Epcoritamab + GemOx in Patients With R/R DLBCL Ineligible for ASCT: EPCORE NHL-2 Updated Results

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OBJECTIVE

To evaluate the long-term safety and efficacy of epcoritamab + GemOx in patients with R/R DLBCL who failed or are ineligible for ASCT

CONCLUSIONS

Epcoritamab in combination with GemOx led to high ORR and CR rates in this difficult-to-treat, high-risk R/R DLBCL population

ORR 80%, CR rate 57%

Responses were deep and durable

Median duration of CR: 13.3 mo
Median overall survival: Not reached

High ORR and CR rates were observed across subgroups and were notably higher in second-line and CAR T–naive patients

The safety profile remained consistent with those of the individual drugs

These results are encouraging and continue to underscore the combinability of epcoritamab for the treatment of R/R DLBCL

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Disclosures
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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, 33% of patients treated with rituximab and gemcitabine + oxaliplatin (GemOx) achieved complete response, with a median progression-free survival of 5 mo and median overall survival of 10 mo[3]
- Epcoritamab SC is the only approved subcutaneously administered CD3xCD20 bispecific antibody[4-9]
  - Approved for the treatment of adults with different types of 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]

[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 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

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

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/m² IV	Q2W					
GemOx	Oxaliplatin 100 mg/m² IV	Q2W					

- **Primary objective:** Assess 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.

RESULTS

Baseline Characteristics and Prior Treatments

High-Risk, Refractory Patient 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 and Prior Treatments	**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)
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[b] 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.

Efficacy Results

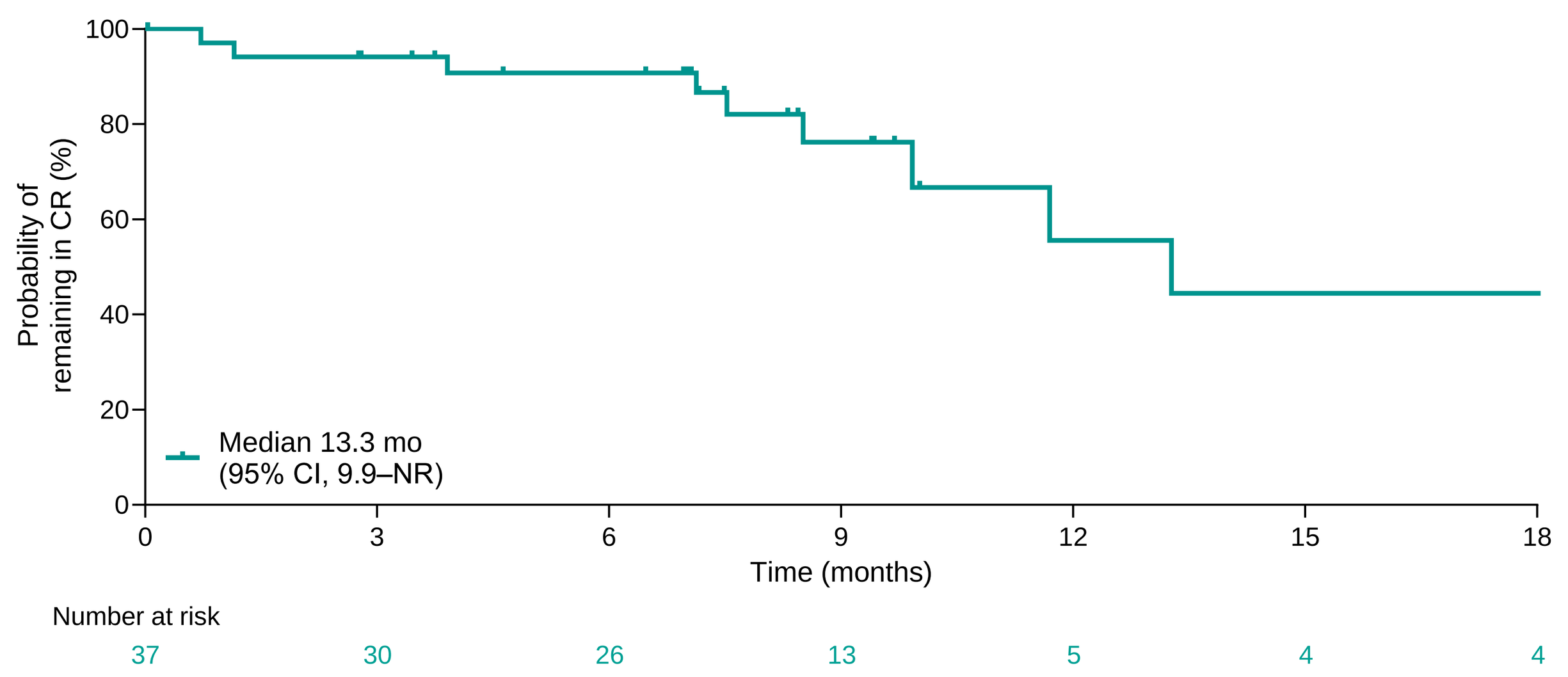
Responses Occurred Early and Rates Were High

