Genmab

2023 R&D Update and ASH Data Review

December 12, 2023

Forward looking statement

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.

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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.

- Seagen Inc.: tisotumab vedotin (Tivdak®)
- AbbVie Inc: epcoritamab (EPKINLY®, TEPKINLY®)
- BioNTech SE[1]: Acasunlimab (GEN1046/BNT311), DuoBody-CD40x4-1BB (GEN1042/BNT312), DuoBody-EpCAMx4-1BB (GEN1059/BNT314), HexaBody-OX40 (GEN1055/BNT315)
- Janssen Biotech, Inc. (Janssen)[2]: HexaBody®-CD38 (GEN3014), daratumumab, daratumumab and hyaluronidase-fihj (DARZALEX®, DARZALEX *FASPRO*®), amivantamab (RYBREVANT®), teclistamab (TECVAYLI®), talquetamab (TALVEY®)

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 Janssen Biotech, Inc.; Janssen Biotech, Inc. leads the development and commercialization of DARZALEX and DARZALEX FASPRO; Janssen Biotech, Inc. co-discovered RYBREVANT and leads the development and commercialization; Janssen Biotech, Inc. discovered TECVAYLI and TALVEY and leads the development and commercialization.

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Agenda

11:00 AM	Welcome & Introduction	Dr. Jan van de Winkel, President & CEO
11:10 AM	HexaBody-CD38 at ASH	Prof. Andrew Spencer, MD, PhD Malignant Haematology, Transplantation and Cellular Therapies Service, The Alfred Hospital
11:15 AM	Epcoritamab at ASH	Dr. Martin Hutchings, MD, PhD Department of Hematology, Rigshospitalet, Copenhagen University Hospital
11:55 AM	2024: Advancing Our Proprietary Pipeline	Dr. Jan van de Winkel
12:00 PM	Live Q&A	

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Driving Towards Our 2030 Vision

2023 Company Highlights

- Expanding into I&I: argenx collaboration
- 8 approved medicines based on Genmab's innovation and antibody expertise
  - 2 Genmab co-owned:
    Tivdak (tisotumab vedotin-tftv) and
    EPKINLY/TEPKINLY (epcoritamab)
  - 4 created via DuoBody technology
- Growing recurring revenue streams and significant underlying profitability
- Focused and disciplined investment approach incl. continued strategic growth of team

Our 2030 Vision:
By 2030, our KYSO™ antibody medicines are fundamentally transforming the lives of people with cancer and other serious diseases.

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Tivdak is being co-developed and co-promoted by Genmab and Seagen. EPKINLY is being co-developed and co-promoted by Genmab and AbbVie

Driving Towards Our 2030 Vision

EPKINLY/TEPKINLY (epcoritamab)

- Regulatory approvals in the U.S., Japan, Europe and other territories
- Added to NCCN Guidelines
- EPCORE NHL-1: positive topline results in R/R FL
  - U.S. FDA granted BTD in R/R FL
  - EMA validated Type II variation application in R/R FL
- Additional Ph 3's anticipated to start in 2024

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Epcoritamab is being co-developed by Genmab and AbbVie

Broad & Comprehensive Epcoritamab Clinical Development Plan

B-NHL Type		Intervention	Most Advanced Phase
Front-line			
DLBCL		Epcoritamab + R-CHOP	**Phase 3**
	Anthracycline ineligible elderly patients	Epcoritamab +/- lenalidomide	Phase 2
		Epcoritamab + pola-R-CHP	Phase 1b/2
FL		Epcoritamab + R^2	**Phase 3**
		Epcoritamab + BR	Phase 1b/2
Relapsed or refractory			
DLBCL	ASCT ineligible patients	Epcoritamab + lenalidomide	**Phase 3**
		Epcoritamab vs SOC	**Phase 3**
		Epcoritamab + lenalidomide	Phase 1b/2
		Epcoritamab + lenalidomide + ibrutinib	Phase 1b/2
	ASCT eligible patients	Epcoritamab + R-DHAX/C	Phase 1b/2
	ASCT eligible patients	Epcoritamab + R-ICE	Phase 1b/2
	ASCT eligible patients	Epcoritamab + Salvage	**Phase 3**
		Epcoritamab + GemOx	Phase 1b/2
FL		Epcoritamab + R^2	**Phase 3**
		Epcoritamab + lenalidomide	Phase 1b/2
DLBCL & FL	Outpatient	Epcoritamab monotherapy	Phase 2
B-NHL	DLBCL, FL, MCL	Epcoritamab monotherapy	Phase 2
	Japanese patients	Epcoritamab monotherapy	Phase 1/2
	Pediatric patients	Epcoritamab monotherapy	Phase 1
	Chinese patients	Epcoritamab monotherapy and + SOC	Phase 1
CLL	CLL	Epcoritamab + venetoclax	Phase 2*
	Chemo-ineligible frontline & R/R Richter's Syndrome	Epcoritamab monotherapy	Phase 1b/2
	Chemo-eligible frontline & R/R Richter's Syndrome	Epcoritamab + R-CHOP	Phase 1b/2
	Chemo-ineligible Richter's Syndrome	Epcoritamab + lenalidomide	Phase 1b/2
	Double-exposed CLL	Epcoritamab monotherapy	Phase 1b/2
	CLL	Epcoritamab + venetoclax	Phase 1b/2

B-NHL: B-cell Non-Hodgkin Lymphoma; BR: bendamustine + rituximab; DLBCL: diffuse large B-cell lymphoma; FL: follicular lymphoma; MCL: mantle cell lymphoma; SOC: standard of care; R2 = Revlimid + rituximab: pola-R-CHP: polatuzumab vedotin, rituximab, cyclophosphamide, HCL, prednisone; R-ICE = rituximab, ifosfamide, carboplatin, and etoposide phosphate
*Trial sponsored by Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)

Driving Towards Our 2030 Vision

TIVDAK (tisotumab vedotin)

- Upgraded to preferred regimen in NCCN Guidelines
- innovaTV 301 positive topline results: basis for global regulatory submissions
- innovaTV 207 interim analysis
- Planned engagement with health authorities on next steps in head & neck cancer

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Tisotumab vedotin is being co-developed by Genmab and Seagen

Driving Towards Our 2030 Vision

Mid/Early-stage Pipeline

- Acasunlimab (GEN1046/BNT311)
  - Planned engagement with health authorities on next steps in NSCLC
  - Phase 2 in advanced endometrial cancer

- Pipeline Progress
  - DuoBody-CD40x4-1BB (GEN1042/BNT312)
  - DuoBody-CD3xB7H4 (GEN1047)
  - DuoBody-CD3xCD30 (GEN3017)

- Next in the clinic
  - DuoBody-EpCAMx4-1BB (GEN1059/BNT314)
  - HexaBody-OX40 (GEN1055/BNT315)

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Acasunllimab, GEN1042, GEN1059 and GEN1055 are being co-developed by Genmab and BioNTech

Innovation in Action

Summary of Key 2023 Events: Programs Powered by Genmab's DuoBody Technology

- Janssen
  - Three approved medicines: TECVAYLI, TALVEY, RYBREVANT
- 2023
  - TECVAYLI: continued growth
  - TALVEY: U.S. & EU approvals
  - RYBREVANT: regulatory submissions

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HexaBody-CD38 at ASH

Presented by Prof. Andrew Spencer, MD, PhD,
The Alfred Hospital

GEN3014 (HexaBody®-CD38) in Anti-CD38 mAb–Naive Patients with Relapsed/Refractory Multiple Myeloma: Preliminary Results from a Dose-Expansion Cohort of a Phase 1/2 Trial

Sebastian Grosicki, MD, PhD,[1] Torben Plesner, MD,[2] Wojciech Jurczak, MD, PhD,[3] Jakub Radocha, MD, PhD,[4] Ehsan Malek, MD,[5] Ida H. Hiemstra, PhD,[6] Lauren K. Brady, PhD,[7] Jenny Chen, MD, PhD,[7] Nian Gong, PhD,[7] Charlotte Hindsberger, MS, PhD,[8] Andrew Spencer, MD[9]

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Presented at the American Society of Hematology Annual Meeting; December 9–12, 2023; San Diego, CA

Introduction

- Anti-CD38 monoclonal antibody (mAb)–containing regimens have changed the treatment paradigm for patients with multiple myeloma (MM)[1]
  - As monotherapy in 3L+ relapsed or refractory multiple myeloma (RRMM), anti-CD38 mAbs have shown limited response rates (24%–41%), with complete responses (CRs) very rarely observed (1%–2%)[2-5]
- In preclinical studies, GEN3014, a next-generation anti-CD38 mAb, demonstrated enhanced complement-dependent cytotoxicity (CDC) against primary MM cells from newly diagnosed or RR patients and stronger inhibition of CD38 cyclase activity compared with daratumumab[6]
- Preliminary dose-escalation data from the first-in-human phase 1/2 trial of GEN3014 in RRMM patients (NCT04824794) showed clinical activity with deep responses, including 2 CRs, and a tolerable safety profile (recommended phase 2 dose, 16 mg/kg)[7]; based on these findings, expansion was initiated

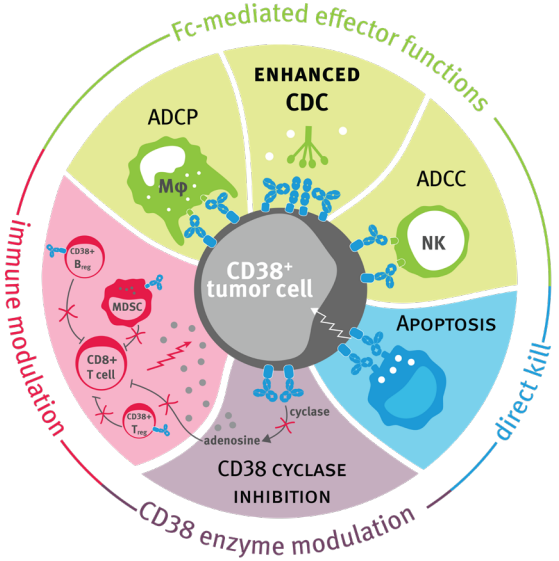
HexaBody® platform

- The HexaBody® platform is designed to enhance IgG1 hexamer formation upon target-specific binding to the cell surface, thereby promoting CDC, target clustering, outside-in signaling, or apoptosis

1. Pick M, et al. *Eur J Haematol*. 2018;100:494-501. **2.** Lokhorst HM, et al. *N Engl J Med*. 2015;373:1207-19. **3.** Lonial S, et al. *Lancet*. 2016;387:1551-60. **4.** Mateos MV, et al. *Lancet Haematol*. 2020;7:e370-80. **5.** Martin T, et al. *Blood Cancer J*. 2019;9:41. **6.** Hiemstra IH, et al. *eBioMedicine*. 2023:93:104663. **7.** Spencer A, et al. ASH 2022. Poster 3254.

GEN3014 Mechanism of Action and Study Objective

- GEN3014 (HexaBody®-CD38) is a next-generation human IgG1 anti-CD38 mAb containing E430G, a hexamerization-enhancing mutation
- GEN3014 facilitates highly efficient CDC and other Fc-mediated effector functions to induce antitumor activity
- GEN3014 has been shown to induce CDC activity across a broad range of CD38 expression levels
- By targeting CD38+ immune cells and inhibiting CD38 enzyme activity, GEN3014 may relieve immune suppression in the tumor microenvironment



Objective

- The primary objective is to evaluate the antitumor activity of GEN3014 in anti-CD38 mAb–naive RRMM patients from dose expansion part A of the phase 1/2 trial (NCT04824794)
- Secondary objectives include assessment of safety and pharmacokinetics; exploratory objectives include pharmacodynamics

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; B_{reg}, regulatory B cell; CDC, complement-dependent cytotoxicity; Mφ, macrophage; MDSC, myeloid-derived suppressor cell; NK, natural killer cell; T_{reg}, regulatory T cell.

Methods

A phase 1/2, open-label, multicenter trial of GEN3014 (HexaBody®-CD38) in adults with RRMM

GEN3014 was administered[a] IV in 28-day cycles until disease progression or unacceptable toxicity

Key inclusion criteria (part A)

- RRMM with disease progression on most recent treatment based on IMWG criteria
- ≥3 prior lines of therapy including PI and IMiD, double refractory to PI and IMiD, or ≥2 prior lines of therapy if 1 included a combination of PI and IMiD
- No prior anti-CD38 antibody
- Acceptable laboratory test results
- ECOG PS of 0–2

Dose expansion part A

RP2D 16 mg/kg[b]

RRMM anti-CD38 mAb–naive (N=11)

Current analysis
Median (range) follow-up: 7.4 mo (0.6–11.3)
Data cutoff: August 14, 2023

Head-to-head expansion part B (recruiting)
A randomized comparison of GEN3014 vs daratumumab in adults with RRMM

Endpoints (part A)

Primary

- Antitumor activity

Key Secondary

- Safety
- Immunogenicity

Exploratory

- Pharmacodynamic markers

[a]Premedication (corticosteroids, antipyretics, antihistamines, and a leukotriene receptor antagonist) and postinfusion medications (corticosteroids) were to be given to reduce the risk of infusion-related reactions and systemic administration-related reactions. During cycle 1, all patients were required to remain in the clinic after each GEN3014 infusion for at least 4 h for close observation. Dosing schedule for GEN3014 was as follows: cycle 1 days 1, 2, 8, 15, and 22; cycle 2 days 1, 8, 15, and 22 (QW); cycles 3–6 days 1 and 15 (Q2W); cycles 7+ day 1 (Q4W). [b]Preliminary safety findings from the escalation phase have found the optimal RP2D to be 16 mg/kg with near-complete target saturation, NK cell depletion, and complement consumption. ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory imide drug; IMWG, International Myeloma Working Group; PI, protease inhibitor; RP2D, recommended phase 2 dose.

Patient Population

- Overall, patients in the RRMM anti-CD38 mAb–naive cohort were heavily pretreated **(Table 1)**

Table 1. Baseline demographics and characteristics

	Total N=11
Median age, y (range)	66 (56–75)
Male, n (%)	5 (45)
Race, n (%)	
White	9 (82)
Black or African American	1 (9)
Asian	1 (9)
ECOG performance status, n (%)	
0	0
1	11 (100)
Subtype of measurable MM disease, n (%)	
IgG	6 (55)
IgA	3 (27)
Light chain	2 (18)
Median M-protein level (range)	
In serum, g/L	18.8 (0–61.0)
In urine, mg/day	5.7 (0–7745)

	Total N=11
Patients with ≥1 extramedullary plasmacytoma, n (%)	1 (9)
ISS stage at screening, n (%)	
Stage I	3 (27)
Stage II	6 (55)
Stage III	2 (18)
Median number of prior lines of therapy (range)	4 (3–6)
Best response to most recent prior therapy, n (%)	
Very good partial response or better with prior therapy	1 (9)
Partial or minimal response with prior therapy	6 (55)
Stable disease with prior therapy	3 (27)
Unknown response with prior therapy	1 (9)

Exposure

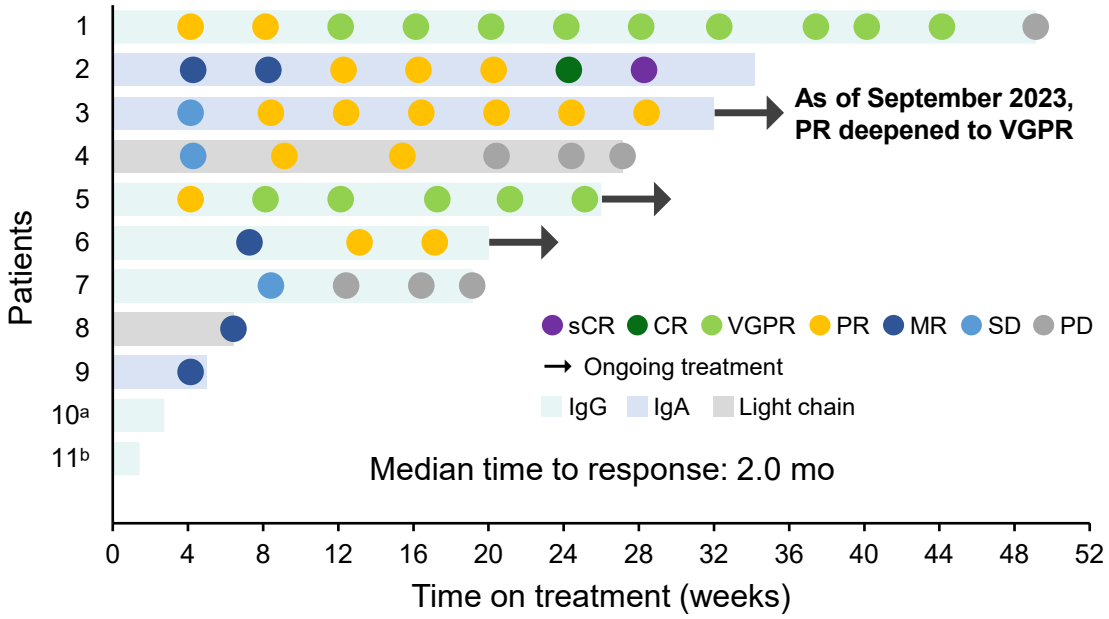
Table 2. Treatment exposure and discontinuation

	Total N=11
Treatment exposure	
Median number of cycles initiated (range)	5 (1–13)
Median duration of treatment, mo (range)	4.6 (0.2–11.3)
Discontinued treatment, n (%)	8 (73)
Reasons for discontinuation, n (%)	
Adverse event	4 (36)
Related to treatment	2 (18)
Disease progression	4 (36)

Response Profile

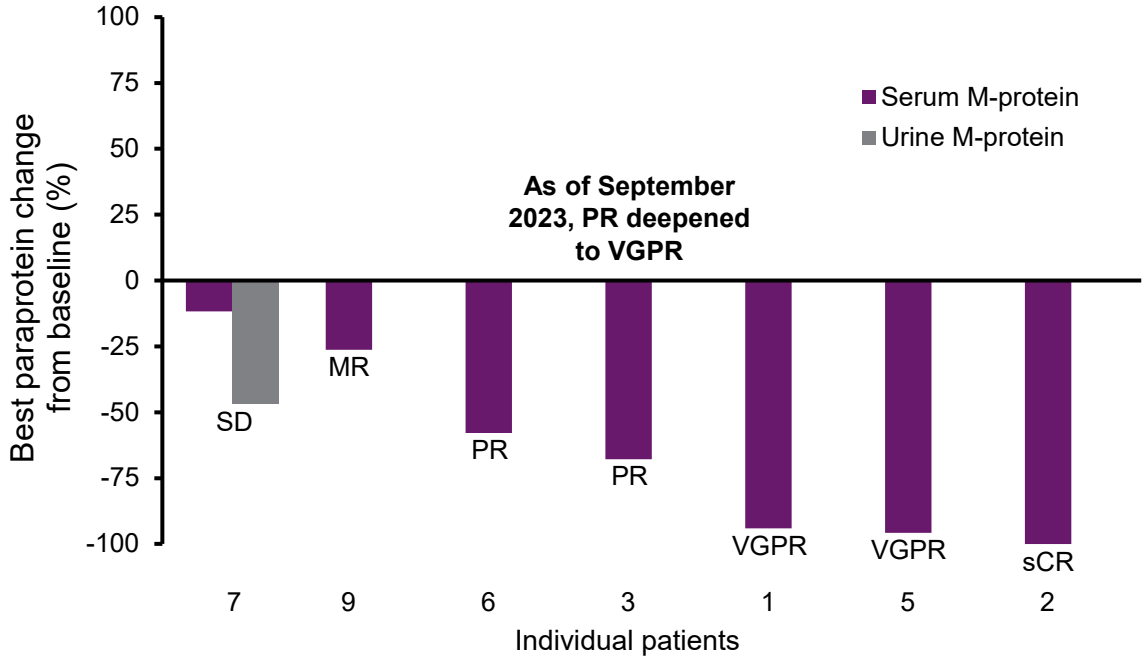
- Clinical benefit was shown in more than half of anti-CD38 mAb–naive patients **(Figures 1 and 2)**
- As of the August 14, 2023, data cutoff, 6 (55%) of 11 patients achieved a response: 1 sCR, 2 VGPR, and 3 PR

Figure 1. Swimlane plot



Patients received GEN3014 16 mg/kg IV in 28-day cycles (QW, cycles 1–2; Q2W, cycles 3–6; Q4W, cycles ≥7). [a]Discontinued due to COVID-19, which was assessed by investigator as not related to treatment. [b]Discontinued due to PD. CR, complete response; MR, minimal response; PD, progressive disease; PR, partial response; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

Figure 2. Best percentage change from baseline in paraprotein

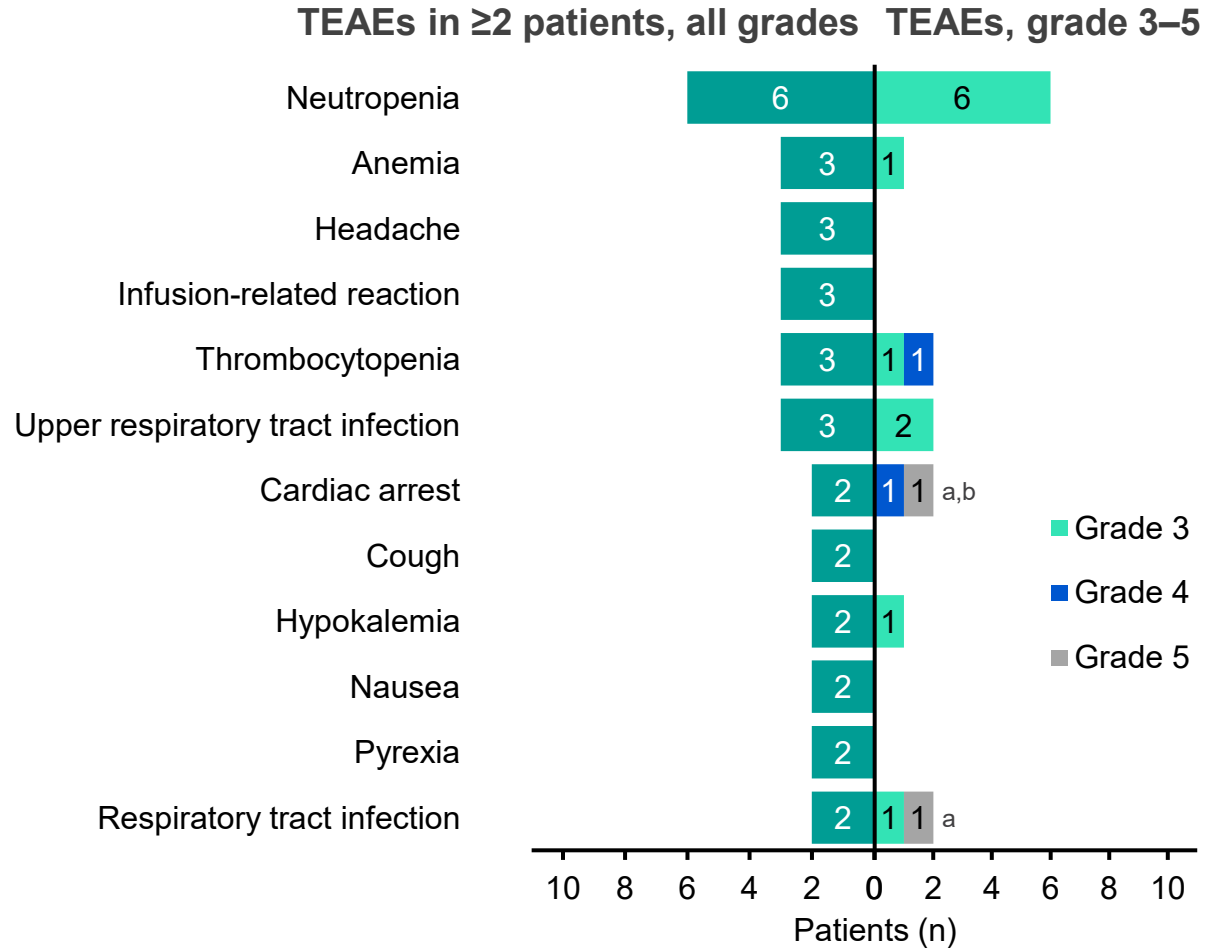


Plot includes 7 patients with postbaseline measurements; 2 patients did not have postbaseline assessments, and 2 patients had light-chain MM disease not shown on waterfall plot.

