

**Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Committee Meeting
September 2011**

Protocol Number: **457**

Protocol Title: **An Open-Label, Phase I, Dose-Escalation Study of TNFerade™ Biologic with Radiation Therapy as an Adjunct to Surgery or for Palliation of Soft Tissue Sarcoma of the Extremities.**

DocID#	Receipt Date	Event Description
11195	05/23/2011	Approximately one year post gene transfer dosing, the subject developed gangrenous necrosis in the affected limb, which required hospitalization. Despite the significant time interval between administration of the study agent and the serious adverse event, the Principal Investigator deemed the event as being possibly related to the study agent. After treatment at the hospital, the subject made a full recovery from this event.
11194	05/23/2011	Eleven days after the injection of the gene transfer agent, the subject developed a skin infection at the site of the injection.

Protocol Number: **624**

Protocol Title: **Phase I Trial of Conditionally Replication-Competent Adenovirus (Delta-24-RGD) for Recurrent Malignant Gliomas**

DocID#	Receipt Date	Event Description
11199	06/01/2011	Approximately one week after receiving the gene transfer agent, the subject developed fever, headaches, nausea and vomiting. Analysis of cerebral spinal fluid (CSF) showed inflammatory cells. No bacteria or fungus was found in the CSF but adenovirus was detected. Subject recovered after administration of steroids.

Protocol Number: **817**

Protocol Title: **Reduced Intensity Stem Cell Transplantation for Advanced Chronic Lymphocytic Leukemia Followed by Vaccination with Lethally Irradiated Autologous Tumor Cells Admixed with Granulocyte Macrophage-Colony Stimulating Factor Secreting K562 Cells**

DocID#	Receipt Date	Event Description
11241	07/11/2011	Following the fifth dose of study agent, the subject developed transient Common Terminology Criteria for Adverse Event (CTCAE) Grade 4 neutropenia (low white blood cell count). This event was determined to be expected in the post-HSCT (stem cell transplant) setting but was also felt to be possibly related to vaccination. The neutrophil counts returned to normal levels.

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
11152	04/15/2011	Subject received the gene transfer agent and then chemotherapy. Shortly after starting the chemotherapy, the subject developed swelling and pain in the knee. The subject was diagnosed with an infection in the knee joint (septic arthritis) and was treated surgically and with antibiotics. Subject was taken off treatment.

Protocol Number: 937

Protocol Title: **Vaccination With Lethally Irradiated Autologous Myeloblast Admixed With Granulocyte Macrophage-Colony Stimulating Factor Secreting K562 Cells (Gm-K562) In Patients With Advanced MDS Or AML After Allogeneic Hematopoietic Stem Cell Transplantation**

DocID#	Receipt Date	Event Description
11208	05/23/2011	This event was discussed at the December 14, 2011 RAC Meeting. Please refer to http://oba.od.nih.gov/rdna/rac_past_meeting_2011_webcasts.html#dec .

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 or Stage IV Disease**

DocID#	Receipt Date	Event Description
11254	07/28/2011	Subject had received several doses of the gene transfer when the subject was admitted to the hospital for treatment of an open leg wound. The subject had a previous wound that was deemed related to previous radiation for melanoma. Infection of the gene transfer agent may have led to worsening of this chronic wound.
11249	07/26/2011	Subject developed a vasculitis at the site of the cutaneous metastatic melanoma lesion where she had received injections with the gene transfer agent for nine months as well as radiation. The vasculitis may have been due to a number of factors, including an underlying autoimmune disorder, radiation therapy and inflammation secondary to the gene transfer agent.

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
11239	07/11/2011	Subject developed a pleural effusion (fluid around the lungs) and pericardial effusion (fluid around the heart) while receiving the gene transfer agent. The subject was symptomatic with shortness of breath. The symptoms resolved with steroids. Subject was taken off the study.

Protocol Number: 977

Protocol Title: **Direct CNS Administration of a Replication Deficient Adeno-Associated Virus Gene Transfer Vector Serotype rh.10 Expressing the Human CLN2 cDNA to Children with Late Infantile Neuronal Ceroid Lipofuscinosis**

DocID#	Receipt Date	Event Description
11228	06/27/2011	Approximately six days after administration of the vector by intracranial delivery, the subject had a seizure. The seizure occurred in the setting of multiple precipitants: bright lights, sleep deprivation, and subtherapeutic levels of valproic acid, one of the medications used to control the subject's seizures.

Protocol Number: 1013

Protocol Title: **A Phase III Study of Chemotherapy and Chemoradiotherapy With or Without HyperAcute®-Pancreatic Cancer Vaccine in Subjects with Surgically Resected Pancreatic Cancer**

DocID#	Receipt Date	Event Description
11151	04/15/2011	Subject was given second injection of hyperacute vaccine in left forearm and developed signs of inflammation that resolved. The remaining injections did not lead to a local reaction. However, after receiving chemotherapy subjects developed a CTCAE Grade 3 injection site reaction at the site of the first injection.
11153	04/15/2011	Approximately 16 weeks from first injection of study agent, subject developed pain and swelling in both legs. The injections were given into the thighs. Imaging revealed myositis (inflammation of the muscle) with small areas of necrosis. Subject was taken off of the study.

Protocol Number: 1042

Protocol Title: A Phase I/II Study using Allogeneic Tumor Cell Vaccination with Oral Metronomic Cytosin in Patients with High-Risk Neuroblastoma (ATOMIC)

DocID#	Receipt Date	Event Description
e-Filed	07/08/2011	The subject was enrolled and has received four vaccinations per the protocol. The day after the fourth vaccination, the subject was admitted to hospital due to pain in leg and back (in areas known to have evidence of disease). The subject felt that the outpatient pain medication schedule was not able to control symptoms. Subject denied any trauma, fever or vomiting since last visit.