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

Protocol Number: **359**

Protocol Title: **Phase I Trial of Adenoviral Vector Delivery of the Human Interleukin-12 cDNA by Intratumoral Injection in Patients with Primary or Metastatic Colorectal Cancer to the Liver.**

DocID#	Receipt Date	Event Description
10596	11/06/2009	Following injection of the study agent into a liver metastasis, the subject was found on laboratory testing to have increased values of liver enzymes. The subject was asymptomatic with no complaints of abdominal pain or nausea. Four days after the study agent was given, the lab values normalized. An ultrasound and CT scan of the abdomen showed no liver abnormalities.

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
10577	10/16/2009	The subject received only one dose of study agent. That same day, the subject came to the emergency room with complaints of fever and chills. In the emergency room, the subject was noted to have low blood phosphorous levels and was treated. The subject was discharged the following day in stable condition.

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
10637	12/24/2009	Three weeks after the last dose of the study agent, the subject was noted to have bilateral leg swelling and blisters. The subject was treated with medications that help remove fluid. There no evidence of a deep vein thrombosis.
10630	12/23/2009	The subject expired due to a gastrointestinal bleed approximately five months after study agent administration.
10634	12/24/2009	The subject was readmitted with bilateral lower extremity edema. The subject experienced difficulty walking. The subject was discharged two days later and the event was considered resolved.

Protocol Number: **552**

Protocol Title: **A Phase I/III 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
10598	11/12/2009	The subject was seen two days post vaccine administration. The skin reaction over the vaccine site on the left forearm was minimal. The subject returned home and a week after vaccine administration, informed the investigators that the left forearm was red and swollen at the vaccine site and that the site was tender and painful. The subject denied any drainage from the wound. One day later, the subject reported that pus was draining from the vaccine site. The subject went to the local oncologist where a wound culture was done and the subject was prescribed antibiotics. Two days later, the subject notified the investigators that the site was draining and was very painful. The subject informed the investigators of the decision to return for further evaluation. The subject was told to come to the hospital on arrival for evaluation. The wound over the left arm was a 1 cm area of crusted ulcer with redness and small amount of drainage. A 4 to 5 cm area surrounding the ulcer was hard and tender. Wound cultures and a gram stain were done and the dressing was re-applied. Gram stain showed gram-positive cocci in clusters. The culture is pending at this time. The subject is without fever and reports that the wound is improving and not as painful. Culture results from the local MD were negative. The grade 3 injection site reaction/infection/ulceration is an expected adverse event and mentioned in the protocol consent. The subject received vaccination with the same vaccine lots as the 10 prior subjects dosed on this study and no similar reaction was seen, suggesting that this is NOT a microbial contamination issue with the vaccine. This vaccine lot had passed all safety and sterility certifications at the manufacturer at the time of release. It is suspected this adverse event was a skin infection that occurred at the time of vaccine injection and is unlikely to be a reaction to the vaccine gene therapy product.

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
10592	11/02/2009	The subject had been reporting persistent diarrhea and was initially treated with fluids and blood pressure medications were held. The subject subsequently presented with a rapid heart rate in the 150s and was restarted on a medication known as a beta blocker that slows the heart rate. The subject also underwent a cardioversion, a procedure to normalize the heart rhythm. The subject's heart rate then stabilized in the 80s. Stool studies looking for infection were all negative. Because of low red blood cell counts, the subject also received a blood transfusion. Five days after admission, the subject was in stable condition and discharged.

Protocol Number: 863

Protocol Title: **A Pilot Study To Evaluate the Safety and Feasibility of Cellular Immunotherapy Using Genetically Modified Autologous CD20-Specific T cells for Patients with Relapsed or Refractory Mantle Cell and Indolent B Cell Lymphomas**

DocID#	Receipt Date	Event Description
10641	12/21/2009	Following the second infusion of T cells, the subject experienced some mild shivering at the end of the two hour observation period. The subject subsequently received a platelet transfusion for a known low platelet count following cyclophosphamide. An hour after the platelet transfusion was completed, the subject developed a fever and was given tylenol. An hour later, the fever had resolved, although the subject was noted to have a blood pressure that was lower than the baseline and a heart rate that was slightly increased. On standing, the subject's blood pressure dropped further and the heart rate increased as well. The subject was admitted to the hospital for administration of intravenous fluids. Blood cultures were drawn and the subject was started on empiric antibiotics. The subject was discharged the following day. This event was assessed as probably related to the study agent.
10642	12/21/2009	The subject completed the third infusion of T cells without incident, but developed mild chills at the end of the two hour observation period. The subject went on to receive the first dose of low dose IL-2. A chest x-ray was done which showed no acute process. A few hours later, the subject developed a fever and had a drop in the oxygen saturation. The subject was given tylenol and supplemental oxygen therapy. The fever resolved. The subject was admitted for observation to ensure availability of care if required. A repeat chest x-ray showed no abnormality. The subject's oxygen saturation improved as well. The second dose of low dose IL-2 was administered the following morning without incident and the subject was discharged later that same afternoon. The event was considered possibly related to the T cell infusion and possibly related to IL-2.

