INTERVIEW

## Melody A Cobleigh, MD

Dr Cobleigh is Professor of Medicine and Director of the Section of Medical Oncology at Rush University Medical Center in Chicago, Illinois.

### Tracks 1-8

Track 1 **Case discussion:** A 53-year-old woman who developed liver, lung and chest wall metastases seven years ago and subsequently underwent treatment for CNS metastases is currently receiving sixth-line therapy with metronomic cyclophosphamide/methotrexate 12 years after treatment for node-negative TNBC

Track 2 **Case discussion:** A 59-year-old woman with ER-positive, HER2-positive mBC whose disease has progressed through multiple lines of anti-HER2 therapy during the past five years has a significant response to T-DM1 on protocol

Track 3 Clinical experience with T-DM1 in patients with HER2-positive mBC

Track 4 Treatment options for patients who experience relapse during or after adjuvant chemotherapy/trastuzumab

Track 5 NSABP-B-47: A Phase III trial of adjuvant chemotherapy with or without trastuzumab in HER2-normal BC

Track 6 Clinical utility of the Onco*type* DX assay

Track 7 NSABP-B-43 trial: Radiation therapy with or without trastuzumab in HER2-positive ductal carcinoma in situ

Track 8 Perspective on community BC practice

## Select Excerpts from the Interview

### Tracks 2-4

**Case discussion**

A 59-year-old woman with ER-positive, HER2-positive mBC whose disease has progressed through multiple lines of anti-HER2 therapy during the past five years is treated with T-DM1 on protocol.

**DR COBLEIGH:** Since diagnosis, this patient's disease has progressed through multiple lines of treatment, including dose-dense AC/paclitaxel followed by radiation therapy, capecitabine/trastuzumab, trastuzumab alone, vinorelbine/trastuzumab, lapatinib with and without trastuzumab, trastuzumab/bevacizumab, trastuzumab/letrozole and trastuzumab with metronomic therapy.

She became eligible for the expanded-access T-DM1 protocol and experienced a dramatic response and was transformed from someone who was unable to work into a person who was able to hike seven miles during a recent vacation in Arizona. Her tumor measurements markedly decreased — this was interesting because previously her liver disease was so extensive that it was impossible to measure. Using volumetric measurements, we found that her tumor had shrunk by approximately 66 percent. She remains on the study.

**DR LOVE:** Did she experience any side effects?

**DR COBLEIGH:** The only side effects she had were bleeding gums and transient thrombocytopenia, which most patients experience after about a week of therapy with this agent. Otherwise she felt terrific.

**DR LOVE:** How do you believe T-DM1 will fit into the future treatment algorithm for breast cancer?

**DR COBLEIGH:** Most clinicians would like to see this agent used in the adjuvant setting in place of chemotherapy. Although T-DM1 contains trastuzumab bound to a chemotherapeutic agent, it doesn't cause the toxicity associated with chemotherapy.

**DR LOVE:** You mentioned that this patient experienced a response to the combination of trastuzumab and bevacizumab. What has been your experience with this regimen for metastatic disease?

**DR COBLEIGH:** I believe it to be an active combination. I've administered it to patients who, like this one, were responding to trastuzumab and then experienced disease progression and subsequently responded when bevacizumab was added back in.

**DR LOVE:** What is your approach for patients who experience relapse after previous adjuvant chemotherapy/trastuzumab?

**DR COBLEIGH:** Thankfully, that is not a common scenario, so I don't have a specific algorithm. I don't believe lapatinib is as well tolerated or as active as trastuzumab. Information from neoadjuvant trials confirms that lapatinib is not as active an agent (Baselga 2010; [1.1, page 4]; Untch 2010). I administer lapatinib to patients for whom a number of trastuzumab-containing regimens have failed. I have also used the combination of trastuzumab with lapatinib, which is associated with less toxicity than combinations of trastuzumab with chemotherapy drugs.

## Tracks 5, 7

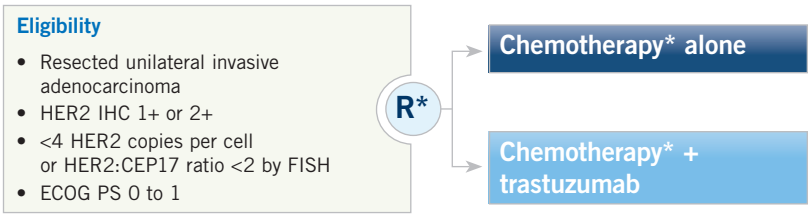
**DR LOVE:** What are your thoughts on the NSABP-B-47 trial, which is evaluating adjuvant chemotherapy with or without trastuzumab for patients with HER2-normal breast cancer?

**DR COBLEIGH:** The first time Dr Soon Paik presented information on the purported benefit of adjuvant trastuzumab for patients with HER2-normal

**4.1**

**NSABP-B-47: A Phase III Trial of Adjuvant Chemotherapy with or without Trastuzumab for Patients with Node-Positive or High-Risk Node-Negative, HER2-Normal Invasive Breast Cancer**

**Protocol IDs:** CDR0000692574; NCT01275677 **Target Accrual:** 3,260 (Open)




* Investigator preference: Docetaxel/cyclophosphamide OR doxorubicin/cyclophosphamide → paclitaxel

**www.clinicaltrials.gov**, June 2011.

breast cancer at an NSABP meeting, I was skeptical, as were most of the people sitting around the table. As a result, he conducted more research and his hypothesis became more robust (Paik 2008) and is definitely worthy of testing in a clinical trial (4.1).

**DR LOVE:** Would you describe your NSABP-B-43 study of trastuzumab in ductal carcinoma in situ (DCIS)?

**DR COBLEIGH:** The B-43 trial is enrolling patients with HER2-positive DCIS resected by lumpectomy. Patients receive two doses of trastuzumab during radiation therapy as a radiosensitizer. The primary endpoint is breast tumor recurrence, and one of the secondary endpoints is the effect of trastuzumab on the contralateral breast tumor.

An interesting study of neoadjuvant trastuzumab for patients with DCIS was recently published by Dr Kuerer from MD Anderson (Kuerer 2011). The study focused on the underlying immunologic effects of trastuzumab and demonstrated that antibody-dependent cell-mediated cytotoxicity skyrocketed within two weeks of a single dose of trastuzumab. ■

## SELECT PUBLICATIONS


Baselga J et al. **First results of the NeoALTTO trial (BIG 01-06/EGF 106903): A Phase III, randomized, open label, neoadjuvant study of lapatinib, trastuzumab, and their combination plus paclitaxel in women with HER2-positive primary breast cancer.** San Antonio Breast Cancer Symposium 2010;**Abstract S3-3**.

Kuerer HM et al. **Biologic and immunologic effects of preoperative trastuzumab for ductal carcinoma in situ of the breast.** *Cancer* 2011;117(1):39-47.

Paik S et al. **HER2 status and benefit from adjuvant trastuzumab in breast cancer.** *N Engl J Med* 2008;358(13):1409-11.

Untch M et al. **Lapatinib vs trastuzumab in combination with neoadjuvant anthracycline-taxane-based chemotherapy: Primary efficacy endpoint analysis of the GEPARQUINTO study (GBG 44).** San Antonio Breast Cancer Symposium 2010;**Abstract S3-1**.