
LAY ABSTRACT

Cancerous tumors produce molecules that suppress the immune system. The immune suppression in cancer patients is mainly due to production of molecules known as Transforming Growth Factors-betas (TGF- β). Production of TGF- β by tumor cells paralyzes the immune cells that are responsible to defend the body against infections and abnormal cells that may be produced in the body. We have shown that injection of tumor cells which have been genetically engineered to reduce the production of TGF- β production makes these gene modified cells potent vaccines. Such vaccines can stimulate the patients' immune system to produce a response against the tumor. Activation of the immune system by the vaccine may cause the tumor to stop growing or perhaps regress. We have previously shown these effects in animal tumor models and in human clinical trials involving patients with brain tumors and non-small cell lung cancer. Thus, we propose to use this approach in a phase III clinical trial in patients with stages IIIA, IIIB or IV non-small cell lung cancer. Historically, the two and five year survivals for stage IIIB are 10.8 and 3.9 and for stage IV are 5.4 and 1.3 percent respectively.

In this Phase III clinical trial patients will be randomly assigned to one of two treatment groups. Patients assigned to one treatment group will receive standard chemotherapy for non-small cell lung cancer. This will consist of monthly treatment with the approved drug pemetrexed (Alimta®). Patients randomly assigned to the second treatment group will receive the unapproved cellular vaccine described above. This vaccine consists of four human non-small cell lung cancer cell lines that have been adapted for growth in the laboratory. In addition, these cells have been previously genetically modified in the laboratory to block their TGF- β secretion. The vaccine is produced at the clinical site by mixing together the four genetically modified cell lines; it is this mixture that is injected in the upper arm, similar to that of a flu vaccine. Patients assigned to the vaccine treatment group will be injected monthly for a total of 18 months, and then once each quarter for two quarters. Thus patients may receive up to a total of 20 vaccine injections.

Patients enrolled in either treatment group will be evaluated each month while they are receiving therapy. Patients that respond to therapy may receive additional injections to evaluate whether their response to therapy can be continued or improved. Finally, patients will be monitored periodically for 5 years following the end of their therapy.

Patients enrolled in either treatment group will be evaluated for survival, clinical response, and time to tumor progression. Patients will be monitored and evaluated according to standard evaluation criteria.

The results of this study may be used as the basis of an application to the US Food and Drug Administration seeking marketing authorization for the sale of the vaccine in the United States.