Safety

- Nine patients experienced ≥1 treatment-emergent adverse event
- Three patients had grade 2 infusion-related reactions; none led to treatment discontinuation **(Figure 3)**
- Two grade 5 events were observed, both deemed not related to GEN3014
- Two patients experienced treatment-related serious adverse events
  - One patient had grade 3 anemia in cycle 4, was hospitalized for a transfusion, was discharged, and continued therapy with GEN3014, with no further transfusion need
  - One patient with multiple underlying cardiovascular comorbidities (hyperlipidemia, hypertension, AV block [Mobitz I], atrial fibrillation, congestive heart failure, morbid obesity, and uncontrolled diabetes mellitus) had nonfatal cardiac arrest in cycle 8 and discontinued study treatment

Figure 3. Treatment-emergent adverse events



[a]Grade 5 events of cardiac arrest (n=1) and respiratory tract infection (n=1) were assessed by investigator as not related to treatment. [b]Patient with grade 4 cardiac event had underlying comorbidities of hyperlipidemia, hypertension, AV Mobitz I, atrial fibrillation, congestive heart failure, morbid obesity, and uncontrolled diabetes mellitus.

Pharmacodynamics

- Treatment with GEN3014 was associated with a rapid, sustained decrease in peripheral blood NK cells **(Figure 4)**
- A transient T-cell decrease was observed after C1D1, and T-cell expansion (≥50% increase from C1D1 for ≥2 visits) was observed in 4 of 7 evaluable patients **(Figure 5)**
- GEN3014 induced transient reduction in total complement lytic activity (CH50), suggesting CDC activity; however, treatment did not exhaust complement **(Figure 6)**

Figure 4. Change in NK cells ($CD3^-CD56^+/CD16^+$ cells, % change from baseline)

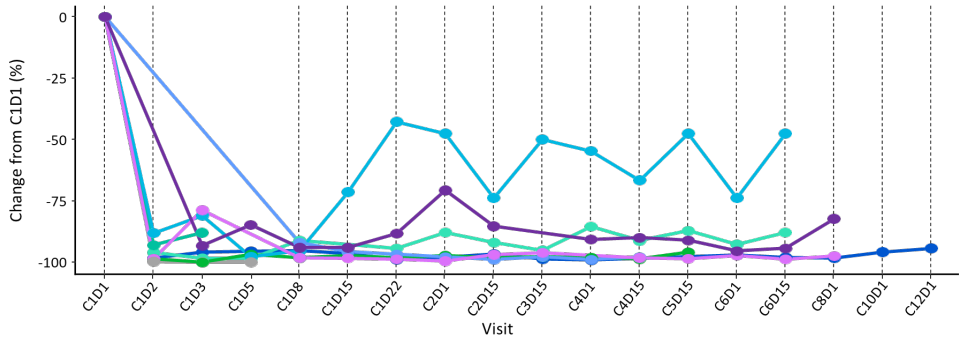


Figure 5. Change in T cells ($CD3^+$ cells, % change from baseline)

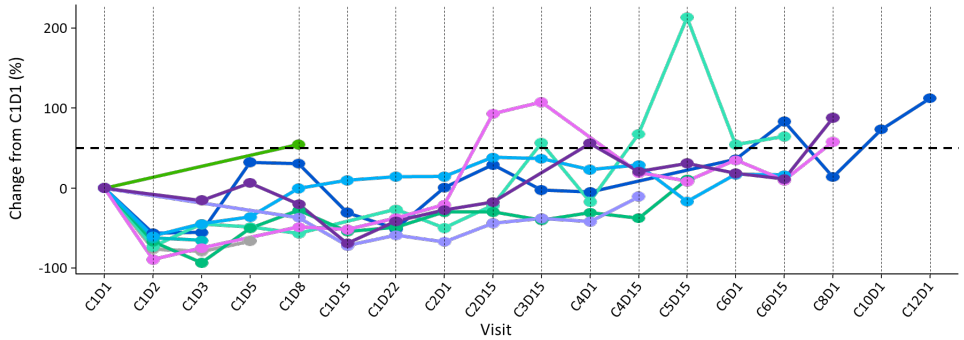
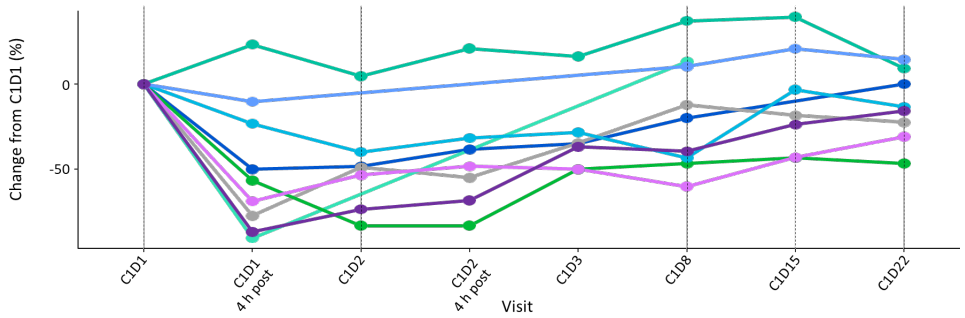


Figure 6. Complement lytic activity in serum (CH50, % change from baseline)



Conclusions

- In this first clinical data disclosure, GEN3014 showed encouraging clinical activity, including rapid, deep responses, in heavily pretreated anti-CD38 mAb–naive RRMM patients
  - As of September 2023, 4 of 11 patients had VGPR or better
  - Compared with responses in immediate prior line of treatment, responses to GEN3014 were very encouraging
- The most common treatment-emergent adverse events were hematologic events, headache, infusion-related reactions, and upper respiratory tract infection
- Pharmacodynamic findings support the mechanism of action and confirm potent CDC
- Based on these encouraging data, a head-to-head comparison of GEN3014 versus daratumumab in anti-CD38 mAb–naive RRMM patients was initiated and is actively enrolling

- 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 graphical support were provided by Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and funded by Genmab.

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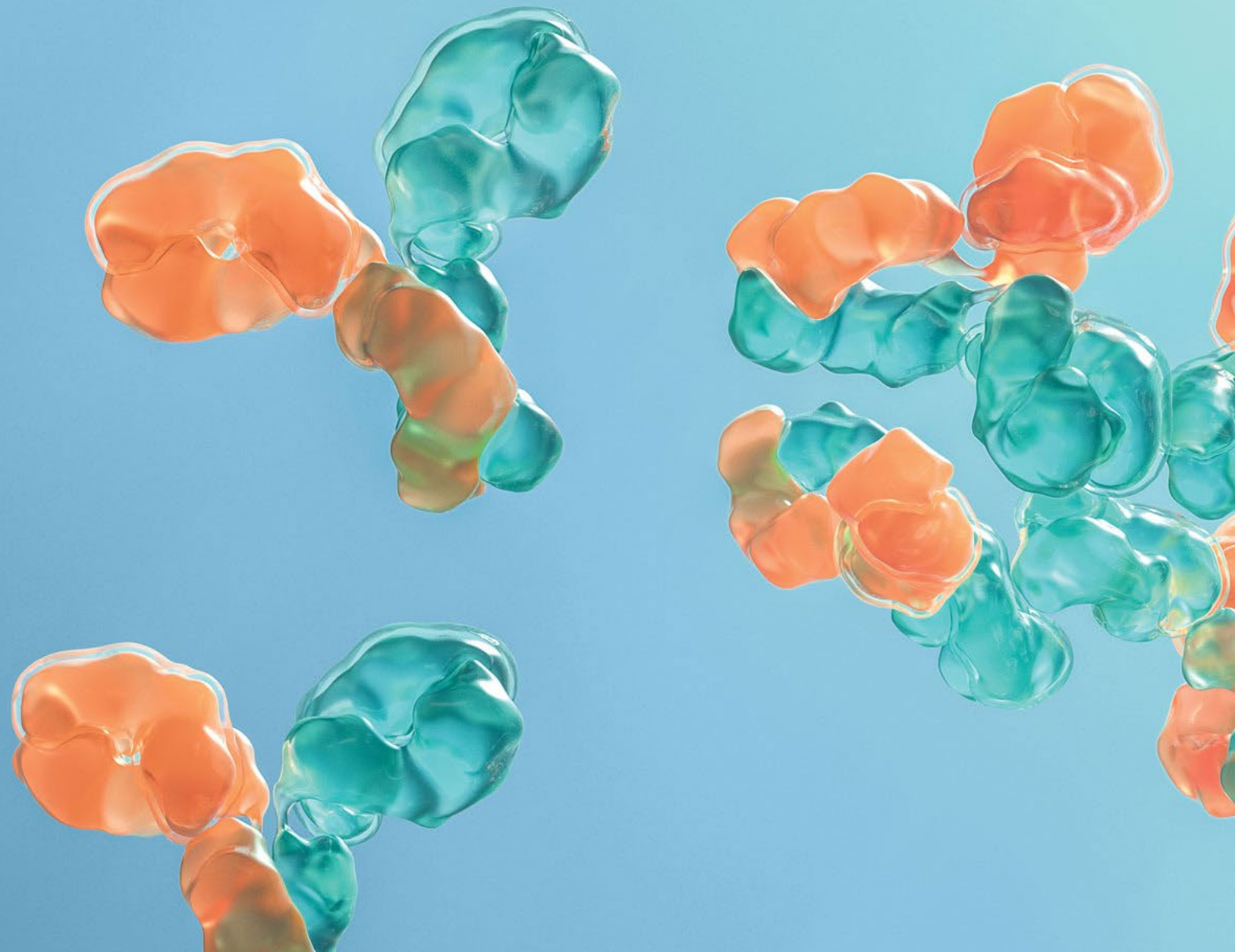
Epcoritamab at ASH



Presented by Dr. Martin Hutchings, MD, PhD, Department of Hematology, Rigshospitalet, Copenhagen University Hospital

Epcoritamab SC Monotherapy Leads to Deep and Durable Responses in Patients with Relapsed or Refractory Follicular Lymphoma: First Data Disclosure from the Pivotal EPCORE NHL-1 Follicular Lymphoma Dose-Expansion Cohort

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[1]The Christie NHS Foundation Trust and Manchester Cancer Research Centre, Manchester, UK; [2]MSC National Research Institute of Oncology, Kraków, Poland; [3]On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Erasmus MC Cancer Institute, University Medical Center, Department of Hematology, Rotterdam, Netherlands; [4]Centre Hospitalier Universitaire de Tours, Tours, France; [5]Institut Català d'Oncologia, Hospital Duran i Reynals, IDIBELL, Universitat de Barcelona, L'Hospitalet de Llobregat, Barcelona, Spain; [6]Odense University Hospital, Odense, Denmark; [7]Medical University of South Carolina, Charleston, SC, USA; [8]Centre Henri Becquerel, Rouen, France; [9]Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [10]University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth, UK; [11]Oregon Health & Science University Knight Cancer Institute, Portland, OR, USA; [12]Rigshospitalet and University of Copenhagen, Copenhagen, Denmark; [13]Vejle Hospital, Vejle, Denmark; [14]Candiolo Cancer Institute, FPO-IRCCS, Candiolo (Turin), Italy; [15]Gold Coast University Hospital, Southport, Queensland, Australia; [16]University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; [17]On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Amsterdam UMC, VU University Medical Center, Amsterdam, Netherlands; [18]AbbVie, North Chicago, IL, USA; [19]Genmab, Copenhagen, Denmark; [20]Genmab, Plainsboro, NJ, USA; [21]Genmab, Utrecht, Netherlands; [22]Assistance Publique & Hôpitaux de Paris (APHP), Hôpital Saint-Louis, Hémato-oncologie, Université de Paris, Paris, France

Presented at the American Society of Hematology Annual Meeting; December 9–12, 2023; San Diego, CA

Background

- Despite recent advances in therapy, patients with relapsed/refractory follicular lymphoma (R/R FL) are still underserved by current treatment options; there remains a need for highly efficacious, easy-to-administer therapies that induce durable remissions, particularly in later lines of therapy[1-3]
- Particularly poor outcomes are observed in patients with POD24, double-refractory disease, and disease refractory to the last prior therapy[4-7]
- Epcoritamab is the only approved subcutaneously administered (SC) CD3xCD20 bispecific antibody for the treatment of (D)LBCL
  - Approved in the US, EU, the UK, Japan and Canada[a]

1. Link BK, et al. *Br J Haematol*. 2019;184:660-3. **2.** Batlevi CL, et al. *Blood Cancer J*. 2020;10:74. **3.** Ghione P, et al. *Haematologica*. 2023;108:822-32. **4.** Casulo C, et al. *J Clin Oncol*. 2015;33:2516-22. **5.** Casulo C, et al. *Blood*. 2022;139:1684-93. **6.** Salles G, et al. *Hemasphere*. 2022;6:e745. **7.** Andorsky DJ, et al. *J Clin Oncol*. 2017;35(suppl). Abstract 7502. **8.** EPKINLY [prescribing information]. Plainsboro, NJ: Genmab US, Inc.; 2023. **9.** Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; 2023. **10.** Tepkinly [summary of product characteristics]. Maidenhead, UK: AbbVie Ltd; 2023. **11.** EPKINLY [prescribing information]. Tokyo, Japan: Genmab K.K.; 2023. **12.** EPKINLY [product monograph]. St-Laurent, Canada: AbbVie; 2023. [a]Approved in Europe and the UK for adults with R/R DLBCL after ≥2 lines of systemic therapy. [b]Approved in Japan for adults with the following R/R large B-cell lymphoma: DLBCL, HGBCL, primary mediastinal large B-cell lymphoma, and FL grade 3B after ≥2 lines of systemic therapy

First disclosure: Pivotal EPCORE™ NHL-1 Study in R/R FL

Dose expansion

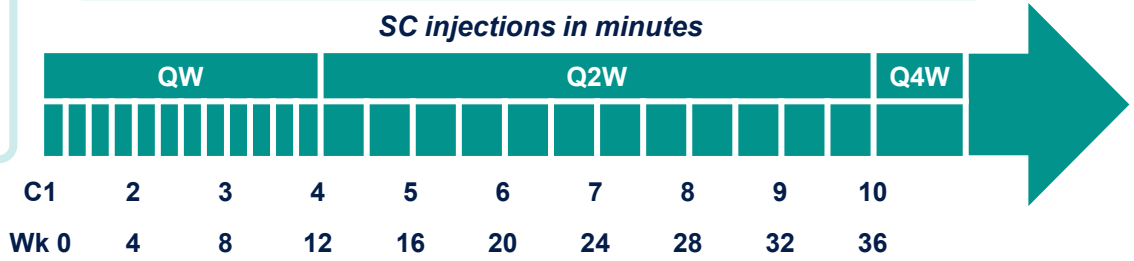
Key inclusion criteria[a]:

- R/R CD20+ R/R FL (Gr 1-3A)
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- Prior treatment with an alkylating agent or lenalidomide
- Prior CAR T allowed
- FDG PET–avid and measurable disease by CT/MRI

Data cutoff: April 21, 2023
Median follow-up: 17.4 mo

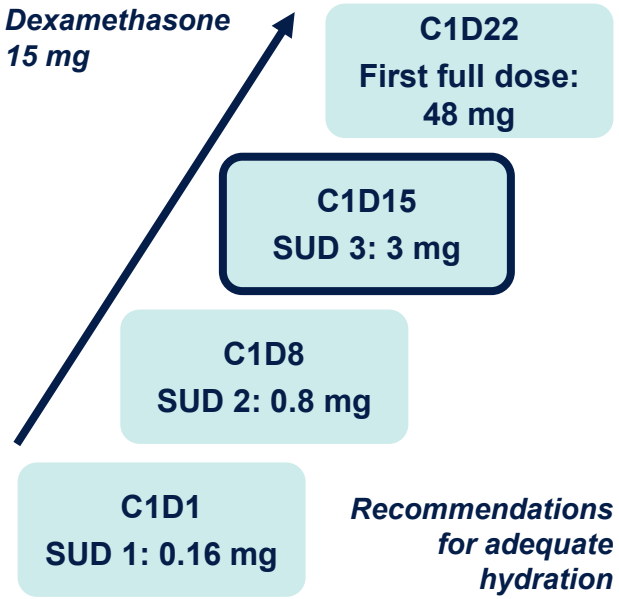
Step-up dosing[b]

Epcoritamab SC RP2D 48 mg
Treatment until PD[c] or unacceptable toxicity
R/R FL grade 1–3A expansion cohort, N=128



- **Primary endpoint:** ORR by independent review committee
- **Key secondary endpoints:** CR rate, MRD[d], DOR, TTR, PFS, OS and safety/tolerability

C1 optimization



- Hospitalization not mandated
- **Primary objective:** Incidence and severity of CRS

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

Baseline Characteristics: High proportion of poor risk patients

Demographics	N=128
Median age, y (range)	65 (39–84)
Male, n (%)	79 (62)
Ann Arbor stage, n (%)[a]	
III	32 (25)
IV	77 (60)
FLIPI, n (%)[b]	
2	31 (24)
3–5	78 (61)
Beta-2 microglobulin, n (%)[c]	
High	79 (62)

Treatment History	N=128
Median time from diagnosis to first dose, y (range)	5.8 (0.6–35)
Median time from end of last line of therapy to first dose, mo (range)	5.2 (1–105)
Median time from end of last anti-CD20 therapy to first dose, mo (range)	10.3 (1–159)
Median number of prior lines of therapy (range)	3 (2–9)
≥3 prior lines, n (%)	81 (63)
≥4 prior lines, n (%)	40 (31)
POD24,[d] n (%)	54 (42)
Double refractory,[e,f] n (%)	90 (70)
Primary refractory,[e] n (%)	69 (54)
Refractory[e] to last prior systemic therapy, n (%)	88 (69)

- All patients had prior treatment with an anti-CD20 mAb and an alkylating agent
- Other prior treatments included anthracyclines (77%), bendamustine (63%), nucleoside analoges (48%), topoisomerase inhibitors (36%), IMiDs (31%), PI3K inhibitors (23%), and CAR T (5%)