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

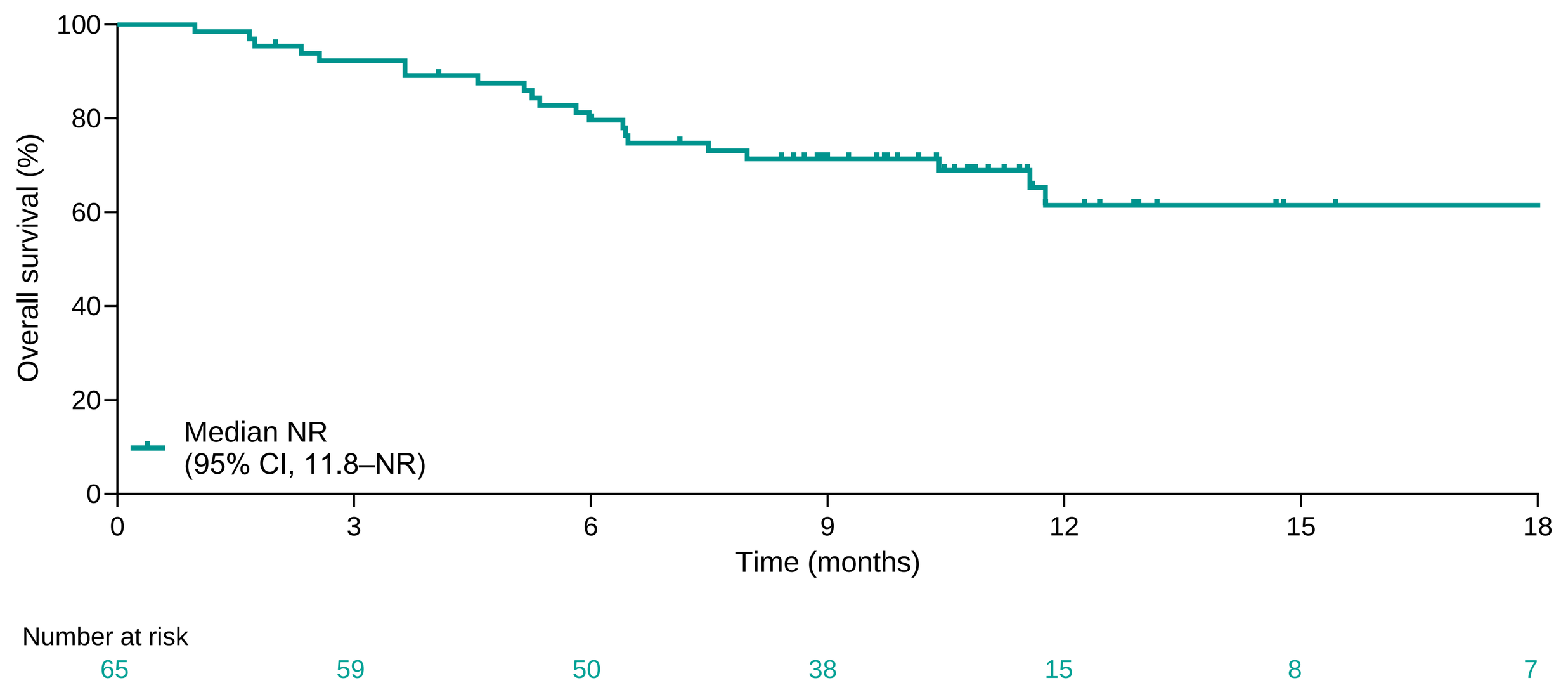
[a]5 patients were not evaluable for response.

