IL13Ralpha2-specific Hinge-optimized 41BB-co-stimulatory CAR Truncated CD19-expressing Autologous T-Lymphocytes

National Cancer Institute

Source

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A preparation of ex vivo expanded, genetically modified autologous central memory-enriched T-cells (Tcm) 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, 41BB-co-stimulatory CAR/truncated CD19 expressing T-lymphocytes 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 tumor cell proliferation, migration and invasiveness. The costimulatory 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 quantify and track the gene modified T-cells in vivo.