Autologous Anti-CD19/Anti-CD20-CAR-CD28-4-1BB-CD3zeta-EGFRt+-expressing Tn/mem Cells

National Cancer Institute

Source

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A preparation of genetically modified autologous naive/memory T-cells (Tn/mem), that have been transduced with a self-inactivating (SIN) lentiviral vector to express a bispecific chimeric antigen receptor (CAR) consisting of a single chain variable fragment (scFv) of anti-CD19, derived from the anti-CD19 monoclonal antibody FMC63, in tandem with an anti-CD20 scFv, derived from the anti-CD20 monoclonal antibody Leu16, and fused to the hinge domain of human immunoglobulin (Ig) G4, the transmembrane domain of human CD28, and the cytoplasmic signaling domains of 4-1BB (CD137) and the T-cell antigen receptor complex zeta chain (CD3-zeta) (BBz), and linked via the T2A sequence to a truncated form of the human epidermal growth factor receptor (EGFRt), with potential immunostimulating and antineoplastic activities. Upon transfusion, autologous anti-CD19/anti-CD20-CAR-CD28-4-1BB-CD3zeta-EGFR+-expressing Tn/mem cells recognize and induce selective toxicity in CD19/CD20-expressing tumor cells, resulting in tumor cell lysis. Both CD19 and CD20 are B-cell-specific cell surface antigens overexpressed in 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 (ADCC) response.