
**Gene Transfer Safety Assessment Board
Adverse Event Report
NIH Office of Biotechnology Activities
December 2013**

Protocol Number: 776

Protocol Title: Phase I Study of CD19 Chimeric Receptor Expressing T Lymphocytes in B-Cell Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia (CRETI-NH)

DocID#	Receipt Date	Event Description
	08/27/2013	The subject who had mantle cell lymphoma, underwent an autologous stem cell transplant about 40 days prior to infusion of anti-CD19 T cells. Six days after the infusion of the T cells, subject developed fevers and received antibiotics but fever continued and subject was admitted for antibiotics. All cultures were negative except for a low level Herpes Simplex Virus (HSV) serum Polymerase Chain Reaction (PCR). Subject also received steroids and fevers abated within several hours. Subject recovered. While this event could be due to the fact that subject was still immunosuppressed from the transplant, because of the timing of the event, it is difficult to definitively rule out a role for the T cells.

Protocol Number: 793

Protocol Title: Pilot Study of Redirected Autologous T Cells Engineered to Containing Anti-CD19 Attached to TCR ζ and 4-1BB or CD28 Signaling Domains in Patients with Chemotherapy Resistant or Refractory CD19+ Leukemia and Lymphoma

DocID#	Receipt Date	Event Description
11853	05/28/2013	After infusion of gene modified T cells, the subject had low grade fevers and slight fatigue. Subject was monitored for several hours and temperature continued to rise to 101° F. All other vital signs were stable. Subject was admitted for management of fevers. The subject recovered.
11854	05/28/2013	Subject was admitted to the hospital approximately 22 months after the last infusion of gene modified CART-19 T cells. Subject presented with chills and moderate fever. Subject was diagnosed with pneumonia, received antibiotics and recovered.
11855	05/28/2013	<p>Subject received 10% of the total planned dose of CAR CD-19 specific T cells. The next evening the subject reported a fever and the remaining dose of CAR CD-19 specific T cells were not infused. The subject reported chills and fever and was told to go to the emergency room.</p> <p>The subject was admitted for moderate fever and mild chills. Subject was neutropenic (low white blood cell count) and started on prophylactic antibiotics. Subject was worked up for infection versus cytokine release syndrome. Serum levels of D-dimer and ferritin started to increase in a few days, consistent with low grade disseminated intravascular coagulation (DIC) and subject continued to have high fevers.</p> <p>Two days later, subject became short of breath and hypoxic (low blood oxygen levels) and developed some hypotension (low blood pressure). Tocilizumab (an antibody against IL-6 receptor) was administered. The subject was transferred to the intensive care unit (ICU) for further observation and management of severe hypoxia.</p> <p>One hour post administration of tocilizumab, the subject's temperature was within normal limits for the first time in 24 hours, systolic blood pressure was within normal limits and oxygen requirement decreased. A few days later, the subject again developed a fever, and the blood pressure dropped to ~70/40. Levophed (a medicine to increase blood pressure) was started.</p> <p>Labs revealed elevated serum LDH and serum ferritin levels with low haptoglobin. Subject received methylprednisolone and by the next morning, subject's blood pressure was normal, the subject was afebrile, and the serum ferritin decreased.</p> <p>Subject was transferred to the oncology floor, to recover from hemophagocytic lymphohistiocytosis (HLH) and DIC and continued on oxygen.</p>
11856	05/28/2013	Approximately 11 hours post T cell infusion, the subject developed severe fevers and was admitted to the hospital for observation and management. Subject became mildly hypotensive (low blood pressure) and hypoxic (low blood oxygen level) requiring 100% oxygen. Subject was transferred to the intensive care unit for better management. Subject's chest X-ray suggested pulmonary edema. Subject's condition improved, but subject continued to spike fevers, despite acetaminophen. Subject ultimately returned to baseline on antibiotic therapy.

