

Breast Cancer

Highlights from the 25th Annual San Antonio Breast Cancer Symposium
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Women in the US Are More Likely to Have Mastectomies

By Orly Aridor

SAN ANTONIO, TEXAS—At the general session of the San Antonio Breast Cancer Symposium, **Gershon Locker, MD**, Professor of Medicine at Northwestern University, representing the ATAC Trialists' group, presented analyses on the rates of mastectomy as opposed to breast conservation in women with early breast cancer. There were 9366 postmenopausal women from 21 countries who had participated in the ATAC trial. A retrospective analysis was conducted to check for factors that could predict for having had a mastectomy versus conservative surgery. Although there was an equal distribution of prognostic and therapeutic factors across the treatment arms, there were differences

in the mastectomy rates between countries represented in this study.

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In the UK (n=3228), a mastectomy was performed in 42% of women compared with 51% in the US (n=2222), with a hazard ratio of 1.43. Dr Locker presented a univariate analysis of factors that predicted mastectomy, which included a larger tumor size (≥ 2 cm), node positivity (>4), age older than 69, a poorly differentiated tumor, and use of adjuvant chemotherapy. During the ATAC trial, patients in centers enrolling ≤ 40 patients (used

as a marker for surgical experience) were more likely to receive a mastectomy than patients enrolled in sites with >40 patients. In comparison, patients with an ER-positive tumor or weighing more than 70 kilograms resulted in breast conservation. A multivariate analysis showed that being from the US remained an independent predictor for mastectomy, although the reasons for this difference are not clear. Breast conservation rates in US women enrolling in the ATAC study were comparable to the rates published by the NIH SEER database. "Given the desirability of breast conservation, increased educational efforts should be supported to promote its greater use," said Dr Locker. ■

Experts Discuss the Changing Face of Adjuvant Therapy

By Orly Aridor

SAN ANTONIO, TEXAS—A minisymposium was held at the 25th Annual San Antonio Breast Cancer Symposium that focused on *The Changing Face of Adjuvant Therapy*. **Hyman Muss, MD**, of the University of Vermont, discussed how to optimize the use of anthracyclines in the adjuvant setting, including selecting the optimal agent, dose, and schedule. There are two anthracyclines available, epirubicin and doxorubicin, and both are superior to CMF (cyclophosphamide, methotrexate, and 5-fluorouracil). There is no difference between the two, but epirubicin is less cardiotoxic, so it may be preferable. Based on the CALGB 9741 study, which was reported earlier during the meeting, high and moderate doses were superior to low doses (sequential vs concurrently). Dr

Comparison of three trials using paclitaxel adjuvant therapy for breast cancer

Trial	Patients	Treatment	Median Follow-up	Disease-Free Survival	Overall Survival
CALGB 9344	3170	Escalating dose of doxorubicin + fixed dose of cyclophosphamide (AC) AC + 4 cycles of sequential paclitaxel	52 mos	70%	81%
NSABP (B-28)	3060	4 cycles of AC 4 cycles of AC + paclitaxel	34 mos	81% 81%	90% 92%
(BCIRG) 001	524	8 cycles of FAC (5-fluorouracil, adriamycin, and cyclophosphamide) 4 cycles of paclitaxel followed by 4 cycles FAC	60 mos	83% 86%	Not reported

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Muss also described ongoing and planned trials by the CALGB.

Jean Marc Nabholz, MD, of the University of California-Los Angeles, discussed advances in the use of taxanes (paclitaxel and docetaxel) for breast cancer in the adjuvant setting. Dr Nabholz mentioned that at ASCO 1997, a few first-line therapies with taxanes were presented in a small number

of studies. "The 90's were the decade of taxanes. This was the turning point for Taxol," said Dr Nabholz. Monotherapy with taxanes was used first, followed by the combinations of taxanes and anthracyclines. "We are moving from the metastatic setting to the adjuvant setting," said Dr Nabholz.

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Hormone Replacement Therapy Increases Risk of Breast Cancer

“The concerns raised recently about hormone replacement therapy may also be applicable to many treatments currently used for breast cancer,” **Rowan Chlebowski, MD, PhD**, of the Harbor-UCLA Research and Education Institute, Torrance, California, reported at the recent San Antonio Breast Cancer Symposium. Tamoxifen and anastrozole affect the function of the estrogen receptor and the levels of estrogen in the body. Due to tamoxifen's positive estrogen function in some normal tissues, it may be used to supplement levels of hormones such as estrogen and progesterone. The Women's Health Initiative study, published earlier in 2002, showed that hormone replacement therapy (HRT) resulted in an increased risk of breast cancer. This study was a randomized, controlled, prevention trial with a

planned duration of 8.5 years, for which 16,608 postmenopausal women were recruited. It was designed to determine the health benefits and risks of supplemental estrogen and progesterone as compared to treatment.

