Integrated Analysis of B-cell Maturation Antigen-Specific CAR T Cells (CT053) in Relapsed and Refractory Multiple Myeloma Subjects by High-Risk Factors

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Introduction

- Various clinical trials of B-cell maturation antigen (BCMA) targeted chimeric antigen receptor (CAR) T-cell clinical trials are under way, which have shown an exciting effect in relapsed and refractory multiple myeloma (RRMM).

- Prior studies of CT053 (Zevorcabtagene autoleucel, Zevo-cel), including 3 investigator-initiated trials (NCT03380039, NCT03716856, NCT03302403) and LUMMICAR STUDY 1 (NCT03975907), demonstrated deep and durable responses in heavily pretreated subjects with RRMM (reported in ASH 2020 presentation #132 and #1396).

- Here we report integrated efficacy and safety of CT053 (Zevo-cel) in Chinese subjects with RRMM based on high-risk factors.
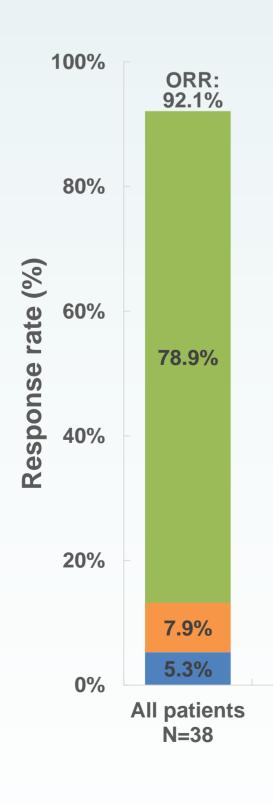
Objectives
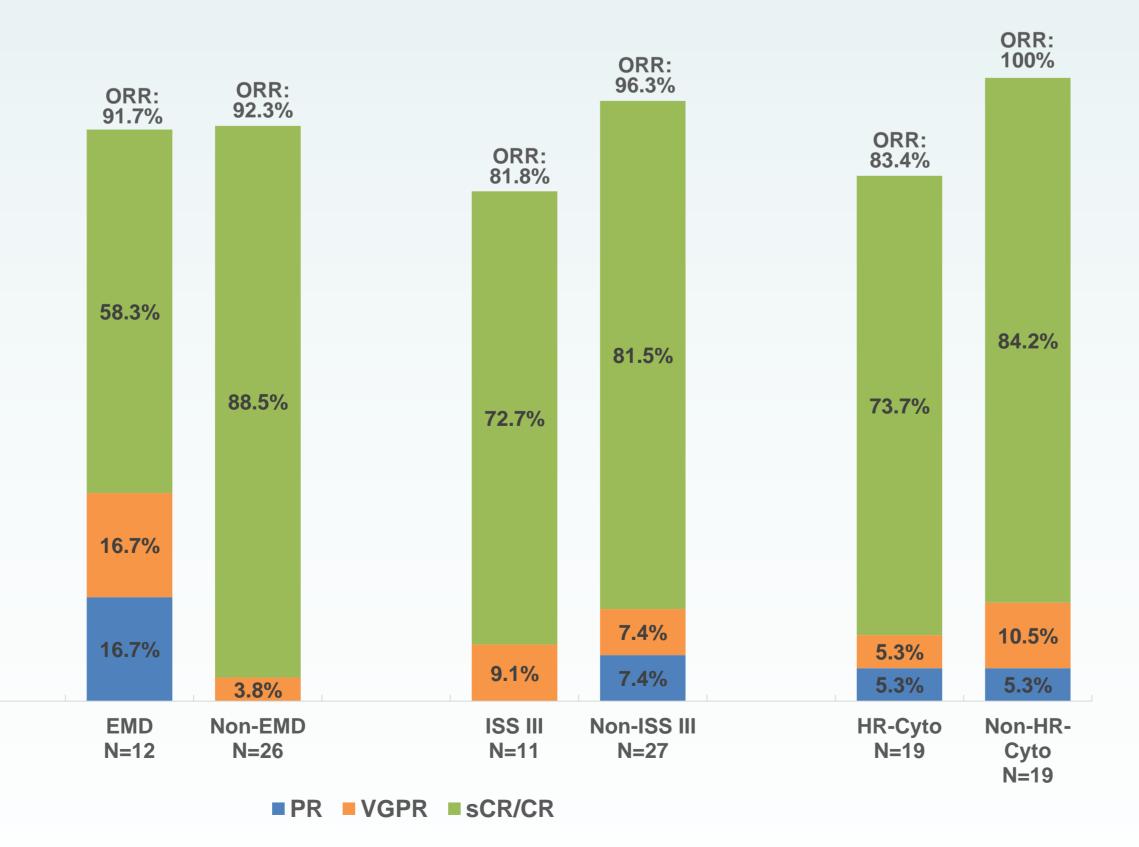
- Evaluate efficacy and safety of CT053 (Zevo-cel) in Chinese subjects with RRMM by combined prior studies.