- 11857 05/28/2013 In the evening after the first 10% of the planned dose of the gene modified T cells, subject reported a fever, and the 30% and 60% of CAR CD-19 specific T cell doses were not infused.
- Approximately two months after the subject received the first dose of the CAR CD-19 specific T cells, the subject presented to an outside hospital with a moderate fever and chills. There were no complaints of cough, shortness of breath, upper respiratory infection symptoms, nausea, vomiting, diarrhea, abdominal pain, rash or urinary symptoms.
- The physician noted that the subject continued to have pancytopenia, neutropenia and increased blood transfusion requirements. The subject was transferred to the trial site hospital and was worked up for possible infection, but fevers continued and no source of infection was found.
- Subject continued to receive antibiotics, and white blood cell counts returned to normal. Subject continued to be transfusion dependent.
- Subject was discharged to home.
- 11858 05/28/2013 Subject received 10% of the planned dose of CAR CD-19 specific T cells. Subject reported fever of 100.5° F and was instructed to go to the emergency room, given underlying neutropenia due to recent chemotherapy. Subject was admitted, but remained afebrile during the initial admission. Subject received the next 30% dose of CAR CD-19 specific T cells and developed a fever that evening and did not receive the remaining 60% dose of CAR CD-19 specific T cells. Subject continued as inpatient, received antibiotics and was discharged home in a few days.
- 11859 05/28/2013 Approximately two months after the last dose of CAR CD-19 specific T cells, subject underwent a CT-guided lymph node biopsy of an abdominal mass. Cytology was non-diagnostic for malignancy. Research samples showed chronic lymphocytic leukemia (CLL) and no evidence of CAR CD-19 specific T cells. Subject reported low grade fevers and chills after biopsy.
- Subject was then admitted to a different hospital with high fevers, rigors, and difficulty breathing. Subject received antibiotics and acetaminophen. A CT scan, chest X-ray and cultures were negative with no evidence of obvious infection. Blood counts (neutrophils and lymphocytes) started to drop, while serum liver enzyme levels tripled since admission. Subject developed progressive leukopenia (low white blood cell counts) and thrombocytopenia (low platelet counts).
- Subject was transferred to trial site hospital, and continued to have persistent fevers. Blood pressure was stable, but subject had tachypnea (increased respiratory rate) and low pulse oximetry (blood oxygen levels) of 92% on room air. Subject's respiratory status worsened, and subject was sent to the intensive care unit (ICU) and was intubated. Serum ferritin level was elevated and subject developed symptoms consistent with cytokine release syndrome. The next day, subject was treated with tocilizumab (antibody against IL-6 receptor). After receiving tocilizumab, overall status began improving. Subject's hospital course was complicated by acute kidney failure which required hemodialysis.
- While inpatient, subject had a CAT scan, bone marrow biopsy and peripheral blood for research. Flow cytometry showed "essentially no B cells, unremarkable T cells, and NK cells. There is no immunophenotypic evidence of a clonal lymphoproliferative disorder. CAT scan revealed dramatic improvement of mediastinal and axillary lymphadenopathy since the prior study. Bone marrow biopsy showed mildly hypocellular marrow with tri-lineage hematopoiesis and no evidence of involvement by chronic lymphocytic leukemia/lymphoma.
- Subject was transferred out of the ICU, extubated and was discharged home.

