Subcutaneous epcoritamab in patients with relapsed or refractory large B-cell lymphoma (EPCORE NHL-1): pivotal results from a phase 2 study

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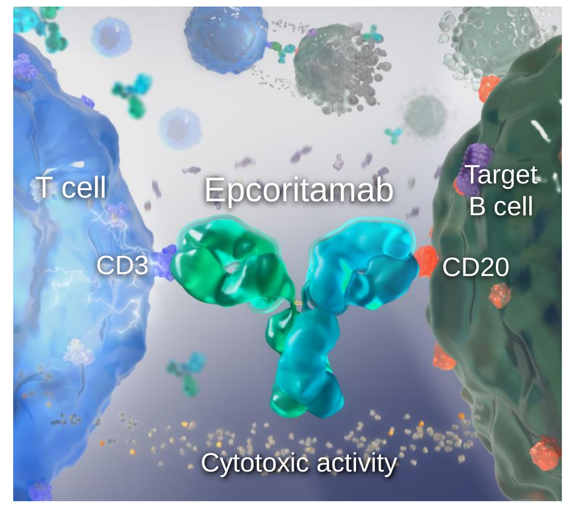
Conclusions

- Epcoritamab is a first-in-class subcutaneously administered T-cell–engaging bispecific antibody
- In this pivotal dataset, single-agent epcoritamab demonstrated:
  - High ORR (63%) and CR rate (39%)
  - Consistent responses across key subgroups
  - Deep and durable responses; median duration of response for CR patients not reached
  - A correlation between MRD negativity and PFS
- Epcoritamab is well tolerated
  - AEs, including CRS, were primarily low grade
  - CRS time of onset was predictable; events occurred early and were transient
  - Few discontinuations due to AEs

Epcoritamab is well tolerated and drives deep and durable responses in challenging-to-treat, highly refractory patients with R/R LBCL

Previously presented at the European Hematology Association Annual Congress; June 9–17, 2022; Vienna, Austria, and virtual

Epcoritamab, a Novel Subcutaneous (SC) Bispecific Antibody in Development



- Despite therapeutic advances, most relapsed or refractory (R/R) large B-cell lymphoma (LBCL) patients have a poor prognosis
- There is a need for convenient, efficacious, well-tolerated, and readily available treatment options
- In the EPCORE NHL-1 dose-escalation cohort across histologies,[1] SC epcoritamab demonstrated:
  - Notable single-agent activity with clinically meaningful overall and complete response rates
  - Manageable safety profile
- Here, we present pivotal dose-expansion results in patients with R/R LBCL

EPCORE NHL-1: LBCL Expansion Cohort

Dose escalation

B-NHL:
- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

Dose expansion data cutoff: January 31, 2022
Median follow-up: 10.7 mo

Key inclusion criteria:
- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- Prior CAR T allowed

Step-up dosing[a] → **Epcoritamab SC RP2D 48 mg** QW C1–3, Q2W C4–9, Q4W C10+ → **Treatment until PD[b,c] or unacceptable toxicity** → **LBCL Cohort N=157** DLBCL, HGBCL, PMBCL, and FL Gr3B

- To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 h in this part of the study
- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

[a]Step-up dosing (priming 0.16 mg and intermediate 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [b]Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. [c]Measurable disease with CT or MRI scan with involvement of ≥2 lesions/nodes with a long axis >1.5 cm and short axis >1.0 cm (or 1 lesion/node with a long axis >2.0 cm and short axis ≥1.0 cm) and FDG PET scan that demonstrates positive lesion(s) compatible with CT-defined (or MRI-defined) anatomical tumor sites for FDG-avid lymphomas. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

