NON-TECHNICAL ABSTRACT

Patients bearing tumors of different histologic origin have elevated levels of Transforming Growth Factors-βs (TGF-βs). TGF-βs are growth factors that are associated with immunosuppression. Suppression of the patients' immune system results in their inability to recognize and destroy tumors when they first appear. Furthermore, suppression of patients' immunity makes them susceptible to frequent infections. We have shown that injection of genetically engineered tumor cells to block their TGF-β production makes the gene modified cells potent vaccines that are recognized by and that can activate the immune system against the tumor. Activation of the immune system subsequently causes the recognition and destruction of the parental, tumors in the patients body at various sites. We have shown this phenomenon to be true in animal tumor models and in human clinical trials. Survival of patients who received ≥ 2.5×10^7 cells in # IND 8868 (Figure 1D) was greater than patients who received lower dose vaccine. Moreover, comparison of survival to historical patients receiving Taxotere or Iressa demonstrates substantial improvement (Figure 10). However, it's difficult to determine which patients will be the most responsive to vaccination. Thus, we propose use of a recently FDA approved device which identified a certain marker contained on the surface of circulating cancer cells to measure cancer cells in the blood. We propose to study this in patients with advanced stage (IIIB/IV) NSCLC.

In this pilot clinical trial we will use the same four human non-small cell lung cancer cell lines that have been previously established in tissue culture laboratory as used in IND # 8868. We will gene modify these tumor cells in the laboratory to block their TGF-β secretion. We will inject the genetically engineered cells as vaccines in patients with stages IIIB/IV non-small cell lung cancer. Patients will be monthly for 16 months if deemed medically acceptable. Our rationale for using other people's tumor cells is that lung tumor cell lines belonging to different people have been shown to share common characteristics that are recognized by non-self immune systems.

Response, time to tumor progression, and tumor free survival will be monitored in patients and compared to levels of circulating cancer cells at baseline and over time during and after treatment. Patients will be monitored and evaluated according to standard evaluation criteria of no response, stable disease, partial response and complete response. The results of this study will be used to evaluate the feasibility of measuring circulating cancer cells in a subsequent phase III clinical trial with TGF-β antisense gene modified tumor cells.