GPRC5D-TARGETED CAR T-CELL THERAPY CT071 FOR THE TREATMENT OF RELAPSED/ REFRACTORY MULTIPLE MYELOMA

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INTRODUCTION

Despite significant progress in the therapeutic landscape, relapsed/refractory multiple myeloma (RRMM) remains incurable[1].

G protein-coupled receptor, class C, group 5, member D (GPRC5D) has emerged as a promising target[2], even for those who are refractory to B-cell maturation antigen (BCMA) targeted therapies.

CT071 is a fully human GPRC5D-targeting autologous CAR T cell product manufactured using an expedited CARcelerate® platform which shortens the manufacturing process to around 30 hours.

AIM

In this first-in-human, single-arm, open-label exploratory clinical trial, we evaluated the safety, pharmacokinetics, and preliminary efficacy of CT071 in patients with RRMM (NCT05838131).

METHODS

Patients with RRMM who had previously received ≥ 3 prior lines of therapy or patients who experienced progression or lack of response having been treated with a proteasome inhibitor and an immunomodulatory agent or those who were double class-refractory, and with ECOG score of 0-2 were enrolled. CT071 was administered as a single infusion at doses of 0.1×10^6 or 0.3×10^6 CAR-positive T cells/ kg using i3+3 design for dose-escalation.

RESULTS

Patient Characteristics

Baseline characteristic	0.1×10^6 (n=8)	0.3×10^6 (n=9)	All (N=17)
Age, median (range), years	64 (51,72)	55 (37,70)	63 (37,72)
Male, n (%)	6 (75.0)	5 (55.6)	11 (64.7)
Time since diagnosis; median (range), years	2.9 (0.8,10.1)	6.0 (2.1,10.9)	5.0 (0.8,10.9)
R-ISS disease stage, n (%)			
I	0	1 (11.1)	1 (5.9)
II	4 (50.0)	8 (88.9)	12 (70.6)
III	4 (50.0)	0	4 (23.5)
ECOG PS, n (%)			
0	3 (37.5)	4 (44.4)	7 (41.2)
1	4 (50.0)	5 (55.6)	9 (52.9)
2	1 (12.5)	0	1 (5.9)
Extramedullary Disease [a], n (%)	2 (25.0)	2 (22.2)	4 (23.5)
High-risk cytogenetics, n (%)	6 (75.0)	6 (66.7)	12 (70.6)
Prior Lines of Therapy, median (range)	4 (1, 12)	5 (3, 7)	5 (1, 12)
Double-class Refractory [b], n (%)	7 (87.5)	9 (100)	16 (94.1)
Triple-class Refractory [c], n (%)	4 (50.0)	7 (77.8)	11 (64.7)
Penta-drug Refractory [d], n (%)	3 (37.5)	1 (11.1)	4 (23.5)
Prior CAR T, n (%)	2 (25.0)	2 (22.2)	4 (23.5)
Prior ASCT, n (%)	2 (25.0)	7 (77.8)	9 (52.9)
Bridging therapy, n(%)	0	1 (11.1)	1 (5.9)

Note, a) defined as soft tissue or paramedullary plasmacytomas; b) Double-class: one or more PI, and one or more IMiD; c) Triple-class: one or more PI, one or more IMiD, and one or more anti-CD38 antibody; d) Penta-drug: two or more PIs, two or more IMiDs, and one or more anti-CD38 antibody.
Abbreviations: Proteasome inhibitor, PI; Immunomodulatory drug, IMiD; R-ISS, Revised International Staging System; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ASCT, Autologous Stem Cell Transplantation. CAR: Chimeric Antigen Receptor.

Safety Summary

Adverse Event (AE) n (%)	0.1×10^6 (n=8)	0.3×10^6 (n=9)	All (N=17)
Treatment-emergent AE	8 (100)	9 (100)	17 (100)
Treatment-related SAE	4 (50.0)	2 (22.2)	6 (35.3)
≥Grade 3 Hematologic TRAE	8 (100)	9 (100)	17 (100)
Leukopenia	8 (100)	7 (77.8)	15 (88.2)
Neutropenia	6 (75.0)	7 (77.8)	13 (76.5)
Thrombocytopenia	6 (75.0)	3 (33.3)	9 (52.9)
Anemia	4 (50.0)	4 (44.4)	8 (47.1)
CRS	6 (75.0)	5 (55.6)	11 (64.7)
Grade 1	5 (62.5)	3 (33.3)	8 (47.1)
Grade 2	1 (12.5)	2 (22.2)	3 (17.6)
ICANS	0	0	0
Onychomadesis	4 (50.0)	0	4 (23.5)
Skin rash	0	1 (11.1)	1 (5.9)
≥Grade 3 treatment-related Infections	2 (25.0)	1 (11.1)	3 (17.6)
AE leading to death	0	0	0

Abbreviations: TRAE, Treatment-related Adverse Event; SAE, Serious Adverse Event; CRS, Cytokine Release Syndrome; ICANS, Immune Effector Cell-associated Neurologic Syndrome.

