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Autologous HER2-CAR-modified Adenovirus-specific Cytotoxic T-lymphocytes

National Cancer Institute

Source

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A population of autologous cytotoxic T-lymphocytes (CTLs) specifically reactive to human adenovirus (Ad) that have been transduced with a retroviral vector expressing a second-generation human epidermal growth factor receptor type 2 (HER2; EGFR2; ErbB2)-specific chimeric antigen receptor (CAR) comprised of an exodomain based on a anti-CD22 single chain variable fragment (scFv) from the anti-HER2 monoclonal antibody FRP5 that is linked to the costimulatory domains of CD28 and the zeta chain of the T CR/CD3 complex (CD3zeta), with potential immunostimulating and antineoplastic activities. Upon intravenous administration, the autologous HER2-CAR-modified Ad-specific CTLs are directed to and induce selective toxicity in HER2-expressing tumor cells. Additionally, these cells may help reconstitute Ad-specific CTL responses in immunocompromised individuals and others at risk of developing Ad-infection. HER2, a receptor tyrosine kinase (RTK) overexpressed by a variety of tumor cell types, belongs to the EGFR superfamily and plays a key role in tumor cell proliferation.