



Key SABCS Presentations
Issue 4, 2011

**Prognostic Value of Genomic
Analysis After Neoadjuvant
Chemotherapy for Breast Cancer**

CME INFORMATION

OVERVIEW OF ACTIVITY

The annual San Antonio Breast Cancer Symposium (SABCS) is unmatched in its significance with regard to the advancement of breast cancer treatment. It is targeted by many members of the clinical research community as the optimal forum in which to unveil new clinical data. This creates an environment each year in which published results from a plethora of ongoing clinical trials lead to the emergence of many new therapeutic agents and changes in the indications for existing treatments across all breast cancer subtypes. In order to offer optimal patient care — including the option of clinical trial participation — the practicing medical oncologist must be well informed of the rapidly evolving data sets in breast cancer. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets from the latest SABCS meeting, including expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for breast cancer.

LEARNING OBJECTIVE

- Compare and contrast the accuracy with which pre- and postneoadjuvant RS predicts patient risk for disease recurrence.

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FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Harold J Burstein, MD, PhD
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Last review date: February 2011
Expiration date: February 2012

[Click here for key papers on genomic predictors from the 2010 SABCS](#)

Last Friday, our CME group welcomed seven winter-weary breast cancer investigators to the RTP recording studio in sunny Miami, this time for our annual post-SABCS Think Tank. As usual, the best part of the day was when these learned souls presented challenging cases from their practices and asked each other what they would do for the patients discussed.

Probably the least frozen faculty member was Northern Californian Hope Rugo, who put the group on its heels with a challenging situation: A 47-year-old highly informed premenopausal woman seeking another opinion about a recently removed 0.8-cm, Grade I, ER-positive, HER2-negative invasive ductal cancer in which one sentinel node had a 0.9-cm focus of tumor. Ki-67 obtained at the referring community hospital was less than five percent.

**2011 Breast Cancer
Clinical Investigator Think Tank**

Friday, February 4, 2011

Adam M Brufsky, MD, PhD
Harold J Burstein, MD, PhD
Melody A Cobleigh, MD
Charles E Geyer Jr, MD
William J Gradishar, MD
Mark Robson, MD
Hope S Rugo, MD
Antonio C Wolff, MD

“Would you order an Oncotype DX® on this lady?” was Hope’s question, and the answers were quite interesting. Two investigators said no to *Oncotype* and suggested TC followed by hormones. Harold Burstein represented most of the others believing an *Oncotype* would add useful information, particularly when Hope noted that this woman was willing to receive chemo but was not insistent on it. Some of the group had been sipping home-brewed Cuban coffee, which may partially explain the heated discussions on this and other topics (keep an eye open for the upcoming audio highlight program), but all wished to hear the follow-up from Hope about what actually happened.

Dr Rugo related that the patient had actually consulted with two prior oncologists, the first of whom had recommended TC straight up (to be followed by hormones) while the second had recommended hormone therapy only. Dr Rugo decided to obtain an *Oncotype*, which returned a Recurrence Score® of 0 (that’s low!). The patient has been contentedly taking tamoxifen for two years.

As part of the discussion surrounding the case, Antonio Wolff noted that now a good option for a woman in this situation would be entry into the upcoming SWOG/ Intergroup RESPOND trial, randomly assigning patients with ER-positive, HER2-negative tumors, one to three positive nodes and a Recurrence Score of 25 or less to endocrine therapy alone or preceded by chemo. Of course, until that study is complete, we will have to rely on other accumulating evidence in the field, including the following papers presented at San Antonio:

1. **Another data set** (following one at ASCO 2010) from the NSABP on the RSPC — Recurrence Score-Pathology-Clinical risk assessment

According to Chuck Geyer, seven years after Soon Paik's presentation (at San Antonio) of the first *Oncotype DX*/NSABP analysis, the group still is attempting to fulfill the mission of the late statistician and group linchpin John Bryant and figure out how to integrate clinical factors in addition to *Oncotype* into treatment decisions. It is easy to understand the interest in having more information on patients like Hope's, for whom there is a disconnect between the clinical factors predicting the risk of recurrence (small, low-grade, low Ki67 but node-positive). The RSPC calculation uses commonly available variables like tumor size and grade but unfortunately doesn't seem to add much to the Recurrence Score in terms of what's most important — prediction of benefit from chemo.

