EHA2024

JUNE 13 - 16 | MADRID

IN-PERSON AND LIVE STREAMED

PHASE 2 STUDY OF FULLY HUMAN BCMA-TARGETING CAR-T CELLS (ZEVORCABTAGENE AUTOLEUCEL) IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

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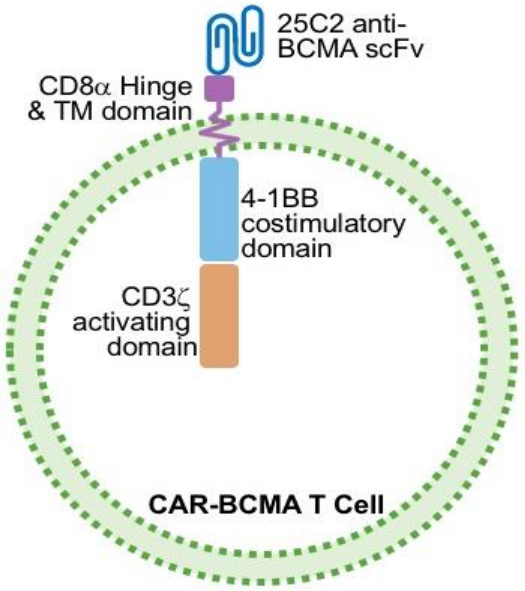
LUMMICAR STUDY 1 (NCT03975907)

Zevorcabtagene autoleucel (zevor-cel or CT053) : BCMA Car T

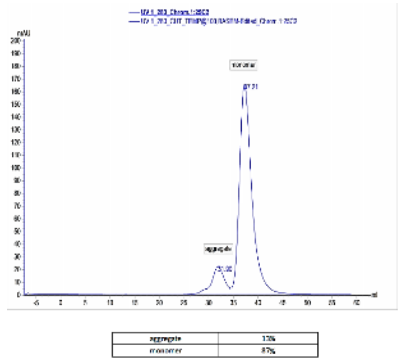
High Binding affinity (pM level)[1]

	KD(M)
BCMA	4.548E-10



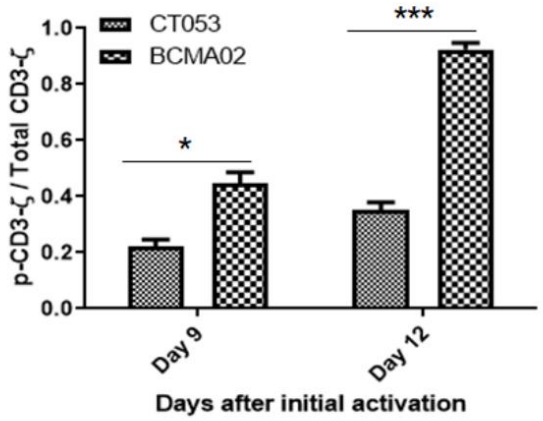
High stability

High Monomer Ratio
(~90%)



Reduced antigen-independent clustering

Less CD3 autophosphorylation



a. BCMA02 CAR was made according to the construct of another CAR-T

1.Yang, Min et al. *Haematologica* vol. 107,8 1960-1965. 2022 Aug 1

Study Background

Investigator Initiated Study[1]

- 24 patients infused with zevor-cel
- Median follow-up 17.4 months
- ORR 87.5%，sCR/CR 79.2%
- Acceptable safety profile

LUMMICAR-1 Phase 2

- 102 patients infused with zevor-cel
- Confirmatory clinical trial in China

LUMMICAR-1 Phase I[2]

- 14 patients infused with zevor-cel
- Median follow-up 37.7 months
- ORR 100%, sCR/CR 78.6%, ≥ VGPR 92.9%
- mPFS 25.0 months (all patients), 26.9 months (patients with sCR/CR)
- DOR 24.1 months (all patients), 26.0 months (patients with sCR/CR)
- CRS 92.9% (all grade 1 or 2), no ICANS
- 2 patients had died at month 42.6 and 32.6, respectively, both were unrelated to zevor-cel