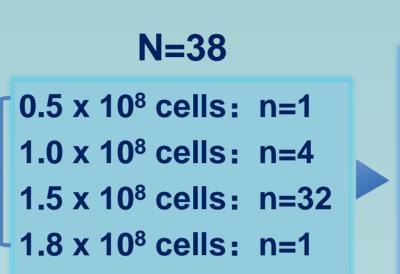- Integrated subgroup analysis of efficacy in subjects stratified by high-risk characteristics.

Investigator-Initiated Trials (IIT) (N=24)

LUMMICAR STUDY 1 (N=14)

Subjects profile:
- 18-75 y
- R/R MM
- ECOG 0-1
- ≥2 prior regimens
- Sufficient organ function

N=38
- 0.5 x 10^8 cells: n=1
- 1.0 x 10^8 cells: n=4
- 1.5 x 10^8 cells: n=32
- 1.8 x 10^8 cells: n=1

Integrated Analysis and Stratification analysis by high-risk factors
High-Risk cytogenetic abnormalities[#]
Extramedullary disease (EMD)
ISS Stage III

Methods

- All subjects received ≥2 prior regimens, including at least an immunomodulatory drug and a proteasome inhibitor. Subjects also could have had exposure to an anti-CD38 antibody. All subjects were refractory to the last therapy per International Myeloma Working Group criteria.

- After lymphodepletion, subjects received a dose of 0.5 (n=1), 1.0 (n=4), 1.5 (n=32), or 1.8 (n=1) × 10^8 CAR+ T cells.

- Integrated subgroup analysis was conducted to evaluate efficacy and safety in subjects stratified by high-risk characteristics, including extramedullary disease (EMD), high-risk cytogenetics [del(17p), t(4;14), t(14;16), t(14;20) and 1q21], and ISS stage III

- The IIT and LUMMICAR STUDY 1 Data cutoff date were Jun 30, 2021 and July 8, 2021, respectively.

Results

Baseline Characteristics

Table 1. Patients' characteristics

Table 1. Patients Characteristics			
	IIT N=24	LUMMICAR STUDY 1 (N=14)	ALL N=38
Age (year)*	60 (38, 70)	54 (34, 62)	56 (34, 70)
Male/Female, %	54.2%/45.8%	50.0%/50.0%	52.6%/47.4%
No. of prior regimens*	5 (2, 12)	6 (3, 11)	6 (2, 12)
High-risk cytogenetic abnormalities[#]	12 (50.0%)	7 (50.0%)	19 (50.0%)
Concomitant extramedullary disease	10 (41.7%)	2 (14.3%)	12 (31.6%)
ECOG			
0	5 (20.8%)	7 (50.0%)	12 (31.6%)
1	11 (45.8%)	7 (50.0%)	18 (47.4%)
>1	8 (33.3%)	0	8 (21.1%)
ISS stage			
I&II	15 (62.5%)	12 (85.7%)	27 (71.1%)
III	9 (37.5%)	2 (14.3%)	11 (28.9%)

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

Efficacy

Table 2. Efficacy Data.

