Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Commitee Meeting
June 2006

Protocol Number: **337**

Protocol Title: **Transduction of CD34+ Cells from the Umbilical Cord Blood of Infants or the Bone Marrow of Children with Adenosine Deaminase (ADA)-Deficient Severe Combined Immunodeficiency (SCID)**

DocID#	Receipt Date	Event Description
8421	03/07/2006	Subject underwent bone marrow harvest and received pre-transplant chemotherapeutic conditioning and transduced cells. Subject received back-up marrow because of persistent cytopenias but back-up marrow did not engraft. A bone marrow biopsy revealed extra chromosomal copies (trisomy 8) in 20 percent of cells. Re-examination of the original bone marrow done prior to dosing also showed trisomy 8.

Protocol Number: **452**

Protocol Title: **A Multicenter, Randomized, Double-Blind, Placebo Controlled, Dose-Response Study to Evaluate the Efficacy and Safety of Ad5.1FGF-4 in Patients with Stable Angina.**

DocID#	Receipt Date	Event Description
8411	02/27/2006	Approximately 27 months after receiving the gene transfer, subject was diagnosed with bladder cancer.

Protocol Number: **530**

Protocol Title: **A Randomized, Phase II, 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
7470	04/10/2006	Subject was undergoing treatment with chemotherapy, gene transfer, and radiation when admitted with a diagnosis of chemotherapy induced intractable vomiting. Subject was treated with intravenous fluids and anti-emetics. Subject also experienced recurrent abdominal pain that had been previously controlled with celiac axis nerve block. After discharge, the investigator elected to allow the subject to continue in the study regimen in order to determine whether the symptoms/events were related to radiation, chemotherapy or study drug as permitted by the protocol. The subject has not experienced any recurrence of the symptoms after re-initiating protocol interventions.

Protocol Number: **543**

Protocol Title: **Phase I Study to Evaluate the Safety of Cellular Immunotherapy for CD19+ Follicular Lymphoma Using Autologous T Cell Cytolytic Clones Genetically Modified to be CD19-Specific and Express HyTK**

DocID#	Receipt Date	Event Description
8504	04/28/2006	Subject found to have low neutrophil count (neutropenia) at week two, prior to the subject's second protocol prescribed gene transfer. The neutropenia was attributed to the protocol chemotherapy. A planned protocol deviation took place and the subject proceeded with the second gene transfer. Approximately 5 hours following the second infusion the subject experienced an episode of chills and temperature elevation. Per standard practice, the subject was started on empiric antibiotics. The subject was observed, found to be asymptomatic and neutropenia resolved. The subject was discharged home.

Protocol Number: **560**

Protocol Title: **A Phase I/II Pilot Study of Sequential Vaccinations with rFOWLPOX-PSA (L155)-TRICOM (PROSTAVAC-F/TRICOM) Alone, or in Combination with rVACCINIA-PSA (L155)-TRICOM (PROSTAVAC-V/TRICOM) and the Role of GM-CSF, in Men with Prostate Cancer.**

DocID#	Receipt Date	Event Description
8524	03/27/2006	Subject received gene transfer and was scheduled for 4 week follow-up appointment but cancelled. In a follow-up phone call, subject's spouse reported that subject was admitted to a hospital over the weekend. Subject was unable to walk at time of admission, but after receiving a muscle relaxant, subject was able to walk to the bathroom that evening. Subject also received a blood transfusion prior to discharge due to anemia. The principal investigator initially reviewed the adverse event report and noted low blood counts (anemia), muscle aches (myalgias) and muscle weakness were not related to the investigational agent but later changed the attribution to possibly related.

Protocol Number: **567**

Protocol Title: **A Multicenter, Randomized, Double-Blind, Dose Ranging Placebo-Controlled Study Evaluating Defined Doses of Percutaneously Delivered Via Boston Stiletto™ Endocardial Direct Injection Catheter System pVGI.1 (VEGF2) (placebo, 20, 200, or 800µg) in Patients with Class III or IV Angina.**

DocID#	Receipt Date	Event Description
8485	04/25/2006	Several hours after injection of the study agent, subject became hypotensive and short-of-breath and was discovered to have a collection of fluid around the heart (pericardial effusion) that required pericardiocentesis. During the pericardiocentesis, the subject developed a ventricular arrythmia requiring defibrillation. The subject was taken to surgery for a pericardial window and evacuation of clots and was discovered to have a posteriolateral perforation of the left ventricle. The subject was admitted to the intensive care unit but did recover and was discharged.
8439	03/13/2006	Five months after receiving gene transfer, subject collapsed, was transported to hospital and expired. The subject's family reported that subject had a heart attack. At this time, the investigator is unable to assess whether the death is related to the study agent.
8490	04/25/2006	Four months after receiving gene transfer, the subject underwent a stress test that was negative for ischemia. After the test, the subject left the hospital and began vomiting. Subject's cardiologist advised subject to go to the emergency room and the subject was admitted and diagnosed with a myocardial infarction. The investigator judged the event as possibly related to study agent, but not related to device or procedure.