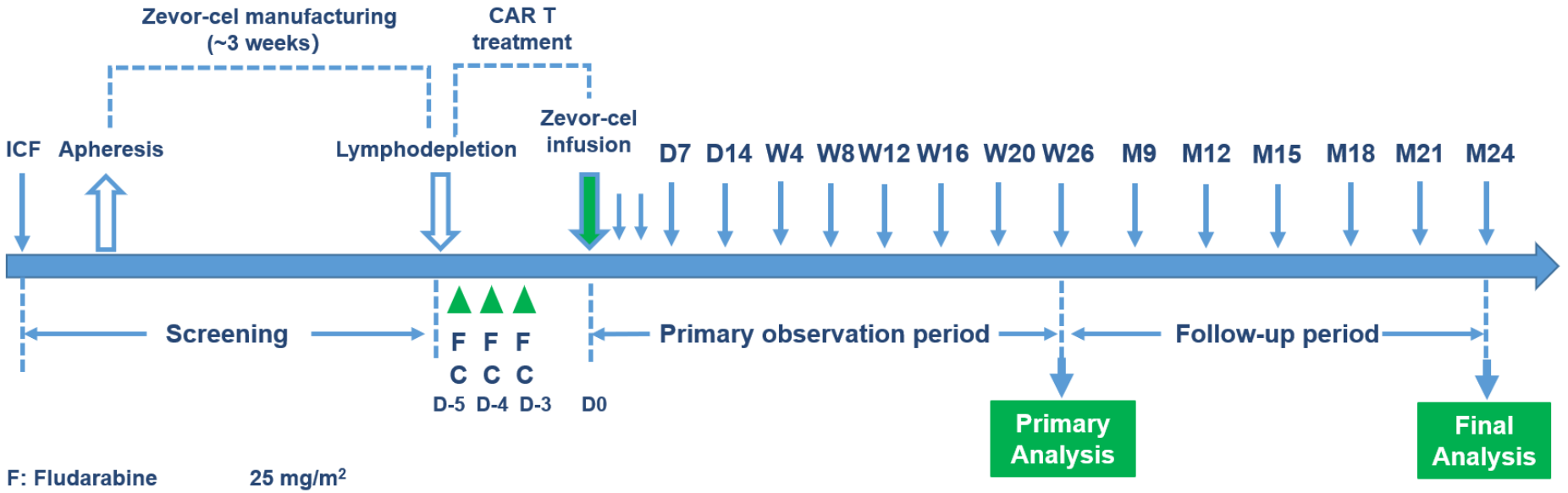
- The initial results from the Phase 2 cohort (n=102) of the ongoing Phase 1/2 study LUMMICAR-1 evaluating zevor-cel showed compelling efficacy with an acceptable safety profile in heavily pre-treated patients with R/R MM (Wenming Chen, et al. Blood 2022;140 (S1):4564–4565).
- Herein, we provide the updated results from the same Phase 2 cohort with a longer follow-up.

1.Yang, Min et al. *Haematologica* vol. 107,8 1960-1965. 2022 Aug 1
2.Chengcheng Fu, et al. *Blood* (2023) 142 *(Supplement 1):* 4845.

LUMMICAR STUDY 1

Study Design

An open label, multicenter, Phase 1/2 clinical study (LUMMICAR STUDY 1) to evaluate the safety and efficacy of autologous zevor-cel in patients with relapsed and/or refractory multiple myeloma (R/R MM).



F: Fludarabine 25 mg/m²
C: Cyclophosphamide 300 mg/m²

Phase 2 dose level:

- **150 × 10^6 cells**
- 180 × 10^6 cells in patients > 80 kg

Key eligibility criteria:

- 18-75 years
- R/R MM
- ECOG 0-1
- At least 3 prior lines of therapy
- Sufficient organ function

Primary endpoint

- Determine the efficacy (ORR) of zevor-cel treatment in patients with R/R MM by an independent review committee (IRC) assessment

Secondary endpoints

- ORR by investigator assessment
- DOR, PFS, OS, CR/sCR, ≥ VGPR, TTR and MRD negativity
- Evaluate the safety and tolerability (AE, SAE, AESI etc.)
- Evaluate PK and biodistribution

AESI: Adverse event of special interest; **ECOG:** Eastern Cooperative Oncology Group performance status; **DOR:** duration of response; **MRD:** minimal residual disease; **ORR:** objective response rate; **OS:** overall survival; **PFS:** progression-free survival; **PK:** pharmacokinetics; **TTR:** time to response

