



Key SABCS Presentations
Issue 4, 2011

**Predicting Chemotherapy Benefit
in Node-Negative, ER-Positive
Breast Cancer Using the Recurrence
Score-Pathology-Clinical (RSPC) Tool**

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

- Recognize the strengths and weaknesses of the novel RSPC relative to the standard Oncotype DX RS as a prognostic and/or predictive breast cancer biomarker.

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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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Predicting Chemotherapy Benefit in Node-Negative, ER-Positive Breast Cancer Using the Recurrence Score-Pathology-Clinical (RSPC) Tool

Presentation discussed in this issue

Tang G et al. **Comparing the prediction of treatment benefit in patients with node-negative, ER-positive breast cancer using the recurrence score and a new measure that integrates clinical and pathologic factors with the recurrence score.** San Antonio Breast Cancer Symposium 2010; **Abstract S4-9**.

Slides from a presentation at SABCS 2010 and comments from Clifford Hudis, MD at an RTP satellite symposium during SABCS 2010 (12/11/10)

Comparing the Prediction of Chemotherapy Benefit in Node-Negative, ER-Positive Breast Cancer Using the Recurrence Score and RSPC, a New Measure Integrating Clinical and Pathologic Data with the Recurrence Score

Tang G et al.

Proc SABCS 2010;Abstract S4-9.

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Objective

- To compare the value of a new clinical tool called the Recurrence Score-Pathology-Clinical (RSPC) risk assessment vs the Oncotype DX® Recurrence Score® (RS) in predicting chemotherapy benefit.
 - The RSPC was developed to assess risk of distant recurrence by integrating:
 - RS
 - Tumor grade
 - Pathologic tumor size
 - Patient age at surgery
 - Hormonal therapy (tamoxifen or anastrozole)

Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Methods

- Retrospective analysis of data from the NSABP-B-20 trial
- Eligibility
 - Participated in the NSABP-B-20 trial (ie, node-negative, ER-positive) of tamoxifen (TAM) or TAM plus chemotherapy (TAM/chemo).
 - Successful Oncotype DX RS
 - ER score ≥ 6.5
- The chemotherapy benefit associated with each risk assessment tool was determined using a Cox proportional hazards regression model to determine RS or RSPC risk benefit x treatment interaction.

Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Patient Characteristics

	TAM alone	TAM/chemo	All
Clinically eligible with evaluable tumor block, n	227	424	651
Oncotype DX and ER ≥ 6.5 , n (%)	225 (99.1%)	400 (94.3%)	625 (96%)
Distant recurrence events, n	31	29	60

Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Patient Characteristics by Treatment Group (N = 625)

	TAM alone	TAM/chemo
RS, mean	20	21
Tumor grade*		
Low	25%	24%
Intermediate	41%	51%
High	34%	25%
Tumor size, mean	2.1 cm	2.1 cm
Age at surgery, mean	52 years	52 years
RSPC, mean	-2.05	-2.05

*p = 0.037 for TAM vs TAM/chemo

Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Prediction of Chemotherapy Benefit

	Hazard ratio (95% CI)	p-value
RS*	2.22 (1.75-2.82)	<0.001
Treatment	0.63 (0.35-1.11)	0.11
RS* x treatment	0.65 (0.44-0.97)	0.034
RSPC*	2.43 (1.68-3.54)	<0.001
Treatment	0.64 (0.35-1.18)	0.156
RSPC* x treatment	0.65 (0.39-1.09)	0.1

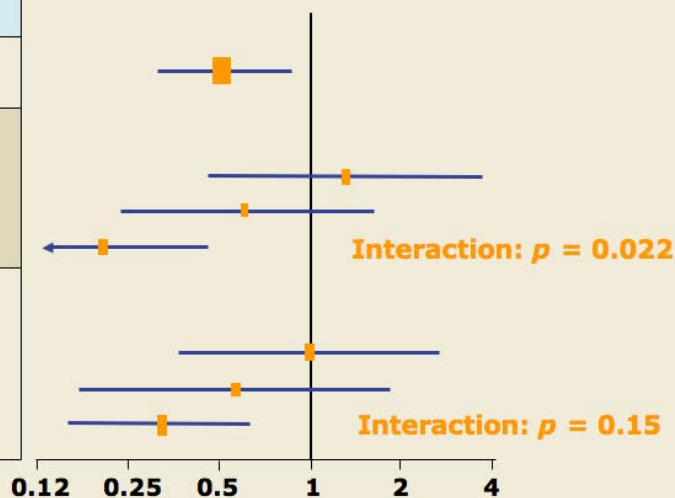
*Standardized with standard deviation = 1.

Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Prediction of Chemotherapy Benefit by Risk Group

	TAM alone	TAM+chemo
Included B-20 Patients	225	400
RS Risk Groups		
Low	135	217
Intermediate	45	90
High	45	93
RSPC Risk Groups		
Low	116	216
Intermediate	48	71
High	61	113



Hazard Ratio (TAM+Chemo vs TAM alone)

With permission from Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Conclusions

- The prediction of chemotherapy benefit was not improved with RSPC compared with RS.
 - Treatment interaction for RS x chemotherapy treatment was significant ($p = 0.034$) compared with that of RSPC ($p = 0.10$).
- The recommended method to predict chemotherapy benefit is RS alone.

Tang G et al. *Proc SABCS 2010*;Abstract S4-9.

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Investigator Commentary: Prediction of Chemotherapy Benefit with the Recurrence Score with or without Clinical and Pathologic Factors

I believe the Recurrence Score-Pathology-Clinical (RSPC) risk assessment approach undermines the value of the *Oncotype DX* assay, which is a gene-based assessment of chemotherapy sensitivity. In this study the investigators added in clinical and pathologic factors — with which, in multivariate analyses performed in the early days, the Recurrence Score was demonstrated to be superior.

The RSPC increased the number of patients who are deemed to have “low-risk” disease, but we lose the distinguishing feature of the *Oncotype DX* assay, which is its ability to predict chemotherapy benefit. The predictive utility is key for me because it’s always been what distinguished the *Oncotype DX* assay from many other available prognostic tests. So, at the moment, it’s difficult to see what advantage the RSPC offers compared to other prognostic tests. Currently, the *Oncotype DX* assay is the only test that has any degree of validation for prediction of benefit from chemotherapy, and that goes away under this RSPC model.

Commentary by Clifford Hudis, MD, December 11, 2010