

# SSRI Escitalopram Rapidly Eases Hot Flashes

BY MARY ANN MOON

FROM JAMA

The selective serotonin reuptake inhibitor escitalopram rapidly reduces the frequency and severity of hot flashes in menopausal women, according to a report.

In a multicenter, randomized clinical trial comparing 10 or 20 mg per day of escitalopram with placebo, the drug's benefit "was only modestly less than that reported in a meta-analysis of estrogen therapy," said Ellen W. Freeman, Ph.D., of the department of obstetrics and gynecology at the

University of Pennsylvania, Philadelphia, and her associates. receive oral escitalopram (10 mg) or a matching placebo for 8 weeks. If they did not show a reduction in hot flash frequency or at least a 50% reduction in hot flash severity at 4 weeks, the dose was escalated to 20 mg of active drug or placebo.

At baseline, the mean frequency of hot flashes was 9.78 per day. After 8 weeks, that decreased by nearly half, to 5.26 per day in women taking escitalopram. This reduction was significantly greater than

the 33% decrease to 6.43 hot flashes per day in the placebo group.

A total of 55% of women receiving active drug showed a decline of at least 50% in hot flash frequency, compared with 36% of women receiving placebo. Similarly, 19% of the escitalopram group showed a decline of at least 75% in hot flash frequency, compared with only 9% of the placebo group.

Data from the study subjects' daily

diaries showed that every week for the duration of the study, the frequency of hot flashes was significantly decreased in the escitalopram group compared with the placebo group, Dr. Freeman and her colleagues said (JAMA 2010;305:267-74).

Escitalopram also diminished the severity of hot flashes by 24%, compared with a decrease of 14% with placebo. Seventy percent of women taking the active drug reported satisfaction with



**'It is noteworthy that women who were not clinically anxious or depressed responded to escitalopram.'**

DR. FREEMAN

University of Pennsylvania, Philadelphia, and her associates.

"Our findings suggest that among healthy women, 10 to 20 mg/d of escitalopram provides a nonhormonal, off-label option that is effective and well tolerated in the management of menopausal hot flashes," they said.

The double-blind trial involved 205 women who were in the menopausal transition, were postmenopausal, or had undergone hysterectomy with one or both ovaries intact. Ninety-five of the women self-reported as African American, 102 as white, and 8 as other. These subjects recorded at least 28 hot flashes or night sweats per week in a daily diary for 3 weeks before enrollment, or hot flashes or night sweats rated as bothersome or severe 4 or more days per week.

The women were randomly assigned to



Image of trabecular bone insert reproduced with permission from David W. Dempster, PhD.

## VITALS

**Major Finding:** Escitalopram decreased the frequency of hot flashes by nearly half, from 9.78 per day to 5.26 per day.

**Data Source:** An 8-week multicenter, randomized, double-blind clinical trial involving 205 women.

**Disclosures:** This study was supported by the National Institute of Aging, the Eunice Kennedy Shriver National Institute of Child Health and Development, the National Center for Complementary and Alternative Medicine, the Office of Research on Women's Health, the Indiana Clinical and Translational Sciences Institute, and the National Center for Research Resources. Forest Laboratories provided the escitalopram and placebo pills. Dr. Freeman reported ties to Forest Laboratories, Wyeth, Pfizer, Xanodyne Pharmaceuticals, Pherin Pharmaceuticals, and Bayer Health Care, and her associates also reported ties to numerous drug companies.

## INDICATION

**Prolia® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.**

## IMPORTANT SAFETY INFORMATION

**Hypocalcemia:** Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Hypocalcemia may worsen, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended. Adequately supplement all patients with calcium and vitamin D.

**Serious Infections:** In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia® group than in the placebo group. Serious skin infections, as well as infections of

the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia®. Endocarditis was also reported more frequently in Prolia®-treated subjects. The incidence of opportunistic infections was balanced and the overall incidence of infections was similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia®, prescribers should assess the need for continued Prolia® therapy.

**Dermatologic Adverse Reactions:** Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate in the Prolia® group compared to the placebo group. Most of these events were not specific to the injection site. Consider discontinuing Prolia® if severe symptoms develop.

**Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia®. An oral exam should

treatment, compared with 43% of those taking placebo.

