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Breast Cancer Prevention Trial Results Published

Researchers from the Breast Cancer Prevention Trial (BCPT) have published a full report and update of the study in the *Journal of the National Cancer Institute*, a peer-reviewed international medical journal.*

With data through March 31, 1998, the BCPT now shows a 49 percent reduction in breast cancer incidence among the high-risk participants who took tamoxifen (Nolvadex®, Zeneca Pharmaceuticals, Wilmington, Del.), a drug used for the past two decades to treat breast cancer. The initial study results had shown a 45 percent reduction in breast cancer incidence.

Investigators had released the initial study results, on April 6, 1998, with data through Jan. 31, 1998, about 14 months earlier than expected. At that time, they notified the 13,388 participating women of the findings so those women who had been taking the placebo could consider starting tamoxifen therapy after consulting with their personal physicians.

* The study is titled, "Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. The authors are B. Fisher, J.P. Costantino, D.L. Wickerham, C.K. Redmond, M. Kavanah, W.M. Cronin, V. Vogel, A. Robidoux, N. Dimitrov, J. Atkins, M. Daly, S. Wieand, E. Tan-Chiu, L. Ford, N. Wolmark, and other NSABP investigators. *Journal of the National Cancer Institute*, Vol. 90, No. 18, Sept. 16, 1998.

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On Sept. 2, 1998, the Food and Drug Administration's (FDA) Oncologic Drugs Advisory Committee recommended expanding the label for Nolvadex to include reduction in the risk of breast cancer in high-risk populations as one of its approved uses. The FDA is not bound by the committee's recommendations, but usually follows them.

BCPT participants will continue to be followed by the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Pittsburgh-based research network that conducted the trial with support from the National Cancer Institute (NCI).

In this trial, healthy women assigned to take tamoxifen developed 89 cases of invasive breast cancer compared to 175 cases in the women assigned to the placebo.

Women on tamoxifen also had 50 percent fewer diagnoses of noninvasive breast cancer, such as ductal or lobular carcinoma in situ (35 cases in the tamoxifen group vs. 69 cases in the placebo group). Nine participants have died of breast cancer, three in the tamoxifen group and six in the placebo group.

Tamoxifen did increase the women's chances of three rare but life-threatening health problems: there were 36 cases of endometrial cancer (cancer of the lining of the uterus) in the tamoxifen group vs. 15 cases in the placebo group; there were 18 cases of pulmonary embolism (blood clot in the lung) in the tamoxifen group vs. six cases in the placebo group; and there were 35 cases of deep vein thrombosis (blood clots in major veins) in the tamoxifen group vs. 22 cases in the placebo group.

Among these women at increased risk for breast cancer, women under age 50 appeared to suffer no excess risk of serious adverse effects from use of tamoxifen compared to the placebo group of the study.

The BCPT was designed to see whether the drug tamoxifen prevents breast cancer in women who are at an increased risk of developing the disease. Women in the study were randomly assigned to receive tamoxifen or a placebo pill, and neither participants nor their physicians were aware of the treatment assignment, a process called "double-blinding."

Launched in April 1992, the BCPT also looked at whether taking tamoxifen decreased the number of heart attacks and reduced the number certain common types of bone fractures in these women. There was no difference in the number of heart attacks between the tamoxifen and placebo group, but women in the tamoxifen group had fewer bone fractures of the hip, wrist, and

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spine (111 cases in the tamoxifen group vs. 137 cases in the placebo group), a finding that nearly reached statistical significance.

As part of the study design, the BCPT data were regularly reviewed by an independent Endpoint Review, Safety Monitoring, and Advisory Committee. At its regularly scheduled meeting on March 24, 1998, the committee recommended that the participants and their physicians be told what pills each participant had been taking because of the clear evidence that tamoxifen reduced breast cancer risk. NSABP presented the data to NCI on March 26 and, together, both NSABP and NCI researchers concurred with the committee's recommendation. It was agreed that any additional information that might be gained from continuing the study in its randomized form did not outweigh the benefits of making the treatment available to the participants in the placebo group and other women at increased risk of breast cancer.

The women in the trial have taken tamoxifen or placebo daily for an average of four years. In spite of extensive efforts to enroll minorities in the BCPT, Black American, Asian American, Hispanic, and other groups together made up only about 4 percent of the participants. About 40 percent of the participants were ages 35 to 49, 30 percent were ages 50 to 59, and 30 percent were age 60 or older. All age groups showed similar reductions in breast cancer incidence from tamoxifen.

Women in the study will continue to be monitored by BCPT investigators. Postmenopausal women ages 35 or older who had been taking the placebo are invited to participate in the upcoming NSABP Study of Tamoxifen and Raloxifene (STAR) that will compare tamoxifen to raloxifene (Evista®, Eli Lilly, and Co., Indianapolis, Ind.). Raloxifene is approved by the FDA for prevention of osteoporosis in postmenopausal women and could also have breast cancer prevention properties. Women on placebo also have the option of seeking tamoxifen from their health care providers.

Only women at increased risk for developing breast cancer participated in the study. Because the risk of breast cancer increases with age, women 60 years of age and older qualified to participate based on age alone. At age 60, about 17 of every 1,000 women are expected to develop breast cancer within five years. Women between the ages of 35 and 59 who demonstrated an increased risk of breast cancer equivalent to or greater than that of an average

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60-year-old woman were also eligible. This breast cancer risk was determined by a computer calculation based on the following factors:

- Number of first-degree relatives (mother, daughters, or sisters) who had been diagnosed as having breast cancer;
- Whether a woman had any children and her age at her first delivery;
- The number of times a woman had breast lumps biopsied, especially if the tissue was shown to have a condition known as atypical hyperplasia;
- The woman's age at her first menstrual period; and
- Whether a woman has had a type of noninvasive breast cancer known as lobular carcinoma in situ.

A computer-based tool that allows health professionals to project a woman's individualized estimate of breast cancer risk is being released in a pilot program by NCI this month. The Breast Cancer Risk Assessment Tool is a computer program that women and their health care providers can use to estimate a woman's chances of developing breast cancer based on several established risk factors. Researchers from NCI and NSABP developed the tool. The disk is available at no charge and in personal computer (PC) and MacIntosh computer formats. To order, call the NCI's Cancer Information Service at 1-800-4-CANCER or visit NCI's CancerTrials Web site at <http://cancertrials.nci.nih.gov>.

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Questions and Answers are available on the NCI media website (<http://rex.nci.nih.gov>) or from the NCI Press Office.

Sources of Information

For information on the Breast Cancer Prevention Trial and easy access to all clinical trials information from the National Cancer Institute, go to: <http://cancertrials.nci.nih.gov>.

For information on National Surgical Adjuvant Breast and Bowel Project clinical trials, including future prevention trials, go to: <http://www.nsabp.pitt.edu>.

The National Cancer Institute's Cancer Information Service (CIS) is a nationwide information and education network for cancer patients and their families, the public, and health professionals. The CIS can provide information about breast cancer prevention, detection, treatment, and research. One toll-free number, 1-800-4-CANCER (1-800-422-6237) connects English- and Spanish-speaking callers all over the country with the office that serves their area. The number for callers with TTY equipment is 1-800-332-8615.