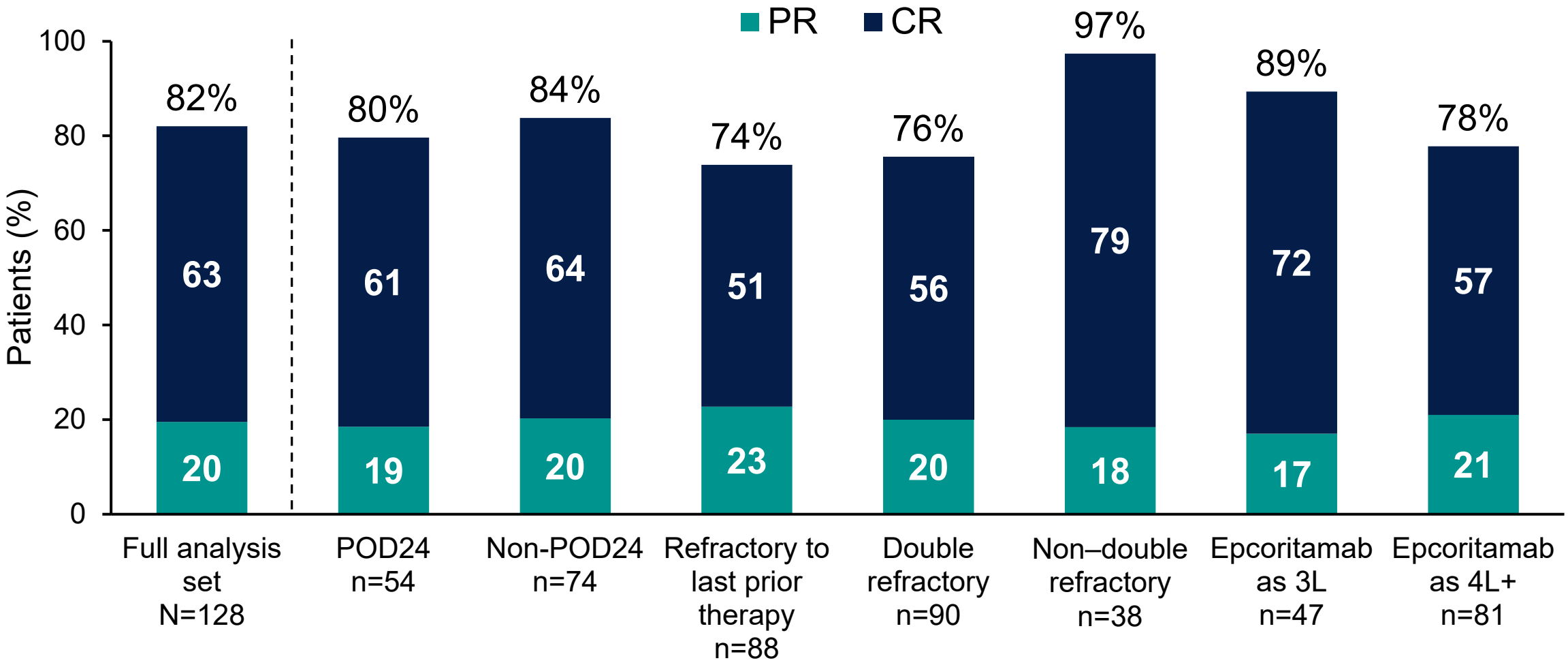
[a]Ann Arbor stage was I–II in 19 patients. [b]FLIPI was 0–1 in 17 patients, unknown for 1 patient, and not applicable for 1 patient. FLIPI was prior to first dose on study. [c]Beta-2 microglobulin was normal in 45 patients and missing for 4 patients. [d]Progression within 2 y of initiating first-line chemoimmunotherapy. [e]Refractory: No response or relapse within 6 mo after therapy. [f]Double refractory: Refractory to both anti-CD20 and an alkylating agent.

Exposure and Follow-up

	N=128
Median follow-up, mo (range)	17.4 (0.2+ to 30.1)
Epcoritamab treatment exposure	
Median number of treatment cycles initiated (range)	8 (1–33)
Median duration of treatment, mo (range)	8.3 (0.03–30)
Ongoing treatment, n (%)	47 (37)
Discontinued treatment, n (%)	81 (63)
PD	44 (34)
AE	24 (19)
COVID-19[a]	12 (9)
Decision to proceed to transplant	4 (3)
Patient withdrawal	3 (2)
Other	6 (5)

[a]Includes COVID-19 pneumonia.

High ORRs and CR Rates Regardless of High-Risk features



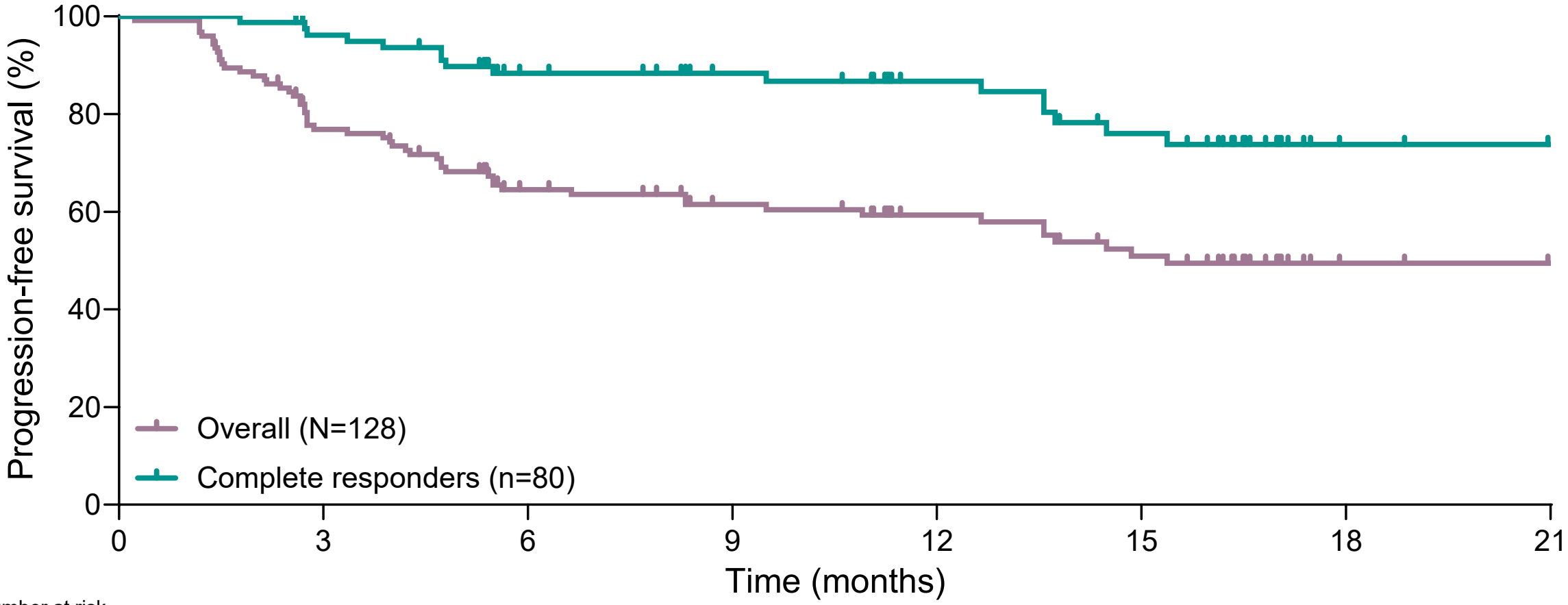
Responses Observed Early and Were Deep and Durable

Efficacy Parameters	N=128
Median time to response, mo (range)	1.4 (1.0–3.0)
Median time to complete response, mo (range)	1.5 (1.2–11.1)
Median duration of response, mo (95% CI)[a]	NR (13.7–NR)
Median duration of complete response, mo (95% CI)[a]	NR (21.4–NR)
MRD negativity, n (%)[b]	61 (67)
Median progression-free survival, mo (95% CI)[a]	
Overall (N=128)	15.4 (10.9–NR)
Complete responders (n=80)	NR (22.8–NR)
MRD-negative patients (n=61)	NR (22.8–NR)
Median overall survival, mo (95% CI)[a]	NR (NR–NR)
Median time to next therapy, mo (range)[a]	NR (0.2+ to 30.0+)

MRD, minimal residual disease; NR, not reached. [a]Based on Kaplan–Meier estimate. [b]Based on MRD-evaluable set (n=91) per clonoSEQ® PBMC assay with 10^{-6} cutoff.

- Responses incl CRs were observed early and were durable
- High MRD negativity rate observed
- MRD was associated with improved progression-free and overall survival
- Long term outcome data continue to mature

Complete Response Associated With Favorable Long-Term Outcomes

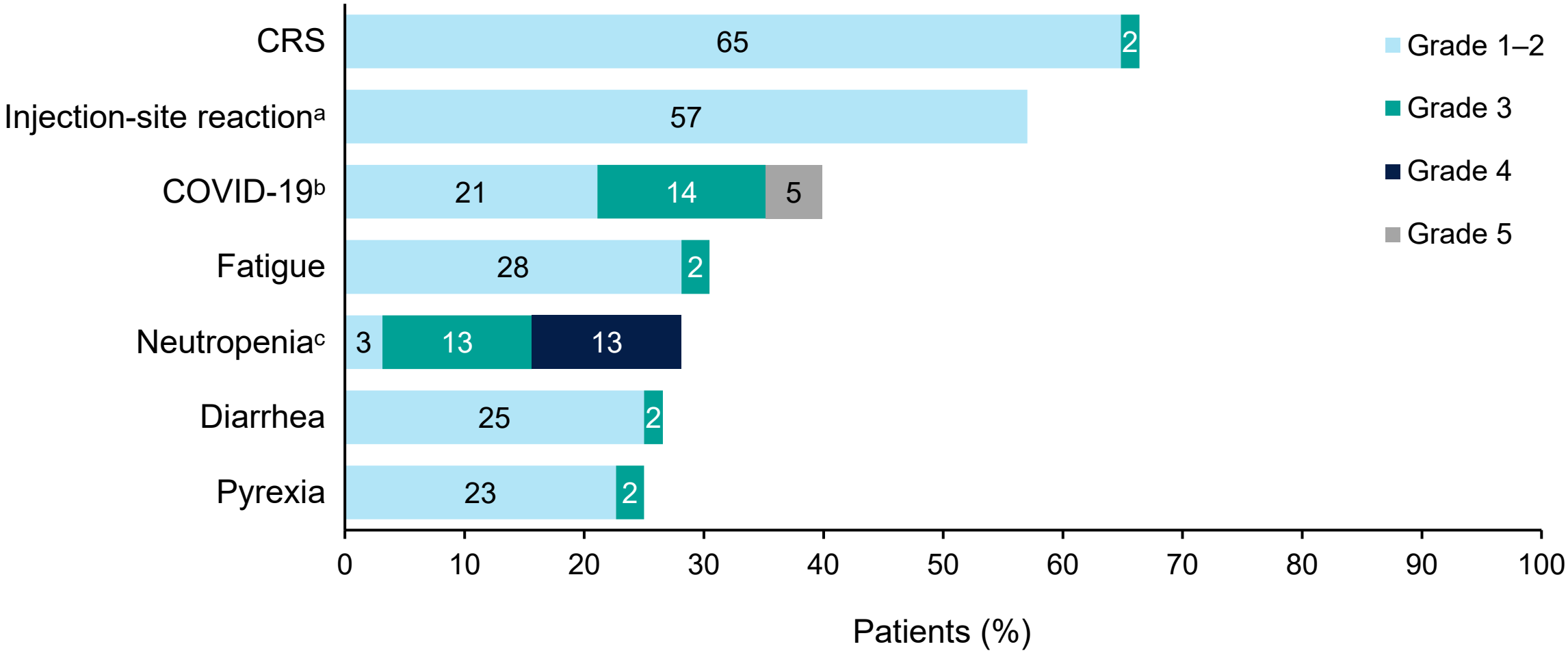


Number at risk

128	90	67	57	43	35	14	12
80	75	61	54	41	34	14	12

Progression-free survival assessed by IRC

Common (>20%) TEAEs Were Mostly Low Grade



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

Manageable Safety

- Safety findings were generally consistent with previous reports of epcoritamab
- 48 patients (38%) had grade ≥3 TEAEs reported as related to epcoritamab
  - Febrile neutropenia was reported in 4 patients (3%; all grade 3)
- The trial was conducted during the global COVID pandemic, and impacted by prevailing COVID trends, including the highly infectious Omicron variant
  - The outcomes of COVID cases were consistent with expected outcomes based on well-known risk factors for severe COVID (eg, age and other comorbidities)
- TEAEs led to treatment discontinuation in 24 patients (19%); half of these TEAEs were due to COVID-19
  - 5 patients (4%) discontinued treatment due to TEAEs reported as related to epcoritamab: 1 patient each with COVID-19, pneumonitis, enteritis, and diarrhea; 1 patient with both fatigue and malaise
- 13 patients (10%) had fatal TEAEs, and 6 (5%) were due to COVID-19
- No clinical tumor lysis syndrome was reported

Cycle 1 Optimization Substantially Reduced the Risk and Severity of CRS

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

- Baseline characteristics were balanced across the cohorts
- Hospitalization not mandated in the optimization cohort
- C1 optimization with 3 SUD substantially reduced rate and severity of CRS, with no impact on efficacy
- In both cohorts, CRS was primarily confined to C1
- There were no cases of ICANS in the C1 optimization cohort; 8 cases observed in the pivotal cohort (all grade 1–2 and resolved; none led to discontinuation)

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

Conclusions

- In this first disclosure of the pivotal expansion data from NHL-1 FL, SC epcoritamab led to deep and durable responses in a challenging to treat R/R FL population with expected poor outcomes
  - ORR 82%, CR rate 63%, 67% MRD negativity
  - High ORR and CR rates observed regardless of high-risk features
  - Depth of response incl. MRD was correlated to long-term outcomes
  - mDOR/mDOCR, mPFS in CR / MRD- pts and mOS were all NR
- Cycle 1 optimization with 3 SUD substantially reduced the risk and severity of CRS, with no impact on efficacy
- Safety was predictable and epcoritamab was generally well tolerated
- Data adds to the growing body of evidence of epcoritamab's activity across B-NHL histologies

Mitigating the Risk of Cytokine Release Syndrome (CRS): Results from a DLBCL Cohort of EPCORE NHL-1

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Presented at the American Society of Hematology Annual Meeting; December 9–12, 2023; San Diego, CA

Background

- CRS is inherent with T-cell engagers like bispecific antibodies or CAR T-cell therapies; current strategies for CRS mitigation vary[1]
- Epcoritamab SC has demonstrated deep, durable responses with a manageable safety profile in patients with R/R large B-cell lymphoma (LBCL) in dose expansion of the pivotal Phase 1/2 EPCORE NHL-1 trial[7,8]
  - SC administration, step-up dosing, premedication incl. prophylactic corticosteroids were used to mitigate CRS during cycle 1
  - CRS events during expansion were primarily low grade (51% overall; 32% G1, 16% G2, 3% G3)[c]; timing was predictable, with the majority of events occurring following the first full dose (C1D15)

[a]Approved in Europe and the UK for the treatment of adults with R/R DLBCL after ≥2 lines of systemic therapy. [b]Approved in Japan for the treatment of adults with the following R/R LBCL: DLBCL, HGBCL, primary mediastinal large B-cell lymphoma, and follicular lymphoma (FL) grade 3B after ≥2 lines of systemic therapy. [c]Data cutoff: November 18, 2022.

1. Shimabukuro-Vornhagen A, et al. *J Immunother Cancer.* 2018;6:56. **2.** EPKINLY [prescribing information]. Plainsboro, NJ: Genmab US, Inc.; 2023. **3.** Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; 2023. **4.** Tepkinly [summary of product characteristics]. Maidenhead, UK: AbbVie Ltd; 2023. **5.** EPKINLY [prescribing information]. Tokyo, Japan: Genmab K.K.; 2023. **6.** EPKINLY [product monograph]. St-Laurent, Canada: AbbVie; 2023. **7.** Thieblemont C, et al. *J Clin Oncol*. 2023;41:2238-47. **8.** Karimi Y, et al. ASCO 2023. Abstract 7525.

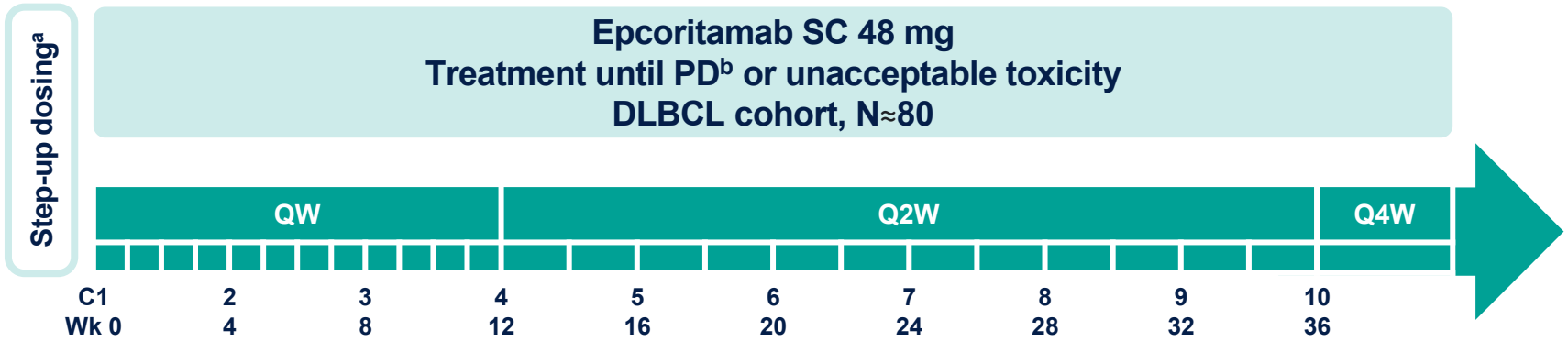
Study Design: EPCORE™ NHL-1 dose optimization Cohort

DLBCL Cycle 1 Optimization

Key inclusion criteria:

- R/R CD20+ DLBCL, NOS (de novo or transformed from FL)
- ECOG PS 0–2
- ≥2 prior lines of systemic antineoplastic therapy, including ≥1 anti-CD20 mAb
- Prior CAR T-cell therapy allowed
- FDG PET–avid and measurable disease by CT/MRI

Data cutoff: July 17, 2023
Median follow-up: 1.7 mo



- **Cycle 1 optimization:** Hospitalization not mandated[c]
  - Dexamethasone 15 mg premedication on D1, D8, D15, and D22 and prophylaxis on D2–4, D9–11, D16–18, and D23–25 was recommended
  - 2–3 L of fluid intake during 24 h prior to each dose
  - Hold antihypertensive medications for 24 h prior to each dose
  - 500 mL of isotonic IV fluids on the day of each dose prior to administration
  - 2–3 L of fluid intake during 24 h following each dose
  - Self-monitoring of temperature 3 times daily for 4 d following each dose
- **Primary endpoint:** Incidence and severity of CRS

[a]Step-up dose (SUD) 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. [b]Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36. [c] Hospitalization not required; patients must remain in close proximity to treatment facility for 24 h following first full dose

Baseline Characteristics and Prior Treatments

Demographics	N=60
Median age (range), y	66 (27–86)
≥75 y, n (%)	13 (22)
ECOG PS,[a] n (%)	
0	20 (33)
1	34 (57)
2	5 (8)
Disease Characteristics and Prior Treatments	**N=60**
DLBCL type,[b] n (%)	
De novo	37 (62)
Transformed	9 (15)
Median time from initial diagnosis to first dose (range),[c] y	1.6 (0.1–24.8)
Median time from end of last therapy to first dose (range),[c] mo	3.1 (1–220)
Median prior lines of therapy, n (range)	3 (2–10)
Prior lines of therapy, n (%)	
2	19 (32)
≥3	41 (68)
Primary refractory[d] disease,[c] n (%)	36 (60)
Refractory[d] to last systemic therapy,[c] n (%)	51 (85)
Refractory[d] to ≥2 consecutive lines of therapy,[c] n (%)	42 (70)
Prior ASCT,[c] n (%)	4 (7)
Prior CAR T therapy,[c] n (%)	33 (55)
Refractory[d] to CAR T therapy, n/n (%)	28/33 (85)

[a]ECOG PS was missing for 1 patient. [b]De novo versus transformed status of 14 patients was unknown or not applicable. [c]Based on available data (n=56). [d]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 mo of completion of therapy.

Exposure and Follow-up

	N=60
Median follow-up (range), mo	1.7 (0.1–6.6)
Mean number of treatment cycles	2
Mean number of doses administered	7
Ongoing treatment, n (%)	42 (70)
Discontinued treatment, n (%)	18 (30)
PD	17 (28)
AE[a]	1 (2)

[a]Grade 3 sepsis, which was diagnosed on C1D6, was considered not related to epcoritamab by the investigator.

