Autologous CD22-4SCAR-expressing T-cells 4SCAR22

National Cancer Institute

Source

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A preparation of genetically modified autologous T-cells transduced with a replication incompetent, self-inactivating lentiviral vector expressing a fourth generation chimeric antigen receptor (4SCAR) consisting of an anti-CD22 single chain variable fragment (scFv) that is coupled to the costimulatory signaling domains CD28, CD137, CD27 and the zeta chain of the T-cell receptor (TCR), and is fused with the suicide gene inducible caspase 9 (iCasp9), with potential immunostimulating and antineoplastic activities. Upon intravenous administration, autologous CD22-4SCAR-expressing T-cells 4SCAR22 are directed to and induce selective toxicity in CD22-expressing tumor cells. iCasp9 consists of a human FK506 drug-binding domain with an F36V mutation (FKBP12-F36V) linked to human caspase 9. If the administered T-cells lead to unacceptable side effects, the chemical homodimerizer AP1903 can be administered. AP1903 binds to the drug binding FKBP12-F36V domain and induces activation of caspase 9, which results in the apoptosis of the administered T-cells and enhances safety of this agent. CD22, a B-lineage-restricted, transmembrane phosphoglycoprotein, is expressed on malignant B cells. CD28, CD137 and CD27, T-cell surface-associated co-stimulatory molecules, are required for full T-cell activation and enhance both proliferation of T-cells and antitumor activity.