

**RAPID AND SIMPLIFIED PROCESS FOR
MANUFACTURING MULTI-TUMOR-ASSOCIATED
ANTIGEN SPECIFIC T CELLS**

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Background 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. Currently, MT-401 is being used for treatment of AML patients following allogeneic stem-cell transplant in both the adjuvant and active disease settings. Although MT-401 has shown promising clinical results, the manufacturing process is time prohibitive for cancer patients with rapid disease progression. 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.

The original manufacturing process for multiTAA-specific T cell products is derived from Baylor College of Medicine studies and begins with the purification of PBMCs from leukapheresis material. Subsequently, dendritic cells (DCs) are matured and pulsed with a pool of exogenous peptides spanning the entire primary sequence of target antigens (Ags). The mature DCs expressing the antigens are co-cultured with T cells in a Gas Permeable Rapid Expansion Device (G-Rex[®]) to stimulate and expand antigen-specific T cells. For MT-401, the following four antigens are used: PRAME, NY-ESO-1, Survivin and WT1. This 36-day manufacturing process results in products containing an average of 83% CD3+ T cells with a predominantly effector memory T cell phenotype, and an average specificity for 4 tumor Ags of 179 spot-forming units (SFU) per 2e5 cells.

Methods We have now simplified the manufacture of multi-TAA-specific T cells and eliminated the need to generate DCs in vitro prior to T cell stimulation.

Results The improved 9-day manufacturing process produces superior T cell products with an average%CD3+ purity of 96%, T cell phenotype showing a uniform distribution of naïve, central memory and effector memory T cells, increased Ag specificity (5-fold), Ag diversity and killing potential.

Conclusions 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. This sophisticated and rapid manufacturing approach has shown to be reproducible regardless of the tumor antigen combination, enabling the extension of this technology to other clinical indications.

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