Autologous Anti-GD2CAR-CD28-CD3zeta-IL-15-expressing Natural Killer T-cells

National Cancer Institute

Source

National Cancer Institute. Autologous Anti-GD2CAR-CD28-CD3zeta-IL-15-expressing Natural Killer T-cells. NCI Thesaurus. Code C158682.

A preparation of autologous natural killer T-lymphocytes (NKTs) that have been transduced with a retroviral vector to express both an extracellular domain consisting of interleukin 15 (IL-15) and a chimeric antigen receptor (CAR) specific for the human tumor associated antigen (TAA) GD2, linked to the CD28 and CD3zeta (TCRzeta; CD247) costimulatory signaling domains, with potential antineoplastic activity. Upon intravenous administration, autologous anti-GD2CAR-CD28-CD3zeta-IL-15-expressing NKTs target, bind to, and induce selective toxicity in GD2-expressing tumor cells. IL-15 is a pro-survival cytokine that promotes T-cell persistence and potentiates the immune response against tumor cells. Incorporation of the costimulatory signaling domains increases T-cell function, expansion, and survival. The CD28 costimulatory molecule signaling domain enhances activation and signaling after recognition of GD2. Additionally, inclusion of the CD28 signaling domain may increase proliferation of T-cells and antitumor activity compared to the inclusion of the CD3zeta chain alone. GD2, a disialoganglioside and tumor-associated antigen (TAA), is overexpressed in a variety of tumor cell types.