SERIOUS, POSSIBLY ASSOCIATED AND UNEXPECTED ADVERSE EVENTS
REPORTED FOR HUMAN GENE TRANSFER PROTOCOLS
REPORTING PERIOD: 08/01/01 -- 11/01/01
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
December 2001

Event	OBA Date	Event	Protocol #	Event Description
			9901-281	**Phase I/II Trial of the Safety, Immunogenicity, and Efficacy of Autologous Dendritic Cells Transduced with Adenoviruses Encoding the MART-1 and gp100 Melanoma Antigens Administered With or Without Low Dose Recombinant Interleukin-2 (rIL-2) in Patients with Stage IV Melanoma. Sponsor: Genzyme Molecular Oncology**
3952	10/11/2001	10/12/2000		Follow-up. Subject had drusen-like hypopigmentation in retinal epithelium after second vaccination. After consultation with the FDA, the subject was allowed to continue with the study. Follow-up ophthalmic exams were performed after each subsequent vaccination. The subject has completed the study and as of the last exam on September 24, 2001 the lesions were stable and there was no change in central or peripheral vision.

Event	OBA Date	Event	Protocol #	Event Description
			0001-385	**Phase I/II Study of GM-CSF Gene-Modified Autologous Tumor Vaccines in Early and Advanced Stage Non-Small Cell Lung Cancer (NSCLC). Sponsor: Cell Genesys, Inc.**
3806	08/07/2001	07/31/2001		A 48 year old male with stage IV non-small-cell lung cancer received three autologous vaccines with cells transduced with the GM-CSF gene. The total number of transduced cells per vaccine was 6.3 X 10^6 with a GM-CSF secretion of 407 ng/10^6 cells/24 hours (or 2.6 μg/dose). The last vaccine was administered on 7-17-01. The next day the subject returned to the emergency room due to lower back and sacral pain, with extension of his cancer noted in that area. While in the hospital, subject developed significant pericardial effusion with tamponade physiology, progressive respiratory distress, and after refusing mechanical ventilation, ultimately respiratory failure and death. Due to the recognized correlation of GM-CSF use and the development of pericardial effusions, the investigator deemed this adverse event as "possibly associated" with the vaccines.
3857	08/17/2001	07/31/2001		Follow-up report to #3806: Autopsy conducted and the preliminary report showed metastatic adenocarcinoma involving multiple sites, including the pericardium. The consent form will be amended to include the potential relationship between GVAX and progression of pericardial effusions. Final autopsy report due in 2-3 weeks.
3914	09/26/2001	08/30/2001		A 76 year old male with stage IB non-small-cell lung cancer received five autologous vaccines with cells transduced with the GM-CSF gene. The total number of transduced cells per vaccine was 5.8 X 10^6 with a GM-CSF secretion of 789 ng/10^6 cells/24 hours (or 4.6 μg/dose). The last vaccine was administered on 2-12-01. On 8-17-01 the subject developed fever and due to persistence of fever, development of shortness of breath and fatigue, was admitted to the hospital on 8-30-01 with a diagnosis of "fever of unknown origin" (FUO). Chest X-ray was negative for pneumonia, but a chest CT done on the second day of admission revealed a "fairly prominent" pericardial effusion with no pulmonary lesions or adenopathy. Elevations in erythrocyte sedimentation rate noted as well. Subject discharged home on 9-14-01 with a final diagnosis of FUO, but a biopsy of the temporal artery is being planned to assess the possible diagnosis of giant cell arteritis. Due to the recognized correlation of GM-CSF use and the development of pericardial effusions, the investigator deemed this adverse event as "possibly associated" with the vaccines.