

## **REQUEST FOR SINGLE PATIENT IND FOR COMPASSIONATE USE**

### **Single Patient IND Protocol: Pancreatic GVAX® for Resected Adenocarcinoma of the Pancreas**

#### **Scientific Abstract**

##### **BACKGROUND**

Cancer of the pancreas is the tenth leading cause of cancer in the United States with an estimated incidence of 29,500 new cases in 1999. It is also one of the most lethal malignancies and is currently the fifth leading cause of cancer death with an estimated number of deaths in 1999 similar to the incidence rate. The death rate in pancreatic cancer is exceeded only by lung, colorectal, breast, and prostate cancer. Despite recent advances in the overall understanding of pancreatic cancer at the molecular level, improved imaging techniques to identify disease at an earlier stage, improved surgical techniques as well, as a growing body of literature that supports the role of adjuvant therapy, the 1-year survival is still on the order of 20% with a median survival of 15 to 19 months for resectable disease and a 5-year survival of approximately 3% for all stages combined. Only one drug, Gemcitabine, is currently approved for this disease. This drug was approved by the FDA based on a significant improvement in quality of life only.

##### **Objectives**

To assess safety and overall survival in a patient treated with adjuvant chemotherapy and radiation therapy followed by an allogeneic pancreatic tumor vaccine.

##### **Patient Population**

Single patient with resected pancreatic cancer having received post-operative chemotherapy and radiation therapy.

##### **Study Design**

Single patient, treatment IND.

##### **Treatment Plan and Schedule**

Following surgical resection and adjuvant chemoradiotherapy, the patient will receive a pancreatic tumor vaccine consisting of two irradiated, allogeneic pancreatic tumor cell lines transfected with the GM-CSF gene.

The Patient will receive his first vaccination 4 weeks after chemotherapy and radiation therapy is complete. He will receive vaccinations every 3 weeks for a total of 6 vaccinations. He will then be followed for safety and progression of disease and enrolled in a long term follow-up study to assess the toxicity of gene therapy.

## **Dose**

The vaccine consists of equal numbers ( $2.5 \times 10^8$  each) of CG 2505 and CG 8020 cells combined into a single vaccination. The patient will receive 16 intradermal injections (0.5 ml/injection) with each vaccination. Vaccine will be administered every 3 weeks for a total of 6 vaccinations.

## **Safety Evaluation**

The patient will be followed for toxicity at treatment visits (every 3 weeks) and at a follow-up clinic visit (4 weeks after the last vaccination). Laboratory monitoring will consist of a complete blood count, liver function tests, creatinine and serum electrolytes at each treatment and follow-up visit. Additionally, a history and physical examination, assessment of vaccination sites, and query for adverse events will be conducted at each treatment and follow-up visit.

All adverse events will be captured from the time of initial vaccination until 4 weeks after the last vaccination. Serious adverse events related to the study drug and all deaths will be reported to Cell Genesys, Inc., the FDA, and the NIH. Treatment with Pancreatic GVAX<sup>®</sup> will stop if any grade 4 adverse events related to the study drug occur. Treatment will not be resumed if a grade 4 adverse event occurs. If a grade 3 adverse event related to the study drug occurs, treatment with Pancreatic GVAX<sup>®</sup> (CG 2505 and CG 8020) will be stopped. Treatment with Pancreatic GVAX<sup>®</sup> (CG 2505 and CG 8020) may be re-started if the grade 3 adverse event resolves to less than grade 2 within 3 weeks. Furthermore, if either of the other two ongoing studies of Pancreatic GVAX<sup>®</sup> is stopped due to toxicity concerns, treatment of the patient under this single patient IND will stop. The NCI Common Toxicity Criteria will be used for safety monitoring and reporting. At the end of the study the patient will be asked to enroll in a long-term follow-up protocol for patients treated on gene therapy protocols.

The toxicity data collected will be descriptive, characterized according to the National Cancer Institute Common Toxicity Criteria. Safety parameters will include physical examination, hematology, and serum chemistry.

## **Product**

Two allogeneic cell lines have been developed from neoplastic tissue harvested from the surgical specimens of patients undergoing pancreaticoduodenectomy at The Johns Hopkins Hospital. These cell lines have been characterized as 100% epithelial by cytokeratin staining (Jaffe et al, Human Gene Therapy 1998;9: 1951–1971). In addition, these cell lines carry the same *k-ras* mutation as the original tumor specimen, which supports the conclusion that these lines are derived from malignant pancreatic tumor cells. The cell lines CG 2505 and CG 8020 were chosen because they contain the most common *k-ras* mutation at codon 12 found in greater than 90% of pancreatic cancer. CG 2505 and CG 8020 were genetically modified to secrete GM-CSF by plasmid DNA transfection (Jaffe et al, Human Gene Therapy 1998;9:1951–1971; Jaffee et al, Cancer J Sci Am 1998;4(3):194–203).