- 11860 05/28/2013 Approximately three days after subject received 10% of the total dose CAR CD-19 specific T cells, subject was admitted to the hospital for high fevers (up to 101°F), respiratory complications requiring intubation, and increased serum ferritin level. Treated with tocilizumab, with improvement and discharged.
- One month after the last dose of CAR CD-19 specific T cells, subject presented with reported fevers (up to 103°F), shaking chills and a diffuse rash covering most of the skin (except face) (legs, abdomen, trunk, and arms), after having a CT scan with contrast dye during the day.
- Subject was seen in clinic, and at the time was afebrile. Labs showed elevated white blood cell count. Subject admitted for fevers, rash, diarrhea and to monitor for possible cytokine release syndrome. Subject was worked up for infection and no sources of infection were found. The fever resolved without intervention in 1-2 days after admission. The rash persisted. Subject was discharged to home.
- 11863 05/28/2013 Subject received 10% of the planned total dose of CAR CD-19 specific T cells. The following day, prior to the next 30% of the planned total dose of CAR CD19 T cells, subject complained of nausea and reported a fever overnight. Intravenous fluids and anti-emetics were ordered. While receiving intravenous (IV) fluids, subject became hypotensive (low blood pressure). Subject was relatively asymptomatic, but had sustained hypotension.
- Subject was taken to emergency room and eventually admitted to the trial site hospital. Subject remained hypotensive despite IV fluids and was transferred to the intensive care unit (ICU) for blood pressure support. While in the ICU, fevers returned. Within four days, blood pressure became stabilized and subject was transferred out of ICU.
- Fevers continued and subject experienced tachypnea (increased respiratory rate). Serum ferritin and C-reactive protein (CRP) levels began to rise. Tocilizumab (anti-IL6 receptor antibody) was administered on day 9 post-infusion of T-cells. Fevers responded to tocilizumab, but tachypnea and bronchospasm continued. Subject was given methylprednisolone to help relieve bronchospasm on day 11 post-infusion of T-cells. Ferritin and CRP levels trended down and blood pressure returned to baseline. Subject was also pancytopenic (low white and red cell counts as well as platelets) and required platelet and packed red blood cells transfusions. Cytokine release syndrome and hemophagocytic lymphohistiocytosis / macrophage activation syndrome were suspected as the cause of subject's symptoms.
- 11869 05/28/2013 Subject developed fevers five days post-infusion of the 30% fraction of the planned dose of CAR CD-19 specific T cells. Subject was admitted to hospital and treated with broad spectrum antibiotics. Labs showed neutropenia (low white blood cell counts). Subject was clinically stable upon admission and vital signs were within acceptable limits, without the need for supplemental oxygen.
- 11870 05/28/2013 Six days after the initial infusion (10%) of the planned total dose of CAR CD-19 specific T cells, the subject developed fevers and myalgias and was admitted to the hospital. Subject was treated with broad spectrum antibiotics. Subject was clinically stable upon admission and vital signs were within acceptable limits without the need for supplemental oxygen.
- Subject experienced high fevers for almost two weeks and some confusion for three day was which was attributed to fever and the T cells. Magnetic resonance imaging (MRI) of the brain was within normal limits and the confusion fully resolved.
- The following adverse events also occurred during this hospital admission: elevated serum ALT, AST, bilirubin, ferritin and LDH. All resolved.
- 11871 05/28/2013 Approximately ten days after infusion of CAR CD-19 specific T cells, subject developed a fever without any other symptoms or complaints. Subject was admitted to the hospital and treated with broad spectrum antibiotics. Subject was clinically stable and vital signs were within acceptable limits without the need for supplemental oxygen. Subject was neutropenic (very low white blood cell count).
- Subject's next dose of CART-19 T cells (30% fraction) was held.

11872	05/28/2013	<p>Subject was two days post-infusion of the 30% fraction of CAR CD-19 specific T cells at the time of these events and tolerated the infusion well and without incident.</p> <p>Subject was admitted for pain and fever. Pain was localized mostly to back and feet, and some intermittent abdominal pain. Subject experienced mildly increased heart rate and hypertension (increased blood pressure), likely secondary to pain. Subject was otherwise, clinically stable.</p>
11873	05/28/2013	<p>Approximately two months after the last dose of CAR CD-19 specific T cells, this pediatric subject underwent a CT-guided lymph node biopsy of an abdominal mass. Cytology was non-diagnostic for malignancy. Research samples showed chronic lymphocytic leukemia (CLL) and no evidence of CAR CD-19 specific T cells. Subject reported low grade fevers and chills after biopsy.</p> <p>Subject was then admitted to a different hospital with high fevers, rigors, and difficulty breathing. Subject received antibiotics and acetaminophen. A CT scan, chest X-ray and cultures were negative with no evidence of obvious infection. Blood counts (neutrophils and lymphocytes) started to drop, while serum liver enzyme levels tripled since admission. Subject developed progressive leukopenia (low white blood cell counts) and thrombocytopenia (low platelet counts).</p> <p>Subject was transferred to trial site hospital, and continued to have persistent fevers. Blood pressure was stable, but subject had tachypnea (increased respiratory rate) and low pulse oximetry (oxygen saturation) of 92% on room air. Subject's respiratory status worsened, and subject was sent to the intensive care unit (ICU) and was intubated. Serum ferritin level was elevated and subject developed symptoms consistent with cytokine release syndrome. The next day, subject was treated with tocilizumab (antibody against IL-6 receptor). After receiving tocilizumab, overall status began improving. Subject's hospital course was complicated by acute kidney failure which required hemodialysis.</p> <p>While inpatient, subject had a CT scan, bone marrow biopsy and peripheral blood for research. Flow cytometry showed "essentially no B cells, unremarkable T cells, and NK cells". There was no immunophenotypic evidence of a clonal lymphoproliferative disorder. CT scan revealed dramatic improvement of mediastinal and axillary lymphadenopathy since the prior study. Bone marrow biopsy showed mildly hypocellular marrow with tri-lineage hematopoiesis and no evidence of involvement by chronic lymphocytic leukemia/lymphoma.</p> <p>Subject was transferred out of the ICU, extubated and was discharged home.</p>
11874	05/28/2013	<p>This pediatric subject with acute lymphoblastic leukemia had an umbilical cord blood transplant on another trial. Subject had infusion of 10% of the total planned dose of CAR CD-19 specific T cells and tolerated infusion well and without incident. Subject was seen in clinic for follow-up and was feeling well, which continued throughout the weekend. Subject had an occasional cough without respiratory distress for approximately one week prior to this hospital admission.</p> <p>Nine days after CAR CD-19 specific T cells subject developed fevers and was admitted to the hospital. The family reported that a sibling had an apparent viral upper respiratory infection recently. Subject was reported to have had intermittent abdominal pain and lower extremity myalgias, but no associated rhinorrhea (runny nose), nasal congestion, emesis (vomiting), diarrhea or rash. Subject was otherwise clinically stable during this admission. Blood cultures during the admission were negative.</p>
11875	05/28/2013	<p>Subject received the 10% of the total proposed dose of CAR CD-19 specific T cells hours prior to this event. Subject tolerated the infusion well and without incident. However, hours after returning home, developed a fever and was admitted to the hospital for observation and antibiotics were begun. Subject appeared well and was clinically stable on admission.</p> <p>No source of infection was found and subject recovered and was discharged.</p>

