Autologous iCasp9-deltaNGFR-CD19CAR-expressing T Cells

National Cancer Institute

Source

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A preparation of autologous T-lymphocytes that are transduced with a retroviral vector encoding a chimeric antigen receptor (CAR) specific for the CD19 antigen, the suicide gene, inducible human caspase 9 (iCasp9 or iC9), and a truncated low-affinity nerve growth factor receptor (deltaNGFR), with potential immunomodulating and antineoplastic activities. The iCasp9 construct consists of the entire coding sequence for the human FK506-drug binding protein (FKBP12) with an F36V mutation (FKBP12-F36V) that is linked to the gene encoding human caspase 9, which is deleted of its endogenous caspase activation and recruitment domains. Upon intravenous administration, autologous iCasp9-deltaNGFR-CD19CAR-expressing T cells are selectively toxic to CD19-expressing tumor cells. If the administered T-cells lead to unacceptable side effects, the chemical homodimerizer AP1903 can be administered, which binds to the FKBP12-F36V drug binding domain, activates caspase 9, and results in apoptosis of the administered CAR19 T-cells. The CD19 antigen is a B-cell specific cell surface antigen expressed in all B-cell lineage malignancies. Prior to administration, deltaNGFR, is used to select the CAR19-transduced T-cells for further enrichment by flow cytometry using an anti-NGFR antibody.