7523

First-line treatment (Tx) with subcutaneous (SC) epcoritamab (epco) + R-CHOP in patients (pts) with high-risk diffuse large B-cell lymphoma (DLBCL): phase 1/2 data update

Lorenzo Falchi, MD,[1]* Fritz Offner, MD, PhD,[2] David Belada, MD, PhD,[3] Joshua Brody, MD,[4] Kim M. Linton, MBChB, PhD,[5] Yasmin Karimi, MD,[6] Raul Cordoba, MD, PhD,[7] Sylvia Snauwaert, MD, PhD,[8] Aqeel Abbas, MS,[9] Liwei Wang, PhD,[9] Jun Wu, MD, MS,[10] Brian Elliott, MD,[9] Michael Roost Clausen, MD, PhD[11]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Universitair Ziekenhuis Gent, Ghent, Belgium; [3]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [4]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]The Christie NHS Foundation Trust and Manchester Cancer Research Centre, Manchester, UK; [6]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [7]Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [8]Department of Hematology, AZ Sint-Jan Hospital, Bruges, Belgium; [9]Genmab, Princeton, NJ, USA; [10]AbbVie, North Chicago, IL, USA; [11]Vejle Hospital, Vejle, Denmark

*Email address for questions: falchil@mskcc.org

Objectives

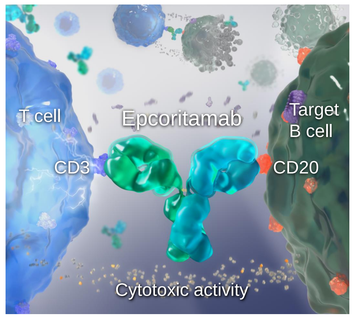
- The EPCORE NHL-2 trial (phase 1/2; NCT04663347) is evaluating epcoritamab combined with different standard of care therapies in patients with B-cell NHL
- To present data from arm 1, which is investigating epcoritamab + R-CHOP in patients with previously untreated high-risk DLBCL

Conclusions

- Epcoritamab + R-CHOP showed encouraging responses:
  - ORR 100%, CMR 77%
- Epcoritamab + R-CHOP has a manageable safety profile; no new safety signals were detected
  - CRS was predictable and generally low grade
  - All CRS events resolved
- These updated data support further exploration of epcoritamab + R-CHOP in first-line DLBCL

Presented at the American Society of Clinical Oncology Annual Meeting; June 3–7, 2022; Chicago, IL, and virtual

Background



- Patients with DLBCL, particularly those considered high/poor risk (ie, with 3–5 risk factors, based on the revised IPI), have poor outcomes with standard first-line therapy (R-CHOP), with 55% overall survival at 4 years[1,2]
  - A significant unmet need remains in this population, and new approaches are needed
- Epcoritamab (DuoBody®-CD3xCD20) is a subcutaneously administered (SC) bispecific antibody that binds to CD3 on T cells and CD20 on B cells to induce T-cell–mediated killing of CD20+ malignant B cells[3,4]
- Epcoritamab-mediated T-cell cytotoxicity is maintained in combination with R-CHOP[3,5]
- In the dose-escalation part of the EPCORE NHL-1 phase 1/2 trial, single-agent epcoritamab had a manageable safety profile and substantial antitumor activity in patients with heavily pretreated B-cell NHL[6]
- Epcoritamab is well suited for combination therapy due to its mechanism of action, distinct from that of the components of standard of care R-CHOP[3,5,7]

Study Design: EPCORE NHL-2 Arm 1

Arm 1 of EPCORE NHL-2, a phase 1b/2, open-label, multicenter trial, is evaluating the safety and antitumor activity of SC epcoritamab + standard R-CHOP for 6 cycles of 21 days, followed by epcoritamab monotherapy for a total of 1 year, in adults with previously untreated DLBCL with high-risk features[a]

Key inclusion criteria
- Newly diagnosed CD20+ DLBCL[b]
  - DLBCL, NOS
  - T-cell/histiocyte–rich DLBCL
  - "Double-" or "triple-hit" DLBCL[c]
  - FL grade 3B
- IPI score ≥3
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Dose escalation, n=10

Step-up dosing: Epcoritamab (SC) 24 mg (n=4) or 48 mg (n=6) QW C1–4, Q3W C5–6, Q4W C7+ + R-CHOP C1–6

Expansion, n=23

Step-up dosing: Epcoritamab (SC) 48 mg QW C1–4, Q3W C5–6, Q4W C7+ + R-CHOP C1–6

Data cutoff: March 25, 2022
Median follow-up: 6.9 mo

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

Primary objective: Antitumor activity[d]
Treatment up to 1 year

[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[8] to mitigate CRS. R-CHOP regimen in C1–6, 21 d each: rituximab 375 mg/m^2 IV Q3W; cyclophosphamide 750 mg/m^2 IV Q3W; doxorubicin 50 mg/m^2 IV Q3W; vincristine 1.4 mg/m^2 IV (with a recommended maximum of 2 mg) Q3W; and prednisone 100 mg/d IV or orally on days 1–5. Subsequent cycles of epcoritamab were 28 d. [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 2014 criteria and LYRIC were used to assess response. AEs were graded by CTCAE v5.0; CRS was evaluated by Lee et al[9] criteria. ClinicalTrials.gov Identifier: NCT04663347.

