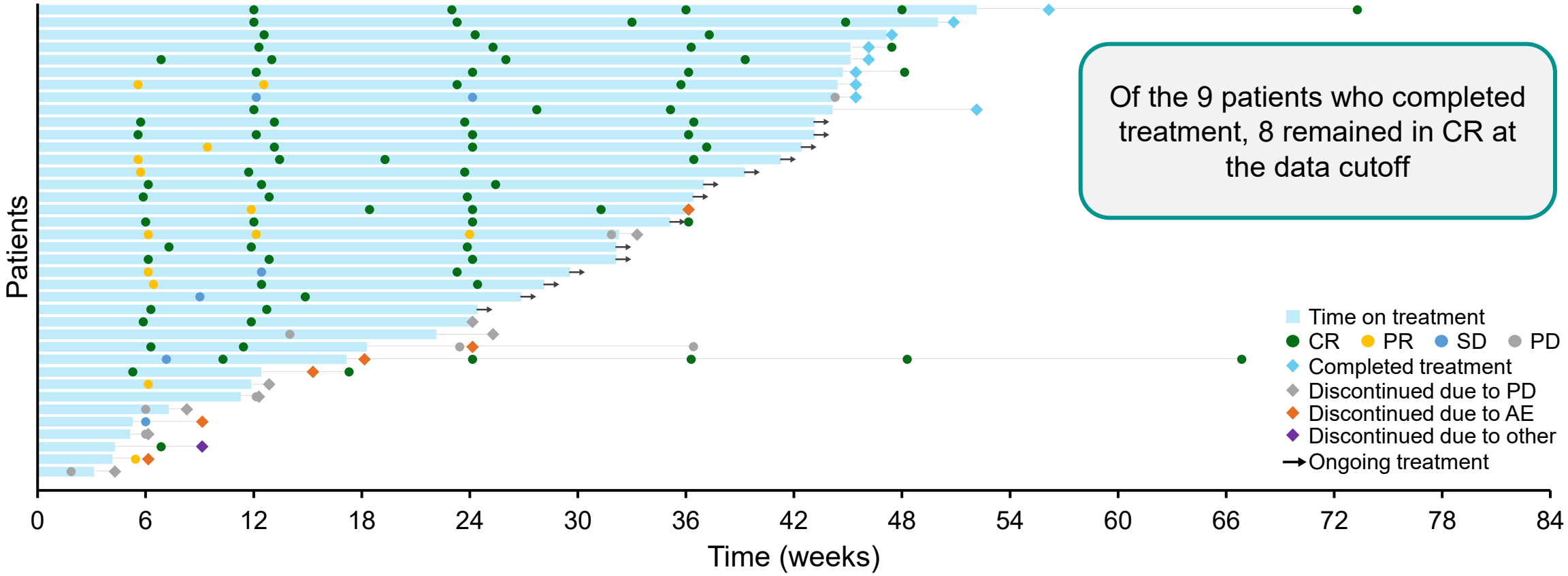
Best Response,[a] n (%)	Full Analysis Set[b] N=45	Response Evaluable[c] n=40
ORR	31 (69)	31 (78)
CR	28 (62)	28 (70)
PR	3 (7)	3 (8)
SD	2 (4)	2 (5)
PD	5 (11)	5 (13)
NA	7 (16)	2 (5)



- 15 responders (14 with CR, 1 with PR) were evaluated for MRD; the overall MRD-negativity rate was 93% (14/15)

[a]Responses are based on investigator assessment and Lugano criteria. [b]Based on the full analysis set, defined as all randomized patients. [c]Based on response-evaluable population, defined as patients who received ≥1 dose of epcoritamab, had measurable disease at baseline, and had ≥1 postbaseline disease evaluation or died within 60 d of first trial treatment. NA, not assessed; SD, stable disease.

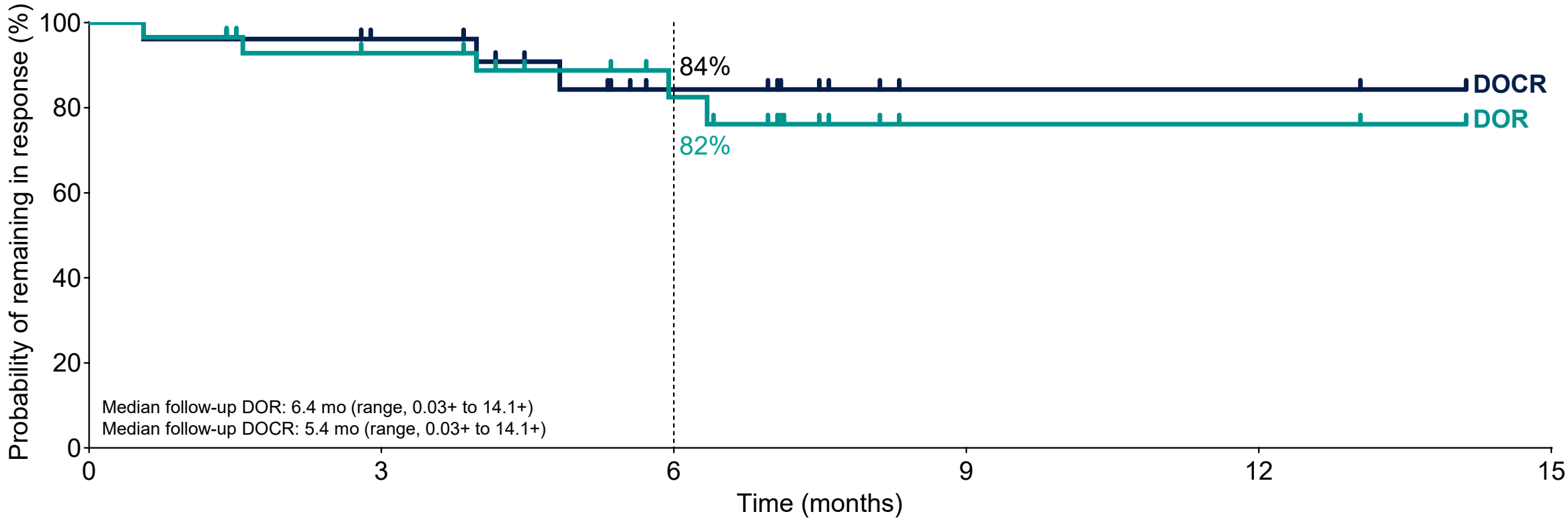
Responses Occurred Early



Of the 9 patients who completed treatment, 8 remained in CR at the data cutoff

- Median time to response: 1.5 mo (range, 1.2–3.4); median time to CR: 2.5 mo (range, 1.2–5.4)
- Response deepened from PR to CR in 7 patients

