ABCL-275

Epcoritamab + GemOx Induces Deep, Durable Responses in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma (R/R DLBCL): Updated Results From EPCORE NL-2

Raul Cordoba, MD, PhD,[1] Judit Jørgensen, MD, PhD,[2] David Belada, MD, PhD,[3] Régis Costello, MD, PhD,[4] Marek Trněný, MD,[5] Umberto Vitolo, MD,[6] David John Lewis, MD,[7] Yasmin H. Karimi, MD,[8] Anna Sureda, MD, PhD,[9] Marc André, MD, PhD,[10] Björn E. Wahlin, MD, PhD,[11] Pieternella J. Lugtenburg, MD, PhD,[12] Tony Jiang, MD, PhD,[13] Aqeel Abbas, MS,[14] Yaou Song, MS,[14] Malene Risum, MD, PhD,[15] Joshua D. Brody, MD[16]

[1]Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [2]Aarhus University Hospital, Aarhus, Denmark; [3]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [4]Assistance Publique – Hôpitaux de Marseille (AP-HM), Marseille, France; [5]First Department of Medicine, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; [6]Candiolo Cancer Institute, FPO-IRCCS, Candiolo (Turin), Italy; [7]University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth, UK; [8]University of Michigan Division of Hematology/Oncology, Ann Arbor, MI, USA; [9]Clinical Hematology Department, Institut Català d'Oncologia – L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [10]CHU UCL Namur, Yvoir, Belgium; [11]Karolinska Institutet, Stockholm, Sweden; [12]On behalf of the Lunenburg Lymphoma Phase I/II Consortium HOVON/LLPC, Erasmus MC Cancer Institute, University Medical Center, Department of Hematology, Rotterdam, Netherlands; [13]AbbVie, North Chicago, IL, USA; [14]Genmab, Plainsboro, NJ, USA; [15]Genmab, Copenhagen, Denmark; [16]Icahn School of Medicine at Mount Sinai, New York, NY, USA

OBJECTIVE

- To evaluate the long-term safety and efficacy of epcoritamab + GemOx in a larger cohort of patients with transplant-ineligible R/R DLBCL, with a focus on complete responders and 2L patients

CONCLUSIONS

- Epcoritamab in combination with GemOx continues to yield deep and durable responses in ASCT-ineligible R/R DLBCL
  - ORR 85%, CR rate 61% (by IRC)
  - Complete responders had sustained CRs, as well as favorable PFS and OS
- High CR rates were observed across prespecified subgroups
  - Higher CR rates were seen in 2L and CAR T–naive patients and patients with non–primary refractory disease (CR rates, 68%–74%)
  - These results indicate that earlier use of epcoritamab + GemOx may further improve outcomes
- These encouraging results and the benefit–risk profile of this combination therapy support the combinability of epcoritamab in R/R DLBCL

Acknowledgments

On behalf of all the authors, we thank the patients, study investigators, and site personnel for their participation in this study. We thank Phillip Chen and Liwei Wang for statistical analysis support. This study was funded by Genmab A/S and AbbVie. Medical writing and graphical support were provided by Wenwen L. Weegerly, PhD, of Precision Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and funded by Genmab. These results were previously presented in part at the American Society of Clinical Oncology Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.

References

1. Sehn LH, Salles G. *N Engl J Med*. 2021;384:842-58; 2. Crump M, *et al. Blood*. 2017;130:1800-8; 3. Cazeller C, *et al. Leuk Lymphoma*. 2021;62:2161-8; 4. Garg M, *et al. Clin Lymphoma Myeloma Leuk*. 2024;24:e181-90; 5. Body JG, *et al.* ASH 2023. Abstract 3262; 6. EPKINLY [prescribing information]. Thousand Oaks, CA: AbbVie Inc.; 2024; 7. Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; 2023; 8. EPKINLY [prescribing information]. Tokyo, Japan: Genmab K.K.; 2023.

Abbreviations

2L, second line; Allo, allogeneic; ASCT, autologous stem cell transplant; C, cycle; CAR T therapy, chimeric antigen receptor T-cell therapy; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; d, day(s); DH, double-hit; DLBCL, diffuse large B-cell lymphoma; DOCR, duration of complete response; DOR, duration of response; EOI, end of induction; EOT, end of treatment; FDG, fluorodeoxyglucose; FISH, fluorescence in situ hybridization; GEMOX, gemcitabine and oxaliplatin; HGBCL, high-grade B-cell lymphoma; HL, Hodgkin's lymphoma; HR, hazard ratio; ICANS, immune effector cell–associated neurotoxicity syndrome; IPI, International Prognostic Index; IRC, independent review committee; IRF, independent review facility; LBCL, large B-cell lymphoma; mo, month(s); MOD, not otherwise specified; ORR, overall response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; pLOT, prior line(s) of therapy; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; R/R, relapsed or refractory; SC, subcutaneous; SMQ, standardized MedDRA queries; SUD, step-up dose; TEAE, treatment-emergent adverse event; TH, triple-hit; TTR, time to response; wk, week(s); y, year(s).

