Study tests method to boost immune system response to inoperable cervical cancer

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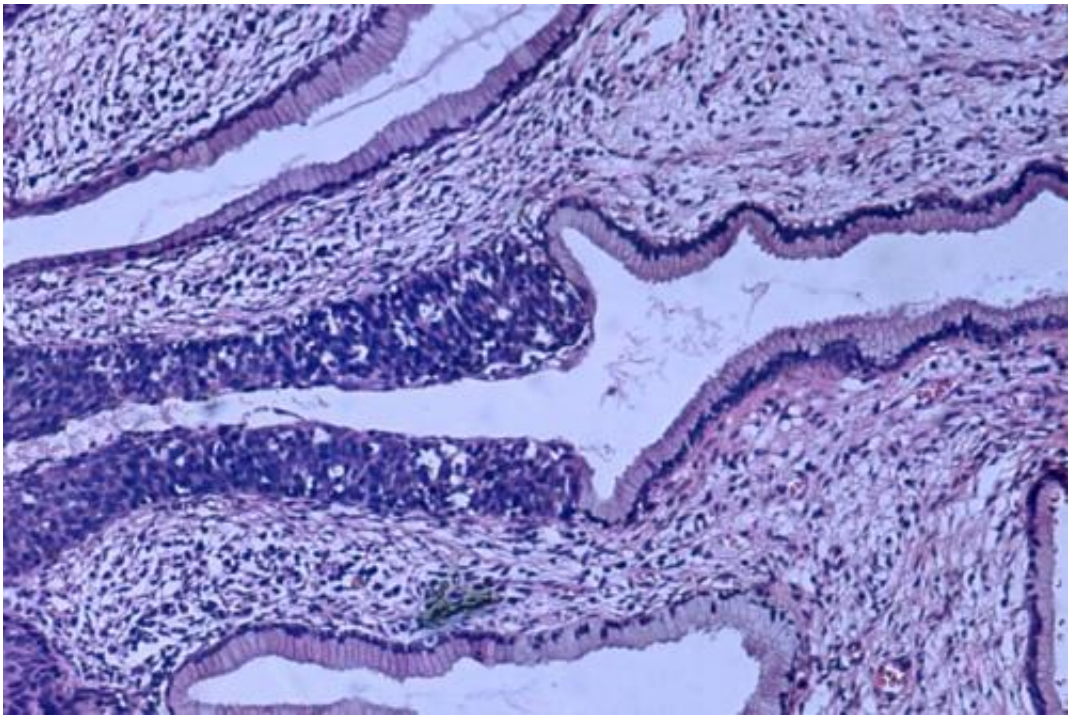

High grade dysplasia (carcinoma in situ) in the uterine cervix. The abnormal epithelium is extending into a mucus gland to the left of centre. This disease can progress to invasive cancer (squamous cell carcinoma) of the cervix. Credit: Haymanj/public domain

The University of Chicago Medicine & Biological Sciences, along with the University of Chicago Medicine Comprehensive Cancer Center at Silver Cross Hospital in New Lennox, is one of three study sites in the United States participating in a clinical trial to determine whether an

investigational DNA cancer vaccine (INO-3112) is safe and can stimulate the immune systems of women with inoperable, recurrent or progressive/persistent cervical cancer to attack malignant cells.

INO-3112 is a DNA immunotherapy. It targets the E6 and E7 proteins of human papillomavirus (HPV) types 16 and 18, a common cause of cervical cancers. It combines two investigational products, VGX-3100 and INO-9012.

VGX-3100 consists of a small piece of DNA that targets HPV. INO-9012 is an immune system activator. It expresses interleukin-12 (IL-12), which can potentially enhance the immune response.

INO-3112 is injected into a muscle followed by electroporation, a technique that uses controlled, millisecond electrical pulses that make it easier for the DNA plasmids to enter muscle cells.

Once the DNA plasmids enter muscle cells, they instruct those cells to produce the E6 and E7 proteins as well as IL-12. These proteins are then presented to the immune system, which alerts the body that an infection and cancer is present. The body, in return, produces an immune response that attacks virally infected cervical cancer cells.

"This one-of-a-kind immunotherapy protocol for cervical cancer subjects, now open to subjects with recurrent or persistent disease, has the potential to have a significant impact," said Yasmin Hasan, MD, assistant professor of radiation and cellular oncology at the University of Chicago and director of the study.

A previous phase II study of VGX-3100 alone to treat women with high-grade cervical cancer showed that 49.5 percent of women who received VGX-3100 had regression to low-grade neoplasia (CIN1) or to no disease. This is almost 20 percentage points higher than women who

received only a placebo (30.6%).

Clearance of the HPV in conjunction with regression of cervical lesions occurred in 40.2 percent of women who received VGX-3100, compared to 14.3 percent of women who received the placebo.

The researchers plan to enroll a total of 30 subjects in two study groups. One is for patients with newly diagnosed but inoperable cervical cancer who have completed chemoradiation therapy.

The other is for subjects with recurrent or progressive/persistent cervical cancer. Subjects will receive four doses into a muscle in the arm over the course of three months.

Enrolling in this study is a commitment. Study participants must return to the clinic every two weeks for the first four months, every eight weeks for the next seven months and every three months for follow-up visits. Participation involves study drug administration, scheduled blood tests, biopsies and swabs, and necessary medical imaging—such as PET and CT scans—which are part of standard follow-up. Over the three-and-a-half-year course of the trial, participants will undergo multiple blood draws at specified intervals.

There are potential risks associated with this study. For example, intramuscular injections can cause pain at the site of the shot. The electroporation device, which uses needles and electrical current to increase DNA uptake, also causes temporary discomfort.

To be eligible for the study, participants must have HPV 16 or 18 positive cervical cancer and have completed standard chemoradiation therapy. Subjects with recurrent or persistent cervical cancer will be eligible if they meet the inclusion criteria.

Although an effective vaccine to prevent HPV infection was approved by the United States Food and Drug Administration in 2006, cervical cancer still remains a major problem worldwide. It is the second leading cause of cancer death in women, with almost 500,000 new cases each year and nearly 275,000 deaths.

The trial, known as the "Open-Label, Safety, Tolerability, and Immunogenicity Study of VGX- 3100 and INO-9012 Delivered by Electroporation in Women with Cervical Cancer after Chemoradiation," is also open at the University of Michigan, Ann Arbor, and Columbia University in New York City.

Provided by University of Chicago