

SCIENTIFIC ABSTRACT

A Phase I/IIb trial using neuroblastoma cells genetically engineered to express gamma interferon (IFN- γ), using a retroviral vector is proposed, in an effort to achieve a therapeutic antitumor immune response. Neuroblastoma is the most common extracranial solid tumor of childhood. Sixty percent of neuroblastoma patients are at risk for developing fatal progressive disease. Despite the success of induction chemotherapy/myeloablative therapy and autologous transplant in attaining complete clinical remissions in the high risk group, approximately 60% develop progressive disease and die. Treatment with retroviral vector mediated transfer/expression of γ -IFN into neuroblastoma cells, is proposed as a means of evoking an active immune response. Autologous neuroblastoma cells will be engineered to express γ -IFN where available. If autologous neuroblastoma cells are not available, single HLA haplotype matched allogeneic cells will be used as an immunogen. Patients at high risk of relapse with minimal or no detectable disease following myeloablative therapy and autologous bone marrow transplant, or patients with progressive/persistent disease despite conventional therapy will be serially immunized with autologous/allogeneic neuroblastoma cells engineered to express γ -IFN. Tumor cell lines will be established from tumor tissue or bone marrow metastasis, transduced with γ -IFN vector, and transduced cells selected for G418. Levels of γ -IFN production, MHC-I and MHC-II expression will be characterized. Following selection, and characterization, transduced cells will be lethally irradiated prior to use as an immunogen. The study will characterize safety/toxicity, clinical, and biological (immune) response.