Disclosures

Cordoba: AbbVie, Janssen, AstraZeneca, Kite, BMS, Gilead, Roche, Takeda, Kyowa Kirin, BeiGene, Lilly. Consultancy: AbbVie, Janssen, AstraZeneca, Kite, BMS, Roche, Takeda. Speakers Bureau: Pfizer. Research Funding: **Jørgensen:** AbbVie, Gilead, Incyte, Orion, Roche, Sobi. Consultancy. **Belada:** AbbVie, BMS, Genmab, Gilead, Morphosys, Roche, Sobi, Takeda. Consultancy: AbbVie, Gilead, Janssen, Morphosys, Roche, Takeda. Honoraria: AbbVie, Recordati, Roche. Travel Expenses/Accommodations. **Costello:** There are no relationships to disclose. **Trněný:** AbbVie, Amgen, BMS, Genmab, Gilead, Incyte, Janssen, Morphosys, Novartis, Roche, Sobi, Takeda. Consultancy: AbbVie, Amgen, BMS, Gilead, Janssen, MorphoSys, Novartis, Roche, Takeda. Honoraria: AbbVie, BMS, Gilead, Janssen, Roche, Takeda. Travel Accommodations/Expenses. **Vitolo:** AbbVie, Genmab, Gilead, Incyte, Regenxbio. Advisory Board: AbbVie, Genmab, Gilead, Incyte, Regenxbio. Consultancy: AbbVie, Genmab, Gilead, Incyte, Regenxbio. Honoraria: AbbVie, Genmab, Gilead, Incyte, Regenxbio. Speakers Bureau: AbbVie, Genmab, Gilead, Incyte, Regenxbio. Travel Expenses/Accommodations: AbbVie, Genmab, Gilead, Incyte, Regenxbio. **Lewis:** AstraZeneca, Roche/Genentech. Honoraria: Research Funding. **Sureda:** Celgene, BMS, Novartis, Janssen, Kite, Amgen, Gilead, Sanofi, Kite, Monopharma Consultancy, Takeda, BMS, Novartis, Janssen, MSD, Amgen, GSK, Sanofi, Kite, Honoraria, Takeda, BMS, Novartis, Janssen, Amgen, Bluebird, Sanofi, Kite. Membership on an Entity's Board of Directors or Advisory Committees: Takeda, BMS, Roche. Travel Expenses: Takeda. Research Funding: Takeda, BMS, Novartis, Janssen, MSD, Amgen, GSK, Sanofi, Kite. Speakers Bureau. **André:** There are no relationships to disclose. **Wahlin:** Roche. Consultancy, Research Funding, Gilead. Research Funding. **Lugtenburg:** Takeda, Servier. Research Grants: BMS, Roche, Takeda, Genmab, AbbVie, Incyte, Regenxbio, Sandoz. Advisory Honoraria, Y-mAbs Therapeutics. Consultancy Honoraria. **Jiang:** AbbVie. Current Employment. **Abbas:** Genmab. Current Employment. **Song:** Genmab. Current Employment. **Risum:** Genmab. Current Employment. **Brody:** AOC Therapeutics, Epicyme, Seagen. Advisory Board: BMS, Genentech, GlaxoKlin, Merck. Research Funding.

BACKGROUND

- Patients with R/R DLBCL who are ineligible for ASCT have a poor prognosis, underscoring the need for novel, effective therapies to improve long-term outcomes[1]
  - Patients whose disease is refractory to standard salvage chemotherapy or who relapse ≤12 mo following ASCT have low response rates (ORR, 26%; CR rate, 7%) and a short median OS of only ~6 mo[2]
- Among patients who received rituximab + GemOx, the CR rate was 33%, with a median PFS of 5 mo and median OS of 10 mo[3]; older patient populations appear to have shorter median OS (~7 mo)[4]
- Low CR rates with rituximab + GemOx present an unmet need for this population[3]
- The addition of a novel agent with a distinct mechanism of action may improve long-term outcomes for patients who are ineligible for ASCT
- 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 chemotherapies[5-8]

