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# Autologous Anti-gp100CAR-CD3zeta-4-1BB-IL-15-PD1-expressing Tri-functional T-lymphocytes

National Cancer Institute

## Source

National Cancer Institute. *Autologous Anti-gp100CAR-CD3zeta-4-1BB-IL-15-PD1-expressing Tri-functional T-lymphocytes*. NCI Thesaurus. Code C162626.

A preparation of autologous T-lymphocytes that have been transduced with a lentiviral vector encoding a tri-functional chimeric antigen receptor (TriCAR) comprised of an extracellular domain consisting of an antigen binding domain specific to glycoprotein 100 (gp100) peptides 209-217 complexed with human leucocyte antigen A2 (HLA-A2), interleukin 15 (IL-15) and programmed cell death 1 (PD1; PDCD1; CD279; programmed death-1), which are linked by a transmembrane domain to the intracellular signaling domains of 4-1BB (CD137) and the zeta chain of the TCR/CD3 complex (TCRzeta; CD247; CD3zeta), with potential antineoplastic activity. Upon administration, the autologous anti-gp100CAR-CD3zeta-4-1BB-IL-15-PD1-expressing tri-functional T-lymphocytes selectively bind to gp100 peptides presented by HLA-A2. Upon binding to the gp100-HLA complex, the T-cells release cytokines and induce selective toxicity in gp100-expressing tumor cells. IL-15 is a pro-survival cytokine that promotes T-cell persistence and potentiates the immune response against tumor cells. The PD1 moiety binds to programmed cell death-1 ligand 1 (PD-L1; cluster of differentiation 274; CD274) on tumor cells, reversing T-cell inactivation caused by endogenous PD1/PD-L1 signaling and enhancing the cytotoxic T-lymphocyte (CTL)-mediated anti-tumor immune response against PD-L1-expressing tumor cells.