



A genetically engineered virus selectively infected and killed cancer tissue without harming adjacent normal tissue, results of a phase I clinical study showed.

The altered poxvirus JX-594 invaded and replicated in cancer tissue from seven of eight patients who received the highest doses of the agent, and six of the eight had tumor shrinkage or stabilization. A transgene inside the virus exhibited dose-related expression in the infected cancer specimens.

Normal tissue was unaffected in all 23 patients who received a single intravenous infusion of JX-594, as reported in the Sept. 1 issue of *Nature*.

"This is the first time in medical history that a viral therapy has been shown to consistently and selectively replicate in cancer tissue after intravenous infusion in humans," John Bell, PhD, of the Ottawa Hospital Research Institute in Ontario, said in a statement.

"The study is also important because it shows that we can use this approach to selectively express foreign genes in tumors, opening the door to a whole new suite of targeted cancer therapies," he added.

Derived from vaccinia vaccine, JX-594 is an oncolytic virus engineered to target cancer cells that express epidermal growth factor receptor (EGFR). After the virus infects and invades

cancer cells, EGFR/Ras signaling fuels viral replication and thymidine kinase gene inactivation.

The altered virus also expresses transgenes that encode for human granulocyte-macrophage colony stimulating factor (GM-CSF). In a previous phase I study, injection of JX-594 directly into liver tumors led to viral replication, expression of biologically active GM-CSF, and tumor destruction (*Lancet Oncol* 2008; 9:533-542).

Bell and colleagues reported findings from a trial involving 23 patients with various types of treatment-refractory, advanced, metastatic solid tumors. Investigators in the multicenter dose-finding trial treated patients with one of six dose levels of JX-594 and obtained biopsy specimens eight to 10 days after treatment.

Evaluation by immunohistochemistry showed granular cytoplasmic staining consistent with viral replication. Investigators also observed evidence of diffuse infection and necrosis of malignant glandular structures. Adjacent and intermixed normal tissue exhibited no evidence of replication. Negative-control biopsy samples from the same patient showed no staining.

Among patients treated with the two highest doses of the virus, new tumor outgrowth occurred less frequently compared with patients who received lower doses ($P=0.05$). Two of five patients treated with the highest dose of JX-594 had antitumor activity by PET imaging (>25% decrease in standardized uptake value).

In general, the therapy was well tolerated. The most common adverse effects were mild flu-like symptoms that lasted no more than 24 hours, including fatigue, headache, nausea, hypotension, vomiting, tachycardia, hypertension, anorexia, and myalgia. Dose-limiting toxicities were not observed.

Source: <http://www.medpagetoday.com/HematologyOncology/Chemotherapy/28330>