Allogeneic Tri-functional Anti-CD19 CAR-NK Cells

National Cancer Institute

Source

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A preparation of allogeneic natural killer (NK) cells transduced with a retroviral vector expressing the immunostimulatory cytokine interleukin-15 (IL-15) and encoding a chimeric antigen receptor (CAR) specific for the tumor-associated antigen (TAA) cluster of differentiation 19 (CD19) that is coupled to the co-stimulatory domains cluster of differentiation 28 (CD28, T-cell-specific surface glycoprotein CD28), cluster of differentiation 137 (CD137; 4-1BB), and the zeta chain of the T-cell receptor (TCR)/CD3 complex (TCRzeta; CD247; CD3zeta); and a blocker for the inhibitory T-cell receptor programmed cell death protein 1 (PD-1; PDCD1; CD279), with potential immunomodulating and antineoplastic activities. Upon transfusion, the allogeneic tri-functional anti-CD19 CAR-NK cells recognize, bind to and induce selective cytotoxicity in CD19-expressing tumor cells. IL-15 enhances the cytotoxic effect of the NK cells and the activated anti-tumor T-cells. The PD-1 inhibitory domain targets and binds to programmed cell death-1 ligand 1 (PD-L1) expressed on tumor cells, thereby preventing the binding of the PD-1 on T-lymphocytes to its ligand, PD-L1 on tumor cells. This prevents PD-1/PD-L1-mediated inhibition of T-lymphocytes and leads to the activation and expansion of T-cells resulting in a cytotoxic T-lymphocyte (CTL) response against tumor cells, thereby enhancing the elimination of tumor cells. CD19 antigen is a B-cell specific cell surface antigen expressed in all B-cell lineage malignancies. The co-stimulatory signaling domains enhance both proliferation of T-cells and anti-tumor activity.