11876 05/28/2013 Subject was four days post-infusion of the 10% of the proposed total dose of the investigational CAR CD-19 specific T cells as of this event. Subject tolerated the infusion well and without incident.

Subject was previously admitted to the hospital for fevers and was discharged. Subject was seen for follow-up visit in clinic and was feeling well.

Within 48 hours of receiving the T cells, the subject was admitted to the hospital with fever, chills, decreased activity and decreased oral intake. Since admission, subject was intermittently febrile with fevers as high as ~104° F. Subject was otherwise clinically stable during the hospital stay. No source of infection identified.

Protocol Number: **940**

Protocol Title: **Assessment of the Safety and Feasibility of Administering T cells Expressing an anti-CD19 Chimeric Antigen Receptor to Patients with B cell Lymphoma or Leukemia**

DocID#	Receipt Date	Event Description
11918	09/19/2013	<p>On day four after administration of the CAR CD-19 specific T cells, subject began exhibiting mild confusion and difficulty finding words. Neurology was consulted, and subject was transferred to the intensive care unit (ICU) for close neurological monitoring.</p> <p>By the next morning, the subject's word finding and speech worsened. Magnetic resonance imaging (MRI) of brain and cerebral spinal fluid (CSF) testing (via an Ommaya reservoir) was performed, but no cause for subject's neurological symptoms were identified. Subject was treated with a single dose of tocilizumab (anti-IL-6 receptor antibody) as an attempt to halt the neurologic process.</p> <p>Because of concerns about impaired swallowing of liquids, subject's oral intake of food and liquids was restricted. In approximately two days, the speech difficulties improved and subject was able to complete parts of an extensive neurological examination. The following day, the subject seemed to become more confused, possibly suggestive of intensive care unit psychosis and also began complaining of some abdominal pain.</p> <p>A computed tomography scan of abdomen was suggestive of colitis (inflammation of colon) and the subject was treated with metronidazole. Subject recovered and was able to sit up in a chair. Subject continued to have some difficulties with speech, but response to commands improved.</p> <p>The subject began recovering significant neurological function and was discharged home with essentially full baseline function.</p>

Protocol Number: **1013**

Protocol Title: **A Phase III Study of Chemotherapy and Chemoradiotherapy With or Without HyperAcute®-Pancreas (Algenpantucel-L) Immunotherapy in Subjects With Surgically Resected Pancreatic Cancer**

DocID#	Receipt Date	Event Description
11984	11/12/2013	<p>Subject developed a diffuse rash, shortness of breath and a sensation of difficulty clearing her throat the morning following dosing of study agent. Subject was seen in the emergency room and treated for anaphylactic reaction (severe allergic reaction). Subject was discharged on histamine blockers and steroids but was readmitted for similar symptoms within 24 hours. Subject was again treated and recovered. Of note, subject had a history of allergies to several drugs as well as latex. Subject withdrew from study.</p>

