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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Epcoritamab SC + R-Mini-CHOP Leads to High Complete Metabolic Response Rates in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma Ineligible for Full-Dose R-CHOP: First Disclosure from Arm 8 of the Epcore NHL-2 Trial

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Background: Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) is a standard of care for previously untreated (1L) diffuse large B-cell lymphoma (DLBCL); however, some patients are not candidates for full-dose R-CHOP due to advanced age, frailty, or underlying comorbidities. For these patients, various attenuated treatment regimens have been evaluated, with low-dose R-CHOP (R-mini-CHOP) being widely adopted as a standard 1L regimen. However, outcomes are suboptimal, with overall response rates (ORRs) and complete metabolic response (CMR) rates around 70% and 40-60%, respectively, and a 2-y progression-free survival rate of only 47%, leaving substantial room for improvement. Epcoritamab, a subcutaneous (SC) CD3xCD20 bispecific antibody, was approved by the US FDA for the treatment of adults with relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after ≥2 lines of systemic therapy. In the 1L setting in patients with high-risk DLBCL, epcoritamab SC with full-dose R-CHOP had a favorable safety profile and showed promising efficacy, including an ORR of 100% (Falchi et al, ASCO 2023). Here we report initial data from arm 8 of the EPCORE™ NHL-2 study (NCT04663347; phase 1/2) evaluating epcoritamab SC + R-mini-CHOP in 1L DLBCL.

Methods: Adults with 1L CD20 $^{+}$ DLBCL who were not considered candidates for full-dose R-CHOP due to age ≥75 y or age ≥65 y with comorbidities (reduced left ventricular ejection fraction, history of myocardial infarction [>6 mo prior to enrollment], exertional chest pain, arrhythmia [grade ≤2], hypertension requiring treatment, or diabetes) were enrolled. Patients received epcoritamab SC (QW, cycles 1-2 [21 d each]; Q3W, cycles 3-6 [21 d each]; Q4W, cycles 7-8 [28 d each]) with R-mini-CHOP in cycles 1-6 (Q3W). A safety run-in was conducted to confirm acceptability of the safety profile. The primary endpoint of arm 8 was ORR as assessed by PET-CT per Lugano criteria.

Results: As of April 24, 2023, 28 patients had received epcoritamab SC 48 mg + R-mini-CHOP. The median age was 81 y, 14 patients (50%) had IPI 3-5, 10 patients (36%) had bulky disease (>6 cm), and 15 patients (54%) had stage IV disease. At the data cutoff, median follow-up was 6.2 mo (range, 2.5+ to 11.7), with 9 patients (32%) having completed treatment and 15 patients (54%) still on treatment. R-mini-CHOP median relative dose intensity was ≥94%. There were no dose-limiting toxicities. The most common treatment-emergent AEs (TEAEs) of any grade were cytokine release syndrome (CRS; 43%), neutropenia (32%), fatigue (25%), anemia (21%), constipation (21%), and hypokalemia (21%). TEAEs decreased over time; 3 patients (11%) discontinued epcoritamab SC due to TEAEs. One grade 5 TEAE (cytomegalovirus infection reactivation) was recorded. CRS events were primarily low grade (grade 1-2: 39%, grade 3: 4%, grade ≥4: 0%), timing was predictable, and a

majority of events were observed after the first full dose (cycle 1, day 15); all events resolved, with a median time to resolution of 3 d (range, 1-7). No ICANS events were reported. All 20 efficacy-evaluable patients had a response (ORR, 100%), with 17 patients (85%) achieving CMR. Median time to response was 1.4 mo (**Figure**). At both month 6 and month 9, most patients who achieved CMR remained in CMR, suggesting durability of response. The study is ongoing and updated results will be presented.

Conclusions: Epcoritamab SC + R-mini-CHOP showed encouraging efficacy with high response rates in patients with 1L DLBCL who cannot tolerate full-dose R-CHOP, including elderly, frail, and high-risk patients. There were no new safety signals, and findings were consistent with previously reported data, supporting the feasibility of the combination. These results warrant further investigation of epcoritamab-based therapies in 1L DLBCL.

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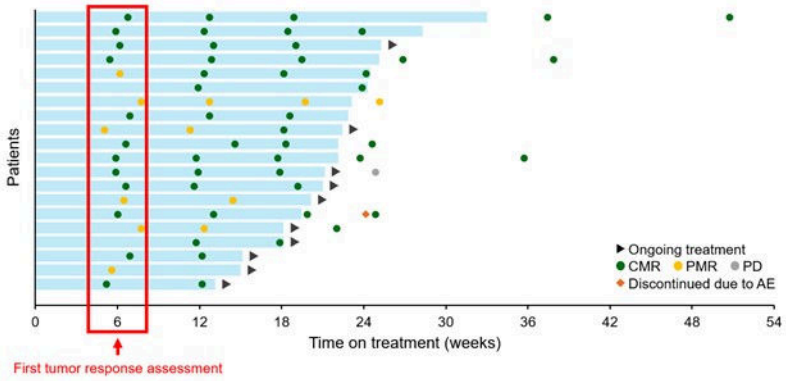
Figure. Onset and durability of responses



Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD.
AE, adverse event; CMR, complete metabolic response; PD, progressive disease; PMR, partial metabolic response.

Figure 1

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