Autologous CD19CAR-CD28-CD3zeta-EGFRt-expressing Tn/mem-enriched T-lymphocytes

National Cancer Institute

Source

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A preparation of genetically modified autologous lymphocytes comprised of CD62L-positive naïve and memory T-cells (Tn/mem), that are transduced ex vivo with a self-inactivating (SIN) lentiviral vector expressing a hinge-optimized chimeric antigen receptor (CAR) specific for the CD19 antigen and containing CD28 and CD3 zeta signaling domains, and a truncated form of the human epidermal growth factor receptor (EGFRt), with potential immunostimulating and antineoplastic activities. Upon isolation of peripheral blood lymphocytes (PBLs), transduction of the CD62L-positive T-lymphocytes, expansion ex vivo and reintroduction of the cells into the patient, the autologous CD19R(EQ)-CD28-CD3zeta-EGFRt-expressing Tn/mem-enriched T-cells target CD19-expressing tumor cells, thereby inducing 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, EGFRt both facilitates in vivo detection of the administered T-cells and can promote elimination of those cells upon a cetuximab-induced antibody dependent cellular cytotoxicity response. Tn/mem T-cells include naïve T-cells, central memory T-cells (Tcm) and stem cell memory T-cells (Tscm). CD19R(EQ) contains two point mutations in the immunoglobulin (Ig) G4 spacer region, thereby preventing recognition of the CAR by Fc receptors (FcRs).