The MAGRIT

(MAGE-A3 as Adjuvant Non-Small Cell LunG Cancer Immunotherapy)

Lung Cancer Vaccine Trial

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After years of modest results, the use of vaccines (immunotherapy) to prevent the recurrence of lung cancer is making a comeback. We examine the role of a major clinical trial that is ongoing to prevent recurrence after surgery for lung cancer.

Surgery, especially minimally invasive ('key-hole') surgery, is an effective and safe treatment for patients with early stage lung cancer. However, between 20 to 30 percent of patients relapse in the first five years following surgical treatment alone in Stage 1 non-small cell lung cancer. In Stage 2, this percentage rises 40 to 50%. There have been many recent attempts to decrease this rate of relapse. Chemotherapy after surgery has been investigated thoroughly. Latest pooled data from the best studies have shown that chemotherapy after surgery improves survival approximately 4% more than surgery alone at five years. Because of these modest results, there has been at least one major study looking at targeted therapy using the drug erlotinib after surgery. Results of this trial are awaited. One other strategy would be to use vaccines (immunotherapy) against lung cancer.

Using the body's own immune system to fight cancer has long been considered a possible anti-cancer strategy. However vaccine therapy for cancer suffers from potential difficulties. One difficulty was that the vaccine should be targeted against the tumor alone, and not normal tissue. In other words, the genetic makeup of the tumor should contain specific targets that the vaccine would act against, leaving normal tissues unaffected.

In the early 1990s, researchers began to look more closely at the genetic makeup of cancers. It was noticed that many cancers contained a specific family of genes, named the 'cancer-testis antigens'. These genes were most pronounced in non-small cell lung cancer. One class of these genes was called the Melanoma Associated Antigen (MAGE). In the following years many teams investigated the details of the MAGE family. Amongst the many MAGE antigens found in lung cancer, the MAGE 3 antigen was considered a good target for development of a vaccine

against the lung cancer that contained this particular antigen. However, only 30% of non-small cell lung cancers contained ('expressed', in medical parlance) the MAGE 3 antigen.

Scientists at GlaxoSmithKline, the pharmaceutical company, are developing a specific vaccine against the MAGE 3 expressing non-small cell lung cancer. The vaccine may induce specific white blood cells to attack the tumor. In addition, the vaccine contains a non-specific immune boosting mechanism that may enhance the effect of these specific white blood cells. Early studies of this vaccine in patients with non-small cell lung cancer were conducted which led to the establishment of a large clinical trial testing this vaccine (called the Phase III MAGRIT trial). Many centers around the world are participating in this trial. There are also smaller trials of various immunotherapy approaches going on at specific institutions in the U.S, however the MAGRIT Trial is the only vaccine trial for post-surgical patients being conducted worldwide at this time.

Patients are consented to participate in the trial following surgery. As a first step, the patient consents for the tumor that was removed at surgery to be tested for the MAGE 3 antigen. If their tumor contains the antigen it means two things – one, that the patients who are MAGE 3 positive do somewhat worse (in the long term) than people who are MAGE 3 negative and two, they are eligible for the trial. MAGE 3 positive patients are then randomized to receive the vaccine over a period of the next two years in 13 injections. The injection is given into the arm or thigh muscle, similar to a flu shot. The patients are randomized on a 2:1 ratio, meaning every 3rd patient receives a placebo and the other two patients receive the vaccine. This is done in a blinded fashion, meaning neither the research staff or the patient knows who is receiving the vaccine versus the placebo. I would encourage all patients who have surgery for lung cancer to discuss with their surgeon or oncologist for possible enrollment in the MAGRIT Trial.

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