

# Low Vitamin D Plus Exemestane Tied to Bone Loss

*The connection between vitamin D insufficiency and breast cancer has not been fully examined.*

BY JANE SALODOF MACNEIL  
Southwest Bureau

ATLANTA — Vitamin D supplementation should be considered for postmenopausal breast cancer patients treated with aromatase inhibitors, Dr. Per E. Lønning reported at the annual meeting of the American Society of Clinical Oncology.

“Low vitamin D status could be one of the factors predisposing patients to breast cancer,” said Dr. Lønning, a professor at Haukeland University in Bergen, Norway.

Postmenopausal breast cancer patients who were treated with exemestane and had vitamin D deficiency lost bone mineral density (BMD) at a higher rate than all other patients in a Norwegian trial, according to Dr. Lønning, who presented the trial’s results.

The double-blind study enrolled early breast cancer patients at six sites between January 1999 and October 2001. Participants were postmenopausal with estrogen

receptor-negative or progesterone receptor-positive breast cancer. Median patient age was 59.5 years, and all had a low risk of breast cancer recurrence after surgery.

Of the patients enrolled in the randomized, controlled trial, 128 of 147 (87%) had low levels of vitamin D, defined as 30 ng/mL or less.

Investigators randomized 73 women to 25 mg of oral exemestane daily and 74 women to a daily placebo for 2 years.

Local guidelines did not routinely offer adjuvant endocrine therapy at the time of the study, the investigators noted. Mean vitamin D levels were reported as 21.6 ng/mL for the exemestane arm and 22.6 ng/mL for the control group.

Average patient change in femoral neck BMD was -4.7% after 2 years of treatment with exemestane, an aromatase inhibitor.

Placebo patients with low vitamin D also had bone loss in the femoral neck, but the reduction was -3.0%.

Women with normal vitamin D levels had similar outcomes whether they were treated with exemestane or placebo: reductions of -3.7% and -3.3%, respectively.

“It has not fully been examined that breast cancer patients on average have a poorer vitamin D status in comparison to the normal population in general,” he added, calling for further investigation of the relationship between vitamin D and breast cancer.

An annual BMD loss of 0.5% is normal for postmenopausal women, according to Dr. Lønning and his fellow investigators from the Norwegian Breast Cancer Screening Program. Interviewed during the poster session where he presented trial data, he said low vitamin D levels could be expected in about 50% of postmenopausal women in Norway.

However, he warned against assuming that low vitamin D levels are entirely explained by reduced sun exposure in northern latitudes, because people in other climates are spending more time indoors and out of the sun.

“You should not think of this as a preventive problem only in the far north,” he said. “This could be a problem to populations all over the world.”

While the investigators reported some significant differences in subgroups and “a trend toward higher loss of BMD in the femoral neck” among women with low vitamin D during the 2 years of exemestane treatment, low vitamin D did not appear to make as much of a difference in lumbar spine BMD.

The reductions were -3.4% for 52 vitamin D-deficient women who completed the study on exemestane and -2.5% for 59 women who stayed on placebo. “Vitamin D has influence on compact bone, not trabecular bone,” Dr. Lønning said.

“When you look at the low toxicity of vitamin D, you are not running much risk with supplementation,” he said. “However, I have to say for research purposes, we need more data.” ■

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## Physical Activity Reduces Breast Cancer Risk by 10% in Postmenopausal Women

BY MELINDA TANZOLA  
Contributing Writer

ATLANTA — In postmenopausal women, an active lifestyle provided about a 10% reduction in the risk of developing breast cancer over a 17-year period in over 36,000 women, according to findings from a prospective cohort study presented at the annual meeting of the American Society of Clinical Oncology.

The protective effect of physical activity was most significant against the risk of developing the more aggressive estrogen receptor (ER)-positive, progesterone receptor (PR)-negative form of breast cancer, providing a 34% risk reduction, said Dr. Aditya Bardia, who was pursuing a degree at the University of Iowa, Iowa City, at the time of the study.

Dr. Bardia and colleagues from the Iowa Women’s Health Study mailed questionnaires addressing leisure time physical activity and breast cancer risk factors to postmenopausal women living in Iowa in 1986; 41,837 women (43%) responded.