Responses Were Durable and Medians Were Not Reached

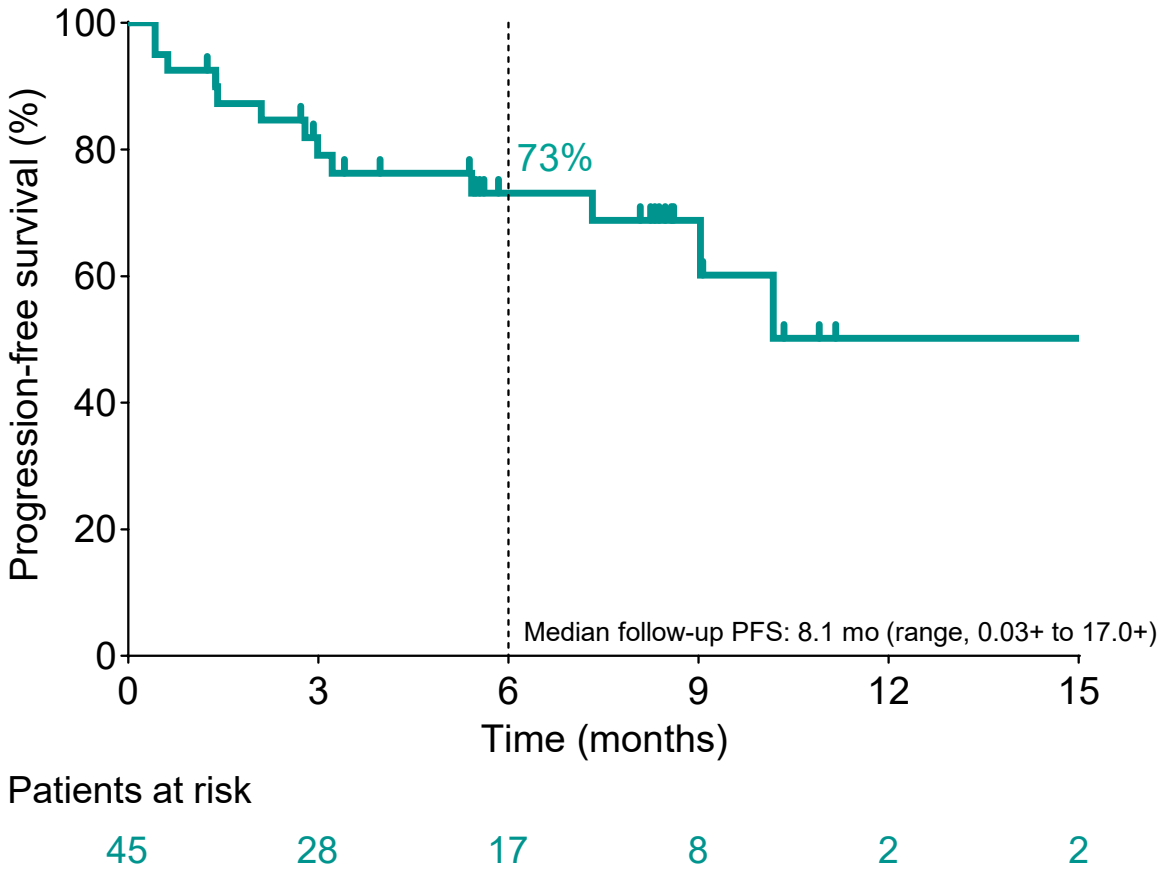


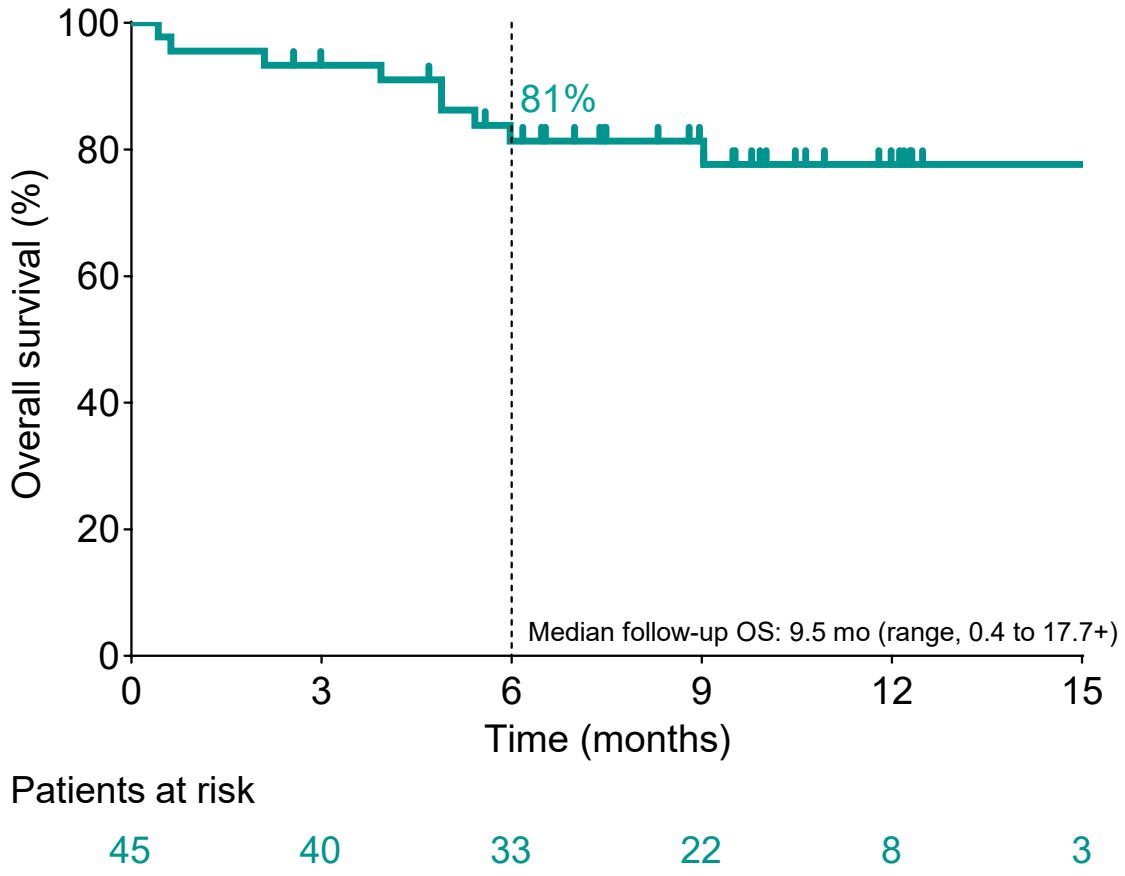
Patients at risk

31	24	13	2	2	0
28	19	9	2	2	0

- At data cutoff, 84% of all responses (26/31) and 89% of complete responses (25/28) were ongoing

Median Progression-Free and Overall Survival Were Not Reached





Conclusions

- Fixed-duration, subcutaneous epcoritamab monotherapy led to high response rates and a generally manageable safety profile in older, anthracycline-ineligible patients with newly diagnosed LBCL, a population with significant unmet need and poor outcomes
  - ORR: 78%; CR rate: 70%
  - 84% of responses and 89% of complete responses were ongoing
- Responses were observed early and were deep, with 14 of 15 MRD-evaluable responders achieving MRD negativity
- Safety was consistent with prior reports for epcoritamab monotherapy
  - CRS timing was predictable, and events were mostly confined to the first cycle of treatment
  - ICANS events were mostly low grade and transient, and all resolved
- Epcoritamab monotherapy is a promising chemotherapy-free treatment option for older patients with comorbidities and newly diagnosed LBCL who are deemed ineligible for anthracycline-based regimens

Fixed-Duration Epcoritamab in Combination with Bendamustine + Rituximab for the Treatment of 1L Follicular Lymphoma: First Disclosure from EPCORE NHL-2 Arm 3

Joshua D. Brody, MD,[1] Lorenzo Falchi, MD,[2] Umberto Vitolo, MD,[3] Marcel Nijland, MD, PhD,[4] Fritz Offner, MD, PhD,[5] Sylvia Snauwaert, MD, PhD,[6] Poliana Patah, MD, PhD,[7] Jennifer Marek,[8] Christopher Morehouse, MS,[8] Andrew J. Steele, PhD,[8] Yi Hao, DrPH,[8] Daniela Hoehn, MD, PhD,[8] Kim M. Linton, MBChB, PhD[9]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Candiolo Cancer Institute, FPO-IRCCS, Candiolo (Turin), Italy; [4]University Medical Center Groningen and University of Groningen, Groningen, Netherlands; [5]Universitair Ziekenhuis Gent, Ghent, Belgium; [6]Department of Hematology, AZ Sint-Jan Hospital, Bruges, Belgium; [7]AbbVie, North Chicago, IL, USA; [8]Genmab, Plainsboro, NJ, USA; [9]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK

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

Background

- Bendamustine + rituximab (BR) is a recommended first-line regimen for FL (ORR, >99%; CR rate, 30%)[1]
- Most patients with newly diagnosed FL eventually experience relapse with currently available options, emphasizing a need for more effective combinations that provide deep and durable remissions[2]

Here we report initial data for efficacy, safety, and T-cell pharmacodynamics of fixed-duration epcoritamab + BR in the treatment of patients with 1L FL

11. Flinn IW, et al. *Blood*. 2014;123:2944-52. **5.** Vidal L, et al. *J Natl Cancer Inst*. 2011;103:1799-806.

Study Design: EPCORE® NHL-2 Arm 3

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + BR in 1L FL patients

Key inclusion criteria

- 1L CD20$^+$ FL
  - Grade 1, 2, or 3A
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: May 15, 2024

Median follow-up: 30.4 mo

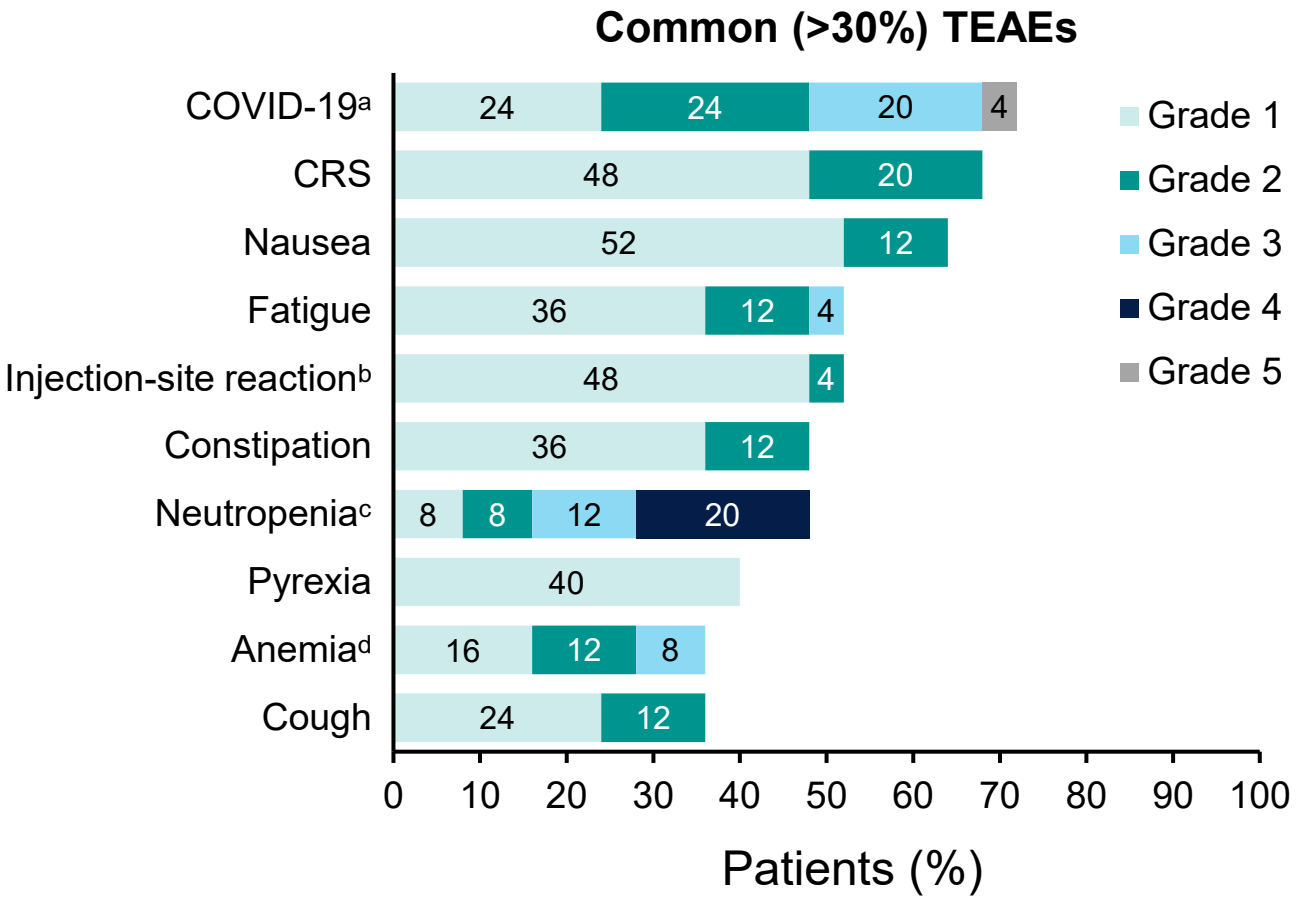
Fixed-duration treatment regimen: Concomitant epcoritamab SC 48 mg + BR

	Agent	C1–3	C4–6	C7–9	C10+ through 2 y
	Epcoritamab SC 48 mg[a]	QW	Q2W	Q2W	Q4W
BR	Bendamustine IV 90 mg/m^2	D1–2 of each cycle			
BR	Rituximab IV 375 mg/m^2	Q4W			

- **Primary endpoint:** Antitumor activity (ORR)[b]
- **Key secondary endpoints:** CR rate, DOCR, PFS, OS, safety/tolerability, and pharmacodynamics
  - Peripheral CD4$^+$ and CD8$^+$ flow cytometry data (cells/µL) were generated using the A167 Q-TBNK assay (IQVIA Laboratories, Durham, NC, USA)

Cycles were 28 d. [a]Epcoritamab was administered with a 2-step step-up dose in C1 followed by 48-mg full doses. Patients were required to be hospitalized for at least 24 h after the first full dose of epcoritamab during C1; additional or longer hospitalization was at the investigator's discretion. [b]Tumor response was evaluated by PET-CT (or separate PET and CT/MRI when PET-CT was not available). ClinicalTrials.gov: NCT04663347. EudraCT: 2023-504805-35.

