

Allogeneic IL13-Zetakine/HyTK-Expressing-Glucocorticoid Resistant Cytotoxic T Lymphocytes GRm13Z40-2

National Cancer Institute

Source

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A preparation of glucocorticoid receptor (GR) negative, allogeneic cytotoxic T-lymphocytes (CTLs) expressing a membrane-tethered interleukin 13 (IL13) cytokine chimeric T-cell antigen receptor (zetakine), with potential antineoplastic activity. Upon transfection of donor T-lymphocytes with a plasmid encoding a fusion protein of the IL13-zetakine and the selection-suicide expression enzyme HyTK, these modified CTLs are expanded and introduced into a patient with glioblastoma multiforme (GBM). This agent specifically targets IL13 receptor alpha2, a glioma-restricted cell-surface epitope; the CTLs exert their cytolytic effect thereby killing IL13Ra2-expressing glioma cells. In addition, IL13-zetakine redirected CTLs induce production of certain cytokines. Furthermore, due to the fact that these CTLs are GR negative, they can be used concomitantly with glucocorticoid therapy. The IL13-zetakine consists of an extracellular IL-13 E13Y mutein-human IgG4 hinge-Fc chimera fused to human cytoplasmic CD3-zeta via the transmembrane domain of human CD4.