5 Minute JournalClub

Key SABCS Presentations
Issue 4, 2011

Meta-Analysis of the Effect of the Oncotype DX® Assay Recurrence Score® (RS) on Clinical Decision-Making

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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

- Effectively integrate the Onco*type* DX RS into risk-stratified adjuvant breast cancer treatment decision-making.

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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
Associate Professor of Medicine
Harvard Medical School
Breast Oncology Center
Dana-Farber Cancer Institute
Boston, Massachusetts

No real or apparent conflicts of interest to disclose.

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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.

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

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.

"Would you order an Onco*type* DX® on this lady?" was Hope's question, and the answers were quite interesting. Two investigators said no to Onco*type* and suggested TC followed by hormones. Harold Burstein represented most of the others believing an Onco*type* 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 Onco*type*, 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 Onco*type* 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 Onco*type* 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 Onco*type* DX on clinical decision-making

Our CME group's national **Patterns of Care studies** have demonstrated that when utilized, Onco*type* 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 Onco*type* 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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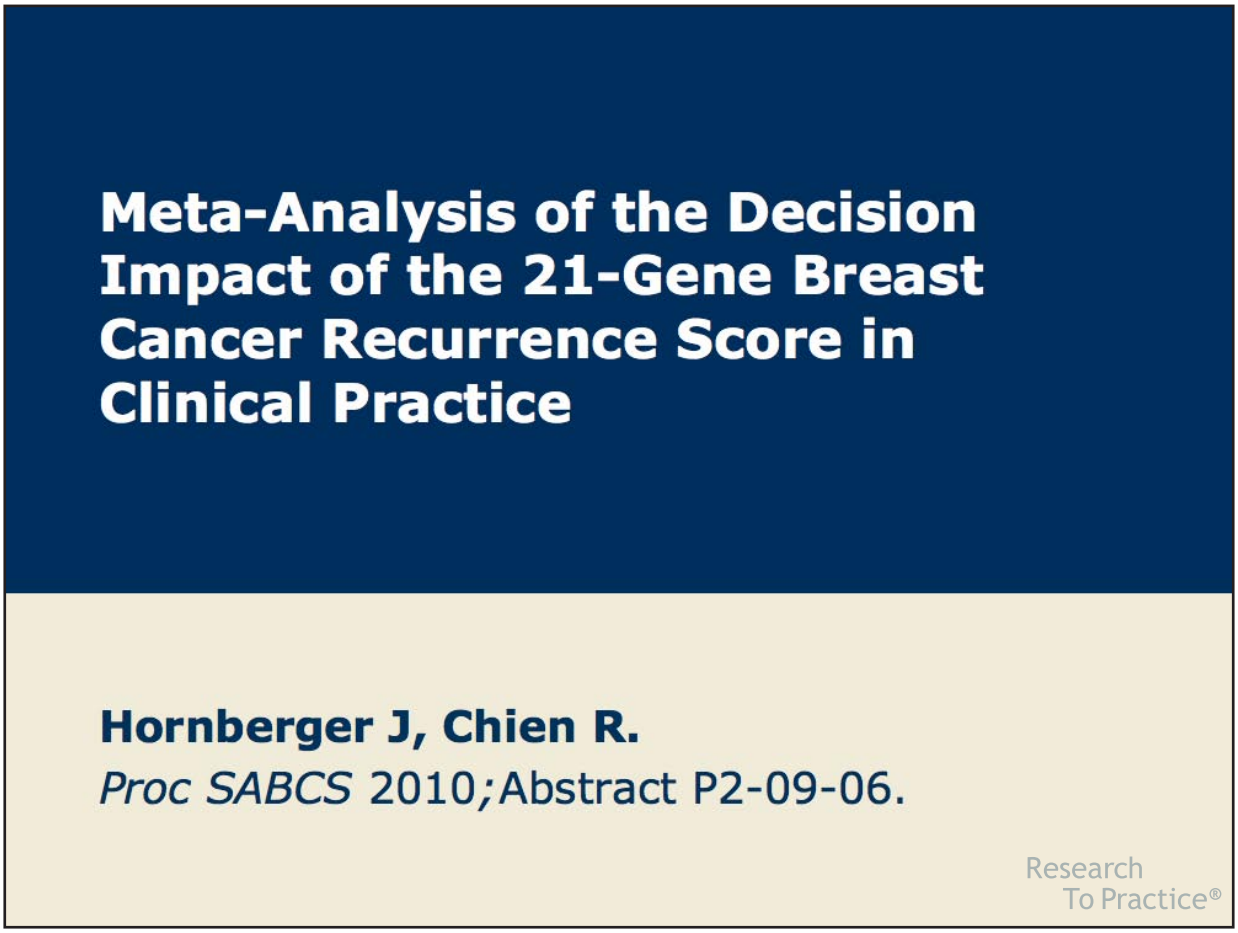
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

Meta-Analysis of the Effect of the Onco*type* DX® Assay Recurrence Score® (RS) on Clinical Decision-Making

Presentation discussed in this issue

Hornberger J, Chien R. **Meta-analysis of the decision impact of the 21-gene breast cancer Recurrence Score in clinical practice.** San Antonio Breast Cancer Symposium 2010;**Abstract P2-09-06**.

