
**Gene Transfer Safety Assessment Board
Adverse Event Report
NIH Office of Biotechnology Activities
September 2012**

Protocol Number: 793

Protocol Title: **Pilot Study of Redirected Autologous T Cells Engineered to Containing Anti-CD19 Attached to TCR ζ and 4-1BB or CD28 Signaling Domains in Patients with Chemotherapy Resistant or Refractory CD19+ Leukemia and Lymphoma**

DocID#	Receipt Date	Event Description
11466	05/22/2012	Pediatric subject with acute lymphoblastic leukemia received autologous T cells expressing an anti-CD-19 chimeric antigen receptor (CAR) and within several days of last dose developed difficulty breathing requiring a breathing tube (intubation), low blood pressure and abnormalities on chest xray consistent with acute respiratory distress syndrome. Subject was treated with steroids, entanercept and an IL-6 antagonist. Subject's clinical condition improved and subject recovered.

Protocol Number: 819

Protocol Title: **Registration Phase III Study of Lucanix™ (belagenpumatucel-L) in Advanced Non-small Cell Lung Cancer: An International Multicenter, Randomized, Double-blinded, Placebo-controlled Study Of Lucanix™ Maintenance Therapy for Stages III/IV NSCLC Subjects who have Responded to or Have Stable Disease Following One Regimen of Front-line, Platinum-based Combination Chemotherapy**

DocID#	Receipt Date	Event Description
11550	08/29/2012	Subject had a history of low blood counts that worsened when on trial. Subject first developed severely low platelet counts which resulted in a severe nosebleed and bleeding from the gums. Subject was then diagnosed with aplastic anemia and was removed from the study. This trial is blinded, so it is unknown whether the subject received the gene transfer agent or placebo.

Protocol Number: 844

Protocol Title: A Phase II Study of Low Dose HyperAcute®-Pancreatic Cancer Vaccine in Subjects with Surgically Resected Pancreatic Cancer

DocID#	Receipt Date	Event Description
11521	06/05/2012	Approximately three weeks after last dose of the study agent, the subject went to the emergency room for nausea, vomiting and dehydration and was admitted. Subject underwent exploratory surgery which revealed a small bowel perforation (hole in the small bowel). Investigator feels the nausea is possibly related to the study drug and that the bowel perforation is most likely related to the chemotherapy and is unlikely related to the study medication.

Protocol Number: 846

Protocol Title: A Phase I, Open-Label, Dose Ranging Study to Assess the Safety and Distribution of Single or Multiple Doses of VB-111 in Patients with Advanced Metastatic Cancer

DocID#	Receipt Date	Event Description
11502	07/09/2012	About three months after the second intravenous dose of the study agent, the subject was admitted with shortness of breath, bilateral leg swelling and weight gain despite a poor appetite. He was diagnosed with new onset congestive heart failure with decreased ejection fraction (efficiency of the heart pumping decreased). This was assessed to be possibly related to the gene transfer agent but it was also noted that subject had received previous chemotherapy agents that have known cardiac toxicity. Subject recovered.

Protocol Number: 930

Protocol Title: A Double-Blind, Placebo-Controlled (Sham Surgery), Randomized, Multicenter Study Evaluating CERE-110 Gene Delivery in Subjects with Mild to Moderate Alzheimer's Disease

DocID#	Receipt Date	Event Description
11526	05/09/2012	Subject had a seizure about two weeks after dosing and recovered. As this study is blinded, it is unclear if the subject received the gene transfer agent or had a sham surgery procedure.

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
11545	08/07/2012	Subject developed pauci-immune glomerulonephritis while receiving the study agent. While the etiology of this event was initially unclear, after further analysis the sponsor concluded that this event is unrelated to the study agent.

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
11541	03/07/2012	Update provided on most recent MRI in which changes seen at twelve months are slightly less prominent on imaging. No clinical correlation between the imaging and behavior seen. For background on these events, see the March 2012 meeting of the RAC. http://oba.od.nih.gov/oba/RAC/meetings/mar2012/RAC_Minutes_03-12.pdf
11471	05/25/2012	Update provided on subject's most recent MRI, in which changes seen at six months are continuing at the subject's Month 12 visit. No clinical correlation between the imaging and behavior seen. For background on these events, see the March 2012 meeting of the RAC. http://oba.od.nih.gov/oba/RAC/meetings/mar2012/RAC_Minutes_03-12.pdf

Protocol Number: 981

Protocol Title: **A Phase 1/2 Trial Assessing the Safety and Efficacy of Bilateral Intraputamin and Intranigral Administration of CERE-120 (Adeno-Associated Virus Serotype 2 [AAV2]-Neurturin [NTN]) in Subjects with Idiopathic Parkinson's Disease**

