ABCL-272

Epcoritamab + R-DHAX/C Induces Deep, Durable Responses in Transplant-Eligible Patients With Relapsed or Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL), Including High-Risk Disease

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OBJECTIVE

- To evaluate safety and efficacy of epcoritamab in combination with R-DHAX/C with longer follow-up in patients with R/R DLBCL eligible for HDT-ASCT, including high-risk patients

CONCLUSIONS

- With longer follow-up and new high-risk subgroup analyses, the efficacy and feasibility of epcoritamab + R-DHAX/C in ASCT-eligible DLBCL continue to provide confidence in further exploring curative-intent regimens with epcoritamab as an emerging alternative to CAR T therapy
- High rates of response were reported and CRs were durable
  - ORR: 76%; CR rate: 69%
  - An estimated 74% of complete responders remained in CR at 24 mo
- The safety profile was manageable and remained consistent with previous reports
- These results support future evaluation of epcoritamab + R-DHAX/C in ASCT-eligible DLBCL

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Abbreviations

AE, adverse event; ASCT, autologous stem cell transplant; AUC, area under the curve; C, cycle; CAR T therapy, chimeric antigen receptor T-cell therapy; CIT, chemoimmunotherapy; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; CTLS, clinical tumor lysis syndrome; d, day(s); DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; G, grade; h, hour(s); HDT, high dose therapy; HGBCL, high grade B-cell lymphoma; ICANS, immune effector cell–associated neurotoxicity syndrome; IV, intravenous; LBCL, large B-cell lymphoma; LYRIC, Lymphoma Response to Immunomodulatory Therapy Criteria; min, minute(s); mo, month(s); MRI, magnetic resonance imaging; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; PR, partial response; PS, performance status; QW, every week; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; R-DHAX/C, rituximab, dexamethasone, cytarabine, and carboplatin or oxaliplatin; R/R, relapsed or refractory; SC, subcutaneous; SD, stable disease; SOC, standard of care; SUD, step-up dose; TEAE, treatment-emergent adverse event; wk, week(s); y, year(s).

Disclosures

Abrisqueta: AbbVie, AstraZeneca, BMS, Janssen: Consultancy, Speakers Bureau; **Falchi:** AbbVie, Genentech: Consultancy, Honoraria, Membership on an Entity's Board of Directors or Advisory Committees, Research Funding; Ecor1mmune, Genmab, Roche: Consultancy, Honoraria, Research Funding; Kaplan: CME Presentation: Projects in Knowledge; Memorial Sloan Kettering Cancer Center: Current Employment; Sanofi: Honoraria; Taylor & Francis: Journal Editor; ADC Therapeutics, Ipsen, Seagen: Membership on an Entity's Board of Directors or Advisory Committees; BeiGene, Innate: Research Funding; Nijland: Janssen: Consultancy, Honoraria, Speakers Bureau; Roche: Consultancy, Honoraria, Membership on an Entity's Board of Directors or Advisory Committees, Speakers Bureau; **de Vos:** AbbVie: Current Employment; **Karimi:** AbbVie, AOC Therapeutics: Consulting or Advisory Role; RichterForemost: Travel Expenses; AbbVie, AstraZeneca, LillyCoJazz, Merck, RichterForemost, Servier: Research Funding; **Cordoba:** AbbVie, Janssen, AstraZeneca, Kite, BMS, Gentrisgt, Roche, Takeda, Kyowa Kirin, BeiGene, Lilly: Consultancy; AbbVie, Janssen, AstraZeneca, Kite, BMS, Roche, Takeda: Speakers Bureau; Pfizer: Research Funding.

BACKGROUND

- For patients with R/R DLBCL, salvage CIT followed by consolidation with HDT and ASCT is potentially curative[1]
  - Among patients who undergo ASCT, ~50% have long-term remission[1]
  - Many patients (40%–60%), especially those with primary refractory disease, do not have an adequate response to salvage CIT and thus are unable to proceed to HDT-ASCT, leading to very poor outcomes[1-4]
  - Some CAR T therapies are approved for LBCL refractory to or that relapsed within 12 months of first-line CIT but may not be appropriate for all patients due to eligibility, required bridging therapy, manufacturing time, and limited accessibility (eg, cost, availability, location)[5-8]
  - A need exists for better off-the-shelf treatment options that improve the rate and depth of response to salvage CIT, enabling more patients to potentially be cured
- Epcoritamab, a subcutaneously administered CD3xCD20 bispecific antibody approved for the treatment of adults with different types of R/R LBCL and FL after ≥2 lines of systemic therapy, has been shown to be safe and efficacious in combination with standard treatments, including rituximab and chemotherapies[9-12]

STUDY DESIGN: EPCORE® NHL-2 Arm 4

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R-DHAX/C in adults with R/R DLBCL who are eligible for transplant

