SAFETY REPORTS AND ADVERSE EVENTS FOR HUMAN GENE TRANSFER PROTOCOLS RECOMBINANT DNA ADVISORY COMMITTEE MEETING JUNE 14, 1999

February 11, 1999 (letter date)	**9804-250 Swisher**	**An Efficacy Study of Adenoviral Vector Expressing Wildtype p53 (Ad5CMV-p53) Administered Intralessionally as an Adjunct to Radiation Therapy in Patients with Non-Small Cell Lung Cancer** **Adverse event:** After second administration of Ad5-p53 patient experienced severe dehydration, inability to swallow, and esophagitis. Patient was hospitalized and given IV fluids, cilastatin/imipenem and fmotidine. Initially, investigator considered these events related to the radiation therapy. This assessment was changed to as possibly related to the study medication.
February 12, 1999	**9701-173 Croop**	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronnectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Adverse event:** Patient experienced Grade III pulmonary hypoxia and infiltrates which were considered as unlikely to be related to these transduced cells. However, the investigators state that: "Hypoxia and pulmonary infiltrates are known toxicities related to peripheral blood stem cell reinfusion."
March 15, 1999 and follow-up dated March 18, 1999	**9804-250 Swisher**	**An Efficacy Study of Adenoviral Vector Expressing Wildtype p53 (Ad5CMV-p53) Administered Intralessionally as an Adjunct to Radiation Therapy in Patients with Non-Small Cell Lung Cancer** **Adverse event:** Patient was hospitalized three days after receiving third dose of Ad5-p53 for pneumonia. Patient was treated with IV and then oral antibiotics. Pneumonia was considered as possible related to study medication.
March 21, 1999	**9705-187 Hall and Woo**	**Phase I Trial of Adenoviral-Mediated Herpes Simplex Thymidine Kinase Gene Transduction in Conjunction with Ganciclovir Therapy as a Neo-adjuvant Treatment for Patients with Clinically Localized (Stage T1c and T2b&c) Prostate Cancer Prior to Radical Prostatectomy** **Adverse event:** Patient experienced a deep vein thrombosis that was related to medical condition (cancer) and lifestyle (inactivity).
March 29, 1999	**9804-246 Yoo *et al.***	**A Multicenter Phase II Study of E1A Lipid Complex for the Intratumoral Treatment of Patients with Recurrent Head and Neck Squamous Cell Carcinoma** **Adverse event:** Patient death due to disease progression.

April 12, 1999	**9701-173 Croop**	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronnectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Adverse events:** Adverse events were reported for two different patients. One patient experienced grade III pulmonary hypoxia. The event was considered to be "...most likely related to sedation from premedications since it occurred prior to reinfusion." A second patient experienced an infection which was a complication of the central venous line. Follow-up to adverse event reported on February 12, 1999. No adverse events were observed after the second infusion for this patient. The adverse events following the first infusion were related to either the respiratory tract infection or the premedications.
May 4, 1999	**9804-246 Yoo *et al.***	**A Multicenter Phase II Study of E1A Lipid Complex for the Intratumoral Treatment of Patients with Recurrent Head and Neck Squamous Cell Carcinoma** **Adverse events:** Two patient deaths due to disease progression and not likely to be related to the study medication. A third patient underwent an endoscopy approximately two weeks after last administration of E1A lipid complex. After the procedure, the patients's oxygen saturation was 80%. Patient was placed on a ventilator and hospitalized overnight. Event is not thought to be related to the study medication.
May 11, 1999	**9804-244 Walsh**	**A Phase I Study Using Direct Combination DNA Injections for the Immunotherapy of Metastatic Melanoma** **Adverse events:** One patient was treated for dehydration. Subsequently, the patient was admitted twice for symptoms that were considered to be related to inappropriate use of pain medications. Neither the dehydration nor the pain medication management were thought to be related to the study medication. A second patient was admitted due to complications from pre-existing pulmonary conditions. These complications were not considered to be related to the study medication.