ABCL-404

Epcoritamab + R-ICE in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma Eligible For Autologous Stem Cell Transplantation: EPCORE NHL-2

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OBJECTIVE

- To report the efficacy and safety results for epcoritamab in combination with R-ICE in patients with R/R DLBCL eligible for ASCT from the NHL-2 trial

CONCLUSIONS

- Epcoritamab + R-ICE demonstrated high overall (87%) and CR (65%) rates in 2L+ patients with R/R DLBCL eligible for ASCT
  - Response rates were consistently high across subgroups, including in patients with disease progression ≤12 months of 1L therapy
- Most patients (65%) completed epcoritamab + R-ICE combination treatment and proceeded to ASCT
- Safety was manageable, with no discontinuations of epcoritamab due to AEs
  - CRS was low-grade, with predictable onset, and all events resolved
- The results of epcoritamab combined with R-ICE in R/R DLBCL continue to show that adding epcoritamab to CIT increases the proportion of patients who respond to treatment and proceed to ASCT, a curative therapy

BACKGROUND

- Approximately 50% of patients with R/R DLBCL are refractory to salvage CIT, limiting transplant eligibility and leading to poor outcomes[1]
  - R-ICE as salvage therapy resulted in an ORR of 64% and a CR rate of 36%[2]
- There is a critical need for effective regimens that increase CR rates, improving transplant eligibility and enabling more patients to undergo ASCT
- Epcoritamab is a subcutaneous CD3×CD20 T cell-engaging bispecific antibody that induces potent T cell-mediated killing of malignant CD20$^+$ B cells
- Epcoritamab + R-DHAX/C salvage therapy has shown high CR rates (69%) and high ASCT rates (55%) in patients with R/R DLBCL[3,4]

EPCORE® NHL-2 STUDY DESIGN

Epcoritamab SC 48 mg + R-ICE
R-ICE up to 3 cycles and epcoritamab until ASCT or progression

	Cycle length: 21 days				*Cycle length: 28 days*	
Agent	**C1**	**C2**	**C3**	**C4**	**C5–9[b]**	**C10+[b]**
Epcoritamab SC 48 mg	QW[a]	QW	QW	QW	Q2W	Q4W
Rituximab[b]	D1	D1	D1			
Ifosfamide IV 5 g/m²/24h	D2	D2	D2			
Carboplatin IV AUC = 5 mg/mL × min	D2	D2	D2			
Etoposide IV 100 mg/m²	D1–3	D1–3	D1–3			

Key inclusion criteria:

- R/R CD20$^+$ DLBCL
  - DLBCL, NOS
  - Double-hit or triple-hit DLBCL
  - FL grade 3B
  - T-cell/histiocyte DLBCL
- Relapsed or refractory to ≥1 prior LOT
- Eligible for R-ICE and HDT-ASCT
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Primary endpoint:
Investigator-assessed ORR per Lugano criteria[5,c]

Key secondary endpoints:
CR rate, DOR, DOCR, PFS, OS, MRD-negativity rate, and safety/tolerability

Data cutoff: 18 Dec 2024

ClinicalTrials.gov: NCT04663347.
[a]Patients received epcoritamab in weekly dosing of 2 step-up doses (0.16 mg; 0.8 mg) before the first full dose. Corticosteroid prophylaxis was used to mitigate CRS, and protocol-mandated hospitalization was required for 24 hours after the first full dose. [b]Dose per local guidelines. [c]Tumor response was evaluated by FDG PET-CT obtained at 9, 18, 24 weeks, and every 24 weeks thereafter until disease progression.

Acknowledgments

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Abbreviations

AE, adverse event; ASCT, autologous stem cell transplantation; AUC, area under the curve; C, cycle; CAR T, chimeric antigen receptor T-cell therapy; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; D, day; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HDT, high-dose therapy; ICANS, immune effector cell-associated neurotoxicity syndrome; IV, intravenous; LOT, line of treatment; MRI, magnetic resonance imaging; NOS, not otherwise specified; ORR; overall response rate; OS, overall survival; PD, progressive disease; PR, partial response; R-DHAX/C, rituximab, dexamethasone, cytarabine, and oxaliplatin or carboplatin; R-ICE, rituximab, ifosfamide, carboplatin, and etoposide; R/R, relapsed/refractory; SC, subcutaneous; SD, stable disease; TEAE, treatment-emergent adverse event.

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RESULTS

Baseline Characteristics and Treatment History

Baseline characteristics	N=31
Median age, years (range)	62 (39–77)
Male sex at birth, n (%)	17 (55)
Race, n (%)	
White	22 (71)
Asian	1 (3)
Black or African American	0
Other	1 (3)
Not reported	7 (23)
ECOG PS, n (%)	
0	14 (45)
1	17 (55)
Ann Arbor stage, n (%)	
I/II	12 (39)
III/IV	19 (61)
Bulky disease (≥7 cm), n (%)[a]	13 (42)
Double hit/triple hit per central lab, n/N[b]	2/10
Median time from diagnosis to first dose, months (range)	10 (1–75)
Median prior LOTs, (range)	1 (1–3)
1 prior LOT, n (%)	25 (81)
2 prior LOT, n (%)	5 (16)
3 prior LOT, n (%)	1 (3)
Primary refractory, n (%)[c]	15 (48)
Progressed within 12 months of 1L therapy, n (%)	20 (65)
Progressed >12 months of 1L therapy, n (%)	11 (35)
Refractory to anti-CD20, n (%)	17 (55)

[a]Bulky disease was classified by largest diameter of any lesion. [b]Double hit/triple hit status was not assessed in 21 (68%) patients. [c]Primary refractory disease was defined as being refractory to 1L antilymphoma therapy.