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

Durable Complete Responses

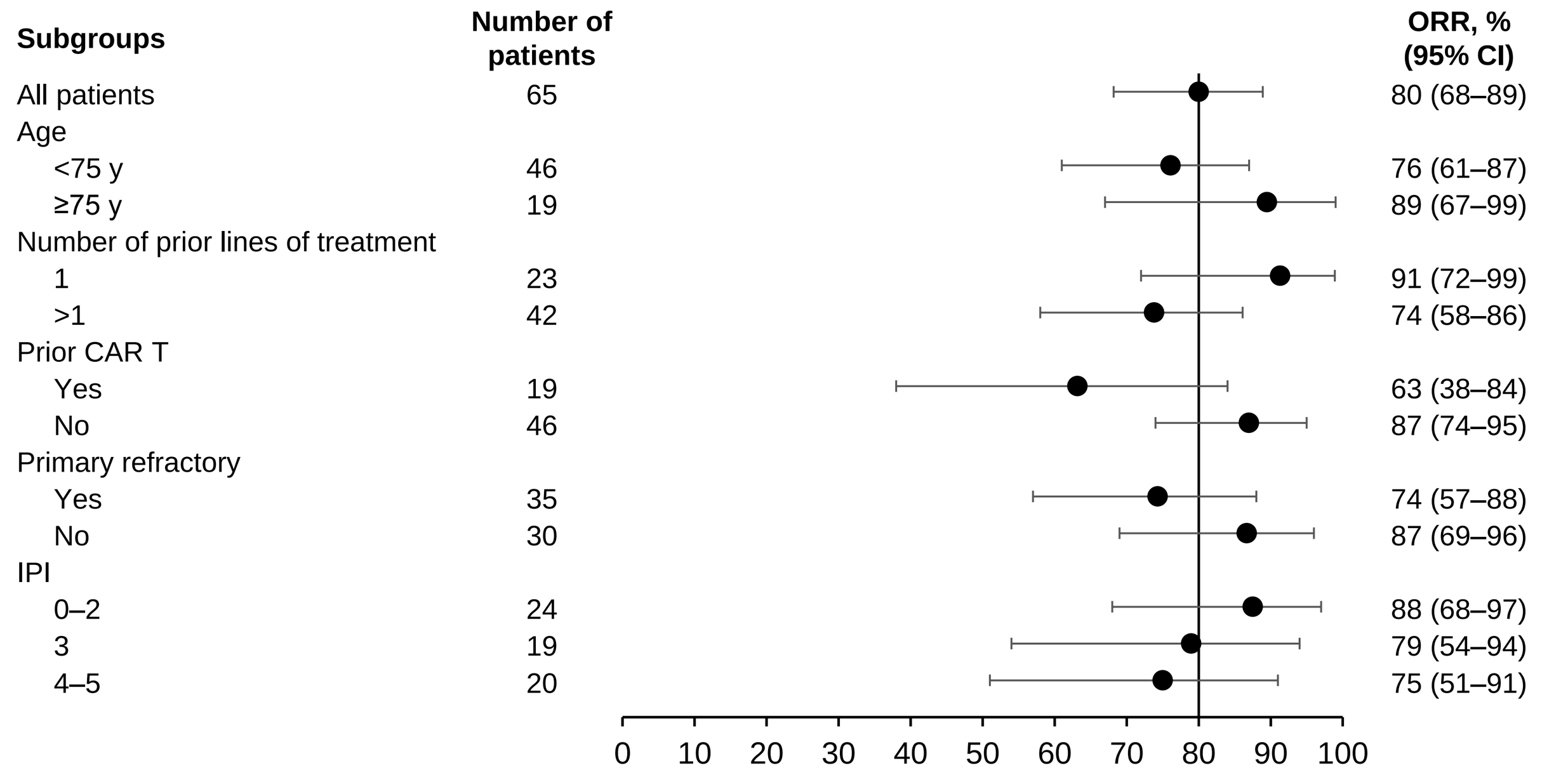


