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

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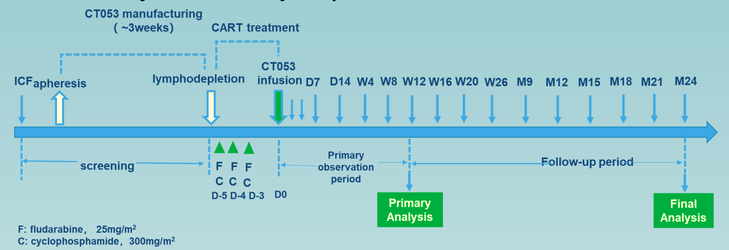
Introduction

- B-cell maturation antigen (BCMA) is a promising therapeutic target in multiple myeloma (MM).
- CT053 (Zevo-cel) is an autologous chimeric antigen receptor (CAR) T cell compound incorporating a fully human BCMA-specific single chain variable fragment (25C2) with high binding affinity and high ratio of monomer.
- Prior studies and results: long term follow up of 24 subjects treated in investigator-initiated trials (IIT) and 14 subjects in current study were ever reported in ASH 2020, showing early, deep and sustainable response of CT053 in RRMM patients with ORR as high as 87.5%-100%.
- We herein reported the results of consistent and sustained efficacy and safety data from the ongoing phase 1 study (LUMMICAR STUDY 1) in China (NCT03975907).

Objectives

- Evaluate safety and tolerability of CT053 (Zevo-cel) and identify the recommended phase 2 dose in subjects with relapsed and/or refractory multiple myeloma (RRMM).
- Evaluate efficacy in RRMM subjects per IMWG 2016.



Methods

- The phase 1 study included RRMM subjects who had received ≥3 prior therapy regimens for evaluation of CT053's safety, efficacy and pharmacokinetics for 24 months.
- CT053 (Zevo-cel) was manufactured in CARsgen's manufacturing center in Shanghai, China.
- All eligible subjects received lymphodepletion preconditioning regimen of fludarabine (25 mg/m^2/day) / cyclophosphamide (300 mg/m^2/day) for 3 days, followed by a single CT053 infusion of 1.0–1.5 × 10^8 CAR+ T cells.
- Dose levels: 3 subjects received one CT053 dose of 1.0 × 10^8 CAR+ T cells; 11 subjects received one CT053 dose of 1.5 × 10^8 CAR+ T cells.
- Between July 2019 and Sep 2020, 14 subjects received CT053 infusion.
- The data cutoff date was July 8th, 2021.

Results

Baseline Characteristics

Table 1. Subject characteristics

Baseline Characteristics	Subjects (N=14)
Age (years)*	54 (34, 62)
Male/female	7/7
Time since diagnosis (years)*	4.7 (1.2, 8.2)
High-risk cytogenetics abnormalities#	7 (50%)
Concomitant extramedullary disease	2 (14.3%)
No. of prior regimens*	6 (3-11)
Proteasome inhibitors	14 (100%)
Immunomodulatory drugs	14 (100%)
Stem cell transplantation	11 (78.6%)
ECOG	
0	7 (50%)
1	7 (50%)
>1	0
ISS	
I&II	12 (85.7%)
III	2 (14.3%)
Tumor BCMA positivity (%)*	42.75 (5.4, 99.7)

- *Median (min, max)
- #High-risk cytogenetic abnormalities included the following: del(17p), t(4;14), t(14;16), t(14;20) and 1q21

