

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

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
10100	12/24/2008	Approximately 4 weeks after receiving TNFerade, a partial thrombosis of the superior mesenteric vein was found on computed tomography scan. Subsequent scans showed progression of this clot. A relationship to the study agent could not be ruled out.
10032	11/06/2008	Subject received the fifth TNFerade injection and later that day was admitted with fevers and complained of watery stools for one week. The absolute neutrophil count (a type of white blood cell) was very low and the admitting diagnosis was neutropenic fever. The subject was diagnosed with an intestinal infection and was treated with antibiotics. The subject recovered and the event was considered resolved.
10005	10/21/2008	The subject died from disease progression 5 months after the last dose of the gene transfer study agent. The Investigator judged the event as possibly related to the gene transfer although the sponsor judged the event as unrelated.
10013	10/24/2008	Approximately one month after receiving the last injection of TNFerade the subject felt "weak" and fell hitting his head. It is unclear whether there was a loss of consciousness. Subject required stitches for the head wound. Blood tests collected in the emergency room revealed new anemia (low blood cell counts) and elevations in the liver enzymes. The subject recovered after a transfusion. The loss of blood was likely due to a peptic ulcer and possibly related to the gene transfer.
10025	10/29/2008	One week after the first dose of the gene transfer the subject developed a clot at the tip of the Mediport intravenous catheter that had to be cleared prior to using.
10027	10/29/2008	One day after the first dose of the gene transfer, the subject had nausea and vomiting with right sided chest pain. Tests done did not indicate this pain was cardiac in origin and subject was admitted to the hospital for supportive care.
10094	12/18/2008	Subject developed an extensive clot in the upper extremity approximately 2 weeks after having an intravenous line placed in a deep vein in the upper extremity and about 12 days after starting on weekly TNFerade injections into the pancreatic tumor. The subject had received two TNFerade injections prior to developing the clots.

Protocol Number: 629

Protocol Title: **A Phase I Dose-Escalation Trial of vvDD-CDSR (Double-Deleted Vaccinia Virus Plus CD/SMR) Administered by Intratumoral Injection in Patients with Superficial Injectable Tumors.**

DocID#	Receipt Date	Event Description
10090	12/11/2008	The subject was in the initial dosing cohort and was admitted to the hospital with a gastrointestinal bleed secondary to the tumor erosion into the stomach, dehydration and shortness of breath. The bleeding was controlled but the subject developed pneumonia requiring ventilator assisted breathing. The subject began to recover but developed a second bacterial infection in the blood and died from infection. Because this is a novel agent, the event was initially assessed as unlikely but possibly related to the gene transfer. However, tests on blood, sputum, ascitic fluid and urine did not show any evidence of the gene transfer viral vector. Autopsy confirmed that subject died from respiratory failure secondary to pneumonia and sepsis with widely metastatic pancreatic cancer and renal failure as contributing factors. The death is not considered related to the gene transfer.

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 $\alpha$ /VP16 in Patients with Intermittent Claudication.**

DocID#	Receipt Date	Event Description
10184	01/29/2009	Two years after receiving either the gene transfer or placebo the subject developed squamous cell carcinoma of the larynx. Subject was a smoker for 30 years.
10189	02/03/2009	323 days after receiving the blinded study treatment (i.e. gene transfer agent or placebo), the subject was diagnosed with non-small cell lung cancer with brain metastases. The investigator considered the event of lung cancer with brain metastases possibly related to the study treatment.

Protocol Number: 693

Protocol Title: **A Phase II study of PROSTVAC-V (Vaccinia)/TRICOM and PROSTVAC-F (Fowlpox)/TRICOM with GM-CSF in Patients with PSA Progression after Local Therapy for Prostate Cancer.**

DocID#	Receipt Date	Event Description
10102	12/29/2008	During week 36 of the study, the subject developed fever, diffuse pain and a joint effusion in the hands and knees after receiving the most recent dose of the gene transfer. The symptoms resolved after approximately 8 weeks. However, the subject withdrew from the study.