Manageable Safety

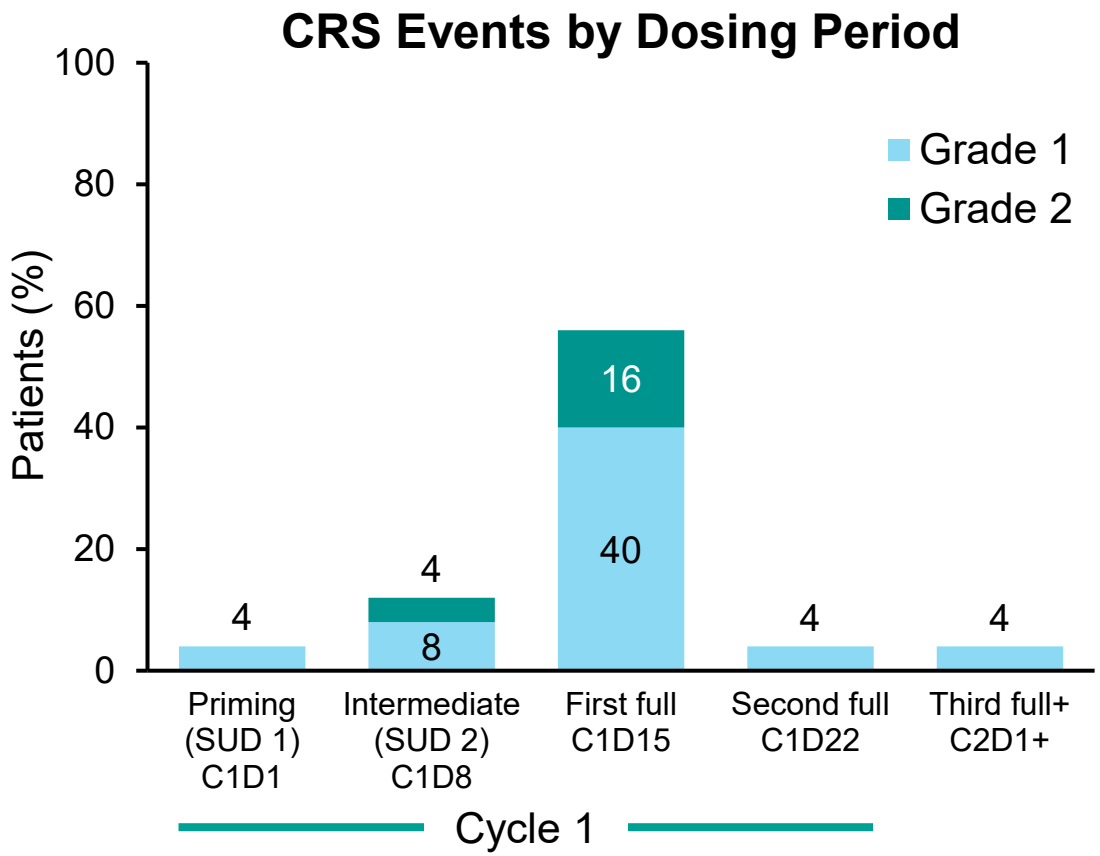


- Common TEAEs were mostly grade 1–2
- Majority of patients were enrolled during the COVID-19 pandemic, 1 patient experiencing a grade 5 event
- TEAEs lead to epcoritamab discontinuationin 9 patients, these were mostly related to COVID (n=7)
- No ICANS or clinical tumor lysis syndrome were observed

[a]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [b]Combined term includes injection-site reaction, erythema, and rash. [c]Combined term includes neutropenia and decreased neutrophil count. One case of febrile neutropenia (grade 4) was reported. [d]Combined term includes anemia and decreased serum ferritin.

CRS Events Were Low Grade, Predictable, All Resolved

	N=25
CRS, n (%)[a]	17 (68)
Grade 1	12 (48)
Grade 2	5 (20)
Median time to onset after first full dose, d (range)	2 (1–6)
CRS resolution, n/n (%)	17/17 (100)
Median time to resolution,[b] d (range)	2 (1–7)
Treated with tocilizumab, n (%)	4 (16)
Leading to epcoritamab discontinuation, n (%)	**0**



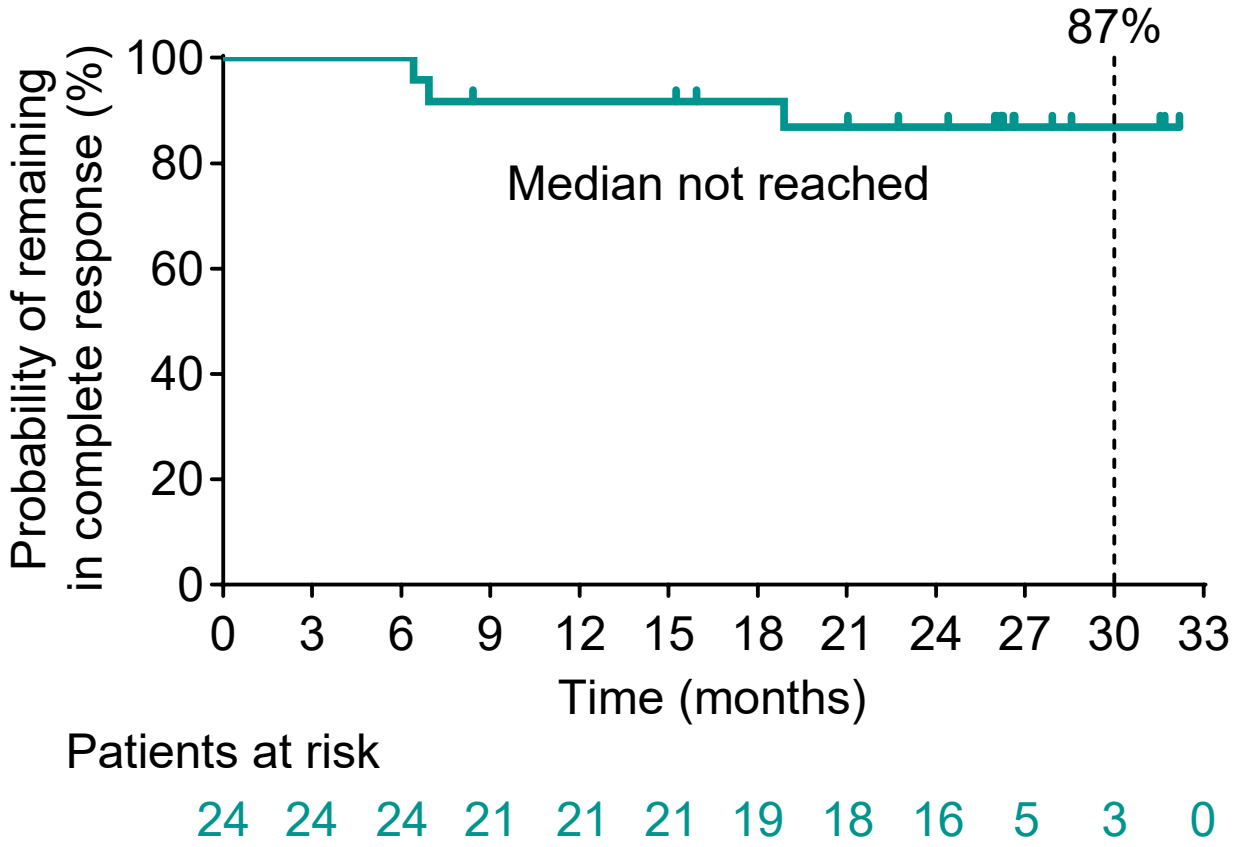
[a]Graded by Lee et al 2019 criteria.[1] [b]Median is based on longest CRS duration in patients with >1 CRS event. **1.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

High Complete Response Rates

Best Response, n (%)	N=25
Overall response	24 (96)
Complete response	24 (96)
Partial response	0
Progressive disease	1 (4)

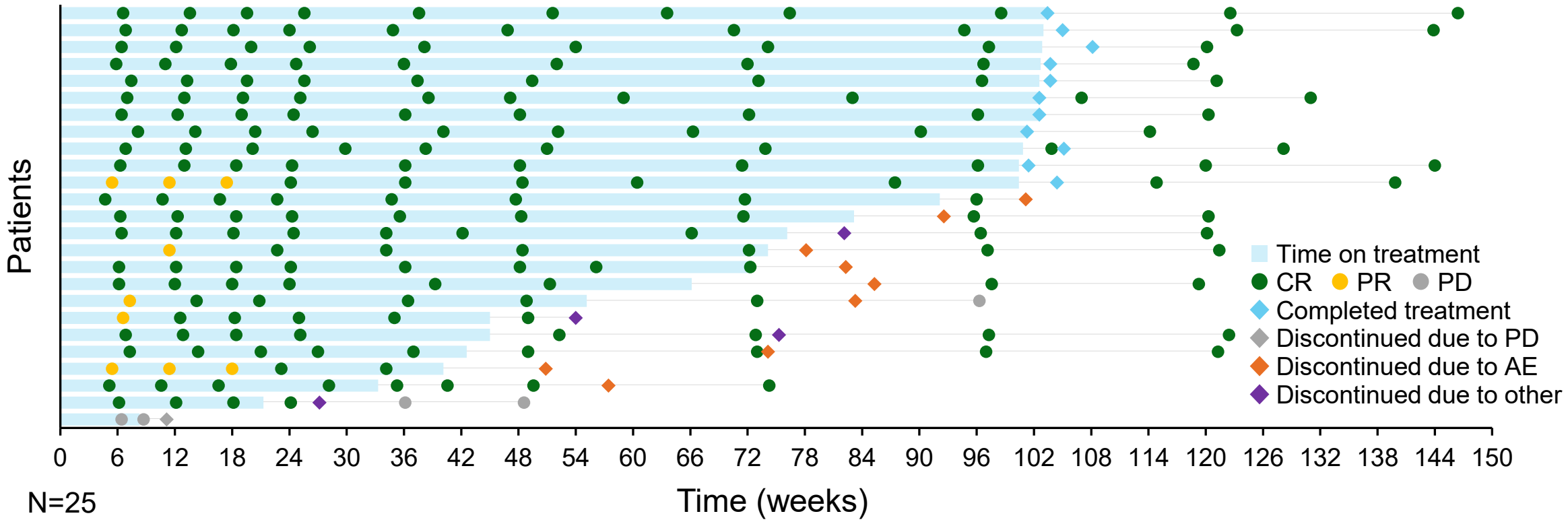
Data cutoff: May 15, 2024

Median follow-up: 30.4 mo



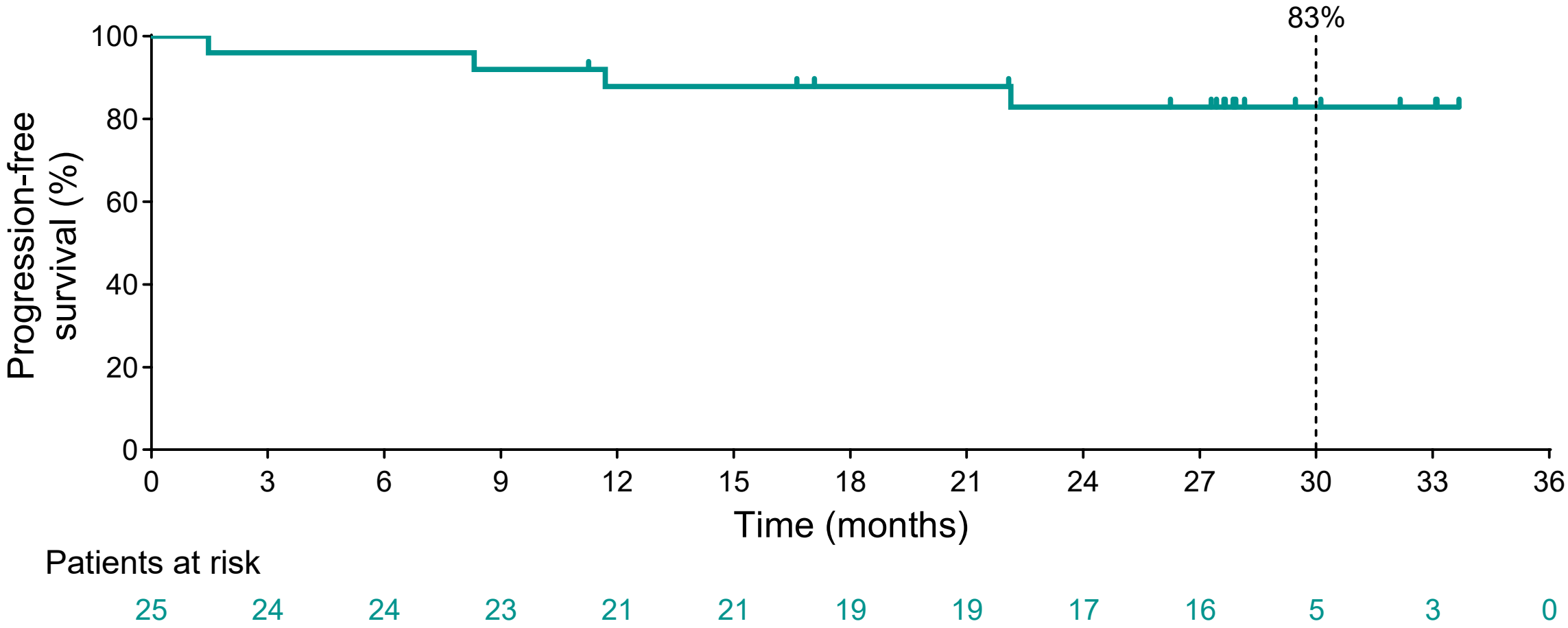
Kaplan–Meier estimate of DOCR assessed by investigator.

