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Autologous iC9-deltaNGFR-CD19CAR-CD3zeta-4-1BB-expressing T-lymphocytes

National Cancer Institute

Source

National Cancer Institute. *Autologous iC9-deltaNGFR-CD19CAR-CD3zeta-4-1BB-expressing T-lymphocytes*. NCI Thesaurus. Code C156479.

A preparation of autologous T-lymphocytes that have been transduced with a retroviral vector to express a chimeric antigen receptor (CAR) consisting of an anti-CD19 single chain variable fragment (scFv) fused to a human immunoglobulin G1 (IgG1) hinge and a CD8alpha transmembrane domain, linked to the co-stimulatory molecule 4-1BB (CD137) and the cytoplasmic portion of the zeta chain of the human T-cell receptor (CD3zeta), containing the apoptosis-inducible suicide gene human caspase 9 (iCASP9 or iC9), linked to a drug binding domain, and a truncated low-affinity nerve growth factor receptor (deltaNGFR), with potential immunostimulating and antineoplastic activities. The iC9 construct consists of the sequence of the human FK506-binding protein (FKBP12) with an F36V mutation, connected through a Ser-Gly-Gly-Gly-Ser linker to the gene-encoding human caspase 9, which is deleted of its endogenous caspase activation and recruitment domain. Upon transfusion, the iCasp9-deltaNGFR-CD19CAR-CD3zeta-4-1BB-expressing autologous T-lymphocytes target and bind to CD19-expressing neoplastic B-cells. Prior to administration, deltaNGFR is used to select the CAR19-transduced T-cells for further enrichment by flow cytometry using an anti-NGFR antibody.