ABCL-517

Phase 3 Trial of Subcutaneous Epcoritamab + R-CHOP Versus R-CHOP in Patients With Newly Diagnosed Diffuse Large B-cell Lymphoma (DLBCL): EPCORE DLBCL-2

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OBJECTIVE

Evaluate epcoritamab in combination with R-CHOP vs R-CHOP in patients with newly diagnosed diffuse large B-cell lymphoma (DLBCL)

STUDY OVERVIEW

NCT05578976

- **P3** Ongoing phase 3
- Multicenter ~379 sites
- International 34 countries
- Open-label
- ~ 900 patients are planned for enrollment

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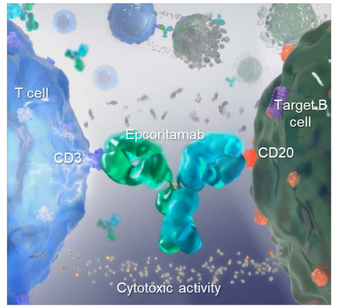
BACKGROUND

- In patients with DLBCL, the standard first-line therapy consists of chemo-immunotherapy with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP).[1] There remains a high unmet need in patients with an International Prognostic Index (IPI) 2–5[2] treated with R-CHOP
  - Approximately 20–35% of patients with IPI 2–5 have primary refractory disease or relapse within 2 years of R-CHOP therapy, requiring additional treatment
  - The 5-year progression-free survival (PFS) estimate was 67.0%, 58.4%, and 45.8% for IPI 2, 3, and 4–5, respectively[2]
- Epcoritamab is a subcutaneously administered, bispecific antibody that binds CD3 on T lymphocytes and CD20 on B cells, inducing potent and selective T-cell–mediated killing of malignant CD20+ B cells[3] (**Figure 1**)
- Epcoritamab received FDA approval for adults with R/R DLBCL not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after ≥2L of systemic therapy
- This study will evaluate whether epcoritamab in combination with standard of care therapy (R-CHOP) is safe and effective in patients with newly diagnosed DLBCL

- In the phase 1/2 EPCORE NHL-2 trial (NCT04663347) in high-risk (IPI ≥3) patients with newly diagnosed DLBCL (N=47, including 11 with double-hit/triple-hit DLBCL), epcoritamab 48 mg combined with R-CHOP showed promising efficacy and a manageable safety profile in high-risk patients with IPI 3–5[4]
  - Overall response rate: 100%
  - Complete metabolic response rate: 76%
    - CMR rate in patients with double-hit/triple-hit DLBCL: 82%
  - Cytokine release syndrome events: 57%, mostly low-grade (grade 1–2; 2% grade 3) and occurred mostly after the first full dose (cycle 1, day 15); all cases resolved

Encouraging data, as well as the distinct mechanisms of action of epcoritamab and R-CHOP, support further evaluation of this combination for its potential to improve clinical outcomes in patients with newly diagnosed DLBCL

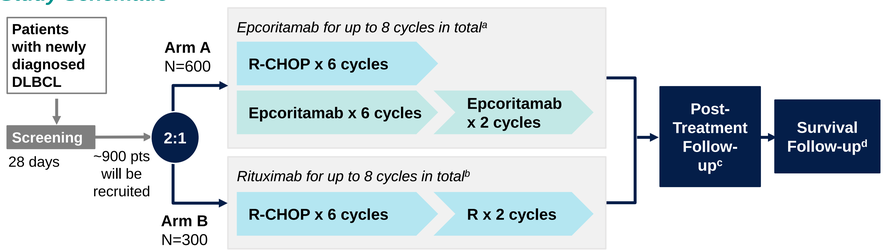
Figure 1: Epcoritamab Mechanism of Action



STUDY DESIGN: EPCORE DLBCL-2 PHASE 3 TRIAL (NCT05578976)

