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Highlights: 2008 San Antonio Breast Cancer Symposium

### CONFERENCE COVERAGE HIGHLIGHTS

Welcome to conference coverage highlights presented by ReachMD Radio on XM160. Conference coverage highlights features the latest clinical information and research findings presented during the 2008 San Antonio Breast Cancer Symposium, which took place on December 10, 2008, through December 14, 2008, in San Antonio, Texas. Your host for this presentation of Conference Coverage highlights will be Dr. Mark Chyna and Sue Berg. Now here is Dr. Mark Chyna.

#### DR. MARK CHYNA:

Breast cancer patients with small HER2-positive tumors may have a significant risk of relapse. Now with the conclusion of the first large study to analyze this cohort of patients, the findings could lead to a shift in treatment of women with early stage HER2-positive breast cancer. Researchers at The University of Texas, MD Anderson Cancer Center studied 965 women diagnosed with tumors measuring 1 cm or less. The patients with HER2 positive tumors have significantly increased risks of recurrence and distant recurrence compared with patients with HER negative tumors. Specifically patients were at 2.5 times higher risk of recurrence and more than 5 times higher risk of distant recurrence. Those with HER2 positive tumors had a 5-year recurrence-free survival rate of about 77%. For HER2 negative patients recurrence-free survival was almost 94%. Also the 5-year distant recurrence-free survival is about 86% in women with HER2 positive tumors compared with about 97% in women with HER2 negative tumors. Current guidelines call for no additional therapy after surgery and radiation if tumors are less than 5 mm. If the tumors are 6 to 10 mm, Herceptin therapy is discussed with the patients. Investigators say their results concretely show that physicians should discuss Herceptin therapy with HER2 positive patients, who have even the smallest of tumors. They also say these patients should be included in ongoing clinical trials with HER2 targeted therapies.

#### SUE BERG:

Combining zoledronic acid with chemotherapy may shrink breast tumors. The drug is also called Zometa and it is approved to treat bone metastasis and osteoporosis. The results from a recent study may lead to an additional indication for breast cancer. Researchers from The University of Sheffield in UK performed a retrospective pathology analysis of more than 200 women enrolled in the AZURE trial. AZURE stands for adjuvant zoledronic acid to reduce recurrence. Women in this trial had stage 2 or 3 breast cancer and they receive either chemotherapy alone or chemotherapy plus zoledronic acid. The investigators found that the average residual invasive tumor size was considerably smaller in the combination group than in the chemotherapy only group. The difference was significant even after adjusting for factors such as estrogen receptor status and duration of treatment. Tumor size was about 28 mm in the combination arm versus 42 mm in the chemotherapy only arm. The combination group also had a significantly higher rate of pathological complete response. Almost 11% compared with about 6%. Adding zoledronic acid also led to a lower rate of subsequent mastectomy. The authors conclude that their data suggest that zoledronic acid when combined with chemotherapy possibly has a direct antitumor effect. They also say their findings indicate that additional perspective studies should be designed to test zoledronic acid's effect in breast

cancer. The large AZURE trial is still being evaluated.

**DR. MARK CHYNA:**

Monitoring a women's breast density can help predict her response to tamoxifen as a preventive measure against breast cancer. That was the conclusion of investigators conducting the international breast intervention study or IBIS-1. This trial of more than 7000 women looked at the potential of tamoxifen for preventing breast cancer. During the study, researchers collected baseline mammograms as well as mammograms at 18, 36, and 54 months to check for breast cancer development. This particular analysis included a subpopulation of the IBIS-1 participants. A 120 women who developed breast cancer and 943 who didn't. The researchers looked to see if the patient's mammograms changed over time and if tamoxifen treatment reduced breast density. The mammogram results indicated a strong correlation between tamoxifen use and reduced breast density as well as lower breast cancer risk. For women taking tamoxifen whose breast density was reduced by 10% or more after a year, the risk of breast cancer was reduced by 52% compared with a control group of women. Conversely the reduction in breast cancer risk was nonsignificant in women, whose density was not reduced. The investigators say that if their findings hold up, women at risk for developing breast cancer should have a baseline mammogram before taking tamoxifen and then a followup scan a year or two later to monitor breast density. If there is a reduction and the agent is having an effect if the density is the same, the drug may not be beneficial to that particular women.