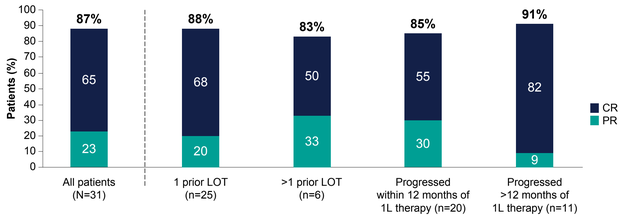
Patient Disposition

	N=31
Median follow-up, months (range)	11 (6–15)
Completed treatment and moved to ASCT, n (%)[a]	20 (65)
Remained on epcoritamab, n (%)	3 (10)
Discontinued treatment, n (%)	8 (26)
PD[b]	6 (19)
AE	0
Other[c]	2 (6)

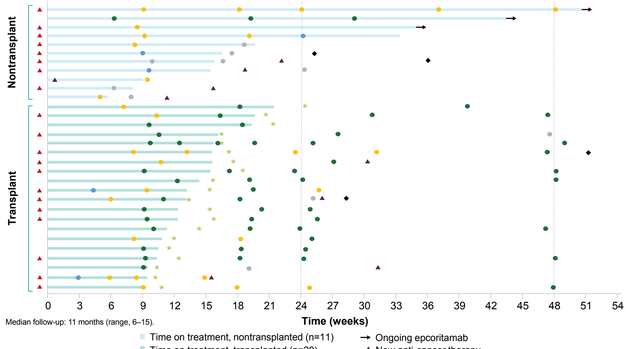
[a]Completed treatment and moved to ASCT indicates that the patient completed epcoritamab + R-ICE and went on to receive transplant. [b]Four patients with PD proceeded to subsequent therapies: 3 to CAR T cell therapy, 1 to a subsequent trial. [c]One patient proceeded to allo SCT and 1 to radiotherapy followed by CAR T cell therapy.

- The median number of treatment cycles initiated was 4 (range, 2–14) for epcoritamab and 3 (2–3) for R-ICE
- Median relative dose intensity remained high throughout 3 treatment cycles: ≥78% and 80% for epcoritamab and R-ICE, respectively

High Response Rates Overall and Across Subgroups



Most Patients Had a CR and Proceeded to HDT-ASCT

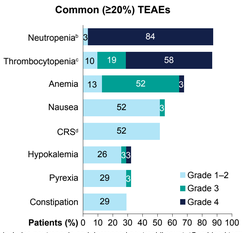


Median follow-up: 11 months (range, 6–15).

- 20 patients completed treatment and received ASCT
  - Prior to transplant, 14 were in CR and 6 in PR
  - 5 PRs deepened to CRs after ASCT
- At 6 months:
  - 81% of CRs were ongoing
  - 74% of patients were progression free
  - 100% of patients were alive

Safety Was Manageable

	N=31
Any grade TEAE, n (%)	31 (100)
Grade 3/4	29 (94)
Grade 5	0
Serious TEAE, n (%)	18 (58)
TEAE leading to trial drug discontinuation, n (%)	3 (10)
TEAE leading to epcoritamab discontinuation	0
TEAE leading to dose delay, n (%)	23 (74)
TEAE leading to epcoritamab dose delay[a]	22 (71)

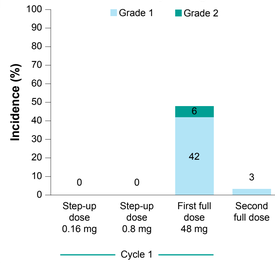


[a]Most common reasons for dose delay were thrombocytopenia and neutropenia (n=11 each). [b]Combined term includes neutropenia and decreased neutrophil count. [c]Combined term includes thrombocytopenia and decreased platelet count. [d]Corticosteroid prophylaxis to mitigate CRS, and protocol-mandated hospitalization for 24 hours after the first full dose.

- Infections occurred in 18 (58%) patients
  - Five (16%) patients had serious infections: bacterial arthritis, cystitis, febrile neutropenia, pneumonia, and septic shock (1 each)
- Febrile neutropenia occurred in 4 (13%) patients; all events resolved
- A grade 1 ICANS event occurred, which resolved in 2 days without treatment
- No clinical tumor lysis syndrome events were reported

CRS was Low Grade and Predictable

	N=31
CRS, n (%)[a]	16 (52)
Grade 1	13 (42)
Grade 2	3 (10)
Grade 3/4	0
Median time to first CRS onset, days (range)	17 (15–42)
Treated with tocilizumab, n/n (%)	5/16 (31)
CRS resolution, n/n (%)	16/16 (100)
Median time to resolution, days (range)	2 (1–8)
Leading to epcoritamab discontinuation, n (%)	0



[a]Graded by Lee et al. 2019 criteria[6].

- CRS occurred predominantly during C1

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