

# Vitamin A Derivative Reduces Risk of Second Cancer in Pre-Menopausal Women with Breast Cancer

Researchers from Italy have reported that the retinoid, fenretinide, significantly reduces the risk of developing a second breast cancer among pre-menopausal women with stage I breast cancer. The details of this study appeared in an early online publication on May 4, 2006, in the *Annals of Oncology* .[1]

Vitamin A and vitamin A analogs have been and are being extensively evaluated for the prevention of a variety of cancers. Vitamin A analogs clearly have potential in reducing the incidence of some cancers, but very little long-term data are available.

The current trial began in 1987 and enrolled 2,867 women with stage I or carcinoma in situ (CIS) treated in 10 Italian hospitals. Patients were between the ages of 30 and 70 years. All were treated with conservative surgery with radiotherapy or mastectomy alone. No patient received adjuvant chemotherapy or hormonal therapy. Patients were randomly allocated to receive 5 years of fenretinide or no further therapy.

An analysis of this trial published in 2001 suggested that fenretinide decreased breast cancer recurrences in pre-menopausal women with a trend for increased recurrences in post-menopausal women. [2] The main side effects of fenretinide were diminished dark adaptation, dermatologic disorders, gastrointestinal symptoms and disorders of the ocular surface. They also reported that symptoms tended to subside with continued fenretinide usage.

The current analysis presents follow-up information after a median of 14.6 years of observation in a cohort of 1,739 women from the original study. Table 1 summarizes the main findings of this recent analysis.

**Table 1:** Fenretinide Versus Control in Stage I and Carcinoma in Situ Patients.

**Fenretinide**

**Control**

Number of Patients

872

867

Number of Second Breast Cancers

168

190

Number of Second Breast Cancers Pre-Menopausal

83

126

Number of Second Breast Cancers Post-Menopausal

85

64

These authors stated that women 40 years of age or younger had a decreased incidence of recurrent breast cancer. This effect disappeared after age 55 years. Also of interest was that there was no apparent effect on prevention of cancers at sites other than breast.

The researchers concluded that treatment with fenretinide for five years following standard therapy appears to drastically reduce the long-term risk of developing a second breast cancer among pre-menopausal women diagnosed with breast cancer. However, there appears to be no benefit from fenretinide for post-menopausal women with breast cancer.

Comments: This study was begun in 1987 and did not include patients receiving adjuvant chemotherapy or hormonal therapy. Today, all of the hormone receptor positive patients in this study would receive anti-estrogen therapy and many would receive adjuvant chemotherapy. Thus, the next study would be to determine if fenretinide adds to the preventative effects of current adjuvant treatments in pre-menopausal women with early breast cancer.

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Reference:

[1] Veronesi U, Mariani L, Decensi A, et al. Fifteen-Year Results of a Randomized Phase III Trial of Fenretinide to Prevent Second Breast Cancer. *Annals of Oncology*. Early online publication May 4, 2006. DOI: 10.1093/annonc/mdl047.

[2] Camerini T, Mariani L, De Palo G, et al. Safety of the synthetic retinoid fenretinide: Long-term results from a controlled clinical trial for the prevention of contralateral breast cancer. *Journal of Clinical Oncology* . 2006;19:1664-1670.

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