Authors: The data included here are not final and will be updated when the final outputs available (end of November)

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

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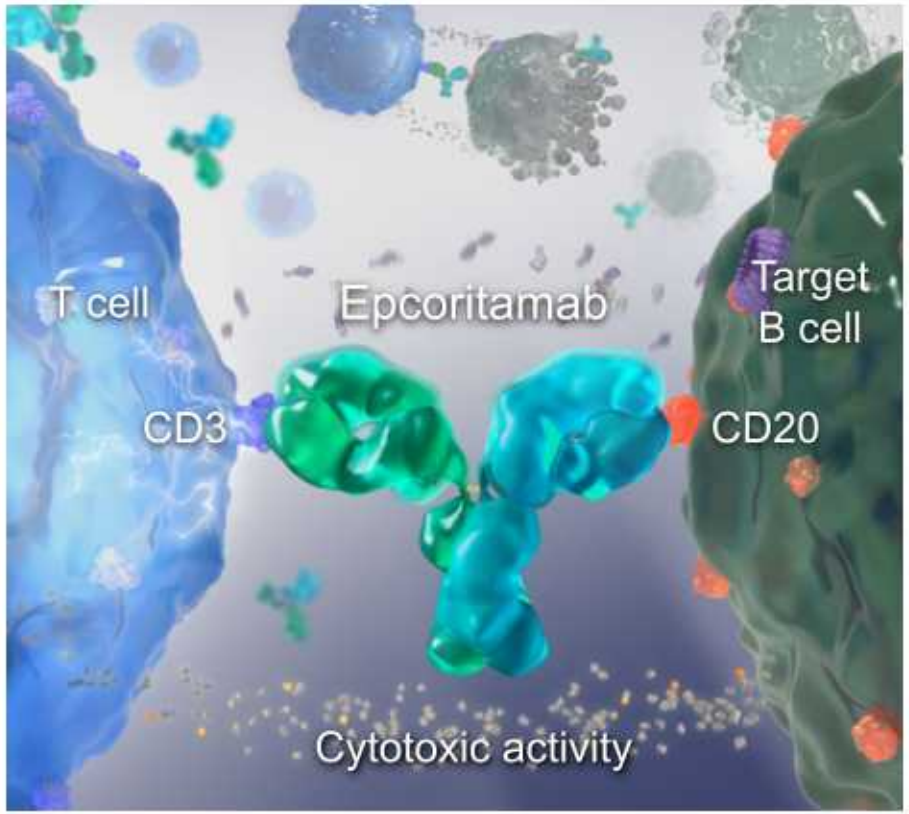
Background

- Patients with relapsed/refractory (R/R) DLBCL have poor outcomes[1-2]
- Epcoritamab is a subcutaneously administered **CD3xCD20 bispecific antibody** that binds to CD3+ T cells and CD20+ B cells, inducing CD3+ T cells to kill CD20+ tumor B cells[3,4]
- Single-agent epcoritamab has demonstrated deep and durable responses and a manageable safety profile in patients with R/R B-cell lymphoma in the EPCORE NHL-1 trial[5]
- Epcoritamab is **approved in the US[6], Europe[7,a], Japan[8,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[6]

We present results from Arm 1 of EPCORE NHL-5, which evaluated combining epcoritamab with lenalidomide in patients with R/R DLBCL

Figure: Epcoritamab Mechanism of Action



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.** Epkinly [package insert] Plainsboro, NJ. Genmab; May 2023. **7.** Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; September 2023. **8.** Epkinly [prescribing information]. Tokyo, Japan: Genmab K.K.; September 2023.

[a]Approved in Europe for the treatment of adult patients with R/R DLBCL ≥2 lines of systemic therapy.

[b]Approved in Japan for the treatment of adult patients with certain types of relapsed/refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 lines of systemic therapy.