Cycle 1 Optimization Substantially Reduced the Risk and Severity of CRS

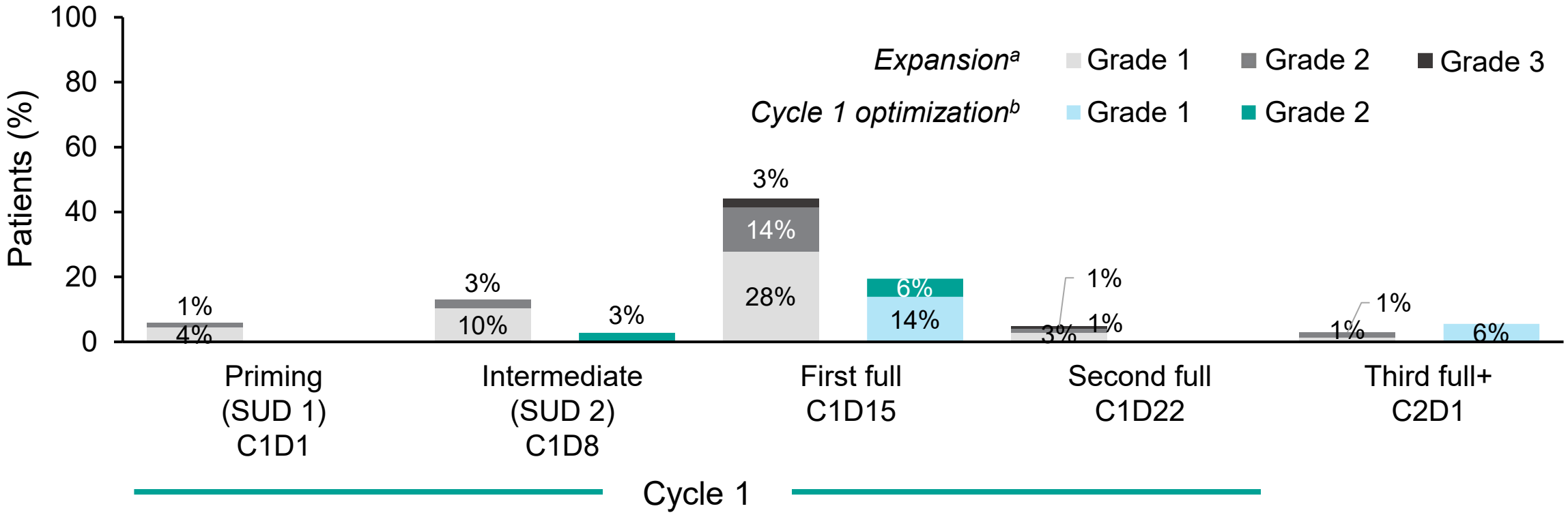
	Expansion[a] N=157	CRS-Evaluable[b] DLBCL Cycle 1 Optimization[c] n=36
CRS, n (%)[d]	80 (51)	8 (22)
Grade 1	50 (32)	5 (14)
Grade 2	25 (16)	3 (8)
Grade 3	5 (3)	0
Signs and symptoms of CRS, n (%)[e]	**n=80**	**n=8**
Fever	79 (99)	7 (88)
Hypotension	24 (30)	3 (38)
Hypoxia	14 (18)	0
Other	15 (19)	1 (13)
Median time to onset after first full dose, h[e]	20	27
Treated with tocilizumab, n/n (%)[e]	23/80 (29)	3/8 (38)
Treated with corticosteroid, n/n (%)[e]	17/80 (21)	2/8 (25)
Leading to treatment discontinuation, n (%)	1 (0.6)	0
CRS resolution, n/n (%)[e]	79/80 (99)	8/8 (100)
Median time to resolution, d (range)[e]	2 (1–27)	2.5 (1–6)

- C1 optimization substantially reduced rate and severity of CRS with no impact on efficacy
- Among the 36 CRS-evaluable patients, pretreatment prior to the first full dose included:
  - IV fluid (86%)
  - Dexamethasone (81%)
  - IV fluid and dexamethasone (69%)
  - Other corticosteroids (19%)

[a]Data cutoff: November 18, 2022. [b]CRS-evaluable population was defined as patients treated with epcoritamab who either met the minimum exposure criterion and completed the CRS-evaluation period with sufficient safety evaluations or experienced a grade ≥2 CRS event during the CRS-evaluation period. [c]Data cutoff: July 17, 2023. [d]Graded by Lee et al 2019 criteria.[1] [e]Among patients with CRS.

1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

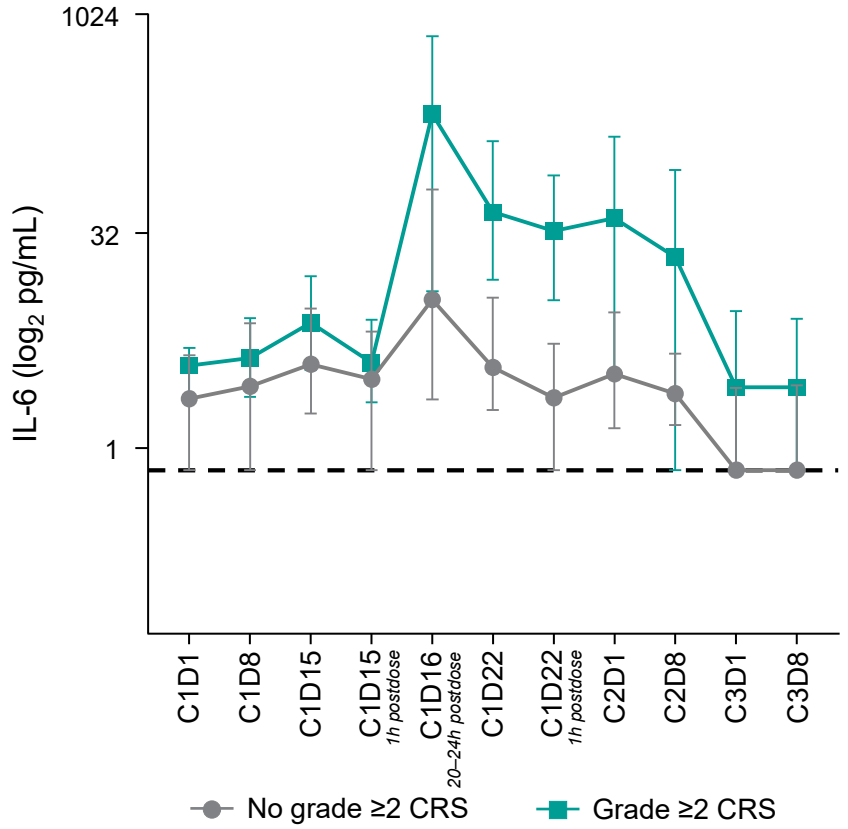
Predictable CRS timing



SUD 1, first step-up dose; SUD 2, second step-up dose. [a]Data cutoff: November 18, 2022. [b]Data cutoff: July 17, 2023. Based on the CRS-evaluable population (n=36), which consists of patients treated with epcoritamab who either met the minimum exposure criterion and completed the CRS-evaluation period with sufficient safety evaluations or experienced a grade ≥2 CRS event during the CRS-evaluation period.

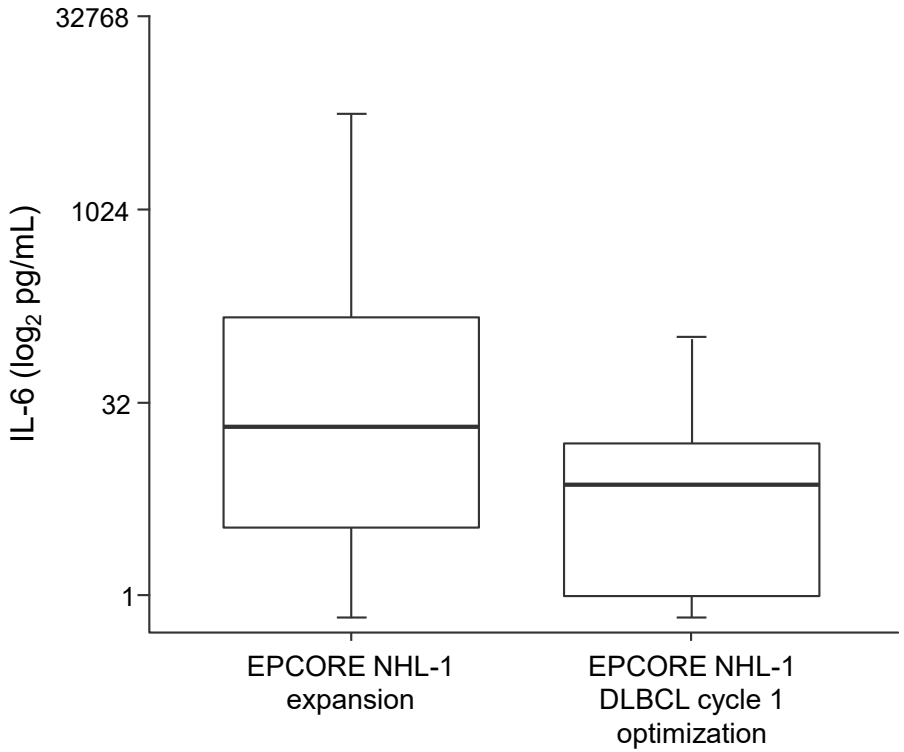
Lower IL-6 levels consistent with lower incidence and severity of CRS

CRS Events in Expansion and Cycle 1 Optimization



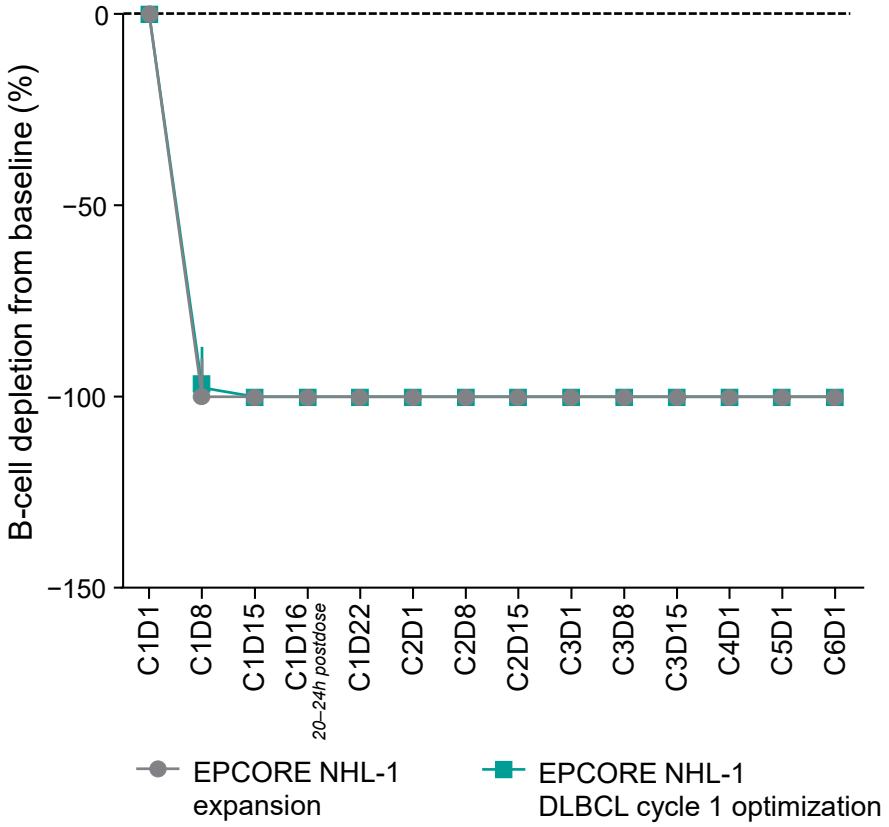
Timepoints are predose unless otherwise specified. The horizontal dashed line indicates the lower limit of quantification (0.695 pg/mL) of the IL-6 assay. Data are presented as median ± interquartile range.

IL-6 Peak Concentration 24 h After First Full Dose



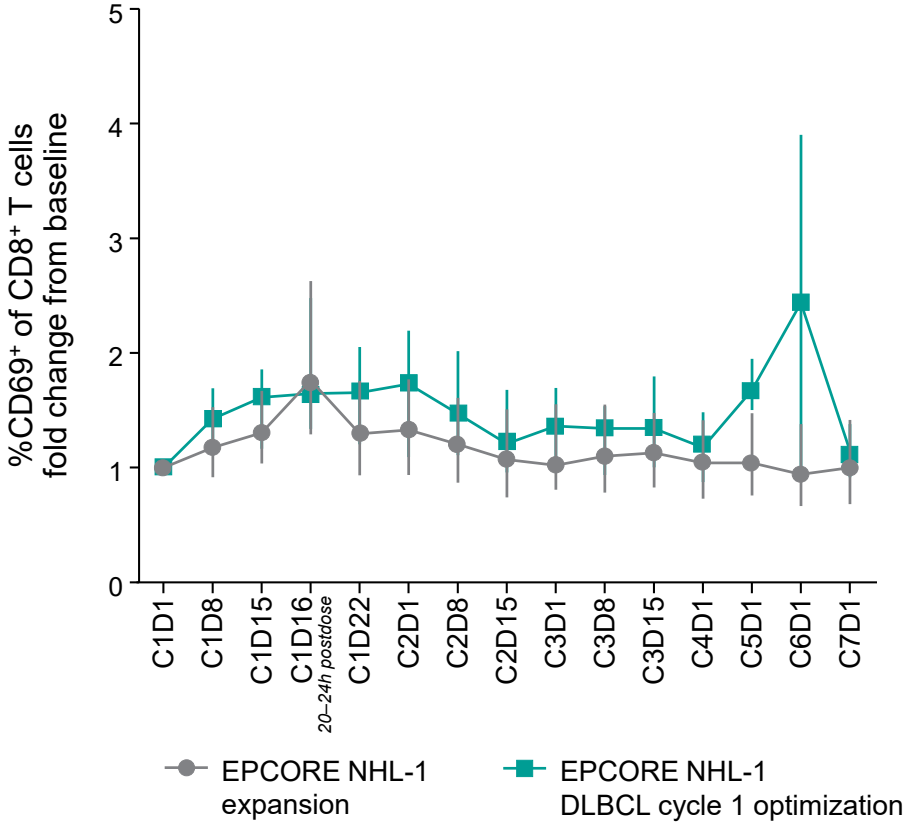
No impact on T-cell activation or B-cell depletion

Peripheral Blood B-Cell Depletion



Timepoints are predose unless otherwise specified. Only patients with ≥10 cells/μL at baseline are included. Data are presented as median ± interquartile range. Common timepoints between the expansion and optimization parts are shown.

Peripheral Blood T-Cell Activation



Timepoints are predose unless otherwise specified. Data are presented as median ± interquartile range. Common timepoints between the expansion and optimization parts are shown.

Conclusions

- First data disclosure of Cycle 1 optimization data from NHL-1 DLBCL
- Incorporation of simple measures of prophylactic dexamethasone and hydration in Cycle 1 effectively decreased rates and severity of CRS with no impact on efficacy
  - Hospitalization was not mandated
  - Overall incidence reduced to 22%, all low grade (14% Gr 1, 8% Gr 2)
  - CRS timing remained predictable
  - No patients discontinued treatment due to CRS
- IL-6 levels were lower with Cycle 1 optimization and consistent with lower observed rates of CRS
  - There was no impact on T-cell activation or B-cell depletion

Subcutaneous Epcoritamab Plus Lenalidomide in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma From EPCORE NHL-5

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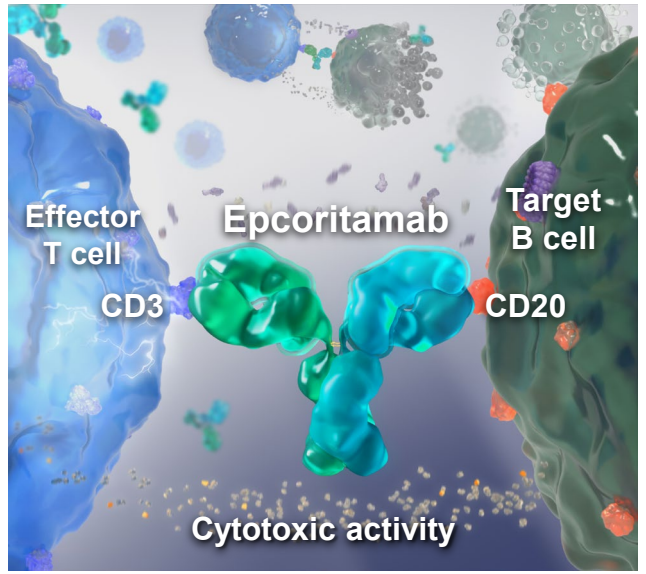
*Presenting author

Presented at the American Society of Hematology; December 9–12, 2023; San Diego, CA, USA

Background

- Patients with R/R DLBCL have poor outcomes[1,2]
- Epcoritamab SC is a CD3xCD20 bispecific antibody developed using the DuoBody® platform[3,4]
- Epcoritamab demonstrated deep and durable responses and a manageable safety profile as monotherapy in patients with R/R B-cell lymphoma in the EPCORE NHL-1 trial[5] and in different lines of therapy and combinations[6,]

Epcoritamab mechanism of action



- Epcoritamab is **approved in the US,[7] Europe,[8,a] Japan,[9,b] and other regions;** in the US, epcoritamab is approved for the treatment of adults with R/R DLBCL not otherwise specified, including DLBCL arising from indolent lymphoma and high-grade B-cell lymphoma after ≥2 lines of systemic therapy[7]
- Lenalidomide activates and enhances T-cell and natural killer cell proliferation, which may complement the T-cell–mediated cytotoxicity of epcoritamab[10]

Here we present the first results of a chemo-free regimen of epcoritamab plus lenalidomide in patients with R/R DLBCL from arm 1 of EPCORE NHL-5

[a]Approved in Europe for the treatment of adult patients with R/R DLBCL after ≥2 lines of systemic therapy.
[b]Approved in Japan for the treatment of adult patients with certain types of R/R LBCL after ≥2 lines of systemic therapy.

1. Sehn LH, Salles G. *N Engl J Med*. 2021;384:842–58. **2.** Crump M, et al. *Blood*. 2017;30:1800–8. **3.** Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. **4.** van der Horst HJ, et al. *Blood Cancer J*. 2021;11:38. **5.** Karimi Y, et al. ASCO 2023, abstract 7525. **6.** Brody JD, et al. ASH 2023, abstract 3092. **7.** Vermaat SP, et al. ASH 2023, abstract 4457. **7.** Epkinly [package insert]. Plainsboro, NJ: Genmab; May 2023. **8.** Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; September 2023. **9.** Epkinly [prescribing information]. Tokyo, Japan: Genmab K.K.; September 2023. **10.** McDaniel JM, et al. *Adv Hematol*. 2012;2012:513702.

Study Design: EPCORE NHL-5 (NCT05283720)

Key inclusion criteria: arm 1

- Adults ≥18 y
- Histologically confirmed CD20+ DLBCL[a]
  - DLBCL, NOS
  - High-grade B-cell lymphoma with *MYC* and *BCL-2* and/or *BCL-6* translocations
  - FL grade 3B
- R/R disease[b] with ≥1 prior anti-CD20 mAb–containing systemic therapy
- ASCT ineligible or failed prior ASCT
- Prior CAR T allowed, but prior CD3/CD20 bispecific antibodies not allowed
- ECOG PS 0–2
- Measurable disease

Data cutoff: Oct 6, 2023
Median follow-up: 8.2 mo

Dose escalation and dose expansion

Arm 1 **Epcoritamab + lenalidomide** **(12 x 28-day cycles)** **R/R DLBCL**	**Arm 2** Epcoritamab + ibrutinib + lenalidomide R/R DLBCL	**Arm 3** Epcoritamab + polatuzumab + R-CHP 1L DLBCL	**Arms 4–5** Epcoritamab + CC-99282 (CELMoD) R/R DLBCL, R/R FL	**Arms 6–7** Epcoritamab + ibrutinib ± venetoclax R/R MCL, 1L MCL

Epcoritamab dosing schedule

Step-up dosing (SUD)

- Cycle 1, day 1: SUD1 (0.16 mg)
- Cycle 1, day 8: SUD2 (0.8 mg)
- Cycle 1, days 15, 22: full dose (48 mg)
- Cycles 2–3, days 1, 8, 15, 22: full dose (48 mg)
- Cycles 4–12, day 1: full dose (48 mg)

Lenalidomide dosing schedule

Cycles 1–12: 25 mg once daily on days 1–21

Premedication and CRS prophylaxis

Diphenhydramine, acetaminophen, and corticosteroids were mandatory for CRS prophylaxis with the first 4 epcoritamab doses

- Prednisone 100 mg for 4 d was initially recommended
- Current recommendation is dexamethasone 15 mg for 4 d[c]

Objectives

Dose escalation: safety, tolerability, and identify expansion dose (RP2D)
Dose expansion: safety, tolerability, and antitumor activity

[a]Per WHO 2016 classification.
[b]Relapsed disease is defined as disease that previously responded to therapy but progressed ≥6 mo after completion of therapy. Refractory disease is defined as disease that either progressed during therapy, failed to achieve an objective response to prior therapy, or progressed within 6 mo after completion of therapy (including maintenance therapy).
[c]Additional information can be found in the following presentation: Vose J, et al. ASH 2023, abstract 1729.

