

**Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
NIH Office of Biotechnology Activities
June 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 |
|--------|--------------|---|
| 10695 | 02/19/2010 | Approximately six weeks after the last dose of the study agent, this subject experienced an episode of dizziness and one episode of dark stool with blood. The subject had recently been discharged for a similar complaint several days earlier. During the previous admission, a Mallory Weiss tear (an ulcer at the gastroesophageal junction) was noted. The subject again presented to the emergency room where low red blood cell counts and low platelets (cells that help blood to clot) were noted. The subject was admitted to the intensive care unit. The subject had a nuclear medicine scan which was unable to pinpoint active bleeding. The subject continued to have episodes of dark stool. During the hospital course, the subject was then noted to have bright red blood coming out from the nasogastric tube that was in the stomach. The subject was taken emergently to interventional radiology where a hepatic (liver) artery aneurysm (typically a bulge in a blood vessel where the wall is weakened and may rupture) was identified. At the time of this report, the subject remained in the intensive care unit and required medications to support blood pressure and mechanical ventilation (a breathing tube). |
| 10699 | 02/24/2010 | Shortly after receiving the third dose of the study agent, the subject was hospitalized for a fever, chills and low blood pressure. Blood cultures did not reveal any bacteria in the blood. Because the subject had lower than normal white blood cells (cells that fight infection), the subject was given a medication to increase the number of these cells, started on antibiotics and intravenous fluids. The next day, the subject's fever resolved and the subject was discharged. |
| 10725 | 03/18/2010 | The subject was in the hospital for the third TNFerade injection. The subject was kept in the hospital overnight for observation due to severe chills that evening. The subject had a fever which decreased with Tylenol. Systolic blood pressure dropped to below 100 mm/hg. The subject received antibiotics and fluids. The chills were thought to be a likely side effect of the 5-Fluorouracil chemotherapy. The subject was discharged the next day. The subject recovered and the event was considered resolved. |
| 10729 | 03/25/2010 | Seven months after the last dose of the study medication, the subject presented with a blood clot in a vein in the right leg. Subject was given anticoagulation medication. Three days after admission, the subject was discharged home with hospice follow-up due to progression of the cancer. |
| 10767 | 04/12/2010 | This subject had multiple previous admissions for a gastrointestinal bleed and a recent embolization (a procedure to selectively occlude a blood vessel) of the bleeding source. More than three months after receiving the last dose of the study agent, the subject was readmitted with a gastrointestinal bleed. The subject was transfused red blood cells. A scan was done to locate the bleeding point and indicated that there was an ulceration near the prior site of embolization and that this may have been caused by the previous procedure. The subject's vital signs and clinical condition stabilized, but unexpectedly the subject's clinical condition deteriorated, with a drop in the blood pressure and oxygen levels in the blood. The subject was treated with intravenous fluids and medications to support the blood pressure. The subject had indicated that he did not want cardio-pulmonary resuscitation or mechanical ventilation and died two days after being admitted to the hospital. |
| 10766 | 04/13/2010 | The day following receipt of the study agent, the subject complained of nausea and was treated with appropriate medications. Radiographic imaging did not show an abnormality to explain the subject's symptoms. |

| | | |
|-------|------------|---|
| 10768 | 04/15/2010 | Six days after completing the last dose of the study agent, the subject was admitted to the hospital with complaints of nausea, vomiting and abdominal pain. Three days after admission, the subject recovered and the event was considered resolved. |
| 10769 | 04/15/2010 | Approximately four days after the administration of the second dose of the study agent, the subject was admitted to the hospital for nausea, vomiting, abdominal pain, constipation and dehydration. The subject was given medicines for control of these symptoms. Three days after admission, the event was considered resolved. Administration of the study agent was not stopped. |
| 10770 | 04/15/2010 | Approximately one week after the second dose of study agent, the subject was hospitalized for generalized weakness and dehydration. The subject was given anti-nausea medication and a liquid diet. The subject has recovered and the event was considered resolved. The study agent will be continued. |

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 |
|--------|--------------|---|
| 10751 | 03/30/2010 | The day after receiving the second dose of the study agent, the subject returned to the hospital complaining of swelling, redness and increased warmth over the area of vaccine administration. The subject was treated with Benadryl, Tylenol and levofloxacin and discharged. Two days later the subject was called and reported improvement in the symptoms. |

Protocol Number: **585**

Protocol Title: **A Phase I Study of Sequential Vaccinations with Fowlpox-CEA(6D)-TRICOM (B7.1/ICAM/LFA3) and Vaccinia-CEA(6D)-TRICOM, in Combination with GM-CSF and Interferon-Alpha-2B in Patients with CEA Expressing Carcinomas.**

| DocID# | Receipt Date | Event Description |
|--------|--------------|--|
| 10714 | 02/01/2010 | The subject received the first dose of the study agent followed by interferon alpha-2B. After the last dose of interferon, the subject complained of flu-like symptoms, fatigue and nausea. Subject was subsequently admitted to an outside hospital with complaints of abdominal pain and confusion. Subject was diagnosed with posterior reversible encephalopathic syndrome, a syndrome characterized by headache, and confusion often secondary to uncontrolled hypertension. The subject was not previously on anti-hypertensives but was noted to have high blood pressures during the hospital course. With treatment, subject improved and was discharged. |

