

ROR1 CAR-specific Autologous T-Lymphocytes

National Cancer Institute

Source

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A mixture of two T-lymphocyte preparations expressing a chimeric antigen receptor (CAR) consisting of an anti-receptor tyrosine kinase-like orphan receptor 1 (ROR1) single chain variable fragment (scFv) fused to either the co-stimulatory signaling domain cluster of differentiation 28 (CD28), and the zeta chain of the T-cell receptor (TCR)/CD3 complex (CD3-zeta) (ROR1CD28zeta), or the co-stimulatory signaling domain cluster of differentiation 137 (CD137; 4-1BB), and the zeta chain of the T-cell receptor (TCR)/CD3 complex (CD3-zeta) (ROR1CD137zeta), with potential immunomodulating and antineoplastic activities. Upon simultaneous administration of the two T-lymphocyte populations ROR1CD28zeta and ROR1CD137zeta, the ROR1 CAR-specific autologous T-lymphocytes are directed to tumor cells expressing ROR1, which may result in a selective toxicity against, and lysis of ROR1-expressing tumor cells. CD28, a T-cell surface-associated co-stimulatory molecule, is required for full T-cell activation, proliferation, and survival. The 4-1BB co-stimulatory molecule signaling domain enhances activation and signaling after recognition of ROR1. ROR1, also known as neurotrophic tyrosine kinase, receptor-related 1, is expressed during embryogenesis and by certain leukemias.