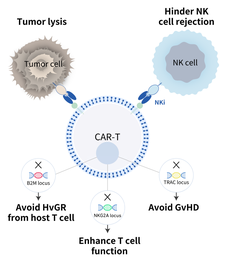
A First-in-Human Study of CT0596, an Allogeneic CAR T-Cell Therapy Targeting BCMA, in Patients with Relapsed/Refractory Multiple Myeloma

J. Du[1,2], L. Jin[1], W. Qiang[1], P. Guo[1], H. He[1], X. Fan[1], X. Zhao[1], D. Yuan[3], Y. Luo[3], and Z. Li[3]
[1] Department of Hematology, Myeloma & Lymphoma Center, Shanghai Changzheng Hospital, Naval Medical University, Shanghai, China.
[2] Department of Hematology, Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.
[3] CARsgen Therapeutics Co. Ltd., Shanghai, China.

INTRODUCTION

Universal CAR T-cell therapy addresses key challenges of autologous CAR T, including high cost, time-consuming, personalized manufacturing and manufacturing failure risks. [1,2]

CT0596



CT0596 is an allogeneic BCMA-targeting CAR T-cell therapy incorporating the knockout of NKG2A, TRAC and B2M genes to mitigate T/NK cell-mediated graft-versus-host disease and host immune rejection, with additional gene editing to further hinder NK cell-mediated rejection from host.

AIM

To evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy of CT0596 in a first-in-human (FIH), open-label, single center, phase I study in relapsed/refractory multiple myeloma (RR MM) and plasma cell leukemia (PCL) patients (NCT06718270).

METHODS

Eligibility:

- Age: ≥18 years;
- Patients with R/R MM had received at least 3 prior lines of therapy. Patients with R/R pPCL had received at least 1 prior line of therapy.
- MM patients have progressive disease following or during the last treatment.
- Patients must have measurable disease.
- ECOG score 0-1.

Dose levels (i3+3 escalating scheme): 1.5×10^8, 3.0×10^8 and 4.5×10^8 CT0596 cells.

CONTACT INFORMATION

Corresponding author: Juan Du

Tel. +86 13962191404; **Email:** juan_du@live.com

RESULTS

Table 1. Patient Characteristics

Baseline characteristic	N=8
Age, median (range), y	63.5 (49, 70)
Sex	
Male, n(%)	4 (50.0)
Female, n(%)	4 (50.0)
Type of Immunoglobulin at Initial Diagnosis, n (%)	
IgG	2 (25.0)
IgA	4 (50.0)
κ Light Chain	2 (25.0)
R-ISS Stage at Screening, n (%)	
I	0
II	5 (62.5)
III	3 (37.5)
Cytogenetic high risk, n(%)	1 (12.5)
Prior Lines of Therapy, median (range)	4.5 (3, 9)
ASCT, n (%)	5 (62.5)
Extramedullary plasmacytoma, n(%)	1 (12.5)
Proportion of Plasma Cells, median (range), %	22.50 (0.5, 53.5)
NKG2A % in NK cells at baseline, median (range), %	20.75 (5.0, 36.7)
Lymphodepletion Dose	
Full Dose[1]	6 (75.0)
Reduced Dose[2]	2 (25.0)
CT0596 Dose (cells) [3]	
1.5×10^8	1 (12.5)
3.0×10^8	5 (62.5)
4.5×10^8	2 (25.0)

Abbreviations: ASCT= Autologous stem cell transplantation; ISS = International Scoring System; NK = Natural killer; NKG2A = Natural killer group 2 member A;

[1] Full dose is defined as fludarabine 30 mg/m² plus cyclophosphamide 500 mg/m² once daily for three consecutive days .
[2] Two patients with reduced dose were 060801002 and 060801006, who received lymphodepletion regimens of fludarabine 30 mg/m²/day and cyclophosphamide 350 mg/m²/day (administered for 3 consecutive days) and fludarabine 22.5 mg/m²/day and cyclophosphamide 375 mg/m²/day (administered for 3 consecutive days), respectively.
[3] PT 04 received a second dose of 4.5 ×10⁸three months after the first infusion of 3.0 ×10⁸ CAR-T cells.

