Autologous Anti-CD19CAR-CD28tm/4-1BB/CD3zeta-HER2tG-expressing CD4+/CD8+ T-lymphocytes SCRI-huCAR19v1

National Cancer Institute

Source

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A preparation of autologous CD4- and CD8-positive T-lymphocytes that have been transduced with a third-generation self-inactivating (SIN) lentiviral vector (LV) expressing a human-derived immunoglobulin G4 (IgG4) hinge-optimized chimeric antigen receptor (CAR) consisting of a single chain variable fragment (scFv) specific for CD19 that is fused to a human CD28 transmembrane domain (CD28tm), the intracellular cytoplasmic domain of 4-1BB (CD137) and the zeta chain of the TCR/CD3 complex (CD3zeta), and linked to a truncated form of the human epidermal growth factor receptor 2 (HER2tG), with potential immunostimulating and antineoplastic activities. Upon administration, the autologous CD4+/CD8+ T-lymphocytes SCRI-huCAR19v1 specifically target and bind to CD19-expressing neoplastic B-cells. This results in a cytotoxic T-lymphocyte (CTL) response against CD19-expressing tumor cells and causes tumor cell lysis. CD19 is a B-cell-specific cell surface antigen that is overexpressed in B-cell lineage tumors. Incorporation of the costimulatory signaling domains of CD28 and 4-1BB increases human T-cell function, expansion, and survival. Devoid of both ligand binding domains and tyrosine kinase activity, the co-expressed HER2tG both facilitates in vivo detection of the administered, transduced T-cells and can promote elimination of those cells through a trastuzumab-induced antibody dependent cellular cytotoxicity (ADCC) response.