Alphavirus-based vaccine may slow some cancers

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An experimental vaccine based on a virus that causes encephalitis in the wild appears to block tumor growth in some cases of advanced cancer, according to researchers at Duke University Medical Center. Scientists say the vaccine is able to stimulate an immune response, even in the face of profound immune system suppression, a condition most patients with advanced cancer experience.

Scientists removed the genes that enable the Venezuelan equine encephalitis virus - an alphavirus - to replicate itself, and replaced them with genes that make the biomarker CEA, present in many malignant colon, breast and lung cells.

"Alphaviruses have been used before in designing treatments for infectious diseases, but we believe this is the first time one has been used in patients with cancer," said Michael Morse, MD, associate professor of medicine at Duke and the lead author of the study appearing online in the Journal of Clinical Investigation.

The Phase I/II study included 28 patients with advanced cases of lung, colon, breast, appendix or pancreatic cancers who had already been treated with multiple courses of chemotherapy, but whose cancers kept coming back.

Cancer vaccines, unlike traditional vaccines, are designed to boost the body's own immune system to recognize and destroy tumors, not prevent disease. Scientists often use genetically altered viruses as vaccines,

stripping the virus of any harmful parts and inserting genes related to their anticancer strategy. But in many cases, the immune system still sees the incoming virus as a foreign invader and springs into action, generating antibodies and T cells that destroy it before it has a chance to do any good.

Based on earlier research, investigators at Duke believed that by using the alphavirus for Venezuelan equine encephalitis as a carrier they might be able to thwart that response.

"The beauty of alphaviruses is that they are naturally attracted to dendritic cells, cells that stimulate the production of large numbers of T cells and antibodies," says Morse. "Essentially, we were hoping that once infected, the dendritic cells would activate T cells and antibodies to go after anything that had the tumor antigen CEA on it - in this case, the quickly growing cancer cells."

Participants received up to four injections plus booster shots of the vaccine over a period of three months. At the end of the study, two patients with no evidence of disease remained in remission; two patients were able to maintain stable disease, and one patient with pancreatic cancer saw a lesion in his liver disappear. The other patients in the trial did not respond to the therapy.

"Remember, these were patients with very advanced disease that nothing else had been able to stop," says Morse, a member of the Duke Comprehensive Cancer Center and a specialist in vaccine design. "We believe that in this small number of patients, the vaccine was able to stimulate the body's defense system to destroy significant numbers of cancer cells despite the presence of an army of neutralizing antibodies and regulatory T cells."

Morse says those who seemed to benefit the most were those who had

the smallest amount of tumor. Because of this, he says his team is planning future trials that will test the vaccine in people with cancers that have been removed, but who are high risk of recurrence. Other trials will couple the vaccine with additional immune system stimulants such as interleukin-12 that may make the vaccine more powerful.

Provided by Duke University Medical Center