Results

Patients Were Challenging to Treat and Highly Refractory

Demographics	LBCL, N=157
Median age (range), y	64 (20–83)
<65 y, n (%)	80 (51)
65 to <75 y, n (%)	48 (31)
≥75 y, n (%)	29 (18)
ECOG PS, n (%)	
0	74 (47)
1	78 (50)
2	5 (3)
Disease Characteristics[a]	**LBCL, N=157**
Disease type, n (%)	
DLBCL	139 (89)
De novo	97/139 (70)
Transformed	40/139 (29)
Unknown	2/139 (1)
HGBCL	9 (6)
PMBCL	4 (3)
FL Gr3B	5 (3)
Prior Treatments	**LBCL, N=157**
Median time from initial diagnosis to first dose, y	1.6
Median time from end of last therapy to first dose, mo	2.4
Median prior lines of therapy (range)	3 (2–11)
≥3 Lines of therapy, n (%)	111 (71)
Primary refractory[b] disease, n (%)	96 (61)
Refractory[b] to last systemic therapy, n (%)	130 (83)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	119 (76)
Prior ASCT, n (%)	31 (20)
Prior CAR T therapy, n (%)	61 (39)
Progressed within 6 mo of CAR T therapy	46/61 (75)

[a]Double/triple-hit patients included, many with responses. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 months of completion of therapy.

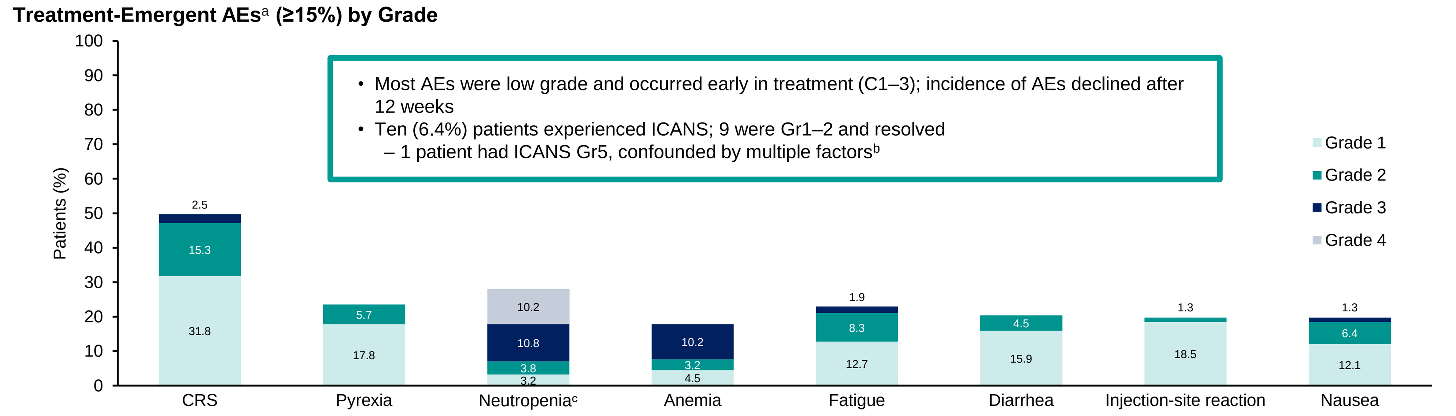
Few Discontinuations Due to AEs; 32% of Patients Remain on Treatment

Follow-up	LBCL, N=157
Median follow-up (range), mo	10.7 (0.3–17.9)
Median number of treatment cycles (range)	5 (1–20)
Ongoing treatment, n (%)	51 (32)
Discontinued treatment, n (%)	106 (68)
PD	83 (53)
AE	11 (7)
Related[a]	3 (2)
Allogeneic transplant	7 (4)
Withdrawal by patient	4 (3)
Other	1 (1)

[a]Worsening CLIPPERS, CRS/fatigue, and ICANS.