Responses Were Observed Early and Sustained After EOT



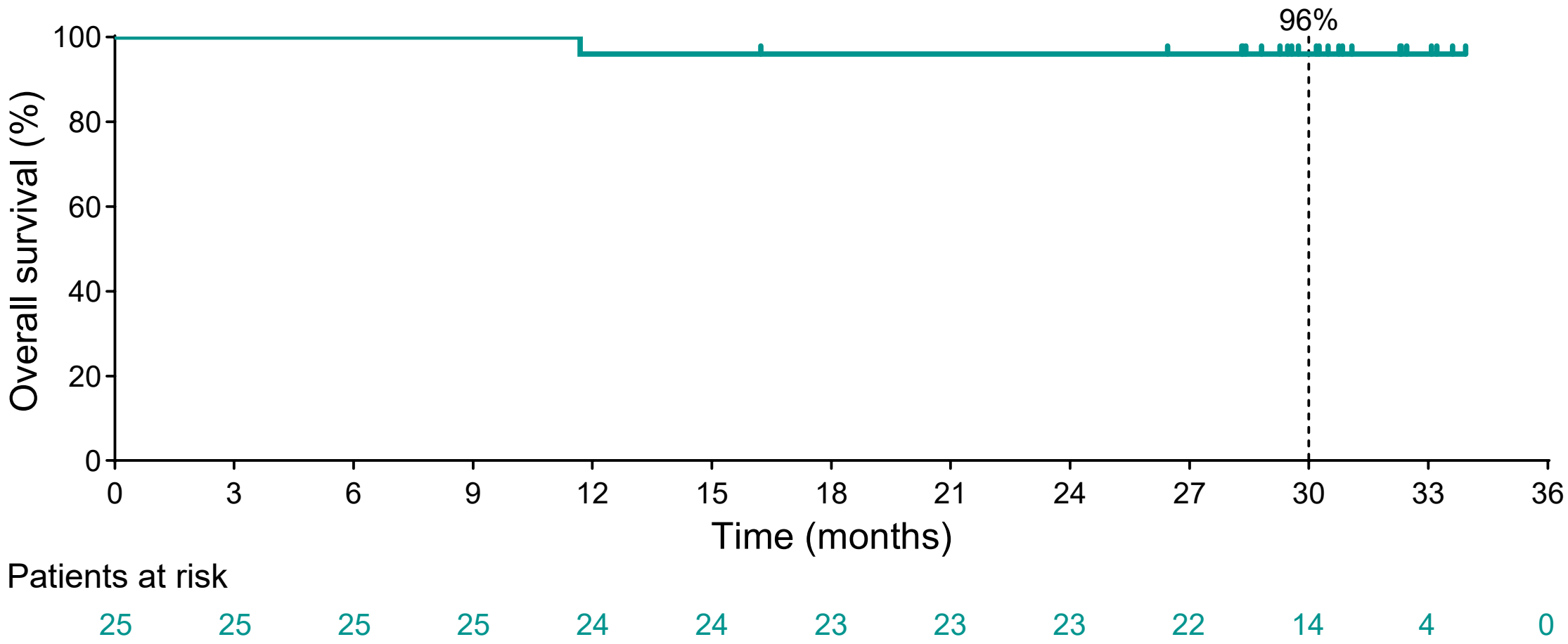
Median time to response was 1.5 mo (range, 1.1–2.6). Median time to CR was 1.5 mo (range, 1.1–5.6).

Median PFS Not Reached at 2.5 Years



Kaplan–Meier estimate of progression-free survival assessed by investigator.

Median OS Not Reached at 2.5 Years



Kaplan–Meier estimate of overall survival.

Conclusions

- Fixed-duration epcoritamab SC + BR showed deep and durable responses in 1L FL that translated to favorable long-term outcomes
  - Nearly all patients had a CR (96%) and most complete responders remained in CR at 30 mo (87%)
  - Median PFS and OS were not reached
- The safety profile was manageable, and consistent with previous reports
- These results compare favorably with BR alone (CR rate, 30%[1]) and support the combinability and further investigation of epcoritamab + BR in 1L FL as well as the continued evaluation of epcoritamab as a core treatment across B-NHL

1. Flinn IW, et al. *Blood*. 2014;123:2944-52.

Fixed-Duration Epcoritamab + R^2 Drives Deep and Durable Responses in Patients with Relapsed or Refractory Follicular Lymphoma: 2-Year Follow-Up from Arm 2 of the EPCORE NHL-2 Trial

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

Background

- R^2 is an approved and widely accepted regimen for R/R FL, though there is still no definitive standard of care[5]
  - R^2 was approved based on data from the AUGMENT trial (ORR 78%; CR 34%; 2-year PFS, 58%)[6]
- Prior reports for fixed duration SC epcortiamab + R^2 in 2L+ R/R FL in the EPCORE NHL-2 trial showed encouraging efficacy and safety

Here we present long-term (>2 years) results from the EPCORE NHL-2 study of fixed duration epcoriamab plus R2 in R/R FL

[a]Approved in the US for adults with R/R DLBCL, NOS, including DLBCL arising from indolent lymphoma, HGBCL, and FL after ≥2 lines of systemic therapy.

Study Design: EPCORE® NHL-2 Arm 2 (NCT04663347)

Key inclusion criteria

- R/R CD20⁺ FL
  - Grade 1–3A
  - Stage II–IV
- ≥1 prior treatment, including an anti-CD20 antibody
- Need for treatment per GELF criteria[9]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: May 15, 2024

Median follow-up: 25.3 mo

(First patient treated March 2021)

Concomitant fixed-duration epcoritamab SC 48 mg + R²
(28-day cycles up to 2 years)

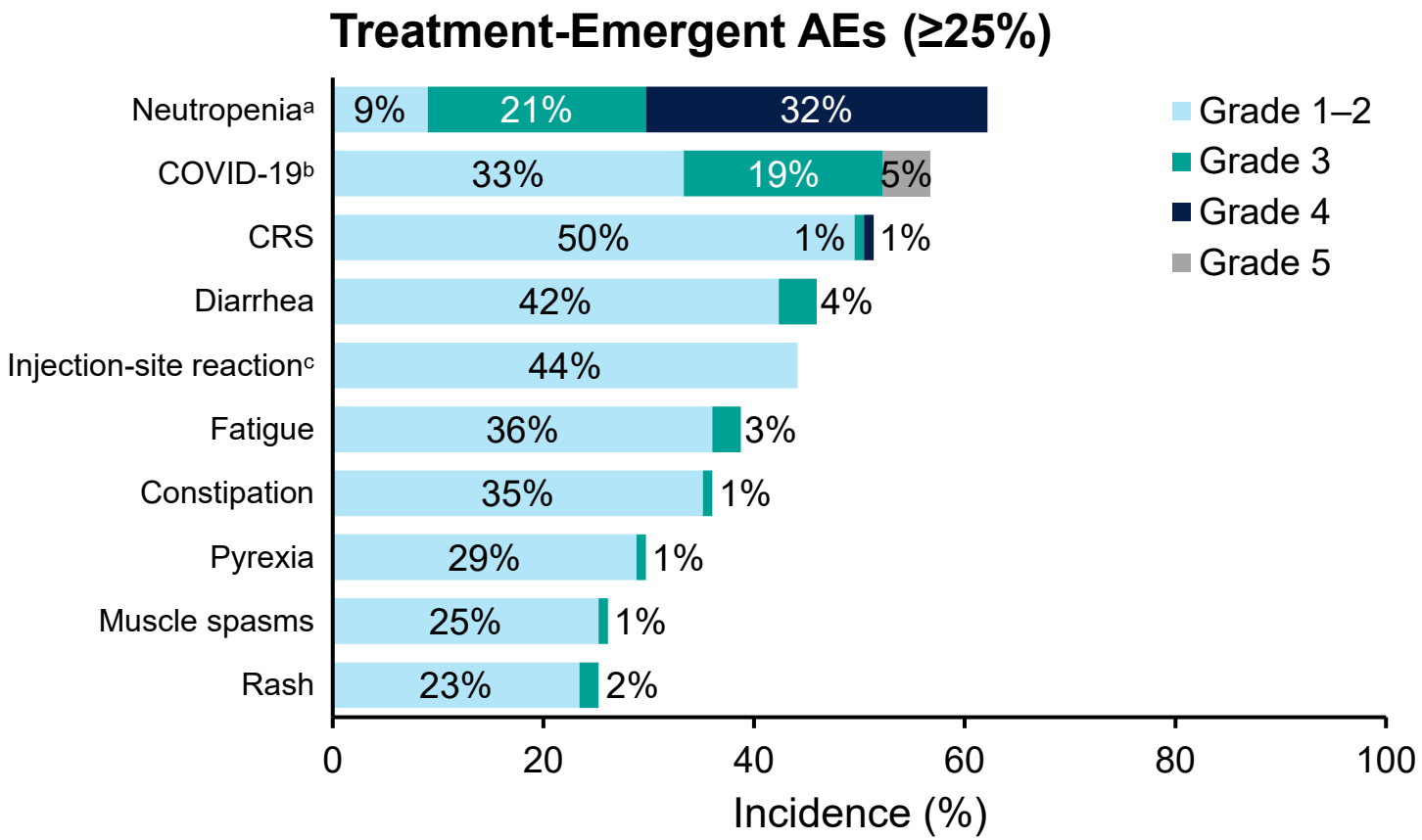
	Agent	C1	C2	C3	C4–5	C6–9	C10–12	C13+
2–step-up-dose regimen[a]	Epcoritamab SC 48 mg							
	Cohort A	QW			Q2W		Q4W	
	Cohort B	QW		Q4W				
R²	Rituximab IV 375 mg/m²	QW	Q4W					
	Lenalidomide PO 20 mg/d	D1–21 of each cycle						

Primary objective: ORR per Lugano criteria[b]

Key secondary objectives: CR rate, DOR, DOCR, PFS, OS, MRD analysis,[d] and safety and tolerability

[a]Patients received epcoritamab SC with 2 step-up doses before the first full dose on C1D15, corticosteroid prophylaxis to mitigate CRS, and protocol-mandated hospitalization for 24 h after the first full dose.. [c]Tumor response was evaluated by PET-CT [d]MRD was assessed in PBMCs using the clonoSEQ® assay

