
**Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Committee Meeting
September 2010**

Protocol Number: **530**

Protocol Title: **A Randomized, Phase II/III Study of TNFerade™ Biologic with 5-FU and Radiation Therapy for First-Line Treatment of Unresectable Locally Advanced Pancreatic Cancer.**

DocID#	Receipt Date	Event Description
10792	05/04/2010	Two months after receiving the last dose of the study agent, the subject was seen in the office with complaints of leg swelling, weakness and pain. An ultrasound of the legs was ordered and clots were present in both legs. The subject was admitted to the hospital and started on a blood thinner. The subject subsequently had an inferior vena cava filter placed to prevent clots from entering the lungs. Two days after admission, the event was considered resolved.
10846	05/27/2010	Three days after receiving the first dose of the study agent, the subject developed abnormal liver blood tests and abdominal pain and subsequently underwent an endoscopic retrograde cholangiopancreatography, a procedure that combines endoscopy and fluoroscopy to diagnose and treat certain problems of the biliary or pancreatic ductal systems. A possibly malignant stricture was noted in the bile duct, but was not biopsied. The subject underwent dilation of the stricture with placement of a stent. The subject recovered and the event was considered resolved three days after the procedure.

Protocol Number: **552**

Protocol Title: **A Phase I/II Study of An Antitumor Vaccination using $\alpha(1, 3)$ Galactosyltransferase Expressing Allogeneic Tumor Cells in Patients with Refractory or Recurrent Non-Small Cell Lung Cancer.**

DocID#	Receipt Date	Event Description
10810	05/19/2010	After receiving the first dose of the study agent, the subject reported experiencing intermittent headaches in the evening, located in the back of the head. After one episode of a headache associated with nausea, the subject took narcotic pain medication and the headache resolved. The subject subsequently received the second dose of the vaccine without problems.

Protocol Number: **741**

Protocol Title: **A Phase 2 Double-Blind, Placebo Controlled, Multi-center Adjuvant Trial of the Efficacy, Immunogenicity, and Safety of GI-4000; an Inactivated Recombinant Saccharomyces cerevisiae Expressing Mutant Ras Protein Combined with a Gemcitabine Regimen Versus a Gemcitabine Regimen with Placebo, in Patients with Post-resection R0/R1 Pancreatic Cancer with Tumor Sequence Confirmation of Ras Mutations.**

DocID#	Receipt Date	Event Description
10911	07/14/2010	The subject had completed cycle one of study agent. Subject had been receiving the study agent for approximately one and a half months. Approximately six days after last dose of study agent, the subject developed chest pain and presented to the Emergency Room and was admitted for extensive bilateral pulmonary embolism. The study is blinded so it was unknown if subject received the gene transfer or placebo. Subject had an inferior vena cava filter placed and was started on a blood thinning medication. The subject remained in the hospital for one week, then transferred to a nursing home for two weeks prior to being discharged home. The event was considered expected, but life threatening and possibly related to study therapy. Blinded study therapy was interrupted as a result of this event. The subject requested to be removed from the study, but continued adjuvant gemcitabine therapy off study.

Protocol Number: **866**

Protocol Title: **A Phase II-a, Open-Label, Randomized Study of JX-594 (Thymidine Kinase-deleted Vaccinia Virus plus GM-CSF) Administered by Intratumoral Injection in Patients with Unresectable Primary Hepatocellular Carcinoma**

DocID#	Receipt Date	Event Description
10806	05/17/2010	Following administration of the blinded study agent (i.e. gene transfer or placebo), the subject was hospitalized for nausea and vomiting. The subject was discharged two days after receiving treatment for this event.