Baseline Characteristics

	Total N=35
Age, median (range), y	72 (41–85)
≥75 y, n (%)	13 (37)
Male, n (%)	21 (60)
Ann Arbor stage, n (%)	
I–II	11 (31)
III	7 (20)
IV	17 (49)
Subtype, n (%)	
DLBCL	31 (89)
FL grade 3b	3 (9)
Double-hit lymphoma	0
Triple-hit lymphoma	1 (3)
ECOG PS, n (%)	
0	24 (69)
1	10 (29)
2	1 (3)
R-IPI, n (%)	
0	2 (6)
1–2	10 (29)
3–5	18 (51)
Unknown	2 (6)
Extranodal disease at screening, n (%)	22 (63)

Treatment History and Prior Systemic Therapies

	Total N=35
Number of prior lines of anticancer therapy, median (range)	2 (1–4)
Prior lines of therapy, n (%)	
1	17 (49)
2	11 (31)
3	5 (14)
≥4	2 (6)
Time from last prior anticancer therapy to first epcoritamab dose, median (range), mo	5.5 (0.7–150.6)
Prior systemic therapies, n (%)	
Prior CAR T therapy	8 (23)
Prior stem cell transplant	2 (6)
Refractory disease, n (%)	
Primary refractory	15 (43)
Refractory to ≥2 consecutive lines of anticancer therapy	8 (23)

Treatment Exposure and Disposition

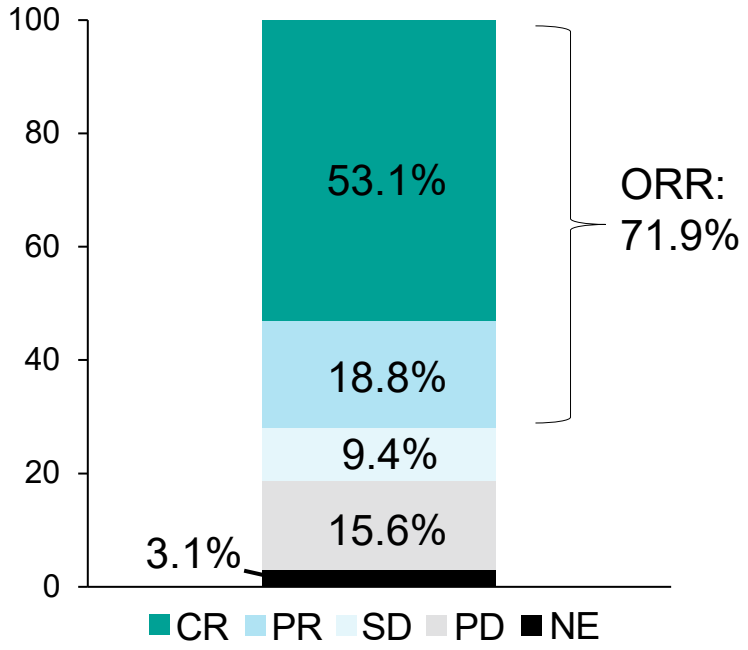
	Total N=35
Study follow-up, median (range), mo	8.2 (1.2–12.7)
Epcoritamab exposure	
Duration, median (range), mo	3.9 (0.03–11.4)
Number of cycles, median (range)	5 (1–12)
Ongoing epcoritamab treatment, n (%)	17 (49)
Completed epcoritamab treatment, n (%)	1 (3)
Discontinued epcoritamab treatment, n (%)	17 (49)
Progressive disease	10 (29)
Patient withdrawal	3 (9)
No longer achieving clinical benefit	2 (6)
AE	2 (6)

	Total N=35
Lenalidomide exposure	
Duration, median (range), mo	4.2 (0.13-11.4)
Number of cycles, median (range)	5 (1–12)
No lenalidomide dose reduction due to AEs, n (%)	24 (69)
Discontinued lenalidomide only due to AE,[a] n (%)	2 (6)

[a]Two additional patients discontinued both epcoritamab and lenalidomide due to AEs.

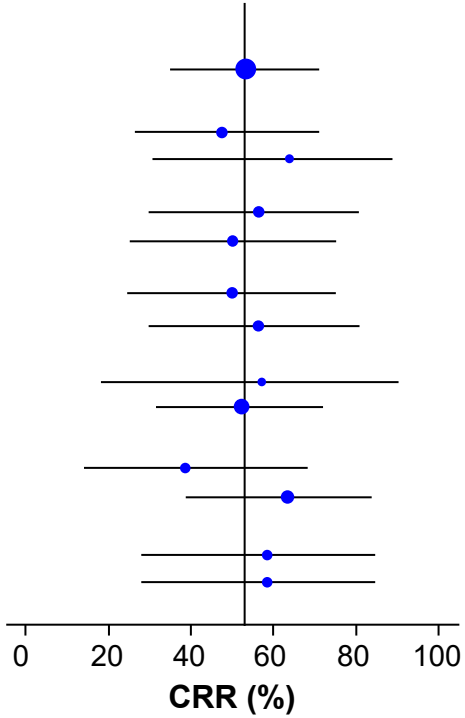
Frequent and Deep Responses Observed

Best overall response[a] (N=32)



Complete response in subgroups (N=32)

Subgroup	N	CRR, % (95% CI)
All patients	32	53.1 (34.7, 70.9)
Age		
<75 y	21	47.6 (25.7, 70.2)
≥75 y	11	63.6 (30.8, 89.1)
Prior lines of therapy		
1	16	56.3 (29.9, 80.2)
≥2	16	50.0 (24.7, 75.3)
Time from end of last therapy to first dose		
<6 mo	16	50.0 (24.7, 75.3)
≥6 mo	16	56.3 (29.9, 80.2)
Prior CAR T therapy		
Yes	7	57.1 (18.4, 90.1)
No	25	52.0 (31.3, 72.2)
Primary refractory status		
Yes	13	38.5 (13.9, 68.4)
No	19	63.2 (38.4, 83.7)
Molecular classification		
GCB	12	58.3 (27.7, 84.8)
ABC/non-GCB	12	58.3 (27.7, 84.8)

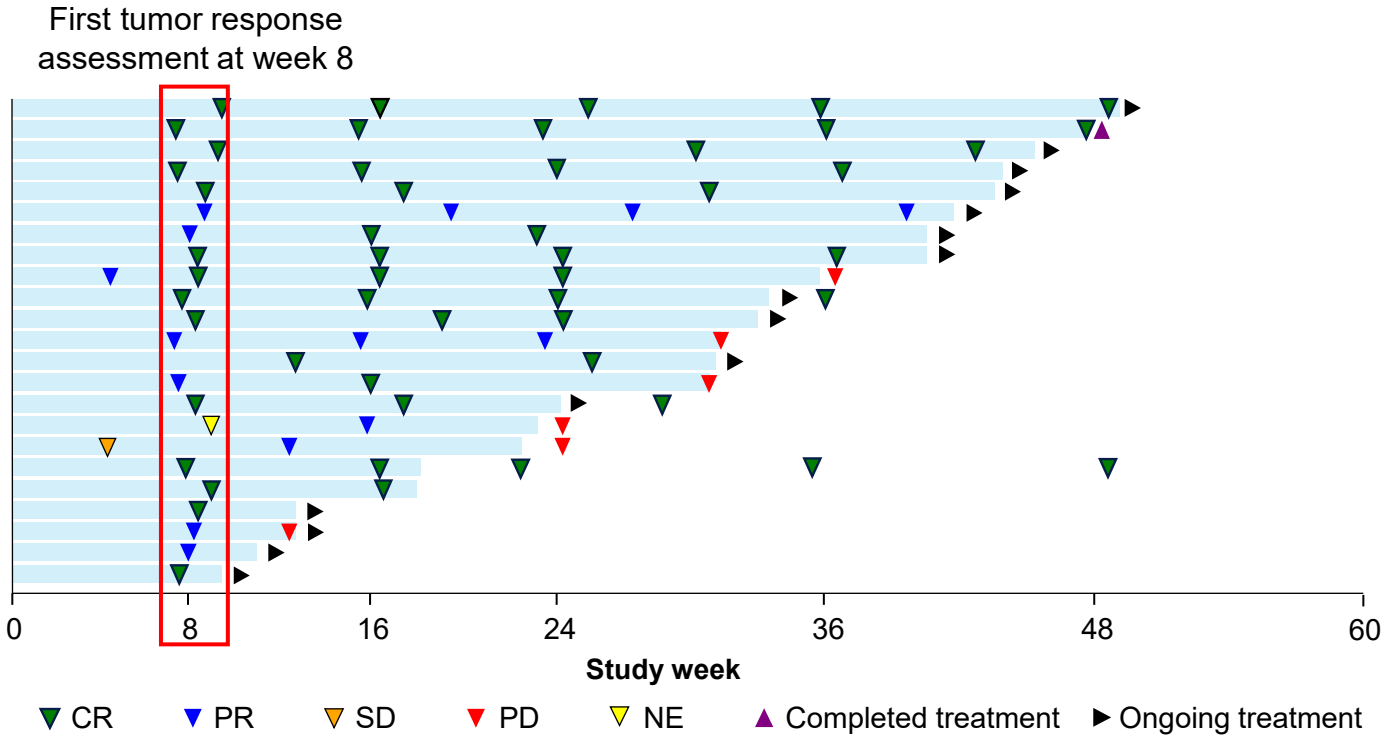


Data cutoff: Oct 6, 2023.

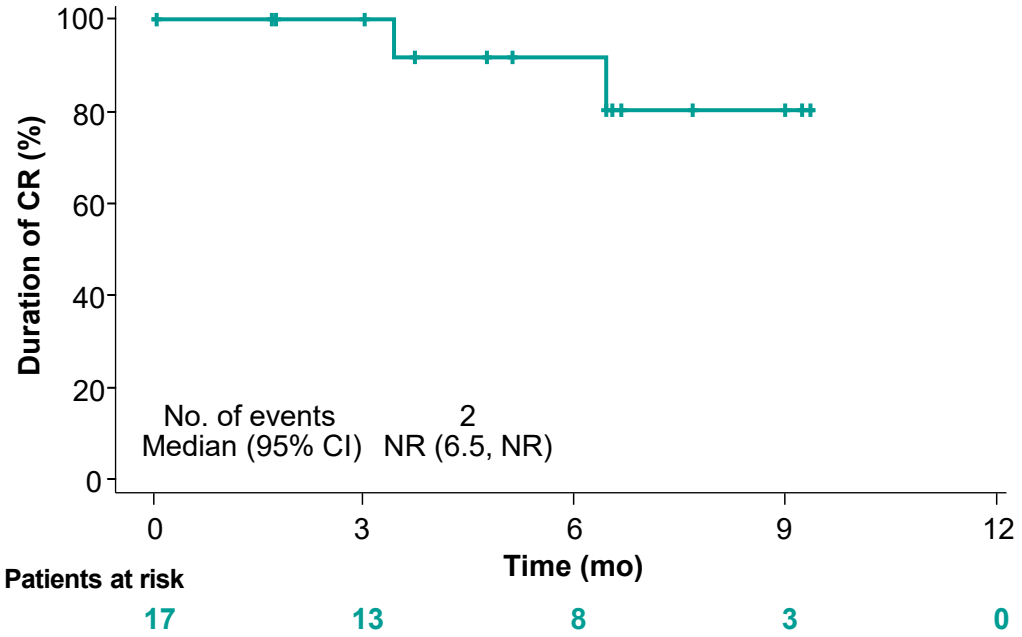
[a]Based on response-evaluable population, defined as patients with measurable disease at baseline and ≥1 postbaseline disease evaluation, or who had died within 60 d of the first dose of study drug without a postbaseline assessment.

Early and Durable Responses Observed[a]

Patients with responses (N=23)[b]



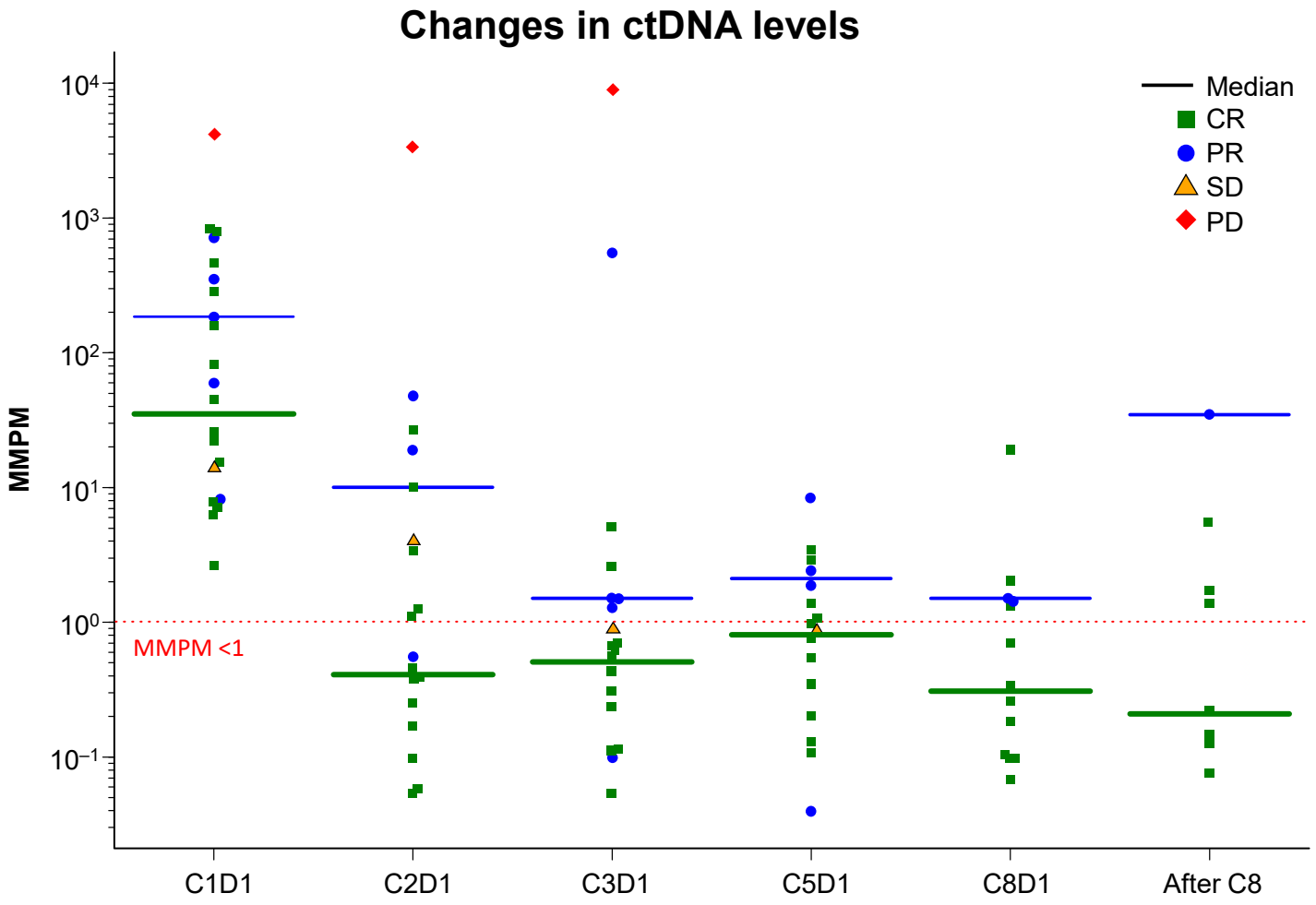
Duration of complete response



- Median time to response was 1.8 mo (range: 1.0–3.6)
- Median time to CR was 1.9 mo (range: 1.6–3.6)
- Median duration of CR was not reached

[a]Based on investigator assessment per Lugano criteria.
[b]Radiographic response assessments occurred Q8W for 24 weeks, Q12W through week 48, then Q24W, and as clinically indicated, until disease progression.

Rapid and Sustained Decline in ctDNA and High MRD Negativity Rates



MRD negativity rates

BoR	MRD negative at C3D1, n (%)	Total
CR	10 (83)	12
PR	1 (20)	5
SD	1 (100)	1
PD	0	1
NE	0	1

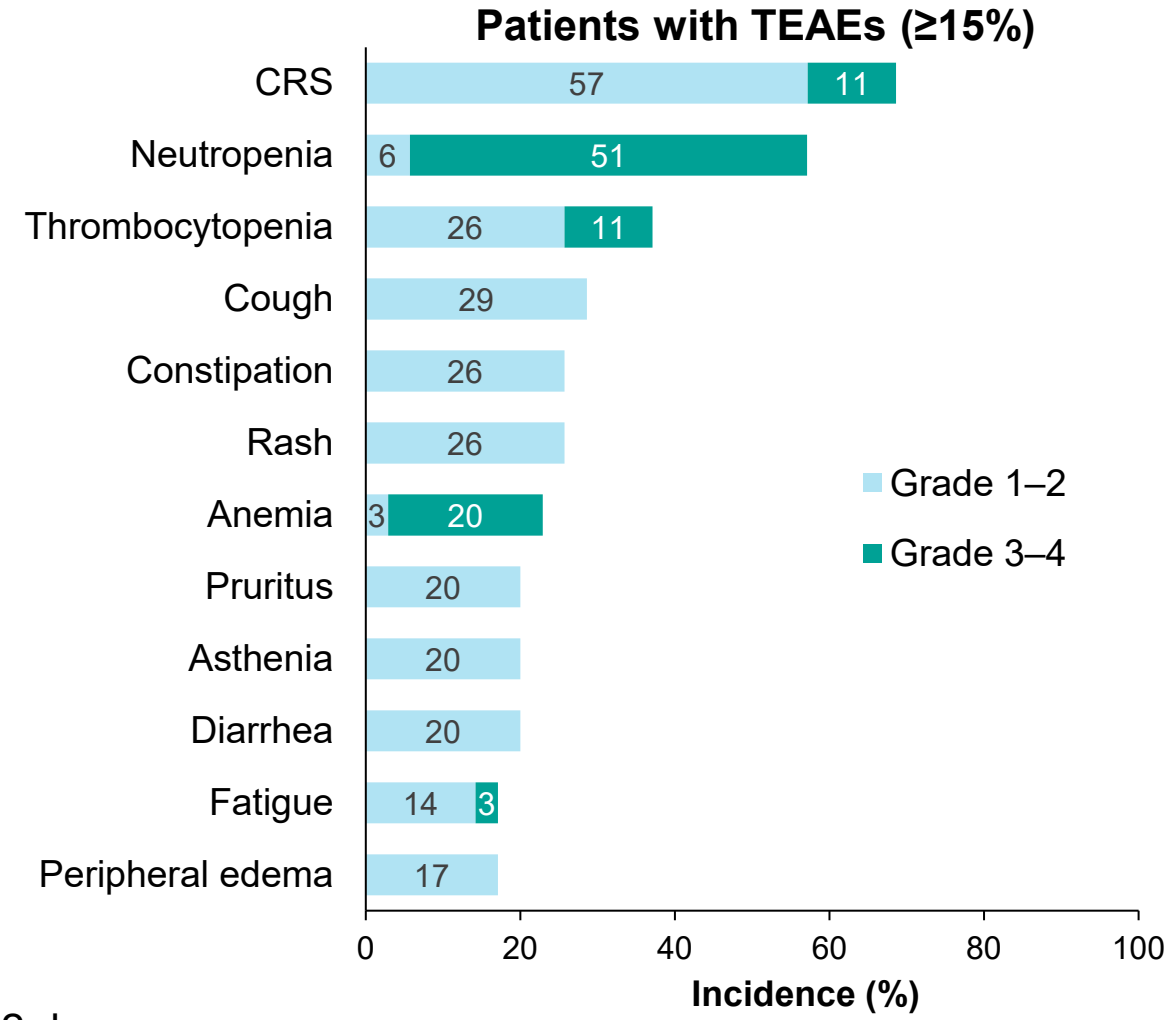
Most patients achieved MRD-negative CR after 2 cycles of treatment

[a]MRD was measured as plasma ctDNA (NGS, Roche Avenio) at protocol-specified time points. ctDNA levels were quantified as mutant molecules per ml (MMPM). MRD negativity was analyzed using a threshold of <1 MMPM.

Safety Was Consistent With Established Profiles

n (%)	Total N=35
Any-grade TEAE	35 (100)
Related to epcoritamab	31 (89)
Grade 3–4 TEAE	30 (86)
Related to epcoritamab	23 (66)
Serious AE	26 (74)
Related to epcoritamab	23 (66)
Epcoritamab delay or interruption due to TEAE	28 (80)
Discontinued epcoritamab due to TEAE	2 (6)
Related to epcoritamab	1 (3)
Grade 5 TEAE[a]	3 (9)
Related to epcoritamab	0

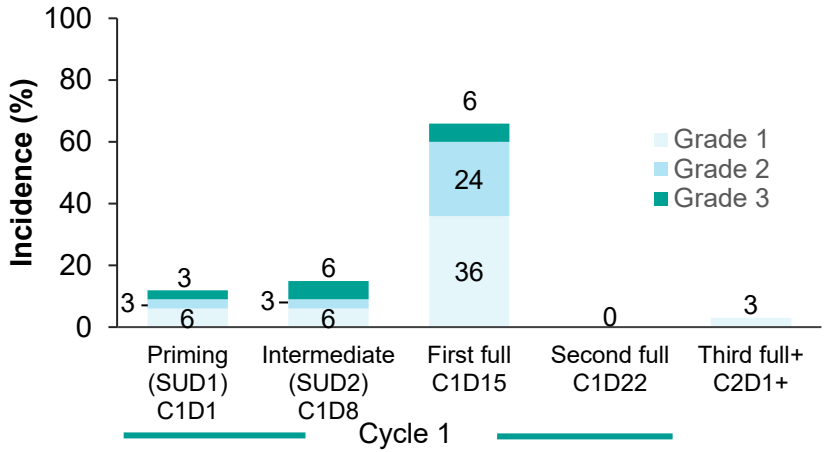
[a]All observed grade 5 TEAEs were due to disease progression.



