Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Commitee Meeting
June 2005

Protocol Number: **223**

Protocol Title: **Phase I Study of Chemokine and Cytokine Gene Modified Allogeneic Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using a Retroviral Vector.**

DocID#	Receipt Date	Event Date	Event Description
6707	12/16/2004	12/26/2003	Follow up Investigator: Received information from site that subject received retrovirus.
6676	02/11/2005	12/26/2003	Follow up Investigator: Screening medical records and baseline laboratory values provided.

Protocol Number: **365**

Protocol Title: **A Phase I/II Study of the Safety, Survival, and Trafficking of Autologous CD4-zeta Gene-Modified T Cells With and Without Exogenous Interleukin-2 in HIV-Infected Patients.**

DocID#	Receipt Date	Event Date	Event Description
6674	02/10/2005	02/09/2005	Subject was premedicated with Tylenol, Benadryl and Zofran prior to the start of interventions. IL-2 given. Infusion of study product completed. Approximately 20 minutes post infusion, the subject experienced shivering, became febrile and heart rate increased (tachycardic). Subject was given Tylenol. Subject became increasingly tachycardic. Additionally, temperature elevated. Blood cultures drawn. Subsequently, subject remained tachycardic with temperature elevations and was admitted for observation. Subject was afebrile, tachycardia resolved and subject was discharged.
6700	02/22/2005	02/09/2005	Follow up Investigator: Subject experiened a fever with chills and tachycardia approximately 20 minutes after completion of the infusion of the investigational agent. The subject was admitted for observation. Blood cultures were negative and the events were self-limited. The subject recovered fully and was discharged to home the next day.

Protocol Number: **366**

Protocol Title: **A Phase III Multi-Center, Open-Label, Randomized Study to Compare the Overall Survival and Safety of Bi-Weekly Intratumoral Administration of RPR/INGN 201 Versus Weekly Methotrexate in 240 Patients with Refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN).**

DocID#	Receipt Date	Event Date	Event Description
6678	02/11/2005	11/09/2004	Follow up Sponsor: Baseline laboratory values provided. No protocol exceptions were granted to enroll this subject. Dosing dates provided; Cycle 1 injections were 7 days and 5 days prior to the event date.

Protocol Number: **393**

Protocol Title: **Phase II Study of a TGF-β2 Antisense Gene Modified Allogeneic Tumor Cell Vaccine in Patients with Stages II-IV Non-Small Cell Lung Cancer.**

DocID#	Receipt Date	Event Date	Event Description
6679	02/11/2005	11/12/2004	Follow up Sponsor: The results of an independent cytogenetics analysis on frozen peripheral blood mononuclear cells. Clinical information regarding prior chemotherapy regimen, radiation regimen, baseline laboratory values received on this subject who was diagnosed with chronic myelocytic leukemia.
6685	02/15/2005	11/12/2004	Follow up Sponsor: Receipt of letter, a supplement to report that documents two tests being developed to further investigate the subject's diagnosis of CML. Assays will be performed to determine whether any parts of the plasmid vector used are present in the peripheral blood lymphocytes collected following CML diagnosis. Also trying to develop PCR methodologies to identify the fusion sites of the BCR/ABL genes in PBLs collected while the subject was on study. These assays will be used to identify the time appearance of the Philadelphia chromosome.
6686	02/17/2005	11/12/2004	Follow up Sponsor: This submission included a Cytogenetic Analysis Report, the final pathologic report on peripheral blood and bone marrow samples, and some background clinical information on this subject who developed CML.

Protocol Number: **400**

Protocol Title: **Transfer of the Multidrug Resistance Gene, MDR-1, to Hematopoietic Progenitors from Patients with High Risk Lymphoma.**

