Abstract: S239

Title: FIRST DATA FROM SUBCUTANEOUS EPCORITAMAB+POLATUZUMAB VEDOTIN, RITUXIMAB, CYCLOPHOSPHAMIDE, DOXORUBICIN, AND PREDNISONE (POLA-R-CHP) FOR FIRST-LINE DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): EPCORE NHL-5

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Session Title: Aggressive lymphoma - Targeted drug therapy

Background:

Pola-R-CHP improved response rates and progression-free survival vs cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) as first-line (1L) treatment (tx) for DLBCL. However, there is still an unmet need to improve outcomes to achieve cure in 1L DLBCL. Epcoritamab (epcor), a subcutaneous CD3xCD20 bispecific antibody, has demonstrated safety and efficacy in 1L DLBCL in combination with R-CHOP and is approved as monotherapy for relapsed or refractory DLBCL after ≥2 lines of systemic therapy in the US, Europe, Japan, and other regions. Combining epcor with antineoplastic agents with varied MOAs may offer enhanced clinical benefit to patients (pts). We report safety and antitumor activity in pts with newly diagnosed DLBCL treated with epcor + pola-R-CHP from the phase 1b/2 EPCORE NHL-5 (NCT05283720) study.

Aims:

To evaluate the safety, tolerability, and antitumor activity of epcor + pola-R-CHP in pts with newly diagnosed DLBCL.

Methods:

EPCORE NHL-5 is an ongoing, multi-arm, open-label, global study. In arm 3, pts had newly diagnosed CD20+ DLBCL (DLBCL not otherwise specified, high-grade B-cell lymphoma [HGBL] with *MYC* and *BCL-2* and/or *BCL-6* translocations [double/triple-hit], or follicular lymphoma [FL] grade 3B) with ECOG PS 0–2 and IPI score 2–5. All pts were treated in 21-d cycles (C) and received epcor + pola-R-CHP until C6, then 2 C of epcor monotherapy. Epcor was given using step-up dosing in C1, followed by full doses (48 mg) QW during C2–4 and Q3W during C5–8. Additional CRS mitigation included prednisone (n=17) or dexamethasone (n=20). G-CSF or pegylated G-CSF was administered 1–2 d after doxorubicin, cyclophosphamide, and pola during C1–6. CNS prophylaxis was allowed. Key endpoints included DLTs, investigator-assessed response (ORR/CR), time to response (TTR), and safety.

Results:

As of Nov 28, 2023, 37 pts received epcor + pola-R-CHP: 51% female; median age 64 y; DLBCL, n=34; HGBL, n=1; FL grade 3B, n=1. No DLTs were observed. Among 27 response-evaluable pts, ORR was 100%, with 89% of pts achieving a CR (n=24; **Table**). Median follow-up was 5.8 mo (95% CI: 4.8, 8.6). Median TTR and time to CR were 2.7 mo (range: 1.3–3.3) and 2.8 mo (range: 1.3–6.7), respectively. Tx-emergent AEs (TEAEs) are summarized (**Table**). Two (5%) pts discontinued epcor due to an AE; 3 (8%) pts discontinued pola-R-CHP due to an AE. The most common grade 3–4 AEs were neutropenia (65%), anemia (14%), and leukopenia (11%). One pt had a fatal TEAE (septic shock) not considered related to epcor. CRS was low grade (32% G1, 16% G2) and primarily occurred after the first full dose (C1D15). CRS events occurred in 6/17 pts (35%; 3 G2) and 12/20 pts (60%; 3 G2) receiving prophylactic dexamethasone or prednisone, respectively. All CRS resolved, with median time to resolution of 2 d (range: 1–6). No ICANS was observed. One pt had G4 hemophagocytic lymphohistiocytosis (HLH), which resolved and the pt completed tx. Biomarker analysis showed pharmacodynamic profiles consistent with the MOA of epcor, including predictable elevations in cytokine levels after the first full dose (IFN-gamma, IL-2, IL-6). Preliminary pharmacokinetic profiles and exposures of epcor were comparable with other tx combinations and monotherapy. Follow-up is ongoing. Additional data will be presented.

Summary/Conclusion: Epcor + pola-R-CHP in newly diagnosed DLBCL showed high ORR and CR rate across all subgroups with a manageable safety profile. Data compare favorably with pola-R-CHP alone and other tx regimens in this setting and support further investigation of this combination. Additional data including MRD will be presented.

Table. Antitumor activity (A) and safety (B) in pts with DLBCL treated with 1L epcor + pola-R-CHP

A.

Antitumor activity in response-evaluable pts	n=27
Overall response rate, % (95% CI)	100 (87.2, 100.0)
Complete response rate	89 (70.8, 97.6)
Overall response by subgroup, % (95% CI)	
Molecular classification	
Germinal B-cell (n=14)	100 (76.8, 100.0)
Activated B-cell/nongerminal B-cell (n=10)	100 (69.2, 100.0)
Unclassified/unknown (n=1 each)[a]	100 (15.8, 100.0)
International prognostic index	
2 (n=12)	100 (73.5, 100.0)
3–5 (n=14)	100 (76.8, 100.0)
Age, years	
<65 (n=15)	100 (78.2, 100.0)
65–74 (n=12)	100 (73.5, 100.0)
Complete response by subgroup, % (95% CI)	
Molecular classification	
Germinal B-cell (n=14)	78.6 (49.2, 95.3)
Activated B-cell/nongerminal B-cell (n=10)	100 (69.2, 100.0)
Unclassified/unknown (n=1 each)[a]	100 (15.8, 100.0)
International prognostic index	
2 (n=12)	91.7 (61.5, 99.8)
3–5 (n=14)	85.7 (57.2, 98.2)
Age, years	
<65 (n=15)	86.7 (59.5, 98.3)
65–74 (n=12)	91.7 (61.5, 99.8)

B.

Safety, n (%)	(N=37)[b]
AEs, grade 3–4	27 (73)
CRS, any grade	18 (49)
Grade 1	12 (32)
Grade 2	6 (16)
Grade ≥3	0
Treated with tocilizumab	7 (19)
Treated with corticosteroid	2 (5)
Treated with tocilizumab + corticosteroid	1 (3)
ICANS, any grade	0
CTLS, any grade	0
Serious AEs, any grade	20 (54)
AEs leading to epcor discontinuation, any grade	2 (5)

[a]One patient was unclassified by NGS, one patient was unknown.
[b]Included 1 ineligible pt with FL grade 3A who was excluded from efficacy analyses.
AE, adverse event; CRS, cytokine release syndrome; CTLS, clinical tumor lysis syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; NGS, next-generation sequencing.

Keywords: Bispecific, Diffuse large B cell lymphoma, DLBCL, Clinical trial