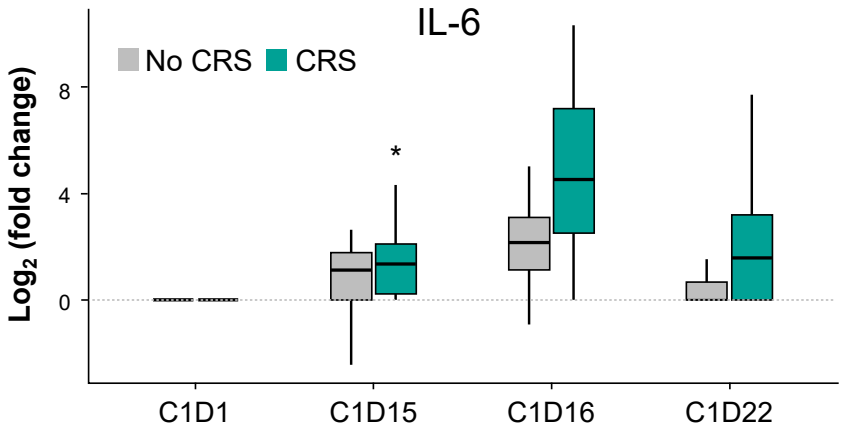
- One patient experienced ICANS (grade 3), which resolved after 2 days
- One patient experienced CTLS (grade 1)
- The most common grade ≥3 TEAE was neutropenia (51%); no neutropenia events led to epcoritamab discontinuation

CRS: Primarily Low Grade and All Resolved

	Total N=35
CRS, n (%)[a]	24 (69)
Grade 1	12 (34)
Grade 2	8 (23)
Grade 3	4 (11)
Time to onset of first CRS event, median (range), d	16 (2–45)
CRS resolution, n (%)[b]	24 (100)
Time to resolution, median (range), d[c]	2 (1–6)
CRS interventions, n (%)	
Treated with tocilizumab	13 (54)
Treated with corticosteroid	10 (42)
Treated with tocilizumab + corticosteroid	7 (29)
Leading to epcoritamab discontinuation, n (%)	0



- 5 of 9 patients (56%) receiving prophylactic dexamethasone had CRS
- Predictable timing of CRS onset; most events occurred after first full dose and were primarily confined to C1



- IL-6 peak occurred at C1D16
- Similar results were seen for IFN-γ and IL-2

[a]Maximum CRS grade is presented for patients with >1 CRS event. [b]Percentages calculated based on patients with ≥1 CRS event. [c]Based on longest recorded CRS duration for patients with >1 CRS event. *Outlier.

Conclusions

- Epcoritamab + lenalidomide showed deep and durable responses in patients with R/R DLBCL, including those with high-risk disease (eg, primary refractory, elderly, prior CAR T therapy)
  - ORR: 72%; CR: 53%
  - Median duration of CR was not reached
- Demonstrated a manageable safety profile with no new safety signals identified
  - Most CRS events were low grade and had predictable timing; all events resolved
- Cytokine peaks occurred immediately after the first full dose
- MRD negativity was achieved early and was sustained throughout treatment
- Data compares favorably to other treatment regimes in this setting
- These data are the first results of a bispecific antibody in combination with lenalidomide for R/R DLBCL and support further exploration of epcoritamab + lenalidomide in these patients

Epcoritamab SC + R-Mini-CHOP Leads to High Complete Metabolic Response Rates in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma Ineligible for Full-Dose R-CHOP: First Disclosure from Arm 8 of the EPCORE NHL-2 Trial

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Presented at the American Society of Hematology Annual Meeting; December 9–12, 2023; San Diego, CA

Background

- R-CHOP is an effective treatment for previously untreated diffuse large B-cell lymphoma (DLBCL), however some patients are not eligible due to advanced age, frailty, or underlying comorbidities[1]
- Low-dose R-CHOP (R-mini-CHOP) is a standard attenuated 1L regimen with suboptimal outcomes;
  - ORR and CR rates around 70% and 40%–60%, 2-year PFS rate 47%[1]
- Novel therapies are needed to improve cure rates
- Epcoritamab SC is the only approved subcutaneously administered CD3xCD20 bispecific antibody[2-4]
  - Offers immediate T-cell engagement and CD20 inhibition with no need for debulking
  - Showed high ORRs and CR rates and manageable safety in combination with R-CHOP in 1L DLBCL[10]
  - Is available off-the-shelf

[a]Approved in Europe and the UK for the treatment of adults with R/R DLBCL after ≥2 lines of systemic therapy. [b]Approved in Japan for the treatment of adults with the following R/R large B-cell lymphoma: DLBCL, HGBCL, primary mediastinal large B-cell lymphoma, and follicular lymphoma (FL) grade 3B after ≥2 lines of systemic therapy.

1. Peyrade F, et al. *Lancet Oncol*. 2011;12:460-8. **2.** Engelberts PJ, et al. *eBioMedicine*. 2020;52:102625. **3.** van der Horst HJ, et al. *Blood Cancer J.* 2021;11:38. **4.** Thieblemont C, et al. *J Clin Oncol*. 2023;41:2238-47. **5.** EPKINLY [prescribing information]. Plainsboro, NJ: Genmab US, Inc.; 2023. **6.** Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; 2023. **7.** Tepkinly [summary of product characteristics]. Maidenhead, UK: AbbVie Ltd; 2023. **8.** EPKINLY [prescribing information]. Tokyo, Japan: Genmab K.K.; 2023. **9.** EPKINLY [product monograph]. St-Laurent, Canada: AbbVie; 2023. **10.** Falchi L, et al. ASCO 2023. Abstract 7519.

Study Design: EPCORE™ NHL-2 Arm 8

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R-mini-CHOP in adults with 1L DLBCL[a]

Key inclusion criteria:

- Newly diagnosed CD20+ DLBCL[b]
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - Double-hit or triple-hit DLBCL[c]
  - FL grade 3B
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function
- Ineligible for full-dose R-CHOP[d]

Data cutoff: September 1, 2023
Median follow-up: 9.4 mo
ClinicalTrials.gov: NCT04663347

Fixed treatment regimen: Concomitant epcoritamab SC 48 mg + R-mini-CHOP

	Agent	C1–C2	C3–C6	C7–C8
	Epcoritamab SC 48 mg	QW	Q3W	Q4W
R-mini-CHOP	Rituximab IV 375 mg/m^2	Q3W		Q4W
R-mini-CHOP	Cyclophosphamide IV 400 mg/m^2			
R-mini-CHOP	Doxorubicin IV 25 mg/m^2			
R-mini-CHOP	Vincristine IV 1 mg			
R-mini-CHOP	Prednisone IV or oral	100 mg/d, D1–5 of each cycle	40 mg/m^2/d, D1–5 of each cycle	

- **Primary objective:** Antitumor activity[e]

[a]Patients received epcoritamab SC with 2 step-up doses (SUD) before the first full dose and corticosteroid prophylaxis to mitigate CRS. R-mini-CHOP was given in 21-d cycles. Subsequent cycles of epcoritamab were 28 d. [b]De novo or histologically transformed from FL or nodal marginal zone lymphoma. [c]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [d]Due to age ≥75 y or age ≥65 y with comorbidities (reduced left ventricular ejection fraction, history of myocardial infarction [>6 mo prior to enrollment], exertional chest pain, arrhythmia [grade ≤2], hypertension requiring treatment, or diabetes). [e]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression.

Patients Were High Risk and Challenging to Treat

	48 mg, N=28
Median age, y (range)	81 (74–90)
Male, n (%)	14 (50)
ECOG PS, n (%)[a]	
0	10 (36)
1	12 (43)
2	5 (18)
Ann Arbor stage, n (%)[b]	
II	3 (11)
III	4 (14)
IV	15 (54)
IPI score, n (%)[c]	
0–2	9 (32)
3	9 (32)
4–5	8 (29)

[a]One patient had an ECOG PS of 3, which was allowed per protocol if score was reduced to 2 prior to first dose. [b]Ann Arbor stage was I for 6 patients. [c]IPI score was unknown for 2 patients.

	48 mg, N=28
DLBCL subtype, n (%)[a]	
De novo	24 (86)
Transformed	3 (11)
MYC/BCL2/BCL6 rearrangements, n (%)[b]	2 (7)
Bulky disease, n (%)	
>6 cm	12 (43)
>10 cm	5 (18)
LDH, n (%)[c]	
High	16 (57)
Normal	10 (36)
Median time from initial diagnosis to first dose, d (range)	37.5 (15–74)

[a]DLBCL subtype was missing for 1 patient. [b]Patients can be classified as having HGBCL (double-hit, n=1; triple-hit, n=1). [c]LDH was missing for 2 patients.

Most Patients Completed Treatment as Planned

	48 mg, N=28
Median follow-up, mo (range)[a]	9.4 (2.5+ to 16.8)
Completed treatment, n (%)	22 (79)
Ongoing treatment, n (%)	2 (7)
Discontinued treatment, n (%)	4 (14)
AE[b]	3 (11)
Failure to meet continuation criteria	1 (4)
Median epcoritamab cycles initiated (range)	8 (1–8)
Median duration of treatment, mo (range)	5.3 (0.2–7.6)

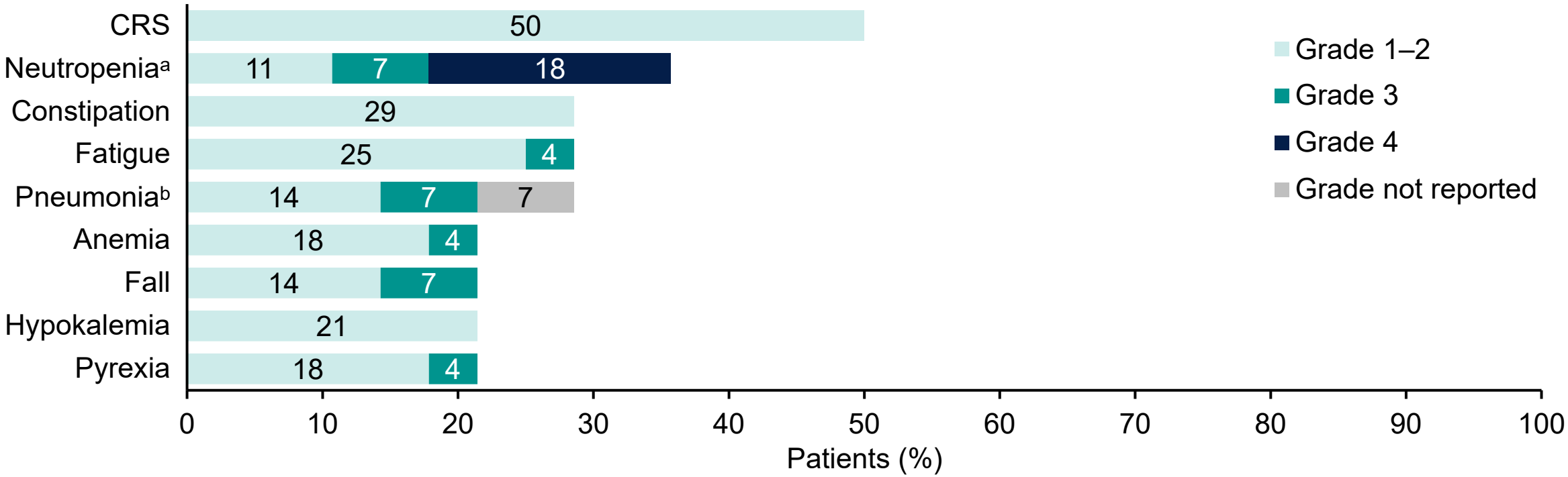
[a]Median is Kaplan–Meier estimate. [b]AEs that led to treatment discontinuation were confusional state and cytomegalovirus infection reactivation, both in the same patient (n=1); CRS (n=1); and rhinitis (n=1).

Epcoritamab Did Not Affect R-Mini-CHOP Dose Intensity

Relative Dose Intensity, %	Rituximab	Cyclophosphamide	Doxorubicin	Vincristine
Mean (SD)	93 (9)	93 (8)	94 (8)	93 (8)
Median	95	94	95	95

R-mini-CHOP was administered in cycles 1–6.

Most TEAEs Were Low Grade



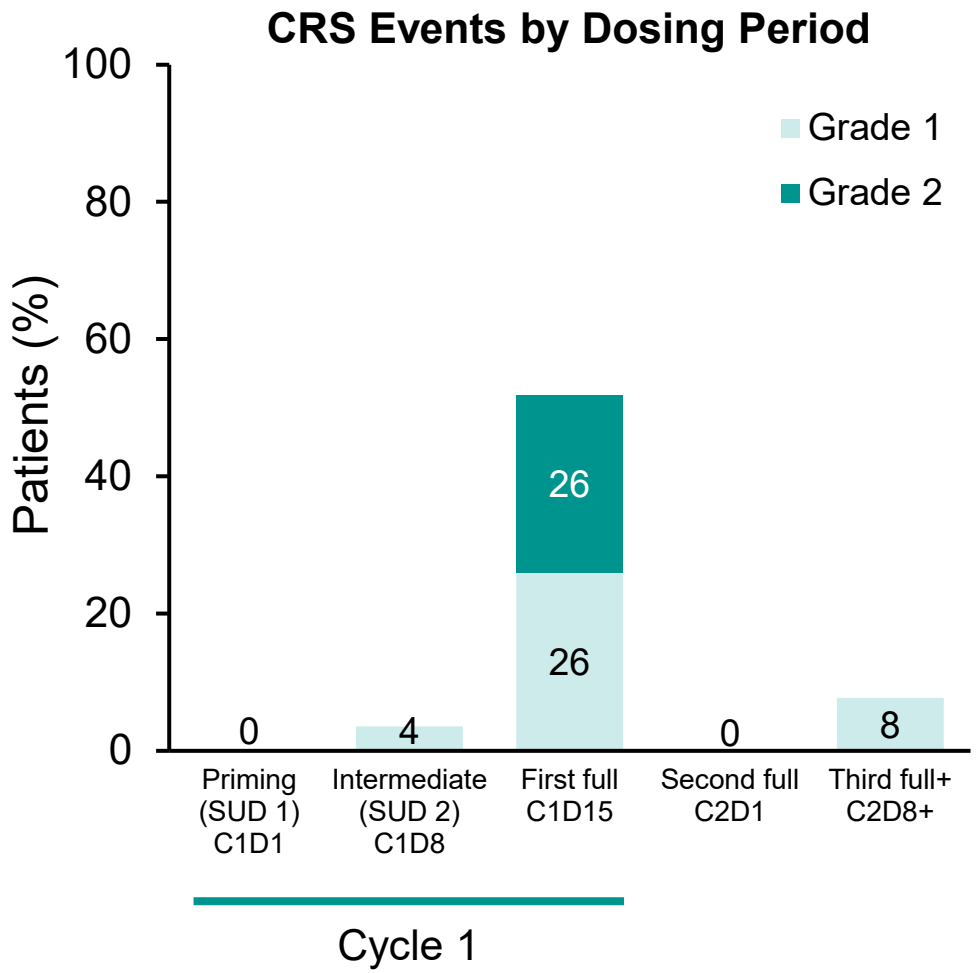
- No ICANS or clinical tumor lysis syndrome
- 2 patients had febrile neutropenia (grade 3 and grade 4)
- 1 patient had Gr 5 TEAEs (confusional state [not related to treatment] and cytomegalovirus infection reactivation [considered related to treatment] in a patient aged 90 years also diagnosed with acute cerebrovascular accident)

Data cutoff: September 1, 2023. [a]Combined term includes neutropenia and neutrophil count decreased. Use of growth factors was allowed, in general, and required for recurring grade ≥3 neutropenia. [b]Grade was not reported for 2 patients with pneumonia.

CRS Was Low Grade, Predictable, and Resolved

	48 mg N=28
CRS, n (%)[a]	14 (50)
Grade 1	7 (25)
Grade 2	7 (25)
Grade 3	0
CRS resolution, n/n (%)	**14/14 (100)**
Median time to onset from first full dose, d (range)	2 (1–3)
Median time to resolution, d (range)[b]	2 (1–7)
Treated with tocilizumab, n (%)	7 (25)
Leading to epcoritamab discontinuation, n (%)	1 (4)[c]

[a]Graded by Lee et al 2019 criteria.[1] [b]Median is based on longest CRS duration in patients with CRS.
[c]Patient had grade 2 CRS.



1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

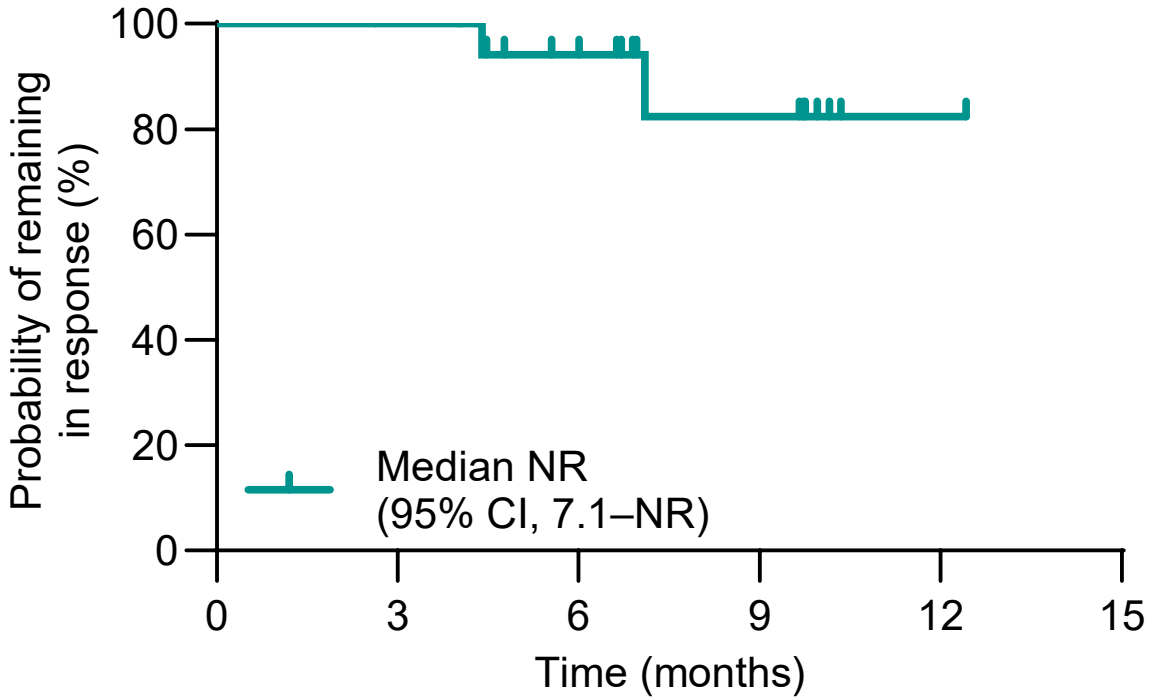
High Rates of Overall and Complete Response

Best Response[a]	Efficacy Evaluable n=23	Patients Who Completed 6C R-Mini-CHOP With Concomitant Epcoritamab n=21
Overall response	100%	100%
CMR	87%	86%
PMR	13%	14%
Progressive disease	0	0

Data cutoff: September 1, 2023. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first trial treatment.

