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# First-in-human Study of GPRC5D-targeted CAR T Cells (CT071) with An Accelerated Manufacturing Process in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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## INTRODUCTION

Despite many recent advances, relapsed or refractory multiple myeloma (RRMM) remains incurable[1] and innovative treatments are still needed. G protein-coupled receptor, class C, group 5, member D (GPRC5D) is an emerging target for the treatment of MM[2]. CT071 is a fully human GPRC5D-targeting autologous second-generation CAR T-cell product manufactured using a CARcelerate™ platform which expedites the manufacturing process to approximately 30 hours resulting in much shorter vein-to-vein time and younger, healthier T cells.

## AIM

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

## METHODS

Patients with RRMM with an ECOG score 0-2 who had previously received at least ≥ 3 prior lines including a proteasome inhibitor (PI) and an immunomodulatory drug (IMID) or 1 prior line of therapy with prior relapse, lack of response or lack of tolerability to a PI and an IMID were enrolled. CT071 was administered as a single infusion at doses of $1.0\times10^5$ or $3.0\times10^5$ CAR-positive (CAR+) T cells/kg using i3+3 design for dose-escalation and dose-expansion.

## CONCLUSIONS

In the ongoing exploratory trial, preliminary data from CT071, an autologous fully human anti-GPRC5D CAR T-cell product with expedited manufacturing, demonstrate an acceptable safety profile and encouraging clinical efficacy in patients with RRMM without the need for bridging therapy, and warrants further clinical evaluation.

## REFERENCE

[1] Moreau P, et al. *Lancet Oncol.* 2021;22(3):e105-e118.

[2] Mailankody S, et al. *N Engl J Med.* 2022;387(13):1196-1206.

## RESULTS

### Patient Characteristics

| Baseline characteristic | $1.0\times10^5$ (n=7) | $3.0\times10^5$ (n=3) | All patients (n=10) |
|---|---|---|---|
| Age, median (range), y | 63.0 (51, 72) | 48.0 (46, 55) | 58.5 (46, 72) |
| Male, n(%) | 6 (85.7) | 2 (66.7) | 8 (80.0) |
| Years since diagnosis, median (range) | 3.7 (0.8, 10.1) | 4.4 (3.9, 10.9) | 4.2 (0.8, 10.9) |
| R-ISS Stage, n(%) | | | |
| II | 3 (42.9) | 3 (100) | 6 (60.0) |
| III | 4 (57.1) | 0 | 4 (40.0) |
| Extramedullary Disease, n(%) | 2 (28.6) | 1 (33.3) | 3 (30.0) |
| ECOG PS, n (%) | | | |
| 0 | 3 (42.9) | 2 (66.7) | 5 (50.0) |
| 1 | 3 (42.9) | 1 (33.3) | 4 (40.0) |
| 2 | 1 (14.3) | 0 | 1 (10.0) |
| High-risk Cytogenetics, (%) | 6 (85.7) | 2 (66.7) | 8 (80.0) |
| Prior Lines of Therapy, median (range) | 5.0 (1, 12) | 5.0 (3, 6) | 5.0 (1, 12) |
| Prior Regimens of Therapy, median (range) | 7 (3, 13) | 8 (6, 9) | 7.5 (3, 13) |
| Double-class Refractory, n (%) | 6 (85.7) | 3 (100) | 9 (90.0) |
| Triple-class Refractory, n (%) | 4 (57.1) | 3 (100) | 7 (70.0) |
| Penta-class Refractory, n (%) | 3 (42.9) | 1 (33.3) | 4 (40.0) |
| CAR-T Refractory, n (%) | 2 (28.6) | 0 | 2 (20.0) |
| Stem cell transplantation, n (%) | 2 (28.6) | 3 (100) | 5 (50.0) |

*Note: y, years; Double-class refractory defined as refractory to one or more immunomodulatory drugs (IMiDs) and one or more proteasome inhibitors (PIs) and the reason for discontinuation is disease progression, lack of efficacy or other. Triple-class refractory defined as refractory to one or more PIs, one or more IMiDs, and at least one anti-CD38 antibody and the reason for discontinuation is disease progression, lack of efficacy or other. Penta-class refractory defined as refractory to two or more PIs, two or more IMiDs, and at least one anti-CD38 antibody and the reason for discontinuation is disease progression, lack of efficacy or other.*