Safety Profile Was Manageable, With No New Safety Signals



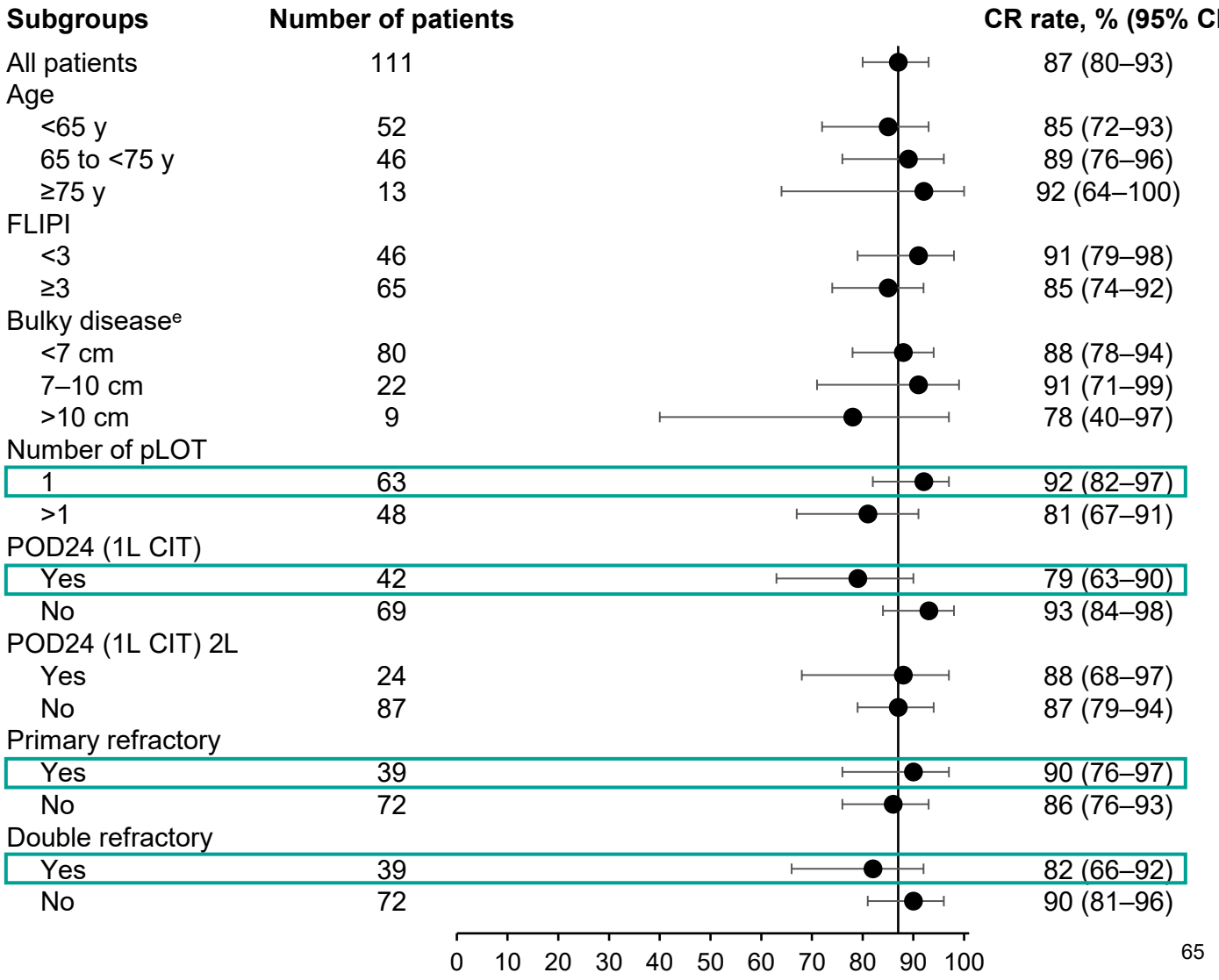
- The safety profile was consistent with previous reports
- CRS was low grade, predictable and all events resolved
- One low grade ICANS events resolved rapidly and did not lead to treatment discontinuation
- Patients were enrolled and treated during the global COVID-19 pandemic, 5 fatal COVID-19[b] events
  - No other fatal TEAEs occurred

[a]Combined term includes neutropenia and decreased neutrophil count. [b]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [c]Combined term includes injection-site reaction, erythema, pain, pruritus, rash, and swelling.

Deep Responses Regardless of High-Risk Features

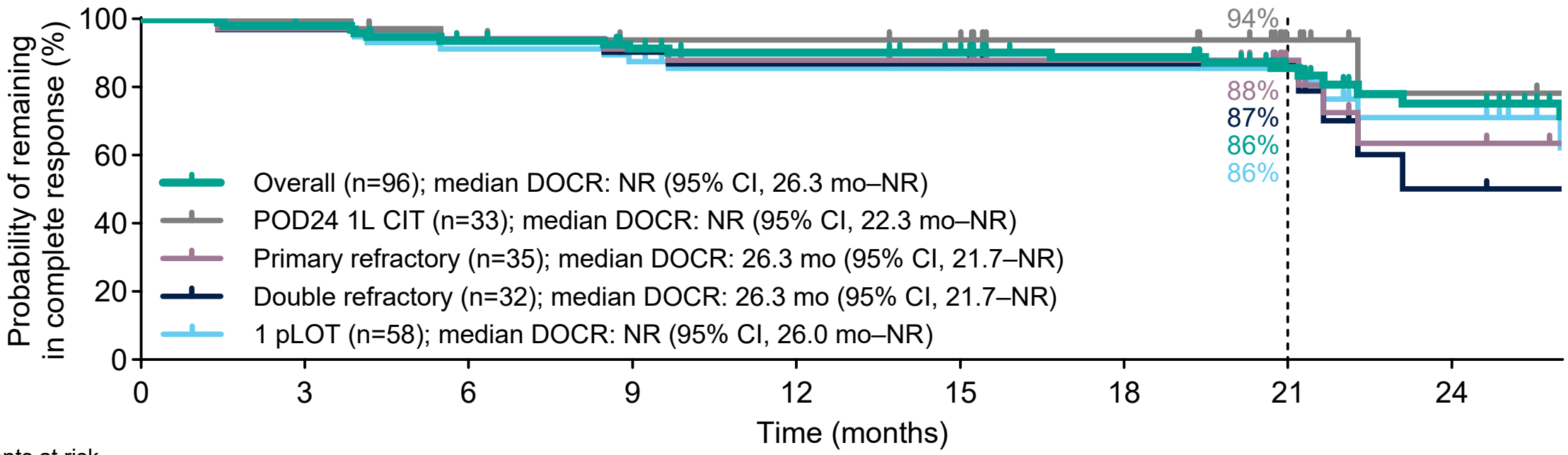
Best Response, n (%)[a]	N=111
Overall response	107 (96)
Complete response	97 (87)
Partial response	10 (9)
Progressive disease	2 (2)

MRD Negativity, n/n (%)	MRD Evaluable
MRD negativity at any time point[b]	66/75 (88)
MRD negative and complete response[c]	63/68 (93)



[a]Two patients were not evaluable for response. [b]MRD negative at any time point with (PBMC assay; clonoSEQ). [c]One patient became MRD positive at a subsequent assessment (C5D1); patient later experienced radiographic PD.

Durable Complete Responses Across High-Risk Subgroups

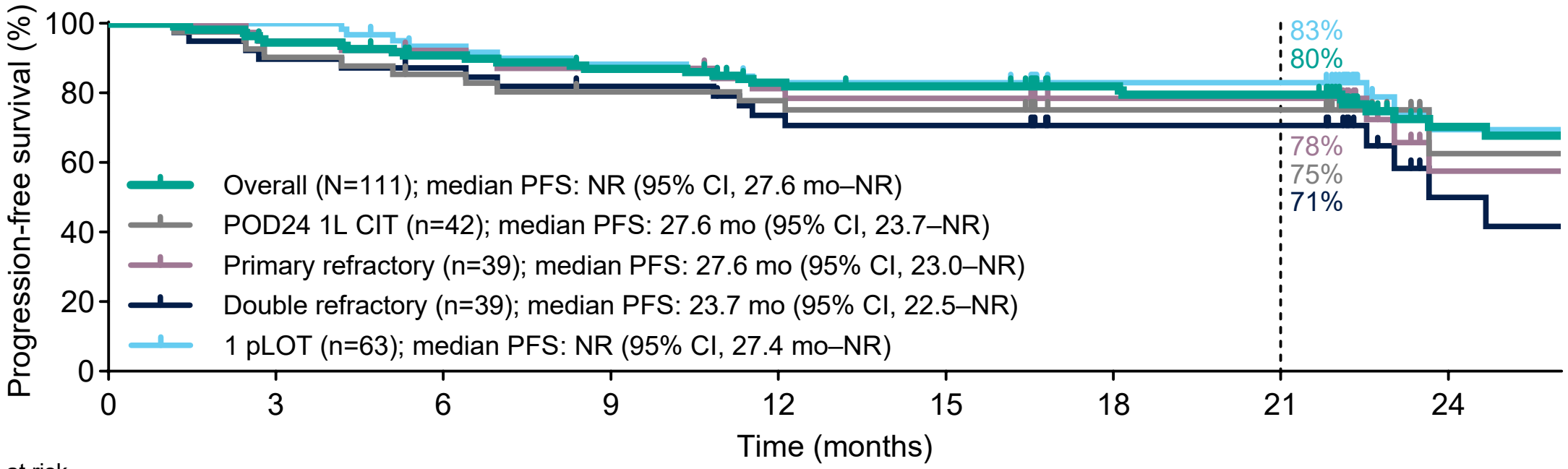


Patients at risk									
Overall	96	92	85	79	75	72	63	37	27
POD24 1L CIT	33	33	30	28	28	27	21	10	5
Primary refractory	35	34	32	28	26	25	22	12	7
Double refractory	32	31	29	26	24	23	18	11	5
1 pLOT	58	56	51	46	42	39	36	20	13

