
**Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Committee Meeting
June 2009**

Protocol Number: 513

Protocol Title: Phase I Study of Intravenous DOTAP:Cholesterol-Fus 1 Liposome Complex (DOTAP:Chol-Fus 1) in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) Previously Treated with Chemotherapy.

DocID#	Receipt Date	Event Description
10188	02/02/2009	The subject developed fever and chills approximately 10 hours after study agent infusion and presented to the Emergency Room. The subject was treated with fluids, acetaminophen and antibiotics and was discharged from the emergency room the following morning.
10316	04/15/2009	The day after receiving the second dose of the study agent, the subject went to the emergency room for fever and was treated with antibiotics. While in the emergency room, the subject also developed some bleeding from the mouth. An evaluation was done by placing a tube with a video through the mouth to visualize the airways. A tumor was seen in the right airway with some bleeding that stopped with the administration of medication. The subject was sent home to return for another evaluation in a month. At that time, the tumor in the right airway was removed and a stent was placed in the airway to keep it open. Palliative radiation therapy to the chest was recommended to help with the continuing cough. The investigator thought the event was possibly related to the study agent. The subject is now off study.

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
10272	03/06/2009	The subject was admitted with trouble swallowing and weakness about two weeks after the last dose of the study agent. A swallow study found abnormal motion that was leading to some food going into the lungs. During this same admission the subject was diagnosed with an infection in the blood that was thought to be from the gallbladder. The subject was also found to have abnormalities on a chest x-ray that indicated possible infection. The subject was treated with antibiotics. The investigator felt that both events could possibly be related to the study agent.
10187	01/30/2009	Six days after the last study agent injection, the subject presented to the emergency room with a fever accompanied by chills and was hospitalized for evaluation and treatment. The subject was discovered to have an infection after blood cultures indicated bacteria in the blood and was treated with antibiotics. The subject was also found to have a low white blood cell count and a low red blood cell count. The subject received a blood transfusion. Administration of the study agent was interrupted.
10173	01/21/2009	The subject was hospitalized two days after the administration of the study agent due to a fever which occurred following an endoscopic retrograde cholangiopancreatogram, a technique used to diagnose and treat certain problems of the biliary or pancreatic ductal systems and used for biliary stent replacement for biliary stent occlusion. The subject recovered and the event was considered resolved. The subject continued on the study.
10177	01/27/2009	The subject presented with a one day history of abdominal pain, cough and nausea without a fever. The subject underwent a computed tomography scan which revealed bilateral blood clots in the lungs and bilateral blood clots in the extremities.
10179	01/29/2009	Approximately four and a half hours after the fourth injection of the study agent, the subject was hospitalized for chills, fever of 101 degrees Fahrenheit and malaise. While in the hospital, the subject was also noted to have a low white blood cell count. A source of infection was not found and the subject recovered. The event was considered resolved. The principal investigator concluded that the event was possibly related to the gene transfer.
10196	02/05/2009	The subject presented with shortness of breath. Vital signs demonstrated a rapid heart rate and low blood pressure. Pulse oximetry (which measures blood oxygen levels) was normal when lying down and would decrease upon standing. The initial assessment was to rule out blood clots in the lungs. The subject was seen in the emergency room for this work-up. The computed tomography (CT) scan was negative for blood clots, but demonstrated hypo-dense liver lesions that were possibly related to pancreatitis or abscess. Metastasis was thought to be unlikely because the lesions were not present on a CT less than one month ago. Hepatic abscess was considered, but aspiration of fluid collection is pending. The subject has not yet recovered and the event is considered ongoing. No action was taken with TNFerade.
10261	03/17/2009	The subject was admitted for intractable nausea and vomiting two months after the last dose of the gene transfer agent. The subject had history of admissions for nausea and vomiting and had a stent placed for obstruction in the duodenum. After further imaging and inspection, it was determined that a duodenal stent was occluded and that this was causing the subject to have nausea and vomiting. Duodenal obstruction was successfully cleared. The subject was started on supplemental feedings.

10242	03/12/2009	The subject experienced nausea, vomiting and dehydration secondary to a gastric outlet obstruction. The subject was hospitalized approximately two months after the last dose of the gene transfer vector. The event resolved after one day with appropriate treatment and the subject was discharged.
10243	03/12/2009	Since starting on the study, the subject has had progressive weight loss and anorexia resulting in the placement of a feeding tube. These symptoms are likely related to the underlying disease but could possibly be related to the gene transfer. The subject completed five doses of the gene transfer.
10320	04/16/2009	One day after the first dose of the gene transfer agent was given, the subject presented to the clinic with a fever and was admitted for further evaluation. The subject complained of chills, sweats, nausea and vomiting that started at the same time as the fever. The subject also complained of abdominal pain that started before taking the study agent. The subject was noted to have an elevation in liver enzymes that decreased by the time of discharge. Pain medications were adjusted during the admission. The subject recovered and fever, sweats and chills resolved. The subject was discharged home.
10348	04/29/2009	On the day the subject received the fourth dose of the study agent, the subject was admitted to the hospital for nausea, vomiting and dehydration, which the subject had experienced throughout receiving the study agent. The subject reported a 30 pound weight loss. The subject also reported abdominal and back pain, as well as intermittent dizziness. On admission, the subject was noted to have abnormally low numbers of red blood cells as well as platelets. The subject was treated with fluids and a blood transfusion. The event resolved and the subject was discharged. Administration of the study agent was interrupted. The investigator and sponsor stated that the event was possibly related to study agent.

