RNA PRIMED SMAR-T\textsuperscript{TM} CELLS AGAINST MULTIPLE DRIVER MUTATIONS, ALL HLA’S, DESIGNED FOR FIRST LINE THERAPY

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Background Success of immune checkpoint inhibitors, e.g., anti-PD1 antibodies have revolutionized cancer immunotherapy by demonstrating that a patient’s own T-cells recognize and treat cancer. The efficacy of PD-1 blockade is driven by recruitment of new T-cells from blood rather than via activation of pre-existing tumor infiltrating lymphocytes.\textsuperscript{1} However, anti-PD1 therapy is most effective in \(-\)5\% of malignancies i.e., cancers with high mutational burden. Hence, the challenge of addressing most lower mutational burden cancers (the \(-\)95\%) needs an alternate treatment strategy.

Methods We address this challenge by using RNA to prime and expand peripheral T-cells to cancer-specific mutations ex-vivo. Using our proprietary, patented, and robust manufacturing method, we can generate T-cell populations reactive to as low as 8 and as high as 40 cancer-specific mutant proteins.

Results In in-vitro cytotoxicity assays, our T-cells have cancer mutation-specific cytotoxicity and do not kill the normal cells. Further, the T-cells express homing receptors enabling them to infiltrate tumors and express high levels of TNF\textalpha and IFN\gamma, which are associated with effective tumor cytotoxicity and pro-inflammatory modification of tumor microenvironment (TME). Additional characterization shows these cells to be predominantly CD4\textsuperscript{+} and CD8\textsuperscript{+} T-cells bearing central and effector memory phenotypic with negligible regulatory or exhausted T-cells.

Conclusions We believe our T-cells can be used for cellular therapy in conjunction with, or as an alternative to, immune checkpoint inhibitors to treat lower mutational burden cancers present in most patients.

REFERENCE

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