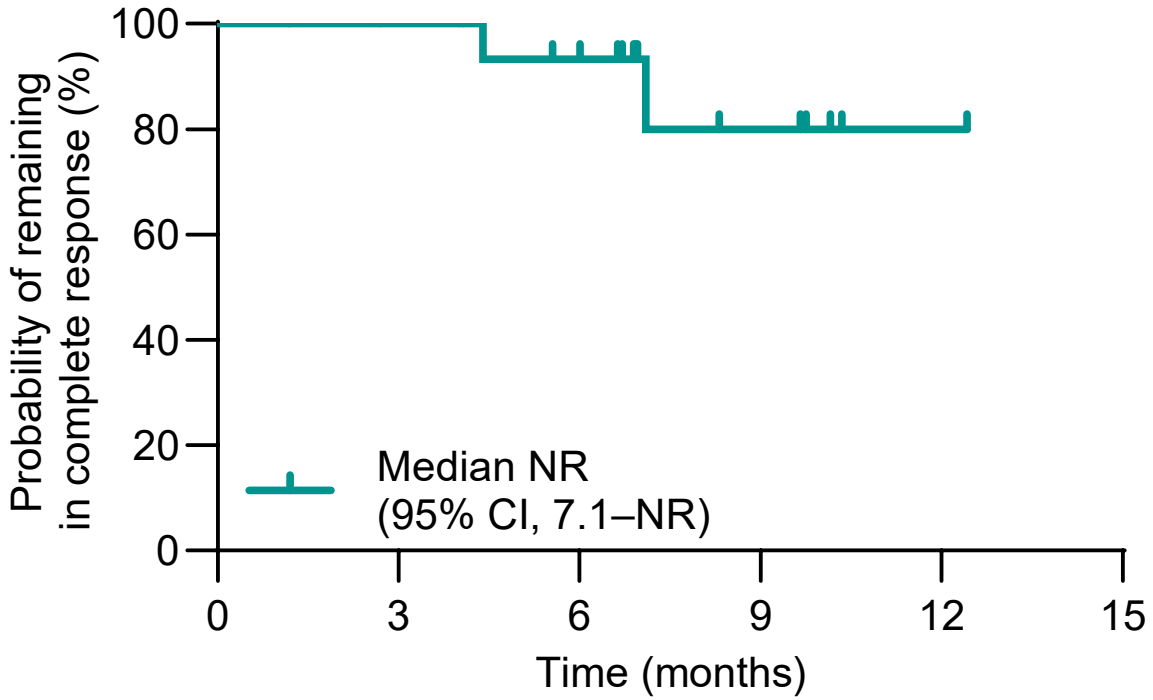
- Responses Observed Early:
  - Median time to response was 1.4 months (range, 1.1–2.7)
  - Median time to complete response was 1.5 months (range, 1.2–5.1)

Durable Responses Observed



Number at risk

0	3	6	9	12	15
23	22	13	7	1	0

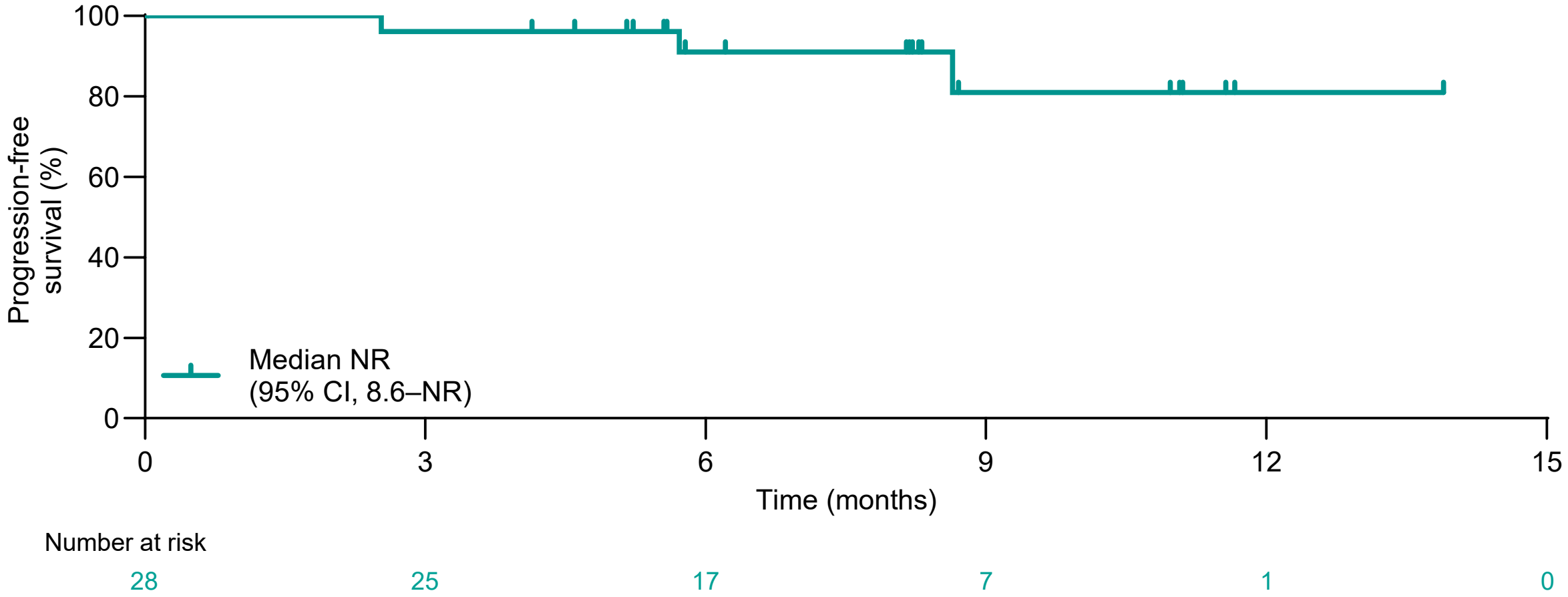


Number at risk

0	3	6	9	12	15
20	17	13	5	1	0

- Responses were durable; an estimated 80% of complete responders remained in complete response at 12 months

Favorable long-term outcomes: Median PFS Not Reached



Conclusions

- Epcoritamab is the first CD3XCD20 bsAb to present data in combination with R-mini-CHOP in 1L DLBCL
- Offers immediate T-cell engagement and CD20 inhibition, with no need for debulking
- Treatment was given for a fixed duration for 8 cycles
- Frequent, deep and durable responses observed
  - 100% ORR with 87% CR compares favorably to R-mini-CHOP alone
  - mDOR, mDOCR and mPFS all NR
- Safety as expected; CRS low grade, predictable and manageable
- These results continue to underscore the combinability of epcoritamab and may inform subsequent clinical development

Epcoritamab SC + GemOx Leads to High Complete Metabolic Response Rates in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma Ineligible for Autologous Stem Cell Transplant: Updated Results from EPCORE NHL-2

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Background

- Patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who fail or are ineligible for autologous stem cell transplant (ASCT) have poor outcomes with standard chemotherapy; novel, effective therapeutic options are needed[1]
- The prognosis for patients whose disease is refractory to standard salvage chemotherapy or who relapse ≤12 mo after ASCT is extremely poor, with an overall response rate (ORR) of 26%, a complete response rate of 7%, and a median overall survival of approximately 6 mo[2]
- In another retrospective analysis, patients treated with rituximab and gemcitabine + oxaliplatin (R-GemOx) achieved a 33% CR rate, with a median PFS of 5 mo and median OS of 10 mo[3]

[a]Approved in Europe and the UK for the treatment of adults with R/R DLBCL after ≥2 lines of systemic therapy. [b]Approved in Japan for the treatment of adults with the following R/R large B-cell lymphoma: DLBCL, HGBCL, primary mediastinal large B-cell lymphoma, and follicular lymphoma (FL) grade 3B after ≥2 lines of systemic therapy. **1.** Sehn LH, Salles G. *N Engl J Med*. 2021;384(9):842-58. **2.** Crump M, et al. *Blood*. 2017;130:1800-08. **3.** Cazelles C, et al. *Leuk Lymphoma*. 2021;62(9):2161-68

Study Design: EPCORE™ NHL-2 Arm 5

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab SC + GemOx in adults with R/R DLBCL ineligible for ASCT

Key inclusion criteria:

- R/R CD20+ DLBCL[a]
  - DLBCL, NOS
  - "Double-" or "triple-hit" DLBCL
  - FL grade 3B
  - T-cell/ histiocyte-rich DLBCL
- Eligible for GemOx
- Ineligible for ASCT or prior ASCT failure
- ECOG PS 0–2
- FDG-avid disease by PET
- Adequate organ function

Treatment regimen: Concomitant epcoritamab SC 48 mg + GemOx

Agent	C1	C2	C3	C4	C5–9	C10+ until progression[c]
Epcoritamab SC 48 mg[b]	QW	QW	QW	Q2W	Q2W	Q4W
GemOx: Gemcitabine 1000 mg/m^2 IV	Q2W					
GemOx: Oxaliplatin 100 mg/m^2 IV						

Data cutoff: September 1, 2023
Median follow-up: 11.4 mo

- **Primary objective:** Antitumor activity
- **Key secondary endpoints:** DOR, DOCR, TTR, PFS, OS, TEAEs

Analysis includes patients with ≥9 mo of study follow-up. Cycles are 28 d. [a]De novo or histologically transformed from FL or nodal marginal zone lymphoma based on World Health Organization 2016 classification. [b]Step-up dose (SUD) 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. [c]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. ClinicalTrials.gov: NCT04663347. EudraCT: 2020-000845-15.

Baseline Characteristics: High risk, refractory population

Demographics	N=65
Median age (range), y	71 (20–87)
≥75 y, n (%)	19 (29)
Male, n (%)	38 (58)
ECOG PS, n (%)	
0	16 (25)
1	39 (60)
2	10 (15)

Disease Characteristics	N=65
DLBCL type,[a] n (%)	
De novo	49 (75)
Transformed	14 (22)
Ann Arbor stage, n (%)	
I	7 (11)
II	12 (18)
III	12 (18)
IV	34 (52)
Median time from initial diagnosis to first dose (range), mo	14 (0.6–178)

Prior Treatments	N=65
Median time from end of last therapy to first dose (range), mo	4 (0.6–85)
Median prior lines of therapy (range)	2 (1–6)
Prior lines of therapy, n (%)	
1	23 (35)
2	15 (23)
≥3	27 (42)
Primary refractory[b] disease, n (%)	35 (54)
Refractory[b] to last systemic therapy, n (%)	49 (75)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	30 (46)
Prior ASCT, n (%)	7 (11)
Relapsed ≤12 mo after ASCT, n/n (%)	5/7 (71)
Prior CAR T therapy, n (%)	19 (29)
Refractory to CAR T therapy, n/n (%)	17/19 (89)

[a]De novo versus transformed status of 2 patients was missing. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 mo of completion of therapy.

Exposure and Follow-up

	N=65
Median follow-up (range), mo	11.4 (1.0+ to 30.6)
Mean number of epcoritamab treatment cycles initiated, n	9
Mean doses administered, n	21
Ongoing treatment, n (%)	28 (43)
Discontinued treatment, n (%)	37 (57)
PD	19 (29)
AE[a]	13 (20)
Death	4 (6)
Maximum clinical benefit[b]	1 (2)

[a]The most frequent AEs leading to discontinuation were COVID-19 (n=3) and pneumonia (n=3). AEs related to epcoritamab that led to discontinuation were pneumonia, multiple organ dysfunction syndrome, small intestinal perforation, and ICANS (in 1 patient each). [b]Patient achieved partial response and subsequently proceeded to allogeneic transplant.

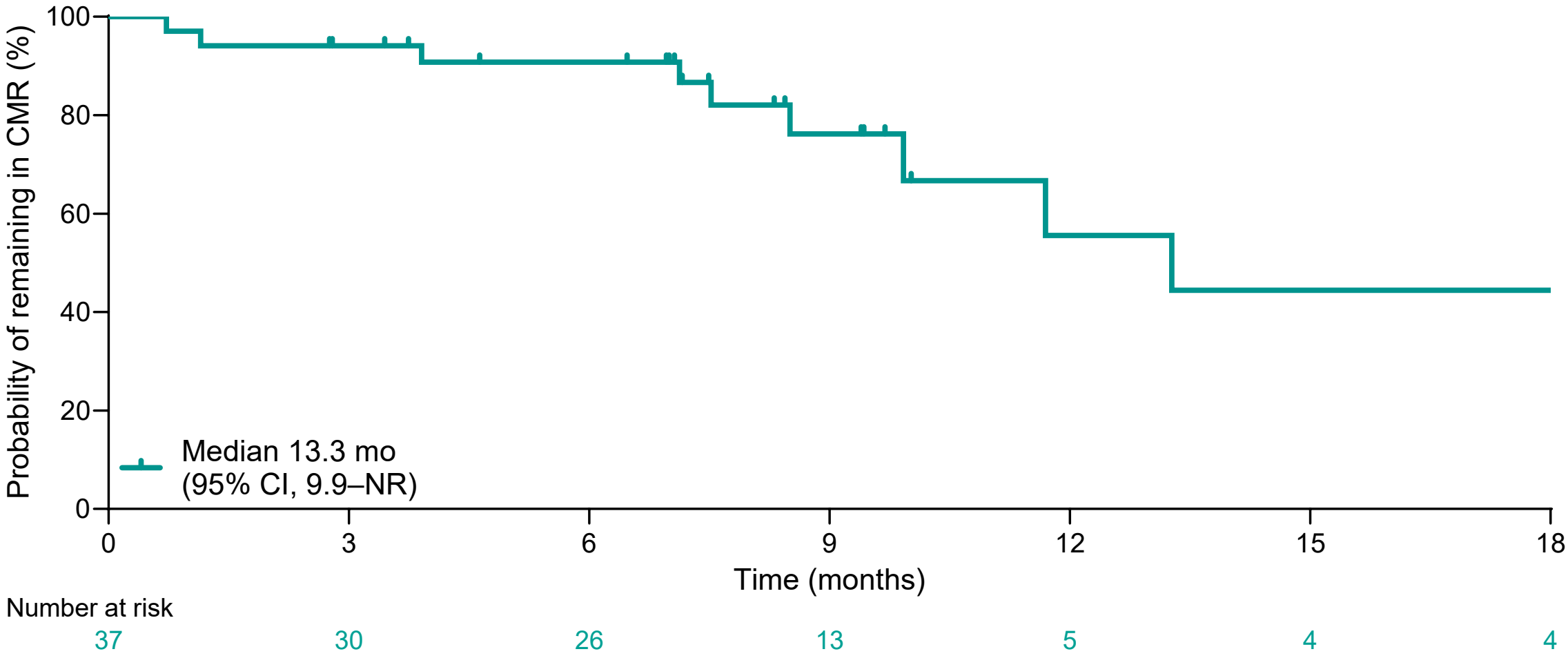
Responses Occurred Early and Response Rates Were High

Best Overall Response, n (%)	N=65[a]
Overall response rate	52 (80)
Complete metabolic response	37 (57)
Partial metabolic response	15 (23)
Stable disease	4 (6)
Progressive disease	4 (6)

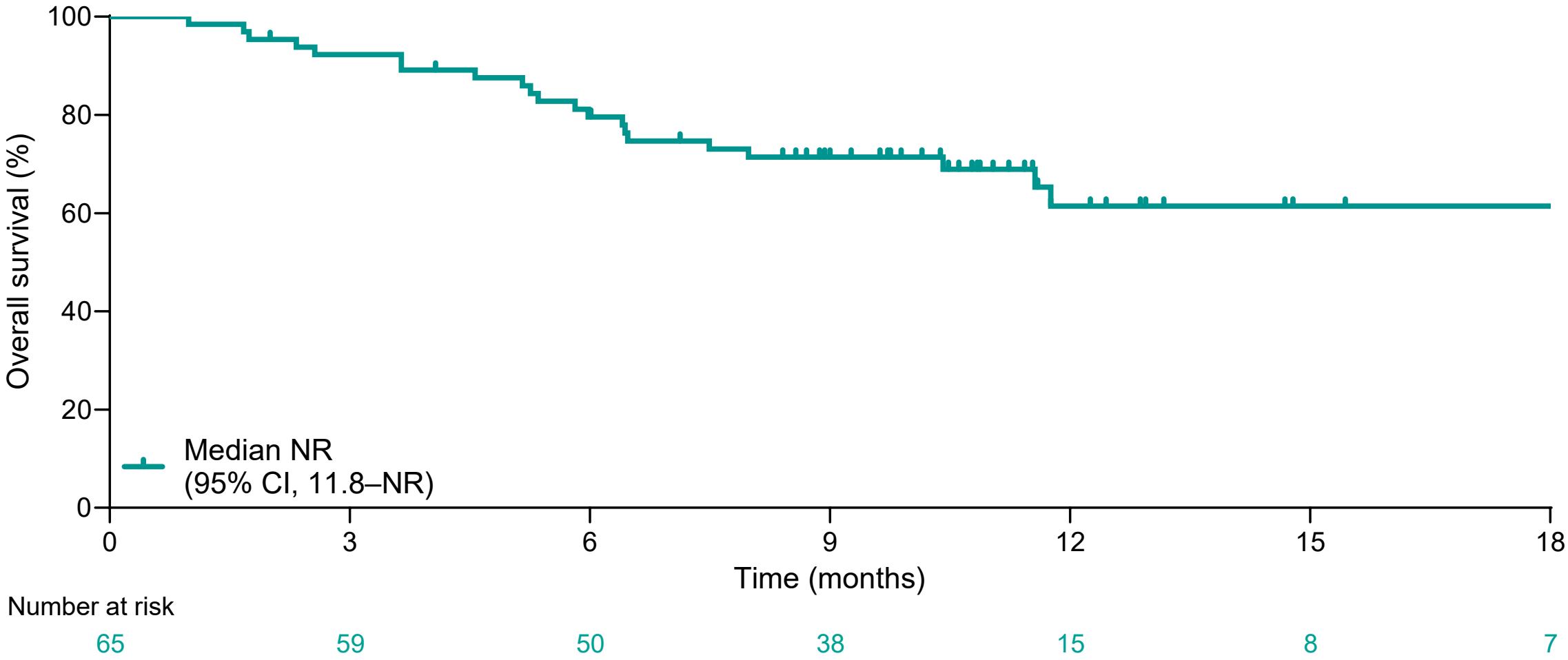
[a]5 patients were not evaluable for response.

- Median time to response was 1.5 mo (range, 0.9–3.0)
- Median time to complete metabolic response was 1.8 mo (range, 1.3–10.7)

Durable Complete Metabolic Responses



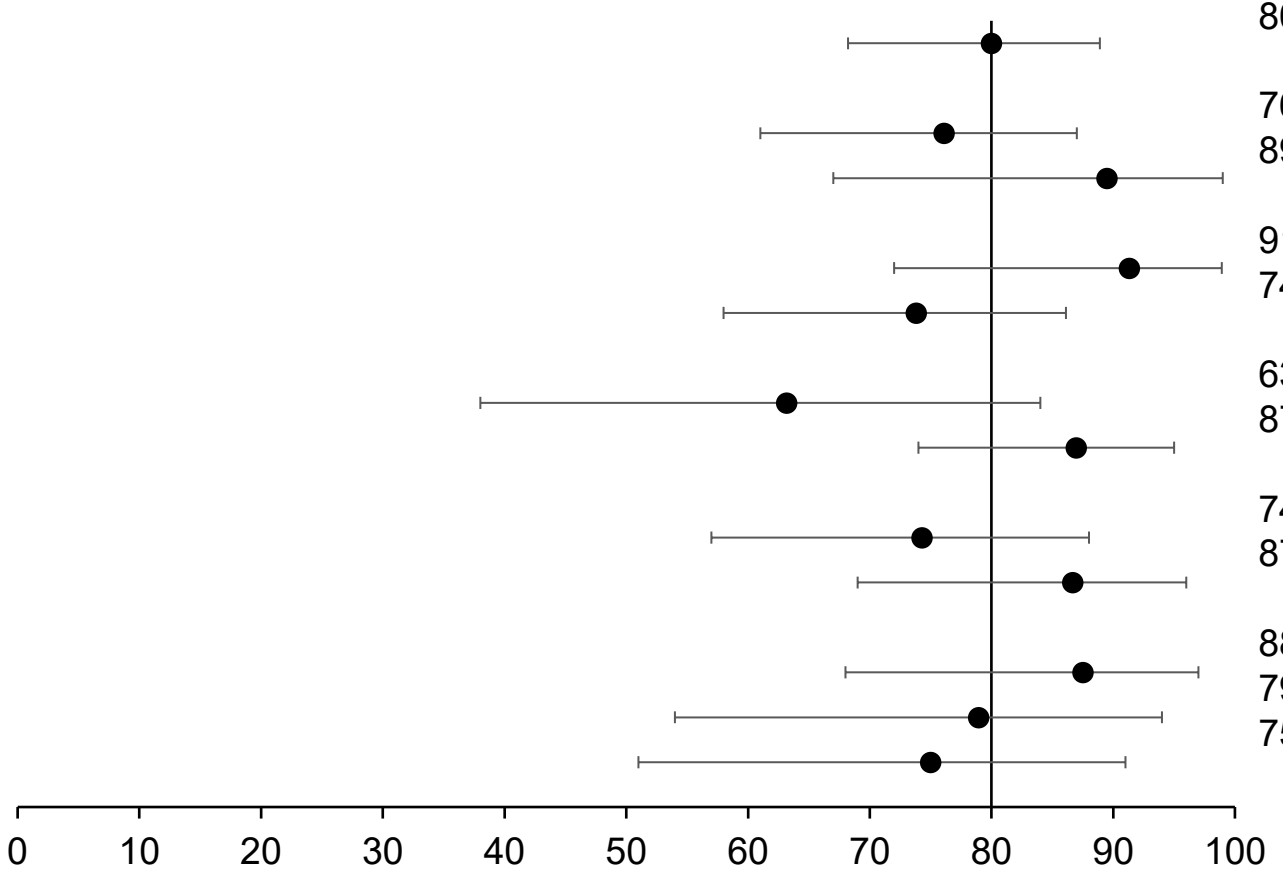
Median Overall Survival Not Reached



Deaths due to COVID-19 have been censored.

