Synthetic HPV Vaccine May Prevent VIN

BY MARY ANN MOON

A vaccine containing peptides targeting HPV-16 oncoproteins E6 and E7 was effective against high-grade, HPV-16–positive vulvar intraepithelial neoplasia, according to small phase II study results.

"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.

In the blood of patients with high-grade vulvar intraepithelial neoplasia (VIN), researchers have noted 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 developed a vaccine containing synthetic long peptides "that represent the entire length" of these two oncoproteins.

The findings from this small study suggest that 'more effective immune responses can be generated against precursor lesions than against late-stage [vulvar] disease.'

They tested the vaccine in 20 women in a single-center observational study 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 to four vaccinations at 3-week intervals and were followed for 24 months.

After 3 months, blood samples showed that 17 subjects had an HPV-16–specific immunologic response and enhanced production of interferon, Dr. Kenter and her associates said.

Eleven patients reported symptom relief. Five patients showed a complete histologic and clinical response, and seven showed partial responses.

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.

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 (N. Engl. J. Med. 2009;361:1838-47).

In an editorial comment accompanying this report, Olivera J. Finn, Ph.D., and Dr. Robert P. Edwards, both of the University of Pittsburgh, noted that this report was the latest in a series from 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."

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"Many cancer vaccines based on non-viral 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," the investigators wrote (N. Engl. J. Med. 2009;361:1899-901).

If the vaccine approach is developed further, it may offer a less invasive and more durable treatment than is currently available for VIN, Dr. Finn and Dr. Edwards said.

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 receiving consulting fees from Fresenius SE and grant support from Sanofi-Aventis. ■