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]
- ≥1 prior anti-CD20 monoclonal antibody–containing combined systemic therapy
- ECOG PS 0–2
- Measurable disease

Data cutoff: Oct 06, 2023
Median follow-up: 9.0 mo

Dose escalation (N=3–12) and dose expansion (N≈20)

↓

Epcoritamab + anti-neoplastic agents in NHL

Arm 1 **Epcoritamab + lenalidomide** **(R/R) DLBCL**	**Arm 2** Epcoritamab + ibrutinib + lenalidomide (R/R) DLBCL	**Arm 3** Epcoritamab + pola-R-CHP 1L DLBCL	**Arms 4–7** Epcoritamab + antineoplastic agents across 1L or R/R DLBCL, FL, MCL

Epcoritamab dosing schedule

Step-up dosing

- Cycle 1, day 1: priming dose (0.16 mg)
- Cycle 1, day 8: intermediate dose (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), Q4W

Lenalidomide dosing schedule

Cycles 1-12: once daily on days 1–21 (25 mg) for 12 cycles of 28 days

Objectives

Dose Escalation: Assess initial safety and tolerability and identify expansion dose (RP2D) of each combination therapy
Dose Expansion: Safety, tolerability, and antitumor activity of each combination therapy

[a]Per WHO 2016 classification.
[b]Relapsed disease is defined as disease that previously responded to therapy but progressed ≥6 months 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 months after completion of therapy (including maintenance therapy).

Baseline Characteristics

	Total N=35
Median age, y (range)	72 (41–85)
Female, n (%)	14 (40)
Ann Arbor stage, n (%)	
I–II	11 (31)
III	6 (17)
IV	17 (49)
Cancer under study, n (%)	
DLBCL	30 (86)
HGBL/DLBCL (Triple hit)	1 (23)
FL grade 3b	3 (9)
ECOG PS, n (%)	
0	24 (69)
1	10 (29)
2	1 (3)
R-IPI category, n (%)	
Very good (0)	2 (6)
Good (1-2)	9 (26)
Poor (3-5)	16 (46)
Unknown	4 (11)
Extranodal disease at screening, n (%)	
Yes/No	22 (63) / 13 (37)

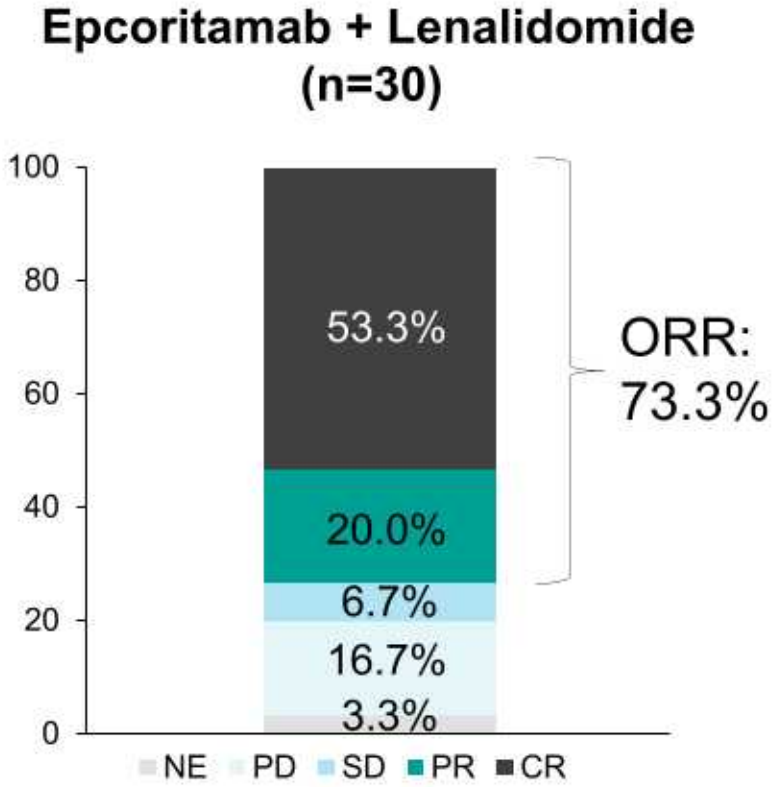
Treatment History and Prior Systemic Therapies

