AN ONGOING PHASE I STUDY SHOWS CLINICALLY MEANINGFUL ACTIVITY AND MANAGEABLE SAFETY OF CEVOSTAMAB MONOTHERAPY IN PATIENTS WITH HEAVILY PRE-TREATED RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) [ENCORE]

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Background: Cevostamab (an FcRH5xCD3 bispecific antibody [BsAb]) facilitates T cell-directed killing of myeloma cells. We present updated safety and efficacy data from the ongoing Phase I study (NCT03275103) of cevostamab monotherapy in patients with heavily pre-treated RRMM.

Methods: Cevostamab (intravenous infusion) is administered in 21-day cycles. Single step-up cohorts receive a step dose (0.05–3.6mg) on Cycle (C) 1 Day (D) 1 and the target dose (0.15–198mg) on C1D8. Double-step up cohorts receive step doses on C1D1 (0.3–1.2mg) and C1D8 (3.6mg), and the target dose (60–160mg) on C1D15. In subsequent cycles the target dose is given on D1 for a total of 17 cycles, unless progressive disease/unacceptable toxicity occurs.

Results: At data cut-off (18 May 2021), 160 patients had been enrolled. Median number of prior lines of therapy was 6 (range: 2–18); 85.0% of patients were triple-class refractory, and 17.5% had received ≥1 prior CAR-T, 8.1% ≥1 prior BsAb, 16.9% ≥1 prior antibody–drug conjugate (ADC), and 33.8% ≥1 prior anti-BCMA agent.
The most common adverse event was cytokine release syndrome (CRS; 80.0%). Most CRS events occurred in C1 (87.2%), were low-grade (Grade 1: 42.5%; Grade 2: 36.3%; Grade 3: 1.3%), and resolved within 48 hours (83.4%).
158 patients were efficacy evaluable. Data suggested a target dose-dependent increase in clinical efficacy, thus two dose-expansion cohorts were opened (160mg and 90mg); overall response rate (ORR) was higher at 160mg (54.5% versus 36.7%, respectively). Among all responders, the estimated median duration of response was 15.6 months (95% CI 6.4, 21.6), with a median follow-up of 8.1 months.

Conclusions: Cevostamab monotherapy shows meaningful activity in patients with heavily pre-treated RRMM. Durable responses are observed, with target dose-dependent increases in ORR but no increase in CRS rate.