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

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LUMMICAR STUDY 1

INTRODUCTION

- Zevorcabtagene autoleucel (zevor-cel or CT053), a fully human, B-cell maturation antigen (BCMA)-targeting autologous CAR T-cell therapy, has been approved by China National Medical Products Administration (NMPA) for the treatment of patients with relapsed/refractory multiple myeloma (RRMM) in Feb 2024.
- In the ongoing Phase I/II study LUMMICAR STUDY 1 (NCT03975907), zevor-cel has shown compelling efficacy with an acceptable safety profile in heavily pretreated patients with RRMM.
- As of 25 Oct 2023, in 102 patients, the objective response rate (ORR) was 92.2% (95% CI: 85.13, 96.55), and 71.6% patients achieved complete response (CR) / stringent CR (sCR). All patients who achieved CR/sCR attained MRD negativity. (EHA 2024 Abstract S209).
- Clinical efficacy could be influenced by patient characteristics such as Age, International Staging System (ISS) stage, and high-risk cytogenetics.

OBJECTIVES

- To assess the potential impact of patient characteristics on the clinical efficacy of zevor-cel in RRMM through subgroup analyses.

METHODS

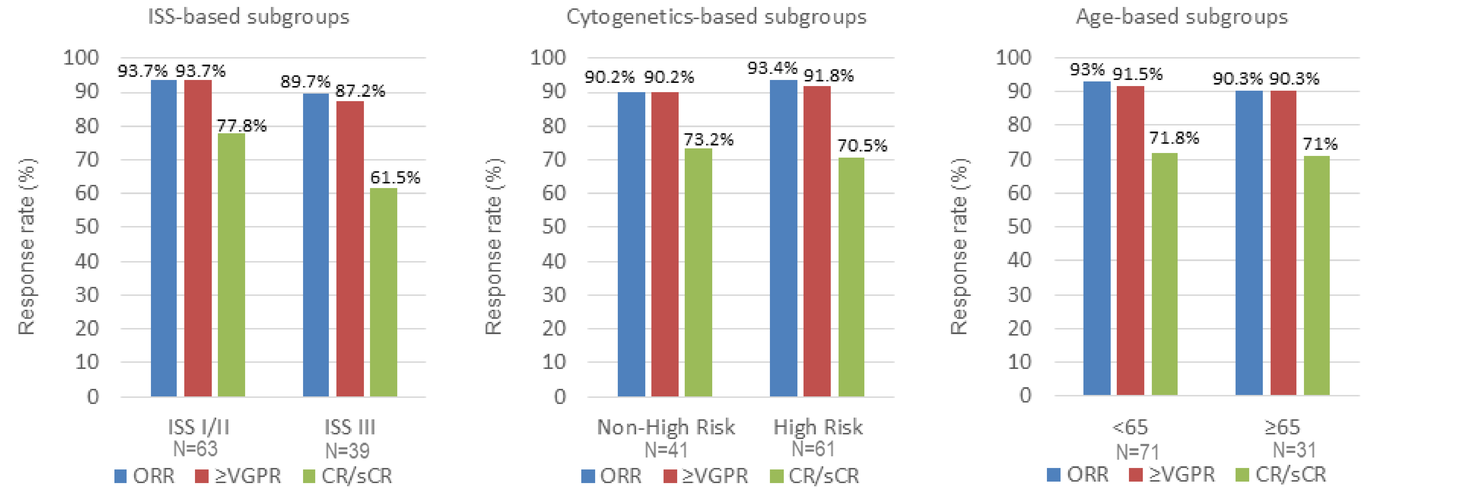
- Patients with RRMM who had received at least 3 prior lines of therapy including an immunomodulatory drug and a proteasome inhibitor were enrolled in the study.
- A single dose of zevor-cel (target dose of 150×10^6 or 180×10^6 CAR-positive T cells based on body weight of ≤80 kg or >80 kg, respectively) was administered 1 to 2 days after the completion of lymphodepletion.
- Response was assessed per the international myeloma working group (IMWG) 2016 criteria by an independent review committee (IRC).
- Subgroups with sample size greater than 20% of the total study population were selected for analyses.

RESULTS

Patient Characteristics

Baseline characteristic	N=102
Age, median (range), years	59.5 (38, 75)
<65, n (%)	71 (69.6%)
≥65, n (%)	31 (30.4%)
Sex	
Male, n (%)	55 (53.9%)
Female, n (%)	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, n (%)	
I or II	63 (61.8%)
III	39 (38.2%)
Cytogenetic risk, n (%)	
Non-High risk	41 (40.2%)
High risk	61 (59.8%)
Extramedullary plasmacytoma, n (%)	11 (10.8%)
Bone marrow plasma cells, n (%)	100
< 50%	83 (81.4%)
≥ 50%	17 (16.7%)
Double-class refractory, n (%)	91 (89.2%)
Triple-class refractory, n (%)	23 (22.5%)

Subgroup Efficacy Analyses



- Between December 1st, 2020, and March 2nd, 2022, a total of 102 patients were enrolled. Data cutoff: Oct 25th, 2023
- 31 (30.4%) patients were aged ≥65 years, 39 (38.2%) patients had ISS Stage III and 61 (59.8%) patients had high-risk cytogenetics.
- With a median follow-up of 20.3 (range: 0.4-27) months, the median duration of response (DOR), progression-free survival (PFS), and overall survival (OS) data were not mature.
- 18-month (18m) and estimated 30-month (30m) event free rates were used as efficacy outcomes for subgroup analyses.

Subgroups	18m DOR (95%CI)	18m PFS (95%CI)	30m OS (95%CI)
ISS-based subgroups			
ISS I/II (N=63)	64% (50%,75%)	63% (50%,74%)	81% (69%,89%)
ISS III (N=39)	57% (38%,72%)	58% (40%,72%)	76% (59%,87%)
Cytogenetics-based subgroups			
Non-High Risk (N=41)	66% (48%,79%)	69% (52%,81%)	85% (70%,93%)
High Risk (N=61)	58% (44%,70%)	56% (42%,68%)	76% (62%,85%)
Age-based subgroups			
<65 (N=71)	62% (49%,73%)	63% (49%,73%)	81% (69%,88%)
≥65 (N=31)	60% (39%,75%)	58% (39%,73%)	77% (58%,89%)

- The DOR, PFS and OS were not impacted by age or ISS. There was a trend towards favorable outcomes which was seen in patients without high-risk cytogenetics compared to those with high-risk cytogenetics, however, none of these differences were statistically significant.

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

CONCLUSIONS

The subgroup analyses of the pivotal Phase II stage of LUMMICAR STUDY 1 demonstrate that the clinical efficacy of zevor-cel is not significantly impacted by baseline characteristics and therefore, even RRMM patients with poor prognostic factors may benefit from zevor-cel.

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Chen W, Fu C, et al. Phase 2 study of fully human BCMA-targeting CAR-T cells (zevorcabtagene autoleucel) in patients with relapsed/refractory multiple myeloma. EHA 2024 Abstract S209.