An estimated 75% of patients with CR remained in CR at 2 years

Data cutoff: May 15, 2024. Median follow-up for DOCR: 20.9 months

PFS Observed in Most Patients

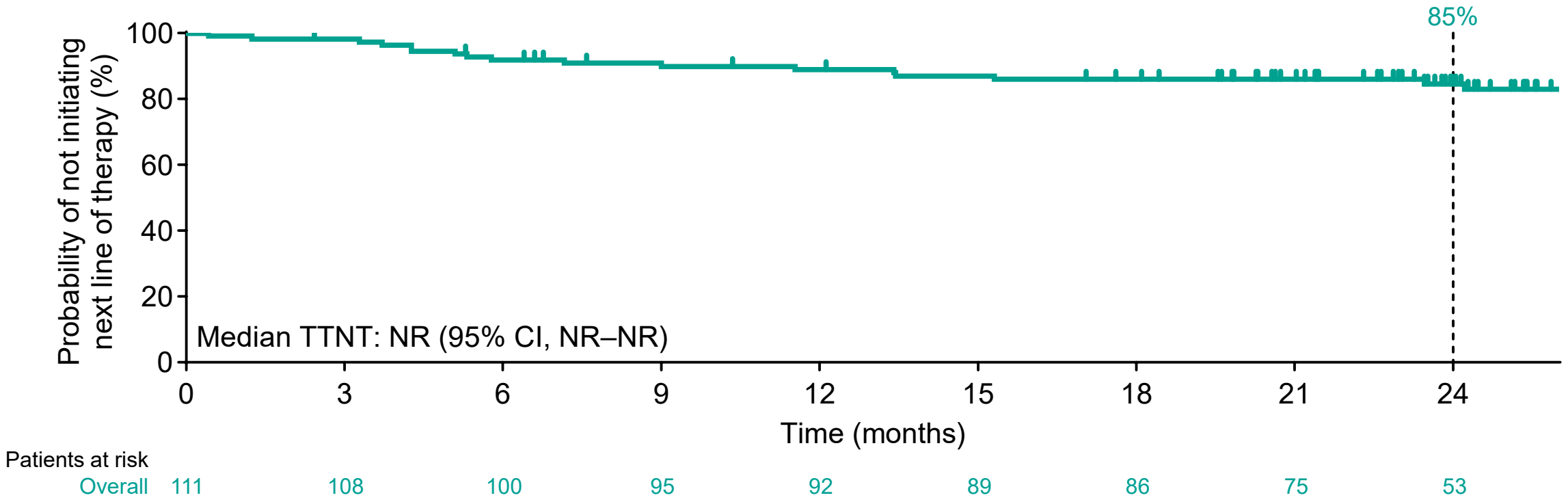


Patients at risk									
Overall	111	102	95	90	82	80	68	66	29
POD24 1L CIT	42	37	34	31	30	29	21	21	5
Primary refractory	39	37	35	32	28	27	22	22	7
Double refractory	39	35	33	30	26	25	18	18	6
1 pLOT	63	61	55	52	45	45	38	38	13

An estimated 70% of patients remained progression free at 2 years

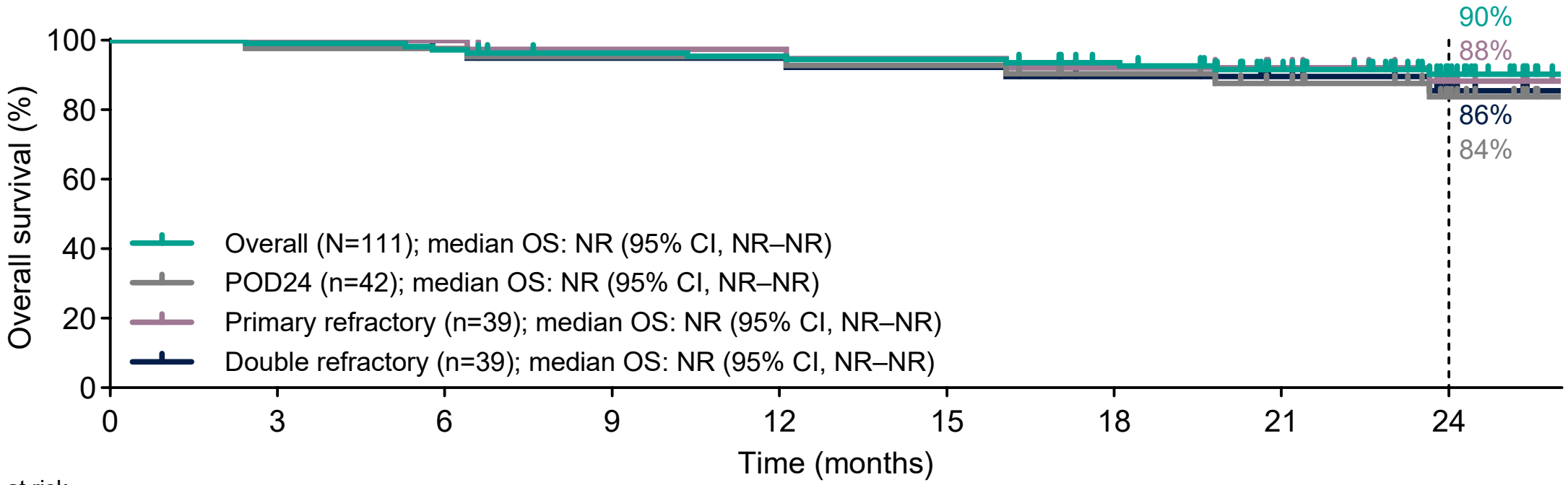
Data cutoff: May 15, 2024. PFS is among the full analysis population. Median follow-up for PFS: 22.3 months.

Next Therapy Not Initiated for Most Patients by 2 Years



Data cutoff: May 15, 2024. TTNT is among the full analysis population. Median follow-up for TTNT: 24.7 months.

Overall Survival



Patients at risk									
Overall	111	110	108	104	103	102	96	83	62
POD24	42	41	41	39	39	38	34	29	19
Primary refractory	39	39	39	37	37	36	32	29	20
Double refractory	39	39	38	36	36	35	30	25	18

Most patients remained alive at 2 years regardless of high-risk features

Data cutoff: May 15, 2024. OS is among the full analysis population. Median follow-up: 25.3 mo (range, 2.4+ to 34.1). Percentages are Kaplan–Meier estimates.

Conclusions

- With more than 2 years of follow-up, fixed-duration epcoritamab + R^2 continued to show deep and durable responses, including in patients with high-risk features
  - **ORR was 96% and CR rate was 87% in the overall population**, with a notably higher CR rate observed in 2L FL patients (CR rate, 92%)
  - MRD-negativity rate was 88% and correlated with PFS
- Safety profile was manageable and consistent with previous reports
- These findings may be practice-informing, as results compare favorably with R^2 alone and support the ongoing phase 3 trial of epcoritamab + R^2 vs R^2 in R/R FL (EPCORE FL-1; NCT05409066)

Epcoritamab Monotherapy in Patients (Pts) with Relapsed or Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): Results from CLL Expansion and Optimization Cohorts of EPCORE CLL-1

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

Background

- Patients with CLL refractory to both a BTK and a BCL-2 inhibitor have a poor prognosis and limited treatment options[1]
- Novel approaches such as CAR T-cell therapy offer limited benefits, with complete responses rates ≤20%, indicating a need for novel, effective treatments[2]
- Initial data from EPCORE CLL-1 have shown encouraging efficacy in both R/R CLL and RT[6,7]

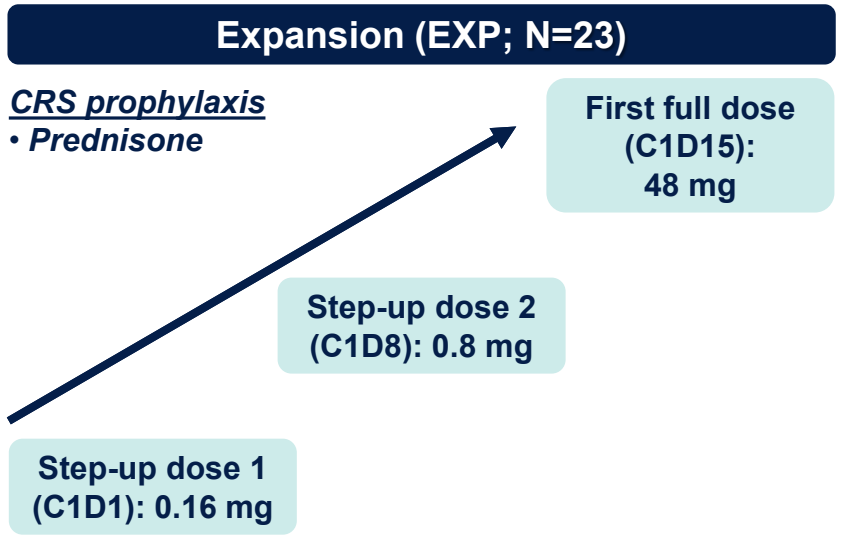
Here we present updated results from the CLL expansion cohort and preliminary results from Cycle 1 optimization from the EPCORE CLL-1 study of epcoritamab monotherapy in R/R CLL

[a]Approved in the US and Europe for the treatment of adults with R/R FL, DLBCL, and HGBCL (US only) after ≥2 lines of systemic therapy.

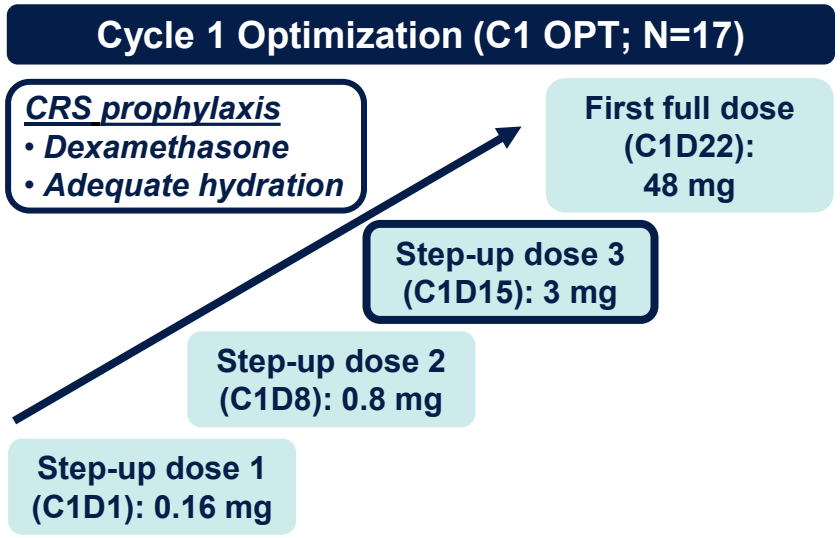
Study Design: EPCORE® CLL-1 Expansion and C1 Optimization

Key inclusion criteria

- CD20+ R/R CLL
- ≥2 prior lines of systemic therapy
- ECOG PS 0–2
- Measurable disease with ≥5×10^9/L B lymphocytes (expansion only)
- No prior allogeneic HSCT



