Autologous Anti-BCMA-CAR-4-1BB-CD3zeta-EGFRt-expressing CD4+/CD8+ T-lymphocytes

National Cancer Institute

Source

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A preparation of an approximately equal ratio of autologous CD4- and CD8-positive T-lymphocytes that have been ex vivo transduced with a genetically-engineered self-inactivating (SIN) lentiviral vector (LV) expressing a chimeric antigen receptor (CAR) containing a single chain variable fragment (scFv) specific for the human tumor-associated antigen (TAA) B-cell maturation antigen (BCMA; tumor necrosis factor receptor superfamily member 17; TNFRSF17) fused to the co-stimulatory domain of 4-1BB (CD137), the CD3-zeta (CD3z) T-cell signaling domain, and a truncated form of the human epidermal growth factor receptor (EGFRt), with potential immunostimulating and antineoplastic activities. Upon administration, the autologous anti-BCMA-CAR-4-1BB-CD3zeta-EGFRt-expressing CD4+/CD8+ T-lymphocytes specifically recognize and induce selective toxicity against BCMA-expressing tumor cells. Devoid of both ligand binding domains and tyrosine kinase activity, the expressed EGFRt facilitates both in vivo detection of the administered, transduced T-cells and can promote elimination of those cells through a cetuximab-induced antibody-dependent cellular cytotoxicity (ADCC) response. BCMA, a tumor-specific antigen and a receptor for both a proliferation-inducing ligand (APRIL) and B-cell activating factor (BAFF), is a member of the tumor necrosis factor receptor superfamily (TNFRSF) and plays a key role in plasma cell survival. BCMA is found on the surfaces of plasma cells and is overexpressed on malignant plasma cells.