# Subcutaneous epcoritamab with gemcitabine + oxaliplatin (GemOx) induced high response rates in patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) ineligible for autologous stem cell transplant (ASCT)


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## Objectives

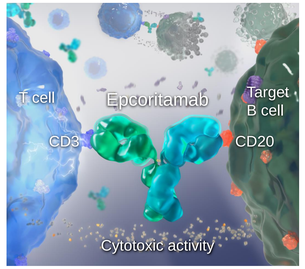
- The EPCORE NHL-2 trial (phase 1/2; NCT04663347) is evaluating epcoritamab combined with standard of care therapies in patients with B-cell NHL
- To present initial data from arm 5, which is investigating epcoritamab + GemOx in patients with R/R DLBCL who are ineligible for ASCT

## Conclusions

- Epcoritamab + GemOx showed encouraging responses in this high-risk, refractory DLBCL population
  - ORR 92%; CMR 60%; PMR 32%
  - CMR rate appears higher than in recent GemOx studies
- Epcoritamab + GemOx had no new safety signals
  - CRS was mostly low grade; all cases resolved
  - One ICANS event (grade 3), resolved
- These initial data warrant further clinical study of epcoritamab + GemOx in this population


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## Background




- Patients with R/R DLBCL remain a challenge to treat; ASCT is the standard of care for eligible patients, but 60–70% of patients are ineligible due to lack of response to salvage therapy, failure to mobilize stem cells, age, comorbidities, or other patient or disease characteristics[1,2]
- Recent studies demonstrate moderate efficacy of GemOx in this setting with CR rate 30–33%, median PFS ~5 months, and especially poor outcomes (CR rate <10%) in patients with prior therapy response <12 months[3,4]; novel treatment options are needed
- Epcoritamab (DuoBody®-CD3xCD20) is a subcutaneously administered bispecific antibody that binds to CD3 on T cells and CD20 on B cells, which induces effective T-cell–mediated killing of CD20+ malignant B cells[5,6]
- Epcoritamab showed substantial antitumor activity and manageable safety in patients with heavily pretreated B-cell NHL in the dose-escalation portion of the first-in-human phase 1/2 trial[7]
- Epcoritamab is well suited for combination therapy due to its mechanism of action and toxicity profile, distinct from GemOx[8]

## Study Design: EPCORE NHL-2 Arm 5

**Arm 5 of EPCORE NHL-2, a phase 1b/2, open-label, multicenter trial, is evaluating the safety and antitumor activity of SC epcoritamab + GemOx for 4 cycles of 28 days, followed by epcoritamab monotherapy until disease progression, in adults with R/R DLBCL ineligible for ASCT[a]**

**Key inclusion criteria**
- R/R CD20+ DLBCL[b]
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - "Double-" or "triple-hit" DLBCL[c]
  - FL grade 3B
- Eligible for GemOx
- Ineligible for ASCT or prior ASCT failure
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

**Dose escalation, n=6** → **Expansion, n=20**

**Step-up dosing**
**Epcoritamab (SC) 24 mg (n=3) or 48 mg (n=3)**
QW C1–3,
Q2W C4–9,
Q4W C10+
**+ GemOx**
C1–4

**Step-up dosing**
**Epcoritamab (SC) 48 mg**
QW C1–3,
Q2W C4–9,
Q4W C10+
**+ GemOx**
C1–4
C = 28 d
GemOx QZW

**Data cutoff: March 25, 2022**
**Median follow-up: 9.2 mo**

**Primary objectives:** DLT/Safety and tolerability
**Key secondary objective:** Antitumor activity[d]

**Primary objective:** Antitumor activity[d]
**Treatment until disease progression**

[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[7] to mitigate CRS. Epcoritamab was administered in 28-d cycles as shown. GemOx regimen: gemcitabine 1000 mg/m$^2$ IV QZW; oxaliplatin 100 mg/m$^2$ IV QZW. [b]De novo or histologically transformed from FL or nodal marginal zone lymphoma; based on World Health Organization 2016 classification.[9] [c]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [d]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. Lugano criteria and LYRIC were used to assess response. AEs were graded by CTCAE v5.0; CRS was evaluated by Lee et al[10] criteria. ClinicalTrials.gov Identifier: NCT04663347.

## Results

### Baseline Demographics, Characteristics, and Prior Therapies

| Characteristic | Total N=26 |
|---|---|
| Median age, y (range) | 71 (47–87) |
| Male, n (%) | 13 (50) |
| Ann Arbor stage, n (%)[a] | |
| II | 3 (12) |
| III | 6 (23) |
| IV | 16 (62) |
| DLBCL subtype, n (%) | |
| De novo | 19 (73) |
| Transformed | 7 (27) |
| IPI score, n (%)[b] | |
| 0–2 | 7 (27) |
| 3 | 5 (19) |
| 4–5 | 10 (38) |
| Median time from diagnosis to first dose, mo (range) | 12 (1–76) |
| Median number of prior lines of therapy (range) | 2 (1–13) |
| 1 prior line, n (%) | 10 (38) |
| 2 prior lines, n (%) | 7 (27) |
| ≥3 prior lines, n (%) | 9 (35) |
| Prior ASCT, n (%) | 3 (12) |
| Prior CAR T, n (%) | 3 (12) |
| Primary refractory disease, n (%)[c] | 16 (62) |
| Refractory to last line of therapy, n (%)[c] | 19 (73) |
| Relapsed within 6 mo after therapy | 12 (46) |
| Refractory to ≥2 consecutive lines of therapy, n (%)[c] | 10 (38) |

