

Non-technical abstract

Small Cell Lung Cancer (SCLC) represents one fourth of the 150,000 lung cancers that occur each year in the United States. Despite a high initial sensitivity to chemotherapy, most of these cancers ultimately relapse. Once relapse has occurred, then the chance of responding to additional conventional chemotherapy is unusual. There has been increasing interest in recent years in developing immunologic approaches to malignancies, and there is some evidence that the growth of SCLC can be modulated by the host's immune system. One therapeutic approach that is being investigated by several groups is to induce expression of a molecule called B7-1 by the tumor cells to enhance the immunogenicity of tumors. Normally, this molecule is expressed by cells of the immune system that recognize foreign or abnormal antigens and "present" them to the T-lymphocytes. B7-1 is necessary for the activation of T-lymphocytes. If it is not present, the T-lymphocytes do not react to the antigen. It has been shown that in mice tolerant to a tumor, the implantation of tumor cells in which the B7-1 gene has been introduced can induce regression of the initial tumor. An additional characteristic of SCLC cells is that they do not express well tumor antigens on their surface. This defect can be restored by interferon gamma stimulation.

Patients enrolled on this protocol will be treated with a combination of interferon gamma in subcutaneous injections and their own tumor cells modified to express B7-1 which will function as a tumor vaccine. Specifically, tumor cells will be taken from the patient at diagnosis and adapted to in vitro culture. The patient will receive standard chemotherapy. The human B7-1 gene will then be introduced into the cultured tumor cells. When relapse occurs, or in case of partial remission not amenable to irradiation in patients with extensive disease, tumor cells will be treated with interferon gamma, irradiated and injected subcutaneously into the patients at 2 week intervals. Interferon gamma will then be given to the patients subcutaneously on the second week after vaccine injection. Clinical response will be assessed in a planned accrual of 30 patients, as well as the reaction of the lymphocytes to the tumor cells in the laboratory.