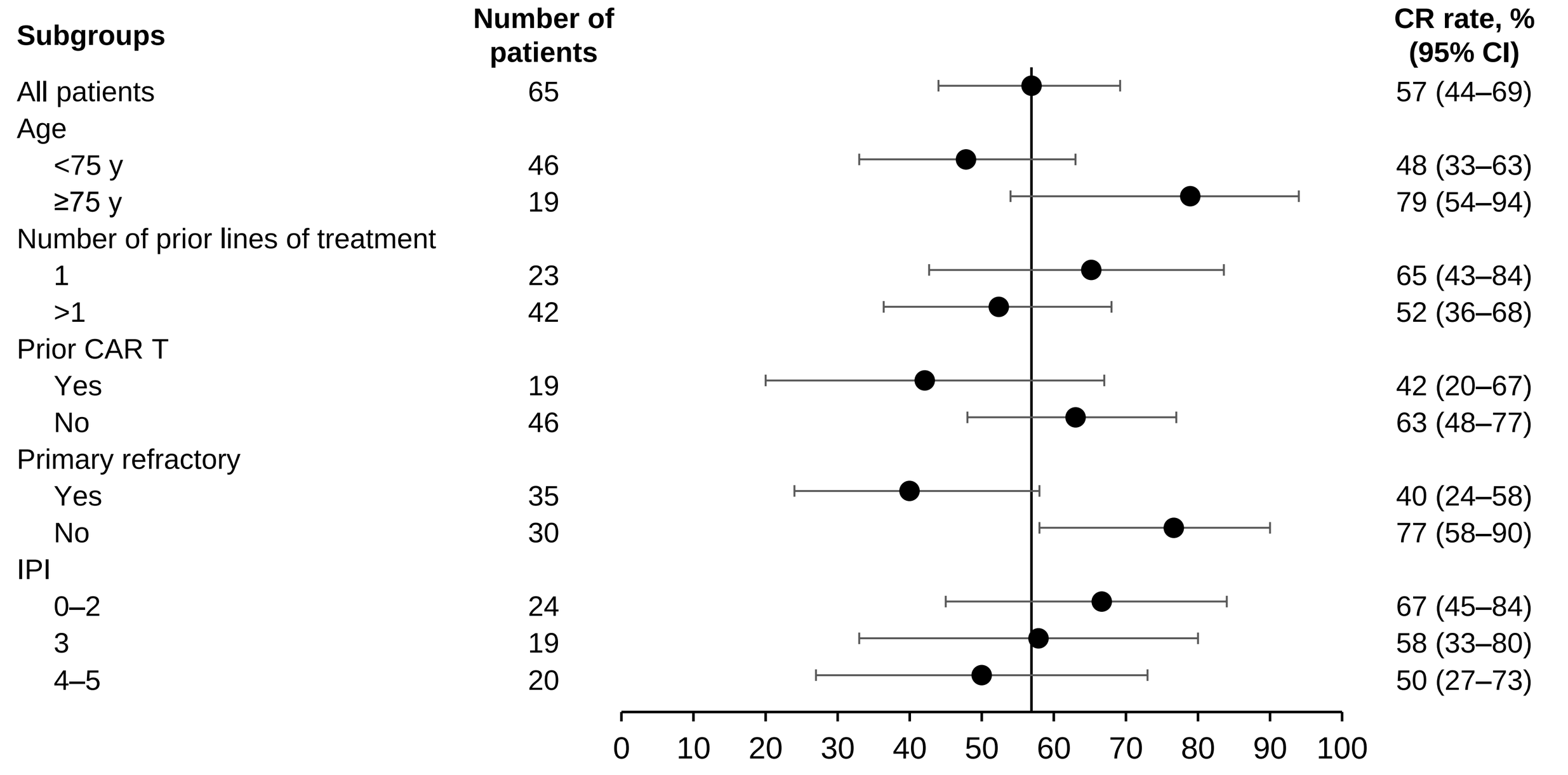
Median Overall Survival[a] Not Reached



[a]Deaths due to COVID-19 (n=6) have been censored.