Protocol Number: 773

Protocol Title: **A Phase I Study of In-Situ, Neoadjuvant, Pre-Radical Prostatectomy RTVP-1 Gene Therapy in Patients with Locally Advanced Adenocarcinoma of the Prostate (Spore #: 11-01-30-15)**

DocID#	Receipt Date	Event Description
10144	01/07/2009	Seven hours after an intraprostatic administration of the gene transfer vector the subject was hospitalized for fever and myalgias. The next day subject also complained of diarrhea, photophobia and dysuria. Bacterial and viral cultures, including for adenoviral virus, were negative. The subject recovered within 24 hours and was discharged. It was felt that the symptoms were probably related to the gene transfer.

Protocol Number: 785

Protocol Title: **TRIST (TroVax Renal Immunotherapy Survival Trial) An International, randomized, double-blind, placebo controlled, parallel group study to investigate whether TroVax added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma**

DocID#	Receipt Date	Event Description
10103	12/29/2008	Subject admitted to hospital for one day with vomiting while being treated for community acquired pneumonia. Subject continued on the study but was withdrawn several months later due to disease progression.
10104	12/29/2008	The subject had blood in the urine that was due to the left renal tumor and required hospitalization. The subject received either the study agent or placebo. Initially, a possible role of the study agent could not be ruled out. However, the event was later assessed as unrelated.
10105	12/29/2008	Six months after starting on the trial, the subject was admitted to the hospital with shortness of breath. The subject had been receiving either the gene transfer or placebo and was diagnosed with an exacerbation of chronic obstructive lung disease. After 2 weeks, the subject was discharged but was also removed from the study due to disease progression. The principal investigator deemed the event to be possible related to the study agent (gene transfer or placebo).
10120	12/30/2008	The subject had been on the study for six months when admitted for ureter obstruction. A catheter was implanted to relieve the obstruction and the subject recovered. However, the last dose of the study agent was given prior to the event. While at first the principal investigator felt the event was due to kidney stones, subsequently the principal investigator noted that the event was possibly related to treatment with the study agent (gene transfer vaccine or placebo).

Protocol Number: 910

Protocol Title: **Closely HLA-Matched Allogeneic Virus Specific Cytotoxic T-Lymphocytes (CTL) to Treat Persistent Reactivation or Infection with Adenovirus, CMV and EBV after Hemopoietic Stem Cell Transplantation (HSCT)**

DocID#	Receipt Date	Event Description
e-Filed	11/17/2008	The subject had a transplant for aplastic anemia in April 2008 and 4 months later was diagnosed with post-transplant EBV-associated lymphoproliferative disorder. The subject was enrolled in this trial and received 3 doses of cells over the next month. However, about 2 weeks after the third dose the subject developed renal failure requiring dialysis and it was determined subject had hemolytic uremic syndrome/thrombotic thrombocytopenic purpura. The etiology of this disorder could be a complication of the total body irradiation done with the transplant, the gene modified cells or an acquired antibody. The subject will no longer be treated on this protocol.

Protocol Number: 932

Protocol Title: **A Randomized, Placebo-Controlled, Double-Blind, Dose-Escalation Study to Evaluate the Safety, Tolerability, and Pharmacodynamics of Multiple Intravenous Doses of ANZ-521 in Treatment-Naïve Hepatitis C Patients**

DocID#	Receipt Date	Event Description
10209	02/17/2009	The trial has been closed after two adverse events. In the most recent event, 2 hours after the IV infusion of the third dose of the study agent, the subject developed a non-productive stridorous cough which was initially treated with diphenhydramine but after the development of decreased oxygenation to the lungs and other signs that indicated a possible anaphylactoid reaction, the subject was treated with epinephrine. Eight hours post end of infusion, a similar episode occurred and the patient was again treated for possible anaphylaxis, with the addition of high dose steroids. Of note, this subject developed a cough with the first and second infusion, the first episode treated with diphenhydramine only. In addition to this subject, another subject developed a cough shortly after infusion. There were no signs or other symptoms to indicate and anaphylactic reaction, but given these reactions a decision has been made to close the trial.