Treatment History	Total N=35
Median time from diagnosis to first dose, mo (range)	0.9 (0–12.9)
Median number of prior lines of anti-cancer therapy, n (range)	2.0 (1–4)
Prior lines of therapy, n (%)	
1 prior line	17 (49)
2 prior lines	11 (31)
3 prior lines	5 (14)
≥4 prior lines	2 (6)
Prior systemic therapies, n (%)	
Prior CAR-T therapy	6 (23)
Prior stem cell transplant	2 (6)

Treatment Exposure and Disposition

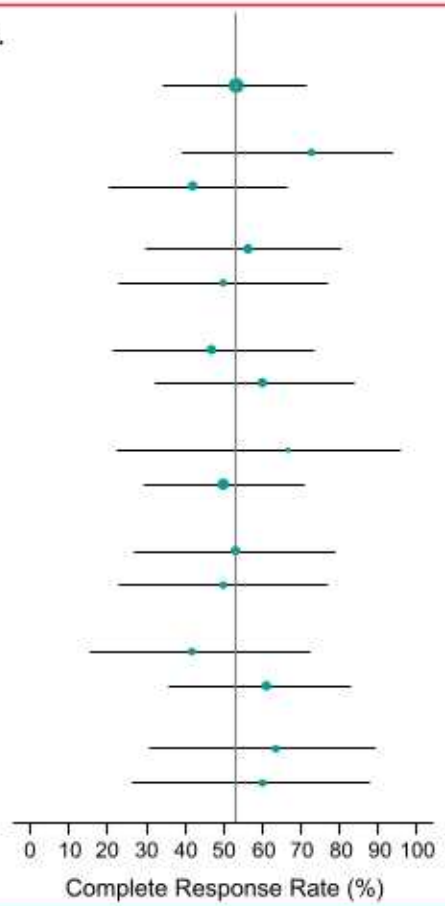
	Total N=35
Median follow-up, mo (95% CI)	9.0 (6.0–9.6)
Epcoritamab exposure	
Median duration, mo (range)	3.9 (0.03–10.2)
Median number of cycles, n (range)	5 (1–12)
Ongoing treatment, n (%)	20 (57)
Discontinued treatment, n (%)	15 (43)
Progressive disease	8 (23)
Patient Withdrawal	3 (9)
AE	2 (6)
Other	2 (4)

Responses With Epcoritamab + Lenalidomide (n=30)[a]



