
**Gene Transfer Safety Assessment Board
Adverse Event Report
NIH Office of Biotechnology Activities
December 2012**

Protocol Number: 906

Protocol Title: **Randomized Phase II Trial of a DNA Vaccine Encoding Prostatic Acid Phosphatase (pTVG-HP) versus GM-CSF Adjuvant in Patients with Non-Metastatic Prostate Cancer**

DocID#	Receipt Date	Event Description
11554	09/06/2012	Subject had received a total of six injections of either the gene transfer agent or placebo. About three weeks after the most recent injection, the subject was admitted to the hospital due to flu-like symptoms. Subject recovered and no source of infection found. Subject may have had a viral infection but a possible relationship to the study agent cannot be ruled out.

Protocol Number: 985

Protocol Title: **A Phase I Trial of Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19**

DocID#	Receipt Date	Event Description
11605	10/24/2012	Subject who is a 55+ year-old male with relapsed acute lymphocytic leukemia, developed high-grade fevers approximately two days after last dose of the anti-CD-19 engineered T-cells and developed fluid responsive hypotension (low blood pressure). Subsequently, the subject had a marked decline in mental status. Subject was transferred to the intensive care unit (ICU) for further care, including intubation (breathing tube) for airway protection due to the altered mental status. Four days later the subject had a seizure and was started on anti-convulsants and seizure activity stopped. The breathing tube was removed and the subject was transferred out of the ICU. A MRI of the brain demonstrated no evidence of acute infarct, hemorrhage or mass. Subject improved clinically and was discharged in stable condition.

Protocol Number: 1037

Protocol Title: Phase I/II Study of Metastatic Melanoma Using Lymphodepleting Conditioning Followed by Infusion of Tumor Infiltrating Lymphocytes Genetically Engineered to Express IL-12

DocID#	Receipt Date	Event Description
11598	10/18/2012	Subject had metastatic disease with previous collapse of the lung and endobrachial laser treatment of a lung mass about a month prior to enrollment. About two weeks after receiving the engineered T cells he developed difficulty breathing and required supplemental oxygen and was admitted to the intensive care unit (ICU). In addition to the breathing problems, the subject developed liver problems with an increase in bilirubin to > 12 (upper limit of normal 1.2). Subject also developed kidney failure and had renal replacement therapy (continuous veno-venous hemofiltration). Subject improved but remained in the ICU at the time of this report.

Protocol Number: 1060

Protocol Title: Phase 1b Open Label, Single Arm, Multicenter Trial to Evaluate the Safety, Tolerance, Response Rate and Immunological and Other Biological Effects of Repeated Intratumoral Injections of Ad-RTS-IL-12 Vector Engineered to Express hIL-12 in Response to an Oral Activator Ligand, Both Administered in Intra-Patient Escalating Doses in Patients With Unresectable Stage III C or IV Malignant Melanoma

Extension Study: An Open-Label Extension Study of Ad-RTS-hIL-12, an Adenovirus Vector Engineered to Express hIL-12, in Combination with an Oral Activator Ligand, in Subjects Who Completed Protocol ATI001-101 with Evidence of Ongoing Clinical Benefit" (ATI001-101-EXT)

DocID#	Receipt Date	Event Description
11594	10/04/2012	Three days after receiving the gene transfer agent and the activator drug, the subject developed fever, mental status changes and low blood pressure requiring hospitalization. Subject's condition worsened and she died likely due to sepsis. Blood cultures grew vancomycin resistant enterococcus. Subject had recently completed a course of steroids for colitis caused by ipilimumab therapy.

Protocol Number: 1064

Protocol Title: Phase I/II Study: Direct CNS Administration of a Replication Deficient Adeno-Associated Virus Gene Transfer Vector Serotype rh.10 Expressing the Human CLN2 cDNA to Children with Late Infantile Neuronal Ceroid Lipofuscinosis Using a Modified Administration Method.

DocID#	Receipt Date	Event Description
11600	10/17/2012	Update provided on subject's most recent MRI, in which changes seen at six months have resolved. For background on these events, see the March 2012 meeting of the RAC. http://oba.od.nih.gov/oba/RAC/meetings/mar2012/RAC_Minutes_03-12.pdf .
11615	10/22/2012	Approximately 114 days post vector, subject's Month 3 follow-up visit was completed by the child's local physician. The doctor noted dystonic posturing of hands. This serious adverse event is considered unexpected, possibly related to the study drug, and unlikely related to the study procedures. Subject's neurologist stated that the event would be observed for now. No changes were made in medications. Dystonia is considered unexpected because it is not listed in the protocol or consent form as a risk, however, it is an expected complication of disease progression. Informed consent has been amended.
11620	11/16/2012	The first subject to receive the lower dose of the study drug developed diffusion changes on the Month 12 follow-up MRI. The subject was asymptomatic. The significance of these changes on imaging with no apparent clinical effect is not clear. For a discussion of similar events on this protocol, please see a presentation by the sponsor at the March 7, 2012, meeting of the Recombinant DNA Advisory Committee Meeting. http://oba.od.nih.gov/oba/RAC/meetings/mar2012/RAC_Minutes_03-12.pdf

Protocol Number: 1120

Protocol Title: A Phase 1 Ascending Dose Trial of the Safety and Tolerability of Toca 511, a Retroviral Replicating Vector, Administered to Subjects at the Time of Resection for Recurrent High Grade Glioma and Followed by Treatment with Toca FC, Extended-Release 5-FC

DocID#	Receipt Date	Event Description
11611	10/12/2012	Subject developed fevers and weakness about two weeks after intracranial administration of this replication competent retroviral vector. Testing for the virus in the blood did reveal RNA from the virus. The level was higher than other subjects but quickly declined and the subject went on to receive the protocol chemotherapy (5-FU) and recovered. For more information on this event see March 2012 RAC meeting. http://oba.od.nih.gov/oba/RAC/meetings/mar2012/RAC_Minutes_03-12.pdf