LUMMICAR STUDY 1

Patient Characteristics

Baseline characteristic	Subjects (N=102)
Age, median (range), years	59.5 (38-75)
Sex	
Men, No. (%)	55 (53.9)
Women, No. (%)	47 (46.1)
Years since diagnosis, median (range)	3.6 (0.7-16)
Prior lines of therapy, median (range)	4.0 (3-15)
Prior antitumor regimens, median (range)	6.0 (3-17)
International Staging System, No. (%)	
I	24 (23.5)
II	39 (38.2)
III	39 (38.2)
Cytogenetic high risk, No. (%)	**61 (59.8)**
Extramedullary plasmacytoma, No. (%)	11(10.8)
Bone marrow plasma cells, No. (%)	100
< 50%	83 (81.4)
≥ 50%	17 (16.7)

102 R/R MM patients enrolled:

- Median age of 59.5 years
- 38.2% of patients had ISS stage III disease
- 59.8% of patients had at least one high-risk cytogenetic abnormality
- 89.2% of patients were double-class refractory
- 22.5% of patients were triple-class refractory
- 23.5% of patients received prior hematopoietic stem cell transplant

Baseline characteristic	Subjects (N=102)
Double-class refractory, No. (%)	91 (89.2)
Triple-class refractory, No. (%)	23 (22.5)
Prior hematopoietic stem cell transplant, No. (%)	24 (23.5)
Bridging therapy, No. (%)	26 (25.5)

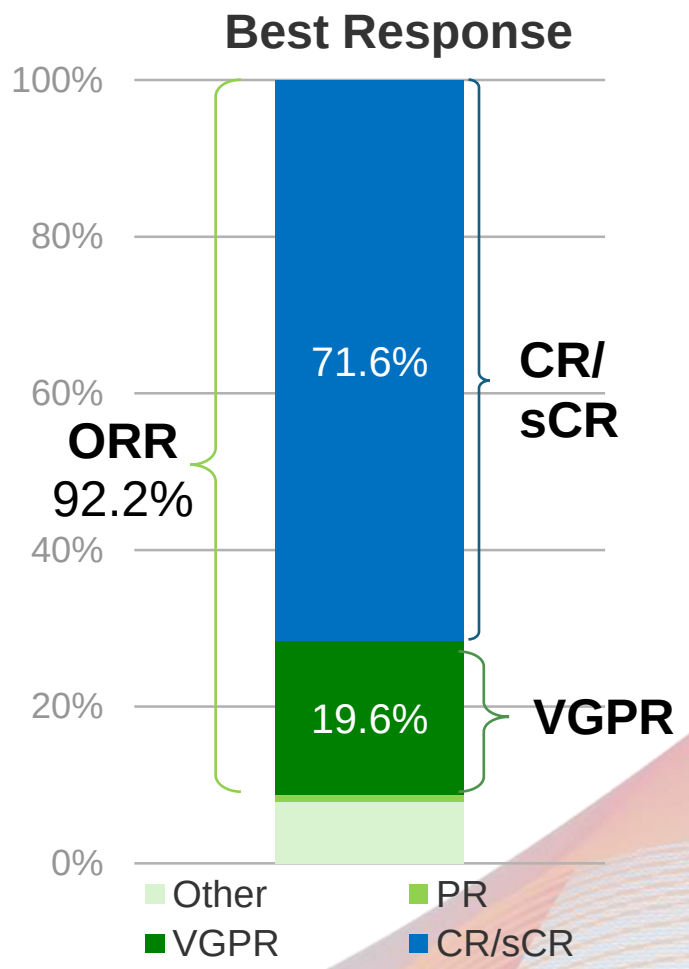
Cytogenetic high risk includes: del(17p13.1); t(4,14); t(14.16); t(14,20); 1q21
Double-class refractory: Refractory to a proteasome inhibitor and immunomodulatory drug;
Triple-class refractory: Refractory to a proteasome inhibitor, immunomodulatory drug and anti-CD38 antibody

Data cutoff: Oct 25, 2023

LUMMICAR STUDY 1

Efficacy Summary

Best overall response by IRC Assessment	Zevor-cel Phase 2 N=102 (%) *
ORR, No. (%) [95% CI]	94 (**92.2**) [85.13, 96.55]
sCR/CR, No. (%) [95% CI]	73 (**71.6**) [61.78, 80.06]
sCR, No. (%) [95% CI]	70 (68.6) [58.69, 77.45]
CR, No. (%) [95% CI]	3 (2.9) [0.61, 8.36]
VGPR, No. (%)	20 (19.6)
PR, No. (%)	1 (1.0)
≥VGPR, No. (%)	93 (**91.2**)



