

SCIENTIFIC ABSTRACT

Small-cell lung cancer is a fatal disease in more than 90% of affected patients despite combined modality therapy with radiation and chemotherapy. The intent of this protocol is to culture small-cell lung cancer cells and transfect them with the gene for Interleukin-2 (IL-2) production. These transfected cells will be returned to patients after cytoreduction of their cancer with conventional chemotherapy. The aim is for the reimplanted, IL-2 producing tumor cells to stimulate the proliferation of a tumor-specific population of cytotoxic lymphocytes capable of destroying the reimplanted tumor. The plasmid vector BMG-Neo is an efficient vector of transfection. It uses as a eukaryotic replication unit an 85.5 kb DNA fragment from the bovine papilloma virus 1. This plasmid replicates extra chromosomally as an episome producing a copy number of 20-100 per cell. In pre-clinical studies in a murine model using the Lewis lung carcinoma cell line, the administration of IL-2 transfected cancer cells led to rejection of subsequently administered non-transfected tumor cells and to regression of established tumors. In this study in humans, IL-2 transfected radiated (to prevent proliferation) tumor cells will be serially injected weekly over 4-6 weeks. Companion laboratory studies will seek to quantify and characterize the nature of the induced cytotoxic lymphocyte response in the patients' peripheral blood. The laboratory component, in part, also will clone out populations of tumor specific lymphocytes for in vitro transfection studies of these cells. Clinical measures of response include regression of established tumor deposits and/or delay in time to disease progression.