

Contributing Faculty Editor:

Gary C. Chamness, PhD

Hot Five Presentations

Abstract # 46

A randomized phase 2 trial of qw or q3w ABI-007 (ABX) vs. q3w solvent-based docetaxel (TXT) as first-line therapy in metastatic breast cancer (MBC).

Gradishar W, Krasnojon D, Cheporov S, Makhson A, Manikhas G, Hawkins MJ. Northwestern University, Chicago, IL; Leningrad Regional, St Petersburg, Russian Federation; Yaroslavl Regional, Yaroslavl, Russian Federation; City Oncology Hospital, Moscow, Russian Federation; St Petersburg Oncology Center, St Petersburg, Russian Federation; Abraxis BioScience, Los Angeles, CA

Abstract # 34

Long term efficacy of tamoxifen for chemoprevention – results of the IBIS-I study.

Cuzick J, on Behalf of the IBIS Investigators. Wolfson Institute of Preventive Medicine, London, United Kingdom

Abstract # 5

A sharp decrease in breast cancer incidence in the United States in 2003.

Ravdin PM, Cronin KA, Howlander N, Chlebowski RT, Berry DA. MD Anderson; National Cancer Institute; Harbor UCLA Medical Center

Abstract # 48

Relationship between quantitative ER and PgR expression and HER2 status with recurrence in the ATAC trial.

Dowsett M, Allred DC, on Behalf of the TransATAC Investigators. Royal Marsden Hospital, London, United Kingdom; Baylor College of Medicine, Houston, TX

Abstract # 32

Mature analysis from the women's intervention nutrition study (WINS) evaluating dietary fat reduction and breast cancer outcome.

Chlebowski RT, Blackburn GL, Elashoff RM, Hoy KM, Thomson CA, Nixon DW, Giuliano AE, McAndrew P, Hudis C, Butler J, Merkel D, Shapiro A. LABioMed, Torrance, CA; Beth Israel Deaconess Hospital, Boston, MA; University of California, Los Angeles, CA; Cancer Prevention Institute, New York, NY; University of Arizona, Tucson, AZ; St Johns Hospital and Health Center, Santa Monica, CA; Cedars Sinai Hospital, Beverly Hills, CA; Memorial Sloan-Kettering Cancer Center, New York, NY; University of California at Irvine, City of Orange, CA; Evanston Hospital, Kellogg Cancer Care Center, Evanston, IL; Park Nicollet Institute, Minneapolis, MN

**San Antonio Breast Cancer Symposium 2006
MODERATORS, REVIEWERS, and PANELISTS**

General Session Moderators

- Martine Piccart
Eric Winer
- Kathy Albain
Suzanne Fuqua
- Ian Smith
George Sledge
- Adrian Lee
Steffi Oesterreich
- Richard Elledge
Kay Blanchard
- Judy Garber
Powel Brown
- Jenny Chang
Mothafar Rimawi

Poster-Discussion Discussants

- Paul E Gos
- Michael Lewis
- Mark Pegram
- Debra Ikeda
- Suzanne Fuqua

Mini-Symposium Moderators

- D Craig Allred
Suzanne Fuqua
- Steffi Oesterreich
Michael Lewis
- Rachel Schiff
Gary Chamness
- Powel Brown
Mamta Kalidas

Case Discussion Panelists

- Friday*
C. Kent Osborne, moderator
Nancy E. Davidson
Clifford Hudis
Monica Morrow
Ian Smith
Emiel Rutgers
Jay Harris
Judy Perotti (advocate)

Saturday

- C. Kent Osborne, moderator
Eric Winer
James N Ingle
Lisa Carey
Martine Piccart-Gebhart
Gabriel Hortobagyi
Sandy Walsh (advocate)
Bob Riter (advocate)

Plenary Lecture Moderators

- Steffi Oesterreich
- Jenny Chang
- Kent Osbourne

McGuire Lecture

C Kent Osbourne

Brinker Lectures

Chandini Portteus (Director, Grants)

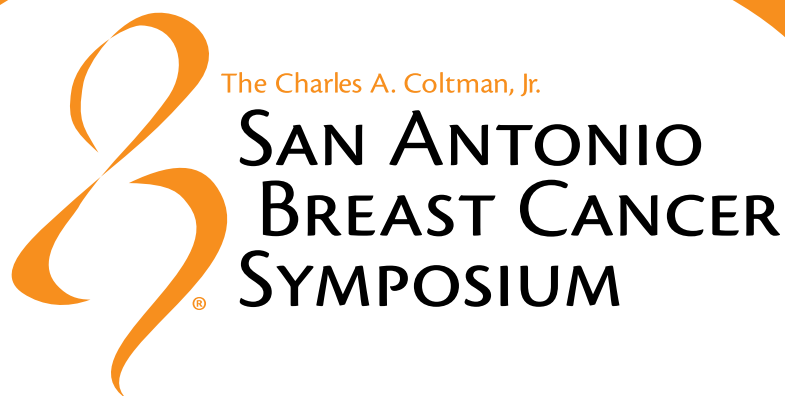
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Differing Treatment Standards for High-Risk Operable Breast Cancer