As of Oct 25, 2023, 102 R/R MM patients with median follow-up of 20.3 months (range 0.4-27.0):

- 92.2% ORR
- 91.2% (93/102) ≥ VGPR and 71.6% (73/102) CR/sCR
- A deepening trend of responses was observed when compared to the initial results of this cohort
- **MRD** negativity at 10^{-5} sensitivity:
  - **100%** in patients who achieved CR/sCR
  - **95.7%** in patients with ≥VGPR

***As of cut-off date, the 102 patients infused with zevor-cel have completed median 20.3 months follow-up , and 32 patients who entered the long-term follow-up have been followed for at least 23.3 months after receiving zevor-cel infusion.**

CR: complete response; **MRD**: minimal residual disease; **ORR**: overall response rate; **PD**: progressive disease; **PR**: partial response; **sCR**: stringent complete response; **VGPR**: very good partial response

Data cutoff: Oct 25, 2023

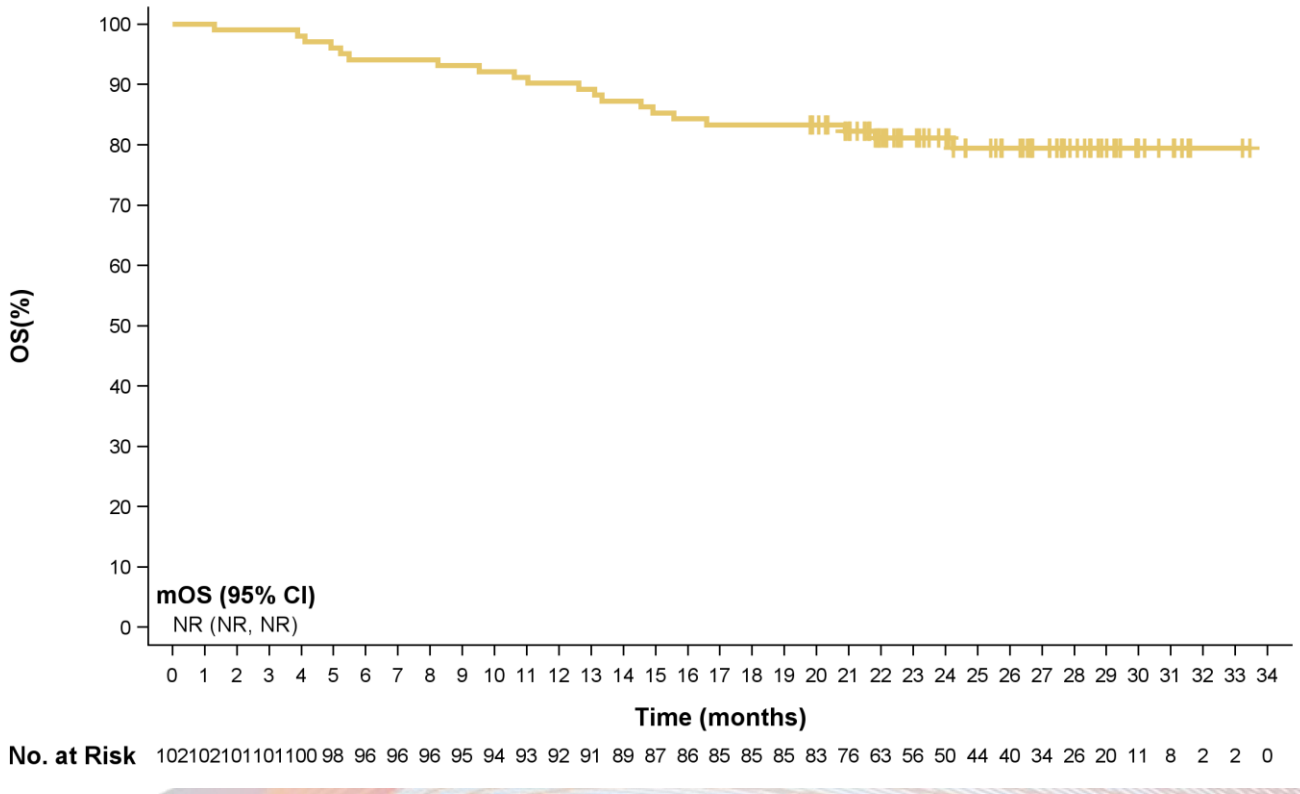
LUMMICAR STUDY 1

Efficacy Summary

With median 20.3 months follow-up:

