MARKER Therapeutics

Pre-Clinical Data of MultiTAA-Specific T Cells in Lymphoma Cells

MT-601 shows anti-tumor activity in CD19 CAR T refractory lymphoma cells *in vitro*

May 31, 2023

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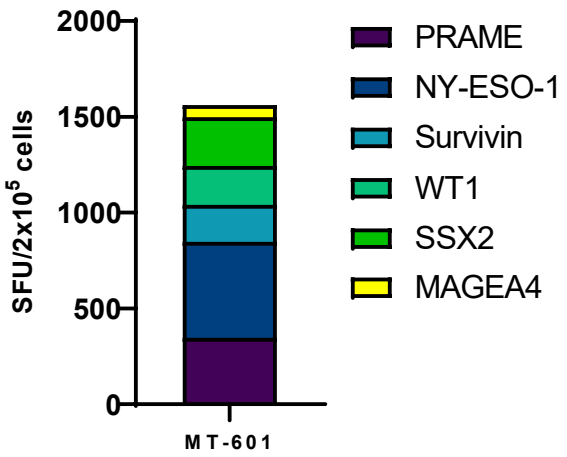
MT-601 demonstrates *in vitro* anti-tumor activity against CAR-naïve lymphoma cells. MT-601 demonstrates broad specificity for 6 target tumor antigens (**Panel A**). The drug product characterization for MT-601 shows that this multiple tumor-associated antigen (multiTAA)-specific T cell product consists almost exclusively of $CD3^+$ T cells (87.9%), with a mixture of $CD4^+$ (40.1%) and $CD8^+$ (38%) T cell subsets that expresses portions of both central (21.7%) and effector (45.2%) memory T cell markers (**Panel B**). A long-term co-culture experiment was performed using MT-601 against HDLM2, a Hodgkin's lymphoma cell line, engineered to overexpress CD19 (**Panel C**). In this experiment MT-601 was able to successfully control the tumor growth of a CD19-expressing lymphoma cell line (CAR-naïve lymphoma cells). Data presented provide non-clinical support for the use of MT-601 as a treatment for patients with lymphoma.

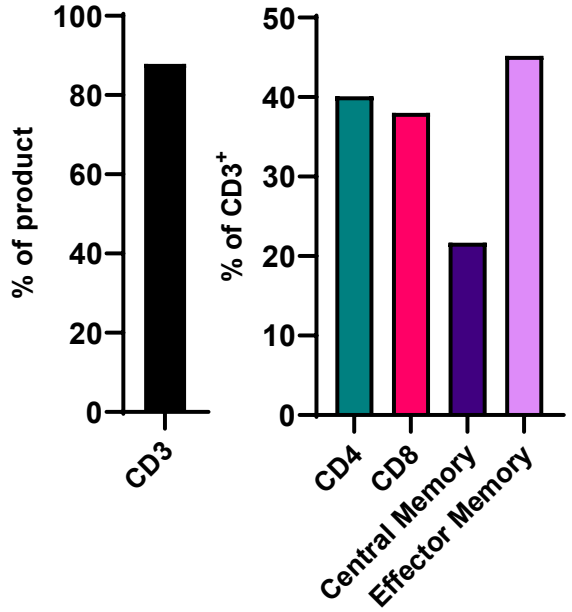
A

MT-601 specifically responds to 6 distinct tumor antigens



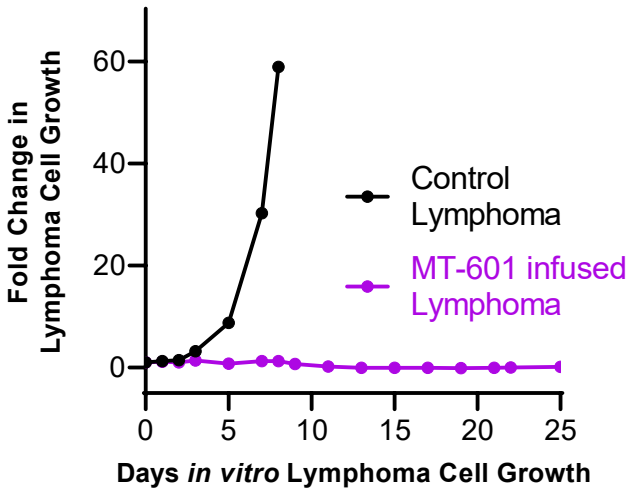
B

MT-601 phenotypic profile



C

CD19 CAR-naïve lymphoma is controlled by MT-601



MT-601 demonstrates *in vitro* anti-tumor activity in a long-term CAR refractory lymphoma cell line model. HDLM2, a Hodgkin's lymphoma cell line, engineered to overexpress CD19 was used (**Panel A**). Although anti-CD19 CAR T cell infusion inhibits CD19⁺ lymphoma growth, 3 weeks after initial treatment anti-CD19 CAR T cell resistant lymphoma cell growth is observed (**Panel B**). When this population of lymphoma cells that grew despite the presence of anti-CD19 CAR T cells were tested for the presence of CD19 antigen, they were found to be negative for CD19 compared to both the control cells and the cells that initially responded to anti-CD19 CAR T cells (**Panel C**). This is the *in vitro* demonstration of clinical relapse associated with antigen loss, whereby CD19 antigen-negative tumor outgrowth is the main cause of relapse in patients treated with anti-CD19 CAR T cells. Indeed, anti-CD19 CAR T cell resistance is confirmed when these CD19 negative lymphoma cells are re-exposed to anti-CD19 CAR T cell administration (**Panel D, upper, blue**). However, unlike anti-CD19 CAR T cells, the broad antigen targeting capability of MT-601 demonstrates the ability to kill lymphoma cells that became anti-CD19 CAR resistant (**Panel D, lower, purple**). Data presented provide nonclinical support for the use of MT-601 as a treatment for patients with lymphoma who have relapsed following anti-CD19 CAR T treatment.