2. **A Meta-analysis** of seven studies (n = 912) evaluating the impact of *Oncotype DX* on clinical decision-making

Our CME group's national **Patterns of Care studies** have demonstrated that when utilized, *Oncotype* changes the clinical decision made in at least a quarter of cases and in this meta-analysis, decisions were changed for 37 percent of patients with a 28 percent overall decrease in the use of chemotherapy.

3. **A translational study** from Dana-Farber evaluating pre- and postneoadjuvant chemotherapy Recurrence Scores

This fascinating report revealed that Recurrence Scores evaluated before and after neoadjuvant chemotherapy did not change substantially and continued to predict outcome, suggesting that treatment did not impact the tumor's genomic profile. Also of interest was a six to 11 percent discordance in ER/PR results with IHC versus RT-PCR.

I first met Soon Paik (for an interview) in San Antonio the night before his classic 2003 presentation of the first *Oncotype* data set that set the stage for a new era in breast cancer and oncology, emphasizing a biologic approach to the development of new

treatments and predictors of response. Seven years later, as evidenced by his [Brinker Award lecture](#) (the last of the Thursday lectures), Dr Paik continues to have a vision for the future of clinical research that is far ahead of the rest of us.

Next up on 5-Minute Journal Club: Endocrine treatment, pregnancy, obesity and breast cancer.

Neil Love, MD

[Research To Practice](#)

Miami, FL

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Prognostic Value of Genomic Analysis After Neoadjuvant Chemotherapy for Breast Cancer

Presentation discussed in this issue

Mayer EL et al. **Prognostic value of genomic analysis after neoadjuvant chemotherapy for breast cancer.** San Antonio Breast Cancer Symposium 2010; **Abstract P3-10-13.**

Slides from a presentation at SABCS 2010 and transcribed comments from a recent interview with Harold J Burstein, MD, PhD (12/22/10)

Prognostic Value of Genomic Analysis After Neoadjuvant Chemotherapy for Breast Cancer

Mayer EL et al.

Proc SABCS 2010;Abstract P3-10-13.

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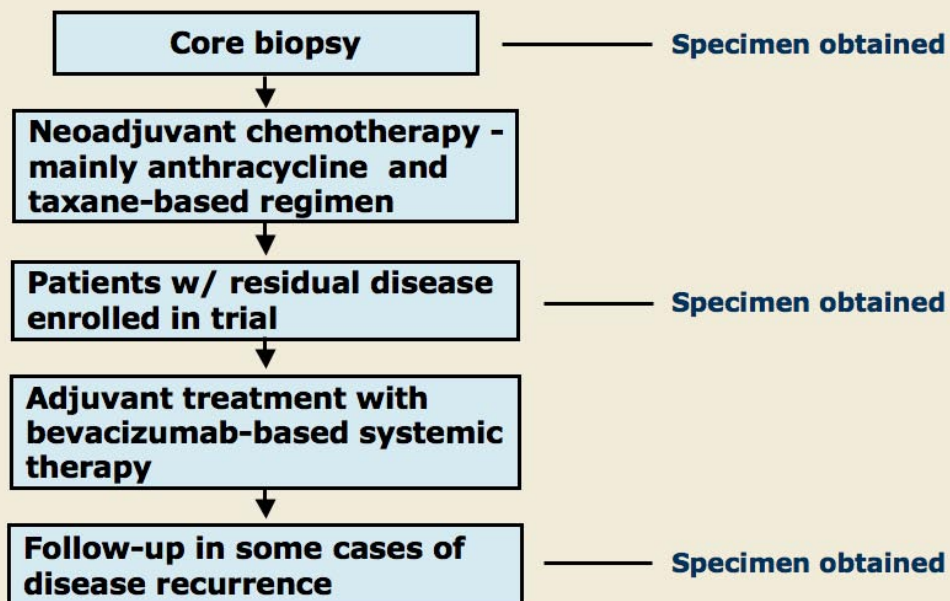
Methods

- Patients were recruited from the Dana-Farber Cancer Institute 05-055 Phase II trial of adjuvant bevacizumab-based therapy for patients with residual disease after neoadjuvant therapy.
 - Accrual between 2005 and 2008
 - Sample size: 162 patients
- Formalin-fixed paraffin-embedded tissue blocks obtained at the following timepoints:
 - Baseline core biopsy
 - Residual tissue from surgery
 - Time of metastatic recurrence
- ER, PR and HER2 determined by IHC and/or FISH for all samples.
- Standard Oncotype DX® testing was performed on all samples.

