Synthetic HPV Vaccine May Prevent Neoplasia

BY MARY ANN MOON

A vaccine that contained peptides targeting the human papillomavirus-16 oncoproteins E6 and E7 was effective against high-grade, HPV-16–positive vulvar intraepithelial neoplasia, according to the results of a small phase II study.

"This clinical efficacy is probably related to a vaccine-induced HPV-16 T-cell response," said Dr. Gemma G. Kenter and her associates at Leiden (the Netherlands) University Medical Center (N. Engl. J. Med. 2009;361:1838-47).

In the blood of patients with high-grade vulvar intraepithelial neoplasia, researchers have noted that there are low or undetectable numbers of T cells directed against the HPV-16 oncoproteins E6 and E7.

Reasoning that "vaccination might overcome this inertia of the immune system," Dr. Kenter and her colleagues proceeded to develop a vaccine containing synthetic long peptides "that represent the entire length" of these two oncoproteins.

They tested the vaccine in 20 women in a single-center observational study conducted in 2004-2007. The study was sponsored by the Dutch Cancer Society, the European Union, and ISA Pharmaceuticals B.V. These subjects were slated to receive three or four vaccinations at 3-week intervals and they were followed for 24 months.

At the 3-month follow-up, blood samples showed that 17 of the subjects had an HPV-16-specific immunologic response and enhanced production of interferon. Eleven of the patients reported symptom relief. Five patients showed a complete histologic and clinical response, and seven showed partial responses, Dr. Kenter and her associates reported.

After 1 year, the number of women showing a complete response increased to nine, and six continued to show a partial response. Twelve women reported symptom relief.

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All nine women who showed a complete response were still free of disease at 2-year follow-up. Tumor microinvasion was found in one woman who had shown a partial response, and carcinoma developed in two other patients 2.5 and 3.5 years after vaccination, the investigators said.

In an editorial comment that accompanied this report, Olivera J. Finn, Ph.D., and Dr. Robert P. Edwards, who are both with the University of Pittsburgh, noted that this study was the latest in a series conducted by the same group of investigators "who over the past several years have tested this vaccine in preclinical settings for its tumor-rejection potential and for its safety and immunogenicity in end-stage cervical cancer."

The findings from this small study suggest that "more effective immune responses can be generated against precursor lesions than against late-stage disease. Many cancer vaccines based on nonviral tumor–associated antigens have been judged to be suboptimal because of their lack of efficacy in advanced disease, yet they might perform very differently if used in patients with premalignant disease," Dr. Finn and Dr. Edwards said.

If the vaccine approach is developed further, it may offer a less invasive and more durable treatment than is currently available for vulvar intraepithelial neoplasia, they said.

The Leiden University Medical Center holds a patent on the use of synthetic long peptides as vaccine. Dr. Kenter reported serving as an unpaid member of the strategy team of ISA Pharmaceuticals. Dr. Edwards reported that he received consulting fees from Fresenius SE and grant support from Sanofi-Aventis. ■