Complete Response in Prespecified Groups

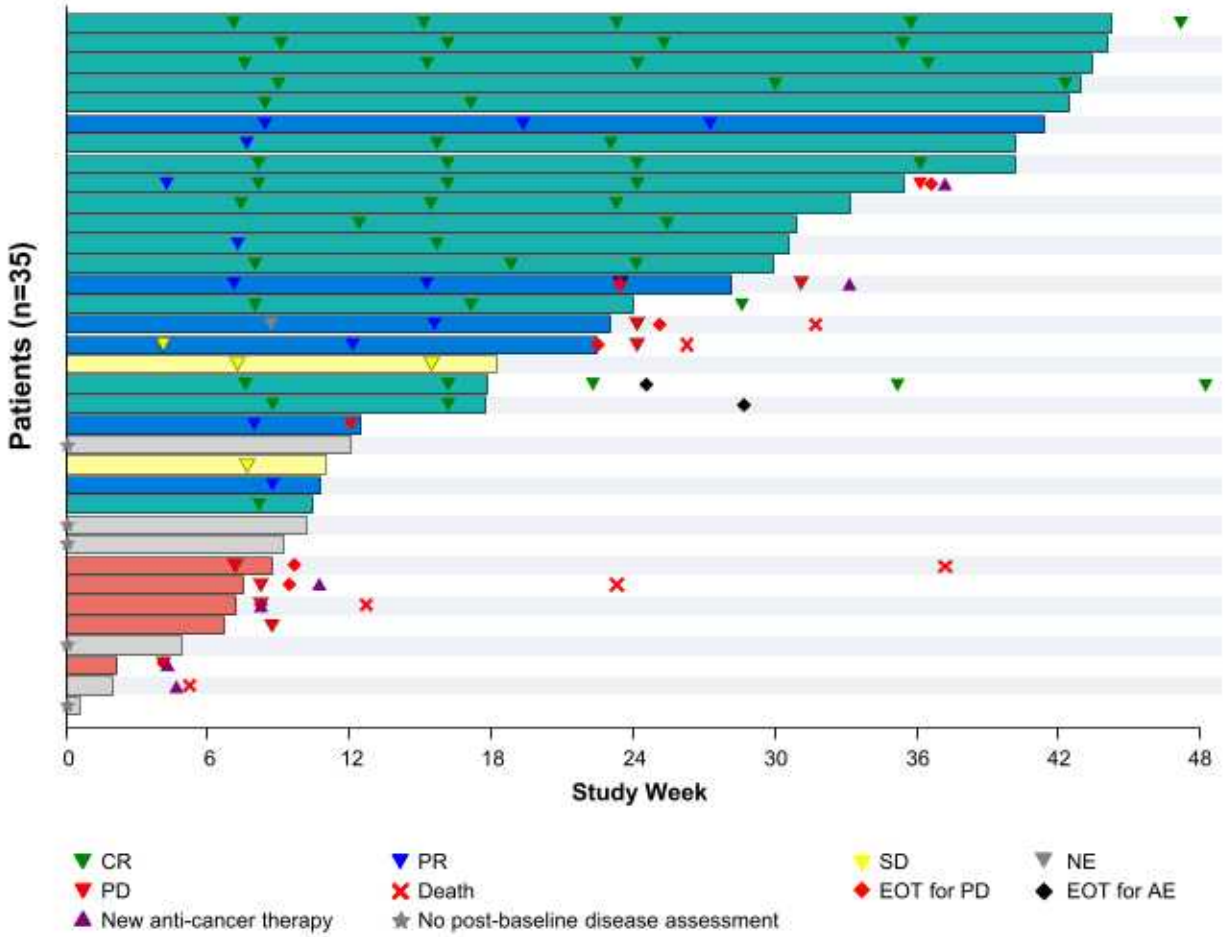
Subgroup	Patients No.	CRR, % (95%CI)
All patients	30	53.3 (34.3 to 71.7)
Age		
<65	11	72.7 (39.0 to 94.0)
≥65	19	42.1 (20.3 to 66.5)
Prior lines of therapy		
1	16	56.3 (29.9 to 80.2)
≥2	14	50.0 (23.0 to 77.0)
Time from end of last line of therapy to first dose		
<6 months	15	46.7 (21.3 to 73.4)
≥6 months	15	60.0 (32.3 to 83.7)
Prior CAR-T experience		
Yes	6	66.7 (22.3 to 95.7)
No	24	50.0 (29.1 to 70.9)
Most recent prior anti-CD20 therapy		
Refractory	15	53.3 (26.6 to 78.7)
Relapsed	14	50.0 (23.0 to 77.0)
Primary refractory status		
Yes	12	41.7 (15.2 to 72.3)
No	18	61.1 (35.7 to 82.7)
Molecular classification		
GCB	11	63.6 (30.8 to 89.1)
ABC/Non-GCB	10	60.0 (26.2 to 87.8)

