Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Commitee Meeting
December 2004

Protocol Number: **274**

Protocol Title: **A Phase I, Multi-Center, Open Label, Safety and Tolerability Study of Increasing Single Dose of NV1FGF Administered by Intra-Muscular Injection in Patients with Severe Peripheral Artery Occlusive Disease.**

DocID#	Receipt Date	Event Date	Event Description
6411	10/01/2004	03/08/2004	Follow up Sponsor: Subject was hospitalized due to infection of amputation wound and resection was performed. Subject remains hospitalized.

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
6395	09/16/2004	2004	Subject expired due to cardiac arrest.
6405	09/23/2004	06/10/2004	Subject admitted for angina, underwent cardiac catheterization.
6463	10/27/2004	08/01/2004	Subject reported increased left leg numbness and new right leg numbness. MRI of spine and brain ordered. Neuro-oncologist consult ordered.
6471	10/26/2004	06/11/2004	Subject was diagnosed with melanoma approximately 14 months after dosing with blinded investigational agent. The work-up was continuing at the time of this report.
6476	10/29/2004	06/11/2004	Follow up Investigator: Subject was hospitalized for a knee replacement. Had a "mole" removed from back and was subsequently diagnosed with melanoma. Discharged. Re-admitted for 3 surgical procedures to remove "moles" and lymph nodes. Subject reported to doctors weakness right side of body. MRI ordered and mass was found in the right side of the brain. Etiology of the mass is still being worked up.

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
6371	08/20/2004	08/05/2004	Follow-up Investigator: The subject underwent angioplasty of the venous stenosis. The graft was working well with an excellent hemodynamic result.
6368	08/20/2004	08/05/2004	Approximately three months after the administration of the investigational agent, the subject experienced graft outflow vein stenosis. The Investigator deemed this possibly related to the investigational agent and the underlying disease.
6409	09/27/2004	07/29/2004	Subject experienced several episodes of graft thrombosis. Admitted for intravenous Heparin and Coumadin therapy. Discharged in stable condition.
6408	09/27/2004	09/22/2004	Subject experienced peri-graft infection. Admitted for observation and intravenous antibiotics. Stable condition. Attributed to routine sticks for dialysis access.
6427	10/06/2004	06/17/2004	Subject experienced mild bleeding after angioplasty for outflow vein stenosis at Week 4 post-investigational procedure. The bleeding resolved. The Investigator assessed the event of outflow stenosis as possibly related to worsened/accelerated intimal hyperplasia, possibly related to the investigational agent. The Sponsor did not concur with this assessment.

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
6362	08/12/2004	07/27/2004	One day post injection with the investigational agent, subject admitted with fever, chills, vomiting, frequent urination, and poor sleep for two nights. Blood cultures were negative. Urine cultures were positive for bacteria. The subject was treated with intravenous fluids, analgesic medications and intravenous antibiotics. Study treatment, chemotherapy and radiation were held. CT scan of the abdomen was suggestive of acute inflammation of the pancreas. The Investigator deemed this event definitely related to the study agent, possible related to the administration procedure and unrelated to the underlying disease.
6365	08/12/2004	08/02/2004	Subject was admitted for fever, nausea, and vomiting six days after injection with the investigational agent. A biliary stent was placed and intravenous antibiotics were administered. The subject improved and was discharged to home on the fourth hospital day.