Protocol Number: **661**

Protocol Title: **A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Dose-Selection Study of Ad2/Hypoxia Inducible Factor (HIF)-1 α /VP16 in Patients with Intermittent Claudication.**

DocID#	Receipt Date	Event Description
10308	04/08/2009	The subject was noted to have a lesion on the back one year after receiving the blinded study agent (placebo or active agent). The lesion was completely removed and the biopsy revealed melanoma, a skin cancer.

Protocol Number: **750**

Protocol Title: **A Phase I/II Safety, Tolerability, and "Proof of Concept" Study of TNFerade™ in Combination with Concomitant Radiotherapy, Fluorouracil, and Hydroxyurea (TNF-FHX) for Patients with Unresectable Recurrent Head and Neck Cancer.**

DocID#	Receipt Date	Event Description
10318	04/16/2009	Eleven days after receiving the study agent and chemotherapy, the subject was admitted for bleeding from the tongue and fever. Laboratory tests showed a low neutrophil count, cells that fight infection. The subject was treated with antibiotics, a medication to raise the white blood cells and pain medications. Chemotherapy was withheld. Administration of the study agent was interrupted. The Investigator and Sponsor judged the event as possibly related to the study agent.

Protocol Number: 829

Protocol Title: **A Phase II Study of HyperAcute Pancreatic Cancer Vaccine in Combination with Chemotherapy and Chemoradiotherapy in Subjects with Surgically Resected Pancreatic Cancer**

DocID#	Receipt Date	Event Description
10146	01/07/2009	The subject received the first set of six intradermal vaccine injections. The area was numbed with ice prior to injections. The subject received two injections in the right forearm, two in the left forearm and one in each thigh. After receiving the injections, the subject complained of severe pain in the left forearm. The subject was unable to use or move the arm and took several doses of extra strength Tylenol. The pain lessened by the evening and the subject was able to use both arms to perform activities of daily living.
10191	02/03/2009	The subject presented to the emergency room with nausea and vomiting two days after receiving the 8th dose of the study agent. The subject had two episodes of vomiting, was unable to eat any solid food and rated nausea as severe. The subject was treated with intravenous fluids and medications to control the nausea.
10295	04/03/2009	Two days after vaccine dosing, the subject was admitted to the hospital with stomach pain, nausea and vomiting. Blood tests revealed possible inflammation of the pancreas. The subject was admitted and recovered.

Protocol Number: 853

Protocol Title: **A Phase 1, Open-Label, Dose-Escalation, Multiple Dose Study of the Safety, Tolerability, and Immune Response of CRS-207 in Adult Subjects with Selected Solid Tumors Who Have Failed or Who Are Not Candidates for Standard Treatment**

DocID#	Receipt Date	Event Description
10236	10/31/2008	The subject developed a fever of 104 degrees Farenheit approximately 22 hours after receiving the first infusion of the study agent. The subject was treated with acetaminophen and temperature returned to baseline within 24 hours after infusion.
10238	10/31/2008	The subject had a significant drop in the white blood cell count (lymphocytes) within 24 hours of the first dose of the study agent. The subject's blood counts recovered to baseline within 4 days.

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
10266	10/01/2008	This event occurred on a trial outside the United States. The subject experienced a rise in serum bilirubin eight days after dosing. There were no associated symptoms but the event was felt to be related to tumor swelling after study agent administration. This was considered a dose-limiting toxicity.

Protocol Number: **939**

Protocol Title: **Phase II Study of Metastatic Melanoma Using a Chemoradiation Lymphodepleting Conditioning Regimen Followed by Infusion of Anti-Mart-1 and Anti-gp100 TCR-Gene Engineered Lymphocytes and Peptide Vaccines**

DocID#	Receipt Date	Event Description
10223	02/27/2009	The subject received the cells and began interleukin 2 treatment. The subject developed renal failure, a rash and somnolence requiring a tube through the mouth to assist with breathing and dialysis. These are known toxicities of interleukin 2. The rash was felt to be a possible expected reaction to the study agent, which targets melanocytes, cells in the skin. Dialysis was discontinued and the subject's breathing tube was removed. The whole body rash nearly resolved. The subject was found to have a moderate eye and a severe hearing impairment which are known toxicities of this therapy and are now being treated and monitored.

Protocol Number: **943**

Protocol Title: **A Pilot and Feasibility Trial of Repeated Dose Intrapleural Adenoviral-Mediated Interferon-alpha (Ad.hIFN- α 2b) Gene Transfer for Malignant Mesothelioma**

DocID#	Receipt Date	Event Description
10297	04/06/2009	Three days after receiving the second dose of study agent, subject presented to the local emergency room with weakness, low blood pressure and trouble speaking. The subject was given fluids intravenously and his condition improved. The subject was admitted to the hospital and discharged after two days.
