Serious and Other Selected Adverse Events
Reported for Human Gene Transfer Protocols
Recombinant DNA Advisory Commitee Meeting
March 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
6568	12/13/2004	2003	Subject, with a history of stage 4 neuroblastoma was admitted to hospital for untreatable hemorrhagic cystitis. During the work-up, further significant progression of neuroblastoma was found, involving bone marrow, liver and central nervous system. Subject developed progressive organ failure and died.
6584	12/17/2004	2003	Follow-up Investigator: Provided additional investigational product details and dosing information.

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
6516	11/22/2004	11/09/2004	Subject was admitted for possible acute inflammation of skin tissue of neck during Week 2 of the investigational regimen. A CT scan showed an increase in tumor size with some areas of tumor necrosis (tumor cell death). Both the Investigator and the Sponsor assess the event as possibly related to the investigational agent.

Protocol Number: **370**

Protocol Title: **Gene Therapy for Patients with Fanconi Anemia: A Pilot Study.**

DocID#	Receipt Date	Event Date	Event Description
6521	11/23/2004	11/20/2004	Subject with chronic neutropenia, related to underlying Fanconi anemia was admitted to Bone Marrow Transplant inpatient unit for observation five days after receiving infusion of investigational agent. Blood work-up indicated neutropenia, elevated lymphocytes, and presence of atypical lymphocytes. Subject was treated for neutropenia, remained afebrile and did well during hospital stay. Subject was discharged within 2 days in good condition. The Investigator considered that the event was not likely to have been caused by the investigational agent.

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
6560	12/08/2004	11/12/2004	Subject was diagnosed with Chronic Myelocytic Leukemia (CML) approximately 6 months after receiving the last injection of investigational vaccine. Treated with Gleevec.
6570	12/14/2004	11/12/2004	Follow up Sponsor: Subject received 16 out of 16 injections of investigational vaccine on approximately a monthly basis. Screening and on-study related labs indicated subject had chronic low white blood cell (WBC) counts throughout the trial. Screening WBC was within inclusion range, 23 of 30 lab tests were below the lower normal limit of $4.1x10^3/mm^3$. The last five on-study WBC tests were all within normal range. Bone marrow biopsy results suggested an abnormal decrease in WBC and normocytic anemia. No evidence of primary or metastatic neoplasm. Marrow was slightly hypercellular with trilineage hematopoiesis and iron stores present. Flow cytometry showed no evidence of lymphoproliferative disorder. Bone marrow sample performed. Pathologic diagnosis: leukocytosis with leukoerythroblastic reaction with packed marrow consistent with myeloproliferative disorder, (CML) probably post chemotherapeutic. Flow cytometry results were suggestive for slightly left-shifted myeloid maturation. Chromosome analysis is pending.

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
6606	12/27/2004	04/20/2004	Subject was diagnosed with Non-Small Cell Lung Cancer approximately three and one-half years after receiving the study agent. The subject received surgery and chemotherapy for the malignancy that was considered by the Investigator to be "possibly related" to the investigational agent previously received. The Sponsor assessment was "unlikely" related to study agent.

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
6522	11/24/2004	06/10/2004	This follow-up report clarifies that the Investigator considered this event of increased chest pain as "possibly related."
6510	11/18/2004	08/01/2004	Folllow up Sponsor: MRI ordered in response to increased left leg numbness and new right leg numbness led to initial diagnosis of a spinal cord tumor and abnormal brain scan. Study is blinded, Sponsor considers the event as "unlikely" related to study product.
6545	12/07/2004	08/01/2004	Follow-up Sponsor: CT scans of abdomen/pelvis and pancreas ordered. Biopsy of pancreas is pending. Attribution remains "unlikely" related to study agent.
6604	12/27/2004	08/01/2004	Follow-up Sponsor: The investigator considers that the spinal cord tumor is "probably related" to the study product. The sponsor assesses the relationship as unclassifiable since the blind is not broken. Further information pending.
6503	11/15/2004	06/11/2004	Follow up Investigator: Subject underwent a second MRI - results are pending.
6583	12/17/2004	06/11/2004	Follow-up Investigator: Biopsy specimen results. The primary lesion was a malignant melanoma of 8mm thickness and only one axillary lymph node was positive for malignancy.
6582	12/17/2004	06/11/2004	Follow up Investigator: Subject was admitted to hospital for total knee replacement surgery.
6624	12/27/2004	06/11/2004	Follow up Investigator: Subject had two follow-up MRI which showed a decrease in the brain lesion. The etiology of the lesion is unclear but the consensus among the physicians involved is that the brain lesion does not represent cancer and a follow-up MRI will be performed at a later date. The event was considered "resolved with persistent damage" since the mass is still present in the brain.
6602	12/27/2004	06/11/2004	Follow-up Sponsor: This report notes that the second MRI showed a brain mass. The Investigator stated that the lesion was probably a brain metastasis from the previously diagnosed melanoma and considered it "possibly related" to the investigational agent.
6625	01/14/2005	06/11/2004	Follow up Investigator: The screening and baseline laboratory values for the subject were provided. Results for Hepatitis C antibody, Hepatitis B surface antigen and HIV were negative.
6504	11/15/2004	10/07/2004	Subject was hospitalized for two days for worsening angina approximately one month before the site called to schedule the 18 month follow-up visit. Details of the hospitalization were not available to the research site at the time of this report, so the event was considered "possibly related."
6505	11/15/2004	09/13/2004	Subject had cholecystectomy at outside hospital two months prior to the 18-month follow-up visit. Event considered "possibly related" because no medical records of the event were available to the research center at the time of this report.
6626	01/14/2005	09/23/2004	Follow up Investigator: After evaluating prior test and scan results, several physicians considered that the subject's weakness was not related to a previously diagnosed brain mass. Additional recent MRI of the neck region showed multi-level degenerative changes and foraminal narrowing. Motor nerve conduction tests showed evidence of inflammatory polyneuropathy and electrodiagnostic evidence of acute degeneration in several muscles. Amyotrophic Lateral Sclerosis was considered a possibility. HTLV I/II tests were negative.

