Allogeneic CD19-specific Universal CAR19-expressing T-lymphocytes

National Cancer Institute

Source

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A preparation of allogeneic, frozen, 'off-the-shelf', universal transcription activator-like effector nuclease (TALEN)-engineered, gene-edited T-lymphocytes expressing a chimeric antigen receptor (CAR) targeting the tumor-associated antigen (TAA) CD19, and containing a RQR8 transgene, with potential immunostimulating and antineoplastic activities. Using TALEN technology, the T-cell receptor (TCR) alpha chain and CD52 genes are deleted from the CAR19 T-cells. Upon infusion, allogeneic universal CD19-specific CAR-modified T cells (UCART19) specifically target and bind to CD19-expressing tumor cells, thereby selectively lysing CD19-expressing tumor cells. CD19 antigen is a B-cell specific cell surface antigen expressed in all B-cell lineage malignancies. Deletion of the CD52 gene makes the modified donor T-cells resistant to the anti-CD52 monoclonal antibody alemtuzumab, which is used during lymphodepletion. The knockout of the TCR alpha gene eliminates TCR expression and is intended to abrogate the potential induction of graft-versus-host disease (GvHD) by the donor T-cells. The gene-edited allogeneic, frozen UCART19 have reduced production times and provide off-the-shelf CAR-T cells when compared to autologous CAR-T cells, which use the patient's own cells and are produced on an individual basis. The protein expressed by the RQR8 transgene contains epitopes from CD34 and CD20, which allows tracking of the UCART19 cells with a clinically-approved anti-CD34 antibody. Additionally if the UCART19 cells cause unacceptable side effects, the CD20 portion of the protein permits selective depletion of the UCART19 cells when the anti-CD20 monoclonal antibody rituximab is administered.