ABCL-429

Epcoritamab + R-CHOP in Patients With Previously Untreated (1L) High-Risk Diffuse Large B-Cell Lymphoma, Including Double-Hit/Triple-Hit Lymphoma: Updated EPCORE NHL-2 Data

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OBJECTIVE

To evaluate longer-term efficacy and safety of concomitant epcoritamab + R-CHOP in 1L high-risk DLBCL

CONCLUSIONS

Epcoritamab + R-CHOP induced a 100% overall response rate in 1L high-risk DLBCL, including in double-hit/triple-hit patients

Responses were durable; all patients remain in remission among those who completed 1 year of epcoritamab + R-CHOP

Safety was manageable with no new safety signals

These data support the ongoing phase 3 trial of epcoritamab + R-CHOP in 1L DLBCL (NCT05578976)

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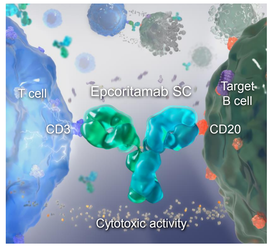
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Disclosures

Falchi: AbbVie, Genentech, Genmab, Roche: Consultancy, Research Funding; AbbVie, ADC Therapeutics, AstraZeneca, Genentech, Seagen: Advisory Board. **Clausen:** AbbVie, Janssen, Gilead, AstraZeneca, Genmab, Incyte: Consultancy. AbbVie, Janssen, Gilead, Genmab: Advisory. AbbVie, Janssen, AstraZeneca, Genmab, Roche: Travel Expenses. **Offner:** There are no relationships to disclose. **de Vos:** There are no relationships to disclose. **Brody:** ADC Therapeutics, Epizyme, Seagen: Advisory Board; BMS, Genentech, GlaxoKlin, Merck: Research Funding. **Linton:** Genmab: Member of the Epcoritamab Global Clinical Committee; AbbVie, BeiGene, BMS, Cegerni, Genmab, Roche: Consulting or Advisory Role. AbbVie, Celgene, Janssen, Roche: Speakers Bureau. **Snauwaert:** AbbVie, Janssen, Roche, Takeda: Consultancy, Honoraria, Speakers Bureau; Gilead, Kyowa Kirin, Regeneron, Roche, Otsp Pharma, Viracta: Research Funding (Paid to Institution); Celgene: Travel Expenses. **Snauwaert:** There are no relationships to disclose. **Cordoba:** AbbVie, Janssen, AstraZeneca, Kite, BMS, Genmab, Roche, Takeda, Kyowa Kirin, BeiGene, Lilly: Consultancy, AbbVie, Janssen, AstraZeneca, Kite, BMS, Roche, Takeda: Speakers Bureau. **Wu:** AbbVie: Current Employment. **Bykhovski:** Genmab: Current Employment. **Wang:** Genmab: Current Employment. **Rana:** Genmab: Current Employment. **Belada:** Genmab: Research Funding.

BACKGROUND

- R-CHOP is a standard therapy for 1L diffuse large B-cell lymphoma (DLBCL), but an unmet need remains
  - Approximately 40% of patients do not achieve cure[1]
  - High-risk patients, such as those with double-hit/triple-hit lymphoma or IPI 3–5, have a worse prognosis[1]
- Epcoritamab SC is a CD3xCD20 bispecific antibody[2-4]
  - Approved by the US FDA for the treatment of adult patients with R/R DLBCL, NOS, including DLBCL arising from indolent lymphoma, and HGBCL after ≥2L systemic therapy[5]
  - Showed encouraging efficacy in preliminary data of epcoritamab + R-CHOP in 1L DLBCL[6]
- Here we present updated results of the ongoing EPCORE NHL-2 arm 1 trial (epcoritamab + R-CHOP in 1L DLBCL)



STUDY DESIGN: EPCORE™ NHL-2 Arm 1

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R-CHOP in adults with previously untreated DLBCL[a]

Key inclusion criteria

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

Data cutoff: January 31, 2023
Median follow-up: 14.2 mo
ClinicalTrials.gov: NCT04663347

