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Updated Results From EPCORE NHL-6: Phase 2 Study of Subcutaneous Epcoritamab as Outpatient Treatment for 2L+ Relapsed/Refractory Diffuse Large B-Cell Lymphoma (R/R DLBCL)

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OBJECTIVE

- To assess whether epcoritamab can be safely monitored in the outpatient setting for patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) across US academic and community sites

CONCLUSIONS

- Patients with R/R DLBCL were successfully administered epcoritamab, monitored in the outpatient setting, and managed inpatient as needed for cytokine release syndrome (CRS)
- Most patients (92% [81/88]) received the first full dose in the outpatient setting; of these, only 13.6% (11/81) were admitted for the management of CRS during the first full dosing period
- Overall response rate was 62% and the complete response rate was 42% in patients with ≥ 1 prior lines of therapy

BACKGROUND

- Immune effector cell therapies such as bispecific antibodies are associated with adverse events (AEs), including cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS)[1]
  - Management of these AEs often requires hospitalization and inpatient monitoring[2]
- Outpatient therapies have the potential to decrease treatment costs and increase patient access, especially in community treatment settings[3]
- Epcoritamab is the only subcutaneous CD3×CD20 bispecific antibody approved for patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL)[4-7]
- The EPCORE NHL-6 trial investigated the feasibility to dose and monitor patients in the outpatient setting for the first full dose
- Initial results from the EPCORE NHL-6 trial (NCT05451810) demonstrated the feasibility of treating and monitoring patients in an outpatient setting following the first dose of epcoritamab[8]
- Here we present updated safety and efficacy data from patients with 2L+ DLBCL treated with epcoritamab monotherapy in the EPCORE NHL-6 (NCT05451810) trial

METHODS

Study Design: EPCORE NHL-6 (NCT05451810)

R/R DLBCL key inclusion criteria:

- Adults ≥ 18 years
- R/R DLBCL[a,b]
  - DLBCL, NOS (de novo or transformed from FL or MZL)
  - HGBCL double-hit or triple-hit lymphoma DLBCL (with *MYC* and *BCL-2* and/or *BCL-6* translocations)
  - FLBL
- R/R disease and ≥ 1 prior line of therapy, including ≥ 1 anti-CD20 monoclonal antibody-containing therapy
- Failed prior ASCT or ineligible for ASCT

Data cutoff: January 15, 2025
Median follow-up: 7.6 months

Epcoritamab: Dose escalation and dose expansion (28-day cycle)

Agent	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10+
Epcoritamab	**Step-up dosing (SUD):** D1: SUD1 (0.16 mg) D8: SUD2 (0.8 mg) D15, D22: full dose (48 mg)	QW full dose (48 mg)		Q2W full dose (48 mg)						Q4W full dose (48 mg)

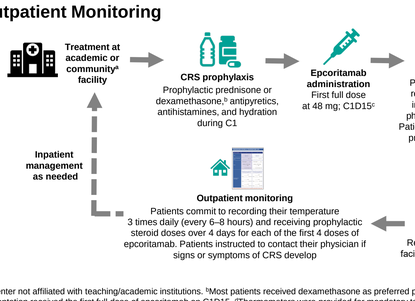
Mandatory CRS prophylaxis
- Administered during C1
- Corticosteroid equivalent to dexamethasone (preferred) 15 mg IV or oral, administered on D1–4, D8–11, D15–18, and D22–25
- Other premedications included diphenhydramine and acetaminophen, administered prior to each epcoritamab dose on D1, D8, D15, and D22 of C1
- Administer 2–3 L of oral fluids during the 24 hours prior to epcoritamab, 500 mL isotonic IV fluids immediately before treatment, and 2–3 L of oral fluids during the 24 hour after treatment; hold antihypertensive medications for 24 hours prior to each epcoritamab treatment

Primary endpoints
- Percentage of patients who experienced grade ≥ 3 events of
  - CRS
  - ICANS
  - Neurotoxicity

Key secondary endpoints
- Investigator-assessed ORR and CRR
- TEAEs

[a]According to the 5th edition of WHO classification of hematolymphoid tumors. [b]Based on most recent representative pathology report.
ASCT, autologous stem cell transplantation; C, cycle; CRR, complete response rate; CRS, cytokine release syndrome; D, day; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; FLBL, follicular large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; IV, intravenous; MZL, mantle zone lymphoma; NOS, not otherwise specified; ORR, overall response rate; QW, once weekly; R/R, relapsed/refractory; SUD, step up dose; TEAE, treatment-emergent adverse event; WHO, World Health Organization.

