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Durable Responses in Patients With Large B-Cell Lymphoma and 2+ Prior Lines of Therapy Who Either Paused or Discontinued Epcoritamab Monotherapy While in Complete Response

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Objective

- To evaluate the durability of response of patients with R/R LBCL in CR who either paused or permanently discontinued epcoritamab treatment in the EPCORE NHL-1 study

Conclusion

- These findings from the EPCORE NHL-1 study of epcoritamab monotherapy demonstrate that patients with R/R LBCL in CR sustain durable remissions despite temporary treatment pauses or discontinuation for reasons other than progression
- While these outcomes highlight the potential flexibility of the epcoritamab regimen, treatment until progression remains the optimal approach as reflected in the primary readout from the EPCORE NHL-1 study and the 4-year follow-up[3,4]
- With a median DOCR exceeding 3 years and the longest reported median DOCR for a bispecific antibody in this setting, epcoritamab continues to show a favorable balance of efficacy and manageability in third line and beyond in patients with R/R LBCL

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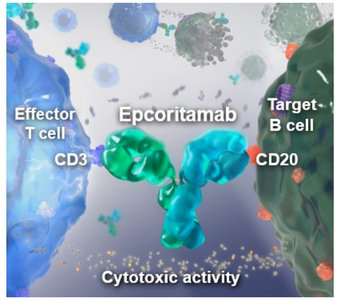
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Introduction

- Outcomes are poor for patients with relapsed/refractory large B-cell lymphoma (R/R LBCL) who have a failed transplant or who are deemed transplant ineligible
- Epcoritamab, a CD3×CD20 bispecific antibody, is approved as monotherapy for adults with R/R LBCL for treatment to progression or unacceptable toxicity after ≥2 prior lines of systemic therapy (**Figure 1**)[1,2]
- Consistent with the previous report at 3 years[3] from the pivotal Phase 2 EPCORE NHL-1 study (NCT03625037), epcoritamab monotherapy continued to result in sustained deep and durable responses, with 41% of patients with LBCL in complete response (CR) achieving a median duration of complete response (DOCR) of 37.7 months (95% CI, 25.1–not reached [NR]) at the 4-year follow-up[4]
  - The median overall survival (OS) in all patients was 18.5 months (95% CI, 11.7–27.7)[4] and the safety was consistent with previous reports[3]
- The efficacy and safety of epcoritamab in patients with LBCL who paused >6 weeks or discontinued treatment are currently unknown and provide the rationale for this exploratory analysis

Figure 1: Epcoritamab Mechanism of Action



Methods

Figure 2: Study Design: EPCORE NHL-1 (NCT03625037)

Phase 1/2, open-label trial of epcoritamab monotherapy in R/R B-cell NHL

Key inclusion criteria:
- Age ≥18 years
- R/R CD20+ LBCL
  - DLBCL (*de novo* or transformed)
  - "Double-" or "triple-hit" DLBCL[a]
  - PMBCL
  - HGBCL
  - FL Grade 3B
- ECOG PS 0−2
- ≥2 prior lines of systemic antineoplastic therapy, including ≥1 regimen with an anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- Prior CAR T therapy allowed

Data cutoff: May 3, 2024
Median follow-up: 18.5 months

Dose Expansion (LBCL cohort, N=157)

Epcoritamab SC
Step-up dosing[b]:
0.16 mg and 0.8 mg followed by 48 mg full doses in 28-day cycles:
- Q1W, cycles 1−3
- Q2W, cycles 4−9
- Q4W, cycles ≥10

Treatment until PD or unacceptable toxicity

- **Primary endpoint:** ORR per Lugano criteria[5]
- **Key secondary endpoints:** CR rate, DOR, DOCR, PFS, OS, TTNT, MRD-negativity rate, and safety/tolerability

Efficacy results were based on investigator's assessment

Patients included in the analysis:
- Patients in CR who had **treatment pauses/dose delays** for >6 weeks while on epcoritamab
- Patients in CR who **permanently discontinued** epcoritamab for reasons other than PD or death

[a]Classified as HGBCL, with *MYC* and *BLC2* and/or *BCL6* translocations. [b]Approved dosing schedule.
CAR T, Chimeric Antigen Receptor T-cell; CR, complete response; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; DOCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG PET, fluorodeoxyglucose positron emission tomography; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; mAb, monoclonal antibody; MRD, minimal residual disease; MRI, magnetic resonance imaging; NHL, non-Hodgkin lymphoma; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; Q1W, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; R/R, relapsed/refractory; TTNT, time-to-next treatment.