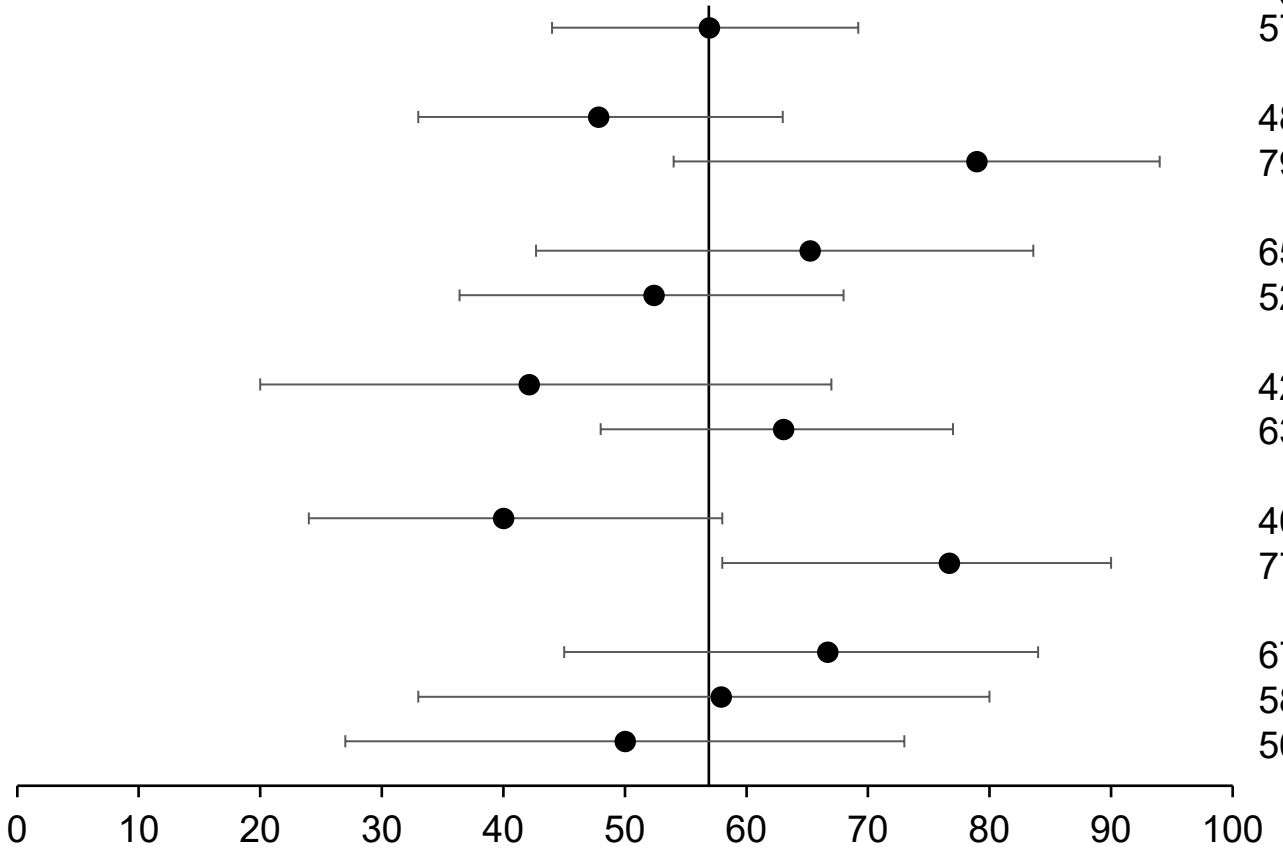
ORR Consistent Across Subgroups, Including in High-Risk

Subgroups	Number of patients	ORR, % (95% CI)
All patients	65	80 (68–89)
Age		
<75 y	46	76 (61–87)
≥75 y	19	89 (67–99)
Number of prior lines of treatment		
1	23	91 (72–99)
>1	42	74 (58–86)
Prior CAR T		
Yes	19	63 (38–84)
No	46	87 (74–95)
Primary refractory		
Yes	35	74 (57–88)
No	30	87 (69–96)
IPI		
0–2	24	88 (68–97)
3	19	79 (54–94)
4–5	20	75 (51–91)

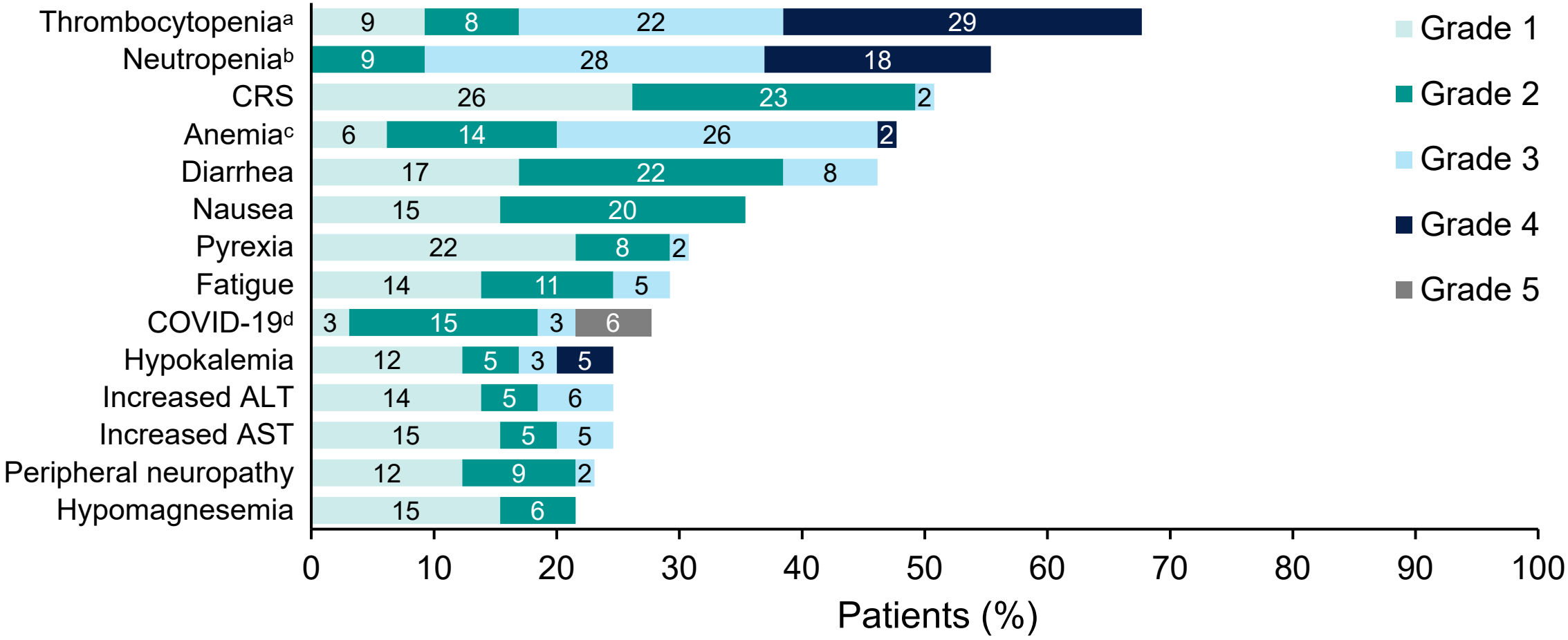


CMR rates Consistent Across Subgroups, Including High-Risk

Subgroups	Number of patients	CMR rate, % (95% CI)
All patients	65	57 (44–69)
Age		
<75 y	46	48 (33–63)
≥75 y	19	79 (54–94)
Number of prior lines of treatment		
1	23	65 (43–84)
>1	42	52 (36–68)
Prior CAR T		
Yes	19	42 (20–67)
No	46	63 (48–77)
Primary refractory		
Yes	35	40 (24–58)
No	30	77 (58–90)
IPI		
0–2	24	67 (45–84)
3	19	58 (33–80)
4–5	20	50 (27–73)



Common (>20%) Treatment-Emergent Adverse Events



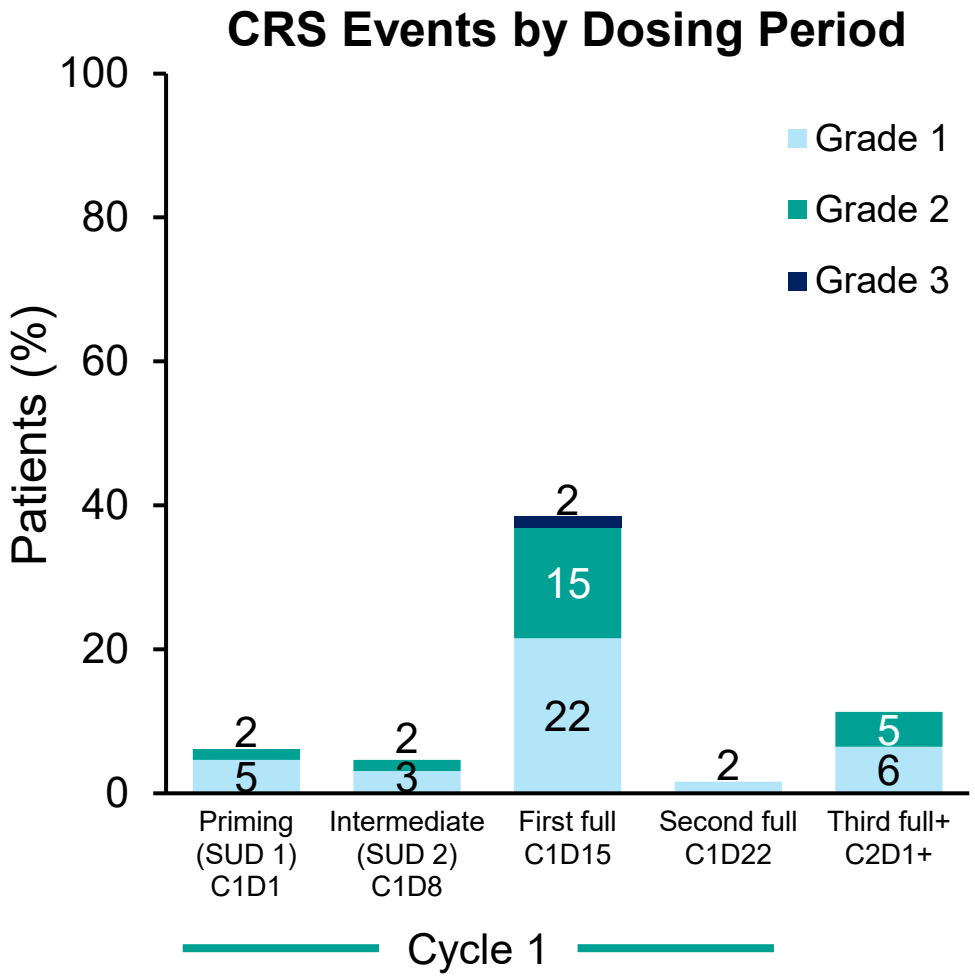
[a]Combined term includes thrombocytopenia and decreased platelet count. [b]Combined term includes neutropenia and decreased neutrophil count. [c]Combined term includes anemia and decreased hemoglobin. [d]Combined term includes COVID-19 and COVID-19 pneumonia.

Safety consistent with previous reports

- 4 patients experienced febrile neutropenia
- ICANS was reported in 2 patients (grade 1 and 3); both events resolved and 1 patient discontinued treatment due to ICANS
- There were no reports of clinical tumor lysis syndrome
- The trial, conducted during the global COVID-19 pandemic, was impacted by prevailing COVID-19 trends, including the highly infectious Omicron variant
- 11 patients had grade 5 TEAEs; 4 events were related to COVID-19
  - The contribution of epcoritamab and GemOx could not be ruled out by the investigator in 2 cases (small intestinal perforation and multiple organ dysfunction syndrome; both patients had multiple confounding factors)

CRS Events Were Primarily Low Grade and Timing Was Predictable

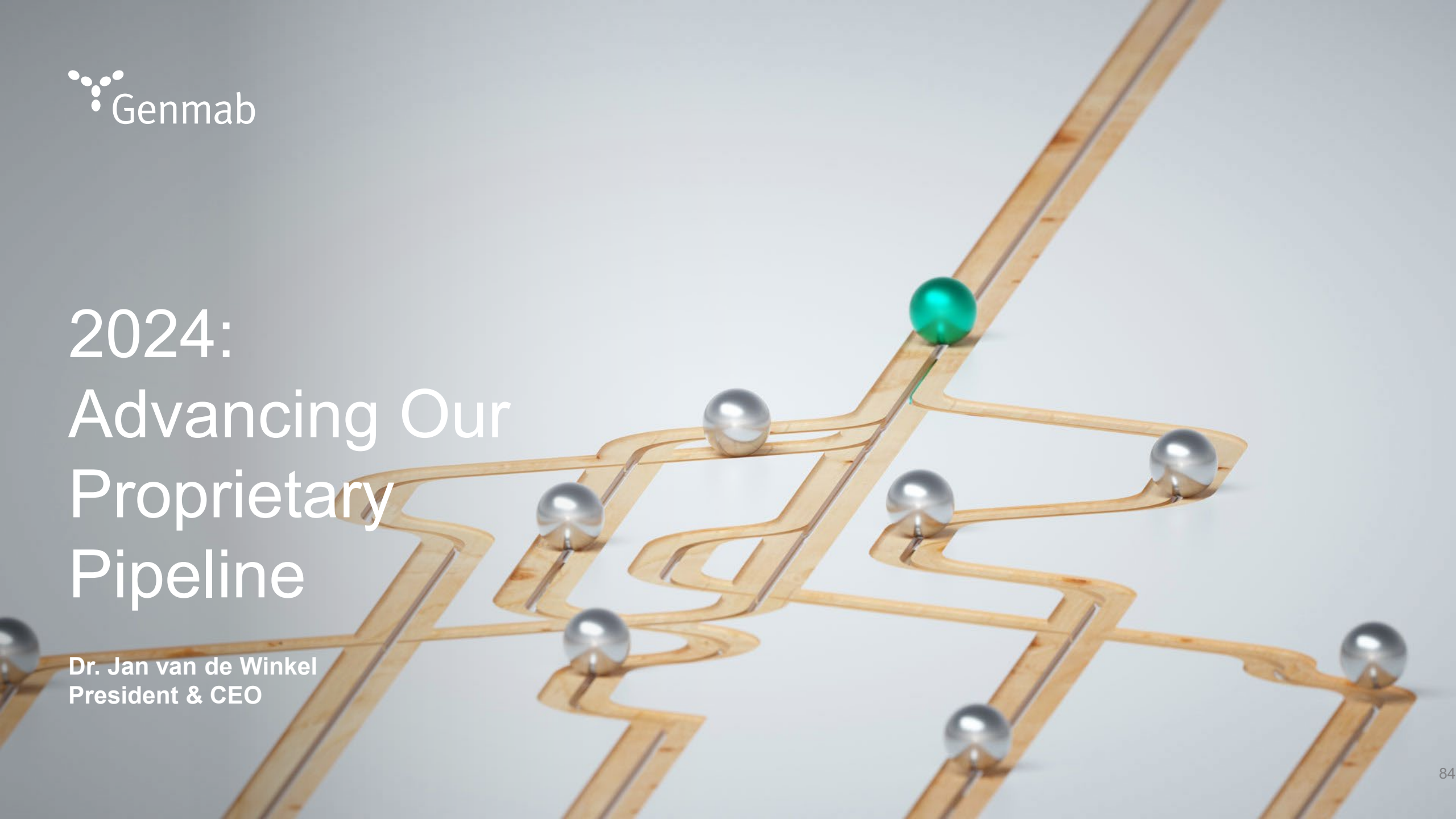
	N=65
CRS, n (%)[a]	33 (51)
Grade 1	17 (26)
Grade 2	15 (23)
Grade 3	1 (2)
Median time to onset after first full dose, d (range)	2 (1–5)
Tocilizumab use, n (%)	12 (18)
Leading to epcoritamab discontinuation, n (%)	0
CRS resolution, n/n (%)	33/33 (100)
Median time to resolution, d (range)[b]	2 (1–13)



SUD 1, first step-up dose; SUD 2, second step-up dose. [a]Graded by Lee et al 2019 criteria.[1] [b]Median is based on longest CRS duration in patients with CRS. **1.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

Conclusions

- This longer follow up reaffirms the previous reported data for Epcoritamab in combination with GemOx in this difficult-to-treat R/R DLBCL population
- Frequent, deep and durable responses observed
  - 80% ORR with 57% CR compares favorably to R-GemOx
  - mDOCR 13.3 mo, mOS NR
- High ORR and CMR rates were observed across subgroups and were notably higher in second vs later lines as well as in CAR T–naive patients
- Safety remained consistent with those of the individual drugs and previous reports
- These results continue to underscore the combinability of epcoritamab for the treatment of R/R DLBCL and may inform clinical practice



2024: Advancing Our Proprietary Pipeline

Dr. Jan van de Winkel
President & CEO

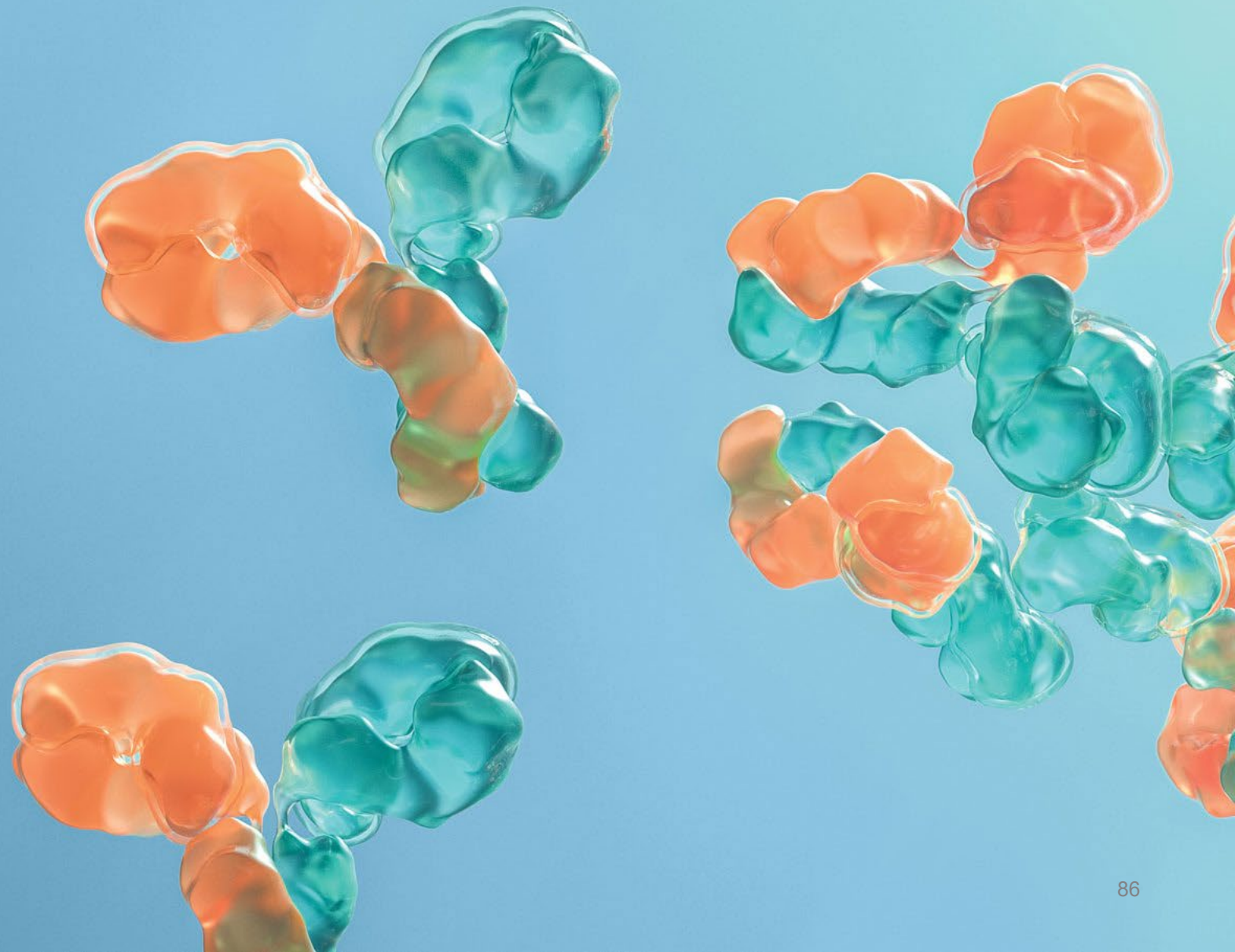
Anticipated 2024 Pipeline Events

Program	Indication	Event	Anticipated Timing
Epcoritamab	3L+ R/R FL	EMA decision	2H 2024
Epcoritamab	3L+ R/R FL	U.S. FDA decision	2H 2024
Epcoritamab	3L+ R/R FL	JP filing	1H2024
Epcoritamab + R^2	1L FL	Phase 3 start	2024
Epcoritamab + Len	2L DLBCL ASCT ineligible	Phase 3 start	2024
Epcoritamab + Salvage	2L DLBCL ASCT eligible	Phase 3 start	2024
Tivdak	2L R/M CC	EU/JP filing	1H 2024
Tivdak	2L+ HNSCC	Engagement with health authorities on next steps	2024
Acasunlimab (GEN1046/BNT311) + CPI	2L+ NSCLC	Phase 2 data	1H 2024
Acasunlimab (GEN1046/BNT311) + CPI	2L+ NSCLC	Phase 3 planning	2024
DuoBody-CD40x4-1BB (GEN1042/BNT312) + SoC	1L solid tumors	Phase 2 data	2024
Duobody-CD3xB7H4 (GEN1047)	Solid tumors	Phase 1 data	2024
HexaBody-CD38 (GEN3014)	Head-to-Head vs DARZALEX *FASPRO*	Data	2H 2024

Genmab

Genmab

Q&A



HAPPY

holidays