Anti-mesothelin iCasp9M28z CAR-transduced Autologous T Lymphocytes

National Cancer Institute

Source

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Genetically modified, autologous T-lymphocytes transduced with a retroviral vector encoding a chimeric antigen receptor (CAR) specific for mesothelin linked to the signaling domains for the co-stimulatory molecules CD28 and CD3 zeta, as well as the suicide gene inducible caspase 9 (iCasp9 or iC9), with potential immunomodulating and antineoplastic activities. Upon intravenous administration, anti-mesothelin iCasp9M28z CAR-transduced autologous T lymphocytes specifically target and kill mesothelin-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, a dimerizing agent can be administered, which binds to the FKBP12-F36V drug-binding domain and activates caspase 9, resulting in the apoptosis of the administered T-cells. Mesothelin, a tumor-associated antigen, is overexpressed in a variety of cancer cell types.