IL13Ralpha2-specific Hinge-optimized 4-1BB-co-stimulatory CAR/Truncated CD19-expressing Autologous TN/MEM Cells

National Cancer Institute

Source

National Cancer Institute. IL13Ralpha2-specific Hinge-optimized 4-1BB-co-stimulatory CAR/Truncated CD19-expressing Autologous TN/MEM Cells. NCI Thesaurus. Code C141460.

A preparation of ex vivo expanded, genetically modified autologous naïve and memory T-cells (TN/MEM) transduced with a replication incompetent, self-inactivating (SIN) lentiviral vector expressing a hinge-optimized, chimeric antigen receptor (CAR) specific for interleukin-13 receptor alpha 2 (IL13Ra2), and containing the cluster of differentiation 137 (CD137; 4-1BB) co-stimulatory signaling domain fused to the signaling domain of the T-cell antigen receptor complex zeta chain (CD3-zeta), and a truncated form of human cluster of differentiation 19 (CD19t), with potential immunostimulating and antineoplastic activities. Upon intratumoral or intracavitary administration, IL13Ra2-specific hinge-optimized 4-1BB-co-stimulatory CAR/truncated CD19-expressing autologous TN/MEM cells are directed to, and induce selective toxicity and cytolysis in, IL13Ra2-expressing tumor cells. IL13Ra2, overexpressed by a variety of tumor cell types, is associated with increased proliferation, migration and invasiveness of tumor cells. The co-stimulatory signaling domain enhances both proliferation of T-cells and antitumor activity. Hinge optimization prevents the recognition and clearance of the CAR by endogenous Fc receptors (FcRs). CD19t is used as a surface marker to both track and quantify the modified T-cells in vivo.