



INTERVIEW

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Tracks 1-10

- Track 1** Results of a Phase II study of adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive BC
- Track 2** Choosing between TCH and paclitaxel/trastuzumab as adjuvant therapy for HER2-positive BC
- Track 3** Perspective on the BETH trial results: TCH with or without bevacizumab
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- Track 5** Prediction of late distant recurrence after 5 years of endocrine therapy: A combined analysis of patients from the ABCSG-8 and TransATAC studies using the PAM50 risk of recurrence score
- Track 6** Direct comparison of risk classification among the MammaPrint®, Mammostrat® and Oncotype DX® assays for patients with early-stage BC
- Track 7** **Case discussion:** A 48-year-old woman who previously received multiple lines of chemotherapy for ER/PR-negative, HER2-positive mBC experiences a prolonged complete response with trastuzumab and dose-reduced vinorelbine
- Track 8** **Second opinion:** Hormonal therapy versus high-dose chemotherapy → radiation therapy for patients with ER-positive, HER2-negative mBC
- Track 9** **Case discussion:** A 46-year-old woman who originally received endocrine treatment in 1999 for Stage I, ER-positive IDC presents with ER-negative, HER2-positive recurrent disease and begins treatment with weekly paclitaxel in combination with trastuzumab
- Track 10** **Case discussion:** A 68-year-old man who previously received a regimen that included an anthracycline for testicular cancer presents with a 2.4-cm, ER-positive, HER2-positive IDC with 1 positive axillary node

Select Excerpts from the Interview

Tracks 1-2

- **DR LOVE:** What are your thoughts on the Phase II APT trial that was presented at the 2013 SABCS by a group from Dana-Farber evaluating adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer (Tolaney 2013; [3.1])?
- **DR MILLER:** This was an important single-arm study that came out of the recognition that a population of patients with smaller, HER2-positive, node-negative breast cancer has been largely excluded from adjuvant trastuzumab trials. The goal of this Phase II trial was to find a treatment that would have an excellent outcome while minimizing the duration, cost and toxicity of therapy. The trial enrolled approximately 400 patients

Phase II APT Trial of Adjuvant Paclitaxel and Trastuzumab for Node-Negative, HER2-Positive Breast Cancer

Efficacy	Paclitaxel and trastuzumab	
Three-year disease-free survival (DFS)		
All patients (n = 406)	98.7%	
Tumors >1 cm (n = 205)	98.0%	
Tumors ≤1 cm (n = 201)	99.5%	
DFS events		
Any recurrence	2.5%	
Local/regional recurrence (ipsilateral axilla and breast)	0.9%	
Distant recurrence	0.5%	
Select adverse events	All grades	Grade 3 or 4
Neuropathy	13%	3%
Neutropenia	11%	<5%
Leukopenia	9%	2%
Anemia	7%	<1%
Symptomatic congestive heart failure: 0.5%; asymptomatic declines in left ventricular ejection fraction: 3.2%		

Tolaney S et al. San Antonio Breast Cancer Symposium 2013; **Abstract S1-04**.

with tumors 3 centimeters or smaller. Patients received paclitaxel and trastuzumab for 12 weeks followed by trastuzumab for 9 months.

The majority of patients had tumors that were between 1 and 2 centimeters in size, and their outcomes were excellent (Tolaney 2013; [3.1]). The side effects, including cardiac toxicity, were minimal. Although questions remain, we now have a fairly large data set we can use in this setting.

► **DR LOVE:** In this study, 19% of the patients had T1a tumors that were 5 millimeters or smaller and may not have experienced a recurrence without treatment. What is your approach for managing these tumors?

► **DR MILLER:** I believe that, even with the most aggressive biology, tumor size still matters. Where you set that bar for treatment is where we differ. I find it difficult to advocate systemic therapy for patients with tumors smaller than 5 millimeters.

I may or may not recommend systemic treatment for tumors in the 5- to 10-mm range, depending on a discussion with the patient. We consider factors such as the size of the tumor, tumor biology and whether the patient is more concerned about recurrence or about the toxicities of therapy.

► **DR LOVE:** What adjuvant therapy do you recommend for patients with node-negative, HER2-positive breast cancer?

► **DR MILLER:** Since participating in the Phase II APT trial, I generally recommend that regimen of paclitaxel and trastuzumab for 12 weeks. It was well tolerated, and I am comfortable recommending that abbreviated regimen to patients outside of a trial setting. I have administered both TCH and anthracyclines followed by paclitaxel/trastuzumab depending on tumor size and nodal burden.

Track 4

► **DR LOVE:** Would you discuss the results from trials reported at SABCS 2013 evaluating the benefits of primary tumor resection for patients with Stage IV breast cancer?

► **DR MILLER:** Two randomized trials — in Turkey and India — were presented at SABCS to address this question (Badwe 2013; Soran 2013). These studies did not report any significant benefits for resection of the primary tumor (3.2).