The participants’ levels of physical activity were classified as low, medium, or high based on the frequency and intensity of their exercise.

The investigators determined cancer incidence between 1986 and 2003 using the Iowa Surveillance, Epidemiology, and End Results (SEER) Cancer Registry and mortality information from state and national resources. Periodic follow-up surveys confirmed continued residence in Iowa in greater than 99% of the women each year.

Classification of Physical Activity		
Level	Intensity	Frequency
High	Vigorous	≥2 times per week
	Moderate	>4 times per week
Medium	Vigorous	1 time per week
	Moderate	1-4 times per week
Low	Any	<1 time per week

Source: Dr. Bardia

After exclusion of women with cancer, a full or partial mastectomy, and those with incomplete data, the cohort included 36,363 women. During the 17-year follow-up period, 2,548 women were diagnosed with breast cancer at an average age of 71 years.

Overall, 47% of women reported low physical activity, 28% reported medium physical activity, and 25% were highly active. In addition to having a lower body mass index (BMI), active women were more likely to have received education beyond high school and reached menopause at an older age.

A high level of physical activity was associated with a 13% reduction in the risk of developing ER-positive breast cancer and an 8% reduction in ER-negative breast cancer, compared with low physical activity. The risk reduction for PR-positive and PR-negative breast cancer was 5% and 27%, respectively.

After the 34% risk reduction for ER-positive/PR-negative breast cancer, the next greatest benefit was a 20% reduction in the risk of developing ER-nega-

tive/PR-negative cancer.

The risk of ER-negative/PR-positive breast cancer was increased by 42% with a high activity level, but Dr. Bardia said the confidence intervals were high on this association due to a small number of women in this group.

Modifiable risk factors such as obesity and a sedentary lifestyle may be contributing to the increasing incidence of breast cancer. However, previous prospective studies have yielded mixed results on the correlation between physical activity and breast cancer risk. Furthermore, such prospective cohort studies have until now evaluated only the link between physical activity and breast cancer risk as a whole. Associations between physical activity and certain types of breast cancer would not have been detected.

Dr. Bardia commented that future studies should investigate the association between physical activity and breast cancer incidence in premenopausal women.

Dr. Banu Arun, of the department of breast medical oncology at the M.D. Anderson Cancer Center, Houston, noted that future studies should evaluate other factors including the use of hormone therapy and genetic risks. “There may be many other differences in lifestyle between women who exercise and who do not which could be a confounding factor as well.” ■

## Anogenital IN Found To Require Lengthy Surveillance Term

ATLANTA — High-grade anogenital intraepithelial neoplasia has remarkably high recurrence and malignancy potential despite repeated treatments; thus long-term surveillance is mandatory, according to Dr. Mathias K. Fehr of University Hospital, Zurich, Switzerland.

A retrospective study of 442 patients with biopsy-proven grade 2-3 intraepithelial neoplasia of the vulva (VIN), vagina (VAIN), or perianal skin (PAIN) showed that progression to invasive disease occurred in 4% of the 433 treated patients within a mean of 8 years, Dr. Fehr reported in a poster at the annual meeting of the American Society of Clinical Oncology.

Recurrent disease, defined as VIN, VAIN, or PAIN diagnosed at least 1 year after the initial diagnosis, occurred in 32% of the treated patients, and among treated patients with a follow-up of longer than 5 years, 14% continued to experience recurrences. On multivariate analysis, immunosuppression was shown to be associated with recurrence (odds ratio 2.33), and immunosuppression and smoking were shown to be independent risk factors for disease progression (odds ratios 3.31 and 3.12, respectively).

Patients had a mean age of 47 years at initial diagnosis, and were treated with biopsy and laser evaporation in 62% of cases, surgical excision in 33% of cases, and other local destructive methods in 3% of cases. Nine patients (2%) refused treatment, Dr. Fehr noted.

Particular attention should be paid to long-term surveillance of VIN, VAIN, and PAIN in immunosuppressed patients and in patients who smoke, he concluded.

—Sharon Worcester