Data cutoff: May 28, 2024
Median follow-up: 22.8 months



Data cutoff: May 28, 2024
Median follow-up: 2.9 months

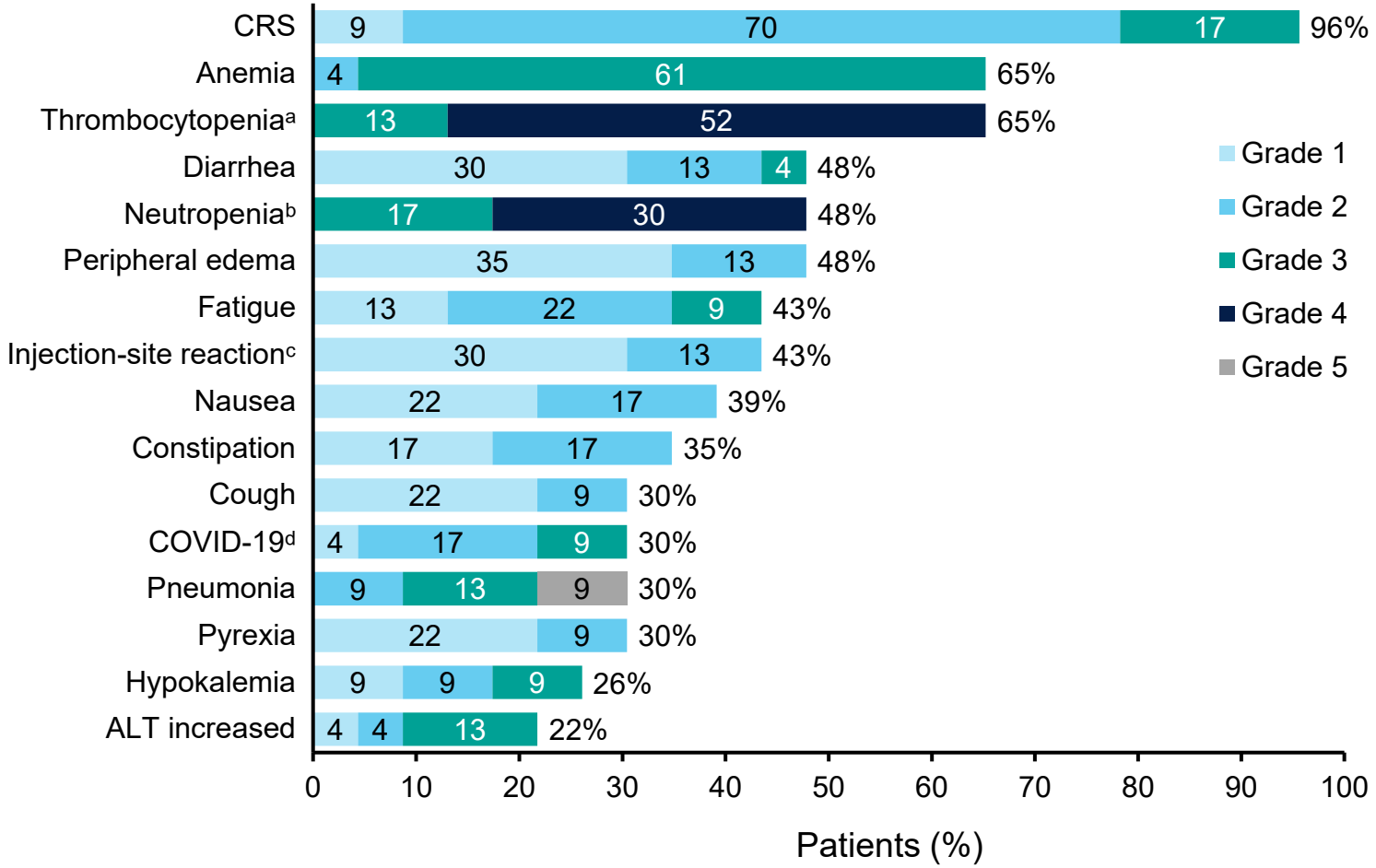
- **Primary endpoint (EXP):** Overall response rate
- **Primary endpoint (C1 OPT):** Incidence and severity of CRS, ICANS, and clinical TLS
- **Key secondary endpoints (EXP):** CR rate, time to response, MRD (PBMCs using the clonoSEQ® assay), and safety/tolerability

- To ensure patient safety and better characterize CRS, inpatient monitoring was required for at least 24 hours after each epcoritamab dose in C1

ClinicalTrials.gov: NCT04623541; EudraCT: 2023-504828-25.

Safety Profile Was Manageable, With No New Safety Signals

Treatment-Emergent AEs (>20%) in EXP



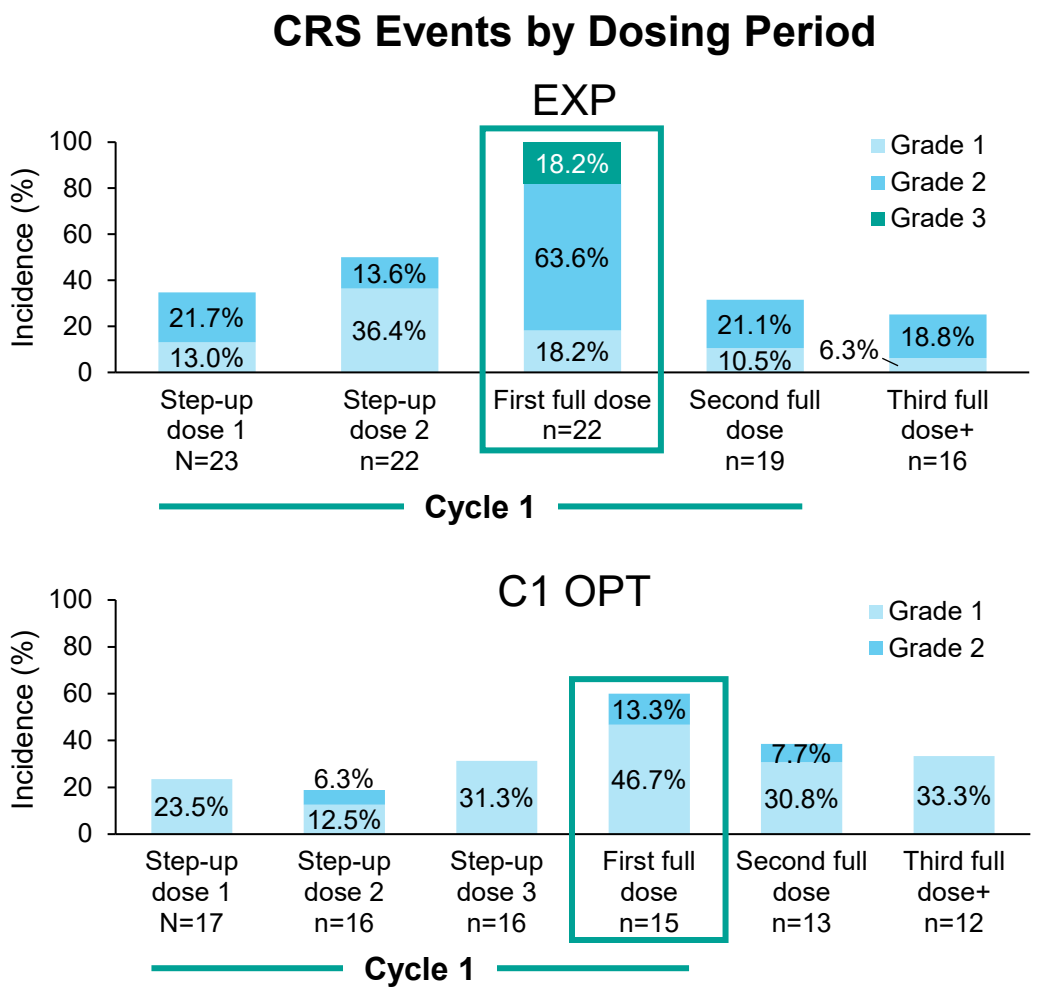
Patients With ≥1 Event, n (%)	EXP N=23
Neutropenia	11 (48)
At study entry	1 (4)
In first 8 weeks	4 (17)
Thrombocytopenia	15 (65)
At study entry	14 (61)
In first 8 weeks	5 (22)
Anemia	15 (65)
At study entry	14 (61)
In first 8 weeks	15 (65)

- TEAEs were primarily low grade (G1–2)
- TEAEs led to treatment discontinuation in 5 pts from EXP and 1 pt from OPT
- 4 fatal TEAEs[e] occurred in EXP; none in OPT

[a]Combined term includes thrombocytopenia and decreased platelet count. [b]Combined term includes neutropenia, decreased neutrophil count, and febrile neutropenia. Three patients had febrile neutropenia (EXP, n=2 [grades 1 and 3]; OPT, n=1 [grade 3]). [c]Combined term includes injection-site reaction, bruising, erythema, rash, and swelling. [d]Combined term includes COVID-19 and COVID-19 pneumonia. [e]Fatal TEAEs were pneumonia (n=2), sepsis (n=1), and squamous cell carcinoma of the skin (n=1); 1 case of pneumonia was considered related to epcoritamab.

C1 OPT Mitigated Adverse Events of Interest Including ICANS and Clinical TLS

	EXP N=23	C1 OPT N=17
CRS, n (%)	**22 (96)**	**14 (82)**
Grade 1	2 (9)	12 (71)
Grade 2	16 (70)	2 (12)
Grade 3	4 (17)	0
Treated with tocilizumab, n (%)	20 (87)	6 (35)
Leading to treatment discontinuation, n (%)	**0**	**0**
CRS resolution, n/n (%)	22/22 (100)	14/14 (100)
Median time to resolution, days (range)	3 (1–16)	3.5 (1–7)
ICANS, n (%)	**3 (13)**	**0**
Grade 1	1 (4)	0
Grade 2	2 (9)	0
Clinical TLS, n (%)	**1 (4)**	**0**
Grade 2	1 (4)	0



Deep Responses Across Subgroups

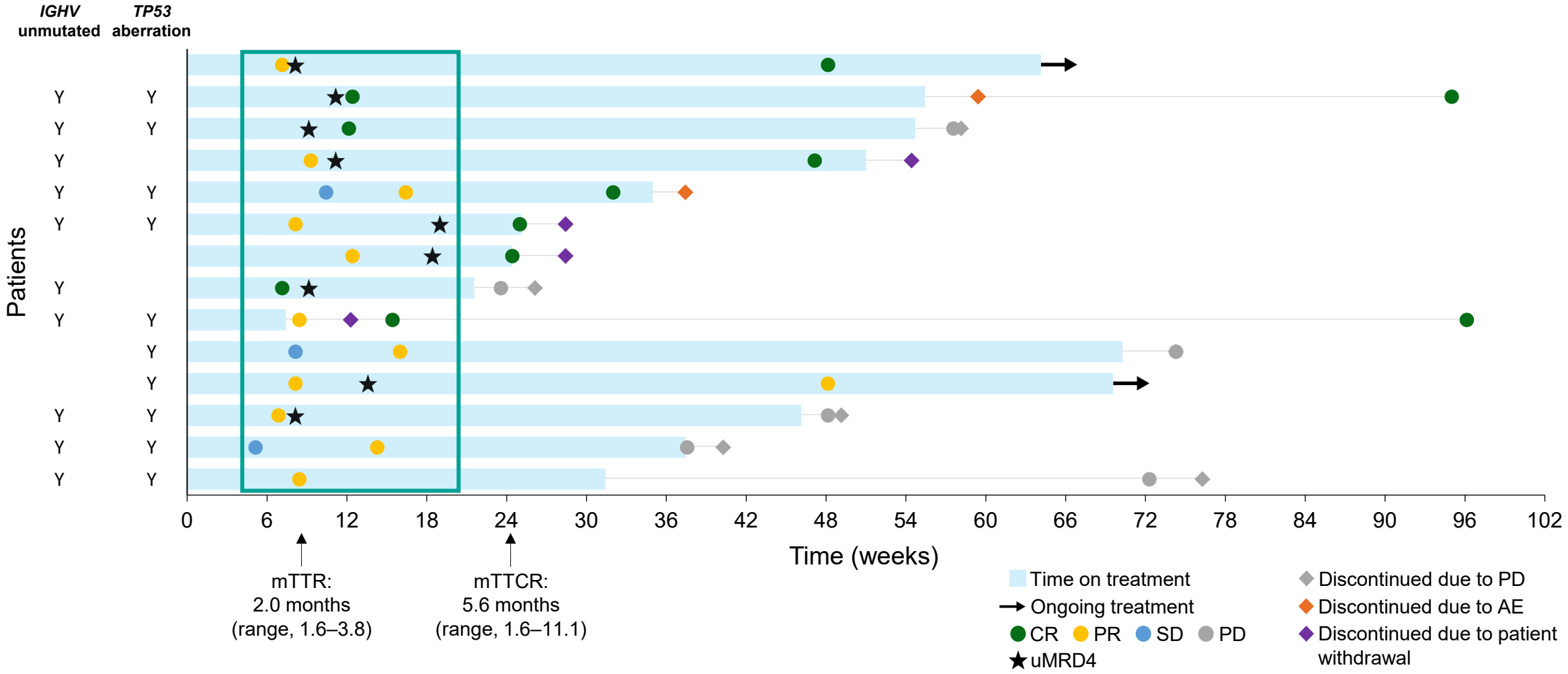
Response, n (%)	EXP mFU: 22.8 months					C1 OPT mFU: 2.9 months
	Full Analysis Set N=23	Response Evaluable n=21	*TP53* Aberration n=15	*IGHV* Unmutated n=16	Double Exposed[a] n=19	Response Evaluable n=10
Overall response[b]	**14 (61)**	**14 (67)**	**10 (67)**	**10 (63)**	**10 (53)**	**6 (60)**
Complete response	9 (39)	9 (43)	5 (33)	7 (44)	7 (37)	1 (10)
Partial response	5 (22)	5 (24)	5 (33)	3 (19)	3 (16)	5 (50)
Stable disease	4 (17)	4 (19)	2 (13)	3 (19)	4 (21)	2 (20)
Progressive disease	1 (4)	1 (5)	1 (7)	0	1 (5)	1 (10)