Treatment regimen: Concomitant epcoritamab SC 48 mg + R-CHOP

	Agent	C1–C4	C5–C6	C7+
	Epcoritamab SC 48 mg	QW	Q3W	Q4W Up to 1 year
R-CHOP	Rituximab IV 375 mg/m^2	Q3W		
R-CHOP	Cyclophosphamide IV 750 mg/m^2	Q3W		
R-CHOP	Doxorubicin IV 50 mg/m^2	Q3W		
R-CHOP	Vincristine[d] IV 1.4 mg/m^2	Q3W		
R-CHOP	Prednisone IV or oral 100 mg/d	D1–5 of each cycle		

Primary objective: Antitumor activity[e]

[a]Patients received epcoritamab SC with 2 step-up doses (SUD) before the first full dose and corticosteroid prophylaxis to mitigate CRS. R-CHOP was given in 21-d cycles. Subsequent cycles of epcoritamab were 28 d. [b]De novo or histologically transformed from FL or nodal marginal zone lymphoma. [c]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [d]Recommended maximum 2 mg. [e]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.

RESULTS

Baseline Characteristics

	48 mg N=47
Median age, y (range)	64 (19–82)
Male, n (%)	23 (49)
ECOG PS, n (%)	
0	15 (32)
1	26 (55)
2	6 (13)
Ann Arbor stage, n (%)	
II	1 (2)
III	9 (19)
IV	37 (79)
IPI score, n (%)	
3	33 (70)
4–5	14 (30)
DLBCL subtype, n (%)[a]	
De novo	37 (79)
Transformed	8 (17)
MYC/BCL2/BCL6 rearrangements, n (%)[b]	
Double-hit	6 (13)
Triple-hit	5 (11)
Bulky disease, n (%)	
>6 cm	27 (57)
>10 cm	16 (34)
LDH, n (%)[c]	
High	31 (66)
Normal	15 (32)
Median time from initial diagnosis to first dose, d (range)	28 (9–423[d])

Data cutoff: January 31, 2023. [a]DLBCL subtype was missing for 2 patients. [b]Three additional double-hit/triple-hit patients were identified after the data cutoff for a total of 14 (30%). Double-hit/triple-hit status was missing in 13 patients (28%). [c]LDH was missing for 1 patient. [d]The patient who received a first dose at 423 d delayed treatment due to personal preference.

Patient Disposition and Treatment Exposure

	48 mg N=47
Median follow-up, mo (range)[a]	14.2 (0.8–17.7)
Completed 1 year of treatment, n (%)	19 (40)
Ongoing treatment, n (%)	16 (34)
Discontinued treatment, n (%)[b]	12 (26)
Progressive disease	4 (9)
Adverse event[c]	3 (6)
Other[d]	5 (11)
Median epcoritamab cycles initiated (range)	11 (1–15)
Median duration of treatment, mo (range)	8.3 (0.6–13.2)

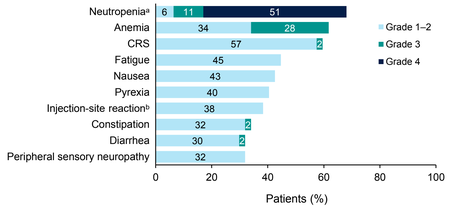
Data cutoff: January 31, 2023. [a]Median is Kaplan–Meier estimate. [b]Three patients (1 PD, 1 AE, and 1 discontinuation due to withdrawal by patient) did not complete 6C of R-CHOP. [c]AEs that led to treatment discontinuation were COVID-19 events (n=2) and heart failure (n=1). [d]Five patients discontinued treatment due to other reasons (withdrawal by patient, n=2; COVID-19 control measures, n=1; other, n=2).

Epcoritamab Did Not Affect R-CHOP Dose Intensity (C1–6)

Relative Dose Intensity, %	Rituximab	Cyclophosphamide	Doxorubicin	Vincristine
Mean (SD)	96 (6)	94 (8)	94 (8)	89 (14)
Median	98	98	97	95

Data cutoff: January 31, 2023. Relative dose intensity is actual dose intensity divided by planned dose intensity. Actual dose intensity is defined as average (full) doses taken within the treatment period for epcoritamab (mg/wk), rituximab (mg/m^2/cycle), cyclophosphamide (mg/m^2/cycle), doxorubicin (mg/m^2/cycle), and vincristine (mg/cycle).

