

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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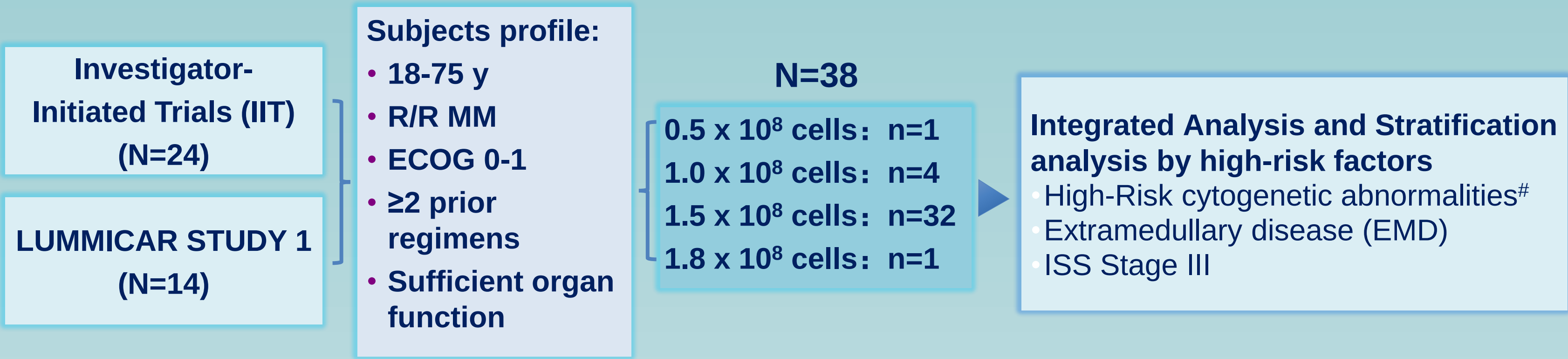
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Introduction

- 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 autoleucl, 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.



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) × 10⁸ 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

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	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)

