

## **New Selective Estrogen-Receptor Modulator for Treating Women with Osteoporosis?**

*Lasofoxifene is unlikely to offer net benefits greater than those of existing therapies.*

Clinicians and menopausal women alike would welcome new agents that can prevent osteoporotic fractures with minimal adverse nonskeletal outcomes. In a manufacturer-sponsored international trial, investigators enrolled 8556 women (mean age, 67) who met bone-mineral density criteria for osteoporosis; participants received placebo or the investigational selective estrogen-receptor modulator (SERM) lasofoxifene (0.25 mg or 0.5 mg daily) for 5 years. The manufacturer is seeking FDA approval for this drug.

Women who received 0.5-mg lasofoxifene had substantially lower risk for vertebral (hazard ratio, 0.58) and nonvertebral (HR, 0.76) fractures than did women who received placebo. This dose of lasofoxifene was also associated with lower risk for estrogen-receptor (ER)-positive breast cancer (HR, 0.19), coronary heart disease events (HR, 0.68), and stroke (HR, 0.64) but with twofold higher risk for venous thromboembolic events overall and more than fourfold higher risk for pulmonary embolism. Incidence of endometrial cancer and endometrial hyperplasia was low ( $\leq 3$  women in each group); however, endometrial polyps and hypertrophy were substantially more common among women who received either dose of lasofoxifene.

**Comment:** Although these results show that lasofoxifene lowers risk for *radiologic* vertebral fractures, data submitted to the FDA showed that risk for *clinical* vertebral fractures was not lower at 3 years. Both raloxifene and lasofoxifene are associated with excess risk for venous thromboembolic events. The authors note that lasofoxifene did not raise risk for endometrial neoplasia or hyperplasia — but rates of other endometrial outcomes suggest that this agent has a proliferative effect on the endometrium. Although the attenuated risks for ER-positive breast cancers and coronary artery events are intriguing, an editorialist points out that one would need to treat 492 women for 1 year to prevent one major coronary artery event. Lasofoxifene seems to offer no clinically important benefits over existing SERMs; moreover, alendronate, a generic bisphosphonate proven to prevent clinical vertebral and nonvertebral fractures, often fills the bill for preventing osteoporotic fractures in menopausal women.

— [Andrew M. Kaunitz, MD](#)

Published in [Journal Watch Women's Health](#) February 24, 2010

### **Citation(s):**

Cummings SR et al. Lasofoxifene in postmenopausal women with osteoporosis. *N Engl J Med* 2010 Feb 25; 362:686.