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Autologous Anti-CD19CAR-4-1BB-CD3zeta-EGFRt-expressing T Lymphocytes

National Cancer Institute

Source

National Cancer Institute. *Autologous Anti-CD19CAR-4-1BB-CD3zeta-EGFRt-expressing T Lymphocytes*. NCI Thesaurus. Code C116914.

A preparation of genetically modified CD8⁺ central memory (T_{cm}) and CD4⁺ autologous T-lymphocytes (1:1) transduced with a replication incompetent, self-inactivating (SIN) lentiviral vector expressing a chimeric antigen receptor (CAR) containing an anti-CD19 single chain variable fragment (scFv) derived from the murine IgG1 monoclonal antibody (mAb) FMC63, fused to the signaling domain of 4-1BB (CD137), the zeta chain of the TCR/CD3 complex (CD3-zeta), and a truncated form of the human epidermal growth factor receptor (EGFRt), with potential immunostimulating and antineoplastic activities. Upon intravenous administration, autologous anti-CD19CAR-4-1BB-CD3zeta-EGFRt-expressing T lymphocytes are directed to and induce selective toxicity in CD19-expressing tumor cells. CD19 antigen is a B-cell specific cell surface antigen expressed in all B-cell lineage malignancies. Devoid of both ligand binding domains and tyrosine kinase activity, the expressed EGFRt both facilitates in vivo detection of the administered, transduced T-cells and can promote elimination of those cells through a cetuximab-induced antibody dependent cellular cytotoxicity response. The 4-1BB costimulatory signaling domain enhances both proliferation of T-cells and antitumor activity.