Epcoritamab + R-Mini-CHOP Induces High Complete Metabolic Response (CMR) Rates in Patients With Previously Untreated (1L) Diffuse Large B-Cell Lymphoma (DLBCL) Ineligible for Full-Dose R-CHOP: EPCORE NHL-2 Arm 8 Results

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OBJECTIVE

To evaluate efficacy and safety of epcoritamab + R-mini-CHOP in patients with 1L DLBCL ineligible for full-dose R-CHOP

CONCLUSIONS

Epcoritamab + R-mini-CHOP induced 100% overall response and 87% complete response rates in a high-risk population

Offers rapid T-cell engagement and CD20 inhibition, with no need for debulking

Frequent, deep, and durable responses were observed

Median PFS was not reached with a median follow-up of 9.4 months

An estimated 91% and 81% of patients remained progression free at 6 and 9 months, respectively

Safety was as expected

Data are reported without cycle 1 optimization

CRS was low grade and predictable, and all events resolved

Encouraging results compare favorably to R-mini-CHOP alone

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Disclosures

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BACKGROUND

- Although rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) is an effective treatment for previously untreated (1L) diffuse large B-cell lymphoma (DLBCL), some patients are not eligible for full-dose R-CHOP due to advanced age, frailty, or underlying comorbidities[1]
- Low-dose R-CHOP (R-mini-CHOP) is a standard attenuated 1L regimen, although outcomes are suboptimal, with overall response rates (ORRs) and complete response (CR) rates of approximately 70% and 40%–60%, respectively, and a 2-year progression-free survival (PFS) rate of 47%[1]
- Novel therapies that can be safely combined with standards of care are needed to improve outcomes
- Epcoritamab SC is the only approved subcutaneously administered CD3xCD20 bispecific antibody[2-4]
  - Approved for the treatment of adults with different types of relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 lines of systemic therapy in various geographies, including the US, Europe, and Japan[a-c,5-9]
  - Showed high ORRs and CR rates and manageable safety in combination with R-CHOP in 1L DLBCL[10]
- We present initial results from arm 8 of the ongoing EPCORE NHL-2 trial (epcoritamab SC + R-mini-CHOP in 1L DLBCL), the first results of a CD3xCD20 bispecific antibody with this regimen

[a]Approved in the US for the treatment of adults with R/R DLBCL, not otherwise specified (NOS), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma (HGBCL) after ≥2 lines of systemic therapy. [b]Approved in Europe and the UK for the treatment of adults with R/R DLBCL after ≥2 lines of systemic therapy. [c]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.

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]

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	Q3W		
R-mini-CHOP	Doxorubicin IV 25 mg/m^2	Q3W		
R-mini-CHOP	Vincristine IV 1 mg	Q3W		
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	

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

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.

RESULTS

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

[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. [d]DLBCL subtype was missing for 1 patient. [e]Local analysis is reported; patients can be classified as having HGBCL (double-hit, n=1; triple-hit, n=1). [f]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)

