402 Subcutaneous Epcoritamab Induces Complete Responses with an Encouraging Safety Profile across Relapsed/Refractory B-Cell Non-Hodgkin Lymphoma Subtypes, Including Patients with Prior CAR-T Therapy: Updated Dose Escalation Data

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Introduction

Despite advances in the treatment of B-cell non-Hodgkin lymphoma (B-NHL), more efficacious, less toxic, off-the-shelf therapies are needed for patients (pts) with relapsed or refractory (R/R) disease. Epcoritamab is a novel, subcutaneously (SC) administered bispecific antibody (bsAb) that simultaneously binds to CD3 on T cells and CD20 on B cells, inducing activation and cytotoxic activity of T cells for killing of target lymphoma cells. In an open-label, phase 1/2 trial (NCT03625037), initial data demonstrated an encouraging safety profile and potent single-agent clinical activity, even at low doses, in heavily pretreated pts with R/R B-NHL (Hutchings M. EHA 2020, Poster EP1218). Herein, we present updated dose-escalation data, including initial results for the 48-mg recommended phase 2 dose (RP2D) and for pts with mantle cell lymphoma (MCL).

Methods

Adults with R/R CD20+ B-NHL after prior therapy, including an anti-CD20 monoclonal antibody (mAb), receive a SC 1-mL injection of flat-dose epcoritamab in 28-day cycles (q1w: cycles 1-2; q2w: cycles 3-6; q4w thereafter) until disease progression or unacceptable toxicity. Risk mitigation for cytokine release syndrome (CRS) includes starting with priming and intermediate doses and use of corticosteroids. Objectives include dose finding, safety, and antitumor activity.

Results

As of July 6, 2020, 67 pts were enrolled, which included 45 pts (67%) with diffuse large B-cell lymphoma (DLBCL), 12 (18%) with follicular lymphoma (FL) and 4 (6%) with MCL. Pts were heavily pretreated, with a median (range) of 3.0 (1-6) prior lines of therapy for pts with DLBCL and 4.5 (1-18) for pts with FL; in total 6 pts had received prior CAR-T therapy. Over one-half of pts (37/67; 55%) were refractory to their most recent systemic therapy; 35/67 (52%) were refractory to their most recent anti-CD20 mAb therapy. At a median overall follow-up of 8.3 months, treatment is ongoing in 25 pts (37%); median follow-up is 8.3 months for pts with DLBCL and 8.8 months for pts with FL. Epcoritamab was well tolerated and there were no discontinuations due to treatment-related adverse events (AEs). The most common treatment-emergent AEs (TEAEs) were pyrexia (70%), local injection-site reactions (48%), and fatigue (45%). With increased doses, TEAEs of special interest were consistent with previous reports: CRS events were all grade 1/2 (58%) with no grade 3/4 CRS events, and limited neurotoxicity was observed (6%; grade 1: 3%; grade 3: 3%; all transient). There were no dose-limiting toxicities or febrile neutropenia events, and no deaths due to treatment-related AEs. Antitumor activity in evaluable pts with DLBCL and FL is shown in the Table. In 18 pts with DLBCL receiving epcoritamab ≥12 mg, overall response rate (ORR) was 66.7% with 6 pts achieving a complete response (CR). Of the 7 pts who received epcoritamab ≥48 mg (48-mg RP2D n=4; 60-mg n=3), all achieved a response, including CR in 2 pts (28.6%) with limited follow-up. All pts with DLBCL who were previously treated with CAR-T therapy achieved a response (4/4: 2 CR, 2 partial response [PR]). ORR was 100% for the 8 pts with FL receiving epcoritamab ≥0.76 mg, with 2 pts achieving a CR (PET scans were not mandatory and disease assessment by PET was not available in 4/6 pts who achieved a PR). Of the 4 pts with MCL, responses have been observed in 2 pts with blastoid variant MCL (1 CR; 1 PR). Data on duration of response are not yet mature. Longer follow-up data, including additional response evaluations at 48-mg dose and in pts with MCL, will be presented.

Conclusions

Epcoritamab, a novel SC bsAb, demonstrates a consistent and favorable safety profile, with no grade ≥3 CRS events and limited neurotoxicity, in support of outpatient administration. Emerging

data with longer follow-up are highly encouraging, with substantial single-agent efficacy, including CR in heavily pretreated pts with FL, MCL, and DLBCL.

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Table: Antitumor activity of epcoritamab in evaluable patients with R/R B-NHL

	DLBCL		FL	
	≥12 mg	≥48 mg	≥0.76 mg	≥12 mg
Evaluable patients	18[a]	7	8	3
Overall response rate, %	66.7	100	100	100
Complete response, n (%)	6 (33.3)	2 (28.6)	2 (25.0)	2 (66.7)
Partial response, n (%)	6 (33.3)	5 (71.4)	6 (75.0)[b]	1 (33.3)
Stable disease, n (%)	1 (5.6)	0	0	0
Progressive disease, n (%)	5 (27.8)	0	0	0

Based on data snapshot taken on July 6, 2020. Response assessments were based on Lugano 2014 response criteria by investigator assessment (modified response evaluable population).

[a]Excludes 1 patient who discontinued before first assessment due to COVID-19.

[b]4/6 patients with partial response did not have PET scans (not mandatory until recent protocol amendment).