Mayer EL et al. *Proc SABCS 2010*;Abstract P3-10-13.

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Study Design



Mayer EL et al. *Proc SABCS 2010*;Abstract P3-10-13.

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Clinical Samples Summary

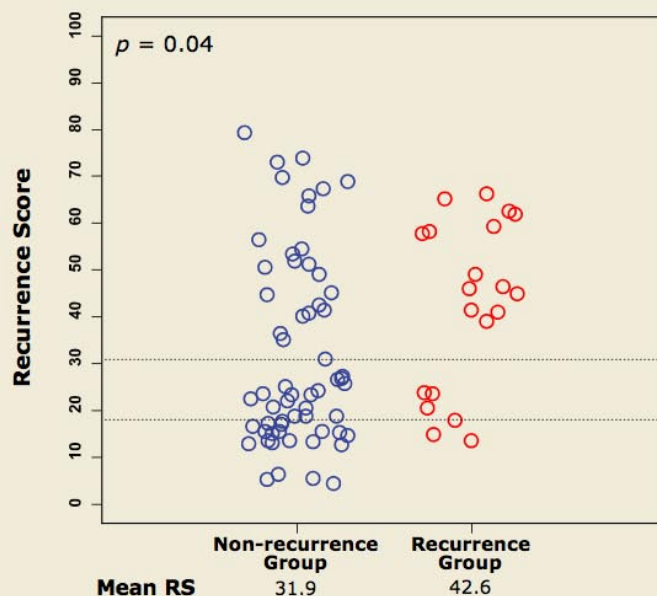
	Samples	Patients
Included in data analysis	116	80
Core biopsy samples	47	—
Surgical excision samples	67	—
Core biopsy and surgical specimen pairs	68	34
Recurrence specimen	2	2

- A total of 20 patients experienced distant recurrence.
- A majority of patients were ER-positive and/or PR-positive and HER2-negative.

Mayer EL et al. *Proc SABCS 2010*;Abstract P3-10-13.

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Distribution of Recurrence Score (RS) Values



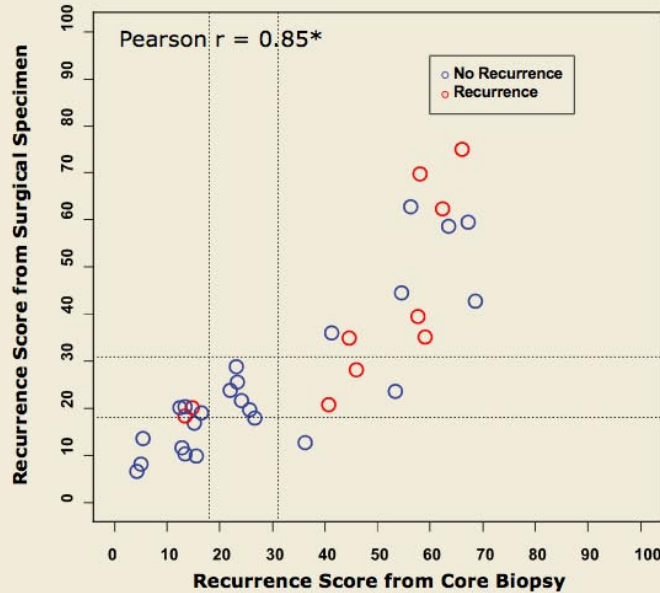
n = 80 samples
47 core biopsies
33 surgical specimens

- A high RS was positively associated with distant recurrence

With permission from Mayer EL et al. *Proc SABCS 2010*;Abstract P3-10-13.

