SOHO ANNUAL MEETING 2024

CT-165

Safety and Efficacy of 9 days vein-to-vein Decentralized Manufactured anti-CD19 CAR-T Cells for Relapsed or Refractory B Cell Leukemia and Lymphoma: Results From the First Phase 1 Indian Trial (VELCART)

Hamenth Kumar Palani, Arun Kumar Arunachalam, Mohammed Yasar, Phaneendra Datari, Uday Kulkarni, Sushil Selvarajan, Anu Korula, Aby Abraham, Biju George, Vikram Mathews

Department of Haematology, Christian Medical College, Ranipet Campus, Vellore 632 517, India.

Introduction

- Anti-CD19 CAR-T cells are an effective therapeutic modality against relapsed/ refractory CD19+ve B-cell leukemia and lymphomas (r/r B-cell ALL/ Lym).
- Decentralized or point-of-care manufacturing using fresh products, and a short vein-to-vein time can potentially improve access and efficacy of CAR-T cell therapy while reducing logistic challenges and costs.
- These are especially relevant in low/ middle-income countries (LMIC) like India.

Aim

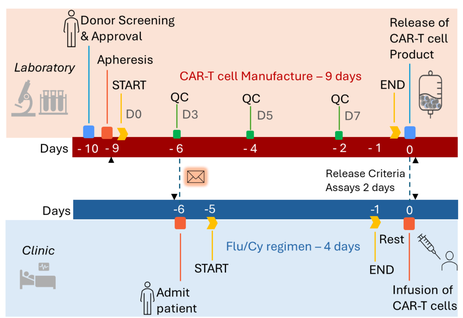
To evaluate the safety and efficacy of decentralized manufacture of anti-CD19 CAR-T cells for treating relapsed or refractory B cell leukemia/ lymphoma and evaluate its total cost of therapy in an academic not-for-profit setting in India.

Methods

- Patients aged 2 to 60 years with r/r B-cell ALL/Lym who failed ≥ 2 lines of therapy with ECOG PS ≤ 2 and measurable disease were enrolled.
- Autologous T cells were transduced with an anti-CD19 second-generation lentiviral vector (LTG1563, Lentigen, Miltenyi Biotec).
- GMP-compliant CAR-T cell manufacture was done using the CliniMACS prodigy system in a 9-day culture protocol.
- Phase 1 study was designed with a dose escalation strategy of 3+3 design with increasing doses at each level (0.5 X 106 / Kg (n=3), 1 X 106 / Kg (n=3), and 2 X 106 / Kg (n=4).
- Lymphodepletion was done with Cyclophosphamide 40-60 mg/ kg on day -6 and Fludarabine 30 mg/ m2 daily on days -5 to -2.
- The response was assessed by bone marrow (BM) minimal residual disease by multi-parametric flow cytometry (MFC) for B cell leukemia and PET-CT for B-cell lymphoma per NCCN and IWG criteria.
- The CRS and ICANS were graded and treated as per ASTCT guidelines.
- Hematotoxicity was graded as per EHA/ EBMT recommendations, and other toxicities were graded as per CTCAE v5

Results

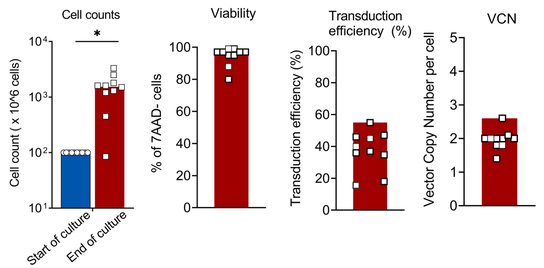
1. VELCART study workflow for manufacturing anti-CD19 CAR-T cells using Prodigy and fresh infusion into patients



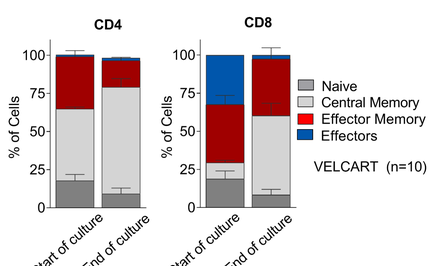
2. Table demonstrates the patient characteristics and toxicities

Indications	B-ALL (n=6)	B-Lymphoma (n=4)
Patient Characteristics		
Age	35 (2 – 59)	52 (43 - 59)
Prior line of therapy	3 (2 – 4)	3 (2 - 6)
Refractory disease (BM blast percentage)	5 (0.06 – 2.27%)	2
Bulk disease	1 (28%)	2
CAR-T post infusion		
CRS (Grade ≥2)	1 (Grade2) 1 (Grade 3)	Nil
ICANS	Nil	Nil
Hematotoxicity (Grade ≥2)	1 (Grade 3)	2 (Grade 2)

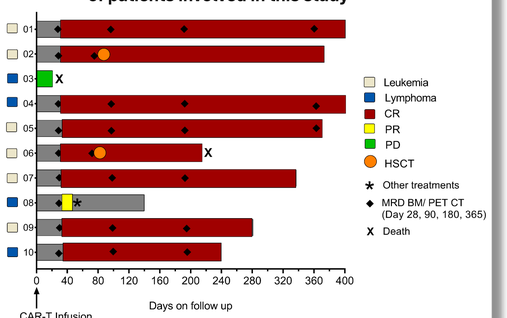
3. Characterization of anti-CD19 CAR-T cells before infusion by flow cytometry and QPCR



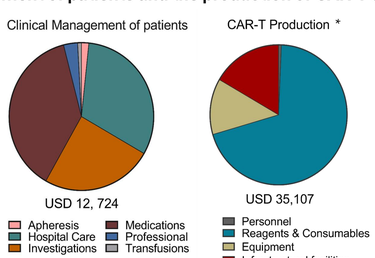
4. Immunophenotypic characterization of CAR-T cells and their differentiation status



5. Swimmer plot demonstrates the response and outcome of patients involved in this study



6. The pie diagram illustrates the cost analysis for the management of patients and the production of CAR-T cells



• *Excluding the cost of lentiviral vector, Palani et al, BMT 2023*

Conclusion

- Data from 10 patients enrolled in this phase 1 VELCART trial demonstrates that decentralized, point-of-care manufacturing of CAR-T cells with nine days vein-to-vein time is feasible using the CliniMACS prodigy system.
- The safety profile of this CAR-T cell product is comparable to other CAR-T cell therapies, with high CR rates across different doses in heavily pre-treated patients. Our data highlights the safety, efficacy, low cost, and potential to improve accessibility of CAR-T cell therapy in LMIC using a fully automated point-of-care manufacturing platform.

References

Palani et al., "Decentralized manufacturing of anti-CD19 CAR-T cells using CliniMACS Prodigy: real-world experience and cost analysis in India," Bone Marrow Transplantation volume 58, pages 160–167 (2023).

Contact: hamenth@cmcvellore.ac.in

The authors have no relevant conflicts of interest to disclose.