Autologous Anti-PSCA-CAR-4-1BB/TCRzeta-CD19t-expressing T-lymphocytes

National Cancer Institute

Source

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A preparation of autologous T-lymphocytes that have been immunomagnetically depleted of CD14+ myeloid cells and CD25+ regulatory T-cells (Tregs), activated with anti-CD3 and anti-CD28 beads, and transduced with a self-inactivating (SIN) lentiviral vector (LV) encoding a chimeric antigen receptor (CAR) containing a prostate stem cell antigen (PSCA)-specific, humanized and affinity matured A11 single chain variable fragment (scFv), a human immunoglobulin G4 (IgG4) Fc spacer lacking the CH2 domain, a human CD4 transmembrane domain, a costimulatory human 4-1BB (CD137) cytoplasmic signaling domain linked to the zeta chain of the human T-cell receptor (TCR)/CD3 complex (CD3zeta), and a truncated human CD19 sequence (CD19t), with potential immunostimulating and antineoplastic activities. Upon intravenous infusion, the autologous anti-PSCA-CAR-4-1BB/TCRzeta-CD19t-expressing T-lymphocytes recognize and induce selective toxicity in PSCA-expressing tumor cells. PSCA, a glycosyl-phosphatidylinositol (GPI)-linked cell surface antigen, is uniquely and highly expressed in certain cancers including bladder, pancreatic, and prostate cancers. Co-expression of CD19t provides an inert, non-immunogenic surface marker that allows for measurement of genetically modified cells and tracking of T-cells following adoptive transfer. The costimulatory signaling domains improve T-cell function, selectivity, expansion and survival.