Key inclusion criteria

- R/R CD20+ DLBCL
  - DLBCL, NOS
  - "Double-hit" or "triple-hit" DLBCL[a]
  - FL grade 3B
  - T-cell/histiocyte-rich DLBCL
- Eligible for R-DHAX/C and HDT-ASCT
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Dose escalation, n=8

Step-up dosing[b]

Epcoritamab (SC)
24 mg (n=3) or 48 mg (n=5)
QW C1–4, Q2W C5–9, Q4W C10+*
+ R-DHAX/C
C1–3

Expansion, n=21

Step-up dosing[b]

Epcoritamab (SC)
48 mg
QW C1–4, Q2W C5–9, Q4W C10+*
+ R-DHAX/C
C1–3

Primary objectives: DLTs/Safety and tolerability
Key secondary objective: Antitumor activity

Primary endpoint: ORR per Lugano criteria[c]
***Epcoritamab treatment until HDT-ASCT or PD (whichever is earlier)**

Data cutoff: January 31, 2024
Median follow-up: 27.7 mo

R-DHAX/C regimen in C1–3, 21 d each: rituximab 375 mg/m^2 IV Q3W; dexamethasone 40 mg/d IV or orally on D1–4; cytarabine 2 g/m^2 IV repeated after 12 h Q3W; carboplatin AUC = 5 mg/mL x min (Calvert formula) or oxaliplatin 100 mg/m^2 IV Q3W. Cycle 4 was 21 d. Cycles 5+ were 28 d. [a]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [b]SUD 1: 0.16 mg; SUD 2: 0.8 mg. Corticosteroid prophylaxis was used in C1 to mitigate CRS. [c]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until PD. ClinicalTrials.gov: NCT04663347. EudraCT: 2020-000845-15.

RESULTS

Baseline Characteristics and Prior Treatments

Characteristic	N=29
Median age, y (range)	58 (28–75)
Male, n (%)	24 (83)
Ann Arbor stage, n (%)	
II–III	9 (31)
IV	20 (69)
Transformed from indolent lymphoma, n (%)	11 (38)
ECOG PS, n (%)	
0	11 (38)
1	18 (62)
Median time from diagnosis to first dose, mo (range)	10.8 (0.3–54.1)
Median number of prior lines of therapy (range)	1 (1–3)
Prior CAR T therapy, n (%)	3 (10)
Primary refractory[a] disease, n (%)	18 (62)
Progressed within 12 mo of initial therapy, n (%)	24 (83)
Relapsed[b] after last line of therapy, n (%)	12 (41)

[a]Refractory indicates no response or disease progression within 6 mo after therapy. [b]Relapsed indicates disease progression >6 mo after therapy.

Patient Disposition and Exposure

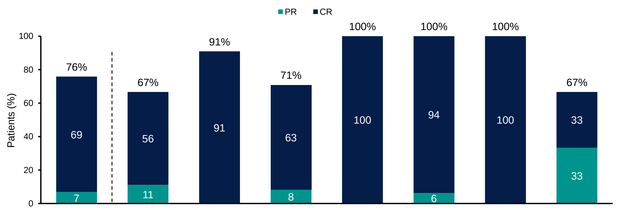
	N=29
Median follow-up (range), mo	27.7 (2.0+ to 33.8)
Ongoing treatment with epcoritamab monotherapy, n (%)	2 (7)
Discontinued treatment, n (%)	27 (93)
Proceeded to transplant	16 (55)
PD	6 (21)
AE[a]	3 (10)
Withdrawal by patient[b]	1 (3)
Other[c]	1 (3)

Symbol '+' indicates a censored value. [a]AEs that led to treatment discontinuation were ICANS, Guillain-Barré syndrome, and pneumonia. [b]Patient requested to stop treatment after reaching CR. [c]Biopsy of target lesion confirmed PD and treatment was discontinued per investigator.

- Median relative dose intensity of SOC ranged from 87% to 100%

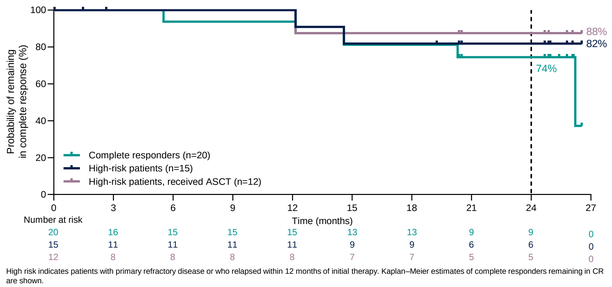
Efficacy Results

Response Rates Were High Regardless of High-Risk Status



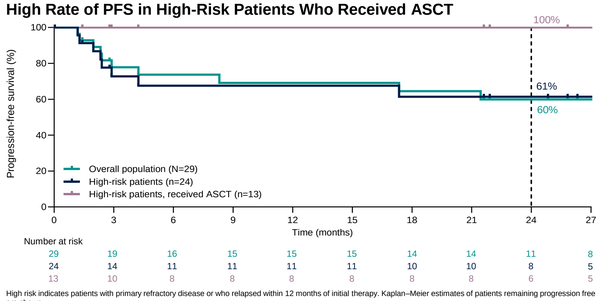
- Overall, median time to response was 1.4 mo (range, 1.2–4.2) and median time to CR was 1.5 mo (range, 1.2–15.5)