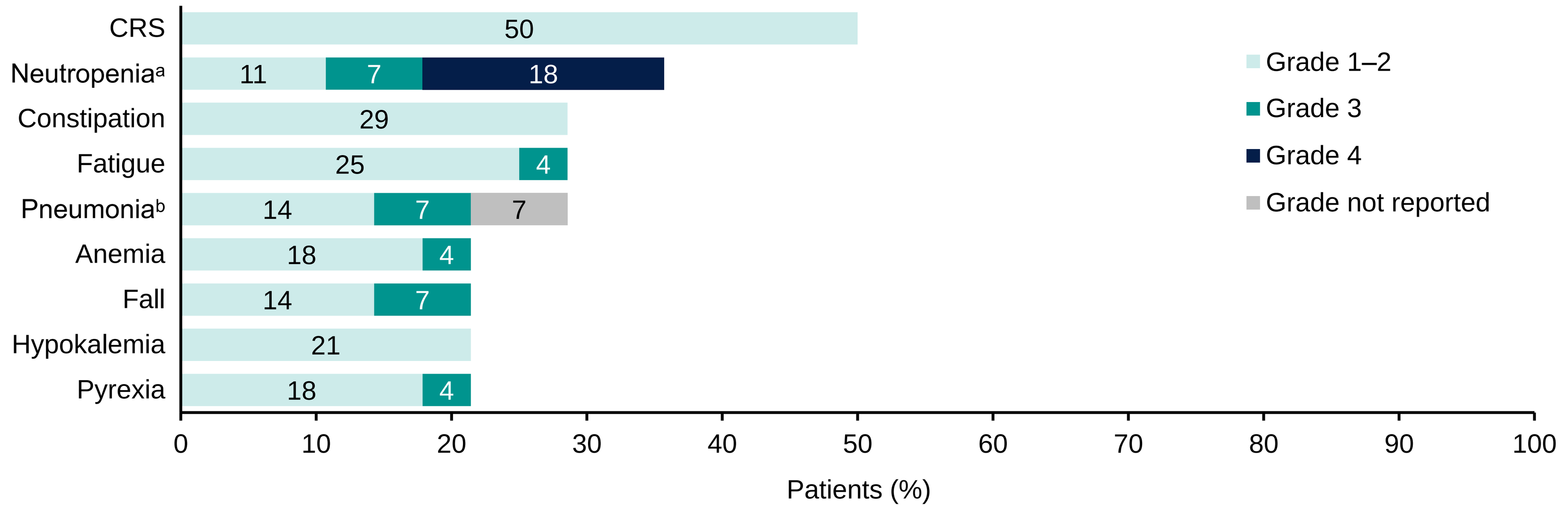
[a]Median is Kaplan–Meier estimate. [b]AEs that lead to treatment discontinuation were confusional state and cytomegalovirus infection reactivation, both in the same patient (n=1); CRS (n=1); and rhinitis (n=1).

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



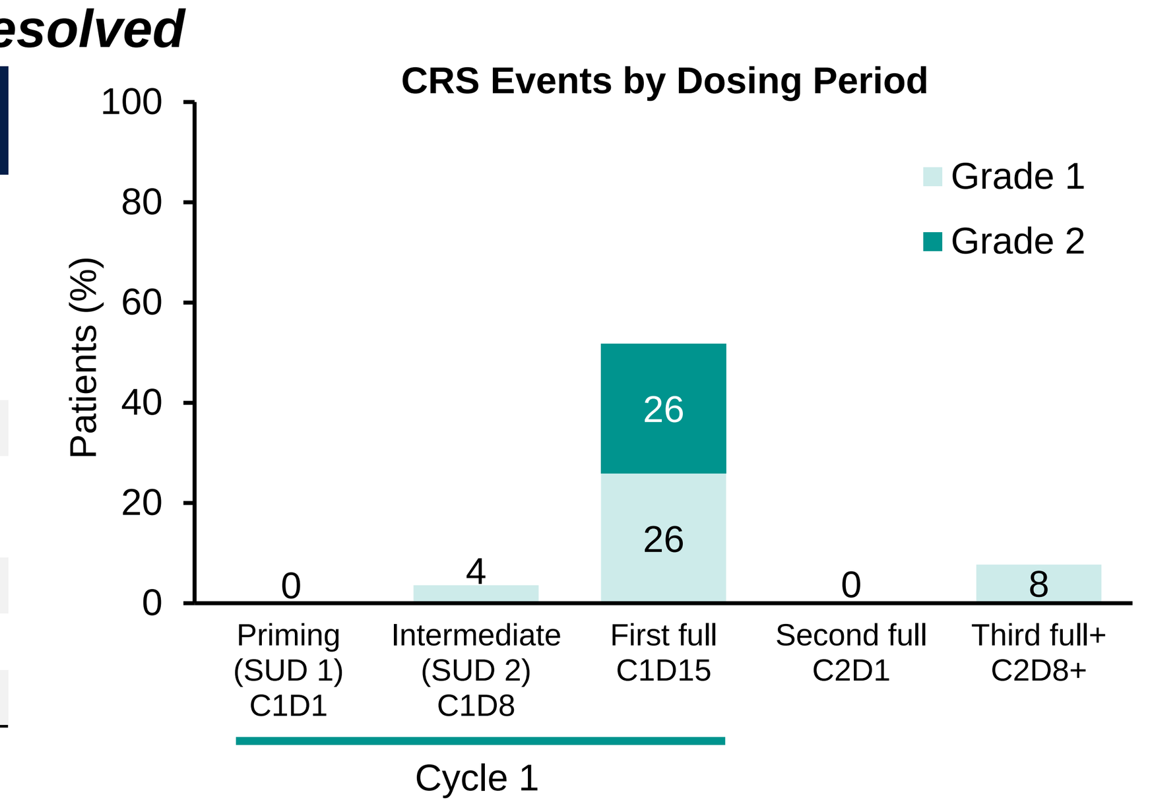
Data cutoff: September 1, 2023. [a]Combined term includes neutropenia and neutrophil count decreased. Use of growth factors was allowed, in general, and required for recurring grade ≥3 neutropenia. [b]Grade was not reported for 2 patients with pneumonia.

