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Novel Analysis of 3-Year Results From the Pivotal EPCORE NHL-1 Study: Outcomes in Patients With Relapsed/Refractory Large B-Cell Lymphoma and Complete Response at 2 Years With Epcoritamab Monotherapy

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OBJECTIVE

- To report results from a novel, post hoc analysis evaluating long-term outcomes in patients with R/R LBCL who remained in CR 2 years after starting epcoritamab monotherapy in the EPCORE NHL-1 trial

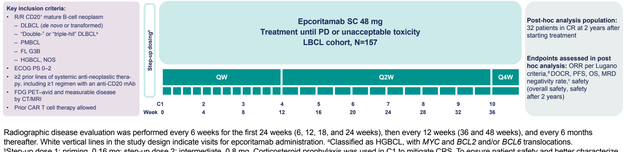
CONCLUSIONS

- This subgroup analysis of patients with R/R LBCL in CR at 2 years after starting epcoritamab highlights durable, long-term disease-free remission and OS with epcoritamab in the subset of patients who achieved a CR
  - An estimated 96% of patients in CR at 2 years remained alive and in CR at 3 years
    - Median DOCR, median PFS, and median OS were all not reached
- Long-term safety was consistent with the established safety profile of epcoritamab
- These findings underscore the durable benefits of epcoritamab in the 3L+ setting and indicate that some patients obtain long-term remission
- Epcoritamab is being explored in earlier LOTs, including in ongoing trials for 1L and 2L+ DLBCL

BACKGROUND

- In patients with DLBCL, deep and durable responses to treatment are associated with favorable long-term outcomes[1]
- Epcoritamab, a CD3×CD20 T-cell–engaging bispecific antibody, is a novel treatment approved for use in different types of R/R LBCL or R/R FL after ≥2L of systemic therapy until PD[2–4]
- The long-term efficacy and safety of epcoritamab was assessed in a recent 3-year follow-up from the pivotal EPCORE® NHL-1 trial (NCT03625037) in patients with R/R LBCL[5]
  - Results demonstrated durable efficacy in patients with CR, with a median DOCR of 36 months, median PFS of 37 months, and median OS not reached; long-term safety was consistent with previous reports[5]
    - These data compare favorably with other treatment options and support long-term disease-free survival with treat-to-progression epcoritamab for patients with 3L+ LBCL
      - Other bispecific antibodies have reported median DOCRs of 17.9–29.8 months[6,7]
  - To explore these favorable long-term efficacy outcomes further, we conducted a novel subgroup analysis of patients in the EPCORE NHL-1 trial who remained in CR 2 years after starting epcoritamab treatment

EPCORE NHL-1 PHASE 2 STUDY DESIGN



Radiographic disease evaluation was performed every 6 weeks for the first 24 weeks (6, 12, 18, and 24 weeks), then every 12 weeks (36 and 48 weeks), and every 6 months thereafter. White vertical lines in the study design indicate visits for epcoritamab administration. *Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. †Step-up dose 1: priming, 0.16 mg; step-up dose 2: intermediate, 0.8 mg. Corticosteroid prophylaxis was used in C1 to mitigate CRS. To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 hours; this requirement has since been removed in the C1 optimization cohort. ‡Exploratory MRD analyses were performed using the clonoSEQ® (Adaptive Biotechnologies, Seattle, WA, USA) next-generation sequencing assay to evaluate plasma ctDNA. Samples collected on D1 of C 3, 5, 7, 10, and 13, then every 6 months (±1 month) for up to 3 years from C1D1. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

RESULTS

Patient Demographics and Baseline Characteristics

- In the EPCORE NHL-1 overall population, 41% (65/157) of patients had a CR
- 32 patients remained in CR 2 years after starting epcoritamab, accounting for 20% (32/157) of all patients enrolled and 49% (32/65) of patients who achieved a CR
- Compared with the overall population, patients in CR at 2 years had lower tumor burden at baseline (bulky disease >7 cm 19% vs 31%; LDH 294 vs 338 U/L), lower baseline ferritin levels (383 vs 406 µg/L), and similar CAR T therapy exposure (38% vs 39%)