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



Methods

- Meta-analysis performed on seven studies (n = 912)
  - Six retrospective chart reviews
  - One prospective analysis (Lo S et al. *J Clin Oncol* 2010)

- Studies were included that reported the following:
  - Number of patients who switched from treatment plan of chemotherapy plus hormone therapy (CT+HT) to hormone (HT) only based upon Onco*type* DX® Assay Recurrence Score® (RS) (CT+HT → HT)
  - Number of patients who switched from HT-only treatment plan to CT+HT (HT → CT+HT) based upon RS

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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Study Summaries

Before RS	CT + HT		HT	
After RS	**CT + HT**	**HT**	**CT + HT**	**HT**
Asad J et al. *Am J Surg* 2008 (n = 81)	24	36	8	13
Henry L et al. *J Surg Oncol* 2009 (n = 29)	6	7	2	14
Klang S et al. *Value in Health* 2010 (n = 313)	69	105	20	119
Liang H et al. *Proc SABCS* 2007 (n = 260)	125	85	3	47
Lo S et al. *J Clin Oncol* 2010 (n = 83)	20	20	3	40
Oratz R et al. *J Oncol Pract* 2007 (n = 68)	19	14	3	32
Thanasoulis T et al. *Proc ASBS* 2008 (n = 78)	8	30	2	38

- Before RS testing: 568 (62%) of patients were recommended to be treated with adjuvant CT+HT.
- After RS testing: 312 (34%) of patients were recommended to be treated with adjuvant CT+HT.

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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Probabilities of CT + HT

	Before RS	After RS	Difference
Asad J et al. *Am J Surg* 2008	74%	40%	-35%
Henry L et al. *J Surg Oncol* 2009*	45%	28%	-17%
Klang S et al. *Value in Health* 2010	56%	28%	-27%
Liang H et al. *Proc SABCS* 2007	81%	49%	-32%
Lo S et al. *J Clin Oncol* 2010	48%	28%	-20%
Oratz R et al. *J Oncol Pract* 2007	49%	32%	-16%
Thanasoulis T et al. *Proc ASBS* 2008	49%	13%	-36%
All studies	62%	34%	-28%
Excluding Liang H et al.	55%	28%	-27%

*All studies except Henry et al had statistically significant differences in CT recommendation before and after RS testing.

- Results: Net reduction of CT+HT recommendation of 28%

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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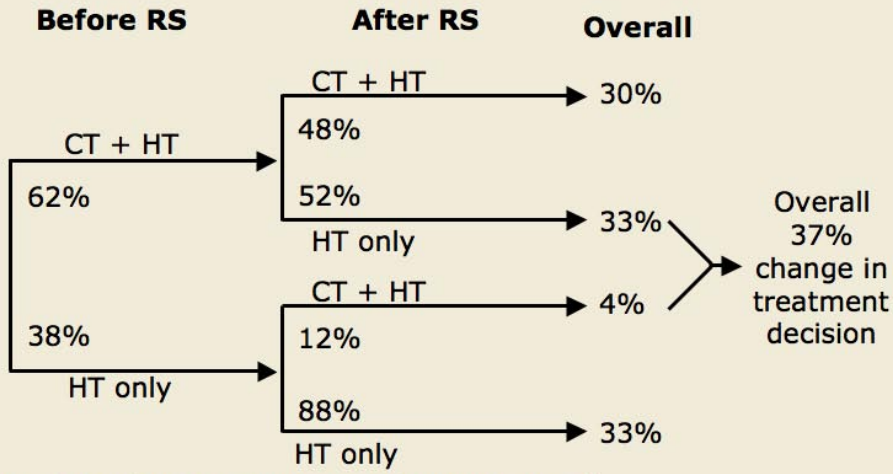
Effect of Recurrence Score on Treatment Plans



- RS led to 37% change in treatment decisions overall.
- RS testing led to 52% switch in treatment recommendations in patients who were initially recommended to adjuvant CT+HT.
- RS testing led to 12% switch in treatment recommendations in patients who were initially recommended to HT only.

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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Decision Impact of the 21-Gene Breast Cancer Recurrence Score in Clinical Practice

Rx Plan Before RS	Rx Plan After RS	N = 912 (%)
CT	CT	271 (30%)
HT only	HT only	303 (33%)
HT only	CT	41 (4%)
CT	HT only	297 (33%)

37%

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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Discussion

- Overall reduction of CT recommendation or use is approximately 28%.
- One study (Liang H et al. *Proc SABCS* 2007) reported treatment recommendation based on NCCN guidelines against the RS.
  - Mean chemotherapy difference of 27% with this study excluded from analysis.
- The RS led to approximately 37% change in treatment decision.
- This meta-analysis summarizes the experience with RS in both academic institutions and community-based centers.

Limitations:

- Data are predominately US-based and may not reflect the regional variation in chemotherapy use around the world.
- Data from recently published prospective TRANSGEICAM study were not available at the time of this analysis.
  - Reported 15.5% of patients switched from CT+HT to HT and 12.7% of patients switched from HT-only to CT+HT (Albanell J et al. *Proc ESMO* 2010).

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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Conclusions

- This meta-analysis shows approximately 27-28% reduction in the recommendation of chemotherapy after Onco*type* DX assay Recurrence Score testing.
- Overall, the RS changed more than a third of treatment decisions:
  - 33% of the overall population switched from CT+HT to HT only after RS testing.
  - 4% of the overall population switched from HT only to CT+HT after RS testing.

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06.

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Investigator Commentary: Meta-Analysis of the Effect of the Onco*type* DX Assay on Clinical Decision-Making

In this meta-analysis of seven published reports with approximately 1,000 patients, the investigators attempted to evaluate the effect of the Recurrence Score on clinical decision-making. They demonstrated consistently that the use of the Recurrence Score resulted in less administration of adjuvant chemotherapy.

On one hand, these findings are not surprising because the Recurrence Score performs well in identifying patients in the low- to intermediate-risk zone who do not need chemotherapy. A back-of-the-envelope calculation would quickly suggest that it should lower the use of adjuvant chemotherapy. On the other hand, it's a nice confirmation of that expectation and this is important to third-party payers and other regulators — because even an expensive test that spares patients chemotherapy will quickly pay for itself, because of the relatively high cost of chemotherapy.

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