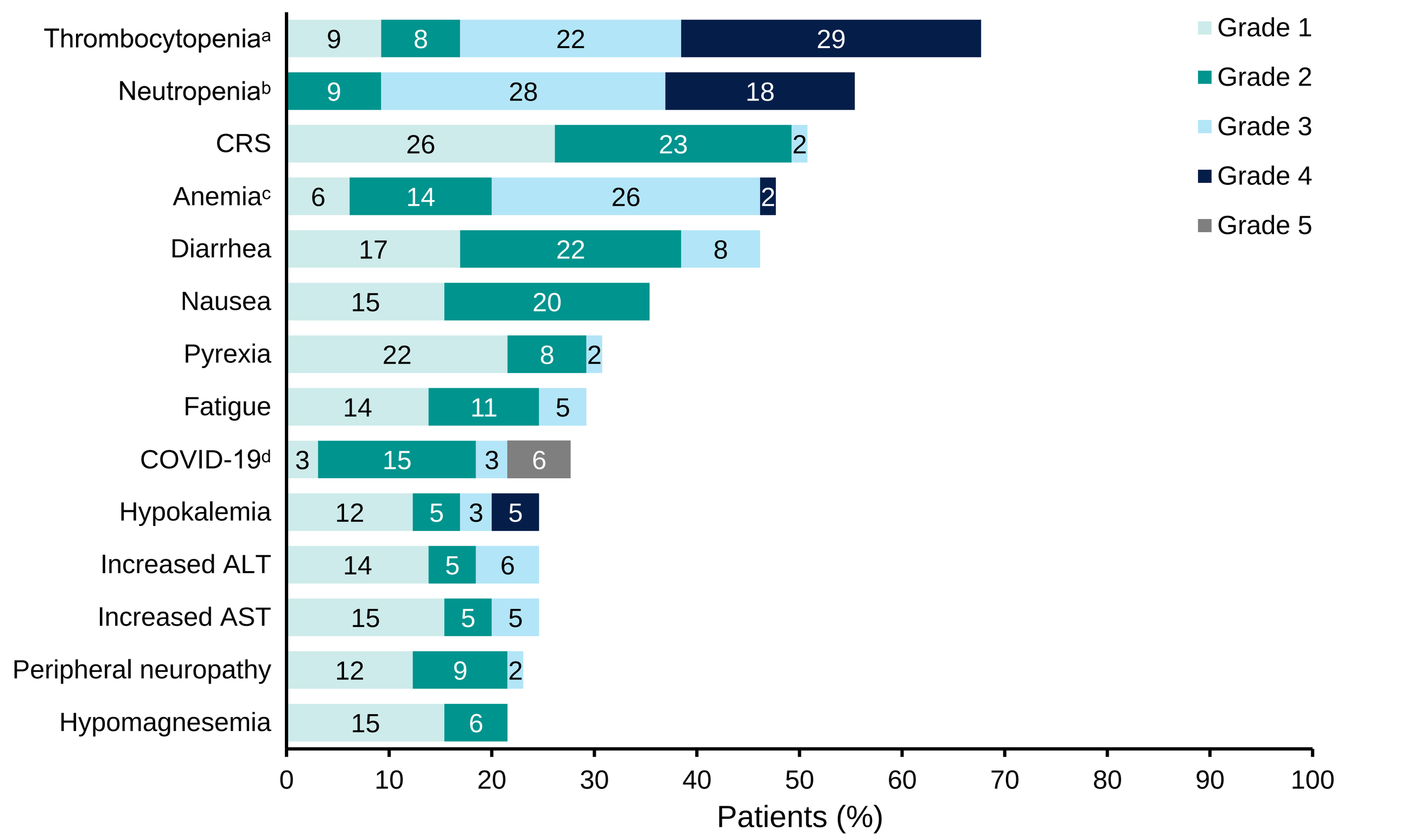
Response Rates Remained Consistent Across Subgroups, Including High-Risk Patients