- No ICANS or clinical tumor lysis syndrome events were reported
- 2 patients (7%) had febrile neutropenia (grade 3 and grade 4)
- 1 patient (4%) had grade 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)

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.[11] [b]Median is based on longest CRS duration in patients with CRS. [c]Patient had grade 2 CRS.



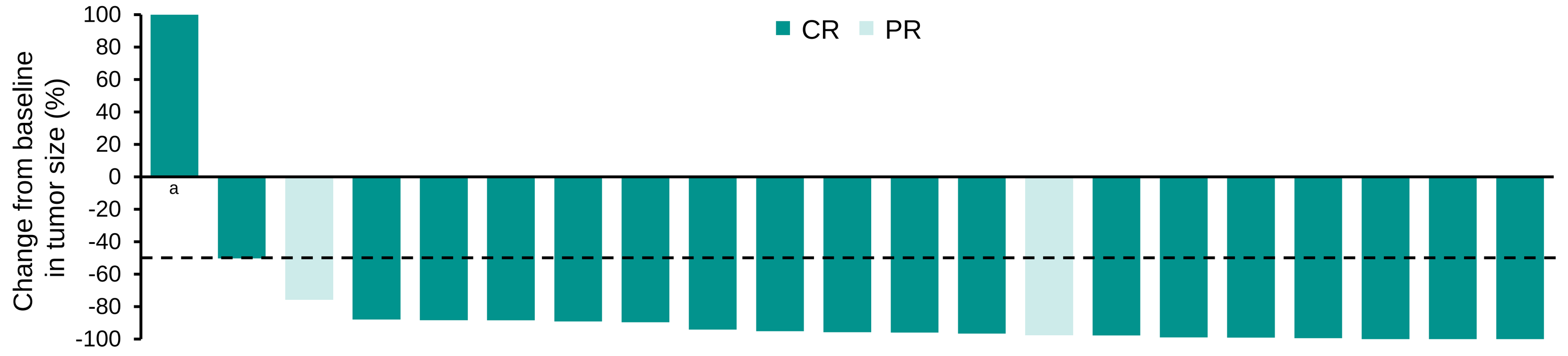
High Rates of Overall and Complete Response

Best Response[a]	Efficacy Evaluable n=23	Patients Who Completed 6C R-Mini-CHOP With Concomitant Epcoritamab n=21
Overall response	100%	100%
CR	87%	86%
PR	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.

- 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)

Consistent Antitumor Activity Observed

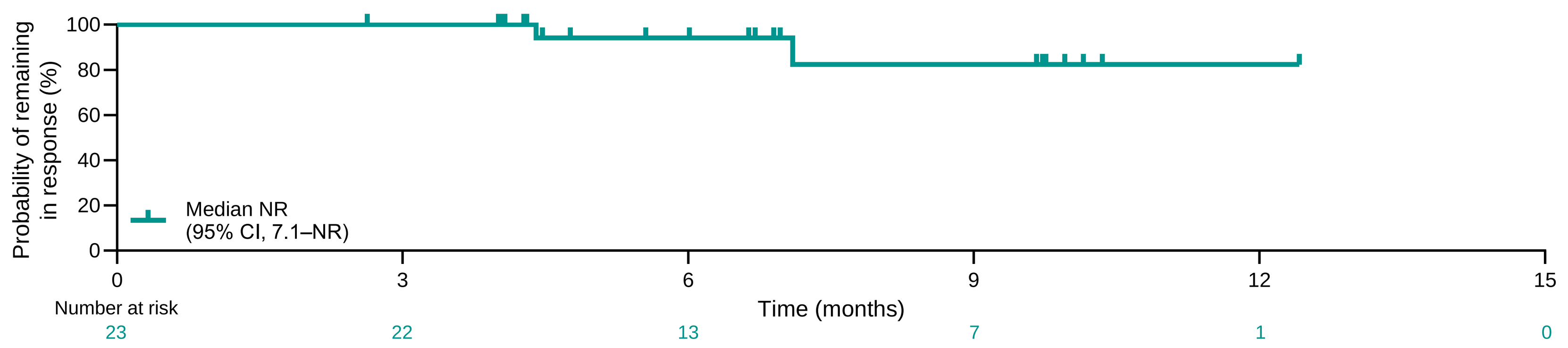


A total of 21 patients were evaluable for change from baseline in tumor size. [a]Baseline target lesion measurements were pending confirmation at the data cutoff.