Safety Profile of Concomitant Epcoritamab + R-CHOP

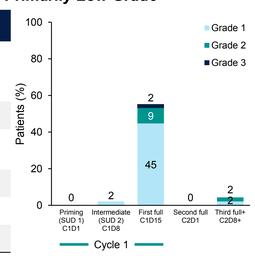


- No clinical tumor lysis syndrome events
- 6 patients (13%) had febrile neutropenia
- 2 patients (4%) experienced ICANS (G1, G2), which resolved
- 12 patients (26%) had G3+ infections; of these, 3 patients had G3–4 COVID-19[c], and 1 patient had G5 COVID-19[c]

Data cutoff: January 31, 2023. Treatment-emergent AEs with frequency >30% are shown in the graph. [a]Combined term includes neutropenia and neutrophil count decreased. [b]Combined term includes injection-site reaction, pruritus, rash, discoloration, erythema, hematoma, and pain. [c]Combined term includes COVID-19 and COVID-19 pneumonia.

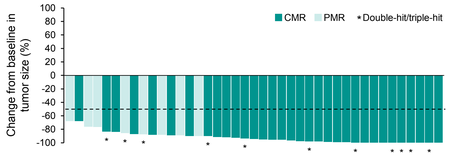
CRS Was Predictable and Primarily Low Grade[7]

	48 mg N=47
CRS, n (%)	28 (60)
Grade 1	22 (47)
Grade 2	5 (11)
Grade 3	1 (2)
CRS resolution, n/n (%)	28/28 (100)
Median time to onset from first full dose, d (range)	2 (1–7)
Median time to resolution, d (range)[a]	2 (1–12)
Treated with tocilizumab, n (%)	5 (11)
Leading to treatment discontinuation, n (%)	0



[a]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.

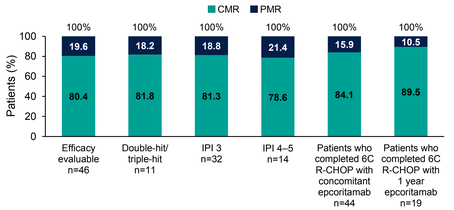
Consistent Antitumor Activity Observed



- Epcoritamab + R-CHOP induced responses across all patients, including high-risk double-hit/triple-hit patients

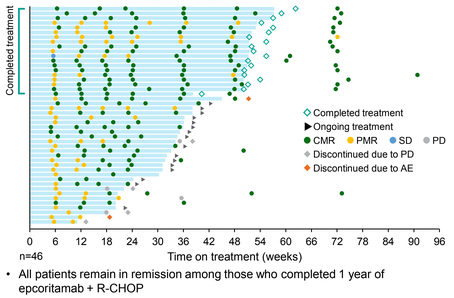
Five patients had missing postbaseline lesion data.

High Rates of Complete Response Across Subgroups



Data cutoff: January 31, 2023. Best response was 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 trial treatment prior to first assessment. One patient was not considered response evaluable because this patient withdrew consent from the trial without receiving a response evaluation.

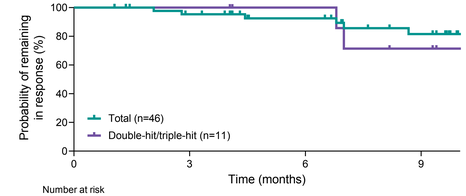
Onset and Durability of Responses



- All patients remain in remission among those who completed 1 year of epcoritamab + R-CHOP

Data cutoff: January 31, 2023.

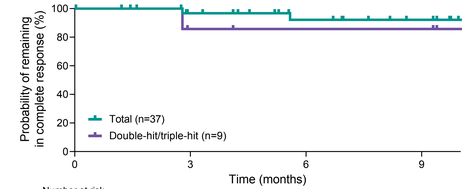
Duration of Response



- Median duration of response was not reached in the overall population

Kaplan–Meier estimated probability of remaining in response.

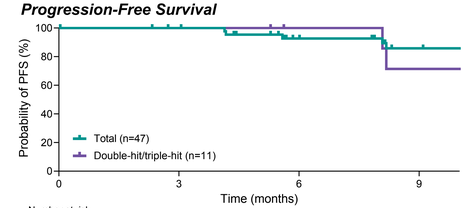
Duration of Complete Response



- Median duration of complete response was not reached in the overall population

Kaplan–Meier estimated probability of remaining in complete response.

Progression-Free Survival



- Median PFS was not reached in the overall population

Kaplan–Meier estimated probability of progression-free survival.

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