6623	01/14/2005	09/23/2004	Subject was diagnosed with melanoma approximately 14 months after dosing with blinded investigational agent. Prior MRIs one and two months prior showed a decrease in in the size of a brain lesion. Subject's present condition is progressively worsening requiring continuous use of a cane or walker.
6633	01/21/2005	2005	Notification that the subject expired at home. No details were available at the time of this report.

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
6601	12/27/2004	12/16/2004	Subject had a nonmalignant growth found on colonoscopy 195 days after the last dose of blinded study agent. The subject was referred to a surgeon. The Investigator considered this event "possibly related" to the investigational agent.

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
6565	12/10/2004	2004	Follow up Sponsor: Emergency room medical notes and pathology reports provided. Chronology of events as reported by the Investigator included. Death certificate pending.
6572	12/15/2004	2004	Follow up Sponsor: Death certificate states esophageal cancer as primary cause of death. No other causes or contributing causes were listed on the death certificate.

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
6544	12/03/2004	10/20/2004	Follow up Sponsor: Subsequent to the inadvertant seven-fold dosing, the Sponsor submitted a copy of the corrective action plan.
6590	12/20/2004	10/20/2004	Follow-up Sponsor: Subject's platelet count normalized with values reported out to one-month post-cessation of oral steroids. Additional laboratory parameters, including liver transaminases, were unremarkable.

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
6492	10/19/2004	09/19/2004	Follow up Investigator: Medical records were provided.
6511	11/18/2004	09/19/2004	Follow up Investigator: Subject tested negative for viral hepatitis A, B, and C.
6527	11/24/2004	10/08/2004	Follow up Sponsor: Copies of the Certificates of Analysis on the investigational agents provided. All release criteria were met.
6500	11/15/2004	10/15/2004	Follow up Investigator: Subject's liver enzymes are within normal limits.
6531	11/24/2004	10/15/2004	Follow up Sponsor: Copies of the Certificates of Analysis for the investigational agents provided. All release criteria were met.
6490	11/05/2004	07/04/2004	Follow up Investigator: Medical records provided.
6530	11/24/2004	07/04/2004	Follow up Sponsor: Copies of the Certificates of Analysis for the investigational agents provided. All release criteria were met.
6491	11/05/2004	10/29/2004	Follow up Investigator: Medical records provided.
6513	11/18/2004	10/29/2004	Follow up Investigator: Hepatitis panel results were negative. Hepatitis B surface antibody results were positive, consistent with a prior immunization.
6529	11/24/2004	10/29/2004	Follow up Sponsor: Copies of the Certificates of Analysis for the investigational agents provided. All release criteria were met.
6591	12/20/2004	10/29/2004	Follow up Investigator: Lab tests performed approximately six weeks after discharge showed normalization of liver function (tests were for enzymes AST and Alk Phos). One enzyme test (ALT) remained mildly elevated but the research participant was asymptomatic.

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
6528	11/09/2004	10/10/2004	Follow-up Sponsor: The subject continues to receive dialysis and plasmaphoresis as an outpatient but the TTP was considered to be resolved with sequelae and the myocardial infarction was considered resolved. At the follow-up visit the subject reportedly looked well.