

**SAFETY REPORTS AND ADVERSE EVENTS FOR
HUMAN GENE TRANSFER PROTOCOLS
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
SEPTEMBER 2-3, 1999**

<p>May 21, 1999 (letter date)</p>	<p>9804-244 Walsh</p>	<p>A Phase I Study Using Direct Combination DNA Injections for the Immunotherapy of Metastatic Melanoma</p> <p>Adverse event:</p> <p>Patient death due to progressive disease.</p>
<p>May 26, 1999</p>	<p>9712-226 Dreicer <i>et al.</i></p>	<p>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)</p> <p>Adverse event:</p> <p>Patient was hospitalized with a urinary tract infection three days after receiving first course of three injections of Ad5CMV-p53. Event was considered by the investigator as possibly related to Ad5CMV-p53.</p>
<p>May 28, 1999</p>	<p>9712-226 Dreicer <i>et al.</i></p>	<p>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)</p> <p>Follow-up/Adverse events:</p> <p>1) In a follow-up to the event reported on May 26, the relationship of the adverse event to the study drug is now considered by the investigator as remotely related.</p> <p>In addition during hospitalization for urinary tract infection, it was noted that the patient's airway was obstructed. Investigator considered airway obstruction as remotely related to Ad5CMV-p53.</p> <p>2) A second patient experienced a grade 3 carotid bleed approximately three weeks after receiving the second injection of the first course of treatment. Event was considered by the investigator as due to disease progression and other treatments performed (surgery and radiation therapy) and unlikely to be related to Ad5CMV-p53.</p>
<p>July 8, 1999</p>	<p>9712-226 Dreicer <i>et al.</i></p>	<p>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)</p> <p>Follow-up:</p> <p>Patient that experienced the carotid artery bleed reported on May 28 experienced a second episode. Patient received a transfusion and right carotid artery was embolized; patient was taken off study. It was determined that the initial carotid artery bleed reported on May 28 was not related to Ad5CMV-p53.</p>
<p>July 12, 1999</p>	<p>9804-244 Walsh</p>	<p>A Phase I Study Using Direct Combination DNA Injections for the Immunotherapy of Metastatic Melanoma</p> <p>Adverse event:</p>

Patient was hospitalized due to a bowel mass obstruction. Patient was removed from study due to progressive disease. Obstruction was not related to study drug.