Safety

Table 2. Adverse event (AE) summary

Adverse Event	1.0x10^8 cells (N=3)	1.5x10^8 cells (N=11)	Total (N=14)
All AEs	3 (100%)	11 (100%)	14 (100%)
DLT	0	0	0
SAE	0	2 (18.2%)	2 (14.2%)
AE leading to withdrawal	0	0	0
AE leading to death	0	0	0
Grade 3-4 AEs	3 (100%)	11 (100%)	14 (100%)
≥ Grade 3 fever*	0	2 (18.2%)	2 (14.2%)
Grade 3	0	2 (18.2%)	2 (14.2%)
Grade 4	0	0	0
Grade 3-4 hematological toxicity*	3 (100%)	11 (100%)	14 (100%)
Cytokine release syndrome (CRS)*	3 (100%)	10 (90.9%)	13 (92.9%)
Grade 1	2 (66.7%)	7 (63.6%)	9 (64.3%)
Grade 2	1 (33.3%)	3 (27.2%)	4 (28.6%)
Grade 3-4	0	0	0
Grade 3-4 neurotoxicity*	0	0	0
≥ Grade 3 infections and infestations*	0	4 (36.4%)	4 (28.6%)
Grade 3	0	4 (36.4%)	4 (28.6%)
Grade 4	0	0	0

*Treatment related AE, including lymphodepletion-related AEs or CAR-BCMA T-cell infusion-related AEs.

Efficacy

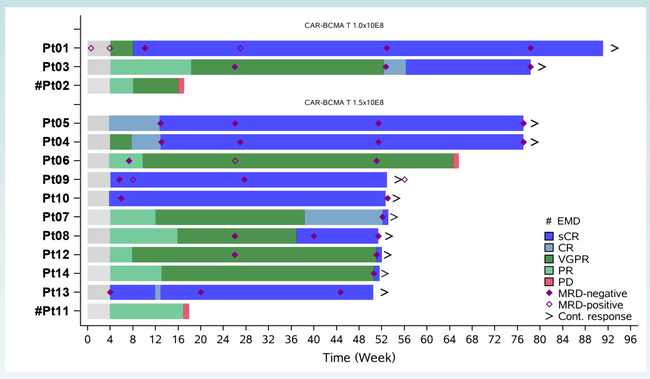


Figure 1. Tumor response by patients

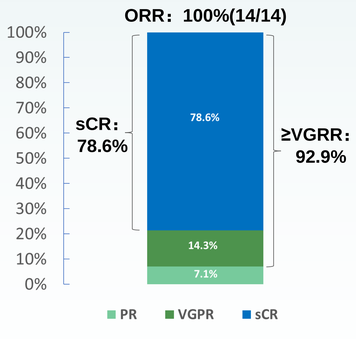


Figure 2. Best response

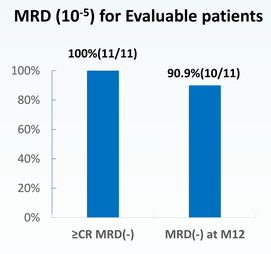


Figure 3. MRD (10^{-5}) Status for evaluable patients

Summary

- At data cutoff on July 8th, 2021, the median follow-up was 13.6 months (range, 4.2–22.4 months).
- CT053 (Zevo-cel) was well tolerated. The most common ≥ grade 3 AE was hematological toxicity which occurred within 3m post infusion.
- No dose-limiting toxicities (DLT) and no death occurred.
- No ≥ grade 3 CRS and Neurotoxicity.
- The ORR was 100% (14/14), including 78.6% (11/14) with MRD-negative sCR , ≥VGPR rate was 92.9% (13/14).
- The CR/sCR rate for the subjects without EMD is 91.7% (11/12)
- 12m-PFS rate was 85.7%, and 100% for subjects without EMD.
- No immunogenicity was detected.

Conclusion

- LUMMICAR STUDY 1 demonstrated that CT053 (Zevo-cel), an investigational fully-human BCMA-targeted CAR T-cell therapy, infused at a target dose of 1.0–1.5×10^8 CAR-T cells delivered early and deep responses, including MRD-negativity in all complete responders, with an acceptable safety profile in subjects with heavily pretreated RRMM.

• Pivotal Phase 2 study is ongoing now.

We are deeply grateful for the contributions of all study participants, especially the study subjects and their families.

Learn more about our ongoing CT053 clinical studies at clinicaltrials.gov:

- LUMMICAR STUDY 1 (NCT03975907)
- LUMMICAR STUDY 2 (NCT03915184)
- China IITs (NCT03380039; NCT03716856; NCT03302403)