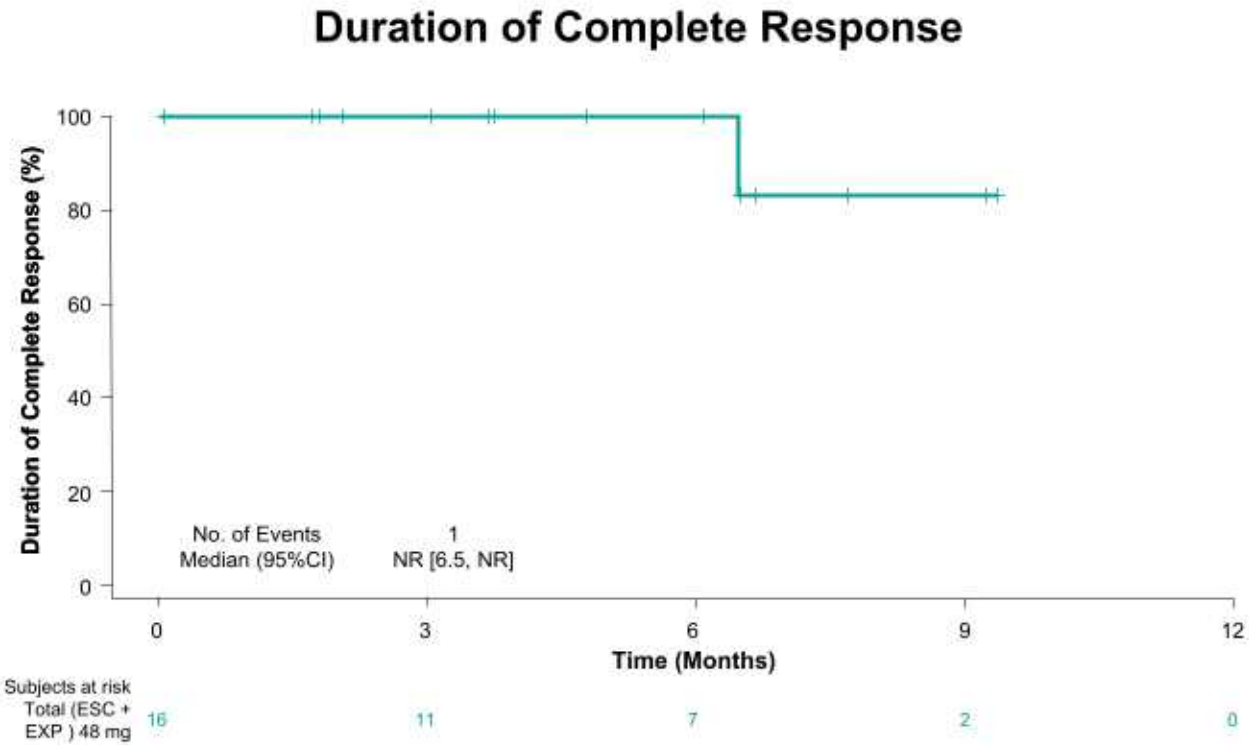


Data cutoff: Oct 06, 2023.

[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 days of the first dose of study drug without a postbaseline assessment.

Onset and Durability of Response (n=35)[a]

