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Autologous CD123CAR-CD28-CD3zeta-EGFRt-expressing T Lymphocytes

National Cancer Institute

Source

National Cancer Institute. Autologous CD123CAR-CD28-CD3zeta-EGFRt-expressing T Lymphocytes. NCI Thesaurus. Code C116329.

A preparation of genetically modified autologous T-cells transduced with a replication incompetent, self-inactivating lentiviral vector expressing a hinge-optimized, chimeric antigen receptor (CAR), containing a CD28 co-stimulatory signaling domain fused to CD3 zeta, the single-chain variable fragment of CD123 (Interleukin-3 receptor alpha chain or IL3RA) antigen, and a truncated form of the human epidermal growth factor receptor (EGFRt), with potential immunostimulating and antineoplastic activities. Upon intravenous administration, autologous CD123CAR-CD28-CD3zeta-EGFRt-expressing T Lymphocytes are directed to and induce selective toxicity in CD123-expressing tumor cells. CD123 is normally expressed on committed blood progenitor cells in the bone marrow; its overexpression is associated with increased leukemic cell proliferation and aggressiveness. Devoid of both ligand binding domains and tyrosine kinase activity, EGFRt both facilitates detection of the administered T-cells in vivo and can promote elimination of those cells following a cetuximab-induced antibody-dependent cellular cytotoxicity response. The costimulatory signaling domain enhances both proliferation of T-cells and antitumor activity. Hinge optimization prevents recognition of the CAR by Fc receptors (FcRs).