Protocol Number: 1049

Protocol Title: Phase 1/2 Open-Label, Multiple-Dose, Dose-Escalation Study to Evaluate the Safety and Tolerability of SNS01-T Administered by Intravenous Infusion in Subjects with Relapsed or Refractory Multiple Myeloma, Mantle Cell Lymphoma, or Diffuse Large B Cell Lymphoma

DocID#	Receipt Date	Event Description
11847	08/28/2013	<p>Subject experienced acute kidney injury (after completing first infusion of study agent), which required hospitalization.</p> <p>Two hours after completion of the infusion of study drug, subject developed an infusion reaction characterized by rigors and fever. Subject was treated with hydrocortisone, acetaminophen and meperidine. The investigator had planned to admit the subject to the hospital overnight for observation due to the expected infusion reaction, based on experience with another subject at this dose level. In the hospital, serum creatinine (a measure of kidney function) was elevated compared to screening and baseline. Subject was given intravenous fluids and creatinine returned to baseline.</p> <p>The subject was discharged from the hospital the next day. The subject was also noted to have a low platelet count and the second scheduled treatment with study drug was held for 24 hours until the platelet count was improved. The subject received his second dose of study treatment and remains on study.</p> <p>The event of acute kidney injury was unexpected and possibly related to study drug.</p>

Protocol Number: 1056

Protocol Title: A Phase I, Dual, Cohort, Two Site, Clinical Trial Evaluating the Safety and Activity of Redirected Autologous T-cell Expressing a High Affinity TCR Specific for MAGE-A 3/6 or NYESO-1 Administered Post ASCT in Patients With Advanced Myeloma

DocID#	Receipt Date	Event Description
11992	11/13/2013	<p>Approximately two months after the modified T cells were infused, subject developed fever (in the setting of low white blood cell count), diarrhea and tingling around the mouth that was found to be due to a low serum calcium level. The persistent diarrhea was likely due to chemotherapy or graft-versus-host disease triggered by modified T cells leading to low serum electrolytes.</p> <p>Labs showed low calcium, magnesium, and potassium levels, likely due to diarrhea. Neutropenia (low white blood cell count) was likely related to chemotherapy, but the modified T cells could also cause graft-versus-host disease and diarrhea, leading to low serum electrolytes.</p>
11889	04/17/2013	<p>Subject received autologous stem cell transplant followed by chemotherapy, and steroids to prevent graft versus host disease. The following day, subject received the gene modified T cell infusion. One week later the subject developed diarrhea. Subject underwent a colonoscopy and was diagnosed with graft-versus-host disease of the gastrointestinal tract possible related to the T cells.</p>

Protocol Number: 1060

Protocol Title: A Phase I/II, Open Label Study of Ad-RTS-hIL-12, an Adenovirus Vector Engineered to Express hIL-12, in Combination with an Oral Activator Ligand, in Subjects with Unresectable Stage III or IV 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
11986	11/08/2013	Two days after the first injection of the gene transfer agent and receipt of the activator drug, the subject was seen in clinic and reported low blood pressure, chills, fever and fatigue. These symptoms led to admission to the hospital. Subject was found to have low white blood cell counts and elevated serum liver enzymes. Subject recovered and was discharged but was removed from the study.
11961	10/17/2013	Shortly after receiving the gene transfer agent (with the activator drug), subject experience low grade fever, generalized weakness, lightheadedness and confusion and was admitted to the hospital. It was noted that subject was on narcotic pain medications and received additional narcotic therapy before the intratumoral injection, which may have contributed to the symptoms. The subject recovered with oral hydration, intravenous fluids and anti-pyretics (to lower tremor). No infection or other etiology for the confusion was found.
11979	11/06/2013	Subject developed low grade fever and delirium shortly after starting the fourth cycle of study drug. Subject was hospitalized and found to have anemia and hyponatremia (low serum sodium). Subject was treated with intravenous fluids, anti-pyretics, and transfusions. Subject was transferred to a rehabilitation facility. Subject was then readmitted about a week later with hypercalcemia (high calcium level) likely due to known bone metastases, which improved after intravenous fluids.