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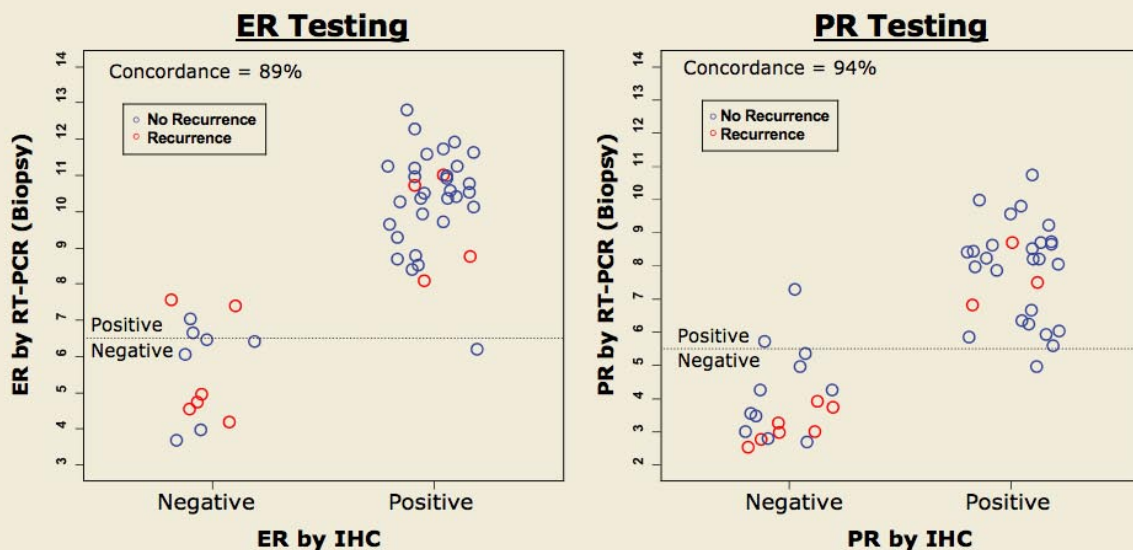
Comparison of RS Values from Patients with Core Biopsy and Surgical Specimens (n = 34)



* RS was highly correlated before and after exposure to chemotherapy (95% CI 0.72-0.92)

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Concordance of ER/PR Testing by IHC vs RT-PCR in Prechemotherapy Samples



- Good concordance exists in ER/PR testing by local IHC vs RT-PCR for the prechemotherapy samples (n = 47 core biopsies)

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Summary

- A high RS appeared to be associated with disease recurrence for the entire study cohort ($p = 0.04$).
- The RS determined either before or after neoadjuvant chemotherapy also appeared to be associated with disease recurrence (Pearson $r = 0.85$).
- RT-PCR results for ER/PR/HER2 remained consistent despite interval chemotherapy (data not shown).
- Despite high concordance between IHC and RT-PCR for ER/PR, the observed 6-11% discordance is of unclear origin and may have meaningful clinical consequences.
- Confirmation of the potential prognostic role of postneoadjuvant chemotherapy RS warrants additional study.

Mayer EL et al. *Proc SABCS 2010*;Abstract P3-10-13.

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Investigator Commentary: Prognostic Value of Genomic Analysis After Neoadjuvant Chemotherapy

Our group conducted a series of studies in which we evaluated treating a unique and high-risk group of patients with breast cancer who had residual disease after neoadjuvant chemotherapy. On a series of protocols we offered them additional treatments, mostly built around bevacizumab.

We wanted to know how the pre- and post-treatment biopsy Recurrence Scores® correlated and whether we could study the residual tumors with an *Oncotype DX*® assay to predict disease recurrence. Our studies were limited by a small sample size, but we showed a good correlation between tumor biopsy preneoadjuvant therapy and postneoadjuvant therapy. So whatever chemotherapy is doing to the tumor, it's not changing its Recurrence Score phenotype that much.

We also showed that if you review the post-treatment biopsy results by Recurrence Score, they remain robust predictors of the chance of disease recurrence in the years ahead. So we saw no real surprises in these findings — rather, it was another demonstration of the power of these molecular diagnostic tests.

Interview with Harold J Burstein, MD, PhD, December 22, 2010