Phase II Study of Fully Human BCMA-Targeted CAR T Cells (Zevorcabtagene Autoleucel) in Patients with Relapsed/Refractory Multiple Myeloma

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Introduction

B-cell maturation antigen (BCMA) is an established target for multiple myeloma.

Zevorcabtagene autoleucel (zevor-cel or CT053) is an autologous chimeric antigen receptor (CAR) T-cell product with a fully human BCMA-specific single chain variable fragment (25C2) with high binding affinity and high monomer ratio (Yang 2022).

Prior studies: Results for 14 subjects treated in phase I of LUMMICAR STUDY 1 showed a well-tolerated safety profile and early, deep and sustainable responses with an ORR of 100% and a 78.6% stringent complete response/complete response (sCR/CR) rate (Chen 2021).

We report the consistent safety and efficacy results of zevor-cel in Chinese patients with R/R MM who have failed at least prior 3 lines in the ongoing phase II LUMMICAR STUDY 1 (NCT03975907).

Objectives

Evaluate the safety and efficacy of zevor-cel in subjects with R/R MM

Primary endpoint was objective response rate (ORR) by independent review committee (IRC) assessment according IMWG 2016 criteria.

Methods

The phase II study included subjects with R/R MM who had received ≥3 lines of therapy to evaluate zevor-cel safety, efficacy and pharmacokinetics for 24 months.

Zevor-cel products were manufactured in CARsgen's facility in Shanghai, China.

Prior to infusion, subjects received the lymphodepletion regimen (**Figure 1**):

- Fludarabine (25 mg/m^2/day) for 3 days
- Cyclophosphamide (300 mg/m^2/day) for 3 days

Phase II dose: 102 subjects received zevor-cel with a target dose of 150×10^6 CAR+ T cells.

Characteristic	Subjects (N=102)
Age, median (range), y	59.5 (38-75)
Sex	
Men, No. (%)	55 (53.9)
Women, No. (%)	47 (46.1)
Years since diagnosis, median (range)	3.6 (0.7-16)
Prior lines of therapy, median (range)	4.0 (3-15)
Prior antitumor regimens, median (range)	6.0 (3-17)
International Staging System, No. (%)	
I or II	63 (61.8)
III	39 (38.2)
Cytogenetic high risk, No. (%)	46 (45.1)
Extramedullary plasmacytoma, No. (%)	11 (10.8)
Bone marrow plasma cells, No. (%)	
< 50%	83 (81.4)
≥ 50%	17 (16.7)
Dual-class refractory, No. (%)	91 (89.2)
Triple-class refractory, No. (%)	23 (22.5)
Previous stem cell transplant, No. (%)	24 (23.5)

Table 3. Efficacy summary in zevor-cel treated patients

Results

- Grade 3: 6.9% (7/102)
- All subjects with CRS recovered

Immune cell-associated neurotoxicity (ICANS): 2% (2/102), both grade 1

Treatment-related adverse event (AE) infections

- Grade 3: 29.4% (30/102)

No AEs led to discontinuation of zevor-cel infusion, 1 treatment-related death reported

e 2. Adverse event summary for subjects treated zevor-cel at target dose

*Treatment related AEs indicate lymphodepletion-related AEs or zevor-cel infusion-related AEs.

M%Q|

° CAR+ T cells

Data cutoff date: August 16, 2022

Figure 3. Duration of response

Figure 4. Progression-free survival

Best

Media (range

Conclusions

We deeply appreciate the contributions of all study participants, especially the study subjects and their families.