Complete Responses Were Durable



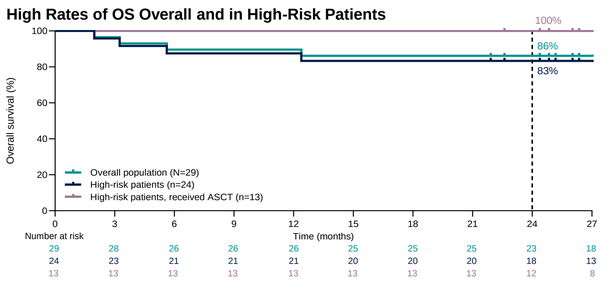
High risk indicates patients with primary refractory disease or who relapsed within 12 months of initial therapy. Kaplan–Meier estimates of complete responders remaining in CR are shown.

High Rate of PFS in High-Risk Patients Who Received ASCT



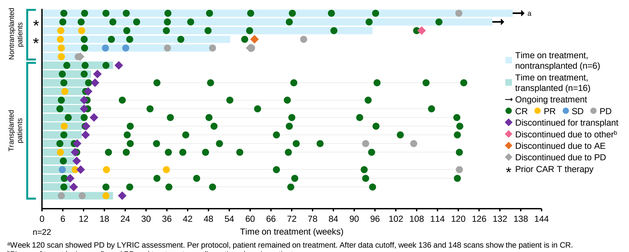
High risk indicates patients with primary refractory disease or who relapsed within 12 months of initial therapy. Kaplan–Meier estimates of patients remaining progression free are shown.

High Rates of OS Overall and in High-Risk Patients



High risk indicates patients with primary refractory disease or who relapsed within 12 months of initial therapy. Kaplan–Meier estimates of patients remaining alive are shown.

Most Patients Had a CR and Proceeded to HDT-ASCT

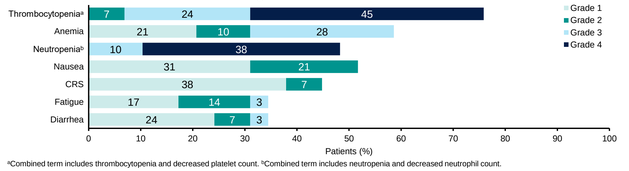


[a]Week 120 scan showed PD by LYRIC assessment. Per protocol, patient remained on treatment. After data cutoff, week 136 and 148 scans show the patient is in CR. [b]Biopsy of target lesion confirmed PD and treatment was discontinued per investigator.

- 12 (75%) of 16 patients who proceeded to HDT-ASCT remained in remission as of data cutoff

Safety Profile

Common (>30%) Treatment-Emergent Adverse Events



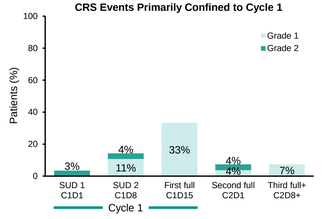
[a]Combined term includes thrombocytopenia and decreased platelet count. [b]Combined term includes neutropenia and decreased neutrophil count.

- Febrile neutropenia was reported in 5 patients (17%; all G3)
- 11 patients had TEAEs that led to R-DHAX/C dose modification; 3 patients discontinued R-DHAX/C due to TEAEs
  - TEAEs that led to discontinuation of R-DHAX/C were anemia, decreased neutrophil count, decreased platelet count, and streptococcal endocarditis (n=1), Guillain-Barré syndrome (n=1), and lower respiratory tract infection, pneumonia, and thrombocytopenia (n=1)
- 1 patient had ICANS (G2), with confusional state as a symptom
  - ICANS resolved; the patient discontinued epcoritamab treatment
- No patients experienced CTLS and there were no fatal TEAEs

All CRS Events Were Low Grade and Resolved

	N=29
CRS, n (%)[a]	13 (45)
Grade 1	11 (38)
Grade 2	2 (7)
Grade 3–5	**0**
Median time to onset after first full dose, d (range)	2 (2–2)
Treated with tocilizumab, n (%)	2 (7)
Leading to epcoritamab discontinuation, n (%)	**0**
CRS resolution, n/n (%)	**13/13 (100)**
Median time to resolution, d (range)[b]	2 (1–7)

[a]Graded by Lee et al 2019 criteria.[13] [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.



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