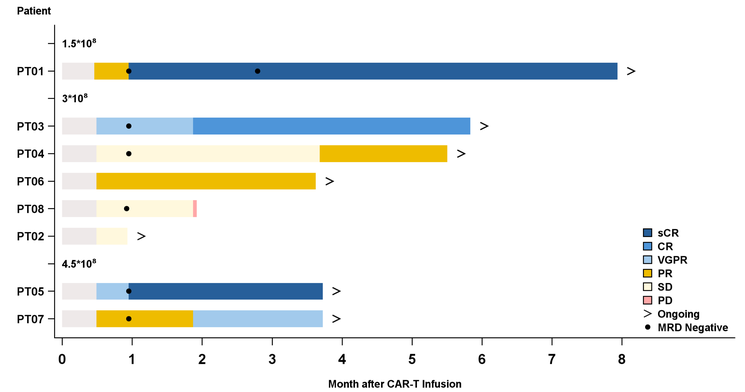
Table 2. Safety Summary

	N (%)
TEAE	8 (100.0)
SAEs	2 (25.0)
≥Grade 3 AEs	8 (100.0)
Treatment related TEAEs	8 (100.0)
SAE	2 (25.0)
≥Grade 3	8 (100.0)
≥Grade 3 Leukopenia	8 (100.0)
≥Grade 3 Neutropenia	7 (87.5)
≥Grade 3 Lymphopenia	7 (87.5)
≥Grade 3 Thrombocytopenia	3 (37.5)
≥Grade 3 Anemia	2 (25.0)
≥Grade 3 Infections	0
CRS	4 (50.0)
ICANS	0
GvHD	0
AEs leading to withdrawal	0
AEs leading to death	0
DLT	0

Abbreviations: AEs = adverse events; CRS = cytokine release syndrome; DLT = dose limiting toxicity; GvHD= graft-vs-host disease; ICANS = immune-cell associated neurotoxicity syndrome; SAEs = serious adverse events; TEAE = treatment emergent adverse events.

- As of 24-June-2025, cytopenias were reported in all 8 patients.
- ≥Grade 3 treatment-related cytopenias:
  - Leukopenia [n=8]
  - Lymphopenia [n=7]
  - Neutropenia [n=7]
  - Thrombocytopenia [n=3]
- Four patients experienced Grade 1 CRS
  - No ≥ Grade 2 CRS
  - Time to onset was 2 (1, 8) days post-infusion
  - Duration was 6 (2, 10) days.
- No cases of ICANS or GvHD were observed.
- No DLTs, no study discontinuation due to AE, no deaths due to AE.

Efficacy Summary



Abbreviations: CR =complete response; MRD = minimal residual disease; PD = progressive disease; PR = partial response; sCR = stringent complete response; SD =stable disease; VGPR = very good partial response

Figure 1. Swimming Plot for All Patients

- As of 31-Aug-2025, 8 infused patients were all evaluable for efficacy, with the median follow-up time of 4.14 months (range 0.9, 7.9).
- Six patients achieved PR or above: 3 CR/sCR (all 3 received full lymphodepletion dose), 1 VGPR and 2 PR. Five out of 6 with full lymphodepletion dose achieved PR or above.
- Six patients achieved MRD negativity at Week 4.
- Disease progression after infusion was observed in one patient with pre-treatment-refractory and aggressive disease.
- PT01 has ongoing sCR and MRD negative until Month 8.
- PT04 achieved PR along with response in extramedullary disease after a second infusion..
- In dose level 4.5×10^8, PT05 got sCR and PT07 exhibited deepening treatment response over time.

CONCLUSIONS

Preliminary results of this FIH study of CT0596, an allogeneic CAR T-cell therapy targeting BCMA for the treatment of RRMM, demonstrate a manageable safety profile while achieving durable clinical responses. Additional clinical studies are warranted to further evaluate the clinical utility of CT0596.

ACKNOWLEDGEMENTS

This trial was funded in part by The National Natural Science Foundation of China (No. 82270210), the National Key Research and Development Program of China (No. 2023YFC3403700) and CARsgen Therapeutics Co., Ltd.

REFERENCES

[1] Lonez C, Breman E. Allogeneic CAR-T Therapy Technologies: Has the Promise Been Met? *Cells*. 2024 Jan 12;13(2):146. doi: 10.3390/cells13020146.
[2] Lin H, Cheng J, Mu W, Zhou J, Zhu L. Advances in Universal CAR-T Cell Therapy. *Front Immunol*. 2021 Oct 6;12:744823. doi: 10.3389/fimmu.2021.744823.