Autologous WT1-TCRc4 Gene-transduced CD8-positive Tcm/Tn Lymphocytes

National Cancer Institute

Source

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Autologous, human CD8 T-lymphocytes, comprised of both central memory T-cells (Tcm) and naïve T-cells (Tn), that are transduced, ex vivo, with a self-inactivating (SIN) lentiviral vector encoding a high-affinity T-cell receptor (TCRc4) specific for the human tumor antigen Wilms tumor 1 (WT1) epitope 126-134 (RMFPNAPYL), with potential antineoplastic activity. Upon isolation of peripheral blood lymphocytes (PBLs), transduction, expansion ex vivo, priming of the Tn subset, but not the Tcm subset, with interleukin-21 (IL-21) and reintroduction of equal amounts of Tcm and Tn cells into the patient, WT1-TCRc4 gene-transduced CD8-positive Tcm/Tn lymphocytes redirect T-lymphocytes to WT1-expressing tumor cells and specifically bind to and lyse those cells. This inhibits proliferation of WT1-expressing tumor cells. WT1 protein, a zinc finger DNA-binding transcriptional regulator, is overexpressed in most leukemias and various solid tumors, while expression in normal, healthy tissues is very limited; its expression is correlated with aggressiveness and poor prognosis.