Protocol Number: **549**

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

DocID#	Receipt Date	Event Date	Event Description
6402	10/14/2004	2004	One day prior to presentation in the emergency room, subject experienced an episode of heart palpitations lasting approximately one hour. The next day, subject complained of shortness of breath which rapidly worsened and was transport to ER. In ER, the subject experienced cardiopulmonary arrest from which subject could not be revived. An autopsy revealed a large pulmonary saddle embolus, bilateral pulmonary edema, and a pulmonary infarct.
6434	10/14/2004	2004	Follow up Sponsor: Baseline labs provided: WNL. Intrinsic interventions provided: cisplatin 75mg/m² Day 1 and Day 29, 5-FU 1000mg/m² over 96 hours Day 1 and Day 29, 45 Gy external radiotherapy administered in 1.8 Gy fractions over 5 weeks. To deliver TNFerade via endoscopy the subject received conscious sedation (Demerol, Versed, viscous lidocaine, and Ciprofloxacin IV and oral per protocol. Famotidine or rabeprazole and fluconazole for one week for candida esophagitis, one-time double lumen catheter administration of TPA to declot the central line. At the time of death, subject was only receiving Timoptic eye drops, atenolol 50 mg and Prilosec OTC prn.
6462	10/14/2004	2004	Follow up Sponsor: Baseline labs provided: within normal limits. Intrinsic interventions provided: Cisplatin 75mg/m² Day 1 and Day 29, 5-FU 1000mg/m² over 96 hours Day 1 and Day 29, 45 Gy external radiotherapy administered in 1.8 Gy fractions over 5 weeks. To deliver TNFerade via endoscopy, the subject received conscious sedation (Demerol, Versed, viscous lidocaine, and Ciprofloxacin IV and oral per protocol. Famotidine or rabeprazole and fluconazole for one week for candida esophagitis, one-time double lumen catheter administration of TPA to declot the central line. At the time of death, subject was only receiving Timoptic eye drops, atenolol 50 mg and Prilosec OTC prn.

Protocol Number: **562**

Protocol Title: **A Phase I Trial Using a Universal GM-CSF-Producing and CD40L-Expressing Bystander Cell Line (GM.CD40L) in the Formulation of Autologous Tumor Cell-Based Vaccines for Cancer Patients with Stage IV Disease.**

DocID#	Receipt Date	Event Date	Event Description
6398	09/28/2004	07/23/2003	Two days after the subject received Vaccination #2, the lab notified the Investigator that the final study product culture results showed bacterial contamination. The subject was treated prophylactically with oral antibiotics without experiencing any untoward reaction.

Protocol Number: **568**

Protocol Title: **A Phase II Multi-Center, Double-Blind, Placebo-Controlled, Trial of VLTS-589 in Subjects with Intermittent Claudication Secondary to Peripheral Arterial Disease.**

DocID#	Receipt Date	Event Date	Event Description
6379	09/02/2004	01/12/2004	Follow up information: Chest xray showed changes that suggested scarring and granulomas. No acute illness.

Protocol Number: **569**

Protocol Title: **A Multicenter, Double-Blind, Placebo-Controlled, Phase II Study of Aerosolized tgAAVCF for the Treatment of Cystic Fibrosis.**

DocID#	Receipt Date	Event Date	Event Description
6396	09/16/2004	08/23/2004	Subject experienced an expected adverse event of subacute pulmonary exacerbation but this was accompanied by the unexpected event of hemoptysis (coughing up of blood from the respiratory tract). The subject underwent bronchial artery embolization with resolution of the hemoptysis. Treated with antibiotics. The Sponsor considered the hemoptysis as possibly related to the investigational agent/procedure.

Protocol Number: **572**

Protocol Title: **A Phase I Trial of Intraprostatic Injection of CG7870 Followed by Three-Dimensional Conformal Radiation Therapy (3D-CRT) in Patients with Clinically-Localized Intermediate-Risk Prostate Cancer.**

DocID#	Receipt Date	Event Date	Event Description
6483	11/03/2004	10/20/2004	Subject inadvertantly received a seven-fold dose of the investigational agent. On Day 10 post-dosing, the subject had an asymptomatic and isolated thrombocytopenia (decrease in blood platelets). The thrombocytopenia was considered to be immune mediated and the subject responded well to oral steroids. Both the Investigator and Sponsor assessed the thrombocytopenia as "related" to the investigational agent.

Protocol Number: **581**

Protocol Title: **Phase I Study of Intravesical Recombinant Fowlpox-Gm-CSF (rF-GM-CSF) and/or Recombinant Fowlpox-Tricom (rF-TRICOM) in Patients with Bladder Carcinoma Scheduled for Cystectomy.**

