Autologous Prostate Stem Cell Antigen-specific CAR T Cells BPX-601

National Cancer Institute

Source

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A preparation of autologous T-lymphocytes expressing a chimeric antigen receptor (CAR) consisting of an anti-human prostate stem cell antigen (PSCA) scFv (single chain variable fragment) coupled to the zeta chain of the T-cell receptor (TCRzeta) and a drug-induced co-stimulatory molecule, composed of an inducible, chimeric MyD88/CD40 (inducible MC; iMC) co-stimulatory domain, in which both the MyD88 and CD40 lack their extracellular domains, with potential antineoplastic activity. Upon administration of BPX-601, the T-cells target and bind to PSCA-expressing cancer cells. Upon subsequent administration of the chemical inducer of dimerization (CID) agent rimiducid, this agent targets and binds to the drug binding domain, which leads to iMC expression, activation of both CD40- and MyD88-mediated signal transduction pathways, and an induction of selective cytotoxicity in, and eradication of PSCA-expressing cancer cells. iMC activation by rimiducid increases T-cell survival and anti-tumor activity of the administered T-cells, compared to T-cells without the drug iMC activation-switch. As these T-cells are engineered to only be fully activated by binding to both antigen and rimiducid, T-cell proliferation, activity and toxicity can be controlled by adjusting the dose of rimiducid, thereby preventing uncontrolled T-cell activation which increases the safety of the administered T-cells. PSCA is a glycosylphosphatidylinositol (GPI)-anchored cell surface antigen overexpressed in many cancer cell types.