STUDY DESIGN: EPCORE® NHL-2 Arm 5

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab SC + GemOx in adults with R/R DLBCL ineligible for ASCT

Key inclusion criteria

- R/R CD20+ DLBCL[a]
  - DLBCL, NOS
  - "Double-" or "triple-hit" DLBCL
  - FL grade 3B
  - T-cell/histiocyte-rich DLBCL
- Eligible for GemOx
- Ineligible for ASCT or prior ASCT failure
- ECOG PS 0–2
- FDG-avid disease by PET
- Adequate organ function

Data cutoff: December 15, 2023
Median follow-up (range): 13.2 mo (1.0+ to 34.6)

Treatment regimen: Concomitant epcoritamab SC 48 mg + GemOx

	Agent	C1	C2	C3	C4	C5–9	C10+ until progression[c]
	Epcoritamab SC 48 mg[b]	QW	QW	QW	Q2W	Q2W	Q4W
GemOx	Gemcitabine 1000 mg/m² IV	Q2W					
GemOx	Oxaliplatin 100 mg/m² IV	Q2W					

- **Primary objective:** Assess antitumor activity
- **Key secondary endpoints:** DOR, DOCR, TTR, PFS, OS, TEAEs

Cycles are 28 d. [a]De novo or histologically transformed from FL or nodal marginal zone lymphoma based on World Health Organization 2016 classification. [b]SUD 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. [c]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. ClinicalTrials.gov: NCT04663347. EudraCT: 2020-000845-15.

RESULTS

Baseline Characteristics and Prior Treatments

Demographics	N=103
Median age (range), y	72 (20–87)
≥75 y, n (%)	36 (35)
Male, n (%)	57 (55)
Disease Characteristics and Prior Treatments	**N=103**
ECOG PS, n (%)	
0	33 (32)
1	57 (55)
2	13 (13)
IPI, n (%)	
<3	38 (37)
≥3	65 (63)
Bulky disease,[a] n (%)	
>10 cm	20 (19)
DLBCL type,[b] n (%)	
De novo	75 (73)
Transformed	24 (23)
DH/TH by local assessment,[c] n (%)	15 (15)
DH/TH by central lab,[c] n (%)	6 (6)
Ann Arbor stage, n (%)	
I/II	22 (21)
III	18 (17)
IV	63 (61)
Median time from initial diagnosis to first dose (range), mo	13 (0.6–178)
Median time from end of last therapy to first dose (range), mo	5 (0.6–99)
Median prior lines of therapy (range)	2 (1–6)
Prior lines of therapy, n (%)	
1	39 (38)
2	27 (26)
≥3	37 (36)
Primary refractory[d] disease, n (%)	54 (52)
Refractory[d] to last systemic therapy, n (%)	72 (70)
Refractory[d] to ≥2 consecutive lines of therapy, n (%)	38 (37)
Prior ASCT, n (%)	10 (10)
Relapsed ≤12 mo after ASCT, n/n (%)	5/10 (50)
Prior CAR T therapy, n (%)	29 (28)

[a]Bulky disease per IRC assessment; 12 patients had bulky disease >10 cm per investigator assessment. [b]De novo versus transformed status of 4 patients was missing. [c]DH/TH status not assessed in 45 patients. [d]Refractory disease is defined as disease that either progressed during therapy or progressed within 6 mo of completion of therapy.

Exposure and Follow-Up

- Patients initiated a median of 8 epcoritamab treatment cycles (range, 1–37) and received a median of 22 doses (range, 2–52); all but 1 patient received the first full dose
- As of data cutoff, treatment was ongoing in 44 patients (43%)
- Reasons for treatment discontinuation among the 57% of patients who discontinued were progressive disease (31%), AEs (19%), death (3%), withdrawal by patient (3%), and maximum clinical benefit (1%)
  - The most frequent AEs leading to discontinuation were COVID-19 (n=6) and pneumonia (n=5)
  - The patient with maximum clinical benefit had a partial response and subsequently proceeded to allogeneic transplant
- Mean (SD) relative dose intensities of gemcitabine and oxaliplatin were 76% (20%) and 76% (19%), respectively

Efficacy Results

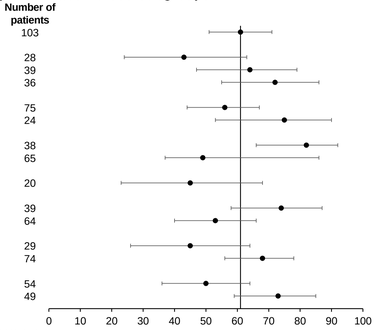
Responses Occurred Early and Rates Were High

Best Overall Response	Investigator Assessment N=103[a]	IRC Assessment N=103[b]
Overall response rate, n (%)	82 (80)	88 (85)
Complete response	60 (58)	63 (61)
Partial response	22 (21)	25 (24)
Median time to response (range), mo	1.5 (0.9–11.1)	1.5 (0.9–3.0)
Median time to complete response (range), mo	1.7 (1.3–10.7)	2.6 (1.3–22.1)

[a]Five patients were not evaluable for response per investigator. [b]Four patients were not evaluable for response per IRC.

