Genetically-modified Anti-HER2-CAR-CD28zeta-expressing Allogeneic NK-92/5.28.z Cells

National Cancer Institute

Source

National Cancer Institute. Genetically-modified Anti-HER2-CAR-CD28zeta-expressing Allogeneic NK-92/5.28.z Cells. NCI Thesaurus. Code C154568.

A preparation of genetically-modified natural killer (NK) cells derived from the allogeneic NK-92 cell line that are transduced with a lentiviral vector expressing a codon-optimized chimeric antigen receptor (CAR) consisting of a single chain variable fragment (scFv) of the anti-human epidermal growth factor 2 (HER2; ErbB2) monoclonal antibody FRP5, and fused, via hinge and transmembrane regions, to the intracellular domain of the costimulatory molecule CD28, and the intracellular signaling domain of the T-cell antigen receptor complex zeta chain (CD3-zeta), with potential cytolytic, immunomodulating and antineoplastic activities. Upon infusion of the genetically modified anti-HER2-CAR-CD28zeta-expressing allogeneic NK-92/5.28.z cells, the NK cells recognize and bind to HER2 expressed on tumor cells. This leads to the secretion and release of perforins, granzymes, cytokines and chemokines, which results in selective tumor cell lysis in HER2-expressing tumor cells. HER2, a receptor tyrosine kinase (RTK) mutated or overexpressed in many tumor cell types, plays a significant role in tumor cell proliferation and tumor vascularization. The NK-92 cells are derived from a human cytotoxic cell line composed of allogeneic, activated, interleukin-2-(IL-2) dependent-NK cells from a 50-year old male patient with rapidly progressive non-Hodgkin's lymphoma. As NK-92 cells are devoid of killer inhibitory receptors (KIRs; also called killer cell immunoglobulin-like receptors), which are negative regulators of NK cell activity, cancer cells are unable to suppress the cancer cell killing ability of the NK-92 cells.