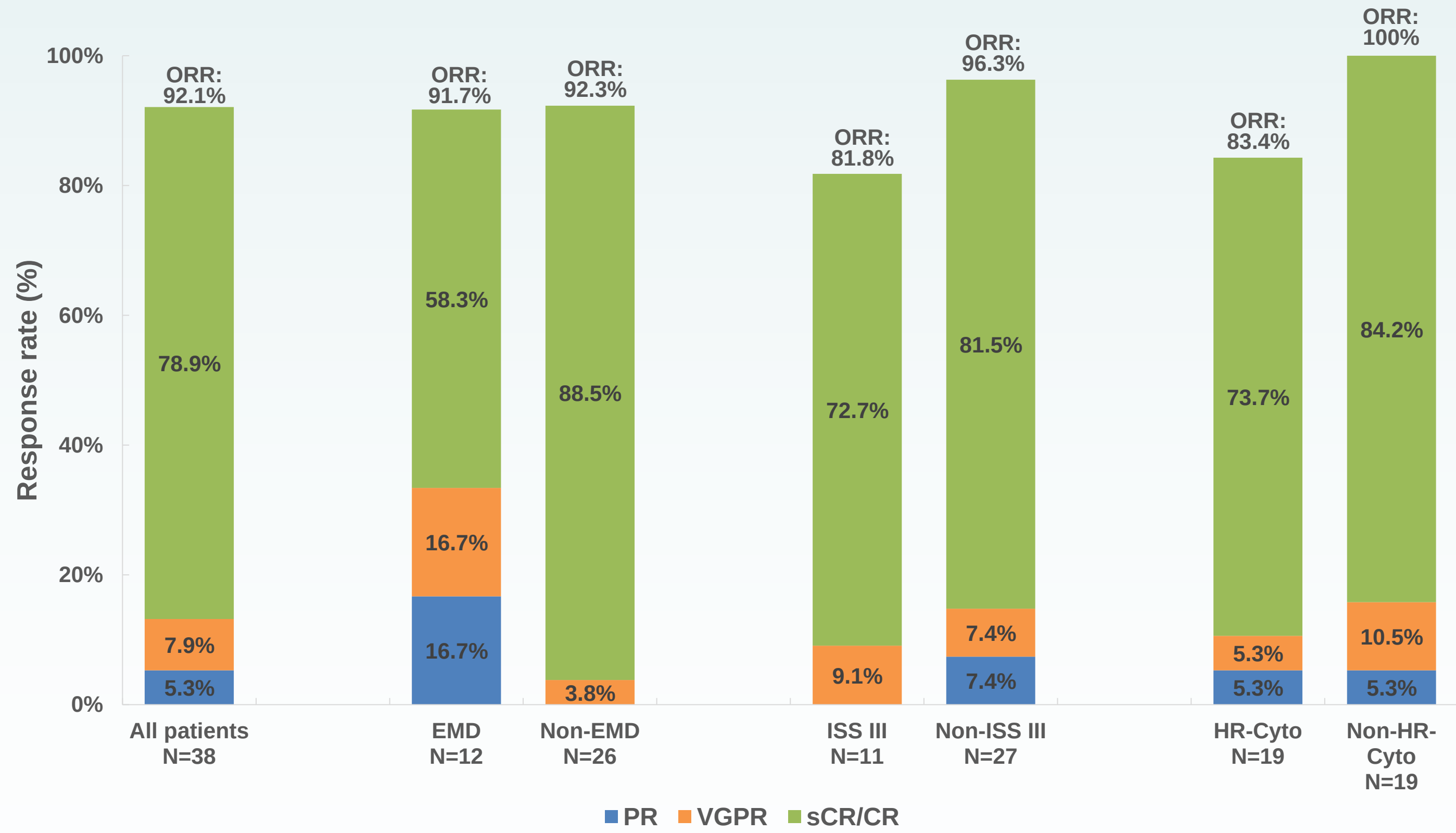


Figure 1. Best response

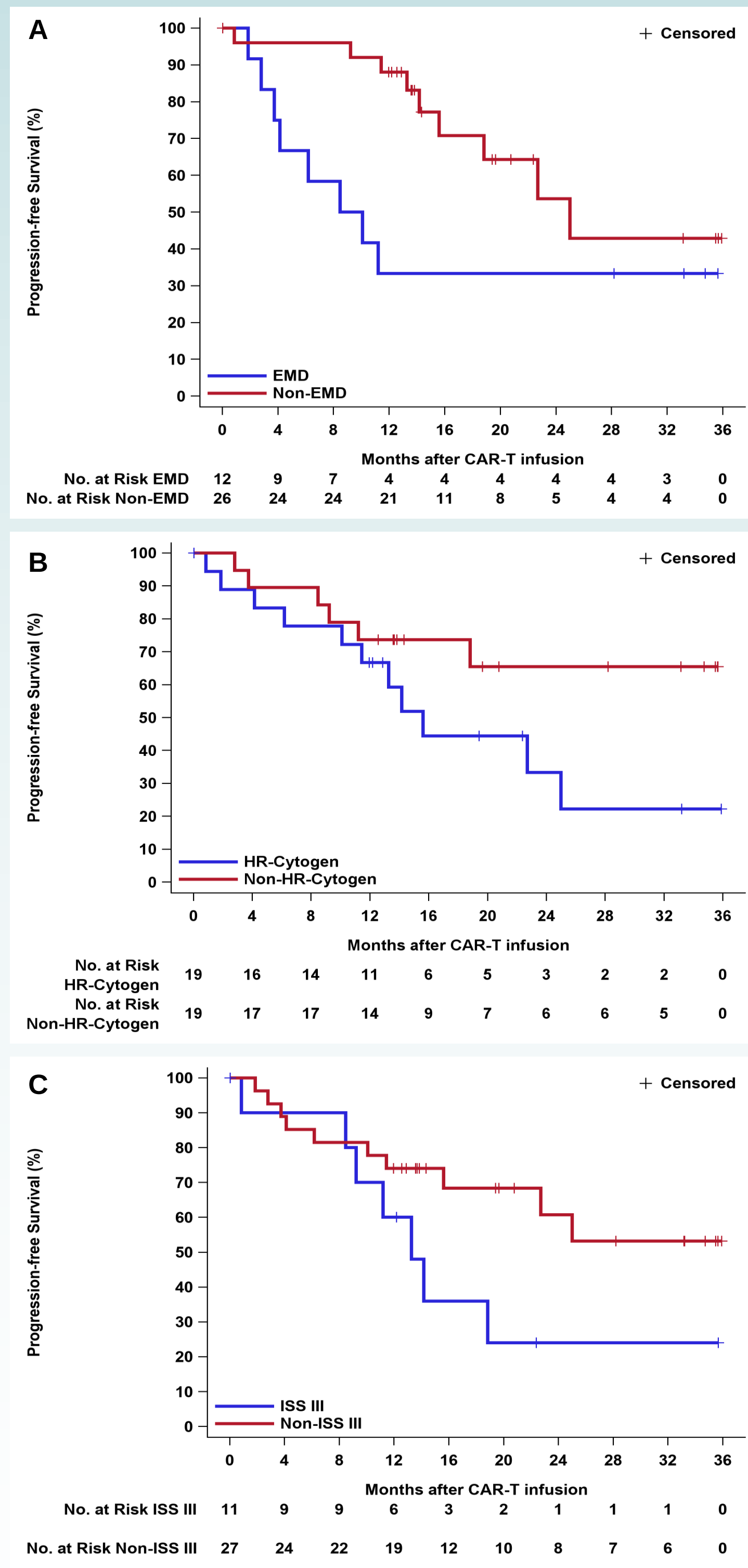


Figure 2. Progression-free survival, stratified by (A) EMD; (B) High-Risk Cytogenetics; (C) ISS stage.

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.

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)

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