### Safety Summary

| Characteristic, n (%) | $1.0\times10^5$ (n=7) | $3.0\times10^5$ (n=3) | All patients (n=10) |
|---|---|---|---|
| TEAE | 7 (100) | 3 (100) | 10 (100) |
| Treatment-emergent SAE | 4 (57.1) | 0 | 4 (40.0) |
| Treatment-related SAE | 4 (57.1) | 0 | 4 (40.0) |
| CRS, any grade | 5 (71.4) | 0 | 5 (50.0) |
| Grade 1 | 4 (57.1) | 0 | 4 (40.0) |
| Grade 2 | 1 (14.3) | 0 | 1 (10.0) |
| ICANS, any grade | 0 | 0 | 0 |
| ≥Grade 3 Infections | 4 (57.1) | 0 | 4 (40.0) |
| Treatment-related Infections | 2 (28.6) | 0 | 2 (20.0) |
| ≥Grade 3 hematologic TRAE | 7 (100) | 3 (100) | 10 (100) |
| Neutropenia | 5 (71.4) | 1 (33.3) | 6 (60.0) |
| Thrombocytopenia | 5 (71.4) | 0 | 5 (50.0) |
| Anemia | 3 (42.9) | 2 (66.7) | 5 (50.0) |
| Death due to TEAE | 0 | 0 | 0 |

*Note: AE, Adverse Events; TEAE, Treatment-emergent AE; TRAE, Treatment-related AE; CRS, Cytokine Release Syndrome; SAE, Serious Adverse Events; ICANS, Immune Effector Cell–associated Neurologic Syndrome.*

- As of February 28, 2024, all 10 infused patients experienced Grade 3 or higher hematologic toxicities.
- Five patients (50%) had CRS, all at Grade 1 (n=4) or 2 (n=1).
- Four patients experienced treatment-related SAE, including pneumonia (n=1), decreased appetite (n=1) and thrombocytopenia (n=2), and all recovered.
- No dose limiting toxicity, AESI, ICANS, or death due to TRAE occurred.
- One patient in $1.0\times10^5$ cells/kg dose group had died due to progressive disease 134 days after cell infusion, which was unrelated to CT071.

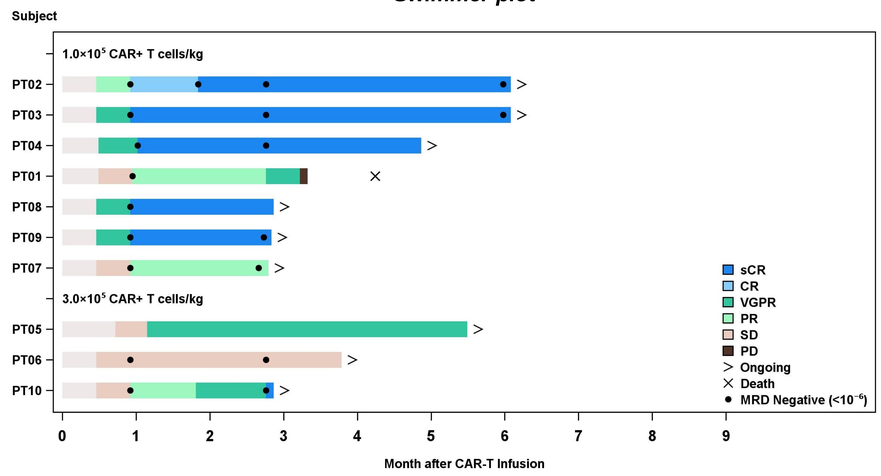
### Efficacy and Pharmacokinetics Summary

