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New Data Provide In-Depth, Safety Information on Long-Term use of EVISTA®

Eight years of data provide new information for postmenopausal women and physicians regarding osteoporosis treatment

INDIANAPOLIS, IN - Data compiled from an eight-year study provide new in-depth, long-term safety information about EVISTA® (raloxifene HCl), the first and only selective estrogen receptor modulator (SERM) approved for the prevention and treatment of osteoporosis in postmenopausal women. These data, which appear in the September issue of Current Medical Research and Opinion, represent the experience of more than 4,000 postmenopausal women, and reinforce the known safety profile of EVISTA.

The data are from the Multiple Outcomes of Raloxifene Evaluation (MORE) and the Continuing Outcomes Relevant to EVISTA (CORE) trials, the primary endpoints of which were efficacy in fracture risk reduction and breast cancer risk reduction, respectively.

"Because of the chronic nature of osteoporosis, a physician who diagnoses a woman with the condition expects his or her patient to be on an antiresorptive for a number of years. Understanding the long-term safety profile of the treatments available is very important," said Silvana Martino, DO, Director, Breast Cancer Section, The Angeles Clinic and Research Institute and lead investigator of the CORE study. "The results of these studies reinforce EVISTA's safety profile over an extended period of time, providing physicians and patients with information they need to weigh the risks and benefits of treatment and decide if EVISTA is right for that person."

These data demonstrated that EVISTA posed no increased risk for side effects over time compared to placebo of:

- myocardial infarction (heart attack)
- stroke
- endometrial hyperplasia
- postmenopausal bleeding
- uterine and ovarian cancer

In addition to analysis of all adverse events, the above adverse events were specifically analyzed to ascertain EVISTA's gynecologic and cardiovascular safety. This is important because EVISTA is designed to produce estrogen-like effects in some tissues while blocking the effect of estrogen in other tissues.

Similar to the findings from MORE, results from the CORE trial found an increased risk for developing venous thromboembolism (VTEs) as compared to placebo (1.7 percent with Evista versus 1.0 percent with placebo). While in this paper the increase in VTEs was not statistically significant, this finding does not alter the previously established early increased risk for VTEs, an infrequent but serious adverse event with EVISTA. EVISTA is contraindicated in women with an active or past history of VTE events, including deep vein thrombosis, pulmonary embolism and retinal vein thrombosis. Being immobile for a long time may add to a person's risk for developing a VTE.

The study also confirmed the most common side effects such as hot flashes and muscle cramps which were previously associated with EVISTA. Side effects with EVISTA have usually been mild, and most women didn't find them serious enough to stop taking it. Benign uterine polyps were also more commonly detected in women who took EVISTA, as reflected in the product label.

"As a company committed to advancing women's health, Lilly is pleased to be able to provide this meaningful long-term safety information about this first-in-class therapy for the prevention and treatment of osteoporosis," said K. Shaw Lamberson, M.D., Medical Director of U.S. Osteoporosis, Urologic Medicine and Women's Health, Eli Lilly and Company. "Given that a large number of postmenopausal women are affected by osteoporosis, we believe these results will be valuable to physicians and patients."

Trial Design

Data were collected in two separate trials, MORE and CORE. MORE was an international, 4-year double-blind, randomized, placebo-controlled study designed to assess the effect of EVISTA® on bone mineral density and vertebral fracture incidence in 7705 postmenopausal women with osteoporosis.

The CORE trial, also a 4-year placebo-controlled trial, was a follow up to MORE. CORE participants included 4011 (placebo-1286; EVISTA-2725) postmenopausal women with osteoporosis. The CORE data analysis includes all reported adverse events collected during doctor visits of both MORE and CORE participants.

CORE study participants received the FDA approved dose of EVISTA 60 mg/d or placebo.

Data Highlights

Safety of EVISTA was evaluated through analysis of all adverse event (AE) data, following standard clinical trials. Below are key findings, which support the known safety profile of EVISTA:

- No statistically significant difference was reported in the incidence of myocardial infarction (MI) or stroke between EVISTA and placebo treatment groups.
 - 108 women reported MI during the 8-year period, with incidence of 2.7 percent in the EVISTA treatment group and 2.6 percent in the placebo group ($p>0.99$).
 - In the case of stroke ($n=110$ women), the incidence in the EVISTA and placebo treatment groups was 2.9 percent and 2.5 percent, respectively ($p=0.54$).
- Long term safety data was obtained on cancer, and found:
 - No significant difference in the incidence of uterine cancer, endometrial hyperplasia, ovarian cancer or postmenopausal bleeding between the EVISTA and placebo treatment groups (all $p\geq 0.66$).
 - In addition, there was no increase in the incidence of hospitalization or mortality in the EVISTA treated population compared to placebo.

HOW EVISTA WORKS

EVISTA attaches to the estrogen receptor within bone. EVISTA works through the cellular pathways of the estrogen receptor to prevent and treat osteoporosis.

In other cells that have estrogen receptors, EVISTA may either stimulate or block the estrogen receptor. EVISTA does not pose any significant cardiovascular safety concerns.

EVISTA blocks the action of estrogen on the breast and uterus, and does not have any significant negative effects on these organs. EVISTA is the only osteoporosis treatment with this unique profile.

Additional Important Safety Information about EVISTA

EVISTA is not for everyone. If you are or still can become pregnant, are nursing, have severe liver problems, or have had blood clots that required a doctor's treatment, you should not take EVISTA.

You may be at increased risk for osteoporosis if you are Caucasian (white) or Asian, have a slender build, don't exercise, or have a family history of the disease. If you don't get enough calcium and/or vitamin D in your diet, you should also take these supplements. For detailed information about EVISTA, and for a copy of the product's prescribing information visit Lilly's website at <http://www.EVISTA.com>.

About Osteoporosis

More than 50 percent of all women over the age of 75 are estimated to have osteoporosis, and due to their advanced age, have a high risk of fracture. In fact, most American women over the age of 50 will experience one or more osteoporosis-related fractures during their lifetimes, and women with osteoporosis who have two or more previous fractures have up to a nine times greater risk of future fracture compared with women who have not suffered a previous fracture.

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers - through medicines and information - for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

Evista® (raloxifene hydrochloride, Lilly)