Abstract: S234

Title: EPCORITAMAB INDUCES DEEP RESPONSES IN RELAPSED OR REFRACTORY (R/R) FOLLICULAR LYMPHOMA (FL): SAFETY AND POOLED EFFICACY DATA FROM EPCORE NHL-1 PIVOTAL AND CYCLE (C) 1 OPTIMIZATION (OPT) FL COHORTS

Abstract Type: Oral Presentation

Session Title: Follicular and mantle cell lymphoma - Role of bispecifics

Background:

Epcoritamab, a CD3xCD20 bispecific antibody, led to deep, durable responses in patients (pts) with multiply R/R FL (overall response rate [ORR] 82%, complete response [CR] rate 63% per independent review) in the pivotal cohort of EPCORE™ NHL1 (phase 1/2; NCT03625037). Safety was manageable; most CRS events were low grade (G; 66% overall; 40% G1, 25% G2, 2% G3), all resolved, and none led to treatment (tx) discontinuation. Further mitigation of CRS and ICANS may increase epcoritamab accessibility and reduce healthcare resource use. Enhanced CRS mitigation strategies and omission of mandatory hospitalization for CRS monitoring are being investigated in a C1 OPT cohort.

Aims:

To report the largest population of patients (pts) with R/R FL receiving epcoritamab to date, with efficacy (including minimal residual disease [MRD]) from the EPCORE NHL1 FL pivotal and C1 OPT cohorts and safety from the fully enrolled C1 OPT cohort.

Methods:

In the C1 OPT cohort, pts with CD20+ R/R FL G1–3A and ≥2 prior lines of systemic tx received subcutaneous epcoritamab in 28-d Cs, including a third stepup dose in C1 (D1, 0.16 mg; D8, 0.8 mg; D15, 3 mg), followed by 48-mg full doses (QW, C1–3; Q2W, C4–9; Q4W, C≥10) until disease progression. In C1, adequate hydration and dexamethasone (preferred steroid for mandatory CRS prophylaxis) were recommended. Hospitalization for CRS monitoring was not mandated. Primary endpoints were rates of any-grade and G≥2 CRS events. Secondary endpoints included response (Lugano), MRD in peripheral blood (clonoSEQ® assay; 10−6 cutoff), and safety/tolerability. A pooled analysis of response per investigator and MRD negativity was conducted.

Results:

As of the data cutoff (Jan 8, 2024; median follow-up, 5.7 mo), 86 pts with R/R FL had received epcoritamab in this C1 OPT cohort (median of 2 prior tx lines [range, 2–9], 92% stage III–IV FL, 63% double-refractory disease, 44% primary refractory disease, and 42% POD24). All CRS events were low grade (49% overall; 40% G1, 9% G2), most occurred during C1, and none led to tx discontinuation. Corresponding with reduced CRS rate and severity with C1 OPT, IL6 levels 24 h after the first full dose were lower with C1 OPT vs the pivotal cohort. No ICANS or clinical tumor lysis syndrome occurred. Most pts in C1 OPT who received the first full dose (44/82; 54%) were monitored for CRS as outpatients. Of the 38 pts who were hospitalized, 18 were hospitalized to monitor for potential CRS and 20 were hospitalized for logistical/social reasons or other AEs. Among the 214 pts in the pivotal and C1 OPT cohorts, which had similar demographics and disease characteristics, ORR was 84% and CR rate was 65% (**Figure**). In each cohort, median times to response and CR were 1.4 mo and 1.5 mo, respectively. CR was associated with improved progression-free survival (PFS). Among MRD-evaluable pts in both cohorts (n=135), MRD negativity was observed in 89 pts (66%), and MRD negativity overall and at C3D1 (prespecified time point) were associated with improved PFS (**Figure**). Additional data, including subgroup analyses, will be presented.

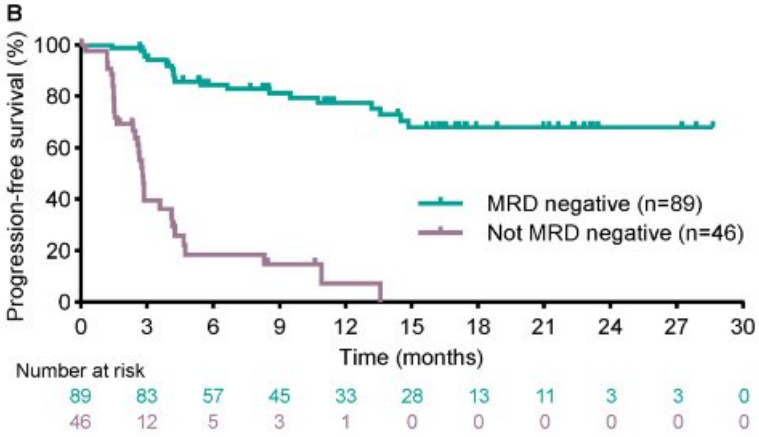
Summary/Conclusion:

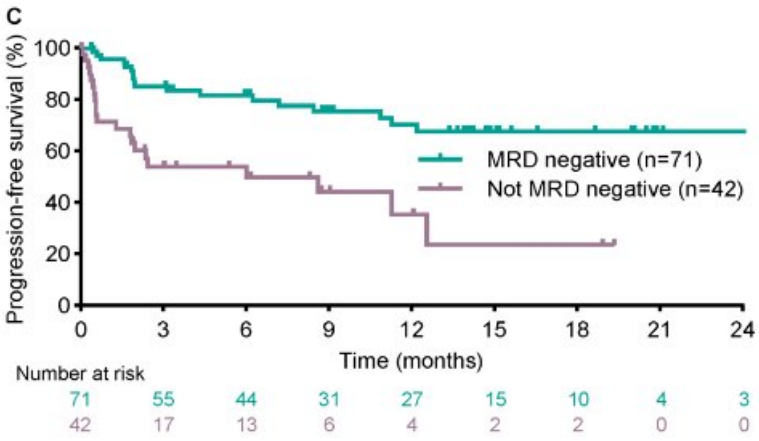
Epcoritamab monotherapy showed early, deep responses in the largest R/R FL population treated with a Tcell−engaging therapy to date. CR and MRD negativity, including at C3D1, were associated with improved PFS. Safety was manageable in both cohorts, and CRS rate and severity were substantially reduced with C1 OPT, with few G2 and no G≥3 events. The data suggest that mandatory hospitalization for CRS monitoring is not necessary and support further evaluation of outpatient epcoritamab tx for pts with R/R FL.

Figure. Individual cohort and pooled response rates per investigator assessment among pts in the pivotal and C1 OPT cohorts (**A**) and pooled Kaplan–Meier plots of investigator-assessed progression-free survival by MRD status[a] across all MRD-evaluable pts (**B**) and among pts for whom MRD data were available at the C3D1 landmark (**C**)

A

n (%)	Pivotal cohort[b] N=128	C1 OPT cohort N=86	Pooled N=214
ORR	106 (83)	74 (86)	180 (84)
CR rate	84 (66)	55 (64)	139 (65)





[a]Based on PBMC assay with 10^{-6} cutoff.
[b]Data cutoff: Apr 21, 2023; median follow-up, 17.4 mo.
C1, cycle 1; C3D1, cycle 3 day 1; CR, complete response; MRD, minimal residual disease; OPT, optimization; ORR, overall response rate; PBMC, peripheral blood mononuclear cell; pt, patient.

Keywords: Follicular lymphoma, Bispecific, Hematological malignancy, Non-Hodgkin's lymphoma