- High concordance (90%) between investigator and IRC assessment
- By IRC assessment, median duration of response among complete responders was 25.4 mo (range, 2.2 to 31.9+)

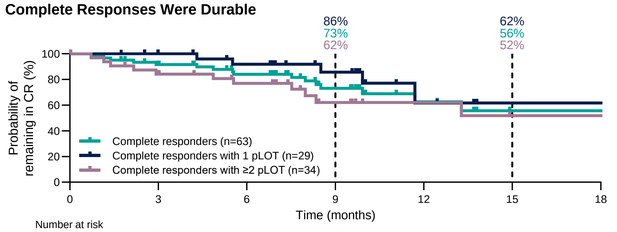
High Complete Response Rates Across Subgroups



[a]Complete response rates per IRC assessment.

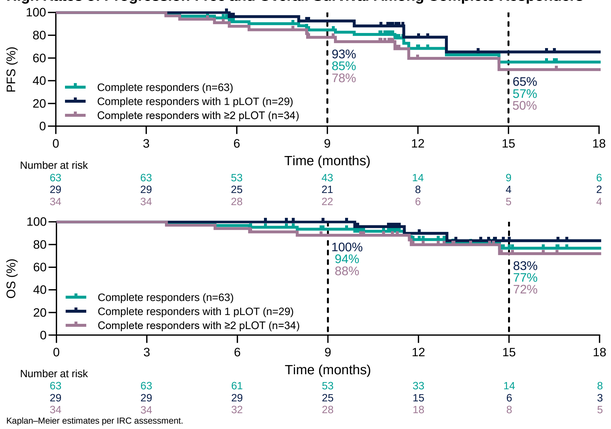
- Higher complete response rates in 2L patients indicate that earlier use of epcoritamab + GemOx may further improve outcomes

Complete Responses Were Durable



Kaplan–Meier estimates per IRC assessment.

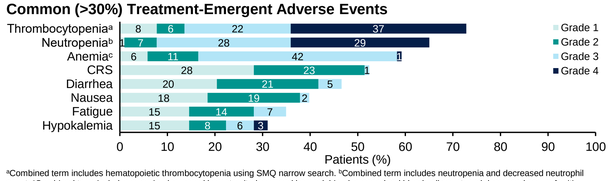
High Rates of Progression-Free and Overall Survival Among Complete Responders



Kaplan–Meier estimates per IRC assessment.

Safety Profile

Common (>30%) Treatment-Emergent Adverse Events



[a]Combined term includes hematopoietic thrombocytopenia using SMQ narrow search. [b]Combined term includes neutropenia and decreased neutrophil count. [c]Combined term includes anemia, decreased hematocrit, decreased hemoglobin, decreased red blood cell count, and decreased serum ferritin.

- 7 patients experienced febrile neutropenia
- ICANS was reported in 3 patients (grade 1–3, n=1 each); all events resolved and 1 patient discontinued treatment due to ICANS
- No clinical tumor lysis syndrome
- 13 patients had grade 5 TEAEs
  - 5 events were related to COVID-19; all patients had ≥1 risk factor for severe COVID, and 3 of the 5 patients who had grade 5 COVID had a CR

Low-Grade CRS With Predictable Timing

- CRS was primarily low grade (52% overall; 28% grade 1, 23% grade 2, 1% grade 3) and had predictable timing, with most events occurring following the first full dose (median time to onset after first full dose, 2 d)
- Overall, 24 patients (23%) received tocilizumab
- CRS events all resolved (median time to resolution, 2.5 d) and did not lead to epcoritamab discontinuation

Rate of Infections Over Time

- In the overall population, the rate of serious infections, excluding COVID-19, was higher in the first 8 weeks of the study (15%) than during subsequent 12-week time intervals until week 72 (range, 1%–10%)
- There is an increased risk of morbidity and mortality due to infections for patients with hematologic malignancies being treated with B-cell–depleting therapies

Presented at the Society of Hematologic Oncology Annual Meeting; September 4–7, 2024; Houston, TX