

SCIENTIFIC ABSTRACT

The overall objective of this project is to perform a Phase I Clinical Trial in glioblastoma patients of cytokine gene transfer comprising subcutaneous injections of autologous or allogeneic HLA-A2 matched tumor cells genetically modified to secrete interleukin-2 (IL-2). The Phase I study will evaluate the safety, anti-tumor effects and immune responses induced by subcutaneous injections with escalated doses of irradiated HLA-A2 positive autologous or allogeneic tumor cells transduced with a replication incompetent IL-2 retroviral vector. We have treated one patient with glioblastoma multiforme who had failed conventional therapy with IL-2 gene therapy employing autologous tumor cells and fibroblasts transduced with an IL-2 retroviral vector. No significant morbidity was noted at the injection sites and post treatment monitoring of complete blood counts, serum chemistries and urinalyses revealed no significant changes from pre-treatment values. Cellular anti-tumor immune responses and tumor necrosis were observed during the course of therapy. This patient's tumor has an HLA-A2 positive haplotype and the IL-2 transduced tumor has been established as a continuous cell line. This cell line, termed GT9, will be utilized as the allogeneic HLA-A2 positive IL-2 transduced cell line for immunizations in this study. In the Phase I study, a group of patients will be injected with IL-2 transduced HLA-A2 positive autologous tumor cells and a second group will be treated with IL-2 transduced GT9 allogeneic irradiated tumor cells. Patient cohorts will receive injections with increasing doses of transduced tumor cells. All patients enrolled in the study will also have an established autologous tumor cell line for application in humoral and cellular immune response monitoring assays. The patients will be monitored for toxicity, anti-tumor responses and the induction of anti-tumor immunity. The results of the Phase I trial should permit an assessment of the safety of this form of cytokine gene therapy and provide initial data to evaluate the potential utility of IL-2 gene therapy with either autologous or partially HLA matched allogeneic tumor cells.