Autologous Anti-MUC1*-CAR-4-1BB-CD3zeta-expressing T-lymphocytes

National Cancer Institute

Source

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A preparation of autologous T-lymphocytes transduced with a lentiviral vector encoding a human CD8 alpha leader sequence, a humanized MNC2-single chain variable fragment (scFv) targeting the extracellular domain of the cleaved form of mucin-1 (MUC-1), known as MUC1*, portions of human CD8 hinge and transmembrane domains, and human 4-1BB and human CD3-zeta costimulatory domains, with potential antineoplastic and immunostimulating activities. Upon re-introduction into the patient, the autologous anti-MUC1*-CAR-4-1BB-CD3zeta-expressing T-lymphocytes specifically recognize and induce selective toxicity in MUC1*-expressing tumor cells. MUC1* is a post-translationally modified form of MUC1, a single pass type I transmembrane protein that is normally expressed in the glandular or luminal epithelial cells of the esophagus, stomach, duodenum, pancreas, uterus, prostate, and lungs, and may be aberrantly expressed in certain tumor types. MUC1* is a growth factor that is activated by ligand-induced dimerization of its extracellular domain, which may stimulate mitogen-activated protein kinase (MAP kinase, MAPK) signaling and promote tumor cell growth. MUC1* is frequently expressed in certain cancer types, with increased expression noted in higher grade lesions and tumor cells resistant to certain chemotherapies.