SAFETY REPORTS AND ADVERSE EVENTS FOR HUMAN GENE TRANSFER PROTOCOLS RECOMBINANT DNA ADVISORY COMMITTEE MEETING SEPTEMBER 24-25, 1998

May 21, 1998 (letter date)	**9303-038 Heslop *et al.***	**Administration of Neomycin Resistance Gene Marked EBV Specific Cytotoxic T Lymphocytes to Recipients of Mismatched-Related or Phenotypically Similar Unrelated Donor Marrow Grafts** **Adverse event:** One patient death due to relapsed secondary acute myeloid leukemia.
May 21, 1998	**9510-130 Roskrow *et al.***	**Administration of Neomycin Resistance Gene Marked EBV Specific Cytotoxic T Lymphocytes to Patients with Relapsed EBV-Positive Hodgkin Disease** **Adverse event:** One patient death due to disease progression.
June 5, 1998	**9709-214 Breau *et al.***	**A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)** **Adverse event:** Patient experienced vomiting, chills, and fever (39 C) 11 hours after receiving first dose (4 x 10^{10} pfu) of Ad5CMV-p53. Chills and fever were considered by investigator to be probably related to the study medication.
July 29, 1998	**9709-214 Breau *et al.***	**A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)** **Adverse events:** One patient experienced, on day 19 of cycle 2, and was hospitalized for dehydration, renal failure, and gastroenteritis. These events were considered by the investigator as possibly related to the study medication. An additional related trial is being conducted with Ad5CMV-p53 in Europe only. Two patients have experienced adverse events under this trial. This information has been submitted to NIH/ORDA voluntarily. 1) On day 27 after receiving drug, one patient experienced fever (39.6 C), hypotension (80/50 mm Hg), local pain grade 4, and probable septicemia. Patient was hospitalized and given antibiotics (pyperacillin and tazobactam). Event was considered by the investigator as possibly related to the study medication. 2) A second patient experienced swelling, on day 15 after receiving the study medication, in the left cheek around the mandibulae. Two days later, the patient developed dyspnea and a tracheostomy was performed. These events were considered by the investigator as possibly related to the study medication.

August 13, 1998	**9712-226 Dreicer *et al* .**	**A Phase II, Multi-Center, Open Label, Study to Evaluate Effectiveness and Safety of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 39 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)** **Adverse event:** Patient completed first course and received one injection of second course of Ad5CMV-p53. One day after first injection of second course, patient experienced an increase in tumor size that was considered to be disease progression and not due to swelling from the injection. Patient was removed from the study. Patient was hospitalized for IV antibiotics, cultures were positive for S. aureus, and abscess was drained. Two days later, patient was discharged after resolution of the infection. Infection was considered by the investigator as possibly related to the study medication.
August 18, 1998	**9709-214 Breau *et al.***	**A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)** **Adverse events:** These are follow-ups to events that were reported on July 29, 1998. Patient that experienced dehydration, renal failure, and gastroenteritis was hospitalized for over three weeks. During this hospitalization, the patient went into cardiac arrest. Cardiac arrest was not considered to be related, by the investigator, to the study medication. These two follow-ups concern the two patients being treated under the European-only trial. 1) Antibiotics given to the patient that experienced fever, hypotension, pain, and septicemia resolved the fever. Cultures were negative. The investigator now considers that the original event was due to the injections themselves and not to the study medication. 2) The dyspnea experienced by the second patient is now considered by the investigator not to be related to the study medication. The investigator believes that the event was caused by either the injection itself, the swelling, or was due to tumor progression.
August 24, 1998	**9403-069 Walker**	**A Phase I/II Pilot Study of the Safety of the Adoptive Transfer of Syngeneic Gene-Modified Cytotoxic T-Lymphocytes in HIV-Infected Identical Twins** **Adverse event:** There has been one patient death since the last continuing review. Death was due to rectal lymphoma and was considered to be remotely related to the study.