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704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Promising Safety and Efficacy of Trovocabtagene Autoleucel (C-CAR088) Followed ASCT in Ultra High-Risk Multiple Myeloma (UHR-MM) Patients Who Failed or Had Suboptimal Response to Standard First Line Triplet Based Therapy

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Background:
The prognosis of MM has improved significantly nowadays. However, patients with ultra-high-risk features (UHR-MM) had dismal outcomes even treated with standard front-line therapy. This study (NCT05632380) explores the potential of new CAR-T therapy in addressing the unmet need of these patients.
Trovocabtagene autoleucel (trovo-cel), an anti-BCMA CAR T-cell manufactured by Cellular Biomedicine Group, Inc., showed deep and lasting responses with a good safety profile in relapsed or refractory multiple myeloma (R/R MM). Hereby, we are reporting a phase I, open-label, single-arm study, assessing the feasibility of trovo-cel followed ASCT in UHR-MM patients who failed or had suboptimal responses to the first-line standard therapy.
Methods:
Eligible patients are 18-70 years old, transplant-eligible and confirmed as UHR-MM defined as follows: 1) Genetic ultra-high risk: del(17p)≥60%; or ≥2 high-risk cytogenetic abnormalities including TP53 mutation, del(17p)/P53 deletion, t(4;14), t(14;16), t(14;20), 1q21 gain/ amplification, and did not reach CR or better response after 4 cycles standard first-line therapy; 2) Primary refractory: <MR after 2 cycles or <PR after 4 cycles standard first-line therapy; 3) Early relapse: lost best response within 6 months from the standard first-line therapy; 4) primary PCL history and < CR after 4 cycles standard first-line therapy. Standard first-line therapy should be a potent standard triplet-based regimen including one PI, one IMIDs, and glucocorticoid. Quadruplet or quintuplet regimens might be used. Prior ASCT, BCMA-targeted therapy, or CAR-T treatment are excluded.

Patients undergo conditioning (melphalan alone or plus fludarabine) followed by ASCT on Day 0 and trovo-cel 3.0 or 6.0×10^6 cells/kg single intravenous infusion on Day 3. Maintenance is allowed after 3 months post-transplantation per investigator's decision.

Results:

As of July 24, 2023, 8 UHR-MM patients completed ASCT and trovo-cel infusion. Five patients received melphalan and 3 received fludarabine combining melphalan pretreatment. Trovo-cel was administrated at 3×10^6 cells/kg for all 8 patients. The median age of patients was 54.5 years (range: 39-66). The median number of prior lines of therapy was 2 (range: 1-2), with VRD exposure rate of 100%. Seven patients (87.5%) had received daratumumab, with six having been treated with dara-based quadruplet or quintuplet therapy as a front setting. Two patients (25%) had genetic ultra-high risk features, four patients (50%) had primary refractory myeloma, two (25%) had early relapse myeloma, and three patients (37.5%) had primary PCL history, two (25%) had extramedullary disease. Five patients (62.5%) received bridging and 6 received maintenance therapy.

The combination of ASCT and Trovo-cel was well tolerated. With a median follow-up of 184 days (range: 13-332 days), no unexpected adverse events was observed. Among evaluable 7 patients, six (85.7%) had experienced grade 1 CRS and fully recovered. Two patients (28.6%) received tocilizumab and glucocorticoid for CRS. No ICANS event was reported. As expected, hematological toxicities are the most common AEs. All 7 patients achieved hematopoietic reconstitution successfully, with a median time of 14 days for ANC ($\geq0.5\times10^9$/L) and 13 days for PLT ($\geq20\times10^9$/L) post ASCT. The ORR was 100%, with 6 CR with MRD negative (NGF, 10^{-5}) (85.7%), 1 VGPR (14.3%). Robust CAR T-cell expansion was observed in blood of all patients. The median time of peak of CAR-T expansion (T_{max}) was 7 days (range 4~7), the median peak CAR-T copy number (C_{max}) was 891,963 copies /μg gDNA and the median AUC $_{0\text{-}28day}$ was 6,009,475.5 copies /μg gDNA/day. The PK profile is similar to trovo-cel single agent treatment [1] but with earlier peak of CAR-T expansion.

Conclusion:

The preliminary results of this clinical trial show a promising safety and efficacy profile of trovo-cel followed ASCT in UHR-MM patients. Although the follow-up time is relatively limited, we are looking forward to a consistently good safety and efficacy outcome in long-term follow-up and in more patients recruited later.

Research Sponsor: Institute of Hematology & Blood Diseases Hospital
Collaborator: Cellular Biomedicine Group, Inc.

Disclosures Li: *Cellular Biomedicine Group Inc:* Current Employment. **Zhu:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Huang:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Zheng:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Lan:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company.

OffLabel Disclosure: Trovocabtagene autoleucel (C-CAR088)

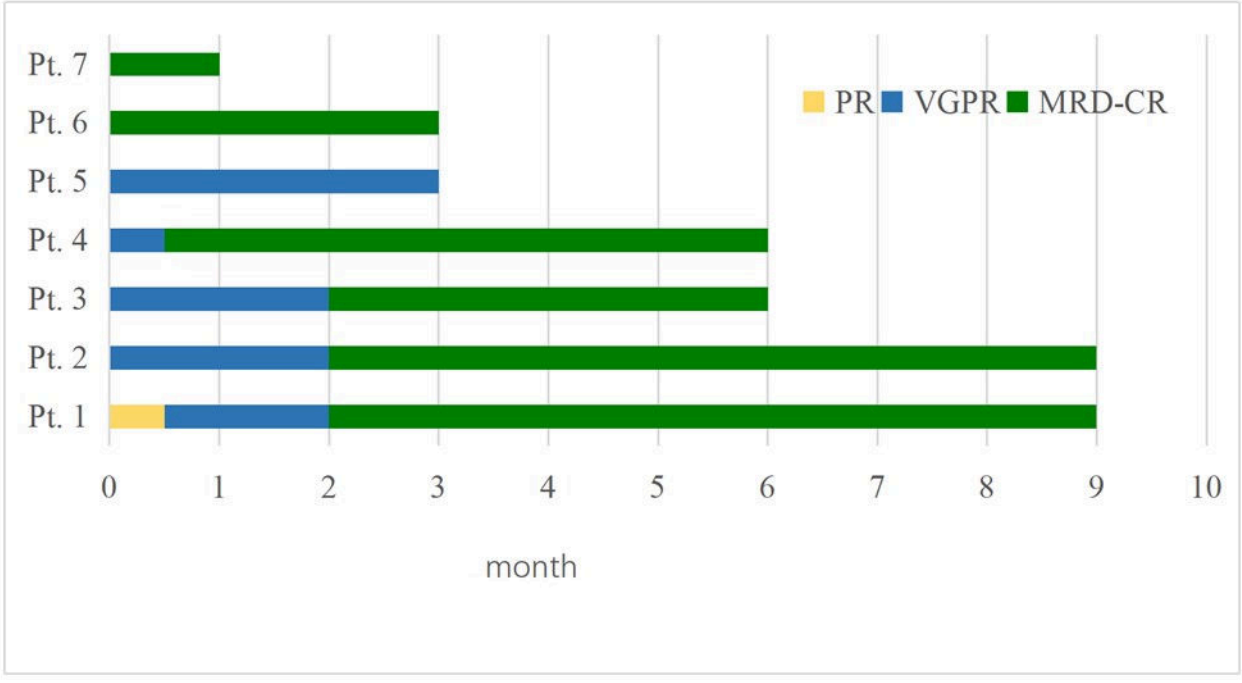

Figure 1

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