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S222 EPCORITAMAB WITH RITUXIMAB + LENALIDOMIDE (R2) PROVIDES DURABLE RESPONSES IN PATIENTS WITH HIGH-RISK FOLLICULAR LYMPHOMA, REGARDLESS OF POD24 STATUS

Topic: Indolent and MCL - Clinical

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Background:

Follicular lymphoma (FL) is a heterogeneous disease. Early progression after initial treatment with chemoimmunotherapy, or POD24, occurs in approximately 20% of patients and is a strong predictor of poor outcomes. There is no standard treatment approach for patients with high-risk, relapsed or refractory (R/R) FL, including those with disease that is primary refractory, double refractory, or refractory to prior anti-CD20 treatment and those with POD24. In these patients with a high unmet need, novel options are needed to improve efficacy. Epcoritamab, a subcutaneous T-cell–engaging bispecific antibody, demonstrated impressive single-agent antitumor activity and a manageable safety profile in R/R FL (Hutchings et al, *Lancet* 2021) and shows promise combined with standards of care.

Aims:

To present pooled analyses from cohorts 2a and 2b of the ongoing phase 1/2 EPCORE™ NHL-2 trial (NCT04663347) of epcoritamab + R^2 in R/R FL.

Methods:

Patients with R/R $CD20^+$ FL received subcutaneous epcoritamab + R^2 for 12 cycles (28 d each). Epcoritamab was dosed QW in cycles 1–3, Q2W in cycles 4–9, and Q4W in cycles ≥10 (2a) or QW in cycles 1–2 and Q4W in cycles ≥3 (2b) for ≤2 y. Informed consent was obtained.

Results:

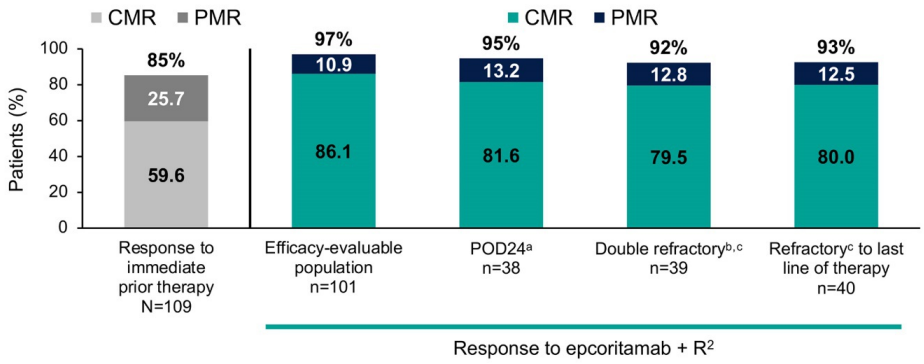
As of October 31, 2022, 109 R/R FL patients had received epcoritamab 48 mg + R^2 in 2a and 2b. Median age was 65 y, 56% of patients had FLIPI 3–5, 61% had stage IV disease, and 59% had only 1 prior line of treatment. Most had received alkylating agents (92%) or anthracyclines (62%); 2 had prior CAR T. At a median follow-up of 8.8 mo (range, 1.2–18.5), 82% were still on treatment. The most common treatment-emergent AEs were CRS and

neutropenia (48% each), injection-site reactions (38%), and fatigue (33%). CRS events were mostly low grade (G; 46% G1–2, 2% G3) and mostly occurred following the first full dose (cycle 1, day 15); all resolved and none led to discontinuation. ICANS occurred in 2 patients (G1, G2) and resolved. In 101 efficacy-evaluable patients, overall response rate (ORR) was 97%, with complete metabolic response (CMR) in 86%. Median time to any response and CMR was 1.4 mo. Estimated 6-mo progression-free survival was 93%. Notably, patients achieved higher ORR/CMR rates with epcoritamab + R^2 vs their immediate prior therapy (ORR, 97% vs 85%; CMR, 86% vs 60%; **Figure**). High ORR/CMR rates were consistent across high-risk subgroups: POD24 (progression within 2 y of first-line treatment with chemoimmunotherapy, n=38; **Figure**), 95%/82%; subset of POD24 patients that received epcoritamab in second line (n=20), 95%/90%; double refractory (refractory to anti-CD20 and an alkylating agent, n=39; **Figure**), 92%/79%; refractory to last line of therapy (no response or relapse within 6 mo after last line of therapy, n=40; **Figure**), 93%/80%; primary refractory (no response or relapse within 6 mo after first-line treatment, n=39), 97%/87%; refractory to prior anti-CD20 treatment (n=49), 94%/84%. Additional data with longer follow-up will be presented.

Summary/Conclusion:

Epcoritamab + R^2 showed potent antitumor activity and a manageable safety profile in a large R/R FL population. Encouraging responses were seen in patients with high-risk disease, suggesting subcutaneous epcoritamab may abrogate negative effects of high-risk features. A separate POD24 cohort is planned, and epcoritamab + R^2 is being studied in the phase 3 EPCORE FL-1 trial (NCT05409066).

Figure. Response rates, overall and among high-risk R/R FL subgroups, including POD24



[a]POD24 indicates progression within 2 y of first-line treatment with chemoimmunotherapy. [b]Double refractory indicates refractory to both anti-CD20 and an alkylating agent. [c]Refractory indicates no response or relapse within 6 mo after therapy.