# Autologous Anti-HER2-CAR-4-1BB-CD3zeta-CD19t+-expressing Tcm-enriched T-lymphocytes

National Cancer Institute

## Source

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A preparation of genetically modified autologous central memory (Tcm) enriched T-cells transduced with a lentiviral vector expressing a chimeric antigen receptor (CAR) consisting of an anti-human epidermal growth factor 2 (HER2) single chain variable fragment (scFv) derived from trastuzumab, with a 4-1BB (CD137) costimulatory domain that is linked to the signaling domain of the T-cell antigen receptor complex zeta chain (CD3-zeta) (BBz), and truncated CD19 (CD19t), with potential immunostimulatory and antineoplastic activities. Upon intravenous infusion, Anti-HER2-CAR-4-1BB-CD19t+-expressing Tcm-enriched T-lymphocytes are directed against HER2-expressing cells, thereby inducing selective toxicity in HER2-expressing tumor cells. HER2, a receptor tyrosine kinase, is mutated or overexpressed in many tumor cell types, plays a significant role in tumor cell proliferation and tumor vascularization. The BBz costimulatory signaling domain enhances proliferation of T-cells and antitumor activity, while CD19t, a marker for transduction, is utilized to calculate CAR T-cell dosing and for CAR-expressing cell tracking. Tcm cells have the capacity for long-lived persistence and retain their ability to proliferate upon antigen re-encounter. The immunoglobulin G4 (IgG4) extracellular spacer contains a double mutation, (L235E;N297Q) (EQ) within the CH2 region to reduce Fc receptor recognition.