- The duration of response (DOR) and progression-free survival (PFS) data were not mature.
  - The probabilities of the responders remaining in response at 12 months and 18 months were 76.8% (95% CI: 66.67, 84.24) and 62.4% (95% CI: 51.24, 71.64).
  - 12-month and 18-month PFS rate were 76.3% (95% CI: 66.45, 83.56) and 61.9% (95% CI: 51.19, 70.85).
- The overall survival (OS) data was not mature.
  - In all patients, 12-months and 30-months OS rate was 90.2% (95% CI: 82.55, 94.60) and 79.4% (95% CI: 69.69, 86.29).
  - In patients who achieved CR/sCR, 12-months and 30-months OS rate was 95.9% (95% CI: 87.80, 98.66) and 87.7% (95% CI: 76.56, 93.77).
- The median time to response were 29.0 days (range: 26 to 93).
- The median time to reach CR/sCR were 146 days (range: 28 to 609).

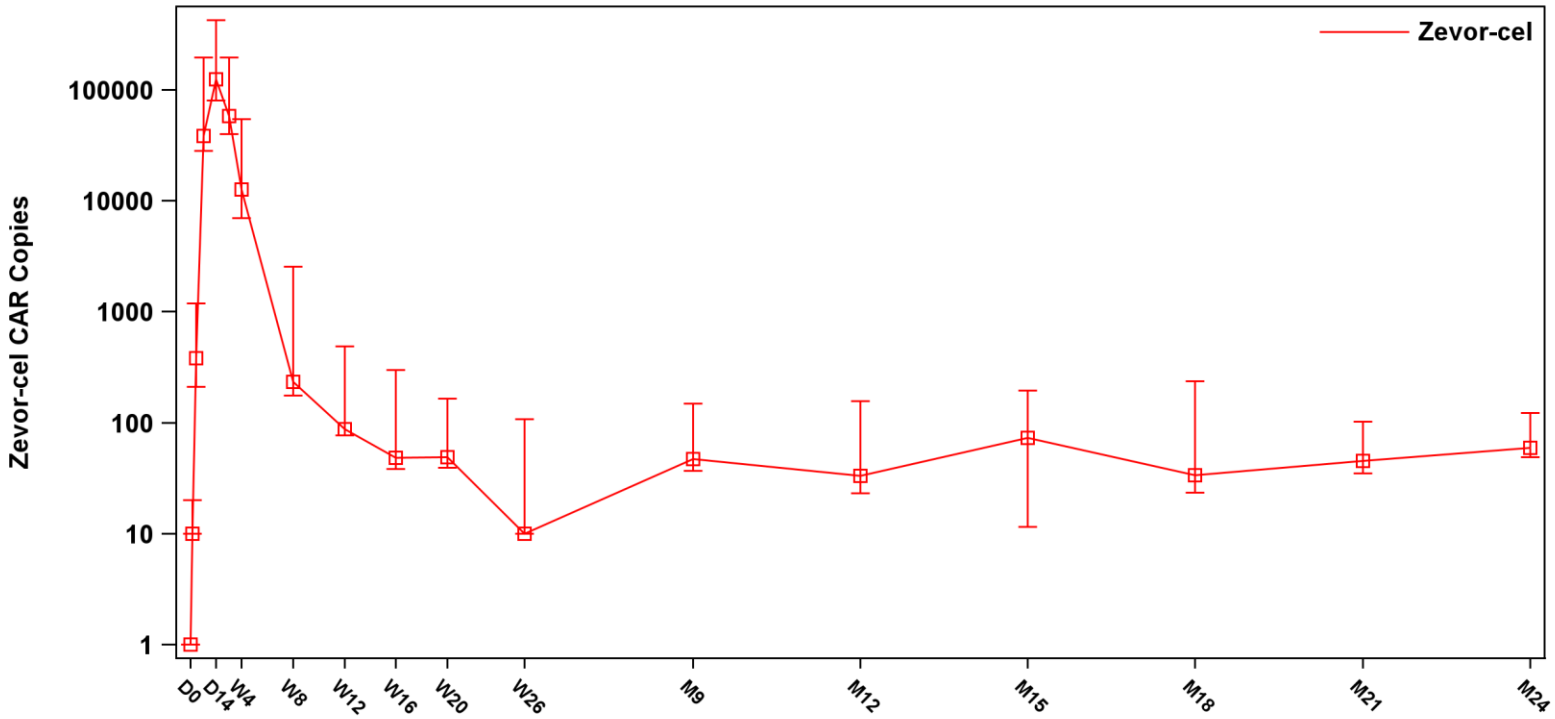
Overall survival



Data cutoff: Oct 25, 2023

LUMMICAR STUDY 1

Pharmacokinetics and Immunogenicity



PK figure: Semi-log plot of Median CAR Copies for 102 Subjects by time. The lower limits is the first quartile (Q1), and the upper limits is the third quartile (Q3).

