Rapid and Simplified Process for Manufacturing Multi-Tumor-Associated Antigen Specific T Cells

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Introduction

AML is a malignant neoplasm of the myeloid lineage arising in the bone marrow and outgrowing normal hematopoietic elements. In 2022, there will be estimated 20,050 new cases of AML with ~11,500 deaths. Marker Therapeutics, Inc. has developed MT-401, a multi-tumor-associated antigen (multiTAA)-specific allogeneic T cell product capable of recognizing multiple targets expressed on the tumor simultaneously, minimizing tumor escape. Here we demonstrate how additional process improvements streamlined the manufacturing process and resulted in products with superior T cell phenotype and potency, both of which have the potential to enhance clinical responses.

Objective

To streamline the manufacturing process and produce T cells with superior phenotype and potency, both of which have the potential to enhance clinical responses.

Methods

To commercialize the multiTAA-specific T cell therapy, the complexity and duration of the manufacturing process needed to be reduced.

Results

New Manufacturing Process Yields Products With Higher Purity, Improved Memory Phenotype and Greater Antigen Specificity Compared to Old Process

A. CD3\(^{\text{pos}}\) Cell Purity

B. Original Process vs. New Process

C. Memory Phenotype

To evaluate how the new manufacturing process affects T cell purity and phenotype multiTAA-specific T cells from healthy donors were manufactured using the original process with dendritic cells and three stimulations (Original) or with one stimulation and no dendritic cells (New). Graphs depict: Comparison of the CD3\(^{\text{pos}}\) T cell purity of the final product negative for antigen and product positive for antigen (A). Comparison of the CD3\(^{\text{pos}}\) cell purity of the final product manufactured using the original and new process (B), four T cell memory populations from products manufactured using the original and new process as measured by flow cytometry (C).

Conclusions

- We have shortened the manufacturing of multiTAA-specific T cells to 9 days and eliminated the need to generate DCs prior to T cell stimulation.
- The improved manufacturing process produces superior T cells with significantly higher CD3\(^{\text{pos}}\) cell purity, increased naïve and central memory phenotype, greater antigen specificity and diversity for all four tumor antigens and anti-tumor activity compared to T cells generated using the original process.
- We demonstrated that the new process is scalable to a G-Rex\(^{\text{®}}\)500M device without affecting the fold expansion and viability of the final product.
- These process improvements significantly reduced the number of interventions needed during manufacturing, thereby decreasing both the possibility of manufacturing failures and product manufacturing time, which translates to faster patient treatment.