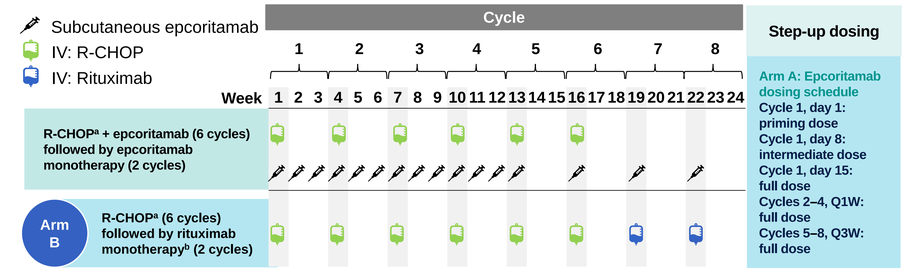
Epcoritamab in Combination With R-CHOP vs R-CHOP Alone in Patients With Newly Diagnosed DLBCL

Study Schematic



[a]Patients randomized to arm A will receive R-CHOP in combination with epcoritamab for 6 cycles followed by 2 additional cycles of epcoritamab.
[b]Patients randomized to arm B will receive R-CHOP for 6 cycles followed by 2 additional cycles of rituximab.
[c]Patients who complete treatment or prematurely discontinue the assigned treatment arm for reasons other than disease progression will proceed to post-treatment follow-up until 5 years after first patient first dose.
[d]Patients who display disease progression or refuse post-treatment follow-up visits will proceed to survival follow-up.

Dosing Schedule



Step-up dosing

Arm A: Epcoritamab dosing schedule
Cycle 1, day 1: priming dose
Cycle 1, day 8: intermediate dose
Cycle 1, day 15: full dose
Cycles 2–4, Q1W: full dose
Cycles 5–8, Q3W: full dose

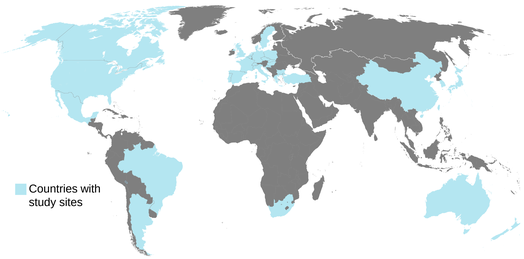
[a]R-CHOP regimen: rituximab 375 mg/m^2 IV on day 1;cyclophosphamide 750 mg/m^2 IV on day 1; doxorubicin 50 mg/m^2 IV on day 1; vincristine 1.4 mg/m^2 IV on day 1; and prednisone 100 mg/d orally on days 1–5.
[b]Rituximab monotherapy: 375 mg/m^2 IV on day 1.
IV, intravenous; Q1W, once weekly; Q3W, once every 3 weeks.

Key Inclusion Criteria[a]

- Age ≥18 and <80 years old
- Newly diagnosed, histologically confirmed CD20+ DLBCL per the 2016 revision of WHO classification of lymphoid neoplasms
  - DLBCL, NOS
  - High-grade B-cell lymphoma with *MYC* and *BCL-2* and/or *BCL-6* rearrangement
  - T-cell/histiocyte-rich LBCL
  - Epstein-Barr virus–positive DLBCL, NOS
  - FL grade 3b
- IPI ≥2 (patients with IPI 2 not to exceed ~30% of total patients)
- ECOG PS 0–2
- At least 1 measurable disease site
- No history of prior systemic antilymphoma therapy for DLBCL

[a]Not a comprehensive list of eligibility criteria.
ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; IPI, International Prognostic Index; NOS, not otherwise specified.

Enrollment



- Enrollment began in 2023 globally at ~379 study locations across 34 countries

Study Endpoints

Primary endpoint

Progression-free survival (PFS) in patients with IPI 3–5 as assessed by independent review committee per Lugano criteria

Key secondary efficacy endpoints

- PFS in patients with IPI 2–5
- Event-free survival
- Complete metabolic response
- Overall survival
- Minimal residual disease negativity

Safety endpoints

- Incidence and severity of treatment-emergent adverse events (TEAEs), serious AEs
- Incidence and severity of AEs of special interest
  - Cytokine release syndrome
  - Immune cell–associated neurotoxicity syndrome
  - Clinical tumor lysis syndrome
- Incidence and severity of changes in laboratory values
- Incidence of dose interruptions, delays, and discontinuations

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