Results

Table 1: Baseline Characteristics and Treatment History

Characteristic	Patients in CR who had treatment pauses/ dose delays (n=16)	Patients in CR who permanently discontinued treatment (n=32)
Median (range) age, years	69 (20−83)	63 (20–82)
Female, n (%)	9 (56)	13 (41)
Race, n (%)		
White	11 (69)	12 (38)
Asian	1 (6)	9 (28)
Other	0	2 (6)
Not reported	4 (25)	9 (28)
ECOG PS, n (%)		
0	8 (50)	17 (53)
1	8 (50)	15 (47)
Disease type, n (%)		
DLBCL[a]	15 (94)	27 (84)
De novo	9 (56)	21 (66)
Transformed	6 (38)	6 (19)
From FL	5 (31)	5 (16)
From SLL	1 (6)	-
Other	-	1 (3)
NA	1 (6)	5 (16)
Median prior LOT (range)	3 (2–7)	3 (2–11)
Primary refractory disease, n (%)[b]	9 (56)	17 (53)
Refractory to ≥2 consecutive prior LOTs, n (%)[c]	12 (75)	22 (69)
Prior CAR T therapy, n (%)	5 (31)	12 (38)

[a]DLBCL include double-hit and triple-hit lymphoma: pauses/delays: double hit: n=1 (6%) and triple hit: (n=1) 6%; discontinuation: double hit: n=1 (3%); triple hit: 0. [b]Disease refractory to frontline anti-lymphoma therapy. [c]Disease progression or stable disease as best response or disease progression within 6 months after therapy completion.
CAR T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; LOT, line of therapy; NA, not applicable; SLL, small lymphocytic lymphoma.

- **Patients in CR who had treatment pauses/delays (n=16) (Table 1):**
  - Median age was 69 years (range, 20–83)
  - 15/16 (94%) patients had DLBCL (*de novo*: 56%; transformed: 38%)
  - Median number of prior lines of therapy was 3 (2–7)
  - 12/16 (75%) patients were refractory to ≥2 consecutive prior lines of therapy
- **Patients in CR who permanently discontinued treatment (n=32) (Table 1):**
  - Median age was 63 years (range, 20–82)
  - 27/32 (84%) patients had DLBCL (*de novo*: 66%; transformed: 19%)
  - Median number of prior lines of therapy was 3 (2–11)
  - 22/32 (69%) patients were refractory to ≥2 consecutive prior lines of therapy

Patients with LBCL in CR who had TREATMENT PAUSES/DELAYS

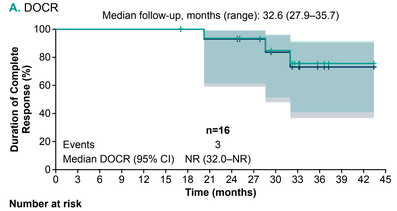
Table 2: Duration of Treatment and Most Common Reason for Pauses/Delays

	Patients in CR who had treatment pauses/dose delays >6 weeks (n=16)
Median duration of treatment hold, months (range)	2.3 (1.6–8.4)
Median duration of treatment prior to pause, months (range)	18.9 (9.3−31.7)
Most common reason for treatment pauses/delays	TEAEs (12/16)[a,b]

[a]Including COVID-19 (8/12), COVID-19 control measures and other (n=4). [b]Of these 16 patients, 15 had a post-pause lymphoma assessment scan and all 15 maintained their CR following treatment reinitiation.
CR, complete response; LBCL, large B-cell lymphoma; TEAE, treatment-emergent adverse event.

Figure 3: DOCR[a] and DOR[b] in Patients in CR Who Had Treatment Pauses/Delays

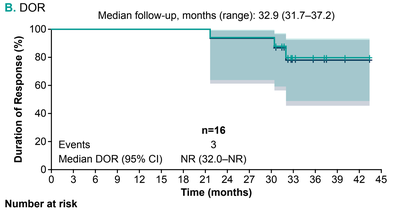
A. DOCR



Number at risk

LBCL	16	16	16	16	16	16	15	14	14	12	9	6	3	1	1	0
DLBCL	15	15	15	15	15	15	14	13	13	11	8	6	3	1	1	0

B. DOR



Number at risk

LBCL	16	16	16	16	16	16	16	16	15	15	15	6	4	2	1	0
DLBCL	15	15	15	15	15	15	15	15	14	14	14	6	4	2	1	0

[a]From time of first CR. [b]From time of first PR or CR.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOCR, duration of complete response; DOR, duration of response; LBCL, large B-cell lymphoma; NR, not reached; PR, partial response.