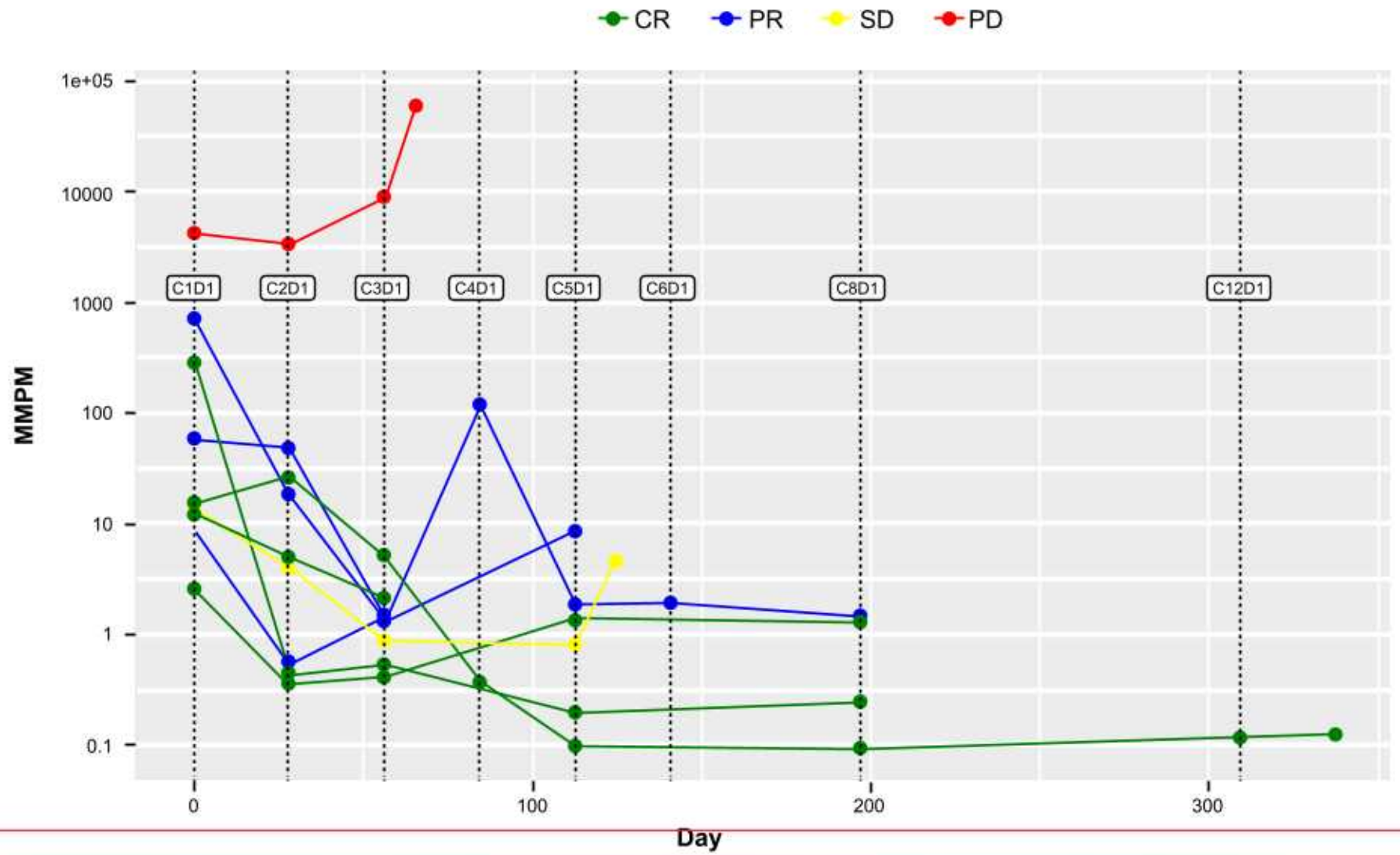




- Median time to response (TTR) was 1.9 mo (range, 1.6–3.6)