DocID#	Receipt Date	Event Date	Event Description
6784	03/04/2005	02/28/2005	Subject with a history of Non-Hodgkins Lymphoma and status post autologous stem cell transplant was admitted to hospital with difficulty breathing and bilateral lower extremity swelling. Treated with antibiotics, oxygen.
6784	03/04/2005	02/28/2005	Subject with history of Non-Hodgkins lymphoma, status post autologous stem cell transplant, admitted to hospital with difficulty breathing and bilateral lower extremity edema. Evaluation was positive for myocardial infarction and CT Scan showed lung infiltrates. Initially considered to be consistent with congestive heart failure (CHF) or pneumonia. A right heart catheterization was performed and was not consistent with CHF. Subject unable to undergo bronchoscopy due to unstable pulmonary status. Treated with antibiotics, including Bactrim for PCP. Requires oxygen via face mask at this time.
	04/13/2005	02/28/2005	Follow up Investigator: "Although subject had signs of a small myocardial infarction as previously noted, it seems most likely to be a secondary event, induced by the stress of the pulmonary condition. The association of the subject's transplant and the event is seen as possible, without a clear etiology it makes it difficult to pinpoint the exact association. It is hypothesized that the subject had an initial viral and/or toxic insult and subsequently suffered a dysregulated immune system response, possibly because of the transplant. Subject was day +388 post transplant."
	04/13/2005	02/28/2005	Follow up Investigator: Subject was admitted with shortness of breath and bliateral lower extremity edema. Pulmonary x-rays showed non-specific ground glass pattern with scattered interstitial infiltrates. Evaluation also showed a myocardial infarction. Despite extensive evaluation and antibiotic therapy, subject's pulmonary status did not improve and comfort measures only were implemented. Subject expired approximately five weeks after admission. The Investigator could not rule-out an association with the investigational agent, but hypothesized that subject had an initial viral or toxic insult to the lungs and subsequently had a dysregulated immune response (possibly due to prior transplant).
7175	04/13/2005	04/12/2005	Subject had no improvement despite appropriate antibiotic therapy and was intubated. Ventilator support was discontinued and subject expired.

Protocol Number: **403**

Protocol Title: **A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Effect of Ad5FGF-4 on Myocardial Perfusion Defect Size and Safety in Patients with Stable Angina.**

DocID#	Receipt Date	Event Date	Event Description
6670	02/04/2005	04/20/2004	This follow-up report notes that the subject had an uncomplicated post-operative course and chemotherapy was recommended for prevention.
6677	02/04/2005	04/20/2004	Follow up Sponsor: The subject's baseline laboratory values were provided.

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 Date	Event Description
6718	02/28/2005	01/19/2005	Follow up Investigator: Death certificate received by site lists cause of death as "congestive heart failure and coronary artery disease", interval between onset and death stated as "years."

Protocol Number: **480**

Protocol Title: **A Phase II, Open-Label, Ascending Dose Study of the Safety and Efficacy of Trinam™ (EG004) in Stenosis Prevention at the Graft-Vein Anastomosis Site in Dialysis Patients.**

DocID#	Receipt Date	Event Date	Event Description
6673	02/09/2005	01/20/2005	Approximately one month after the administration of the investigational agent, subject experienced AV graft site hemorrhage after angioplasty of outflow graft narrowing. The event was considered serious, unexpected, and possibly related to the study agent and study device.
6675	02/10/2005	01/20/2005	Follow up Investigator: Baseline laboratory values for subject received.
7143	03/28/2005	01/20/2005	Approximately two months after angioplasty of the outflow graft, the subject experienced graft occlusion requiring TPA and angioplasty, including that of the stents placed at the time of previous angioplasty.

Protocol Number: **513**

Protocol Title: **Phase I Study of Intravenous DOTAP:Cholesterol-Fus 1 Liposome Complex (DOTAP:Chol-Fus 1) in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) Previously Treated with Chemotherapy.**

DocID#	Receipt Date	Event Date	Event Description
6681	02/14/2005	01/05/2005	A few hours after receiving the investigational agent, subject presented with fever to 104.6°F. Subject was admitted to hospital for observation but was discharged to home in less than 24 hours. The Investigator considered the fever to be definitely related to the investigational agent.
6682	02/14/2005	01/12/2005	Following the first dose of the investigational agent, subject was admitted to hospital for low blood pressure and fever. The Investigator considered the fever to be related to the investigational agent. The subject was discharged on the second hospital day in improved condition.

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 Date	Event Description
7114	03/09/2005	07/02/2004	Follow up Sponsor: Subject admitted with complaints of abdominal pain, nausea, vomiting and pancreatitis. Had a long hospital course characterized by resolving pancreatitis, completion of chemo radiation therapy, abdominal pain and nausea, infections. Underwent treatment for pancreatitis with intravenous fluids, anti-emetics, and proton pump inhibitors. Discharged home. Readmitted with complaints of vomiting bright red blood. Endoscopy showed duodenum was obstructed due to circumferential extrinsic tumor. A CT scan showed liver metastases and ascites. Discharged to home hospice and expired due to progressive disease.
7115	03/09/2005	07/27/2004	Follow up Sponsor: Subject was admitted to the hospital one day post study injection with fever and confusion. CT scan of the abdomen showed acute pancreatitis. Treated with intravenous fluids and antibiotics. Discharged in stable condition. A CT scan revealed resolution of pancreatitis and a large pancreatic mass.

