Abstract: S209

Title: PHASE 2 STUDY OF FULLY HUMAN BCMA-TARGETING CAR-T CELLS (ZEVORCABTAGENE AUTOLEUCEL) IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Abstract Type: Oral Presentation

Session Title: CAR T cell therapy for the treatment of Multiple Myeloma

Background:

Zevorcabtagene autoleucel (zevor-cel) is a fully human B-cell maturation antigen (BCMA)-specific autologous chimeric antigen receptor (CAR) T-cell therapy. The initial results from the Phase 2 cohort (n=102) of the ongoing Phase 1/2 study LUMMICAR-1 (NCT03975907) evaluating zevor-cel showed compelling efficacy with an acceptable safety profile in heavily pre-treated patients with relapsed and/or refractory multiple myeloma (RRMM) (Wenming Chen, et al. *Blood* 2022;140 (S1):4564–4565). Herein, we provide the updated results from the same Phase 2 cohort with a longer follow-up.

Aims:

To evaluate the safety and efficacy of zevor-cel in patients with RRMM.

Methods:

Patients with RRMM, who had received at least 3 prior lines of therapy including at least an immunomodulatory drug and a proteasome inhibitor, were enrolled in the study. A single infusion of zevor-cel (target dose of 150 × 106 or 180 × 106 CAR-positive T cells based on body weight of ≤80 kg or >80 kg, respectively) was administered 1 to 2 days after the completion of lymphodepletion (fludarabine 25 mg/m2 and cyclophosphamide 300 mg/ m2 daily for 3 consecutive days). Response was assessed per the international myeloma working group (IMWG) 2016 criteria by an independent review committee (IRC).

Results:

Between 01 Dec 2020 and 02 Mar 2022, 102 patients (53.9% males) with median age of 59.5 years (range: 38 to 75) and a median of 4 prior lines of therapy (range: 3 to 15) were treated with zevor-cel. Ninety-one patients (89.2%) were double-class refractory, and 23 (22.5%) were triple-class refractory. Overall, 61 patients (59.8%) had high-risk cytogenetics, 39 (38.2%) had International Staging System (ISS) Stage III, 24 (23.5%) had received prior hematopoietic stem cell transplant and 11 (10.8%) had extramedullary disease. Twenty-six (25.5%) patients received bridging therapy.

As of 25 Oct 2023, the objective response rate (ORR) was 92.2% (95% CI: 85.13, 96.55); 73 (71.6%) patients achieved stringent complete response (sCR, n= 69) or complete response (CR, n=4), 20 (19.6%) achieved very good partial response (VGPR), 1 (1.0%) achieved partial response (PR). A deepening trend of responses was observed when compared to the initial results of this cohort. At a median follow-up of 20.3 (range: 0.4 to 27) months, the duration of response (DOR), progression-free survival (PFS) and overall survival (OS) data were not mature. The median time to response and the median time to reach CR/sCR were 29.0 days (range: 26 to 93) and 146 days (range: 28 to 609), respectively. All 73 patients with CR/sCR achieved MRD negativity at 10-5 threshold.

There were no new safety signals identified compared to the initial results. Cytokine release syndrome (CRS) was reported in 92 (90.2%) patients, including Grade 3 or 4 events in 7 (6.9%) patients, and all recovered. Immune effector cell-associated neurotoxicity syndrome (ICANS) which were all Grade 1 in severity occurred in 2 (2.0%) patients, and all recovered. There was no zevor-cel related Grade 3 or higher neurotoxicity event reported. Zevor-cel related Grade 3 or higher infections were observed in 28 (27.5%) patients and all grade hypogammaglobulinaemia was observed in 27 (26.5%) patients. There was one death due to zevor-cel related

pneumonia 149 days after zevor-cel infusion.

Summary/Conclusion:

The longer follow-up data reaffirmed that zevor-cel induces deep and durable responses that mature over time in heavily pre-treated patients with RRMM with an encouraging safety profile.

Keywords: B-cell maturation antigen, CAR-T, Multiple myeloma, relapsed/refractory