Protocol Number: **591**

Protocol Title: **An Open-Label Safety Study of Escalating Doses of SGT-53 for Systemic Injection in Patients with Advanced Solid Tumor Malignancies.**

| DocID# | Receipt Date | Event Description |
|--------|--------------|---|
| 10684 | 02/04/2010 | This subject, with squamous cell carcinoma of the vagina with metastases to the liver and lungs, received the fifth dose of the study agent and two hours later developed a fever to 102 degrees Fahrenheit and chills along with an increased heart rate and chest discomfort. The subject's electrocardiogram did not show changes indicating reduced blood flow to the heart (myocardial ischemia) or possible heart attack. However, due to continuing chest discomfort, the subject was sent to the emergency room and admitted to the hospital for observation. The subject's blood tests were normal and the chest discomfort resolved without any intervention. The subject was discharged. Due to progressive disease, the subject was removed from the study. At the time of this report the Data Safety Monitoring Board was reviewing this event and enrollment into the same dose level was on hold. |

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 |
|--------|--------------|---|
| 10657 | 01/19/2010 | The subject presented to the emergency department with facial and right upper extremity swelling. The subject had normal temperature and blood pressure. The subject was admitted to the hospital and had a computed tomography (CAT) scan of his chest, which confirmed a clot in a vein in the right shoulder. The subject was discharged with a prescription for Lovenox. The subject has recovered and the event is considered to be resolved. No action was taken with the study agent. |
| 10660 | 01/21/2010 | Approximately one month after the last study agent administration, the subject presented to a local hospital's emergency department with complaints of right upper extremity swelling that had been present for one day. The subject was admitted to the hospital and had an x-ray of the lower jaw. The subject had recently had a resection of the angle of the left lower jaw with a side plate and screw device affixing a bone graft. The subject had a computed tomography (CAT) scan of his chest, which revealed a occlusion of a vein. There were also lung nodules that appeared to be metastases, bilateral moderate lung fluid collections, fluid in the abdomen, and wall thickening of the colon and stomach. The subject had a sample taken from the jaw area which showed bacteria. The subject was treated with anticoagulants (medications to prevent blood from clotting) and antibiotics. The subject has recovered and the event is considered to be resolved. |
| 10680 | 02/03/2010 | About one month after the last dose of the study agent, the subject had a scheduled CAT scan of the head and neck that demonstrated interval development of a clot in the left distal transverse and sigmoid sinuses (areas that drain blood into the internal jugular vein). Since the thrombus was an incidental finding, the date of onset is unknown. The subject had previously been on anticoagulant medication for right internal jugular and right subclavian thrombus. The subject has recovered and the event is considered to be resolved. |

Protocol Number: 798

Protocol Title: **A Phase I/II Study of Active Immunotherapy with GRNVAC1, Autologous Mature Dendritic Cells Transformed with mRNA Encoding Human Telomerase Reverse Transcriptase (hTERT), in Patients with Acute Myelogenous Leukemia (AML) in Complete Clinical Remission**

| DocID# | Receipt Date | Event Description |
|--------|--------------|--|
| 10726 | 03/24/2010 | The subject was treated for a low platelet count with immunoglobulin (a blood product consisting of pooled antibodies from multiple donors) and steroids. The subject was discharged two days after being admitted as the platelet count increased after these treatments. |

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 |
|--------|--------------|---|
| 10749 | 03/29/2010 | Five days after receiving the study agent, the subject was admitted for increased serum bilirubin levels, a substance produced when the liver breaks down old red blood cells. The subject did not receive any treatment for this and levels improved the next day, when the subject was discharged on an antibiotic. It was thought that post treatment swelling of the tumor could have blocked a duct which clears bilirubin and, therefore, led to increased levels in the blood. |

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 |
|--------|--------------|---|
| 10784 | 04/19/2010 | Three weeks after receiving the study agent, the subject was admitted to the hospital for a surgical consultation. A colonoscopy on the same date revealed an area of chronic bleeding in the colon concerning for malignancy. The subject reported bloating with discomfort for months along with painless rectal bleeding. Physical exam upon admission was significant for weight loss, palpitations, abdominal pain and a decreased appetite. The event was ongoing at the time of this report. |

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 |
|--------|--------------|---|
| 10703 | 02/04/2010 | Two hours after receiving the infusion of the study agent, the subject developed nausea and had four episodes of vomiting. The subject was admitted for overnight observation and discharged the following day. |