Antihormone Therapy Anastrozole May Provide New Option for Breast Cancer Prevention

SAN ANTONIO — Breast cancer incidence among postmenopausal women at high risk for developing the disease was significantly reduced by the antihormone therapy anastrozole, indicating that the drug may be an effective new option for breast cancer prevention for this group of women, according to initial results of a double-blind, randomized, placebo-controlled trial presented here at the 2013 San Antonio Breast Cancer Symposium, held Dec. 10–14. The study is being simultaneously published in the *The Lancet*.

About 80 percent of women diagnosed with breast cancer in the United States each year have tumors with high levels of hormone receptors. These tumors are fueled by the hormone estrogen. Anastrozole is a drug that prevents the body from making estrogen, and it has been used to treat postmenopausal women with hormone receptor-positive breast cancer for more than 10 years.

“We initiated the International Breast Cancer Intervention Study II (IBIS-II) Prevention trial to investigate whether anastrozole can be used effectively to prevent breast cancer,” said Jack Cuzick, Ph.D., chairman of the IBIS-II Steering Committee. “Our initial results show that for postmenopausal women who do not have breast cancer, but are at high risk for developing the disease, anastrozole reduced breast cancer incidence by 53 percent with very few side effects.

“Two other antihormone therapies, tamoxifen and raloxifene, are used by some women to prevent breast cancer, but these drugs are not as effective and can have adverse side effects, which limit their use,” explained Cuzick, who is also head of the Cancer Research U.K. Centre for Cancer Prevention and director of the Wolfson Institute of Preventive Medicine at Queen Mary University of London. “Hopefully, our findings will lead to an alternative prevention therapy with fewer side effects for postmenopausal women at high risk for developing breast cancer.”

Cuzick and colleagues enrolled 3,864 postmenopausal women at increased risk for developing breast cancer in the IBIS-II Prevention study from 2003 to 2012. Women were considered to be at high risk for breast cancer if they fulfilled any one of a number of criteria, including having...
two or more blood relatives with breast cancer, having a mother or sister who developed breast cancer before the age of 50, and having a mother or sister who had breast cancer in both breasts. Among the participants, 1,920 were randomly assigned to anastrozole for five years and 1,944 to a placebo.

After a median follow-up of just more than five years, the researchers found that women assigned to anastrozole were 53 percent less likely to have developed breast cancer compared with women assigned to the placebo. In addition, very few side effects were reported, mostly small increases in muscle aches and pains, and hot flushes, according to Cuzick.

“We are planning to continue following the IBIS-II Prevention participants for at least 10 years, and hopefully much longer,” said Cuzick. “We want to determine if anastrozole has a continued impact on cancer incidence even after stopping treatment, if it reduces deaths from breast cancer, and to ensure that there are no long-term adverse side effects.”

This study was supported by funds from Cancer Research U.K., the National Health and Medical Research Council of Australia, AstraZeneca, and Sanofi-Aventis. Cuzick is on the speaker’s bureau for AstraZeneca.

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The mission of the 2013 San Antonio Breast Cancer Symposium is to produce a unique and comprehensive scientific meeting that encompasses the full spectrum of breast cancer research, facilitating the rapid translation of new knowledge into better care for patients with breast cancer. The Cancer Therapy & Research Center (CTRC) at The University of Texas Health Science Center at San Antonio, the American Association for Cancer Research (AACR) and Baylor College of Medicine are joint sponsors of the San Antonio Breast Cancer Symposium. This collaboration utilizes the clinical strengths of the CTRC and Baylor and the AACR’s scientific prestige in basic, translational, and clinical cancer research to expedite the delivery of the latest scientific advances to the clinic. For more information about the symposium, please visit [www.sabcs.org](http://www.sabcs.org).

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**Title:** First results of the International breast cancer intervention study II (IBIS-II): A multicentre prevention trial of anastrozole versus placebo in postmenopausal women at increased risk of developing breast cancer

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Background: Third generation aromatase inhibitors have been widely used in postmenopausal women for the adjuvant treatment of hormone receptor positive breast cancer. Anastrozole has shown significantly prolonged disease-free survival, lower rates of recurrence and distant recurrence, and significantly reduced contralateral breast cancer in patients treated with anastrozole compared with tamoxifen. Here, we assess the efficacy of anastrozole compared to placebo in postmenopausal women who do not have breast cancer but are at high risk of developing the disease.

Material and Methods: Postmenopausal women at increased risk of developing breast cancer were recruited into a double-blind trial of anastrozole (1mg/day) versus matching placebo. The primary objective of this study was to determine the efficacy of anastrozole in preventing breast cancer (both invasive and ductal carcinoma in situ). Secondary endpoints included prevention of oestrogen receptor positive breast cancer, breast cancer mortality, other cancers, cardiovascular disease, fractures, adverse events and non-breast cancer deaths.

Results: Between 2003 and 2012, a total of 3864 postmenopausal women were recruited into the IBIS-II Prevention study. 1920 women were randomly assigned to receive anastrozole and 1944 women matching placebo. Median follow-up for this first analysis is 5.04 years and 125 breast cancer events have been recorded, exceeding the protocol-specified events for the first main analysis. Median age was 59.3 years (SD 5.7) and 47.0% of women had used hormone replacement therapy (HRT) before joining the trial. Of the 125 breast cancers reported, 25 were ductal carcinoma in situ (DCIS), 62 invasive oestrogen-receptor (ER) positive, 25 invasive ER-negative, and for 13 breast cancers details are currently not available. A total of 35 deaths have been reported.

Conclusion: We will present a comprehensive analysis of the efficacy of anastrozole for preventing breast cancer and also major adverse events by intention to treat (ITT).