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Experimental radioprotective drug safe for lung cancer patients: study

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Patients with advanced non-small cell lung cancer can safely take an experimental oral drug intended to protect healthy tissue from the effects of radiation, according to a study led by researchers at the University of Pittsburgh Cancer Institute (UPCI) and published in this month's issue of *Human Gene Therapy*.

The findings support further clinical testing of the agent, called manganese superoxide dismutase (MnSOD) plasmid liposome, to determine if giving it alongside chemotherapy and radiation will prevent damage to normal cells that is the typical cause of side effects in cancer treatment, said senior investigator Joel S. Greenberger, M.D., professor and chair, Department of Radiation Oncology, Pitt School of Medicine, and co-director of the lung and esophageal cancer program at UPCI.

"If we can sufficiently protect tissues that are normal, we should be able to deliver our cancer treatments more effectively and perhaps even at higher doses," he explained. "Our aim is to improve the quality of life of patients by minimizing side effects while providing the best treatment for their cancers."

For the safety study, 10 patients with inoperable stage III non-small cell lung cancer took oral doses of MnSOD plasmid liposome twice weekly for a total of 14 doses during seven weeks of conventional chemotherapy and radiation treatment. The agent, which boosts levels of an antioxidant the body makes naturally, is made of fat droplets containing the gene that produces MnSOD. When swallowed, it is absorbed by cells in the

esophagus, which is a common site for severe side effects during radiation treatment for lung cancer.

One patient experienced mild heartburn and a slight rash and another had mild constipation and a fluctuation in blood sodium, problems that might be associated with MnSOD treatment. No other toxicities were thought to be due to the experimental drug.

"The results of this initial trial indicate that MnSOD plasmid liposome can be safely administered," Dr. Greenberger said. "It did not linger in normal cells after treatment, nor did it protect cancer cells from radiation treatment. The next study, which is underway at UPCI, is to determine whether it protects normal tissue, particularly the esophagus, from radiation exposure."

A common toxicity of lung cancer radiation therapy is esophagitis, or inflammation of the esophagus, he explained. Within a few weeks of treatment, patients typically experience painful swallowing that over time can become so severe that narcotics or a break from radiotherapy may be necessary for patient comfort.

Preclinical testing has shown that generating higher levels of MnSOD in healthy cells can suppress the production of inflammatory molecules and reduce cell death, micro-ulceration and esophagitis. Because the agent is delivered to healthy tissue, it does not protect tumor cells from radiation treatment. In fact, Dr. Greenberger noted, experiments hint that when it is given to cancer cells, it actually encourages cell death because of abnormalities in their cellular metabolism.

He and his team plan to investigate the use of MnSOD plasmid liposome for other cancers, such as protecting the rectum from radiotherapy for prostate cancer and protecting the bladder during ovarian or endometrial cancer treatment.

Provided by University of Pittsburgh