Women with node-positive or high-risk node-negative breast cancer are almost always encouraged to undergo adjuvant chemotherapy. In Canada, the usual recommendation is a combination of cyclophosphamide, epirubicin, and fluorouracil (CEF), although recent studies have indicated that 3 months of dose-dense EC is equivalent to 6 months of CEF. In the United States, the usual recommendation is a combination of doxorubicin (A) and C, followed by paclitaxel (AC/T). There has been considerable interest in determining whether the combination regimens based on these two anthracyclines have similar outcomes.

On Sunday morning, Margot Burnell, MD, FRCPC, from the Atlantic Health Sciences Corporation in St. John, New Brunswick, presented interim results of a randomized trial comparing CEF vs dose-dense EC followed by paclitaxel vs AC/T. Patients included in the study were no more than 60 years of age, and had node-positive or high-risk node-negative cancer (histological grade 3 or estrogen receptor [ER]-negative) or lymph vascular invasion. The primary outcome was relapse-free survival; secondary outcomes were overall survival, toxicity, and quality of life. A total of 2100 patients were recruited to the study, stratified by number of positive axillary lymph nodes, ER status, and type of surgery (partial vs mastectomy). The median follow-up time for this interim analysis was 30.4 months. Three-year relapse-free survival was 90.1% for CEF, 89.5% for EC/T, and 85.0% for AC/T ($P = .001$). For the one-by-one comparison of AC/T vs CEF, the hazard ratio (HR) was 1.40 ($P = .005$); for AC/T vs EC/T, HR = 1.68 ($P = .0006$). The increased efficacy of epirubicin-containing regimens compared with doxorubicin-containing regimens was seen only in ER-negative patients—there was no significant difference in ER-positive patients.

In terms of toxicity, febrile neutropenia, cardiac toxicity, and thromboembolic events were all more frequent in patients receiving the epirubicin-containing regimens than in those treated with the doxorubicin-containing regimens. The higher rate of cardiac toxicity was somewhat surprising, because epirubicin had previously been reported to be less toxic than doxorubicin for the treatment of patients with metastatic breast cancer. Neurologic effects were more frequent in regimens containing paclitaxel.

The conclusions reached from this interim analysis are that (1) epirubicin-containing chemotherapeutic combinations result in significantly better rates of relapse-free survival compared with AC/T, and (2) taxanes, which might result in significant neurologic toxicity, did not seem to affect the outcome of patients receiving epirubicin, and may not be necessary for all patients. The observation that epirubicin efficacy may be associated with ER status, while interesting, should be viewed as preliminary.

(continues on page 2)

Routine Surveillance Mammography After Breast Reconstruction

Philip Barnsley, MD, from Dalhousie University in Halifax, one of this year's AstraZeneca scholars, presented the results of a study designed to see if mammographic screening of reconstructed breast mounds after reconstructive surgery is cost effective. For those women who prefer or need to receive a mastectomy, breast reconstruction is now often considered a standard treatment. Many women (and some clinicians) may believe that, because the breast has been removed, screening mammography is no longer necessary. However, residual breast tissue can be found in up to 60% of mastectomy sites, and this number may be as high as 81% if skin flaps >5 mm thick are left. This breast tissue can be the site of future recurrences, and can be imaged with mammography.

Dr Barnsley and colleagues conducted an economic study to determine the cost effectiveness of scheduling regular bilateral mammograms in women with breast reconstruction. They conducted a Markov analysis, with transition probabilities based on historic estimates of rate of local recurrence, rate of metastasis, sensitivity of surveillance mammography, false-positive rate, and salvage rate. Cost estimates were based on data from the Ontario Health Insurance Plan and the Canadian Consumer Index for Health Care.

The analysis indicates that routine bilateral surveillance mammography for women with a reconstructed breast is cost effective even if only 1 woman in 30 with local recurrence is prevented from developing metastatic spread.