Patient Disposition

- 81% (26/32) of patients were on treatment at 2 years, and 59% (19/32) remained on treatment at the data cutoff (median follow-up, 37 months)
- At the data cutoff, 41% (13/32) had discontinued epcoritamab, most commonly due to AEs; only 1 patient discontinued due to PD
  - In the 12 patients who discontinued treatment for reasons other than PD, median follow-up after discontinuation was 14 months (range, 2−28). During this time, none of the 12 patients relapsed

Baseline Characteristics and Prior Treatments in Patients in CR at 2 Years

	Patients with CR at 2 years (n=32)
Age, mean (standard deviation), years	63 (14)
Male sex at birth, n (%)	15 (47)
Race, n (%)[a]	
White	19 (59)
Asian	4 (13)
Other	1 (3)
Disease type, n (%)	
DLBCL	28 (88)
FL[b]	1 (3)
HGBCL	2 (6)
PMBCL	1 (3)
IPI score, n (%)[c]	
0–2	10 (31)
≥3	18 (56)
Bulky disease >7 cm, n (%)	6 (19)
Median total metabolic tumor volume (mL)	75
LDH, serum or plasma (U/L)	294
Ferritin levels, serum or plasma (µg/L)	383
Median prior LOTs, n (range)	3 (2–8)
Prior lines of antilymphoma therapy, n (%)	
2	10 (31)
3	10 (31)
4	8 (25)
5	2 (6)
6	0
7	1 (3)
8	1 (3)
Primary refractory disease, n (%)[d,e]	13 (41)
Refractory to ≥2 consecutive prior LOTs, n (%)	21 (66)
Prior CAR T therapy, n (%)	12 (38)
Refractory to prior CAR T therapy, n (%)[f]	8 (25)

[a]Race was not reported for 8 patients. [b]G 3B. [c]IPI score was NA for 4 patients. [d]Primary refractory indicates refractoriness to 1L antilymphoma therapy. [e]Refractory indicates that patients experienced PD or stable disease as best response to antilymphoma therapy or experienced PD within 6 months of therapy completion. [f]Experienced PD within 6 months of CAR T cell therapy.

Patient Disposition

	Patients with CR at 2 years (n=32)
Median follow-up, months (range)	37 (32–46)
Median treatment duration, months (range)	35 (8–43)
Ongoing treatment with epcoritamab at 2 years, n (%)	26 (81)
Ongoing treatment with epcoritamab at data cutoff, n (%)	19 (59)
Discontinued treatment, n (%)	13 (41)
PD	1 (3)
AE	6 (19)
Maximum clinical benefit[a]	1 (3)
Withdrawal by patient	1 (3)
Death	0
Other[c]	4 (13)

[a]Per investigator's discretion. [b]Includes 2 patients that discontinued due to investigator decision, 1 due to repeated infection, and 1 due to benefit/risk (patient had CR and AEs).

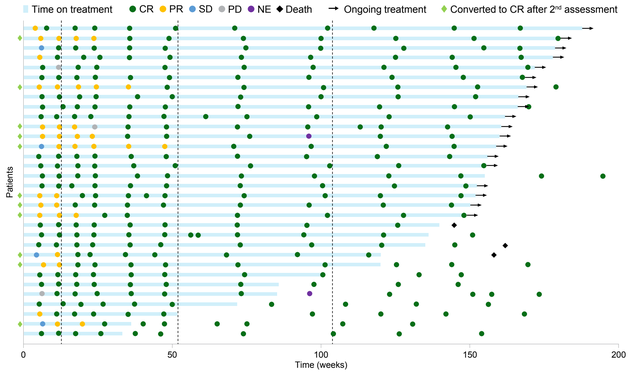
Long-Term Efficacy Outcomes

- Most patients (97%; 31/32) had a response (CR or PR) by the 2nd assessment at week 12
- Responses continued to improve over time, with 11 PRs converting to CRs after the 2nd response assessment
  - 4 patients had SD at their 1st disease assessment; all 4 went on to achieve CR
- Median DOCR was not reached; an estimated 96% of patients remained in CR at 3 years, and the longest ongoing CR was >43 months
- Median PFS and median OS were not reached
  - An estimated 96% and 97% of patients remained progression free and alive, respectively, at 3 years

