INTERVIEW

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CD 2, Tracks 5-16

Track 5 **Second opinion:** Consideration of forgoing chemotherapy for patients with ER-positive BC with 1 positive node and a low Onco*type* DX Recurrence Score

Track 6 Treatment options for patients with ER-positive, node-negative BC

Track 7 Perspective on efficacy and cardiac safety reported on the BCIRG 006 trial — adjuvant AC → T versus AC → TH or TCH for HER2-positive BC

Track 8 **Second opinion:** A 37-year-old woman with locally advanced, ER-positive, HER2-positive BC treated 3 years ago with neoadjuvant AC → TH followed by tamoxifen who now presents with a 5-mm isolated chest wall nodule

Track 9 Toward incorporating pertuzumab into the treatment algorithm for HER2-positive mBC

Track 10 Mechanisms of action of trastuzumab, trastuzumab-DM1 (T-DM1) and pertuzumab

Track 11 A prospective validation study of the Onco*type* DX DCIS Score™ for predicting recurrence risk after resection alone for DCIS

Track 12 **Second opinion:** A patient with low-risk, ER-negative BC and severe skin toxicity after 2 cycles of adjuvant TC

Track 13 Overview of the BOLERO-2 study: Efficacy, toxicities and proposed adjuvant trials of everolimus in BC

Track 14 Current status of the CALGB-40502 study: Weekly paclitaxel, *nab* paclitaxel or ixabepilone with or without bevacizumab as first-line therapy for locally recurrent or metastatic BC

Track 15 Available research on *nab* paclitaxel

Track 16 Adjuvant bisphosphonate therapy in early BC

Select Excerpts from the Interview

CD 2, Track 9

DR LOVE: How do you foresee using pertuzumab if it becomes available in the HER2-positive metastatic breast cancer setting?

DR HUDIS: I believe that pertuzumab will quickly be added to standard first-line therapy for HER2-positive metastatic breast cancer. I'm sure we will hear discussion of administering it after progression as second-line therapy and beyond. Although future studies may demonstrate potential activity of pertuzumab in those settings, the big push now is for its use in early breast cancer. The APHINITY trial evaluating adjuvant pertuzumab/trastuzumab is currently accruing patients (3.1).

We have also initiated a nonrandomized Phase II trial of pertuzumab/trastuzumab with weekly paclitaxel in metastatic disease because we recognize that clinicians may prefer weekly paclitaxel as the chemotherapy partner (NCT01276041). We will be reassured

of paclitaxel as a reasonable substitution if the results resemble those from the experimental arm of CLEOPATRA.

3.1

APHINITY: A Phase III Study of Pertuzumab in Addition to Chemotherapy and Trastuzumab as Adjuvant Therapy for Patients with HER2-Positive Primary Breast Cancer

Protocol ID: NCT01358877

Target Accrual: 3,806

Eligibility
- HER2-positive primary breast cancer
- ECOG PS ≤1
- Baseline LVEF ≥55%
- No prior anti-HER2 therapy

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- Chemotherapy + trastuzumab + pertuzumab
- Chemotherapy + trastuzumab + placebo

LVEF = left ventricular ejection fraction

www.clinicaltrials.gov, May 2012.

CD 2, Track 11

DR LOVE: Would you discuss the SABCS presentation by Dr Solin on the use of the Onco*type* DX assay in DCIS?

DR HUDIS: In this study a subset of the 21 genes from the Onco*type* DX assay were evaluated. Eleven cancer-related genes and 5 reference genes were analyzed and found to be prognostic (Solin 2011; [3.2]). Using the DCIS Score the authors could predict the likelihood of an in-breast event over the coming year.

The problem is that they did not have randomized data for radiation therapy. Although not everyone agrees, it is assumed that the risk is so low, based on the Onco*type* DX DCIS Score being below a certain number, that one could forgo radiation therapy. I believe the role of this test is evolving, and more data are needed. In practice, it would be good if it could be converted from a prognostic to a predictive test, as was done with the Onco*type* DX Recurrence Score.

3.2

ECOG-E5194 Study: 10-Year Outcome of Ipsilateral Breast Events (IBE) by the Onco*type* DX DCIS Score Evaluated by Prespecified Risk Groups

	DCIS Score risk group			
Type of IBE	Low (n = 246)	Intermediate (n = 45)	High (n = 36)	*p*-value*
Any IBE	12.0%	24.5%	27.3%	0.02
Invasive IBE	5.1%	8.9%	19.1%	0.01

* Log-rank *p*-value from a Kaplan-Meier risk curve

"The DCIS Score provides independent information on IBE risk beyond clinical pathologic variables including such important clinical variables as prior tamoxifen use, tumor grade and negative margin width."

Solin LJ et al. San Antonio Breast Cancer Symposium 2011;**Abstract S4-6**.

CD 2, Tracks 14-15

DR LOVE: Would you talk about the current status of the CALGB-40502 study of first-line chemotherapy for metastatic disease?

DR HUDIS: This is an important trial that compared weekly paclitaxel in the control arm to nanoparticle albumin-bound (*nab*) paclitaxel or ixabepilone in the experimental arms. Most of the patients in this trial received bevacizumab without random assignment because at the time of study design it was anticipated that this would be standard practice. The study had to be halted twice. The first time was due to differential toxicities and the lack of superiority of ixabepilone over weekly paclitaxel for progression-free survival, and the second time was a result of lack of superiority of *nab* paclitaxel versus the control arm. The results will be presented at ASCO.

DR LOVE: Your group recently presented a Phase II trial comparing weekly versus every 2-week or every 3-week *nab* paclitaxel with bevacizumab (Seidman 2011; [3.3]). What are your thoughts about the future of *nab* paclitaxel?

DR HUDIS: It may have promise in the metastatic setting as palliative therapy. In the adjuvant setting, I am not aware of a definitive Phase III trial to establish its role. I believe that in some practices it will be the first choice because of the convenience and lack of premedication. In other practices its use will be restricted because of the cost. ■

3.3

Randomized Phase II Trial of Weekly versus Every 2-Week or Every 3-Week Nanoparticle Albumin-Bound (*Nab*) Paclitaxel with Bevacizumab as First-Line Therapy for Metastatic Breast Cancer

Efficacy	***Nab* paclitaxel q3wk** (n = 75)	***Nab* paclitaxel q2wk** (n = 54)*	***Nab* paclitaxel q1wk** (n = 79)
Overall response	44%	41%	46%
Time to tumor progression (TTP)†	8.0 mo	6.3 mo	9.0 mo
Overall survival (OS)†	21.3 mo	19 mo	23.7 mo
Select adverse events (AEs)			
Sensory neuropathy (Grade ≥2)	64%	67%	70%
Hematologic AEs (Grade ≥3)	18%	8%	30%
Nonhematologic AEs (Grade ≥3)			
Fatigue	17%	35%	18%
Bone pain	3%	6%	1%
Hypertension	4%	2%	4%

* Every 2-week arm closed early due to significantly more Grade ≥2 fatigue and bone pain
† No statistically significant difference between treatment arms in TTP and OS

Seidman AD et al. San Antonio Breast Cancer Symposium 2011;**Poster P1-14-01**.

SELECT PUBLICATIONS

Baselga J et al. **CLEOPATRA Study Group. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer.** *N Engl J Med* 2012;366(2):109-19.

Seidman AD et al. **Randomized Phase II trial of weekly vs q 2-weekly vs q 3-weekly nanoparticle albumin-bound paclitaxel with bevacizumab as first-line therapy for metastatic breast cancer.** San Antonio Breast Cancer Symposium 2011;**Poster P1-14-01**.