

Prior chemotherapy negatively impacts the manufacturing and clinical response of Chimeric Antigen Receptor (CAR) T cell therapeutics in DLBCL: A phase I clinical trial experience from India

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Despite remarkable success of CAR-T therapy, complexity of CAR-T manufacturing and high costs limits their accessibility in low-resourced countries including India. Currently, approved CAR-T cells therapy is available to relapsed and refractory patients only. Impact of prior chemotherapy of CAR-T cells manufacturing and clinical response is still a gray area. We have demonstrated efficacy of novel Humanized anti-CD19 CAR-T (HCAR19) cell in preclinical model. Here, we report our experience on scaled manufacturing of HCAR19 from manufacturing to first-in-human Phase I clinical study in r/r B cell malignancies in India along with the impact of prior chemotherapy on patients' T cells, CAR-T manufacturing and clinical response. To examine the feasibility and functionality of the developed manufacturing process and platform, the end-to-end CAR-T cell manufactured in close system for 10 patients was performed. CD3+ T cells from 10 patients of B cell malignancies were enriched/activated and transduction with anti-CD19 lentivirus vectors. CAR-T were manufactured from all the patient's T cell successfully (100% success rate) within 8 days of culture (Robust expansion-20-30 fold, TE:>25%, dosage range: 1.78x10⁶-17x10⁶ viable HCAR19/kg) maintaining antitumor activity with memory phenotype. CAR-T product also qualified release criteria for safety, identity, purity and potency. Patients enrolled for clinical trial were segregated into heavily or less treated based on number of prior chemotherapies. Impact of chemotherapy on CAR T cell therapy was measured on parameter of patient's T cell health, CAR T cells manufacturing capabilities and clinical efficacy. Interestingly, Patients with one line of chemotherapy therapy had superior beneficial impact on patient's T cells health and CAR-T cell manufacturing benefits while maintaining higher memory cells compared to patients with ≥ 1 lines of prior therapies. We developed a novel indigenous anti-CD19 CAR-T product and highly affordable CAR-T manufacturing platform & establish impact of chemotherapy on CAR-T cells manufacturing and its clinical response.



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Biography

Ankesh Kumar Jaiswal, have immense passion in the research and development for improving the health and life of cancer patients. He has earned his expertise in the cell and gene therapy specially CAR-T cell therapy. He have worked on the end-to-end work flow of CAR-T cell therapy, starting from construct design to CAR-T cell manufacturing and its functional validation using multiple tools and technique.

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