Anti-VEGFR2-CAR Retroviral Vector-transduced Autologous T-lymphocytes

National Cancer Institute

Source

National Cancer Institute. Anti-VEGFR2-CAR Retroviral Vector-transduced Autologous T-lymphocytes. NCI Thesaurus. Code C111038.

Autologous human CD8-positive T-lymphocytes transduced with a recombinant retroviral vector encoding a chimeric T cell receptor (chimeric antigen receptor or CAR) consisting of an anti-vascular endothelial growth factor receptor type 2 (VEGFR2) scFv (single chain variable fragment), linked to the transmembrane domain of human CD8alpha and coupled to the costimulatory signaling domains of both CD28 and 4-1BB (CD137), and the CD3 zeta chain of the T-cell receptor (TCR), with potential immunostimulating and antineoplastic activities. Autologous peripheral blood lymphocytes (PBLs) from a patient with VEGFR2-positive cancer are pulsed with a retroviral vector that encodes the CAR gene specific for VEGFR2. After expansion in culture and reintroduction into the patient, the anti-VEGFR2 CAR-gene engineered CD8+ lymphocytes express anti-VEGFR2-CAR on their cell surfaces and bind to the VEGFR2 antigen on tumor cell surfaces. Subsequently, VEGFR2-expressing tumor cells are lysed. VEGFR2, a receptor tyrosine kinase (RTK) overexpressed by a variety of cancer cell types, belongs to the VEGFR superfamily and plays key roles in tumor cell proliferation, survival, invasion and tumor angiogenesis. The co-stimulatory molecules are required for optimal T-cell activation.