CD8+ and CD4+ Donor Memory T-cells-expressing HA1-Specific TCR

National Cancer Institute

Source

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A preparation of CD4+ and CD8+ central memory (CM) T-lymphocytes isolated from the peripheral blood of a transplant donor and transduced with a lentiviral vector (LV) (pRRLSIN) expressing a minor H antigen (HA-1(H); HA1(H)) T-cell receptor (TCR) containing the suicide gene inducible caspase 9 (iCasp9 or iC9)-HA1 TCR2-RQR-CD8 transgene (pRRLSIN iC9-HA1 TCR2-RQR-CD8; HA-1 TCR LV), with potential immunostimulating and antineoplastic activities. Upon intravenous administration and after allogeneic hematopoietic stem cell transplantation (HSCT), the CD8+ and CD4+ donor memory T cells-expressing HA1-specific TCR are directed to and induce selective toxicity in HA1-expressing tumor cells. iCasp9 consists of a human FK506 drug-binding domain with an F36V mutation (FKBP12-F36V) linked to human caspase 9. If administration of the T-cells lead to unacceptable side effects, a dimerizing agent rimiducid (AP1903), which binds to the FKBP12-F36V drug-binding domain and activates caspase 9, can be administered; caspase-9 activation results in the apoptosis of the administered TCR-modified T-cells. HA1(H) is a tumor-associated antigen (TAA) that is selectively and highly expressed on leukemic stem cells and blasts, but not in normal non-hematopoietic cells. RQR includes a CD20 epitope, and a CD34 epitope that facilitates both purification and cell tracking of the transduced T-cells with an anti-CD34 monoclonal antibody.