

2.0 NON-TECHNICAL ABSTRACT

About 164,100 new cases of non-small cell lung cancer were diagnosed in the U.S. in 2000. Forty percent can potentially be cured by surgery. But many patients can only be treated with chemotherapy, radiation or both. Recently researchers have shown that the combination is better than either chemotherapy or radiation alone. In addition, it may be better to give the two types of treatment simultaneously rather than one after the other.

Although this approach has the potential to significantly increase the lifespan of people with this difficult-to-treat cancer, it can be hard for patients to take. Giving chemotherapy and radiation simultaneously in particular appears to make their effects on sensitive body tissues, especially the esophagus, more dramatic. Some patients have trouble swallowing for weeks, can lose significant weight or even be admitted to the hospital for intravenous fluids.

This clinical protocol proposes to test a gene therapy method of reducing some of the ill effects of simultaneous chemotherapy and radiation when used to treat non-operable lung cancer. A protein found in the cells of the esophageal lining called Manganese Superoxide Dismutase (MnSOD) detoxifies cells of some of the harmful byproducts of radiation and chemotherapy-induced damage. The gene for this enzyme can be transferred to cells in the esophagus with a technique that uses DNA encoding MnSOD mixed with highly purified lipids (fat molecules). The lipids help the DNA for the MnSOD gene get absorbed by the cells of the esophagus. Once inside the target cells, the gene directs the production of the protein. Inside cells, the elevated levels of MnSOD protect the cells against the chemotherapy and radiation.

Mice who have been given the MnSOD gene DNA together with lipids have less esophageal damage when exposed to radiation similar to that given to patients receiving lung cancer treatment. If this type of therapy works in people with lung cancer, they will be able to get the treatment they need with less discomfort and may be able to get stronger treatment doses safely.

This clinical trial has been designed to see whether giving the MnSOD gene DNA with lipids by mouth can reduce esophageal damage that results from simultaneous treatment of lung disease with two powerful chemotherapy drugs and radiation. Patients will receive two doses of the MnSOD gene-lipid complex by swallowing on the first and third days of each weekly chemotherapy/radiation cycle. A small group of patients will be treated with gradually increasing doses of the gene to make sure it doesn't have any excessive unsuspected ill effects. Once a well-tolerated dose is determined, additional patients will be treated at this dose. The number of patients who have esophageal damage will be determined and compared to the number who would be expected to have this side effect without the MnSOD gene therapy.