Clinical trial to test whether vaccine can effectively treat melanoma

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Rush University Medical Center is leading a nationwide Phase III clinical trial to determine whether a promising vaccine for advanced melanoma can effectively treat the deadly skin cancer.

An earlier Phase II trial of the experimental drug involving 50 patients with metastatic melanoma had stunning results. Eight patients recovered completely and four partially responded to the vaccine.

"Very few treatment options exist for patients with advanced melanoma, none of them satisfactory, which is why oncologists are so excited about the results we found in our Phase II study," said Dr. Howard Kaufman, associate dean of Rush Medical College and director of the Rush Cancer Program. Kaufman is leading the Phase III study.

Melanoma is a rare but deadly disease whose incidence is rising. According to the National Cancer Institute, there were 68,700 new cases of melanoma in 2009, and more than 8,500 deaths. The cancer typically begins in a mole, but can also lodge in other pigmented tissues, such as in the eye or in the intestines. If caught early, when the disease is superficial, the lesions can easily be removed surgically. But if it advances, the prognosis is poor. Median survival is six months to two years.

The vaccine being tested is called OncoVEX, initially developed to combat herpes virus. Researchers discovered accidentally that the vaccine attacked cancerous tissue when it was inadvertently placed in a

Petri dish of tumor cells. The vaccine includes an oncolytic virus, a reprogrammed virus that has been converted into a cancer-fighting agent that attacks tumor cells while leaving healthy cells undamaged. OncoVEX also carries biological agents that boost the immune response to melanoma.

The vaccine is injected directly into lesions that can be felt or seen, with or without ultrasound. The procedure is generally done in a physician's office.

The earlier Phase II trial, an initial test of the vaccine's efficacy, included 50 patients with metastatic melanoma, or melanoma that had spread to other parts of the body, who had failed to respond to conventional treatment, including chemotherapy and immunological drugs such as interleukin-2. Response rates for those therapies are at best about 15 percent, according to Kaufman.

By comparison, the overall response rate in the OncoVEX trial was 26 percent. Eight of the 50 patients were free of disease by the end of the trial period, which consisted of vaccination every two weeks, for a total of up to 24 injections or until disease disappeared. Four more patients were rendered disease-free after surgery or further vaccination of new lesions. Overall survival was 58 percent at one year, and 52 percent at two years. The results were reported last December in the *Journal of Clinical Oncology*.

"What really surprised, and encouraged, us was that the vaccine worked not just on the cells we injected, but on lesions in other parts of the body that we couldn't reach," Kaufman said. "In other words, the vaccine prompted an immune response that was circulated through the bloodstream to distant sites.

"These are the best results to date for any vaccine developed for

melanoma, but they need to be confirmed in a larger population."

The Phase III trial will enroll a total of 430 patients at centers across the U.S. As with the earlier trial, the vaccine will be injected directly into tumor nodules every two weeks for up to 24 treatments. Patients will be tracked for two years after the first dose is received.

BioVex, in Woburn, Massachusetts, which makes OncoVEX, is funding the study.

Provided by Rush University Medical Center