# Letrozole Stems Breast Ca Return After Tamoxifen

BY MARY ANN MOON
*Contributing Writer*

Use of the aromatase inhibitor letrozole was linked to a significant 63% reduction in disease recurrence in women with early-stage breast cancer who completed 5 years of tamoxifen therapy 1-7 years earlier, results of a phase III study suggest.

"It appears that most cancers remain estrogen dependent for long periods in follow-up and that their clinical courses can be improved by the judicious use of aromatase inhibitors, even very late in follow-up," study investigators reported online in the Journal of Clinical Oncology.

Until now clinicians, regulatory agencies, and health care funders have restricted the use of letrozole to women who were within 3 months of discontinuing tamoxifen, because the evidence supported its use only in these cases. But many, if not most, breast cancer survivors have been off tamoxifen for more than 3 months. They have never been offered letrozole even though they might benefit from it, wrote Dr. Paul E. Goss of Massachusetts General Hospital Cancer Center, Boston, and his associates in the National Cancer Institute of Canada (NCIC) Clinical Trials Group MA.17 study.

Ideally, the question would be settled by a randomized clinical trial. Such a study is under consideration, but even if it proves feasible, the results will not be available for years. In the meantime, assessing outcomes in a subgroup of women in the NCIC MA.17 trial "provides a unique opportunity to determine whether a later intervention with the aromatase inhibitor" is beneficial. These findings "provide the only available information that can be used to inform the decision these women and their physicians face," Dr. Goss and his associates said.

In the MA.17 trial, more than 5,000 postmenopausal women within 3 months of completing approximately 5 years of adjuvant tamoxifen therapy were randomly assigned to receive letrozole or placebo and were to be followed for another 5 years. But an interim analysis after a median of 2.4 years showed a distinct advantage with letrozole, so the trial was unblinded and the placebo group was offered letrozole for the remaining 2.6 years of the trial.

A total of 1,579 women switched to letrozole, while 804 elected no further treatment after unblinding. Thirty-one women (2%) who switched to letrozole developed recurrences, compared with 39 (5%) who did not take letrozole. The drug was associated with an adjusted hazard ratio of 0.37, corresponding to a 63% reduction in disease recurrence (J. Clin. Oncol. 2008;26 [doi: 10.1200/jco.2007.11.6798]).

Distant metastases occurred in 1% of women who switched to letrozole, compared with 2.4% of those who didn't take letrozole; a significant 61% reduction in the risk of developing distant metastases was reported. Similarly, mortality was lower with letrozole than without it (1.3% vs. 4.5%).

Interpreting these results is complicated by the fact that these study subjects self-selected for letrozole therapy or no further therapy. The patients who chose letrozole were at greater risk of recurrence because of tumor characteristics, however.

In addition to the NCIC's funding, this study was supported by the Pharmacia Corp, a Pfizer company, and Novartis Pharmaceuticals Canada Inc. ■

# Use Additional Codes to Cope With Pay for Performance

BY DAMIAN McNAMARA
*Miami Bureau*

Fort Lauderdale, Fla. — Pay-for-performance evaluations of physicians will require additional reimbursement codes to justify the provision of some services.

Medicare and private insurers historically have used coding for financial reimbursement, but the government and insurers began "profiling" all physicians based on claims data about 5 years ago, Dr. Barbara Levy said at a meeting on hysterectomy sponsored by the Cleveland Clinic.

**A physician who uses more resources per patient during a particular period of time will be paid less, per the program's efficiency measures.**

"We are designing additional ICD-9 codes because of pay for performance," said Dr. Levy, a member of the Code and Nomenclature Committee of the American College of Obstetricians and Gynecologists.

For example, one of the quality measures from HEDIS (the Healthcare Effectiveness Data and Information Set) promotes regular pap smears for cervical cancer screening, except for patients who had a hysterectomy for benign disease. "We did not have an ICD-9 code for this until this year: 'Patient no longer has organ.' So now the payers will know that we did not do a pap smear for a good reason. And they are extrapolating this information to judge our quality," said Dr. Levy, also the medical director of the Women's Health and Breast Center, Franciscan Health System, Federal Way, Wash.