DocID#	Receipt Date	Event Description
11532	05/09/2012	<p>This over 65-year-old subject developed a right frontal hemorrhage approximately fifteen days following the study related stereotactic neurosurgical procedure. A CAT scan of the head was performed and was significant for a moderate right frontal lobe hematoma with adjacent edema and mass effect with a 2 mm midline shift to the left.</p> <p>The subject was admitted to the hospital for observation and was treated with steroids. Subject was also treated for urinary tract infection with antibiotics. He responded well to therapy and was discharged the following day. The MRI scan done one month after dosing demonstrated a resolving right frontal lobe hematoma.</p> <p>The investigator and sponsor deemed the severe adverse event of right frontal hemorrhage as possibly related to study drug, definitely related to study surgery, and resolved without sequelae at the one month visit.</p>

Protocol Number: 985

Protocol Title: **A Phase I Trial of Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19**

DocID#	Receipt Date	Event Description
11523	07/26/2012	<p>Within 48 hours of receiving the gene modified T cells, the subject developed fevers, rapid heart rate and a low blood pressure that required the administration of vasopressors (medications to raise blood pressure). Subject also had a seizure. Subject was given steroids and anti-convulsants and is recovering.</p>

Protocol Number: 991

Protocol Title: **A Phase I Study of an IL-2 Expressing, Attenuated Salmonella enterica Typhimurium in Patients with Unresectable Hepatic Spread from any Non-Hematologic Primary Cancer**

DocID#	Receipt Date	Event Description
11508	07/16/2012	<p>Approximately ten days after receiving the gene transfer agent, the subject was admitted for gastrointestinal bleeding. Subject recovered.</p>

Protocol Number: 1042

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

DocID#	Receipt Date	Event Description
	05/22/2012	<p>Pediatric subject with relapsed neuroblastoma has received six vaccines without acute adverse events. At the time of last vaccine administration, creatinine value was slightly high. Subject was seen by primary oncologist and diagnosed with strep throat and started on antibiotics. Labs obtained on that day showed a further increase in creatinine value. At that time, the subject was instructed to stop cytosine and have repeat labs to evaluate kidney function. Results demonstrated a low creatinine clearance (renal function) and with continued increasing creatinine values. Subject was admitted for hydration and further work-up.</p> <p>Per nephrologist (kidney specialist), they obtained a renal ultrasound on admission showed bilateral hydronephrosis and evidence of kidney scarring. They first attempted to decompress the hydronephrosis with the placement of a foley catheter. As there was no evidence of either blood or protein in multiple urine samples to support a diagnosis of acute glomerulonephritis, they continued with supportive measures and stopped all antibiotics and nephrotoxic agents. However, over the next 48 hours, with increasing creatinine values, and a repeat ultrasound showing only mild improvement in the hydronephrosis, subject was started on a steroid pulse to treat a potential diagnosis of acute glomerular nephritis or interstitial nephritis. When no improvement was seen with the steroids and after the subject developed anuria, subject had a kidney biopsy (results currently pending) to better assess the etiology of the acute renal failure. At this time, the nephrologist feels that the subject has an acute, or unrecognized chronic, renal disease of unclear etiology and was due to start dialysis.</p>

Protocol Number: 1043

Protocol Title: A Randomized Phase II Study to Assess the Activity of TroVax® (MVA-5T4) Plus Docetaxel Versus Docetaxel Alone in Subjects with Progressive Hormone Refractory Prostate Cancer

DocID#	Receipt Date	Event Description
11549	08/28/2012	This 70+ year old subject was receiving the gene transfer agent and docetaxel when he tried to get up and felt like he might pass out and had to sit down immediately. He also noted some changes in his vision. Upon hospitalization he was noted to have a low white blood cell count (neutropenia) but no signs of infection. His blood pressure was also low and his red blood cell count was also slightly low. He received antibiotics, fluids, and medication to raise his red blood cell counts. Subject recovered and continued on the study. While docetaxel is known to cause low white blood cell counts it is possible that the gene transfer agent may have contributed to this event.
11482	06/11/2012	Subject developed low white blood cell count (neutropenia) about three months after starting the gene transfer vaccine with docetaxel. Subject recovered. Although neutropenia is expected for docetaxel the gene transfer vaccine may have contributed to this event.
11544	06/22/2012	Subject developed a low white blood cell count, in particular a low neutrophil count (neutropenia), about a month after starting injections of the gene transfer and about a week after starting docetaxel chemotherapy. Although a low neutrophil count is known to occur with docetaxel it is possible the gene transfer agent contributed as well.

Protocol Number: 1113

Protocol Title: **A Phase 1/2a Dose-escalation Study of JX-594 (Thymidine Kinase-Deactivated Vaccinia Virus plus GM-CSF) Administered by Multiple Intravenous (IV) Infusions Followed by Intratumoral (IT) Boosts Alone and in Combination with Irinotecan in Patients with Metastatic, Refractory Colorectal Carcinoma.**

DocID#	Receipt Date	Event Description
11496	07/05/2012	Subject had an episode of low blood pressure within a day of the first dose of the gene transfer agent. A blood test for cardiac muscle injury (troponin) was slightly elevated but additional tests only showed chronic stable coronary artery disease and no acute cardiac event. Subject recovered and no further dosing will occur.