| | $1.0\times10^5$ (n=7) | $3.0\times10^5$ (n=3) | All patients (n=10) |
|---|---|---|---|
| Best Overall Response, n(%) | | | |
| sCR | 5 (71.4) | 0 | 5 (50.0) |
| CR | 0 | 0 | 0 |
| VGPR | 0 | 2 (66.7) | 2 (20.0) |
| PR | 2 (28.6) | 0 | 2 (20.0) |
| SD | 0 | 1 (33.3) | 1 (10.0) |
| ORR, n(%), (95% CI) | 7 (100) (59.0, 100.0) | 2 (66.7) (9.4, 99.2) | 9 (90.0) (55.5, 99.7) |
| CR/sCR rate, n(%) | 5 (71.4) | 0 | 5 (50.0) |
| VGPR or better rate, n(%) | 5 (71.4) | 2 (66.7) | 7 (70.0) |
| Time to Response, Median (range), Month | 0.5 (0.5, 1.0) | 1.1 (1.0, 1.2) | 0.5 (0.5, 1.2) |
| Time to VGPR or better, Median (range), Month | 0.5 (0.5, 1.0) | 1.5 (1.2, 1.8) | 0.5 (0.5, 1.8) |
| Time to CR or better, Median (range), Month | 1.0 (1.0, 1.1) | NA | 1.0 (1.0, 1.1) |
| MRD Negativity ($<10^{-6}$) within subjects with MRD results at Week 4, n (%) | 7 (100) | 2 (100) | 9 (100) |
| MRD negativity ($<10^{-6}$) within CR/sCR subjects, n(%) | 5 (100) | 0 | 5 (100) |

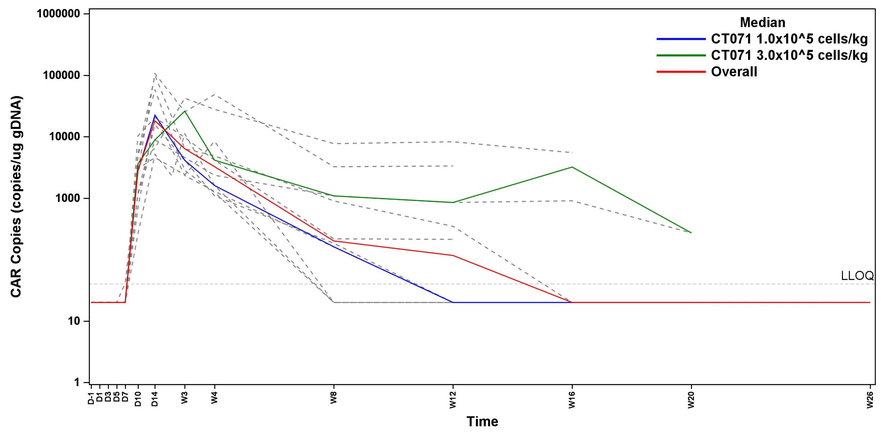
*Note: CI, Confidence Interval; CR, Complete Response; DOR, Duration of Response; MRD, Minimal Residual Disease; NA, Not Applicable; ORR, Objective Response Rate; PR, Partial Response; sCR, Stringent Complete Response; SD, Stable Disease; VGPR, Very Good Partial Response.*

- As of February 28, 2024, the median follow-up time was 4.07 months (range: 2.8 to 7.4).
- The median vein-to-vein time (from leukapheresis to infusion) was 21.5 days (range: 18 to 44).
- The ORR assessed by investigator was 90% (95 CI, 55.5%, 99.7%).
- Two patients had previously received BCMA/CD19 CAR T; both achieved a response (1 sCR and 1 PR).
- All the 9 patients with evaluable MRD achieved MRD negativity ($10^{-6}$ threshold), including all 5 patients with sCR/CR at Week 4.

### Swimmer plot




### Pharmacokinetic plot (semi-logarithmic)




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

- As of February 28, 2024, the pharmacokinetic results of these 10 patients received CT071 infusion showed a good cell expansion and persistence.
- Median $T_{max}$: 14 days (range: 12 to 28).
- Median $C_{max}$: 32280.5 copies/μg gDNA (range: 8372 to 106060).
- Median $AUC_{0\text{-}t}$: 240361.0 day*copies/μg gDNA (range: 81705.0 to 938574.5).
- Median $T_{last}$: 35.5 days (range: 28 to 96).

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## CONTACT INFORMATION

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