

Novel immuno-gene therapy shows promise for the treatment of rare, deadly form of cancer

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(Medical Xpress) -- Researchers at the Perelman School of Medicine at the University of Pennsylvania report promising new results from a small clinical trial using an immune-system-based gene therapy for treating advanced stages of a deadly cancer, malignant mesothelioma. The treatment, immuno-gene therapy, transfers just enough genetic material from an existing virus to trigger a patient's innate defenses to destroy cancer cells. The study results, published in the December 15th issue of the *American Journal of Respiratory and Critical Care Medicine*, may lead to earlier interventions for patients using targeted therapies.

"Given our encouraging results in this trial with advanced stage patients, we believe that multimodality regimens incorporating immuno-gene therapy will have an important role in the treatment of earlier stage patients suffering from malignant mesothelioma," said the study's senior author, Steven M. Albelda, MD, William Maul Measey Professor of Medicine, and vice chief, Pulmonary, Allergy, and Critical Care Division at Penn.

In the current study, Penn researchers, led by Dr. Albelda and Daniel Sterman, MD, associate professor of Medicine, Pulmonary, Allergy, and Critical Care Division, and co-director of the of the Penn Mesothelioma and Pleural Program, tested a new gene therapy approach in which an adenovirus – a modified cold virus – was altered to express high levels of a potent immune system stimulant called interferon-alpha. Interferon-



alpha is a protein made by immune cells that can boost the body's ability to fight off viral infections and some cancers.

Nine subjects with varying stages of malignant mesothelioma were enrolled in the clinical trial. The modified <u>virus</u> was injected directly into the chest cavity containing the tumor. Antibody responses directed against the tumors were seen in almost all of the subjects. No clinical responses were seen in the four subjects with advanced disease. However, evidence of disease stability or tumor regression was observed in the remaining five patients, including one example of partial tumor regression and no major side effects were encountered.

Mesothelioma, one of the most aggressive and deadliest forms of cancer, affects the lining of the lung and is usually caused by exposure to asbestos. It affects thousands of people in the United States and many more worldwide. Current treatments are inadequate, and the cancer is invariably fatal.

"Since there are very few effective treatments for advanced mesothelioma, it is important that we were able to demonstrate radiographic and biochemical evidence of clinical anti-tumor activity in some of our patients," said Dr. Sterman, the study's lead author. "The responses seen in this pilot study, albeit anecdotal, are notable as there are no proven second or third line agents for the treatment of malignant mesothelioma."

The modified adenoviral vector, rAd.IFN-a2b, was originally developed by Merck and is now licensed to FKD Therapies Oy. This new approach is now being tested at Penn in early stage patients in combination with chemotherapy in a trial sponsored by the National Cancer Institute and the Schulze Family Foundation with the vector being supplied by FKD. Dr. Albelda and Dr. Sterman report no conflicts of interest regarding their work on the trial.



Provided by University of Pennsylvania School of Medicine

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