These benefits were consistent across all subgroups of subjects, regardless of the women's race, menopausal status, depression scores, or anxiety scores.

Treatment response was rapid, with women in the escitalopram group showing significant improvement in hot flash frequency and severity within 1 week of starting treatment, the investigators noted.

The study subjects were followed up about 3 weeks after discontinuing their study medication. Hot flash frequency had rebounded by a significantly greater

amount in the escitalopram group (7.18 hot flashes per day) than in the placebo group (6.65 hot flashes per day), as had the severity of hot flashes.

Sixty-four percent of the women taking escitalopram said they wanted to continue taking their assigned medication, compared with only 42% of those in the placebo group.

"It is noteworthy that women who were not clinically anxious or depressed responded to escitalopram," which suggests that the mechanism underlying the drug's effect on hot flashes may differ from that underlying its effect in psychiatric

conditions. This finding also supports the hypothesis that serotonin receptors play a role in the pathogenesis of hot flashes, Dr. Freeman and her associates said.

Overall, 53% of women taking escitalopram and 63% taking placebo reported newly emergent adverse effects, none of which were serious. Nine women in the escitalopram group and two in the placebo group discontinued treatment because of adverse events, including dizziness, vivid dreams, nausea, and excessive sweating.

Dr. Freeman and her colleagues reported that to their knowledge, their

clinical trial is the first to examine whether racial differences exist in response to SSRI treatment for hot flashes. Previous studies have shown that African American women are more likely to report hot flashes than their white counterparts. However, they found that "race did not significantly affect the response to escitalopram in the present study."

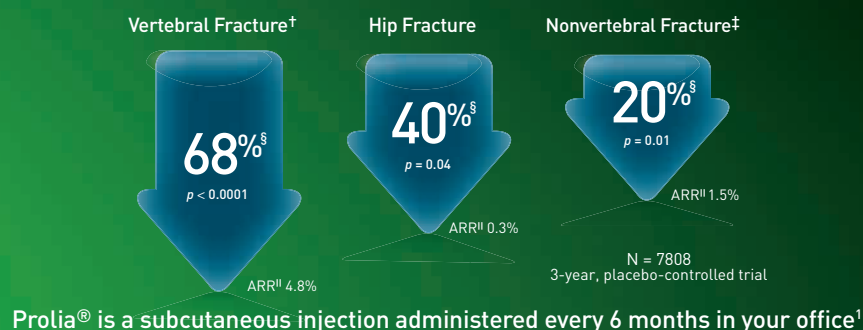
Additional studies are needed to compare the efficacy of SSRIs and selective serotonin norepinephrine inhibitors in treating hot flashes related to menopause, they reported. ■

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Prolia® significantly reduced fracture risk at key sites in a phase 3 trial\*<sup>1,2</sup>



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Please see Brief Summary of Prescribing Information on the following page.

be performed by the prescriber prior to initiation of Prolia®. A dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with risk factors for ONJ. Good oral hygiene practices should be maintained during treatment with Prolia®.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia® should be considered based on individual benefit-risk assessment.

**Suppression of Bone Turnover:** Prolia® resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

**Adverse Reactions:** The most common adverse reactions (> 5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia®.

The overall incidence of new malignancies was 4.3% in the placebo and 4.8% in the Prolia® groups. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

### **Prolia® Postmarketing Active Safety Surveillance Program:**

The Prolia® Postmarketing Active Safety Surveillance Program is available to collect information from prescribers on specific adverse events. Please go to [www.proliasafety.com](http://www.proliasafety.com) or call 1-800-772-6436 for more information about this program.

\* Key sites: vertebral, hip, and nonvertebral.<sup>1,2</sup>

<sup>†</sup> Includes 7393 patients with a baseline and at least one post-baseline radiograph.<sup>1,2</sup>

<sup>‡</sup> Composite measurement excluding pathological fractures and those associated with severe trauma, fractures of the vertebrae, skull, face, mandible, metacarpals, fingers, and toes.<sup>1,2</sup>

<sup>§</sup> RRR = relative risk reduction.

<sup>||</sup> ARR = absolute risk reduction.

References: 1. Prolia® (denosumab) prescribing information, Amgen. 2. Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*. 2009;361:756-765.

For more information, visit [www.ProliaHCP.com](http://www.ProliaHCP.com)

  
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