PRAME-targeting T-cell Receptor/Inducible Caspase 9 BPX-701

National Cancer Institute

Source

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Human allogeneic T-lymphocytes transduced with a retroviral vector encoding a high-affinity T-cell receptor (TCR) specific for human leukocyte antigen (HLA)-A2-01-restricted, preferentially-expressed antigen in melanoma (PRAME) and containing the chemical induction of dimerization (CID) suicide/safety switch, composed of a drug binding domain coupled to the signaling domain of the suicide enzyme caspase-9, with potential antineoplastic activity. Peripheral blood mononuclear cells (PBMCs) are isolated from a patient, transduced with an anti-PRAME-HLA-A2 restricted TCR, expanded ex vivo, and reintroduced into the HLA-A2-positive patient. Upon reintroduction, PRAME-targeting T-cell receptor-based therapy BPX-701 binds to tumor cells expressing PRAME, which may induce cell death in and halt the growth of PRAME-expressing cancer cells. The tumor-associated antigen PRAME is overexpressed by a variety of cancer cell types. If potential T-cell toxicity due to graft-versus-host disease (GvHD) occurs, the chemical dimerizer rimiducid (AP1903) can be adminstered. Rimiducid binds to the drug binding domain expressed by the BPX-701 T-cells, and triggers activation of the caspase-9 domain, which leads to caspase 9-mediated signaling, the induction of apoptosis and to selective and complete elimination of BPX-701 cells.