**SUE BERG:**

A new genetic test can accurately predict breast cancer risk. OncoVue uses a combination of a questionnaire and a saliva test. It takes into account genetic variation in single nucleotide polymorphisms or SNFs. SNFs are small genetic changes within DNA. The OncoVue test is different from the traditional Gail model, which bases risk calculations primarily on traditional risk factors like alcohol consumption. A recent study revealed that the OncoVue model had a much higher accuracy than the Gail model. The study involved about 350 women from Marin County in California. Half had been diagnosed with breast cancer. Marin County has been known for many years to have elevated breast cancer incidence and mortality rates. However, the classical Gail model shows that the Marin women, who develop breast cancer have similar risk factors as Marin women who do not develop cancer. Researchers looked to see if the OncoVue model could do any better at predicting who will develop breast cancer. DNA with genotype for 22 SNFs in 19 genes to determine if a woman had an elevated risk of developing breast cancer. In a blinded analysis, the OncoVue model proved almost 2.5 times more accurate than the Gail model in accurately identifying the Marin breast cancer cases with their increased risk for Marin controls with the reduced risk. The investigators suspect that the OncoVue test will soon become standard in clinics. When physicians know women's breast cancer risks, they can better counsel patients about prevention and early intervention.

**DR. MARK CHYNA:**

Researchers say that postmenopausal women should be tested for the CYP2D6 gene before beginning tamoxifen therapy. The CYP2D6 gene is important for metabolizing tamoxifen from its inactive pill form to an active form once it's in the body. Investigators at the Mayo Clinic studied the DNA of a group of postmenopausal women treated in a clinical trial called ABCSG8. Women whose breast cancer had been surgically removed were randomized to receive 5 years of tamoxifen or tamoxifen for 2 years followed by 3 years or aromatase-inhibitor anastrozole. In group of patients, who received tamoxifen only, women with a deficiency in the CYP2D6 gene had an almost fourfold increase in the risk of breast cancer recurrence by the end of the study compared with women with normal levels of the gene. Patients with the CYP2D6 deficiency who switched to anastrozole had no increased risk of breast cancer recurrence. The study's findings suggested maybe beneficial to switch patients with the CYP2D6 deficiency to anastrozole. The results also highlight the emerging science of pharmacogenomics. Researchers are studying whether therapy can be more individualized by testing for genetic differences and the way patients metabolize drugs.

**SUE BERG:**

Alternating magnetic resonance imaging or MRI with mammography can detect cancers better than mammograms alone. Researchers at the University of Texas MD Anderson Cancer Center reviewed the charts of 334 women, who had taken part in the high-risk breast cancer screening program over the past decade; 86 of these women underwent the alternating screening approach every 6 months. The other women underwent prophylactic mastectomy or were started on chemoprevention agents. After a median of 2 years of followup, the alternating MRI and mammography screening program had detected 9 cancers. Five of these cancers were identified by MRI, but not by mammography, 3 were found by both MRI and mammography and 1 small tumor was overlooked by both screening techniques. No cancer was detected by mammography alone. MRI is more sensitive than mammography for detecting breast cancer. Screening for high-risk women now typically includes MRI along with mammography and a clinical breast exam. One important unanswered question is whether an alternating MRI and mammography screening program will save lives.