- In 102 patients, zevor-cel was detected in 91.2% of patients by 3 days after infusion.
- Median T_{max} was 14 days (7, 22).
- Median C_{max} was 202543.5 copies/μg genomic DNA.
- Median T_{last} was 140 days (26, 740).
- Zevor-cel copies were still detectable in 33.3% (34/102) of patients at 26 weeks, 8（7.8%）at M12 post infusion, showing stable expansion and persistence.
- Anti-drug antibodies were tested negative for 81 (79.4%) patients.

Data cutoff: Oct 25, 2023

LUMMICAR STUDY 1

Safety Summary

Adverse event	Subjects (N=102) No. (%)
Treatment-related AEs (TRAEs)	102 (100)
Grade ≥3 hematologic TRAEs	102 (100)
Cytokine release syndrome (CRS), any grade	92 (90.2)
Grade 1	52 (51.0)
Grade 2	33 (32.4)
Grade 3	5 (4.9)
Grade 4	2 (2.0)
Grade ≥3 neurologic TRAEs	0
ICANS, any grade	2 (2.0)
Grade 1	2 (2.0)
Grade ≥3 infection and infestation TRAEs	28 (27.5)
Hypogammaglobulinaemia, all grade treatment-related	27 (26.5)
Treatment-related SAE	40 (39.2)
Death due to TRAE	1 (1.0)

- Phase 2 target dose was 150×10^6 CAR^+ T cells
- Hematologic toxicities were the most common AEs
- 90.2% of patients experienced CRS, 6.9% patients developed ≥ Grade 3 CRS: 4.9% Grade 3 and 2.0% Grade 4.
- Median onset time for CRS was 4 days (range 1-14 days); and median CRS duration 6 days (range 1-22 days).
- ICANS occurred in 2 patients, both Grade 1. Both patients recovered without use of glucocorticoids.
- No movement disorders were observed
- Treatment-related SAEs occurred in 39.2% patients, comprising hematologic toxicities and infection. One patient died due to pneumonia 149 days after zevor-cel infusion.

AE: adverse event; **ICANS**: Immune effector cell-associated neurotoxicity syndrome;
SAE: serious adverse event

Data cutoff: Oct 25, 2023

LUMMICAR STUDY 1

Summary

LUMMICAR STUDY 1 is a single-arm, open-label, multi-center Phase 1/2 clinical trial, which enrolled patients with R/R MM who had failed at least 3 lines of therapy. China NMPA conditionally approved the registration of zevor-cel on February 23, 2024.

1. Zevor-cel showed clinical benefit in patients with R/R MM.

- In 102 patients, per IRC assessment, the ORR was 92.2% (94/102), the remission rate at VGPR and above was 91.2% (93/102), the CR/sCR rate was 71.6% (73/102). A trend towards deepening of responses was observed with longer duration of follow-up.
- Patients who achieved VGPR and above were 95.7% MRD negative, achieved CR/sCR were 100% MRD negative.
- With 20.3 months median follow-up, median DOR, PFS and OS were not mature.

2. The safety results of zevor-cel showed manageable risk and zevor-cel was well tolerated.

- The incidence of CRS $\geq$ grade 3 was 6.9% (7/102). No grade 5 CRS were reported.
- The incidence of ICANS was 2% (2/102) and both were grade 1.
- One patient died due to pneumonia 149 days after zevor-cel infusion.

3. Zevor-cel PK shows persistence.

- Median T_{max} was 14 days, median C_{max} was 202543.5 copies/μg genomic DNA, and median T_{last} was 140 days, showing zevor-cel had stable expansion and persistence in vivo.

Acknowledgments

- The patients and families who made this study possible
- The clinical teams who participated in the study

This study was supported by CARsgen Therapeutics.

All authors contributed to and approved the presentation.

LUMMICAR STUDY 1