Outpatient Monitoring



[a]A center not affiliated with teaching/academic institutions. [b]Most patients received dexamethasone as preferred prophylaxis for CRS. [c]All patients in this presentation received the first full dose of epcoritamab on C1D15. [d]Thermometers were provided for mandatory temperature checks, and blood pressure cuff and pulse oximeter were provided for optional blood pressure and oxygen saturation checks in C1.
C, cycle; CRS, cytokine release syndrome; CTLS, clinical tumor lysis syndrome; D, day; ICANS, immune effector cell–associated neurotoxicity syndrome.

RESULTS

Table 1. Baseline Characteristics

Characteristic	2L Patients (n = 42)	3L+ Patients (n = 50)	Overall (N = 92)
Median age, years (range)	74.0 (37-87)	64.5 (28-86)	69.0 (28-87)
< 65	11 (26.2)	25 (50.0)	36 (39.1)
65 to < 75	11 (26.2)	14 (28.0)	25 (27.2)
≥ 75	20 (47.6)	11 (22.0)	31 (33.7)
Female, n (%)	15 (35.7)	24 (48.0)	39 (42.4)
Ann Arbor stage, n (%)			
I	5 (11.9)	3 (6.0)	8 (8.7)
II	4 (9.5)	4 (8.0)	8 (8.7)
III	8 (19.0)	11 (22.0)	19 (20.7)
IV	25 (59.5)	32 (64.0)	57 (62.0)
DLBCL type, n (%)			
De novo	38 (90.5)	35 (70.0)	73 (79.3)
Transformed	4 (9.5)	15 (30.0)	19 (20.7)
Double-hit lymphoma	7 (16.7)	9 (18.0)	16 (17.4)
Triple-hit lymphoma	2 (4.8)	2 (4.0)	4 (4.3)
ECOG performance status, n (%)			
0	19 (45.2)	20 (40.0)	39 (42.4)
1	16 (38.1)	28 (56.0)	44 (47.8)
2	7 (16.7)	2 (4.0)	9 (9.8)
IPI, n (%)			
0–2	21 (50.0)	22 (44.0)	43 (46.7)
≥ 3	21 (50.0)	26 (52.0)	47 (51.1)
Bulky disease by investigator at baseline, n (%)			
< 7 cm	33 (78.6)	37 (74.0)	70 (76.1)
7–10 cm	6 (14.3)	6 (12.0)	12 (13.0)
> 10 cm	3 (7.1)	7 (14.0)	10 (10.9)

2L, second line; 3L+, third line and beyond; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group.

Table 2. Treatment History and Prior Systemic Therapies

Characteristic	2L Patients (n = 42)	3L+ Patients (n = 50)	Overall (N = 92)
Number of prior lines of anticancer therapy, median (range)	1.0 (1-1)	3.0 (2-7)	2.0 (1-7)
Prior lines of anticancer therapy, n (%)			
1	42 (100)	0	42 (45.7)
2	0	19 (38.0)	19 (20.7)
3	0	17 (34.0)	17 (18.5)
≥ 4	0	14 (28.0)	14 (15.2)
Time from last prior anticancer therapy to first epcoritamab dose, median (range), months	6.6 (1-207)	4.1 (0-79)	4.3 (0-207)
Prior CAR T therapy, n (%)	0	22 (44.0)	22 (23.9)
Refractory to prior CAR T therapy	0	15 (30.0)	15 (16.3)
Prior stem cell transplant, ASCT, n (%)	1 (2.4)	6 (12.0)	7 (7.6)
Patients refractory to first line anticancer therapy,[a] n (%)	26 (61.9)	30 (60.0)	56 (60.9)
No response	11 (26.2)	16 (32.0)	27 (29.3)
Relapsed within 6 months after therapy completion	15 (35.7)	14 (28.0)	29 (31.5)

[a]Patients were considered refractory if they did not respond to the prior treatment (stable disease or progressive disease) or initially responded (partial response or above) and progressed during therapy or < 6 months after completion of therapy.
2L, second line; 3L+, third line and beyond; ASCT, autologous stem cell transplant; CAR T, chimeric antigen receptor T-cell.

Table 3. Treatment Exposure and Disposition

	Overall (N = 92)
Median study follow-up (95% CI), months	7.6 (6.0, 9.2)
Epcoritamab exposure	
Duration, median (range), day	114.0 (8-717)
Number of cycles, median (range), n	4.5 (1-27)
Ongoing epcoritamab treatment, n (%)	46 (50.0)
Discontinued epcoritamab treatment, n (%)	46 (50.0)
AE	11 (12.0)
Disease progression	27 (29.3)
Withdrawal by patient	2 (2.2)
COVID-19 infection	1 (1.1)
Other	5 (5.4)

AE, adverse event; CI, confidence interval.

