Estriol Gel Reduces Vaginal Atrophy Symptoms

BY RICHARD HYER

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CHICAGO – Estrogen may safely and effectively be administered vaginally in a very low-dose 0.005% estriol gel to treat vaginal atrophy, said Dr. Concepcion Nieto of Italfarmaco S.A. of Madrid.

"The new estriol vaginal gel formulation, providing a very low amount of estriol per application [50 g], is highly efficacious in the improvement of the symptoms related to postmenopausal vaginal atrophy," she said at the meeting.

Dr. Nieto reported the results of a randomized, double-blind, placebo-controlled multicenter study of 167 women randomized 2:1 to the investigational estriol gel or placebo. She said that the gel provides 10 times less hormone per application than the European reference product, Ovestinon 0.1%, and that it is not approved by the Food and Drug Administration for use in the United States.

The 0.005% estriol vaginal gel was approved in Europe in July 2010 and will be proximately marketed in Europe under the brand names of Blissel and Gelistrol, Dr. Nieto said in a later interview. Estriol is a metabolite of estradiol and estrone, but has lower estrogenic potency than estradiol. It also has a greater relative affinity for beta than for alpha estrogen receptors.The study's primary objective was to evaluate the efficacy of 0.005% estriol vaginal gel after 12 weeks of treatment. Safety was a secondary objective. Postmenopausal amenorrheic women with signs and symptoms of vaginal atrophy made up the study population. Symptoms of vaginal atrophy included dryness, dyspareunia, pruritus, burning, and dysuria, and signs included dry vaginal mucosa, pallor, fragility, flattening of vaginal folds, and petechiae. Medication was administered daily in weeks 1-3 and twice weekly in weeks 4-12.

The primary efficacy variable was change in maturation value of vaginal epithelium from baseline to week 12. Symptoms were evaluated by change in global symptom score at baseline and at week 12. The women in the study population (114 active, 53 placebo) averaged 56.7 years, had a mean body mass index of 26.0 kg/m^2, and 9.8 years of menopause. All complained of vaginal dryness at baseline, more than 90% complained of dyspareunia, and more than half, of pruritus. The women also complained of burning and dysuria. The most bothersome symptom was vaginal dryness, in 59% of women. In the active treatment group, 97 of 112 (87%) rated the treatment excellent, good, or acceptable, vs. 37 of 53 (70%) in the placebo group.

"The 0.005% estriol vaginal gel has proved to be significantly more efficacious than the placebo gel over the local symptomatology," said Dr. Nieto. "This effect is clinically relevant, as shown by the evaluation of the patients greatly in favor of estriol regarding the general efficacy of the treatment on finishing the study."

An audience member said, "The FDA requires now an improvement in [the] most bothersome symptom, which you recorded. Was there a statistically significant reduction in [the] most bothersome symptom?"

"Yes," said Dr. Nieto. "We analyzed the most bothersome symptom, and we observed in vaginal dryness that at week 12, 88% of women had improved or were cured from the vaginal dryness, and 66% of women that received the placebo improved or were cured." ■

VITALS

Major Finding: In the active treatment group, 97 of 112 (87%) rated the treatment excellent, good, or acceptable, vs. 37 of 53 (70%) in the placebo group, a significant difference.

Data Source: A study of 167 women randomized 2:1 to estriol 0.005% or to placebo.

Disclosures: Dr. Nieto is the medical director of Italfarmaco SA, maker of ITFE-2026, estriol 0.005% gel. The study was sponsored by Italfarmaco, the Spanish affiliate of Grupo Italfarmaco, a pharmaceutical company operating in Europe and South America. No other member of the investigational team disclosed a financially relevant relationship.