- With limited follow-up, the C1 OPT regimen does not appear to affect epcoritamab efficacy
- uMRD4 in PBMCs was observed in most responders, including all patients with CR who were tested for MRD

EXP MRD Negativity, n/n (%)[c]	uMRD4	uMRD6[d]
Overall response[b]	9/12 (75)	8/12 (67)
Complete response	7/7 (100)	6/7 (86)
Partial response	2/5 (40)	2/5 (40)
Full analysis set	9/23 (39)	8/23 (35)

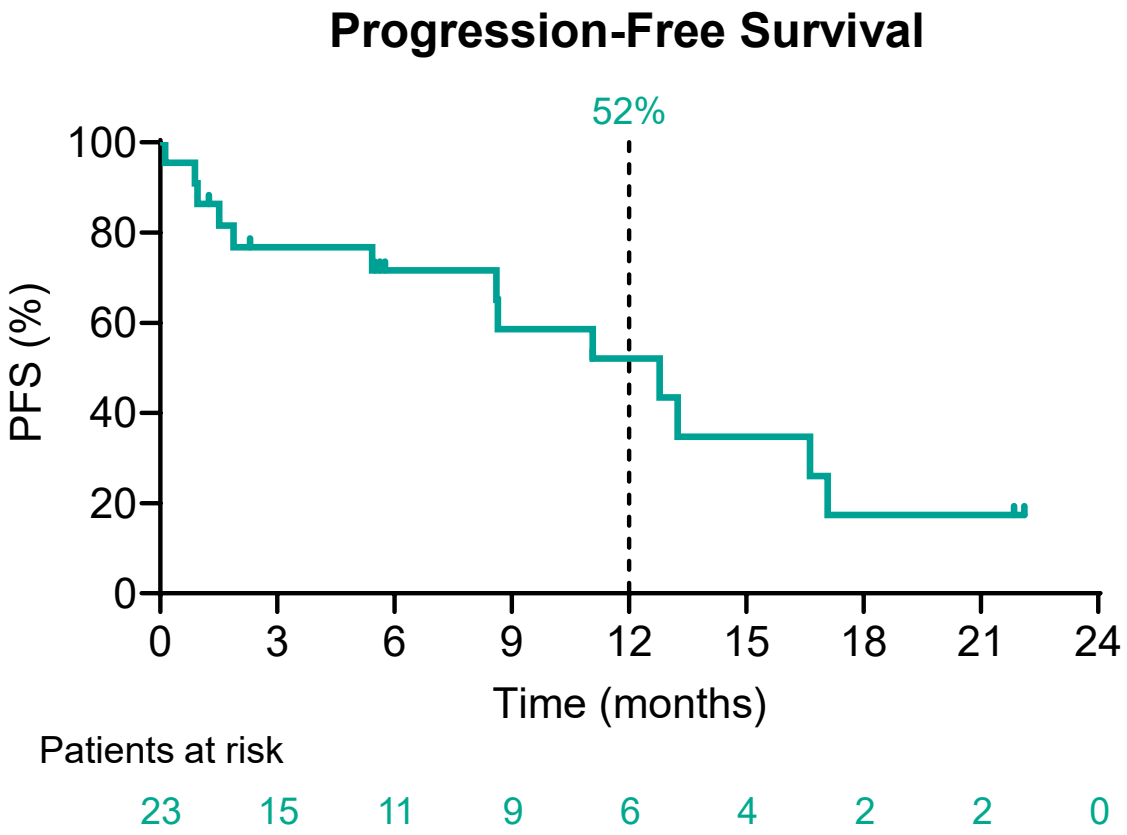
Four patients (*TP53* aberration, n=2; *IGHV* unmutated, n=3; double exposed, n=4) in EXP and 1 in C1 OPT shown above were not evaluable or had no assessment, including 3 in EXP (*TP53* aberration, n=2; *IGHV* unmutated, n=2; double exposed, n=3) and 1 in C1 OPT who died without postbaseline assessment. [a]Patients previously treated with both a BTK inhibitor and a BCL-2 inhibitor. [b]Response assessment according to iwCLL criteria. [c]Patients evaluated for MRD had at least 1 on-treatment MRD result and were not MRD negative at baseline. MRD was only evaluated in patients with CR or PR. [d]Two of 3 evaluated patients had uMRD6 in bone marrow at or shortly after the first CR assessment. mFU, median follow-up.

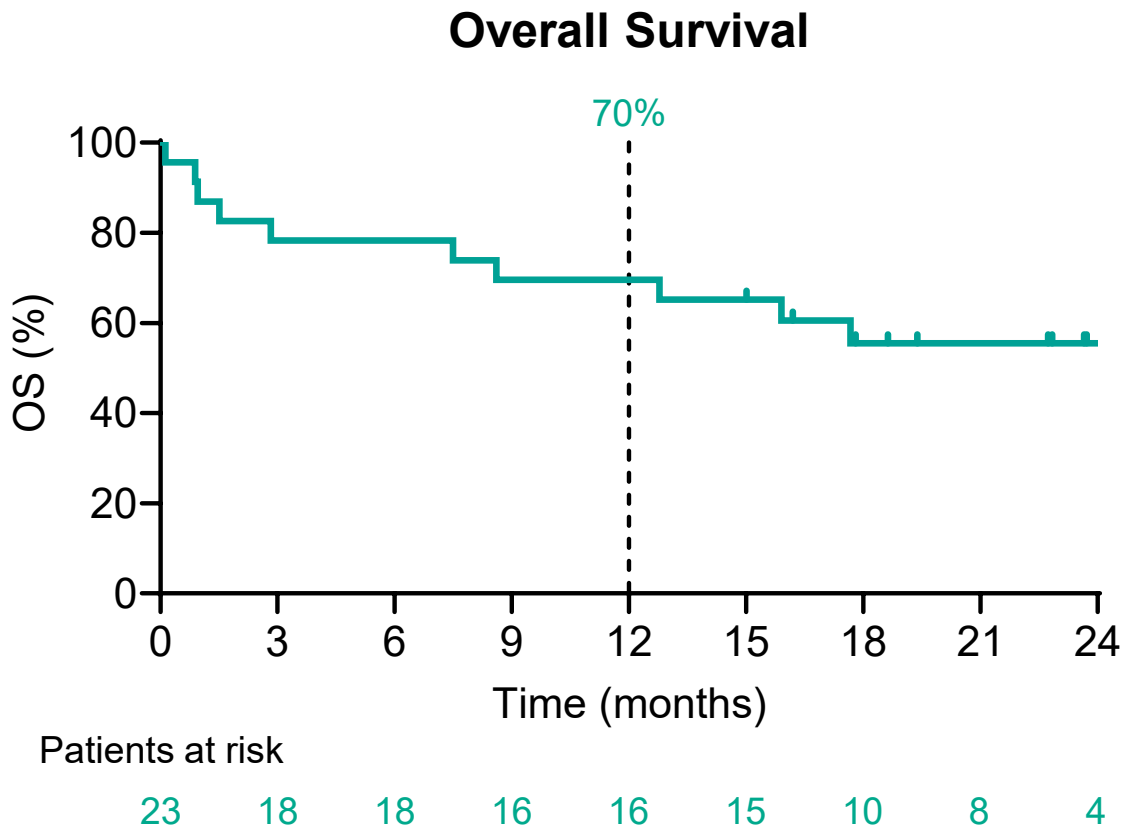
Depth and Duration of Response in EXP



Median follow-up, months (range): 22.8 (0.1+ to 30.0). Median number of treatment cycles initiated (range): 6 (1–18). Median duration of treatment, months (range): 5.8 (0.03–16.2). MRD was assessed in PBMCs using the clonoSEQ® assay (Adaptive Biotechnologies). mTTR, median time to response; mTTCR, median time to complete response.

Progression-Free and Overall Survival in EXP





- Median PFS was 12.8 months (95% CI, 5.4–17.1); median OS was not reached (95% CI, 8.6 months–NR)

Kaplan–Meier estimates are shown.

Conclusions

- Single-agent SC epcoritamab led to deep responses in patients with heavily pretreated R/R CLL, regardless of high-risk features
  - 39% CR rate; uMRD4 in 75% of evaluable responders, all complete responders achieved uMRD
  - Comparable ORR in the EXP and C1 OPT cohorts with limited follow-up for C1 OPT efficacy
- Simple cycle 1 OPT measures of an additional SUD, dexamethasone, and adequate hydration led to decreased incidence and severity of CRS and ICANS
- The EPCORE CLL-1 trial is currently enrolling and evaluating epcoritamab as a single agent and in combination for the treatment of R/R CLL

Conclusion

- ASH24 data reaffirm prior findings across multiple data set and underscore the combinability and versatility of epcortiamab
- Notably, long term data show the favorable long-term safety and highlight the curative potential of epcoritamab across multiple settings
- Additionally, exciting new data for epcoritamab in new indications was presented, including monotherapy data in 1L DLBCL and R/R CLL as well as in novel combination data for epcortiamab+BR in 1L FL

- In summary, these data highlight the potential of epcortiamab as a core therapy across B-NHL

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2025: Strategic Prioritization to Maximize Potential

Dr. Jan van de Winkel
President and Chief Executive Officer

Anticipated 2025 Pipeline Events

Program	Indication	Event	Anticipated Timing
HexaBody-CD38 (GEN3014)	R/R hematologic malignancies	J&J opt-in decision	1Q 2025
Epcoritamab	3L+ R/R FL	JP regulatory decision & launch	1Q 2025
Tivdak	2L R/M cervical cancer	EU regulatory decision	2025
Tivdak	2L R/M cervical cancer	JP regulatory decision & launch	2025
Acasunlimab	2L+ NSCLC	Phase 2 data update	2025
Rina-S	2L+ endometrial cancer	Phase 2 data and next steps	2025
DuoBody-CD40x4-1BB (GEN1042/BNT312)	1L HNSCC	Decision on next steps	2025

Q&A

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