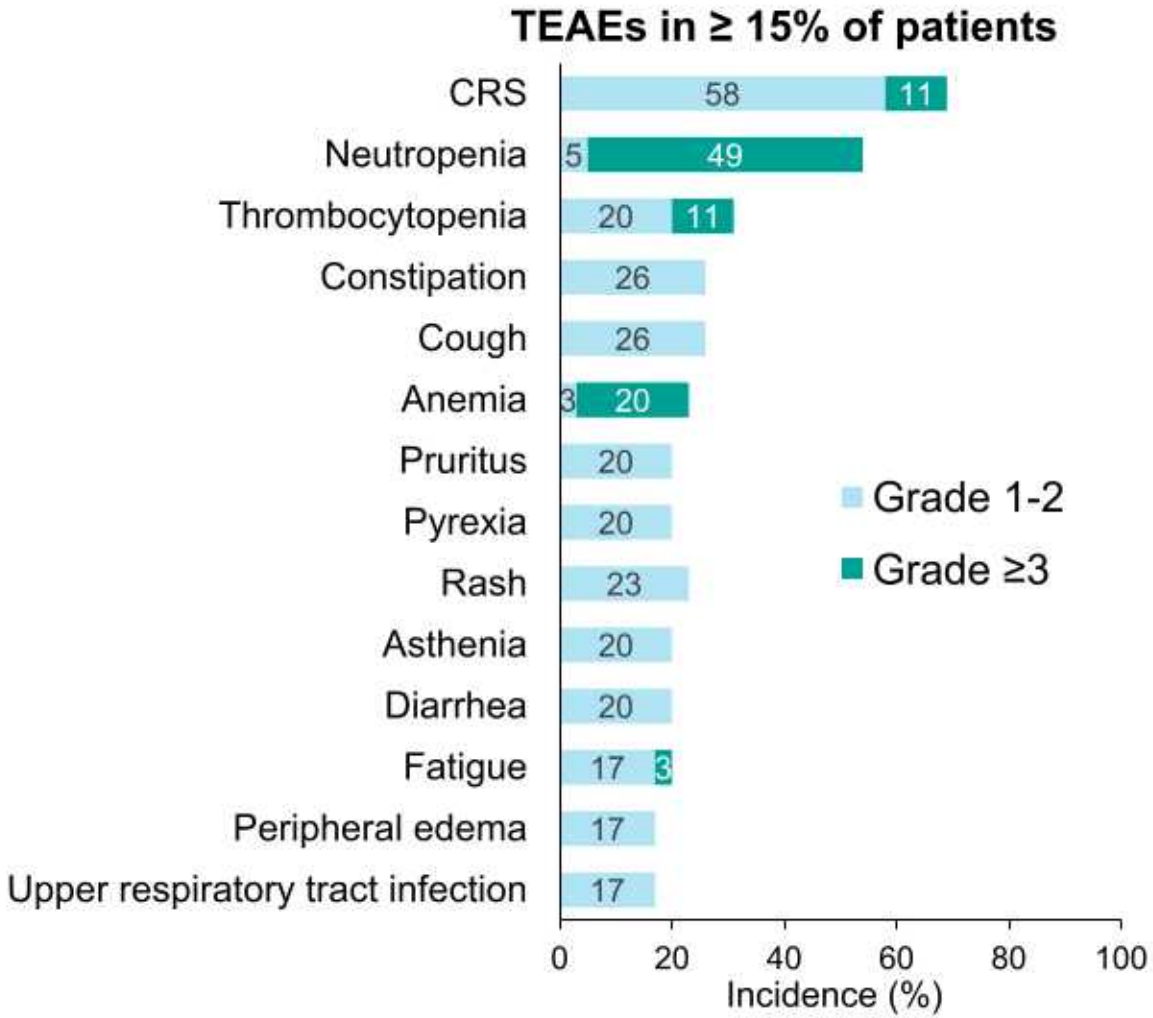
[a]Based on investigator assessment per Lugano criteria.

Rapid and Sustained MRD Negativity Was Consistent With BOR



Safety Profile

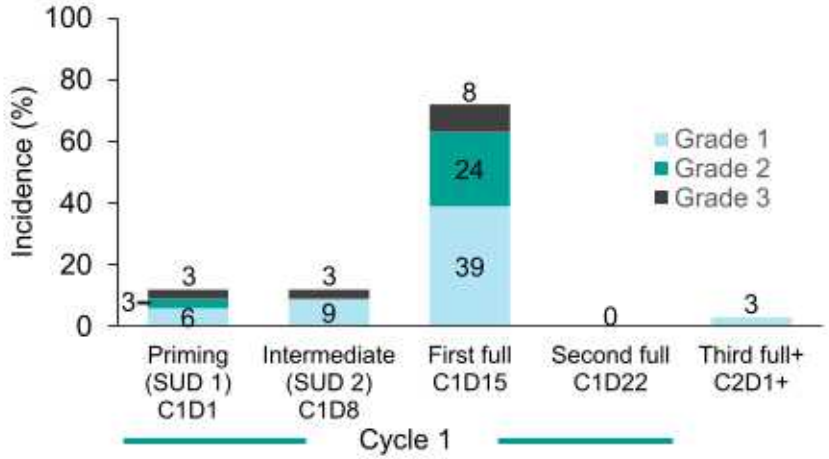
n (%)	Total N=35
Any-grade TEAE	35 (100)
Related to epcoritamab	31 (89)
Grade ≥3 TEAE	30 (86)
Related to epcoritamab	22 (63)
Serious adverse event	26 (74)
Related to epcoritamab	22 (63)
Epcoritamab delay/interruption due to TEAE	28 (80)
Discontinued epcoritamab due to TEAE	2 (6)
Fatal TEAE related to epcoritamab	0