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)


Subgroups
Number of patients
CR 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)

Safety Profile

Common (>20%) Treatment-Emergent Adverse Events


Thrombocytopenia[a] 9 8 22 29
Neutropenia[b] 9 28 18
CRS 26 23 2
Anemia[c] 6 14 26 2
Diarrhea 17 22 8
Nausea 15 20
Pyrexia 22 8 2
Fatigue 14 11 5
COVID-19[d] 3 15 3 6
Hypokalemia 12 5 3 5
Increased ALT 14 5 6
Increased AST 15 5 5
Peripheral neuropathy 12 9 2
Hypomagnesemia 15 6
Grade 1
Grade 2
Grade 3
Grade 4
Grade 5
Patients (%)

[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.

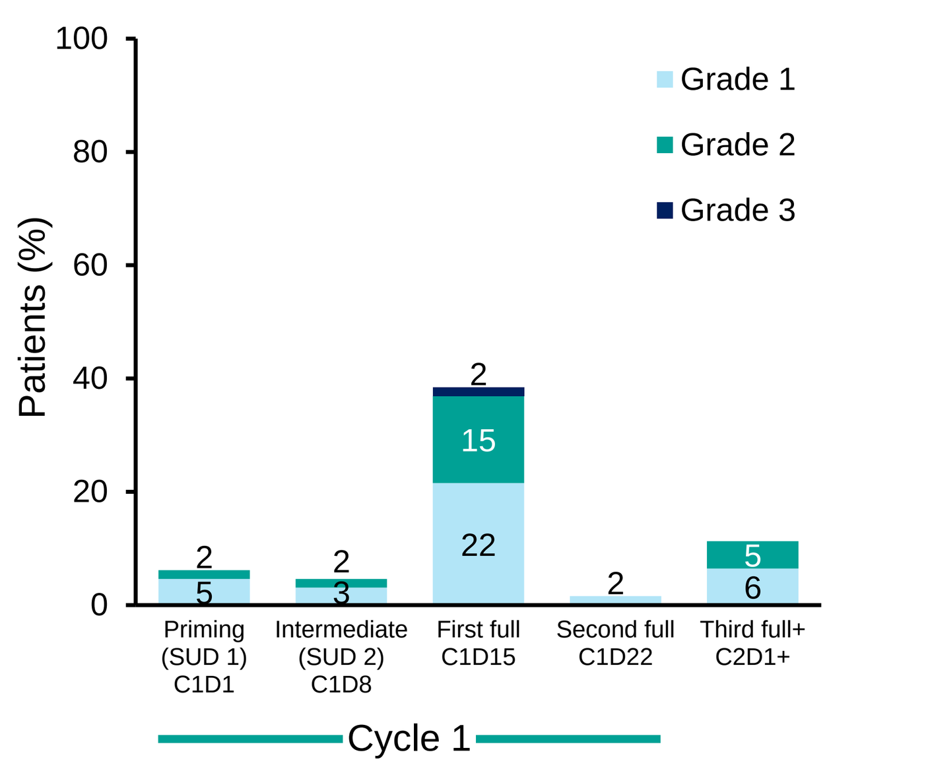
- 4 patients experienced febrile neutropenia
- ICANS was reported in 2 patients (grade 1 and 3); both events resolved and 1 patient discontinued treatment due to ICANS
- There were no reports of clinical tumor lysis syndrome
- The trial, conducted during the global COVID-19 pandemic, was impacted by prevailing COVID-19 trends, including the highly infectious Omicron variant
- 11 patients had grade 5 TEAEs; 4 events were related to COVID-19

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)

[a]Graded by Lee et al 2019 criteria.[10] [b]Median based on longest recorded CRS duration in patients with >1 CRS event.

CRS Events by Dosing Period



SUD 1, first step-up dose; SUD 2, second step-up dose.

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