Elagolix Reduces Endometriosis-Related Pelvic Pain

Elagolix is effective in women with endometriosis-related pain according to the results of a phase 3 trial.

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May 17, 2018 – In women with endometriosis-related pain, both lower and higher doses of elagolix were shown to reduce dysmenorrhea and nonmenstrual pelvic pain in a phase 3 trial.

H.S. Taylor, MD and colleagues reported their findings in the May 19, 2017 issue of *The New England Journal of Medicine*.

Elagolix is an oral, gonadotropin-releasing hormone (GnRH) antagonist. Previous studies have shown that elagolix was effective in improving endometriosis-associated pain by partially suppressing estrogen.

"On the basis of the –"estrogen threshold hypothesis"- complete estrogen suppression may not be needed to control endometriosis-associated pain, and estrogen may be adjusted to a level that is adequate to control pain but minimizes hypoestrogenic effect." Explained R. I. Barbieri in *American Journal of Obstetrics and Gynecology*.

Two 6-month, phase 3 trials, Elaris Endometriosis I and II (EM-I and EM-II), were performed to determine the effects of both lower and higher doses of elagolix compared with placebo. In the lower-dose group, women received 150mg elagolix daily while the higher-dose group received 200mg twice a day.

A total of 872 women were randomly assigned in Elaris EM-I and 817 in Elaris EM-II. Participants were surgically diagnosed with endometriosis and experienced moderate to severe endometriosis-associated pain.

A greater proportion of women who received elagolix met the clinical response criteria for the two primary endpoints at 3 months than those who received placebo. These findings were sustained at 6 months.

The percentage of women who had a clinical response to their dysmenorrhea symptoms in Elaris EM-I was 46.4% in the low-dose group and 75.8% in the high-dose group compared with 19.6% in the placebo group. In Elaris EM-II, the respective percentages were 43.4% and 72.4% compared with 22.7%. ($P<0.001$).

The clinical response in women with nonmenstrual pelvic pain in Elaris EM-I was 50.4% in the low-dose group and 54.5% in the high-dose group compared with 36.5% in the placebo group. In Elaris EM-II, the respective percentages were 49.8% and 57.8% compared with 36.5%. ($P=0.003$ and $P<0.001$).

Adverse effects in those taking elagolix were hypoestrogenic related and included mild to moderate hot flushes, headaches, nausea and an increase in serum lipids. A decrease in bone mineral density was also noted in the elagolix group compared with the placebo group.

“Observed reductions in pain and reports of hypoestrogenic adverse events were consistent with the mechanism of action of elagolix, which competitively inhibits GnRH receptors in the pituitary gland and leads to a rapid reduction in circulating gonadotropins and estradiol.” J. Ng and colleagues noted in *Journal of Clinical Endocrinology and Metabolism*.

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