- As of June 21, 2024, the median follow-up was 6.2 months (range, 1.0 to 11.2).
- The median duration of CRS was 3 days (range, 2 to 8), and all recovered.
- Onychomadesis occurred in 4 patients (23.5%) and skin rash occurred in 1 patient (5.9%), all Grade 1.
- No dose limiting toxicity, ICANS, or death due to AE occurred.

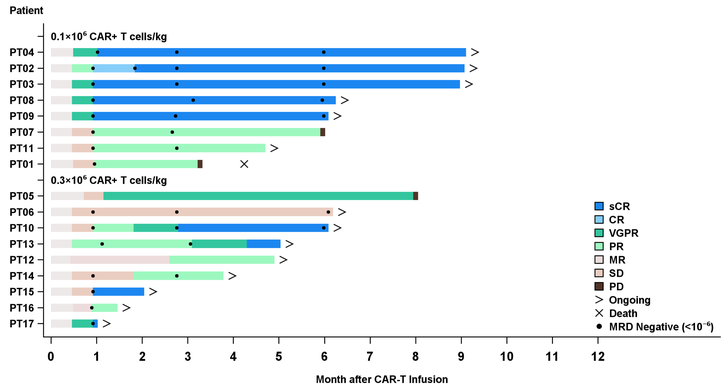
Efficacy and Pharmacokinetics Summary

Efficacy	0.1×10^6 (n=8)	0.3×10^6 (n=9)	All (N=17)
BOR, n (%)			
sCR	5 (62.5)	4 (44.4)	9 (52.9)
CR	0	0	0
VGPR	0	1 (11.1)	1 (5.9)
PR	3 (37.5)	3 (33.3)	6 (35.3)
SD	0	1 (11.1)	1 (5.9)
CR or better, n (%)	5 (62.5)	4 (44.4)	9 (52.9)
VGPR or better, n (%)	5 (62.5)	5 (55.6)	10 (58.8)
ORR, n (%)	8 (100)	8 (88.9)	16 (94.1)
Time to CR or better, median (min, max), months	1 (1.0, 1.1)	1.9 (1.0, 4.3)	1 (1.0, 4.3)
MRD Negativity (10^{-6}) in BM, n (%)	8 (100)	7 (77.8)	15 (88.2)
MRD negativity (10^{-6}) with CR/sCR*, n(%)	5 (100)	4 (100)	9 (100)

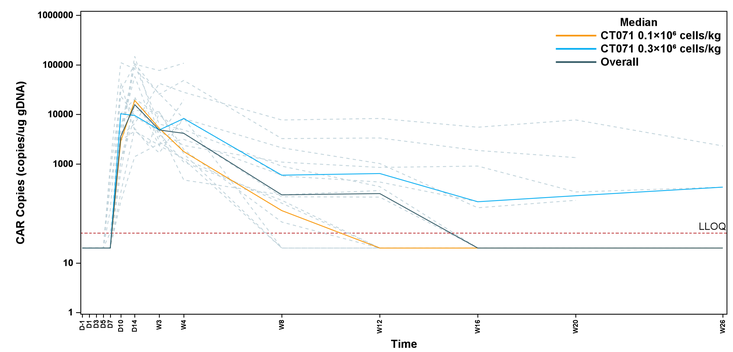
** Percentages were calculated based on CR/sCR patients (n=9).*
Abbreviation: BOR, Best Overall Response; sCR, stringent Complete Response; CR, Complete Response; VGPR, Very Good Partial Response; PR, Partial Response; SD, Stable Disease; ORR, Objective Response Rate; CI, Confidence interval; Min, Minimum; Max, Maximum; MRD, Minimal residual disease; BM, Bone Marrow.

- One patient with SD demonstrated ongoing tumor shrinkage of a large EMD (125 mm×99 mm at baseline) with 38.2% decrease at week 26, along with 93.0% decrease in serum M protein from baseline.
- All 4 patients with previous exposure to BCMA or BCMA/CD19 CAR T responded (2 sCR and 2 PR).

Swimmer Plot



Pharmacokinetics plot



Note: LLOQ, lower limit of quantitation (40 copies/μg gDNA); Concentrations below the limit of quantitation are imputed as ½ of the LLOQ.

- Median T_{max}: 14 days (range: 10 to 28).
- Median C_{max}: 42203.0 copies/μg gDNA (range: 3127 to 156000).
- Median $AUC_{0\text{-}t}$: 295795.0 day*copies/μg gDNA (range: 81705.0 to 2221936.0).
- Median T_{last}: 60.0 days (range: 28 to 189).

CONCLUSIONS

CT071 shows a promising safety profile with compelling clinical response in RRMM patients including in patients with prior BCMA or BCMA/CD19 CAR T exposure.

REFERENCES

[1] National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Multiple Myeloma (Version 1.2025), September 17, 2024
[2] Mailankody S, Devlin SM, Landa J, et al. GPRC5D-Targeted CAR T Cells for Myeloma. N Engl J Med. 2022;387(13):1196-1206.

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