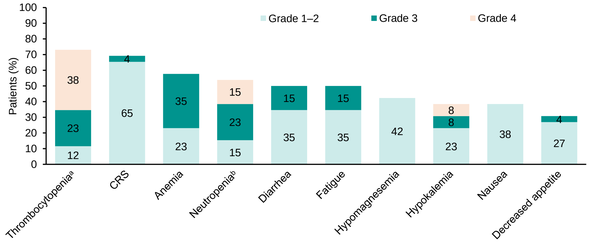
Data cutoff: March 25, 2022. [a]Ann Arbor stage was missing in 1 patient. [b]IPI score was unknown in 4 patients. [c]Refractory indicates no response or relapse within 6 mo after therapy.

### Follow-Up and Patient Disposition

| | Total N=26 |
|---|---|
| Median follow-up, mo (range)[a] | 9.2 (1–15) |
| Ongoing treatment, n (%) | 11 (42) |
| Discontinued treatment, n (%) | 15 (58) |
| PD | 6 (23) |
| AE[b] | 5 (19) |
| Death[c] | 3 (12) |
| Withdrawal by patient | 1 (4) |

Data cutoff: March 25, 2022. [a]Median is Kaplan–Meier estimate. [b]AEs included worsening normal pressure hydrocephalus, *Escherichia* sepsis, subarachnoid hemorrhage, and enterocolitis (not related to epcoritamab) and small intestine perforation (related to epcoritamab). [c]Reasons for death included acute hepatitis/multiorgan failure, COVID-19 pneumonia, and unknown cause.

### Treatment-Emergent Adverse Events (≥30%) by Grade




Data cutoff: March 25, 2022. [a]Combined term includes thrombocytopenia and platelet count decreased. [b]Combined term includes neutropenia and neutrophil count decreased.

- One patient (4%) had ICANS (grade 3)
- One patient (4%) had febrile neutropenia (grade 3)
- Infection rate was 62% for any grade and 31% for grade ≥3
- No clinical tumor lysis syndrome events
- Seven patients (27%) had grade 5 AEs: 2 were related to epcoritamab in patients with transformed DLBCL who achieved a CMR (small bowel perforation and acute hepatitis/multiorgan failure)

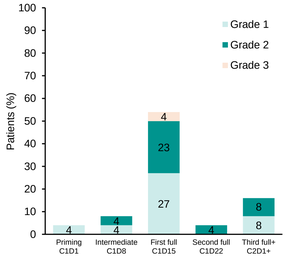
### CRS Graded by Lee et al[10] 2019 Criteria

| | Total N=26 |
|---|---|
| CRS, n (%) | 18 (69) |
| Grade 1 | 7 (27) |
| Grade 2 | 10 (38) |
| Grade 3 | 1 (4) |
| CRS resolution, n (%) | 18 (100) |
| Median time to resolution, d (range)[a] | 2 (1–9) |
| CRS leading to treatment discontinuation, n (%) | 0 |
| Tocilizumab use, n (%) | 5 (19) |

Data cutoff: March 25, 2022. [a]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS; range is defined by shortest and longest CRS duration.

- CRS was mostly low grade and all events resolved

### CRS Events by Dosing Period




Data cutoff: March 25, 2022. Priming dose: n=26; intermediate dose: n=26; first full dose: n=26; second full dose: n=24; third full dose and later: n=24.

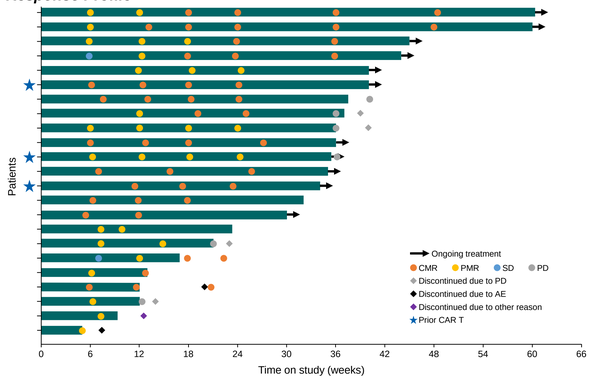
- CRS occurrence was predictable
- Most cases occurred following the first full dose with a median time to onset of 2 days (range, 1–5)

### Best Overall Responses

| Response, n (%)[a] | Total n=25 |
|---|---|
| Overall response | 23 (92) |
| CMR | 15 (60) |
| PMR | 8 (32) |
| Stable disease | 0 |
| Progressive disease | 0 |
| No response assessment[b] | 2 (8) |

Data cutoff: March 25, 2022. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose. [b]Two patients died within 60 d of first dose without assessment.

### Response Profile




Data cutoff: March 25, 2022. Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD.

- Median duration of CMR was 7.5 mo
- At 6 months, an estimated 76% of complete responders remained in CMR


**References**

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