Protocol Number: **546**

Protocol Title: **A Phase I/II Double-Blind, Randomized, Placebo-Controlled Study to Assess the Safety and Efficacy of AMG0001 to Improve Perfusion in Critical Leg Ischemia.**

DocID#	Receipt Date	Event Date	Event Description
7138	03/25/2005	03/14/2005	One day after a single injection of blinded study agent, subject reported pain and edema in the injected lower extremity. Subject has a known history of foot edema and ishcemic foot pain with ulcer, but the Investigator considered the left foot edema as possibly related to the study agent, given the temporal relationship to study agent administration.

Protocol Number: **549**

Protocol Title: **A Phase II, Multi-Center, Single Arm Evaluation of Preoperative Chemoradiation plus TNFerade™ Biologic (Ad$_{GV}$EGR.TNF.11D) Prior to Esophagectomy for Locally Advanced Esophageal Cancer.**

DocID#	Receipt Date	Event Date	Event Description
7116	03/09/2005	05/16/2004	Follow up Sponsor: No protocol exceptions granted. Subject had five weeks of chemotherapy with Cisplatin 75 mg/m^2 and 5-FU 100 mg/m^2 qd for 96 hours and radiation therapy total dose 45Gy. Subject underwent a thoracoscopic esophageal mobilization, laparascopic gastric mobilization with esophago partial gastrectomy, gastric pull-up and jejunostomy tube placement. Had a complicated post op course characterized by an anastomotic leak with empyema. Leak ultimately sealed and subject was discharged Subsequently underwent repeated esophageal dilatations and applications of Indermil Tissue glue to the fistula site. Follow-up endoscopy confirmed the fistula was closed. The Investigator considered the delayed recovery from surgery as possibly related to the study drug and definitely related to the underlying disease and surgery.

Protocol Number: **554**

Protocol Title: **A Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of the HIV-1 DNA Vaccine VRC-HIVDNA009-00-VP (Gag-Pol-Nef-multiclade Env) with the Plasmid Cytokine Adjuvant VRC-ADJDNA004-IL2-VP (IL-2/Ig).**

DocID#	Receipt Date	Event Date	Event Description
6728	03/03/2005	05/17/2004	Subject experienced moderate fatigue and muscle aches, mild headache, mild chills and mild joint pain, following the third set of injections. In addition, subject reported that approximately 12 hours post injection, experienced a sensation of tightness in throat, lasting approximately one hours, without cough or difficulty breathing. The tightness resolved without intervention, and was followed by a sore throat. Did not experience swelling of lips or tongue. That night experienced soaking sweats, without fever. Fatigue increased to severe the day following injection. At that time, experienced earaches and mild dizziness. Also reported that during the post injection period, experienced tenderness at the site of injections, with no more than 1 cm of redness on the day following injections and complete resolution the following day.

Protocol Number: **600**

Protocol Title: **A Phase II Randomized, Double Blind, Controlled Study to Evaluate the Safety and Efficacy of PROSTVAC®-VF/TRICOM™ in Combination with GM-CSF in Patients with Androgen-Independent Adenocarcinoma of the Prostate.**

DocID#	Receipt Date	Event Date	Event Description
6659	02/03/2005	01/17/2005	Approximately one month after beginning the series of experimental vaccinations, and one week after the last dose, this elderly subject presented to the Emergency Room with fever and lower extremity weakness after falling at home. Admitted to the hospital for evaluation. Chest xray and blood cultures (results pending) obtained. Events reported as resolved. The Investigator considered the fever possibly related but the weakness not related to the study agent.
6687	02/18/2005	01/17/2005	Follow up Investigator: Subject had experienced a high fever at home which prompted ER visit. Also noted that subject had history of leg numbness. Blood cultures were negative and the subject was afebrile and able to be discharged to home on the third hospital day with the events considered resolved without sequelae.
6672	02/09/2005	01/21/2005	Approximately 3 months after beginning the investigational agent, and 4 days after the last dose, this elderly subject was admitted for Grade 3 muscle weakness in both lower extremities. The Investigator considered this possibly related to the investigational agent.
7125	03/18/2005	01/21/2005	Follow up Sponsor: Additional details of hospital admission noted subject had bilateral lower extremity edema, renal insufficiency, hyperkalemia, and evidence suggestive of a rhabdomyolysis-like process (breakdown of muscle fibers resulting in the release of muscle fiber contents into the circulation) considered to be possibly related to the statin drug the subject was taking. The subject was given supportive care and on the third hospital day the subject was discharged for rehabilitation.