AEs Were Primarily Low Grade

Treatment-Emergent AEs[a] (≥15%) by Grade



- Most AEs were low grade and occurred early in treatment (C1–3); incidence of AEs declined after 12 weeks
- Ten (6.4%) patients experienced ICANS; 9 were Gr1–2 and resolved
  - 1 patient had ICANS Gr5, confounded by multiple factors[b]

[a]COVID incidence 4.5%. [b]Patient experienced ICANS after intermediate dose with multiple confounders, including extensive opioid use for Gr3 pancreatitis, hyperammonemia, multifocal cerebral infarcts in setting of possible microangiopathy, and tocilizumab administration. [c]Combined term includes neutropenia and decreased neutrophil count.

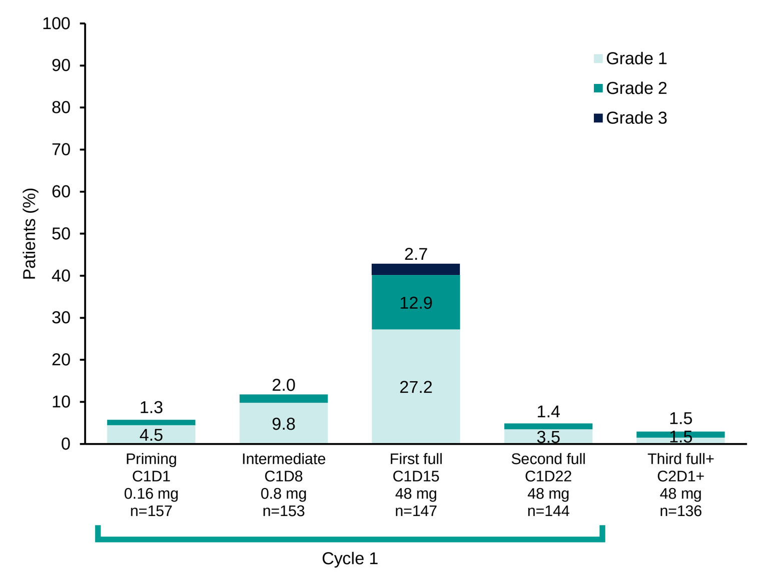
SC Administration and Step-up Dosing May Mitigate CRS

	LBCL, N=157
CRS events, n (%)[a]	78 (49.7)
Grade 1	**50 (31.8)**
Grade 2	24 (15.3)
Grade 3	4 (2.5)
Median time to onset from first full dose, d	**0.8 (20 h)**
CRS resolution, n (%)	77 (98.7)
Median time to resolution from first full dose, d	**2 (48 h)**
Treated with tocilizumab, n (%)	22 (14.0)
Treated with corticosteroids, n (%)	16 (10.2)
Leading to treatment discontinuation, n (%)	**1 (0.6)**

[a]Graded by Lee et al. 2019 criteria.

CRS was primarily low grade and predictable: most events occurred following the first full dose

CRS Events by Dosing Period



High Response Rates Observed

Best Overall Response by IRC, n (%)[a]	LBCL, N=157
Overall response	**99 (63)** [95% CI: 55–71]
Complete response	**61 (39)** [95% CI: 31–47]
Partial response	38 (24)
Stable disease	5 (3)
Progressive disease	37 (24)

