

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

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system,” Dr. Kenter and her colleagues developed 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 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.”

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

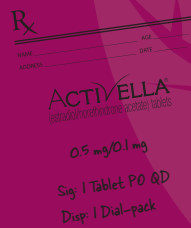
“Many cancer vaccines based on non-viral tumor-associated antigens have been judged to be suboptimal because of their lack of efficacy in advanced disease, yet they might perform very differently if used in patients with pre-malignant disease,” the investigators wrote (N. Engl. J. Med. 2009;361:1899-901).

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. ■



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- The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) per day, relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer in the Prescribing Information)
- The estrogen-alone substudy of the WHI reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with oral conjugated estrogens (CE 0.625 mg) per day, relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders in the Prescribing Information)
- The Women's Health Initiative Memory Study (WHIMS), a substudy of the WHI study, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with CE 0.625 mg combined with MPA 2.5 mg and during 5.2 years of treatment with CE 0.625 mg alone, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See CLINICAL STUDIES, WARNINGS, Dementia and PRECAUTIONS, Geriatric Use in the Prescribing Information)
- Other doses of oral conjugated estrogens with medroxyprogesterone acetate and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical trials and, in the absence of comparable data, these risks should be assumed to be similar. Because of these trials, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman
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Please see brief summary of Prescribing Information on next page.

REFERENCES: 1. The North American Menopause Society. Estrogen and progestogen use in postmenopausal women: July 2008 position statement of The North American Menopause Society. *Menopause*. 2008;15:584-603. 2. Activella® [package insert]. Princeton, NJ: Novo Nordisk Inc; 2007. 3. Loose-Mitchell DS, Stancel GM. Estrogens and progestins. In: Hardman JG, Limbird LE, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York, NY: McGraw-Hill; 2001:1598. 4. Panay N, Ylikorkala O, Archer DF, Gut R, Lang E. Ultra-low-dose estradiol and norethisterone acetate: effective menopausal symptom relief. *Climacteric*. 2007;10:120-131. 5. Data on file. CTR. Novo Nordisk Inc, Princeton, NJ.



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