Results

Baseline Demographics and Characteristics

Characteristic	Total N=33
Median age, y (range)	66 (19–82)
Male, n (%)	18 (55)
ECOG PS, n (%)	
0	13 (39)
1	16 (48)
2	4 (12)
Ann Arbor stage, n (%)	
III	7 (21)
IV	26 (79)
IPI score, n (%)[a]	
3	18 (55)
4–5	10 (30)
DLBCL subtype, n (%)	
De novo	28 (85)
Transformed	5 (15)
MYC/*BCL2*/*BCL6* rearrangements, n (%)	
Double-hit lymphoma	3 (9)
Triple-hit lymphoma	5 (15)
Median time from diagnosis to first dose, d (range)	26 (5–70)

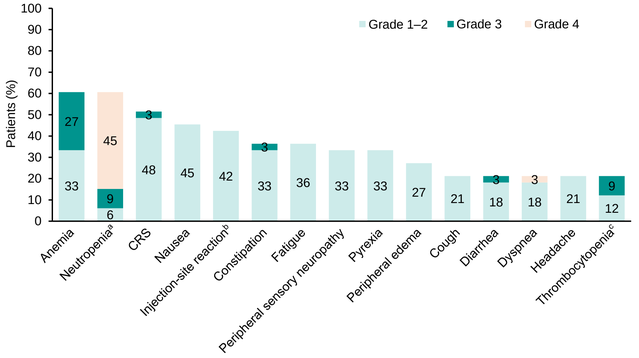
Data cutoff: March 25, 2022. [a]The 5 patients not represented all had IPI scores of ≥3.

Follow-Up and Treatment Exposure

	Total N=33
Median follow-up, mo (range)[a]	6.9 (0.8–14.7)
Ongoing treatment, n (%)	24 (73)
Discontinued treatment, n (%)	6 (18)
PD	2 (6)
AE	1 (3)
Other reason	3 (9)
Completed treatment, n (%)	3 (9)
Treatment exposure	
Median number of epcoritamab cycles initiated (range)	9 (1–15)[b]
Median duration of treatment, mo (range)	6.3 (0.6–11.5)
Patients with epcoritamab dose delay due to TEAE, n (%)	17 (52)
Patients who completed 6 cycles of R-CHOP, n (%)	30 (91)

Data cutoff: March 25, 2022. [a]Median is Kaplan–Meier estimate. [b]One patient received an extra dose due to a reprimimg cycle, causing maximum to be 15.

Treatment-Emergent Adverse Events (≥20%) by Grade



Data cutoff: March 25, 2022. [a]Combined term includes neutropenia and neutrophil count decreased; 4 patients (12%) had febrile neutropenia (grade 1–2, n=1; grade 3, n=3). [b]Combined term includes injection-site pain, pruritus, rash, reaction, and swelling. [c]Combined term includes thrombocytopenia and platelet count decreased.

- No events of clinical tumor lysis syndrome
- One patient (3%) had ICANS (grade 2), which resolved in 4 days

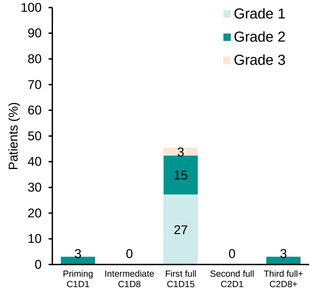
CRS Graded by Lee et al[9] 2019 Criteria

	Total N=33
CRS, n (%)	17 (52)
Grade 1	9 (27)
Grade 2	7 (21)
Grade 3	1 (3)
CRS resolution, n (%)	17 (100)
Median time to resolution, d (range)[a]	2 (1–11)
CRS leading to treatment discontinuation, n (%)	0
Tocilizumab use, n (%)	5 (15)

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; all cases resolved

CRS Events by Dosing Period



Data cutoff: March 25, 2022. Priming dose: n=33; intermediate dose: n=33; first full dose: n=33; second full dose: n=32; third full dose and later: n=32.

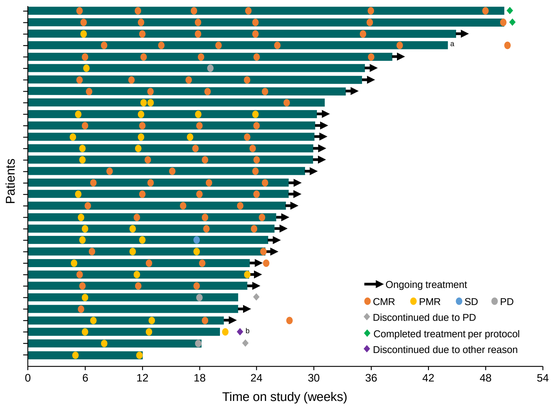
- CRS occurrence was predictable; most cases occurred following the first full dose with a median time to onset of 2 days (range, 1–4)

Best Overall Responses

Response, n (%)[a]	Total n=31
Overall response	31 (100)
CMR	24 (77)
PMR	7 (23)
Stable disease	0
Progressive disease	0

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.

Response Profile



Data cutoff: March 25, 2022. Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD. [a]This patient completed treatment per protocol. [b]Patient did not achieve CMR after completing 6 cycles of R-CHOP.

References

1. Sehn LH, et al. *Blood*. 2007;109:1857-61. **2.** Susanibar-Adaniya S, Barta SK. *Am J Hematol*. 2021;96:617-29. **3.** Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. **4.** van der Horst HJ, et al. *Blood Cancer J*. 2021;11:38. **5.** Chiu CW, et al. AACR 2021. Abstract 1574. **6.** Hutchings M, et al. *Lancet*. 2021;398:1157-69. **7.** Belada D, et al. ASH 2021. Abstract 1413. **8.** Swerdlow SH, et al. *Blood*. 2016;127:2375-90. **9.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

Acknowledgments

On behalf of all the authors, we would like to thank the patients, study investigators, and site personnel for their participation in this study. Medical writing and graphical support were provided by Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and funded by Genmab. This study was funded by Genmab A/S and AbbVie.