Southwest Oncology Group
A National Clinical Research Group

NEWS RELEASE

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Definitive study confirms chemo benefit in postmenopausal breast cancer

But second study finds a subset of patients who may not benefit.

ANN ARBOR, Mich., Dec. 10, 2009 — Chemotherapy added to tamoxifen can improve outcomes for postmenopausal breast cancer patients, according to a landmark study by the Southwest Oncology Group.

But a related study presented today at the 2009 San Antonio Breast Cancer Symposium finds that a multigene test on tumors can identify a subset of patients who may not benefit from that chemotherapy.

Both studies were led by Dr. Kathy Albain, of Loyola University Health System. Both have just been published online, the first in the journal *The Lancet*, the second in *The Lancet Oncology*.

The studies report on a randomized phase III clinical trial of 1,477 postmenopausal women that was conducted at institutions across the U.S. and Canada by the University of Michigan-based Southwest Oncology Group (SWOG), one of the largest federally funded clinical trial networks. All of the women had estrogen receptor-positive (ER+) breast cancer that had spread to the lymph nodes under the arm, known as the axillary lymph nodes.

All women in the trial got daily tamoxifen for up to five years, long the standard therapy for treating ER+ breast cancer, the most common form of the disease. Estrogen latches on to receptors on these cancer cells and promotes tumor growth. Tamoxifen blocks those receptors, locking estrogen out.

Of the 1,477 women in the trial, 361 got only tamoxifen. The rest got tamoxifen plus a regimen of a three-drug chemotherapy treatment known as CAF (cyclophosphamide, Adriamycin®, and 5-fluorouracil).

Albain's team reports in the *Lancet* paper that they saw long-term survival benefits for the women who received CAF chemotherapy. These women's risk of dying or having a cancer recurrence was 24% lower than it was for women who had gotten tamoxifen alone. The team also found that those who got the chemotherapy before the tamoxifen did better than those who got both simultaneously.

The CAF group had higher overall survival rates as well. "Ten years after the start of their treatment, 68% of women who received chemotherapy followed by tamoxifen were still alive, while only 60% of women in the tamoxifen-only arm lived for at least ten years," says William Barlow, Ph.D., of the SWOG Statistical Center in Seattle, who served as lead statistician on both studies.

Initial results from this trial presented at professional conferences in recent years have already changed the standard of practice to include several months of CAF chemotherapy before tamoxifen in treating postmenopausal women with ER+ breast cancer.

The second study, published in *The Lancet Oncology*, was conducted to determine if subsets of women in the SWOG trial could be identified who did not benefit from chemotherapy despite being at higher risk due to lymph node involvement. This study retrospectively analyzed tumor specimens from the trial using a genetic test called the 21-gene recurrence score assay (Oncotype DX®). The assay measures the expression or activity level of 21 specific genes within a tumor sample, and the score predicts risk of recurrence. Testing was conducted by Genomic Health, Inc., who were blinded to the study results.

The study found that women whose tumors scored low on the genetic test appeared to get little or no benefit from CAF chemotherapy added to tamoxifen, while those with higher scores seemed to derive major benefit from this addition.

The 21-gene recurrence score test is now routinely used on the tumors of many patients whose breast cancer has not spread to their lymph nodes – node-negative breast cancer. Doctors use the assay score to help them decide whether a patient is likely to benefit from a course of chemotherapy.

The researchers conclude that this test may similarly predict chemotherapy benefit in patients whose breast cancer *has* spread to their lymph nodes. These patients account for about one-fifth of newly diagnosed breast cancer cases in the U.S.

"There's nothing magic about the biology being different in lymph node-negative versus lymph node-positive breast cancer," says Albain. When it comes to predicting benefit from chemotherapy, "our data suggest that it doesn't seem to matter whether the lymph nodes are involved or not, but the recurrence score on the genetic assay does matter. It identifies for us a group of patients who have a distinct tumor biology, for whom chemotherapy may not reduce the chances of recurrence even though their risk is high."

Currently, several months of chemotherapy after surgery is the standard of care for a patient with node-positive breast cancer, regardless of the hormone receptor or other biomarker status in her tumor tissue. Indeed, chemotherapy in this setting has been credited in part for a marked decline in breast cancer mortality over the last 20 years. But if validated by later studies, the results reported by the SWOG investigators would mean that many of these patients are being treated needlessly, since they do not benefit from the chemotherapy.

The researchers stress that these results only pertain to patients with estrogen receptor-positive breast cancers, and that more work needs to be done to confirm the findings before doctors change clinical practice based on them.

“Many aspects of this retrospective study introduce uncertainty into our results and make our conclusions tentative,” says Dr. Daniel Hayes of the University of Michigan Medical School, who was senior author on the *Lancet Oncology* study. “Prospective studies with larger sample sizes are needed to determine who will benefit from chemotherapy added to hormonal therapy and who should avoid chemotherapy altogether.”

Hayes adds that the Southwest Oncology Group is now designing such a study.

Funding for both studies was provided by the National Cancer Institute. Genomic Health, Inc., maker of the Oncotype DX® genetic assay, also provided support for the second study through an agreement with the Southwest Oncology Group.

References: *The Lancet*, DOI:10.1016/S0140-6736(09)61523-3; *The Lancet Oncology*, DOI:10.1016/S1470-2045(09)70314-6

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*The **Southwest Oncology Group** (swog.org) is one of the largest cancer clinical trials cooperative groups in the United States. Funded primarily by the National Cancer Institute, the group designs and conducts clinical trials to advance the science of cancer prevention and treatment and to improve the quality of life for cancer survivors. The almost 5,000 researchers in the Group’s network practice at more than 500 institutions, including 19 of the National Cancer Institute-designated Comprehensive Cancer Centers. The Group is headquartered at the University of Michigan in Ann Arbor, Mich. (734-998-7140). The Group has an operations office in San Antonio, Texas and a statistical center in Seattle, Wash.*