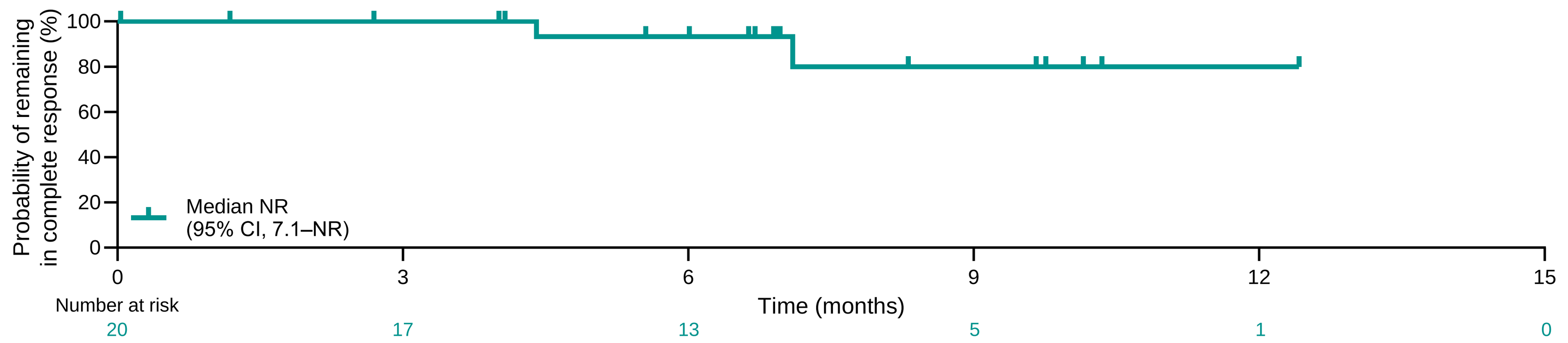
- Epcoritamab + R-mini-CHOP induced responses across all response-evaluable patients

Median Duration of Response, Duration of Complete Response, and Progression-Free Survival Were Not Reached

Duration of Response

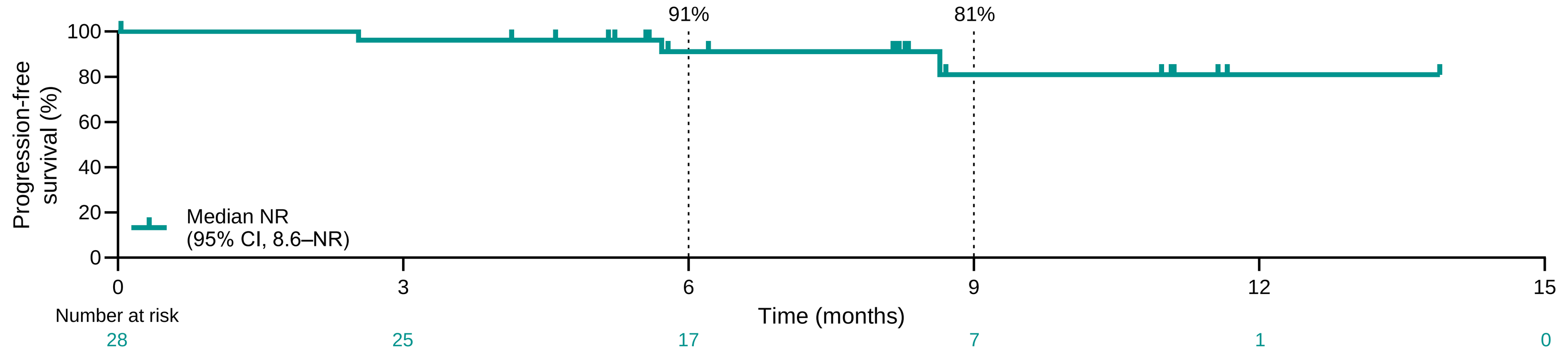


Duration of Complete Response



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

Progression-Free Survival



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