MRD Analysis

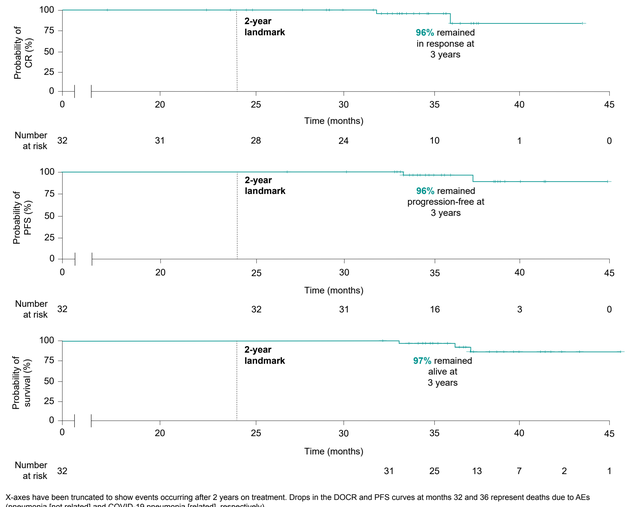
- Among MRD-evaluable patients who had a CR 2 years after starting epcoritamab, MRD negativity was seen as early as C1 and was sustained; 95% (20/21) of these patients were MRD negative at C13D1

Deep and Durable Responses with Epcoritamab Monotherapy



Dotted lines represent 12 weeks, 1 year, and 2 years after treatment initiation.

Long-Term Disease-Free Survival



X-axes have been truncated to show events occurring after 2 years on treatment. Drops in the DOCR and PFS curves at months 32 and 36 represent deaths due to AEs (pneumonia [not related] and COVID-19 pneumonia [related], respectively).

Long-Term Safety

- The most common TEAEs at any time were COVID-19 (66%), CRS (53%), and diarrhea (44%)
- 81% (26/32) of patients had ≥1 TEAE leading to a dose delay during epcoritamab treatment
- The most common TEAEs occurring after 2 years on treatment were COVID-19 (34%), diarrhea (16%), upper respiratory tract infection (16%), neutrophil count decrease (13%), and pneumonia (13%)
- 19% (5/26) of patients still on treatment at 2 years had ≥1 serious infection after 2 years, most commonly pneumonia (n=4)
- 2 patients had fatal TEAEs (pneumonia and COVID-19 pneumonia) after 2 years

Incidence of TEAEs After 2 Years

	Patients with CR at 2 years (n=32)
TEAEs, n (%)	25 (78)
Grade 3+ TEAEs, n (%)	11 (34)
Serious TEAEs, n (%)	7 (22)
TEAEs leading to treatment discontinuation, n (%)	3 (9)
TEAEs relating to dose delay, n (%)	16 (50)
Fatal TEAEs, n (%)	2 (6)
Most common (≥10%) TEAEs of any grade, n (%)	
COVID-19	11 (34)
Diarrhea	5 (16)
Upper respiratory tract infection	5 (16)
Neutrophil count decreased	4 (13)
Pneumonia	4 (13)

Includes TEAEs occurring at any time after 2 years following the start of epcoritamab treatment.

Acknowledgments

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Abbreviations

1L, first line; 2L, second line; 3L+, third line or later; AE, adverse event; C, cycle(s); CAR T, chimeric antigen receptor T cell; CD, cluster of differentiation; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; ctDNA, circulating tumor DNA; D, day(s); DLBCL, diffuse large B-cell lymphoma; DOCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; FL, follicular lymphoma; G, grade; HGBCL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; LOT(s), line(s) of treatment; mAb, monoclonal antibody; MRD, minimal residual disease; MRI, magnetic resonance imaging; NA, not available; NE, not evaluable; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; PR, partial response; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; R/R, relapsed or refractory; SC, subcutaneous; TEAE, treatment-emergent adverse event.

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