**DR. MARK CHYNA:**

A type of benign breast disease called atypical hyperplasia increases young women's risk of developing breast cancer. A recent study found that women with this disease were 6 times more likely to develop breast cancer than other women. Women with atypical hyperplasia were at increased risk of developing breast cancer even if they didn't have a family history of cancer. The study was conducted in more than 4000 women with benign breast disease whose lesions were biopsied between 1967 and 1991. Benign breast disease was diagnosed on average at age 39 years, 2% of the women had been diagnosed with atypical hyperplasia. Young women in the study, who were diagnosed with 2 other forms of benign breast diseases, were at much less risk than patients with atypical hyperplasia. Those with nonproliferative disease had a 0.2% higher risk than normal and the risk was doubled for women with proliferative disease without atypia. In atypical hyperplasia, an increased number of cells bind the milk duct or lobule and the cells do not look normal under a microscope.

**SUE BERG:**

Some women's primary breast cancer spreads to the brain. In these women, those who have tumors that do not express certain receptors have shorter survival times. Two studies conducted at the Mayo Clinic in Jacksonville, Florida looked at molecular markers in about 200 patients with breast cancer who later developed brain metastasis. One study found that patients with tumors that were HER2 positive, but were estrogen receptor and progesterone receptor negative had a significantly shorter median survival from initial diagnosis to death than HER2 positive patients who had estrogen receptor and progesterone receptor positive tumors. The second study found that women with triple-negative tumors had a significantly shorter medial survival from diagnosis to death than other patients. These tumors also do not express HER2. Other researchers looking at brain metastasis found that a combination therapy of lapatinib and capecitabine may benefit patients with HER2 positive cancers. Lapatinib goes by the trade name Tyverb, the trade name of capecitabine is Xeloda. Lapatinib is a tyrosine kinase inhibitor. Capecitabine is an antimetabolite that is taken up by cancer cells and breaks down into 5-fluorouracil. The study was an extension of a phase 2 study called EGF105084. Investigators at the Dana-Farber Cancer Institute in Boston and their colleagues studied the combination regimen in 49 HER2 positive patients with progressive brain metastasis who had previously been treated with trastuzumab and cranial radiotherapy. The researchers found that the brain tumors shrunk at least 20% in 18 of the patients. In 10 patients, tumor shrunk by at least 50%. Other ongoing studies are evaluating the potential of lapatinib in combination with chemotherapies and other targeted agents for the treatment of brain metastases.

**DR. MARK CHYNA:**

Two separate meta analyses of global trials of how aromatase inhibitors are more effective than tamoxifen for preventing breast cancer recurrence in postmenopausal women with early breast cancer. One of these studies also found a significant survival benefit associated with aromatase inhibitors, but researchers say that data are too preliminary to judge whether one drug is truly superior to another for saving lives. Aromatase inhibitors include anastrozole, exemestane, and letrozole. These drugs act by inhibiting an enzyme needed to make estrogen. The researchers divided the major studies into 2 different cohorts. Cohort 1 consisted of clinical trials that randomized

patients to either tamoxifen or aromatase inhibitors for 5 years. Two trials were examined that included nearly 10,000 patients. Cohort 2 included studies with breast cancer patients, who received tamoxifen for 2 to 3 years and then were randomized to complete their 5 years of therapy with tamoxifen or with an aromatase inhibitor. Four studies were examined that enrolled more than 9000 patients. In cohort 1 women using aromatase inhibitors had about a 3% lower recurrence rate at 5 years than women, who received tamoxifen. That decrease in recurrent rate increased to about 4% at 8 years after diagnosis. There were no statistically significant gains in survival between the 2 groups, however. In cohort 2, there was 3.5% reduced risk of breast cancer recurrence in women, who switched to aromatase inhibitors after 6 years compared with women who continued using tamoxifen. There is also a 1.6% reduced risk that patients using aromatase inhibitors would die from their disease.

**We thank you for listening to Conference Coverage highlights of the San Antonio Breast Cancer Symposium held December 10, 2008, through December 14, 2008. Conference Coverage highlights is a presentation of ReachMD Radio, broadcast on XM160 and by live stream at ReachMD.com.**