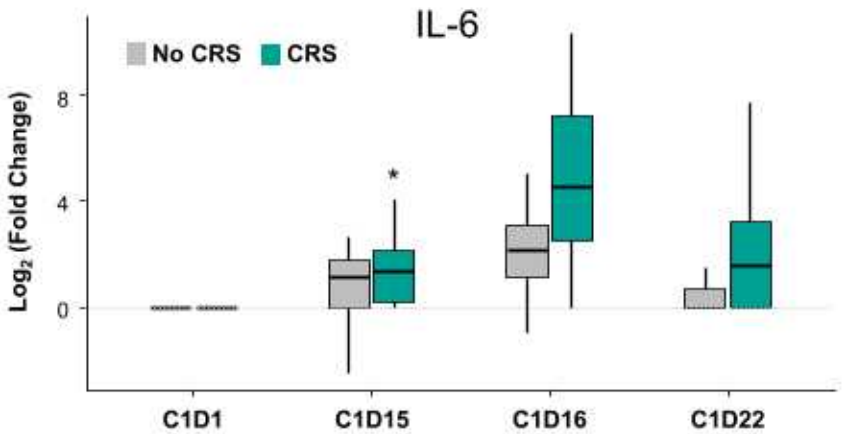
- One patient experienced ICANS (Grade 3), which resolved after 2 days
- One patient experienced CTLS (Grade 1)
- The most common serious AE related to epcoritamab was CRS (51% of all patients)
- The most common Grade ≥3 TEAE was neutropenia (49%) and did not lead to epcoritamab discontinuation

Majority of CRS Events were Low-grade

	Total N=35
CRS, n (%)[a]	24 (69)
Grade 1	12 (34)
Grade 2	8 (23)
Grade 3	4 (11)
Median time to onset of first CRS event, d (range)	16 (2–45)
CRS resolution,[b] n (%)	24 (100)
Median time to resolution, d (range)[c]	2 (1–6)
CRS interventions	
Treated with tocilizumab, n (%)	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 1st full dose



- IL-6 peak was predictable

[a]Maximum CRS grade is presented for patients with more than one CRS event. [b]Percentages calculated based on patients with at least one CRS event. [c]Based on longest recorded CRS duration for patients with more than one CRS event.
CRS, cytokine release syndrome; SUD 1, first step-up dose; SUD 2, second step-up dose.

Conclusions

- Epcoritamab + lenalidomide showed promising antitumor activity in patients with R/R DLBCL (n=30)
  - ORR, 73%; CMR, 53%
- Epcoritamab + lenalidomide demonstrated a manageable safety profile with no new safety signals identified
  - Most CRS events (20/24) were low-grade; CRS occurrence was predictable, and all CRS events resolved
  - One ICANS event that resolved
  - One patient experienced a Grade 1 CTLS event
- Predictable cytokine peaks (IFN-gamma, IL-2, and IL-6) occurred immediately after the first full dose, with a rapid and sustained depletion of peripheral B cells
- These encouraging data support further exploration of epcoritamab + lenalidomide in patients with R/R DLBCL

Disclosures

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