Protocol Number: **579**

Protocol Title: **Virus Specific Cytocoxic T-Lymphocytes for the Prophylaxis of CMV after Allogeneic Stem Cell Transplant: A Dose-Finding Trial.**

DocID#	Receipt Date	Event Description
8484	04/20/2006	Subject received bone marrow transplant and was enrolled in protocol. Subject received the protocol cytotoxic T lymphocytes (CTL) and 3 weeks later was admitted with fever, diarrhea and skin rash. Subject was started on steroids because of a concern about possible graft versus host disease (GVHD). Subsequent investigation revealed the symptoms were not from GVHD. Unfortunately, steroids can destroy adoptively transferred CTLs. Subject began to develop increasing Epstein Barr viral (EBV) titers consistent with the development of EBV-lymphoproliferative disease. PCR tests performed to look for EBV in the CTLs that were transfused were negative. Subject was retreated with cytomegalovirus (CMV) and EBV specific CTLs. EBV titers decreased but CMV immunity was less robust and a third infusion of CMV CTLs were given to correct the residual immunodeficiency caused by the steroid treatment.

Protocol Number: **619**

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

DocID#	Receipt Date	Event Description
8325	01/24/2006	Approximately six months after receiving gene transfer, subject's mother contacted the Principal Investigator to provide an update on subject's recent seizure activity. There was an increase in clusters of brief seizures. Subject's seizure medications were adjusted. The Principal Investigator (PI) reported this event because it is medically significant although the intensity is mild. The PI further noted that there is no way to distinguish whether this event is part of the natural progression of the disease, or due to the study drug and procedures. For this reason, event was reported as possibly related to the study drug and procedures and was expected.
8472	04/17/2006	Approximately two hundred days post gene transfer the subject had a seizure followed by obtundant (decreased alertness) state. Subject recovered and is now stable with controlled seizures.
8345	01/31/2006	Subject one day post intracranial gene transfer developed fever, possibly related to study agent and probably related to procedure.
8383	02/22/2006	The subject's mother reported that the subject had experienced an episode of seizure activity approximately 100 days after gene transfer. The subject's anti-epileptic medication doses were adjusted. The principal investigator wrote "from the information available, we have no way of distinguishing as to whether this event is part of the natural progression of the disease, or due to the study drug and procedures. For this reason, we are reporting this as possibly related to the study drug and procedures."

Protocol Number: **635**

Protocol Title: **A Phase III Randomized, Controlled Study to Evaluate the Safety and Efficacy of PANVAC™-VF in Combination with GM-CSF Versus Best Supportive Care or Palliative Chemotherapy in Patients with Metastatic (Stage IV) Adenocarcinoma of the Pancreas Who Have Failed a Gemcitabine-Containing Chemotherapy Regimen.**

DocID#	Receipt Date	Event Description
8428	03/10/2006	About three weeks after gene transfer, subject presented to the emergency room with two days of abdominal pain that did not respond to narcotic pain medication. An abdominal computed tomography (CT) scan revealed a non-occlusive portal vein thrombus, worsening liver metastases, and peri-portal edema and increased ascites. Subject was admitted for pain management and initiation of anticoagulation therapy. The principal investigator classified the thrombus as possibly related to study drug administration.

Protocol Number: **653**

Protocol Title: **A Phase III Randomized, Open-Label Study of CG1940 and CG8711 Versus Docetaxel and Prednisone in Patients with Metastatic Hormone-Refractory Prostate Cancer Who are Chemotherapy-Naïve**

DocID#	Receipt Date	Event Description
8349	02/01/2006	On the morning following gene transfer, the subject experienced a sudden onset of nausea, vomiting, and vertigo (dizziness) , as well as left-sided hearing loss. Three days following the incident, the subject was seen by a physician who thought that the symptoms were consistent with acute labyrinthitis (inner ear inflammation). Subject was prescribed meclizine with subsequent resolution of vertigo over approximately a week. Subject's hearing loss persisted without improvement over the next month. Brain magnetic resonance imaging (MRI) showed a left small vestibular Schwannoma (benign tumor) superimposed on inflammatory vestibular cochleitis representing two separate processes.
8362	02/08/2006	Approximately one month after gene transfer, subject admitted for worsening unstable gait with accompanying bilateral lower extremity weakness. Subject previously diagnosed with acute labyrinthitis. Neurology consult obtained but results were pending.

Protocol Number: **683**

Protocol Title: **A Staged Phase I Study of the Treatment of Malignant Glioma with G207, a Genetically Engineered HSV-1, Followed by Radiation Therapy.**

DocID#	Receipt Date	Event Description
8398	02/13/2006	Within 24 hours of intratumoral administration of investigational agent, subject experienced a seizure, fever, and developed hemiparesis (partial paralysis) which did not resolve completely.
8399	02/13/2006	Subject experienced a seizure that was characterized as being severe in intensity and possibly related to the gene transfer. The seizure resolved.
8400	02/13/2006	Approximately two months after gene transfer, subject experienced a seizure which resolved with the following sequelae: left sided paresthesias, gait difficulties, and dysphasia. The dose of subject's anti-convulsant medication was increased and the subject was referred to physical and speech therapy. The subject's symptoms improved and the subject was discharged from the hospital .