Protocol Number: 1101

Protocol Title: A Randomized, Double-blind, Phase 3 Efficacy Trial of PROSTVAC ± GM-CSF in Men With Asymptomatic or Minimally Symptomatic Metastatic, Castrate-Resistant Prostate Cancer

DocID#	Receipt Date	Event Description
11989	11/12/2013	Two days after the last dose of blinded study drug (i.e. gene transfer agent or placebo) the subject experienced chest pain, diaphoresis (sweating) and fatigue. Later that day, the subject was seen at an urgent care facility due to shortness of breath, severe leg and back pain, weakness (fever), and complained of generalized body aches. Subject was admitted to cardiac monitoring unit and an acute myocardial infarction / ischemia was ruled out. Subject's symptoms resolved by the next day and subject was discharged. Subject was taken off the study due to this event.
11988	11/12/2013	Approximately two weeks after receiving the first dose of study drug, the subject was admitted to the hospital with weakness of legs after a fall at home. In the emergency department, subject was noted to have tachycardia (rapid heart rate), fever, dizziness and shaking. The heart rhythm was noted to be abnormal and subject was diagnosed with atrial flutter (a rapid heart beat). Subject was treated with antibiotics and it was found that one of his cardiac medications was recently stopped for an unknown reason. The cardiac medication was restarted and the rapid heart beat resolved. Subject was discharged home the next day after admission to the hospital.

Protocol Number: 1108

Protocol Title: A Phase 2b Randomized Open-Label Trial of JX-594 (vaccinia GM-CSF/TK-deactivated virus) Plus Best Supportive Care Versus Best Supportive Care In Patients With Advanced Hepatocellular Carcinoma Who Have Failed Sorafenib Treatment (TRAVERSE)

DocID#	Receipt Date	Event Description
11846	08/27/2013	Subject developed ascites (fluid in the abdomen) and blood clots in the inferior vena cava and the right atrium of the heart about 20 days after the third intratumoral dose. A large volume of fluid was removed from the abdomen (paracentesis). While the gene transfer agent and delivery procedure may have been contributory, the subject had also developed progression of disease. The right heart clot was removed by interventional radiology and pathology of the excised blood clot confirmed metastatic disease originating in subject's primary hepatocellular carcinoma.
11880	09/06/2013	Subject developed nausea and vomiting after the third intratumoral administration of the gene transfer agent. Symptoms prolonged the hospitalization but resolved with supportive treatment.
11878	09/06/2013	In the evening after the intratumoral administration of study drug, the subject experienced nausea and vomiting. Treatment included a proton pump inhibitor. The investigator reported the serious adverse event as vomiting. The subject did not feel well enough to be discharged home and, therefore, hospitalization was prolonged for continued treatment. The subject's condition improved and the subject was discharged in stable condition.
11877	09/06/2013	About five hours after intratumoral (IT) injection of the study drug, the subject had hypotension (very low blood pressure) and a fever, which started on the same day. Subject was treated with intravenous norepinephrine to raise the blood pressure. The subject received antibiotics for possible infection. The subject's vital signs stabilized and supportive care was continued. There were no signs of bleeding observed during or after IT administration. The event of hypotension resolved. The fever resolved and subject was discharged from hospital on the same day.
11976	11/04/2013	Approximately one hour after intratumoral (IT) administration of study drug, the subject experienced hypertension (blood pressure increased) to 160's/110's mmHg but later that same evening subject had hypotension (low blood pressure) to 80's/50's mmHg. The subject also had a fever on the same day. The subject was treated with intravenous fluids, vasopressors (dopamine and norepinephrine), and antibiotics for possible infection. The subject's vital signs returned to normal and supportive care was continued. The event of hypotension resolved the next day and the subject was discharged home in stable condition about one week after the event.

Protocol Number: 1118

Protocol Title: Phase I, open label, dual cohort, triple center clinical trial evaluating the safety and efficacy of autologous T cell expressing enhanced TCRs specific for Mage-A3/6/B18 or NY-ESO-1/LAGE in patients with recurrent or treatment refractory ovarian cancer

