Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Commitee Meeting
September 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
6190	05/26/2004	01/24/2003	Follow up from Another Investigator: A chronological sequence of the event sent to the IBC Chair at University of Miami from the Investigator at University of Miami , also noting that this European study uses the same study product as in the Miami study.
6147	04/30/2004	03/08/2004	Follow up Sponsor: The events of thrombosis and infection occurred on treated leg.
6191	05/26/2004	03/08/2004	Follow up from another PI: Duplicate of report sent in by U.S. site. This was the report to the IRB of the U.S. site notifying them of this AE at the site in Germany.

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
6297	07/28/2004	04/29/2003	This follow-up report from the PI noted that the relationship of the event of breast cancer to the gene transfer product was "possible."
6311	08/02/2004	07/25/2003	Follow-up Investigator: Event relationship was changed from "unrelated" to "possibly associated" and severity of event was changed from "Life Threatening" to "Severe."

Protocol Number: **453**

Protocol Title: **A Multi-Center, Open Label, Two Part, Dose Escalation Study to Determine the Tolerability of Interferon-beta Gene Transfer in the Treatment of Recurrent or Progressive Glioblastoma Multiforme.**

DocID#	Receipt Date	Event Date	Event Description
6295	07/28/2004	2003	The Sponsor reported that the PCR testing for replication competent adenovirus performed on samples from serum, CSF, and brain tissue were all negative and that the clinical hold on this protocol was lifted. However, the Sponsor opted to close the study due to the restrictive population of glioma patients who do not have tumors in locations that might compromise the ventricle.

Protocol Number: **458**

Protocol Title: **Phase II Pilot Study of Safety and Immunogenicity of a ALVAC-CEA/B7.1 Vaccine Administered with Chemotherapy, Alone or in Combination with Tetanus Toxoid, as Compared to Chemotherapy Alone, in Patients with Metastatic Colorectal Adenocarcinoma.**

DocID#	Receipt Date	Event Date	Event Description
6158	05/07/2004	02/13/2004	Approximately two months after Cycle 4 of chemotherapy, and 1 month after the last dose of the experimental vaccine, the subject developed signs and symptoms of congestive heart failure. The subject was treated as an outpatient and was recovering. The Investigator assessed this as possibly related to the study vaccine, malignancy, and hyptertension.
6214	05/27/2004	02/13/2004	The SAE was reported to have an outcome of "recovery".
6213	05/27/2004	02/13/2004	The Sponsor submitted a follow-up report wherein noting that the consulting cardiologist could not offer an etiology for the subject's congestive heart failure. The PI confirmed the assessment that the heart failure is possibly related to the study vaccine. The subject had received six vaccinations.

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
6218	06/09/2004	05/26/2004	Approximately three weeks after the instillation of the investigational agent the subject developed nausea, fever, and chills and was found to have a potassium level of 7.6. There was a Permacath in place but there was no swelling or erythema over the graft. The subject was treated with IV antibiotics for a presumptive diagnosis of central line infection. The Investigator attributed the event to the underlying disease/other suspected cause of Permacath infection, but could not exclude a causal relationship between the event, the study agent and the study device.
6266	07/07/2004	05/26/2004	Follow up Sponsor: Serious criteria amended to include prolonged hospitalization. Medical history amended to include end-stage Renal Disease and Diabetes Mellitus. Concomitant medications provided. Investigator considered the possibility that subject became bacteremic from Trinam agent or device, although highly unlikely. Event resolved. Labs provided show normal LFTs and PCR tests are pending. Sponsor's assessment: Concurs with PI.
6271	07/12/2004	06/28/2004	Twelve days after implantation of the study device the subject presented with an occluded access graft requiring surgical resection and empiric antibiotic therapy. The tissue cultures did grow coagulase negative staphylococci but the subject's wound infection was reported as resolved four days post surgery.

Protocol Number: **502**

Protocol Title: **A Phase II, Randomized, Double-Blind, Placebo Controlled, Parallel Group, Efficacy and Safety Study of Different Doses and Schedules of Administration of NV1FGF in Patients with Severe Peripheral Artery Occlusive Disease.**

DocID#	Receipt Date	Event Date	Event Description
6187	05/07/2004	09/19/2003	Follow up Sponsor: duplicate submission of report from another site.