DocID#	Receipt Date	Event Date	Event Description
6680	02/11/2005	02/02/2005	Approximately eight weeks after last infusion of the investigational agent, and about 16 days after receiving study agent, subject presented with symptoms of fatigue and falling (without loss of consciousness) for several days. The subject was found to have low white blood cells (neutropenia). This was considered to be possibly related to the investigational agent, but fever and neutropenia are expected consequences of the Fowlpox agent.
6793	03/07/2005	02/02/2005	Follow up Sponsor: Subject was treated with intravenous antibiotics and fluids. Neutropenia resolved and subject was afebrile.
6794	03/07/2005	02/19/2005	Subject admitted for fever, chills, shortness of breath and fatigue. Ruled out pneumonia. Treated with antibiotic therapy and subject responded, subsequently discharged. Investigator assessed the event as possibly related to study agent, moderate in severity and expected per protocol. Sponsor assessed the event as not related, since infusion of study agent occurred 9.5 weeks prior to admission.
7137	03/23/2005	02/19/2005	Follow-up report Sponsor: Subject was doing well after recent hospitalization and another follow-up clinic visit was scheduled for three weeks later.

DocID#	Receipt Date	Event Date	Event Description
7118	03/11/2005	02/24/2005	Subject was admitted with one week history of persistent nausea and intermittent vomiting, associated with generalized fatique, constipation, and weight loss. The subject was found to be dehydrated and was given supportive care. The Grade 2 nausea and vomiting and the Grade 3 dehydration were assessed by the Investigator as possibly related to the study agent administration.
7187	03/11/2005	02/24/2005	Follow up Sponsor: Dehydration resloved without sequelae upon completion of treatment.
7119	03/11/2005	03/06/2005	Subject was readmitted, approximately eight days after discharge, for abdominal swelling and lower extremity edema that the Investigator attributed to metastatic disease.
7185	03/11/2005	03/06/2005	Follow up Sponsor: Subject was discharged on the fifth hospital day, having requested removal of the feeding tube and having declined hospice care.
7160	04/01/2005	03/16/2005	Subject was admitted with Grade 3-4 abdominal pain and Grade 2 nausea and vomiting, considered to be possibly related to the study agent administration and concomitant medications.
7161	04/01/2005	03/22/2005	The subject was admitted for Grade 3 abdominal pain and an occluded PICC line. The line was replaced and a continuous infusion of pain medication was begun with resolution of the abdominal pain. The abdominal pain was considered possibly related to study agent administration.
7186	04/18/2005	03/12/2005	Subject expired secondary to progression of underlying malignant disease.
7192	04/22/2005	04/06/2005	Subject was hospitalized with dyspnea and symptoms of pulmonary edema requiring ventilator support. Chest radiographs were suggestive of pneumonia. The findings were consistent with pulmonary edema or disease progression and a causal relationship to the administration of the vaccine could not be ruled out.
7193	04/22/2005	04/10/2005	Subject expired from progressive disease. No autopsy was performed and the possiblity of a causal relationship to the investigational agent could not be ruled out.

Protocol Number: **636**

Protocol Title: **An Open Label Pilot Study to Evaluate the Safety and Tolerability of PANVAC™-V and PANVAC™-F in Combination with Sargramostim in Patients with Metastatic Adenocarcinoma.**

DocID#	Receipt Date	Event Date	Event Description
7159	03/31/2005	03/15/2005	Subject reported shaking chills in the evening of last vaccine/GM-CSF. Subject had a fever of 103.6 that resolved. Experienced lightheadedness and a momentary syncopal event. Went to bed with no subsequent symptoms. Notified staff next day and was told not to take GM-CSF. At evaluation 10 days later, subject was hemodynamically stable and feeling well. Resumed vaccine regimen and no significant findings were noted following EKG and head CT scan. Cardiologist recommended no additional work up and considered that events were "Syncopal/Presyncopal" related to orthostasis and secondary to dehydration/decreased oral intake and fever.
7169	04/12/2005	03/15/2005	Follow up Investigator: The syncope is not expected, nor listed in the informed consent document, but events of fever, fatigue, anorexia that led up to event are in current consent.
7214	04/12/2005	03/15/2005	Follow up Investigator: This event changed to "non-serious and related" to study agent.
7224	05/05/2005	03/15/2005	Follow up Investigator: The subject was rechallenged with the PANVAC-F and no Sargramostim while under observation as in-patient at hospital. The subject experienced no adverse side effects except grade II local injection site reaction which is expected per protocol.