DocID#	Receipt Date	Event Date	Event Description
6432	10/08/2004	10/08/2004	The research participant developed asymptomatic liver enzyme elevations four days after the last vaccination, which was two days after surgical removal of all or part of the urinary bladder.
6447	10/19/2004	10/08/2004	Follow up Investigator: The subject's pre-existing medical conditions, concomitant medications and baseline laboratory values were provided.
6450	10/20/2004	10/15/2004	After receiving the third of four scheduled doses of the investigational agent, the subject developed asymptomatic Grade 3 liver enzyme elevations. The liver enzymes normalized but rose again to Grade 2 levels shortly after surgical removal of all or part of the urinary bladder (cystectomy). By approximately one month post-cystectomy the liver enzymes had returned to normal. The events of liver enzyme elevations were considered to be unexpected and possibly related to the vaccine.
6478	11/03/2004	10/15/2004	Follow up from the Investigator: The subject's liver enzyme values have been decreasing. The subject received transfusion of one unit of packed red blood cells for a Grade 3 level of low hemoglobin which subsequently corrected to a Grade 1 level and the subject was discharged.
6448	10/19/2004	07/04/2004	Six days after receiving the fourth vaccine, and three days after surgical removal of all or part of the urinary bladder (cystectomy), the subject had asymptomatic Grade 2 elevations of liver enzymes.
6461	10/25/2004	07/04/2004	Follow up Investigator: Dosing cohort for subject provided.
6473	10/29/2004	10/29/2004	Approximately three weeks after the fourth vaccine dose and surgical removal of all or part of the urinary bladder (cystectomy), the subject was found to have asymptomatic Grade 3 elevations of liver enzymes. The subject was admitted for further evaluation.
6479	11/03/2004	10/29/2004	Follow-up Investigator: Evaluations showed subject had fatty liver changes but no focal liver mass. Viral hepatitis lab results consistent with previous vaccination to Hepatitis B but no evidence of infectious hepatitis. Liver enzyme elevations were resolving and subject was discharged with a diagnosis of hepatitis.

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
6494	11/09/2004	10/10/2004	Approximately three weeks after the third vaccine dose, the subject was admitted to the hospital with an acute myocardial infarction, thrombotic thrombocytopenic purpura, and acute renal failure. No subsequent investigational agent was given and the subject was treated for the acute conditions. Subject required continued medical care in a skilled-care facility, but was responding to 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 Date	Event Description
6430	10/08/2004	10/05/2004	The subject experienced a seizure post-operatively that was considered to be possibly related to the investigational agent in the setting of neurosurgery and an underlying seizure disorder.
6440	10/18/2004	10/05/2004	Follow up Investigator: An MRI performed after the post-operative seizure showed new burr-holes and a small amount of bifrontal pneumocephalus (presence of air inside of the skull), but no hemorrhage.
6456	10/22/2004	10/19/2004	Two weeks after the investigational agent was administered, subject developed status epilepticus requiring admission to intensive care unit. The Investigator considered this possibly associated with the neurosurgery and the investigational agent in the setting of the subject's baseline seizure disorder.
6474	10/22/2004	10/19/2004	Follow up Investigator: Medical records, progress notes, telephone log documentation from the site with FDA to place themselves on clinical hold.
6460	10/22/2004	10/19/2004	Follow up Investigator: Medical records provided.
6466	10/22/2004	10/19/2004	Follow up Investigator: Medical records, progress notes, telephone log documentation from the site with the FDA to place themselves on clinical hold.
6489	11/08/2004	10/19/2004	Follow-up Investigator : This report was initially submitted as “not yet resolved.” The subject has since experienced a relapse of status epilepticus, and this follow-up is to provide an interval history on the subjects condition.
6464	10/27/2004	10/20/2004	The subject developed a urinary tract infection, considered by the Investigator to be most likely related to the indwelling catheter placed upon admission to the Intensive Care Unit for status epilepticus.
6465	10/27/2004	10/20/2004	The subject developed hypotension which was considered by the Investigator to be possibly associated with the barbiturates administered for treatment of the status epilepticus.
6468	10/28/2004	10/22/2004	The subject developed an anemia that was considered by the Investigator to be most likely dilutional in nature, secondary to the fluids administered in the Intensive Care Unit while being treated for previous event of status epilepticus.
6475	11/02/2004	10/27/2004	The subject developed a decrease in urine output in the setting of normal kidney function and adequate blood pressure, considered by the Investigator to be unlikely related to vector administration. Dopamine was administered to increase diuresis and urine output improved.
6477	11/03/2004	10/30/2004	The subject developed respiratory failure requiring re-intubation considered by the Investigator to be related to high doses of barbiturates administered to supress the seizure activity of status epilepticus. The subject was sucessfully re-intubated and supported with mechanical ventilation.