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Anti-estrogen Drug Therapy Reduces Risk of Invasive Breast Cancer in Older Women

UC San Diego Researchers Lead International Effort

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New analysis of a drug approved for osteoporosis prevention and treatment has provided definitive evidence that the medication is also effective as a breast cancer preventative for certain cancers. Women who took the drug raloxifene were less likely to develop invasive, estrogen-receptor (ER) positive breast cancer compared with women who did not take the drug. The results of the randomized controlled trial will be published in the June 10 online issue of the *Journal of the National Cancer Institute.*

Breast cancer is the most common cancer among women. In 2008, to date, 182,460 new cases of female breast cancer have been diagnosed and 40,480 women have died due to breast cancer (National Cancer Institute).

Raloxifene is a selective estrogen receptor modulator (SERM), which means that the drug has estrogen-like effects on some tissues, such as bone, but anti-estrogen effects on other tissues such as breast. Previous data from the RUTH (Raloxifene Use for The Heart) Trial, which involved more than 10,000 post-menopausal women participants around the world who had an increased risk of coronary heart disease, showed that the drug did not protect against heart disease but it did reduce the risk of invasive breast cancer by 44 percent. The drug is currently approved by the FDA for the prevention and treatment of osteoporosis in postmenopausal women, and invasive breast cancer risk reduction in postmenopausal women with osteoporosis or at high risk for breast cancer.

In this paper, researchers report that, regardless of age, prior hormone use or baseline breast cancer risk, raloxifene reduced the risk of hormone responsive (ER-positive) breast cancers by at least 50 percent for at least 8 years. Most postmenopausal women with breast cancer have this kind of breast cancer.

Non-invasive cancers confine themselves to the ducts or lobules and do not spread to the surrounding tissues in the breast or other parts of the body. They can, however, develop into or raise the risk for a more serious, invasive cancer. Invasive cancers are more aggressive and have started to break through normal breast tissue barriers and invade surrounding areas.

"This research gives older women facing certain medical decisions another option," explained principal investigator Elizabeth Barrett-Connor, M.D., distinguished professor and Chief, Division of Epidemiology, Department of Family and Preventive Medicine, and a member of the Cancer Prevention and Control Program, UC San Diego School of Medicine. "For example, if a woman at risk for osteoporosis is considering taking medication, and has no history of blood clots or stroke, raloxifene might be a more appealing option due to its protective role in invasive breast cancer."

The RUTH trial, the world's largest study of women and heart disease, was a randomized, blinded, placebo-controlled trial conducted at 177 sites, in 26 countries, on five continents. Between June 1998 and August

2000, 10,101 postmenopausal women with coronary heart disease or several heart disease risk factors were randomly assigned to raloxifene or to placebo and followed for a median of 5.6 years. The 5,044 women who took raloxifene had a 55 percent reduction in risk of developing invasive ER-positive breast cancer as compared to the 5,057 women who took placebo.

The initial results of the RUTH trial were published in 2006. The reduction in breast cancer risk was consistent with findings from other trials that involved women who did not have heart disease. However, women who took raloxifene in the RUTH trial had an increased incidence of blood clots and fatal strokes compared to those who took placebo. Thus, the researchers concluded that women considering use of raloxifene need to weigh the risks and benefits.

Study author Deborah Grady, M.D., M.P.H., of the University of California, San Francisco, and colleagues examined the RUTH trial data in more detail in order to investigate the specific types and stages of breast cancer affected by raloxifene, as well as the timing of its action and the types of patients it can help.

"In this study, we looked at whether raloxifene would be more effective in some subgroups of women than others, but found that the relative benefit was the same, regardless of breast cancer risk," said Grady. "Like any therapy, the risk needs to be balanced with the side effects, which for raloxifene include blood clots and fatal stroke. But these findings are important because few drugs actually reduce the risk of breast cancer." noted Grady. "Also raloxifene has been on the market for nearly a decade with good, long term safety data," said Barrett-Connor.

Researchers say women who would have the best risk-benefit ratio would be those at high risk of breast cancer, who have a 30 to 50 percent chance of getting breast cancer in the next five to ten years, and low risk of venous thrombosis and stroke. A reduced risk of spine fractures would be an additional benefit.

Participating institutions included UC San Diego as well as University of California, San Francisco, and the San Francisco VA Medical Center, San Francisco, CA, USA; University of Pittsburgh, Pittsburgh, PA, USA; Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA; School of Public Health, Brussels Free University (ULB), Brussels, Belgium; Columbia University College of Physicians and Surgeons, New York, NY, USA; Royal Brompton Hospital and National Heart and Lung Institute, Imperial College London, London, UK; and Emory University School of Medicine, Atlanta, GA, USA.

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