Ob.gyns. should begin collecting their own case data, including outcomes, instead of waiting for the government or others to do it, Dr. Levy said. "We need to learn to be stewards of our resources and pay attention to what things cost." She calculated a $4,800 overall cost per case for laparoscopic supracervical hysterectomy at her institution, for example. The cost per case for a vaginal hysterectomy is less than $1,000. "We need to think about those things … If we don't do this, someone else will."

Watch for inequities in physician ratings as pay for performance is implemented, Dr. Levy said. The typical measure of physician efficiency is a ratio of actual resource use to expected resource use, given an equivalent quality of care in a particular geographic area. "My practice is primarily gynecologic surgery, so my patients are typically 15 years older than the average ob.gyn. patient in my area," she said.

A physician who uses more resources per patient during a period of time will be paid less, according to the program's efficiency measures. Also, if particular physicians are labeled as higher-cost doctors, a patient might have to pay a higher copay to see them, Dr. Levy said. ■

# Disease Activity, Ethnicity Mediate Risk of Ovarian Failure in SLE

Higher disease activity, treatment with cyclophosphamide, older age, and a certain ethnic background were each linked with a significantly increased risk for developing premature gonadal failure in a study of 316 women with systemic lupus erythematosus.

Disease activity and Texan-Hispanic ethnicity had not previously been reported to boost the risk for premature gonadal failure (PGF) in younger women with systemic lupus erythematosus (SLE), reported Dr. Luis A. González of the division of immunology and rheumatology at the University of Alabama, Birmingham, and his associates (Ann. Rheum. Dis. 2008 Feb. 13 [doi: 10.1136/ard.2007.083576]). The study also confirmed the previously reported findings that cyclophosphamide treatment and older age were linked with PGF in women with SLE.

Alternatives to cyclophosphamide treatment are needed for treating young women with SLE, said Dr. González and his associates.

They used data collected in the Lupus in Minorities: Nature vs. Nurture (LUMINA) study, a longitudinal outcomes study that included SLE patients aged 16 or older who were diagnosed with SLE for 5 years or less. From this group, they focused on women younger than 40 years of age who were not postmenopausal when they entered the study.

This yielded a study group of 316 women, with an average age of about 29 years. Their average duration of SLE at enrollment was 1 year. The group included women from four racial and ethnic groups: Texan-Hispanics, Puerto Rican-Hispanics, African Americans, and whites.

During follow-up, 37 women (12%) developed PGF. The total group of 316 women included 76 who were treated with cyclophosphamide, of whom 33% developed PGF. Women categorized as Texan-Hispanic were about four- to five-fold more likely to develop PGF, compared with white women.

**—Mitchel L. Zoler**

# FDA Finds Injectable Anemia Drug 'Not Approvable'

BY BROOKE McMANUS
*"The Pink Sheet"*

The Food and Drug Administration has issued a "not approvable" letter to Luitpold Pharmaceuticals for its ferric carboxymaltose injection (Injectafer), leaving the company to conduct additional clinical trials for the drug as first-line treatment of iron deficiency anemia in women with postpartum and heavy uterine bleeding.

The Daiichi Sankyo Co. subsidiary said in a statement on March 12 that the studies are needed to address safety issues with Injectafer, particularly a mortality signal that led the Drug Safety and Risk Management Advisory Committee to vote against its approval in February.

The panel concluded that studies conducted by Shirley, N.Y.–based Luitpold Pharmaceuticals Inc. showed that Injectafer was efficacious in replenishing iron and improving hemoglobin concentration, but the mortality data raised a red flag—10 deaths of patients who received the drug, 5 of whom had cardiac abnormalities.

A number of committee members advised that if the FDA chose to approve the product, the label should be limited to women for whom oral iron is not effective. Most of those voting in favor of approval said off-label use should be limited, especially in chronic kidney disease patients.

"While we are disappointed about this latest decision, we are committed to the further development of Injectafer and are working on new studies in support of our application and to address the FDA's concerns," Mary Jane Helenek, Luitpold's president and CEO, said in the company release.

The not approvable letter is the second received by the company related to the mortality signal. Luitpold submitted a statistical assessment of mortality data, study reports for two additional studies, and responses to other FDA questions in September 2007.

The company said its application includes data from 12 multicenter trials including more than 3,000 patients. ■

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