DocID#	Receipt Date	Event Description
11933	09/20/2013	<p>Two days after the first infusion of the gene modified T cells, and one day after the second infusion, (split dose) the subject developed rigors, sore throat, fatigue, and felt ill. The subject was admitted to the hospital and lab results showed evidence of low red blood cell counts. Subject was transfused and was treated with antibiotics. While hospitalized, subject developed additional symptoms approximately a week after the initial study drug administration, which included nausea, low blood pressure, shortness of breath, fever, rash, diarrhea, edema, and impaired renal (kidney) function. A biopsy of the rash revealed epithelium with spongiosis across basal and subbasal epidermal layers with dermal hemorrhage and patchy perivascular mononuclear cell inflammation. The differential diagnosis included dermal hemorrhage secondary to thrombocytopenia/coagulopathy or perhaps a morbilliform drug eruption.</p> <p>The subject was thought to have had cytokine release syndrome and was treated with antibiotics and steroids.</p>
11946	09/27/2013	<p>Approximately three weeks after the initial infusion of the gene modified T cells, the subject presented to the hospital due to malaise and decreased oral intake. The subject was admitted and found to be dehydrated with rapid heart rate and low blood pressure upon standing which responded to intravenous fluids. Subject was discharged the next day and had home intravenous fluid hydration for a few days.</p>

Protocol Number: 1163

Protocol Title: A Phase II, Randomized, Open Label, Parallel Arm Study to Evaluate the Safety and Efficacy of rAd-IFN/Syn3 Following Intravesical Administration in Subjects with High Grade, BCG Refractory, Relapsed or Resistant Non-Muscle Invasive Bladder Cancer (NMIBC)

DocID#	Receipt Date	Event Description
11879	09/10/2013	<p>A few hours after the first dose of the study drug, the subject experienced nausea, vomiting, abdominal pain, and increased urinary frequency. Three days later, lab results showed mild impairment of renal function. Ten days after the first dose of study drug subject complained of nausea and vomiting again during her follow up study visit and urine cultures showed that the subject had a urinary tract infection. Two days later, the subject presented to an emergency department complaining of nausea and poor oral intake. Subject was found to be dehydrated and in acute renal failure and she was admitted to the hospital. Subject was given intravenous fluids and treated with antibiotics and anti-emetics resulting in marked clinical improvement. Subject was discharged home in stable condition two days after admission to the hospital.</p>

Protocol Number: 1165

Protocol Title: A neoadjuvant immunologic study of androgen deprivation therapy combined with a GM-CSF–secreting allogeneic prostate cancer vaccine and low-dose cyclophosphamide in men with high-risk localized prostate cancer undergoing radical prostatectomy

DocID#	Receipt Date	Event Description
11928	09/20/2013	<p>Approximately one month after receiving the study drug and four days after having a radical prostatectomy, the subject experienced abdominal pain, which was not relieved by acetaminophen. At the local emergency department, CT scan showed two hematomas, a larger one under the abdominal muscles and a smaller one near the left inguinal canal. The subject was transferred to a local hospital.</p> <p>On admission, the subject was found to have gross hematuria (blood in urine) and had lower red blood cell counts than usual. Subject's pain was managed with pain medications and he was given intravenous fluids. Hematuria resolved and subject was discharged home the next day on prophylactic antibiotics. He had a follow-up visit at the urology clinic in one week and was found to be well without complaints of pain. The hematoma was most likely due to surgery, although a contributing role of the study drug could not be definitively ruled out.</p>

Protocol Number: 1172

Protocol Title: A Phase I/II Evaluation of ADXS11-001, Mitomycin, 5-fluorouracil (5-FU) and IMRT for Anal Cancer

DocID#	Receipt Date	Event Description
11825	07/30/2013	<p>Subject was admitted for hypotension (low blood pressure) and fever the day of the second dose of the gene transfer agent. The admission labs also showed that subject had a low potassium level which resolved by the next day. Subject recovered with intravenous fluids and was discharged the next day.</p>

Protocol Number: 1179

Protocol Title: A Phase I Study of an Adenoviral Transduced Autologous Dendritic Cell Vaccine Expressing Human HER2/neu ECTM in Adults with Tumors with 1-3+ HER2/neu Expression

DocID#	Receipt Date	Event Description
11993	11/14/2013	<p>Subject had metastatic colon cancer to the liver and lungs. Subject was enrolled in the gene transfer study and received four doses of the vaccine when it was noted that the serum liver tests were starting to become progressively more abnormal. At first, it was thought that this may have been due to some new herbal supplements. However, after the fifth vaccine the liver function worsened and subject died about three weeks after the fifth dose of the vaccine. While there was some concern that this could have been caused by an inflammatory reaction from the vaccine in the liver metastases, the autopsy revealed that the death was due to progression of the metastatic colon cancer.</p>