Highlights From the 2005/2006 EBCTCG Overview

The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) is completing its fifth 5-year cycle of data collection. This update was presented by

Sir Richard Peto, MD, from the Clinical Trial Service Unit, Oxford, viewed by many as the founder of meta-analysis. The ultimate purpose of the overview, according to Sir Richard, is to accumulate data from *every* woman in *all* of the trials. Although large clinical studies are currently accruing 3000 to 5000 or more patients, he said that this is not enough. Treatment advances have resulted in a significant decrease (15% to 17% in the United States and the United Kingdom) in breast cancer-related mortality over the last 15 years in women aged 35 to 60. This has been the result of the combination of many therapeutic advances with only modest individual effects. Clearly, the smaller the effect, the larger the sample size needed to demonstrate it.

The EBCTCG has collected data on 661,000 patients from 823 clinical trials, as of the 2005/2006 review, but much remains to be done. For example, data for chemotherapy trials have been collected from 59,300 patients in 69 trials; data are available, but not yet added to the database, from an additional 7500 patients in 31 trials; and data are not available from 14,000 patients in 35 trials. There are major gaps in the database for the taxane trials, the anthracycline vs CMF (cyclophosphamide, methotrexate, 5-fluorouracil) trials, and for aromatase inhibitor trials. The definitive information currently available from the overview demonstrates: reduction in both local recurrence and breast cancer mortality with the addition of radiotherapy to the treatment of patients receiving mastectomy and AC adjuvant chemotherapy; reduction in local recurrence and breast cancer mortality by adding radiotherapy for patients receiving breast-conserving surgery; and a reduction in recurrence after 5 years of tamoxifen treatment in ER-positive patients, regardless of progesterone receptor status.

Sir Richard strongly cautioned against a current trend towards subdividing data in unplanned subgroup analyses, which are frequently insufficiently powered to generate useful conclusions. He closed by emphasizing that the decline in breast cancer deaths seen since 1990 in the United States and the United Kingdom is the cumulative result of many small advances, and that further moderate advances are still possible and achievable.

Anthracyclines May Not Be for Everyone

Anthracyclines (doxorubicin, epirubicin) are part of the current treatment standard for adjuvant therapy in breast cancer patients. Multiple clinical trials have demonstrated better disease-free survival and overall survival in patients receiving anthracycline-containing regimens compared with those receiving CMF, the previous treatment standard. As with most treatments, however, some patients fail to respond to anthracyclines, and there has been continuing interest in defining predictive factors for drug response. For example, in an earlier paper presented Sunday morning, Dr Burnell shared preliminary evidence indicating that epirubicin response may be associated with ER status. Preventing unnecessary treatment with anthracyclines is especially important because these drugs can cause severe side effects, including potentially life-threatening cardiotoxicity.

At the Sunday morning General Session, Alessandra Gennari, MD, from the National Cancer Research Institute in Genoa, presented her research on the interaction between HER2 status and response to adjuvant chemotherapy. An interaction between HER2 status and response to adjuvant chemotherapy has been reported by some, but not all, prospective trials comparing anthracycline with non-anthracycline regimens. Dr Gennari and colleagues used a meta-analytic approach to combine the results of published studies. They identified several published studies using anthracycline-containing chemotherapeutic regimens that recorded patients' HER2 status. Considered individually, two of these studies showed a significant interaction between HER2 status and response to anthracyclines in disease-free survival, 1 showed a borderline interaction, 3 showed no interaction, and 1 did not measure disease-free survival. A similar picture was seen for overall survival. When the studies were combined in the meta-analysis, anthracycline treatment was associated with a 29% decrease in risk of relapse and a 27% decrease in risk of death in HER2-positive patients, but had no effect on outcomes in HER2-negative patients.

It should be noted that these results were obtained in patients who had not received the anti-HER2 agent trastuzumab. In addition, the meta-analysis was based on abstracted data, so updates in outcome and centralized validation of HER2 status were not available.

Long-term Follow-up From the Royal Marsden Trial

Trevor Powles, PhD, from the Royal Marsden Hospital, presented 20-year follow-up results from the Royal Marsden Tamoxifen Breast Cancer Prevention Trial. Overall, 1238 women completed the trial in the tamoxifen arm and 1233 women in the placebo arm.

Early results from this trial showed only minimal preventive effect, in contrast with other large trials, such as NSABP P-1. Now, with a median follow-up of 13.2 years, we see that tamoxifen did prevent the occurrence of breast cancers at this evaluation, with a highly significant HR of 0.62 ($P = .005$). Of special interest, the difference between the tamoxifen and placebo arms actually increased during the post-treatment period. Significant differences between the study arms were seen only in the development of ER-positive tumors.

The conclusion presented here is that there is a highly significant 39% reduction in the incidence of ER-positive breast cancer ($P = .005$), predominantly occurring after the 8-year treatment period ($P = .004$), indicating a preventive rather than a treatment action by tamoxifen on estrogen-dependent disease.

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