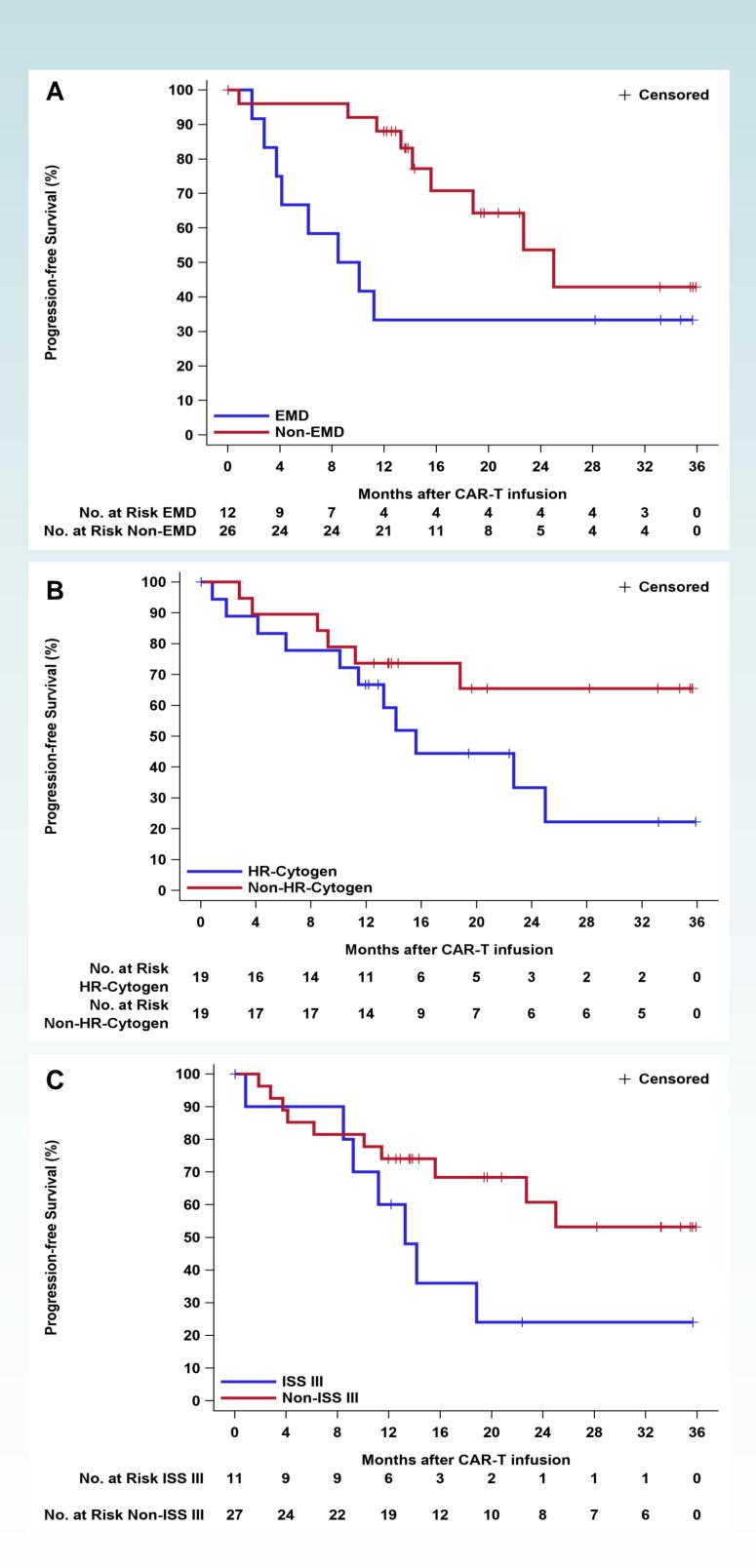|	EMD status		High-Risk Cytogenetics[#]		ISS stage		Total N=38
	EMD N=12	Non-EMD N=26	HR-Cyto N=19	Non-HR-Cyto N=19	ISS III N=11	Non-ISS III N=27	
Median Follow-up time, month	9.3	14.9	12.9	15.4	12.2	15.4	13.9
ORR, n(%)	11 (91.7%)	24 (92.3%)	16 (84.2%)	19 (100%)	9 (81.8%)	26 (96.3%)	35 (92.1%)
sCR/CR, n(%)	7 (58.3%)	23 (88.5%)	14 (73.7%)	16 (84.2%)	8 (72.7%)	22 (81.5%)	30 (78.9%)
mPFS, month (95%CI)	9.3 (2.8, NE)	25.0 (15.6, NE)	15.6 (10.1, 25.0)	NR (11.2, NE)	13.3 (0.9, NE)	NR (15.6, NE)	22.7 (13.3, NE)
mDoR, month (95%CI)	9.2 (2.8, NE)	24.0 (14.8, NE)	18.3 (9.2, NE)	NR (10.3, NE)	13.3 (7.6, NE)	NR (14.8, NE)	24.0 (13.3, NE)

Figure 1. Best response

Figure 2. Progression-free survival, stratified by (A) EMD; (B) High-Risk Cytogenetics; (C) ISS stage.

Summary

- Total of 38 heavily treated R/R MM subjects, including 31.6% with EMD, 50.0% had HR-Cyto, and 28.9% had ISS III disease.

- With a median follow-up of 13.9 month, the ORR was 92.1% with 78.9% achieving sCR/CR, the mPFS and mDoR were 22.7m and 24.0m respectively

- The sCR/CR rate, mPFS and mDOR were 58.3%, 9.3m and 9.2m in subjects with EMD, while those in Non-EMD subjects were 88.5%, 25.0m and 24.0m, respectively; The mPFS and mDOR in subjects with HR-Cyto were 15.6m and 18.3m, and were both 13.3m in ISS III subjects, while those were all had not been reached in subjects without these two high-risk factors.

- Subjects with EMD, HR-Cyto or ISS III at baseline may be the high-risk factors to affect clinical benefit.

- No DLT, treatment-related death or no ≥Grade 3 CRS occurred.

Conclusion

- The results demonstrate that CT053 (Zevo-cel) represents a promising treatment option for subjects with RRMM, including those with high-risk profiles, and shown an acceptable safety profile.

- Pivotal Phase 2 study is ongoing now.

HR-Cyto: High-risk cytogenetic abnormalities; ORR: overall response rate; CR: complete response; sCR: stringent complete response; PR: partial response; VGPR: very good partial response; PFS: progression-free survival ; DoR: duration of response; NR: Not Reached; NE: Not Estimated