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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Epcoritamab SC + GemOx Leads to High Complete Metabolic Response Rates in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma Ineligible for Autologous Stem Cell Transplant: Updated Results from Epcore NHL-2

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Background: Patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who fail or are ineligible for autologous stem cell transplant (ASCT) have poor outcomes with standard chemotherapy, and novel, effective therapeutic options are needed. A retrospective analysis showed that treatment with rituximab and gemcitabine + oxaliplatin (GemOx) in a transplant-ineligible population resulted in a complete response rate of 33% in the overall population; among patients refractory to previous therapy, 10% achieved complete response (Cazelles et al, *Leuk Lymphoma* 2021). Epcoritamab, a subcutaneously administered (SC) CD3xCD20 bispecific antibody, has demonstrated deep, durable responses with a manageable safety profile as a single agent in patients with R/R DLBCL. Based on these data, epcoritamab SC was approved by the US FDA for the treatment of adults with R/R DLBCL, not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma, after ≥2 lines of systemic therapy. In the EPCORE ™ NHL-2 phase 1/2 trial (NCT04663347), epcoritamab + GemOx treatment showed encouraging preliminary efficacy with overall expected and manageable safety in patients with R/R DLBCL who failed or were ineligible for ASCT. Here, we present updated results with longer follow-up.
Methods: Adults with R/R CD20 $^{+}$ DLBCL who had failed or were ineligible for ASCT were enrolled. Patients received epcoritamab SC in 28-d cycles (Cs) as follows: weekly, C1-3; every 2 weeks, C4-9; every 4 weeks, C≥10 until progressive disease or unacceptable toxicity. Patients received GemOx every 2 weeks in C1-4. Step-up epcoritamab dosing (step-up doses 1 and 2 followed by 48-mg full doses) and corticosteroid prophylaxis were required in C1 to mitigate CRS. The primary endpoint was overall response rate (ORR) as assessed by PET-CT per Lugano criteria.
Results: A total of 34 patients (median age, 71 y; range, 47-87) with a median follow-up of 20.3 mo (range, 1.0+ to 26.8) received epcoritamab SC 48 mg + GemOx on or prior to August 24, 2022. At the data cutoff date (April 24, 2023), treatment was ongoing in 35% of patients. A majority of patients (68%) had stage III or IV disease, 53% had primary refractory disease,

38% were refractory to ≥2 consecutive lines of prior therapy, and 79% were refractory to the last line of therapy. The median number of prior lines of treatment was 2 (range, 1-6); 11 patients (32%) had 3 or more prior lines of treatment. A total of 7 patients (21%) had prior CAR T, and 5 patients (15%) had previously received ASCT. The most common treatment-emergent AEs (TEAEs) of any grade (G) were thrombocytopenia/decreased platelet count (68%), diarrhea (59%), anemia (56%), CRS (56%), and neutropenia/decreased neutrophil count (56%). This trial was conducted amid the COVID-19 pandemic and 32% of patients experienced COVID-19. Most CRS events were low grade (53% G1-2; 3% G3) and primarily occurred following the first full dose (C1D15); no incidence of CRS resulted in epcoritamab discontinuation, and all events resolved. ICANS (G1) was reported in 1 patient; this event resolved in 2 d. No clinical tumor lysis syndrome was reported. There were 10 G5 TEAEs; in 2 cases, the contribution of epcoritamab could not be ruled out by the investigator (small intestinal perforation and multiple organ dysfunction syndrome; both patients had multiple confounding factors). The ORR was 91% (31/34), with 59% (20/34) of patients achieving complete metabolic response (CMR). Median times to response and CMR were 1.5 mo and 2.6 mo, respectively. The ORR and CMR rates were 94% and 39% among patients with primary refractory disease, 89% and 78% among patients ≥75 y of age, and 90% and 50% among patients with IPI ≥3 (**Table**). Response rates were comparable for patients with and without prior CAR T treatment: ORR of 86% and CMR rate of 57% among patients with prior CAR T; ORR of 93% and CMR rate of 59% among CAR T-naive patients.

Conclusions: Epcoritamab SC + GemOx led to high CMR rates in this difficult-to-treat R/R DLBCL population ineligible for transplant with high unmet medical need. No new safety signals were identified, and the safety profile was consistent with those of the individual drugs. These data are encouraging and underline the versatility of epcoritamab SC for the treatment of R/R DLBCL. Additional data and subgroup analyses will be presented.

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Table. Response rates among subgroups

	n	ORR, %	CMR, %
Total population	34	91	59
Primary refractory	18	94	39
Age ≥75 y	9	89	78
IPI ≥3	20	90	50
Prior CAR T	7	86	57
CAR T–naive	27	93	59

Figure 1

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