Protocol Number: 947

Protocol Title: **A Randomized Phase 3 Clinical Trial to Evaluate the Efficacy and Safety of a Treatment with OncoVEXGM-CSF Compared to Subcutaneously Administered GM-CSF in Melanoma Patients with Unresectable Stage IIIb, IIIc and IV Disease**

DocID#	Receipt Date	Event Description
10884	07/12/2010	Three weeks after receiving the fourth dose of the study agent, the subject was admitted to the hospital for a surgical consultation due to gastrointestinal bleeding. A metastatic melanoma was found in the colon and removed.
10882	07/08/2010	Two weeks after the second dose of the study agent the subject developed shortness of breath and severe throat pain. A computed tomography scan revealed a new soft tissue mass at the piriform sinus level. Biopsies performed during the work-up only revealed inflammatory tissue, not malignancy. A review of the images done over several weeks indicated that this was an inflammatory lesion of unclear etiology. It is possible the gene transfer contributed to this unusual inflammatory process.
10972	08/18/2010	Subject admitted to hospital with fever, swelling and redness of the leg. Diagnosis was metastatic melanoma lesion with overlying cellulitis. Subject had received injection into that area of the leg.

Protocol Number: 949

Protocol Title: **Treatment of Patients with Metastatic Renal Cancer with T-cells Transduced with a T Cell Receptor which recognizes TRAIL Bound to the DR4 Receptor**

DocID#	Receipt Date	Event Description
10885	07/13/2010	Subject developed respiratory distress and low blood sodium levels four days after receiving the gene modified T cells and three doses of interleukin 2 (IL-2). Due to worsening respiratory status and fatigue, this subject was electively intubated with a breathing tube. Blood cultures revealed three different bacteria in the blood and subject was started on broad spectrum antibiotics. After these interventions the subject was considered stable but remained intubated until further resolution of this possible IL-2 or gene modified T cell toxicity, bacteremia and moderate acute respiratory distress syndrome.

Protocol Number: 951

Protocol Title: **An open label phase I study to evaluate the safety and tolerability of a vaccine consisting of whole, heat-killed recombinant Saccharomyces cerevisiae (yeast) genetically modified to express CEA protein in adults with metastatic CEA-expressing carcinoma**

DocID#	Receipt Date	Event Description
10790	04/30/2010	Three days after receiving a dose of the study agent, the subject was admitted with a fever, increased white blood cell count, increased heart rate, cough and pain over the right side of the chest with inspiration. A chest x-ray revealed a pneumonia and the subject was started on antibiotics. Cultures of blood were negative for any bacteria. The subject was discharged two days after being admitted and was to continue antibiotics and follow-up with their oncologist.

Protocol Number: **1004**

Protocol Title: **An Open Label Dose Escalation Study to Evaluate the Safety of a Single Escalating Dose of ACRX-100 Administered by Endomyocardial Injection to Cohorts of Adults with Ischemic Heart Failure**

DocID#	Receipt Date	Event Description
10885	07/13/2010	Two weeks after receiving the study agent, the subject was hospitalized for body aches, cough, sinus congestion, difficulty walking and neck pain and stiffness. A cardiac work-up was negative and a chest x-ray was normal. Blood and urine cultures were all negative. However, laboratory markers of inflammation were elevated and the subject was treated empirically with doxycycline. A computed tomography scan of the sinuses revealed mild sinus disease. Further work-up revealed an elevated blood anti-nuclear antibody (ANA) and double-stranded anti-DNA antibodies. A diagnosis of systemic lupus erythematosus was made.

Protocol Number: **1029**

Protocol Title: **A Phase II Study of Repeat Intranodal Injections of Adenovirus-CD154 (Ad-ISF35) in Subjects with Non-Hodgkins Lymphoma (Follicular, Diffuse Large Cell, Mantle Cell and Small lymphocytic Lymphoma/Chronic Lymphocytic Leukemia)**

DocID#	Receipt Date	Event Description
10851	06/08/2010	After receiving the third injection, the subject complained of muscle pain, weakness and a fever. The subject was admitted to the hospital for intravenous fluids and observation. The subject recovered and was discharged the next day.