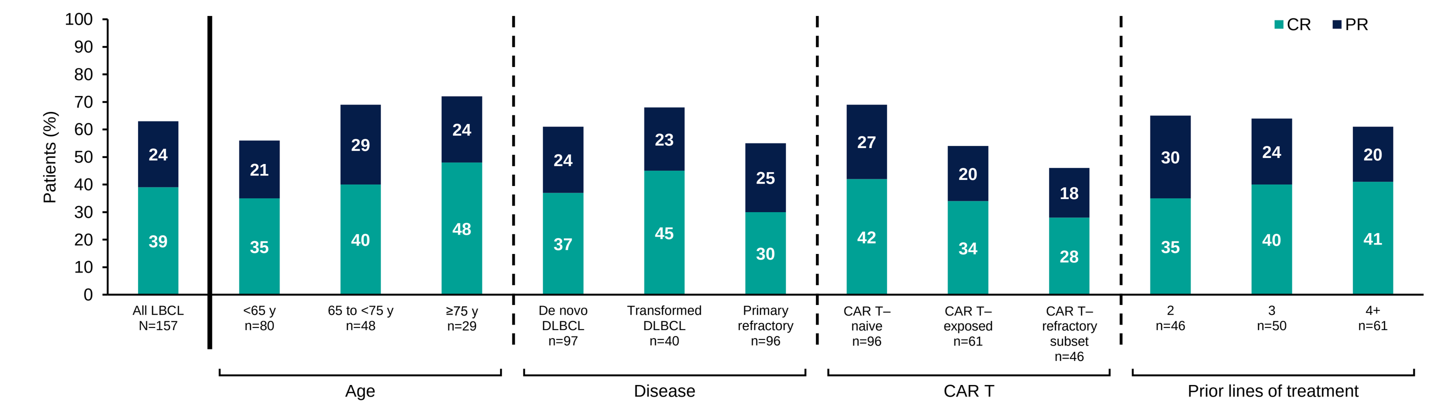
[a]Based on Lugano criteria.

Epcoritamab Induced Deep Responses in R/R LBCL



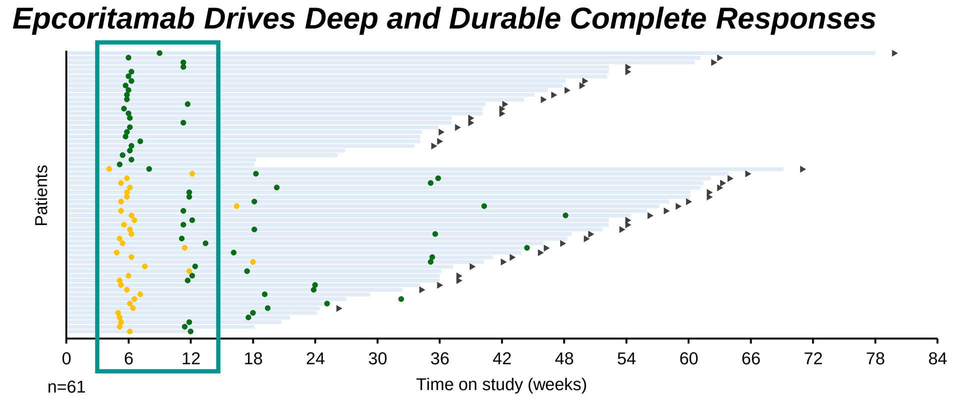
Based on IRC assessment and Lugano criteria.

Deep Responses Consistent Across Key Subgroups



Based on IRC assessment and Lugano criteria.

Epcoritamab Drives Deep and Durable Complete Responses



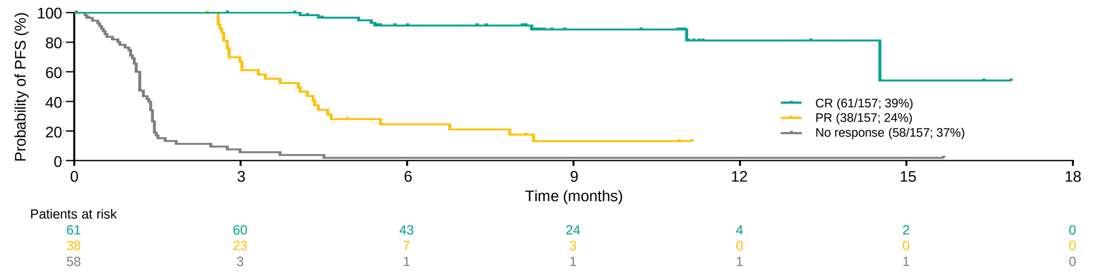
[a]Median duration of response data not yet mature.

Response Characteristics, mo (range)	
Median time to response	1.4 (1.0–8.4)
Median time to CR	2.7 (1.2–11.1)
Median duration of response[a]	12 (0+ to 15.5+)
Median duration of response for patients in CR	Not reached

KM estimates. Based on IRC assessment and Lugano criteria.