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
6305	07/21/2004	07/02/2004	Four days after injection of the investigational agent, this subject presented with signs and symptoms of acute pancreatitis. A CT scan on the day of admission showed the development of pancreatitis since the prior examination one week prior to the study agent administration. The subject responded to usual care and aggressive pain control. The Investigator deemed the event as probably related to the study agent and its administration and probably unrelated to the underlying disease.

Protocol Number: **531**

Protocol Title: **A Phase I Trial of Intrapleural Gene Therapy of Malignant Pleural Disease Using E1-Deleted Adenoviruses Containing the Human Interferon Beta Gene.**

DocID#	Receipt Date	Event Date	Event Description
6309	07/13/2004	06/29/2004	Approximately eleven hours post vector administration the subject experienced a transient fever and oxygen desaturation lasting approximately two hours. The subject responded to inhaled albuterol and supplemental oxygen with resolution of symptoms.

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
6253	07/01/2004	05/16/2004	The subject developed an anastomotic leak with right empyema following laprascopic esophagectomy and partial gastrectomy with gastric pull-up. The leak was surgically repaired, however pleural fluid drainage persisted. 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: **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
6272	07/12/2004	01/03/2004	This follow-up report changes the onset date to Study Day 18 (from 19) and reports the results of screening exams and the testing that was done to establish the diagnosis of Hodgkins disease.
6152	05/03/2004	04/23/2004	Subject presented to emergency room on Study Day 130 with a two-week history of upper and lower extremity weakness. The subject was released from the ER, but returned the next day unable to walk or talk. The subject was found to be comatose and evaluation was ongoing, including consultations with Neurology and Infectious Diseases specialists.
6273	07/12/2004	2004	This follow-up report is the report on the autopsy. The cause of death was not completely clear, however it was thought that it most likely could be related to bronchopneumonia and possible sepsis.
6153	05/03/2004	2004	This report is notification that the subject expired. The Investigator assessed the case as related to the investigational agent as no other proximate cause for the event was known at the time of the report. However, the Medical Monitor for the Sponsor considered that there was insufficient information to assess causality at the time of the report and noted that an autopsy was pending.
6188	05/26/2004	2004	This submission is an autopsy report. The cause of death was not completely resolved by the autopsy, but it may have been due to bronchopneumonia and sepsis. Severe underlying cardiac disease was also noted on autopsy.

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
6235	06/25/2004	06/11/2004	The subject had two self-limited episodes of hemoptysis without hemodynamic compromise. The investigator considered the event to be possibly related to the investigational agent as the subject had no history of hemoptysis.

Protocol Number: **580**

Protocol Title: **Phase II Study Examining the Biological Efficacy of Intratumoral INGN 241 (Ad-mda7) Administration in Patients with In Transit Melanoma.**

DocID#	Receipt Date	Event Date	Event Description
6233	06/24/2004	06/04/2004	Subject was admitted with signs and symptoms of cellulitis of the leg. The subject was successfully treated with antibiotics. The Investigator assessed the event as possibly related to the study agent and the Sponsor assessed it as possibly secondary to bacterial contamination that possibly occured during the injection of the investigational agent or during a biopsy performed three days prior to presentation.

Protocol Number: **587**

Protocol Title: **A Phase II Randomized Trial Comparing TNFerade Biologic with Capecitabine and Radiation Therapy Followed by Surgical Resection versus Capecitabine and Radiation Therapy Followed by Surgical Resection for the Treatment of Rectal Cancer.**

DocID#	Receipt Date	Event Date	Event Description
6238	06/25/2004	04/19/2004	Subject developed lymphopenia and chemotherapy was held as per the protocol. Subject had no signs of infection. This event is an expected toxicity per the protocol.

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
6312	08/03/2004	07/28/2004	The subject developed vomiting which was considered probably associated with the anesthesia and/or the neurosurgical procedure, and possibly related to the investigational agent.