Cancer Research Center Hotline

The Study of Tamoxifen and Raloxifene (STAR Trial) for the Prevention of Breast Cancer

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The Study of Tamoxifen and Raloxifene (STAR) is designed to determine whether the drug used to treat and prevent osteoporosis, raloxifene (Evista®) is as effective as tamoxifen (Novaldex®) in reducing breast cancer in women who are at the greatest risk for the disease. The study has a five-year recruitment plan, which will enroll 22,000 women nationwide, making it one of the largest studies designed to find ways to prevent breast cancer. The study opened in Hawaii at the University of Hawaii's Cancer Research Center of Hawaii in July of 1999. The STAR Study has since recruited 114 of Hawaii's women, all of whom have an increased risk of developing breast cancer.

Tamoxifen was shown to reduce the chance of developing invasive breast cancer by 49% in the Breast Cancer Prevention Trial (BCPT), a study of over 13,000 premenopausal and postmenopausal women at high risk of breast cancer[1]. In the BCPT, half the women took tamoxifen and half took a placebo (an inactive pill that looked like tamoxifen). Participants taking tamoxifen also had fewer fractures of the hip, wrist, and spine than women taking the placebo.

Data regarding breast cancer incidence and raloxifene were obtained from the Multiple Outcomes of Raloxifene Evaluation (MORE) trial. The MORE trial was a multi-center osteoporosis trial that involved 7,705 postmenopausal women with osteoporosis entered at centers around the world. Women were randomized to receive either raloxifene at 60 or 120 mg/d or placebo. The 48 month results from the MORE trial showed a reduction in invasive breast cancer by 72% in women who took raloxifene daily for four years[2]. It is important to recognize that this study was designed as an osteoporosis study. Women were selected because of their pre-existing osteoporosis. Breast cancer risk was not considered. These results emphasize the value of the STAR which will compare the worth of raloxifene in women at increased risk for the disease, and will compare this with tamoxifen in a randomized clinical trial in which breast cancer incidence is a primary study end point.

While tamoxifen has been shown to reduce breast cancer risk in high risk women, the drug increased the women's chances of developing four potentially life-threatening health problems: uterine cancer, deep vein thrombosis, pulmonary embolism, and possibly stroke. Women taking tamoxifen have a two- to three-fold increased risk of uterine cancer. While previous data indicated that tamoxifen increased the risk of only endometrial cancer, recent case studies suggest that tamoxifen may also slightly increase the risk for uterine sarcoma[3]. In the BCPT there are about two cases of uterine sarcoma per 10,000 women taking tamoxifen each year[3,4]. Risk for vascular events are similar to those seen with hormone replacement therapy (HRT).

Information about the safety of raloxifene is limited compared to the data available on tamoxifen. Raloxifene was approved in December 1997 by the FDA to prevent osteoporosis and has been in clinical trials for about five years. Tamoxifen has been approved by the FDA to treat women with breast cancer for more than 20 years and has been in clinical trials for about 30 years. Women taking raloxifene in studies of osteoporosis have had an increased chance of developing a deep vein thrombosis or pulmonary embolism similar to the risk seen with tamoxifen. In these studies, raloxifene did not increase the risk of endometrial cancer. An important objective of STAR will be to compare the long-term safety of raloxifene and tamoxifen in women at increased risk for breast cancer.

Women who participate in STAR must be postmenopausal, at least age 35, and have an increased risk of breast cancer as determined by their age, family history of breast cancer, personal medical history, age at first menstrual period, and age at first live birth. They will also go through a process known as informed consent, during which they will learn about the potential benefits and risks of tamoxifen and raloxifene before deciding whether to participate in STAR. Information sessions for STAR are held monthly at the Cancer Research Center of Hawaii.

Once a woman chooses to participate, she will be randomly assigned to receive either 20 mg tamoxifen or 60 mg raloxifene daily for five years. She will be seen at the Cancer Research Center for follow-up every six months. At that time she will be interviewed regarding her health status and may also receive a clinical breast exam which is required every six months. Each woman will continue her health care with her regular physicians. Annual mammograms and lab tests to include CBC and liver and kidney function studies are required. Pelvic exams will be required annually for all women with the exception of those who have had a total hysterectomy and bilateral oophorectomy. Study drugs are provided without charge and a six months' supply will be given at the time of the follow-up visit. Throughout her participation, a woman will be closely monitored for any adverse events, and updated regarding any new findings.

The STAR presents an important option for women at high risk for breast cancer. Tamoxifen has been approved for this indication. In the recent "American Society of Clinical Oncology Technology Assessment on Breast Cancer Risk Reduction Strategies: Tamoxifen and Raloxifene"[5], it is stated, "It is premature to recommend raloxifene use to lower the risk of developing breast cancer outside of a clinical trial setting."

STAR is now into its fourth year with more than 60% of accrual achieved. Please consider this important trial when counseling women who are at high risk for breast cancer.

The University of Hawaii's Cancer Research Center of Hawaii is one of more that 400 sites participating in STAR. Dr. Nancy Furumoto is the Principal Investigator; Ann Kelminski, R.N. is Program Coordinator.

For more information about STAR, or to refer patients please call the Cancer Research Center at (808)586-2979 or visit the National Surgical Adjuvant Breast and Bowel Project (NSABP) web site at http://www.nsabp.pitt.edu, the NCI clinical trials web site at http://cancertrials.nci.nih.gov, or the Cancer Research Center of Hawaii web site at www.crch.org.

References

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2. Marbaugh, D., Schaefer, J. "Final Data from Landmark MORE Study Show Evista® Continues to Reduce Breast Cancer Risk Through Four Years" Press Release, Eli Lilly and Company, February 12, 2001.
3. Wickerham DL, Fisher B, Wolmark N et al: Association of Tamoxifen and Uterine Sarcoma. Journal of Clinical Oncology Vol 20, No 11 Correspondence.
4. National Cancer Institute. Cancer Information Service. "Cancer Facts" Fact Sheet 4.19, Rev 22 May 2001 <http://cis.nci.gov/fact/4_19.htm>.
5. American Society of Clinical Oncology. "American Society of Clinical Oncology Technical Assessment on Breast Cancer Risk Reduction Strategies: Tamoxifen and Raloxifene." 25 June 2002 <http://www.asco.org>.