

Scientific Abstract:

In the United States, approximately 30,000 people die of pancreatic cancer each year. Despite comprising only 2% of all new cancer diagnoses, pancreatic cancer is the 4th leading cause of cancer-related death in the United States. The disease is difficult to diagnose in its early stages, and 90% of patients have incurable disease at the time of presentation. The overall 5-year survival rate for patients with this disease is less than 5%, so mortality rates approach incidence rates.[1] The only treatment that offers any survival advantage is surgical resection. To date, no effective therapies exist for patients with inoperable disease.

We are proposing a phase II clinical trial that combines two novel therapies in patients with unresectable pancreatic cancer: TNFerade™ to induce apoptosis and autologous dendritic cells to induce an immunologic response. Individually, each therapy has been shown to affect the growth of pancreatic adenocarcinoma and improve clinical outcomes for patients with this disease. The combination of these therapies has never been proposed or executed in a clinical setting, but animal models have shown a therapeutic synergy that leads to tumor regression and protection against subsequent challenge with the same tumor type.[2]

The long-term and broad objectives of this project are to determine whether a lasting immune response can be induced in patients with pancreatic cancer using autologous dendritic cells pulsed with keyhole limpet hemocyanin after the induction of apoptosis in the primary tumor with TNFerade™ (an adenoviral vector coding for human tumor necrosis factor-alpha). The specific aims of this project are as follows: 1) to establish the feasibility and safety of intratumoral injections of activated dendritic cells combined with TNFerade™ in the treatment of locally advanced / metastatic pancreatic cancer; 2) to characterize the immunologic and anti-tumor effects of dendritic cells combined the TNFerade™ in patients with advanced pancreatic malignancy; and 3) to determine the effect of TNFerade™ on the local microenvironment after injection and activation of the vector. Patients with inoperable tumors will be enrolled to receive the treatment protocol. The tumors will be evaluated for the degree of apoptosis, and the systemic response to tumor associated antigens will be evaluated in each individual in the protocol.