

Elicitation of a Cellular Immune Response in Patients with Non-Small Cell Lung Cancer by Immunogenic Tumor Cell Vaccination

SCIENTIFIC ABSTRACT

Non-small cell lung cancer (NSCLC) that is advanced at presentation or recurrent after initial treatment is incurable, with a two-year survival of <5%, despite the administration of chemotherapy and/or radiation therapy. The intent of this protocol is to utilize NSCLC cells from a human Lung adenocarcinoma cell line that are transfected with the genes for B7.1 and either HLA-A1 or -A2 as an approach to enhance the likelihood of an immunologic response. These cells are radiated (to prevent proliferation) and administered by a series of intradermal injections given on three occasions two weeks apart to patients with NSCLC. The aim is for these tumor cells to stimulate the proliferation of a tumor-specific population of cytotoxic lymphocytes capable of destroying the unmanipulated lung cancer cells in the patient. 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 high copy number. In pre-clinical studies in a murine model using the Lewis lung carcinoma cell line, the administration of transfected cancer cells led to rejection of subsequently administered non-transfected tumor cells and to regression of established tumors. In this study in humans, after the completion of a course of therapy, intracutaneous immune reactions (delayed hypersensitivity type) to a panel of transfected and non-transfected cells will be evaluated. Companion laboratory studies will quantify and characterize the nature of the induced cytotoxic lymphocyte response in the patients' peripheral blood, to determine if is a non-specific allogeneic response to the foreign cell line or whether it is HLA-mediated in patients who have the matching HLA-A1 or -A2 tissue type. Regression of established tumor deposits will provide the measure of clinical response.