- In patients with LBCL in CR who had treatment pauses/delays, both DOCR and DOR were NR (range, 32.0–NR) (**Figure 3**)

Patients with LBCL in CR who DISCONTINUED TREATMENT

Table 3: Duration of Treatment and Most Common Reason for Discontinuation

	Patients in CR who permanently discontinued treatment (n=32)
Median duration of treatment prior to discontinuation, months (range)	13.2 (2.6–35.7)
Most common reason for discontinuation	TEAEs (17/32)[a]

[a]Followed by decision to proceed with transplant (n=7), other reasons (n=5), and patient decision to withdraw (n=2).
CR, complete response; LBCL, large B-cell lymphoma; TEAE, treatment-emergent adverse event.

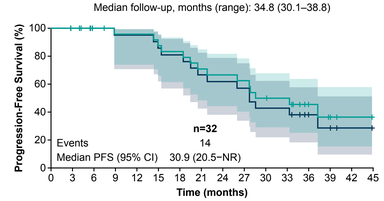
Table 4: TEAEs Leading to Treatment Discontinuation in Patients With LBCL in CR

TEAEs, n (%)[a,b]	Any grade	Grade 1-2	Grade 3-4	Grade 5
COVID-19 pneumonia	8 (25)	0	2 (6)	6 (19)
COVID-19	3 (9)	0	1 (3)	2 (6)
Pneumonia	2 (6)	0	0	2 (6)
Pneumonia bacterial	1 (3)	0	0	1 (3)
Pneumonia pseudomonal	1 (3)	0	1 (3)	0
Myocarditis	1 (3)	0	0	1 (3)

[a]Other TEAEs included anogenital warts (n=1, Grade 1-2) and lung neoplasm malignant (n=1, Grade 3-4). [b]One patient experienced two grade 5 TEAEs (COVID-19 pneumonia and myocarditis) and was counted twice.
CR, complete response; LBCL, large B-cell lymphoma; TEAE, treatment-emergent adverse event.

Figure 4: PFS in Patients in CR Who Discontinued Treatment

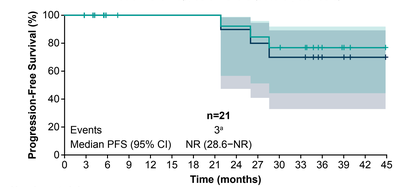
A. PFS in All Patients in CR Who Discontinued Treatment (n=32)



Number at risk

LBCL	32	30	25	23	23	21	20	17	16	15	12	11	5	3	1	0
DLBCL	27	25	21	20	20	18	17	14	13	12	9	9	4	3	1	0

B. PFS in Patients in CR Who Discontinued Treatment Excluding Those Who Experienced Grade 5 TEAEs (n=21)



Number at risk

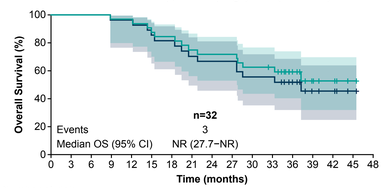
LBCL	21	19	14	13	13	13	13	13	12	11	10	9	4	3	1	0
DLBCL	16	14	10	10	10	10	10	10	9	8	7	7	3	3	1	0

[a]Two deaths and one PD.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; NR, not reached; PD, progressive disease; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

- The PFS NR shows that patients who permanently discontinued epcoritamab and did not have a fatal TEAE did not experience disease recurrence

Figure 5: OS in Patients in CR Who Discontinued Treatment

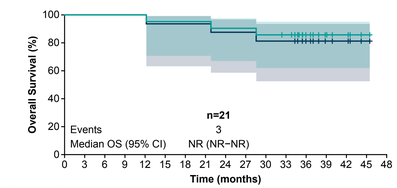
A. OS in All Patients in CR Who Discontinued Treatment (n=32)



Number at risk

LBCL	32	32	32	31	31	28	27	24	23	23	20	19	11	6	4	1	0
DLBCL	27	27	27	26	26	23	22	19	18	18	15	15	10	5	4	1	0

B. OS in Patients in CR Who Discontinued Treatment Excluding Those Who Experienced Grade 5 TEAEs (n=21)



Number at risk

LBCL	21	21	21	21	21	20	20	20	19	19	18	17	10	6	4	1	0
DLBCL	16	16	16	16	16	15	15	15	14	14	13	13	9	5	4	1	0

CR, complete response; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; NR, not reached; OS, overall survival.

- The median time-to-next treatment (95% CI) was NR (13.5–NR) in patients with LBCL in CR who discontinued treatment (n=32). Three events were reported (one death and two initiations of new anti-lymphoma therapy)
- Patients who were in CR and permanently discontinued treatment continued to derive sustained clinical benefit from epcoritamab upon resolution of infection events (**Figures 4 and 5**)