- All patients were in the US
- Overall, 51 (55.4%) patients were treated at a US academic site and 41 (44.6%) were treated at a community site

Table 4. CRS Events Were Primarily Low Grade and All Resolved

	2L Patients (n = 42)	3L+ Patients (n = 50)	Overall (N = 92)
≥ 1 CRS event, n (%)	18 (42.9)	19 (38.0)	37 (40.2)
Grade 1	8 (19.0)	12 (24.0)	20 (21.7)
Grade 2	9 (21.4)	6 (12.0)	15 (16.3)
Grade ≥ 3	1 (2.4)	1 (2.0)	2 (2.2)
Median time to CRS onset from first full dose (range), hours	23.2 (7.7-226.4)	32.2 (11.9-165.1)	24.8 (7.7-226.4)
CRS resolution, n (%)	18 (100)	19 (100)	37 (100)
Median time to resolution (range), days	2.0 (1-7)	3.0 (1-24)	2.0 (1-24)
CRS interventions, n (%)			
Tocilizumab	11 (61.1)	8 (42.1)	19 (51.4)
Corticosteroids	8 (44.4)	7 (36.8)	15 (40.5)
CRS leading to treatment discontinuation	0	0	0

CRS, cytokine release syndrome.

Figure 1. CRS Events by Dose

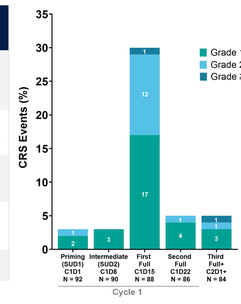
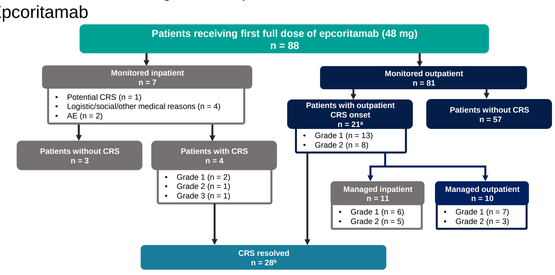


Figure 2. CRS Monitoring and Hospitalizations For the First Full Dose of Epcoritamab



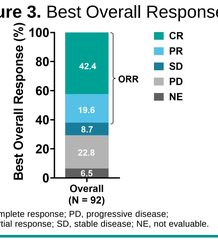
[a]Of the 81 patients who were monitored outpatient, 24 patients had CRS: 21 had outpatient onset of CRS and 3 were admitted for reasons other than CRS and had CRS inpatient. [b]Patients who had CRS after the first full dose: 4 patients monitored inpatient and 24 patients monitored outpatient.
AE, adverse event; CRS, cytokine release syndrome.

Table 5. Low Incidence and Grade of ICANS and CTLS

	2L Patients (n = 42)	3L+ Patients (n = 50)	Overall (N = 92)
ICANS, any grade, n (%)	3 (7.1)	4 (8.0)	7 (7.6)
Grade 1	1 (2.4)	3 (6.0)	4 (4.3)
Grade 2	1 (2.4)	1 (2.0)	2 (2.2)
Grade ≥ 3	1 (2.4)	0	1 (1.1)
Time to onset of first ICANS event from start of treatment (C1D1), median (range), days	25 (15-73)	26 (16-66)	25 (15-73)
ICANS resolution, n (%)[a]	3 (100)	4 (100)	7 (100)
Time to resolution, median (range), days	3 (1-15)	3 (1-6)	3 (1-15)
ICANS leading to epcoritamab discontinuation, n (%)	0	0	0
CTLS[a]	0	1 (2.0)	1 (1.1)

CTLS, clinical tumor lysis syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome.
[a]A non-serious treatment-emergent adverse event grade 3 CTLS (graded per NCI-CTCAE v5.0) was reported in 1 (1.1%) patient, which was not considered treatment-related. Based on review of laboratory data, the patient did not meet Howard's criteria for laboratory TLS. The event of CTLS was resolved and did not lead to dose interruption or treatment discontinuation.

Figure 3. Best Overall Response



- Median follow-up for 2L patients (N = 42) was 5.8 months (95% CI: 3.3, 7.2)
  - The ORR was 64.3% (95% CI: 48.0%, 78.4%); CR was 47.6% and PR was 16.7%
- Median follow-up for 3L+ patients (N = 50) was 10.8 months (95% CI: 8.2, 14.8)
  - The ORR was 60.0% (95% CI: 45.2%, 73.6%); CR was 38.0% and PR was 22.0%

CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; NE, not evaluable.

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