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

LUMMICAR STUDY 1

W Chen[1], C Fu[2], B Fang[3], A Liang[4], Z Xia[5], Y He[6], J Lu[7], H Liu[8], M Hou[9], Z Cai[10], W Yang[11], S Hao[12], S Jiang[13], H Jing[14], J Liu[15], X Du[16], R Fu[17], H Mei[18], Z Zhu[19], Y Yang[20], H Liu[21], D Yuan[22], H Zhao[22], J Xiao[22], W Wang[22], H Wang[22], and Z Li[22]

[1]Beijing Chao-Yang Hospital; [2]The First Affiliated Hospital of Soochow University; [3]Henan Cancer Hospital; [4]Tongji Hospital of Tongji University; [5]Sun Yat-sen University Cancer Center; [6]Xiangya Hospital, Central South University; [7]Institute of Hematology of Peking University; [8]Beijing Hospital; [9]Qilu Hospital of Shandong University; [10]The First Affiliated Hospital of Zhejiang University; [11]Shengjing Hospital of China Medical University; [12]Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine; [13]The First Affiliated Hospital of Wenzhou Medical University; [14]Peking University Third Hospital; [15]The Third Xiangya Hospital of Central South University; [16]Shenzhen Second People's Hospital; [17]Tianjin Medical University General Hospital; [18]Union Hospital of Tongji Medical College, Huazhong University of Science and Technology; [19]Henan Provincial People's Hospital; [20]The First Affiliated Hospital of Bengbu Medical College; [21]Affiliated Hospital of Nantong University; [22]CARsgen Therapeutics Co. Ltd, Shanghai, China

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.

Results

Patient Population

- The phase II study treated 102 patients with relapsed/refractory multiple myeloma (R/R MM) (**Table 1**)
- Target dose: 150×10^6 CAR+ T cells
- Data cutoff date: August 16, 2022

Table 1. Baseline subject characteristics

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)

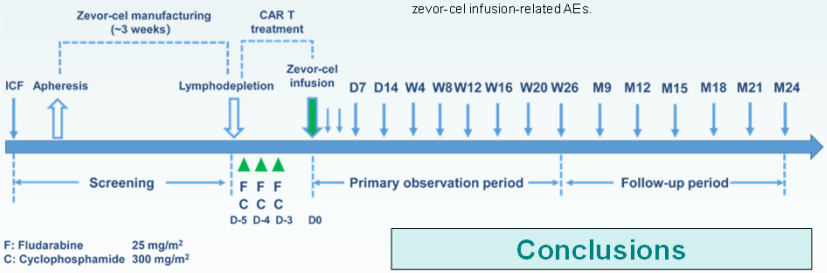

Figure 1. LUMMICAR STUDY 1 schema

Safety

- Zevor-cel was generally well tolerated (**Table 2**)
- Cytokine release syndrome (CRS):
  - ≥ 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

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

Adverse event	Subjects (N=102) No. (%)
Treatment-related AEs (TRAEs) *	102 (100)
Grade ≥3 hematologic TRAEs	102 (100)
Cytokine release syndrome, any grade	92 (90.2)
Grade 1	54 (52.9)
Grade 2	31 (30.4)
Grade 3	5 (4.9)
Grade 4	2 (2.0)
Grade ≥3 neurologic TRAEs	0
ICANS, any grade	2 (2.0)
Grade 1	2 (2.0)
Grade ≥3 infection and infestation TRAEs	30 (29.4)
Treatment-related SAE	38 (37.3)
Death due to TRAE	1 (1.0)

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

Efficacy

- Median follow-up for 102 patients was 9 months (range, 0.4 to 17.8 months)
- Best responses per independent review committee (**Table 3, Figure 2**):
  - ORR was 92.2% (94/102)
  - CR/sCR rate was ≥ 45.1% (46/102), trend to increase with duration of follow-up
  - Remission rate at ≥ VGPR was ≥ 85.3% (87/102)
- Minimal residual disease (MRD) negativity at the 1 in 10^{-5} nucleated cells sensitivity level:
  - 100% in subjects who achieved CR/sCR
  - 96.3% in subjects with ≥ VGPR
- Median DOR and PFS have not been reached (**Figures 3-4**)
  - At Month 9, the DOR rate was 86.1% and the PFS rate was 84.6%.

Table 3. Efficacy summary in zevor-cel treated patients

Best overall response *	≥ 6 months follow-up n=60	≥ 3 months follow-up N=102
Median follow-up duration (range), months	12.1 (0.4-17.8)	9 (0.4-17.8)
ORR, No. (%) [95% CI]	55 (91.7) [81.61, 97.24]	94 (92.2) [85.13, 96.55]
sCR/CR, No. (%) [95% CI]	34 (56.7) [43.24, 69.41]	46 (45.1) [35.22, 55.26]
VGPR, No. (%)	19 (31.7)	41 (40.2)
PR, No. (%)	2 (3.3)	7 (6.9)
≥VGPR, No. (%) [95% CI]	53 (88.3) [77.43, 95.18]	87 (85.3) [76.91, 91.53]

*As of the data cutoff date, per independent review committee assessment. Patients completed the indicated duration of follow-up or withdrew early.

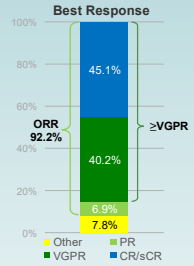

Figure 2. Best response

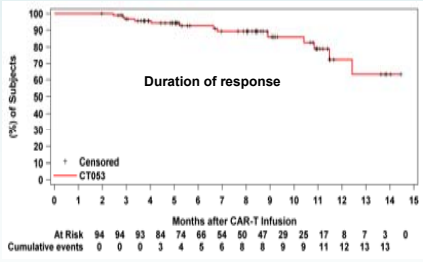

Figure 3. Duration of response

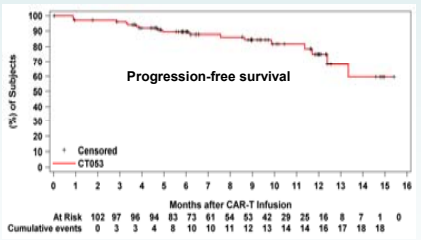

Figure 4. Progression-free survival

Conclusions

LUMMICAR STUDY 1 demonstrated that zevor-cel infused at a target dose of 150×10^6 CAR T cells, delivered deep and sustainable responses, with a well tolerated safety profile in subjects with heavily pretreated R/R MM.

References

- Chen W, Fu C, Cai Z, et al. Sustainable Efficacy and Safety Results from LUMMICAR STUDY 1: A Phase 1/2 Study of Fully Human B-Cell Maturation Antigen-Specific CAR T Cells (CT053) in Chinese Subjects with Relapsed and/or Refractory Multiple Myeloma. Blood 2021; 138 (Supplement 1): 2821.
- Yang M, Zhang W, Yu K, et al. A novel BCMA CAR-T-cell therapy with optimized human scFv for treatment of relapsed/refractory multiple myeloma: results from phase I clinical trials. *Haematologica*. 2022;107(8):1960-1965.

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Learn more about our ongoing zevor-cel clinical studies at clinicaltrials.gov:

- LUMMICAR STUDY 1 (NCT03975907)
- LUMMICAR STUDY 2 (NCT03915184)
- China investigator-initiated trials (NCT03380039; NCT03716856; NCT03302403)