- Majority of CRs were achieved by the first or second assessment
- Some conversions from PR to CR were still observed at ≥36 weeks

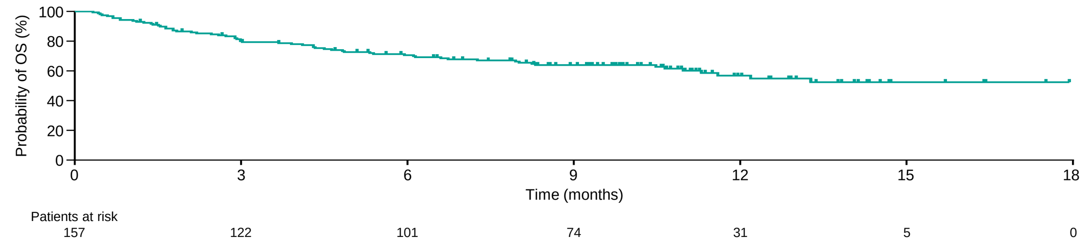
PFS by Best Response per IRC



Kaplan–Meier Estimate	
Median PFS for complete responders	**Not reached**
Complete responders remaining in response at 9 mo	**89%**
Median PFS, mo (95% CI)	4.4 (3.0–7.9)
PFS at 6 mo, % (95% CI)	43.9 (35.7–51.7)

A correlation between depth of response and PFS was observed

Overall Survival

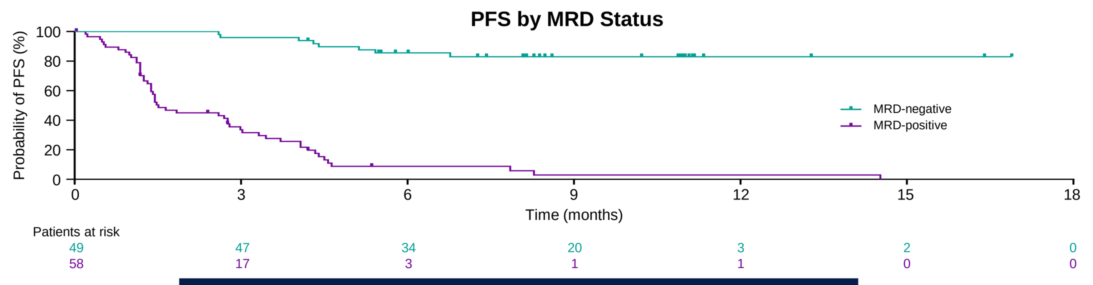


Kaplan–Meier Estimate	N=157
Median OS	**Not reached**
OS at 6 mo, % (95% CI)	70.6 (62.7–77.2)
OS at 12 mo, % (95% CI)	56.9 (47.3–65.4)

Minimal Residual Disease (MRD) Negativity Correlated With Improved PFS

- **Exploratory ctDNA analysis shows that MRD-negative responses were durable and correlated with PFS**

PFS by MRD Status



MRD Results per ctDNA Assay	All LBCL n=107
MRD-negative rate, n (%)	49 (45.8) [95% CI: 36.1–55.7]

Based on MRD-negative evaluable set, which included patients with ≥1 postbaseline MRD sample/evaluation who had detectable disease (n=104) or were not evaluated (n=3) at baseline. MRD negativity was defined as the absence of detectable clone sequences in plasma at any on-treatment time point (clonoSEQ).

Reference

1. Hutchings M, et al. *Lancet*. 2021;398:1157-69.

Acknowledgments

On behalf of all the authors, we thank the patients, study investigators, and site personnel for their participation in this study. This study was funded by Genmab A/S and AbbVie. Medical writing and graphical support were provided by Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and funded by Genmab. Christopher Chiu, Kevin Liu, and David Soong from Genmab provided the MRD data. Huaibao Feng provided statistical support.

