Autologous iCASP9-CD19-expressing T-Lymphocytes

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 tumor-associated antigen (TAA) CD19 and the inducible suicide gene human caspase 9 (iCASP9 or iC9), that is linked to a drug binding domain, 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 iC9, which is a modified form of the CASP9 gene where the sequences encoding the endogenous caspase activation and recruitment domains have been deleted. Upon intravenous administration, autologous iCASP9-CD19-expressing T-lymphocytes (iC9-CAR19 T-cells) target and bind to CD19-expressing tumor cells, thereby selectively lysing these tumor cells. If the administered T-cells cause unacceptable side effects, the chemical homodimerizer AP1903, which binds to the FKBP12-F36V drug-binding domain, can be administered; this induces caspase 9 expression, and results in apoptosis of the administered iC9-CAR19 T-cells. The CD19 antigen is a B-cell specific cell surface antigen expressed in all B-cell lineage malignancies.