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Rowan Chlebowski, MD, PhD
Harbor-UCLA Research and Education Institute, Torrance, California

The impact of HRT on coronary heart disease, breast cancer, stroke, pulmonary embolism, endometrial cancer, colorectal cancer, hip fracture, and death due to other causes was monitored. Conducted by the National Institutes of Health,

this study was halted last summer when results of an increased risk of breast cancer in women on HRT were disclosed. “In older trials, it was not considered important to monitor for issues such as the risk of heart disease and osteoporosis, because the mortality rate for breast cancer was so high,” said Dr Chlebowski. “Now, because such women typically have survival rates of 80% to 90%, the risk of developing chronic disease from a breast cancer treatment is highly relevant,” he added. It has previously been reported that cardiovascular disease and breast cancer were increased, whereas colorectal cancer and osteoporotic fractures were reduced in patients treated with HRT. Dr Chlebowski showed that endocrine treatment in postmenopausal women with breast cancer also impacts chronic problems such as hip fractures and heart disease. ■

Tumor Resistance to Some Endocrine Treatments—New Insights

The first speaker at the plenary session, **Robert Nicholson, PhD**, from the Tenovus Centre for Cancer Research in Cardiff, Wales, talked about how tumors develop resistance to endocrine therapies such as tamoxifen and aromatase inhibitors. Dr Nicholson showed that those tumor cells that are resistant to tamoxifen have greater levels of epidermal growth factor receptor (EGFR) and class I receptor from the tyrosine kinase erbB family (HER2), which contribute to increases in growth rate and ability to invade other sites. Increased numbers of these receptors may also affect the way tumor cells respond to tamoxifen, converting it from an anticancer

drug to a drug that may stimulate the growth of cancer cells instead. In addition, continued stimulation of these pathways can cause tumor cells to stop the syntheses of estrogen receptors, which could explain why endocrine therapies fail. Endocrine therapies are



The banks of the San Antonio River provided a scenic spot for a break during the San Antonio Breast Cancer Symposium

Endocrine treatment resistance results from increased expression of EGF and erbB receptors. Agents designed to block the function of these receptors may enhance endocrine therapy.

effective when tumor growth is stimulated through the estrogen receptor. New agents such as gefitinib and trastuzumab, which block the EGFR and HER2 receptors, respectively, may reduce endocrine resistance. Therefore, these new drugs in combination with endocrine therapy, may have a potential use, based on the hypothesis that targeting both the estrogen receptor and either EGFR or HER2 will turn resistant tumors into tumors sensitive to treatment. ■

Blood Test to Detect Breast Cancer Is on the Horizon

Currently, the best test for detection of breast cancer is mammography. However, in 20% of women's mammograms, breast cancer is not detected. A variety of serum markers for breast cancer have been identified, but none of the markers has a diagnostic value, according to **L.L.L. Wilson, MD**, from the Eastern Virginia Medical School, Norfolk, Virginia. Dr Wilson presented work on the progress of detecting multiple, differentially expressed serum proteins as a profile of biomarkers for breast cancer. One hundred thirty-nine women were enrolled in a single-center study. Serum was isolated

“The sensitivity and specificity of this technique approaches mammography. If confirmed in a larger study, it may serve as a blood test for detection of breast cancer that may be used as adjunct to other existing diagnostic tools.”

L.L.L. Wilson, MD
Eastern Virginia Medical School
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prior to undergoing treatment, and patients were classified as “normal,” “benign,” or “cancer.” Surface enhanced desorption/ionization (SELDI) protein chip mass spectrometry was performed on all samples. No single peak separated the analyzed groups. However, four protein peaks

predicted 93% of the blinded test samples. The sensitivity and specificity for cancer samples as compared to normal samples was 96%. Dr Wilson concluded that the SELDI protein chip mass spectrometry technique together with a classification algorithm identified in a reproducible manner protein profiles for the detection of breast cancer. “The sensitivity and specificity of this technique approaches mammography. If confirmed in a larger study, it may serve as a blood test for detection of breast cancer that may be used as adjunct to other existing diagnostic tools,” Dr Wilson said. ■

Elderly Patients Frequently Not Offered Aggressive Treatment

By Frieda Pearce, PhD

Breast cancer is the most common form of malignancy in women, and 30% of these cancers occur in women over 70 years of age. Previous studies have indicated that elderly patients have been treated less aggressively and not offered standard treatment because of their age. **Srilatha Neerukonda, MD**, from the Scott and White Hospital, Temple, Texas, in a poster session at the San Antonio Breast Cancer Symposium, indicated that some stage I patients and all patients with stage II-IV

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Attendees spend some time studying posters at the San Antonio Breast Cancer Symposium

disease should be offered systemic therapy. In a recent study, 520 women over age 70 who were treated at Scott and White Memorial Hospital and Clinic were retrieved from the tumor registry and then reviewed for the histological type,

Experience has shown that when offered aggressive chemotherapy or hormonal therapy, very few elderly women decline them, despite their age..

stage, treatment offered, and treatment received. Their study agrees with the previous finding, noting that chemotherapy was offered to only 18% of the total patients even though 35% of the patients required chemotherapeutic treatment; hormonal therapy was offered to a larger percentage (61%) of patients. A very small percentage of women declined therapy. The authors concluded that elderly women were not offered adjuvant systemic therapy even though they often would take it. ■