Imiquimod Cream Found Safe, Effective for VIN

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Imiquimod cream, a topical immune-response modifier, cleared vulvar intraepithelial neoplasia lesions and eliminated human papillomavirus DNA expression in a small randomized trial comparing it with placebo.

"As a convenient, self-administered treatment, imiquimod is well tolerated, is less invasive than surgery, relieves itching and pain, and does not influence health-related quality of life, body image, or sexuality. Therefore, we consider imiquimod the first-choice treatment for vulvar intraepithelial neoplasia," said Dr. Manon van Seters of Erasmus University Medical Center, Rotterdam, the Netherlands, and her associates.

The agent has previously been reported as efficacious against vulvar intraepithelial neoplasia (VIN), but "only in small, uncontrolled studies."

After treatment, HPV was no longer detected in 15 of those who had received imiquimod, compared with 2 of those who had received placebo.

Dr. van Seters and her associates conducted a double-blind, placebo-controlled clinical trial in 52 women with multifocal, grade 2 or 3 VIN. The subjects had had the condition for a mean of 5 years, and many had undergone repeated surgeries.

The women were randomly assigned to receive 250 mg of imiquimod 5% or a placebo cream, and were instructed to apply a thin layer to their lesions twice a week for 16 weeks. The cream remained in place overnight, uncovered. Subjects also were advised to use sulfur precipitate in 5% zinc oxide ointment the day after using the cream, to avoid superinfection.

The women recorded adverse effects in a diary and were evaluated every 4 weeks for symptoms and side effects. They underwent pretreatment and posttreatment biopsy of lesions, as well as long-term assessments at 7 months and 12 months after entering the trial.

At 20 weeks, lesion size was reduced by more than 25% in 21 of 26 patients using imiquimod (81%) but in none of the patients using placebo cream. Nine of the women in the imiquimod group had complete clearance of lesions, and they remained free of disease at 1-year follow-up. Another five women had a "strong partial" response, with reductions of 75% in lesion size, at 20 weeks.

In 18 of the 26 women using imiquimod (69%), biopsies showed histologic regression from grade 2 or 3, compared with one woman who used placebo cream (4%).

At baseline, 25 patients in each group had lesions that were positive for HPV DNA. After treatment, HPV was no longer detected in 15 of those who had received imiquimod (58%), compared with 2 of those who had received placebo (8%).

Compared with placebo, imiquimod reduced pruritus and pain at 20 weeks, a difference that persisted through 1-year follow-up. There were no differences between the two groups in health-related quality of life, body image, or sexuality, the investigators said (N. Engl. J. Med. 2008;358:1465-73).

The drug's exact mechanism of action is not yet known, nor was it evident why some patients responded better to treatment than did others, Dr. van Seters and her associates added. ■