Protocol Number: 925

Protocol Title: Phase I/II Study of Metastatic Cancer that Expresses Carcinoembryonic Antigen (CEA) Using Lymphodepleting Conditioning Followed by Infusion of Anti-CEA TCR-Gene Engineered Lymphocytes

DocID#	Receipt Date	Event Description
10606	11/17/2009	One week after receiving chemotherapy, the subject received cells followed by eleven doses of IL-2, stopping for fatigue. One day after discontinuing IL-2, the subject reported increased frequency of diarrhea ranging from seven to nine bowel movements over a 24 hour period with associated cramping. The subject continued to have 15-24 bowel movements per day over the next 72-96 hours. Flexible sigmoidoscopy revealed mild to moderate inflammation of the colon. This grade 3 event is considered related to the study agent and meets dose limiting toxicity criteria per protocol. The subject is recovering.

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
10597	11/09/2009	<p>The subject was seen by the physician with complaints of fever and increased redness in his left upper arm. Antibiotics was initiated for the presumed skin infection. Six days later, the subject was transported to the emergency room as a marked decrease in the level of alertness was noted. The subject had not been using the prescribed CPAP machine for sleep apnea and was recently switched to oxycodone and morphine due to increased pain from a clot in the left shoulder. On examination in the ER, the subject was noted to have an increased heart rate, decreased breath sounds throughout both lung fields and ulceration, swelling and redness over the left upper arm. On neurological exam, the subject was aware of name only. Laboratory analysis indicated dehydration. Chest x-ray demonstrated a possible pneumonia in the left lower lung compared to a previous exam. A CT scan of the head was negative for any abnormality. A dose of vancomycin was administered. The subject was admitted to the hospital with a skin infection and altered mental status. Planned treatment included continued monitoring of neurological status with pain control and further antibiotic coverage. The dose of morphine for pain control was decreased. This was successful in increasing the subject's level of alertness. Two sets of blood cultures were positive for coagulase negative staphylococcus, sensitive to gentamicin, levofloxacin and vancomycin. Ancef was changed to vancomycin as subject spiked a fever. The subject was discharged home with home health care. Following discharge, the subject was contacted in follow-up by the oncology clinic. Per the research nurse, the subject's conversation was difficult to follow. The subject confirmed continuing taking oxycodone but was not sure of the quantity. The subject reported requiring assistance for activities of daily living due to pain and swelling in the left arm. Intravenous antibiotics were to continue for an additional seven days.</p> <p>The Investigator considered the causal relationship of the adverse event of cellulitis to study medication as possibly related and the causal relationship of the event of somnolence to study medication as unrelated, but rather due to the subject's concomitant narcotic medications. The Sponsor considered the causal relationship of cellulitis and somnolence to study medication as not related.</p>

Protocol Number: 952

Protocol Title: Phase Ib Study of Autologous Ad-ISF35-Transduced CLL B Cells and Fludarabine, Cyclophosphamide, and Rituximab (FCR) in Subjects with Fludarabine-Refractory and/or del(17p) Chronic Lymphocytic Leukemia (CLL)

DocID#	Receipt Date	Event Description
10635	12/28/2009	The subject tolerated the gene transfer well, but later the same day, experienced fever and chills, for which tylenol and compazine were given. The subject was evaluated at the day 2 follow-up visit and was noted to have low blood pressure and complaints of dizziness, increased shortness of breath and a brief episode of questionable loss of consciousness lasting less than one minute. Of note, the subject took blood pressure medications in the morning prior to evaluation at the infusion center. The subject was taken to the emergency department and was given intravenous hydration and admitted to the hospital for observation. Overnight, the subject's blood pressure normalized. Blood cultures were negative after 24 hours and the fever resolved.
10654	01/13/2010	After receiving the second dose of study agent, the subject developed fevers, chills and vomiting which were treated with tylenol and compazine. The night after the second infusion, the subject developed low blood pressure, increased heart rate, dizziness and shortness of breath. The subject was given intravenous fluids and blood pressure medications were held. Due to dehydration, the subject's kidney tests were slightly abnormal but normalized after the fluids. The subject's red blood cells were also noted to be low and the subject was transfused two units of packed red blood cells. Liver function tests were slightly abnormal but returned to baseline. All cultures were negative and the subject remained without a fever for 48 hours and was discharged to home.