A subset analysis from one study reported that patients with bone-only metastases had a trend toward longer survival (Soran 2013). I do not generally recommend surgical removal of the primary tumor unless it is symptomatic, and the results from these studies have not affected my practice.

► **DR LOVE:** Dr Seema Khan, the discussant for that session, concluded that locoregional therapy should not be offered to patients with mBC who are at low risk for local recurrence outside the setting of a clinical trial (Khan 2013). Do you agree?

► **DR MILLER:** Dr Khan has been consistent on that front. She has supported the idea that, although surgery might be helpful in some situations, the benefits have not been proven.

It is important to support the ongoing ECOG-E2108 Phase III study (NCT01242800), evaluating early surgery versus standard palliative care for patients with Stage IV breast cancer.

Dr Khan, the principal investigator, has been collaborating with the Turkish and Indian investigators so that they can combine the samples collected in the ECOG trial with their studies. That will allow for a more extensive biobank to identify subsets of patients who might benefit from surgery.

3.2

Results of 2 Phase III Trials Evaluating Primary Tumor Resection for Patients with Stage IV Breast Cancer

Study design	Tata Memorial (India) ¹ (n = 350)	MF 07-01 (Turkey) ² (n = 293)
Initial systemic therapy before randomization	CEF ± taxane	None
Primary endpoint	Overall survival	Overall survival
Efficacy		
Overall survival	LRT vs no LRT HR 1.04, <i>p</i> = 0.79	Surgery vs systemic therapy HR 0.76, <i>p</i> = 0.20
Bone-only metastases	HR 1.43, <i>p</i> = NR	HR 0.60, <i>p</i> = 0.15
Solitary bone metastasis	NR	HR 0.23, <i>p</i> = 0.02

CEF = cyclophosphamide/epirubicin/fluorouracil; LRT = locoregional therapy; HR = hazard ratio; NR = not reported

¹Badwe R et al. San Antonio Breast Cancer Symposium 2013; **Abstract S2-02**; ²Soran A et al. San Antonio Breast Cancer Symposium 2013; **Abstract S2-03**.

Tracks 5-6

► **DR LOVE:** What are your thoughts on the recent study using the PAM50 assay to predict late distant recurrences in cohorts from the ABCSG-8 and TransATAC studies after 5 years of endocrine treatment?

► **DR MILLER:** Although studies like the ATLAS and aTTom trials have shown that extended adjuvant endocrine therapy is beneficial, the benefit was fairly modest. Considering the cost, side effects and compliance issues associated with long-term therapy, it would be valuable to identify patients who have a high recurrence risk after 5 years of endocrine treatment.

The PAM50 analysis was able to identify groups of patients at different risks of recurrence between 5 years and 10 years after endocrine therapy. The high-risk group had approximately a 17% risk of distant recurrence compared to only about 2% in the low-risk group (Sestak 2013). PAM50 analysis has not affected my personal practice because, although it tells us about risk of recurrence, it does not tell us what treatment would be beneficial.

► **DR LOVE:** A study reported at SABCS 2013 comparing the risk classification among the MammaPrint, *Oncotype DX* and Mammostrat assays in early breast cancer demonstrated that these assays classify a large proportion of patients differently. What is your take on these results (Shivers 2013)?

► **DR MILLER:** These assays do classify patients differently, and to an extent that's not surprising. The specific genes incorporated into the different risk-stratifying platforms have little overlap. However, the overlap in the pathways represented by those genes is substantial. Genes involved in ER signaling, proliferation, apoptosis, angiogenesis and invasion are typically represented.

It is important for me to be able not only to determine a patient's risk but also to predict whether a patient will benefit from a specific therapy. Only the *Oncotype DX* assay has been validated as a predictor of benefit from chemotherapy in multiple randomized trials, and that's why I use it in my practice. ■

SELECT PUBLICATIONS

Badwe R et al. **Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial.** San Antonio Breast Cancer Symposium 2013; **Abstract S2-02.**

Khan SA. **Does primary tumor resection improve survival for patients with Stage IV breast cancer?** San Antonio Breast Cancer Symposium 2013; **Abstract S2-04.**

Sestak I et al. **Prediction of late distant recurrence after 5 years of endocrine treatment: A combined analysis of 2485 patients from the ABCSG-8 and transATAC studies using the PAM50 risk of recurrence (ROR) score.** San Antonio Breast Cancer Symposium 2013; **Abstract S6-04.**

Shivers SC et al. **Direct comparison of risk classification between MammaPrint®, *Oncotype DX*® and Mammostrat® assays in patients with early stage breast cancer.** San Antonio Breast Cancer Symposium 2013; **Abstract P6-06-02.**

Soran A et al. **Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01).** San Antonio Breast Cancer Symposium 2013; **Abstract S2-03.**

Tolaney S et al. **A phase II study of adjuvant paclitaxel (T) and trastuzumab (H) (APT trial) for node-negative, HER2-positive breast cancer (BC).** San Antonio Breast Cancer Symposium 2013; **Abstract S1-04.**