# Novel SERM Tested in Vulvovaginal Atrophy

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NATIONAL HARBOR, MD. – A novel selective estrogen–receptor modulator called ospemifene was more effective than placebo for reducing symptoms of vaginal dryness and dyspareunia in a study of 919 postmenopausal women.

Only estrogen-based treatments have been approved in the United States to treat vulvovaginal atrophy (VVA) in postmenopausal women, but concerns about the effects of estrogen on breast and endometrial tissue have prompted doctors and patients to seek alternatives, said Dr. David Portman of the Columbus (Ohio) Center for Women's Health Research.

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"We do need to find alternatives because many of our patients still have concerns even with local estrogen," he emphasized.

Ospemifene (OSP), a selective estrogen–receptor modulator (SERM) – also referred to as a nonsteroidal estrogen–receptor agonist/antagonist – is distinct from other SERMs because its estrogenic activity occurs on the vaginal epithelium, "but not on the endometrium," said Dr. Portman.

Previous studies have shown that ospemifene is well tolerated, with a favorable pharmacologic profile in postmenopausal women with VVA, he added.

In a 12-week randomized, double-blind, placebo-controlled, phase III parallel group study, Dr. Portman and his colleagues assessed the efficacy, safety, and tolerability of ospemifene for women with moderate to severe vaginal dryness or moderate to severe dyspareunia.

Dyspareunia symptoms and severity were self-reported, and use of a nonhormonal vaginal lubricant was permitted as needed.

Demographic characteristics were similar between the two groups.

The women ranged from 40 to 80 years of age at baseline.

Those with a body mass index of 37 kg/m$^2$ or greater were excluded, as were those with clinically significant abnormal gynecologic findings other than vaginal atrophy and those using hormonal medications or other products with possible estrogenic or antiestrogenic effects within a timeframe too close to the study screening.

A total of 314 postmenopausal women who reported vaginal dryness as their primary symptom were randomized to 60 mg of OSP orally each morning or a placebo, the researchers said.

In the intent-to-treat population, the change in the vaginal dryness severity score improved in the OSP group vs. the placebo group (–1.3 vs. –1.1).

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**VITALS**

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**Data Source:** A 12-week study of 314 postmenopausal women who had vaginal dryness and were randomized to 60 mg of OSP orally each morning or a placebo.

**Disclosures:** The study was sponsored in part by Shionogi, which developed and markets ospemifene, and several coinvestigators were Shionogi employees. Dr. Portman has received consulting fees, honoraria, and/or grant support from multiple companies including Shionogi, Bayer, Boehringer Ingelheim, Teva, Warner Chilcott, and Watson Pharmaceuticals.

superficial and parabasal cells were significantly different in the OSP group vs. the placebo group (12% vs. 3% and –32% vs. –4%, respectively).

Measuring these types of cells indicates changes in the vaginal microflora, which have been shown to affect vaginal dryness and pain.

The mean change in vaginal pH was –1.01 in the OSP group, compared with –0.25 in the placebo group, respectively.

An additional 605 women who reported dyspareunia as their primary symptom were randomized to 60 mg OSP orally each morning or a placebo.

In the intent-to-treat population, the change in the dyspareunia severity score improved in the OSP group vs. the placebo group (–1.5 vs. –1.2, $P = .0001$), a significant difference.

In addition, the percentages of superficial cells and parabasal cells were significantly different in the OSP vs. the placebo groups (12% vs. 2% and –40% vs. 0%, respectively).

The mean change in vaginal pH also differed significantly between the OSP and placebo groups (–1.0 vs. –0.06, respectively).

Overall, ospemifene had "a very clean safety profile," Dr. Portman said.

The total number of treatment-emergent adverse events was not significantly different between the OSP and placebo groups (290 vs. 232).

A total of 122 treatment-related adverse events occurred in the OSP group, compared with 62 in the placebo group.

The number of serious adverse events and severe adverse events were similar between the groups (6 vs. 7 and 28 vs. 29, respectively).

The most common treatment-emergent adverse events in the OSP group were urinary tract infection (8%), hot flashes (7%), and vaginal discharge (5%).

No deaths, myocardial infarctions, and or breast cancer cases were reported in any of the patients during the study period.

While the drug is not yet approved for VVA, "this investigational SERM has the potential to be an efficacious, nonestrogen oral prescription therapy for this prevalent, bothersome, and undertreated condition," according to Dr. Portman. ■