Disclosures

Thieblemont: Bristol Myers Squibb/Celgene, Hospira, Roche: Research Funding; AbbVie, Amgen, Bristol Myers Squibb/Celgene, Cellectis, Gilead Sciences, Kite, Novartis, Roche: Consultancy; AbbVie, Amgen, Bayer, Cellectis, Gilead Sciences, Incyte, Janssen, Kite, Novartis, Takeda: Honoraria; AbbVie, Amgen, Bristol Myers Squibb/Celgene, Cellectis, Gilead Sciences, Incyte, Janssen, Kite, Novartis, Roche, Takeda: Membership on an Entity's Board of Directors or Advisory Committees; AbbVie, Amgen, Bristol Myers Squibb/Celgene, Cellectis, Gilead Sciences, Kite, Novartis, Roche: Other: Travel, Accommodations, Expenses. **Phillips:** Seattle Genetics, Pharmacyclics, Incyte, Genentech, Bayer, Gilead Sciences, Curis, Kite/Gilead, Celgene, Genmab, TG Therapeutics, ADC Therapeutics: Consulting or Advisory Role; Seattle Genetics, Lymphoma & Myeloma Connect: Honoraria; AbbVie, Pharmacyclics/Janssen, Bayer: Research Funding. **Ghesquieres:** Gilead Sciences, Celgene, Janssen, Roche, Mundipharma, Takeda: Consultancy/Honoraria. **Cheah:** Roche, Janssen, MSD, Gilead, Ascentage Pharma, AstraZeneca, Lilly, TG Therapeutics, BeiGene, Novartis, Bristol Myers Squibb: Consulting/Advisory/Honoraria; Bristol Myers Squibb, Roche, AbbVie: Research Funding; Roche: Travel Expenses. **Clausen:** AbbVie, Janssen, Gilead, AstraZeneca, Genmab: Consulting/Advisory; AbbVie, AstraZeneca: Travel Expenses. **Cunningham:** MedImmune/AstraZeneca, Clovis, Lilly, 4SC, Bayer, Celgene, Roche: Research Grants (paid to institution, Royal Marsden Hospital). **Do:** There are no relationships to disclose. **Feldman:** There are no relationships to disclose. **Gasiorowski:** MSD, Otsuka, Novartis, Astellas, Janssen, AbbVie, Takeda: Honoraria. **Jurczak:** AbbVie, Bayer, BeiGene, Celgene, Janssen, Roche, Takeda, TG Therapeutics, AstraZeneca, MEI Pharma, Lilly: Research Funding; Janssen, AstraZeneca, MEI Pharma, Lilly, Takeda, Roche, AbbVie, BeiGene: Consultancy. **Kim:** AstraZeneca, Boryung, F. Hoffmann-La Roche Ltd/Genentech, Janssen, Novartis, Sanofi, Takeda, Yuhan: Consulting or Advisory Role; AstraZeneca-KHIDI: Research Funding Outside This Work. **Lewis:** Janssen, Lilly, Roche, BeiGene, Kite: Advisory Boards/Consultancy. **van der Poel:** There are no relationships to disclose. **Poon:** There are no relationships to disclose. **Doerr:** AbbVie: Current Employment. **Kilavuz:** Genmab: Current Employment. **Chen:** Genmab: Current Employment. **Sacchi:** Genmab: Current Employment. **Elliott:** Genmab: Current Employment; P158-US-PSP3: Patents & Royalties. **Hutchings:** AbbVie, Celgene, Genmab, Janssen, Roche, Takeda: Scientific Advisory Boards; Celgene, Genentech, Genmab, Incyte, Janssen, Novartis, Roche, Takeda: Research Support (paid to institution). **Lugtenburg:** Takeda, Servier: Research Grants; Celgene, Roche, Takeda, Genmab, AbbVie, Incyte, Regeneron: Advisory Honoraria.