INTERVIEW

Adam M Brufsky, MD, PhD

Dr Brufsky is Professor of Medicine at the University of Pittsburgh, Associate Director for Clinical Investigation at the University of Pittsburgh Cancer Institute, Co-Director of the Comprehensive Breast Cancer Center and Associate Division Chief in the Department of Medicine's Division of Hematology/Oncology in Pittsburgh, Pennsylvania.

Tracks 1-14

Select Excerpts from the Interview

Track 1

DR LOVE: Would you discuss what was reported at ASCO on the NSABP-B-38 trial comparing adjuvant TAC to dose-dense AC → P with or without gemcitabine for patients with node-positive breast cancer?

DR BRUFSKY: NSABP-B-38 is an interesting trial. The results were long awaited, but I believe that many of us had already taken sides. The dose-dense aficionados

thought the dose-dense regimen was going to work, the TAC aficionados thought TAC was a superior regimen and other people thought more was better and that adding gemcitabine would be an improvement.

Also interesting is that the trial didn't evaluate what I believe to be a very favorable regimen, at least in terms of tolerability and efficacy, which is AC followed by weekly paclitaxel from the ECOG-E1199 study (Sparano 2008). It is unfortunate that this regimen wasn't one of the arms on the trial.

The bottom line from the study was that, at least statistically, no difference was evident — only a slight trend was detected in favor of dose-dense therapy. Absolutely no benefit was seen with the use of gemcitabine (Swain 2012; [3.1]).

The fact that no benefit was evident with the addition of gemcitabine did not surprise me. If you consider past neoadjuvant studies that have taken similar approaches to adding beyond standard AC → T, you can argue that regardless of the choice of agent not much of a difference is observed.

3.1

NSABP-B-38: Definitive Analysis of an Adjuvant Trial Comparing Dose-Dense (DD) AC → Paclitaxel with Gemcitabine to DD AC → Paclitaxel and to TAC for Patients with Operable, Node-Positive Breast Cancer

Efficacy	DD AC → PG	DD AC → P	TAC
Five-year disease-free survival (n = 1,613; 1,618; 1,610)	80.6%	82.2%	80.1%
Five-year overall survival (n = 1,618; 1,624; 1,617)	90.8%	89.1%	89.6%

AC = doxorubicin/cyclophosphamide; P = paclitaxel; G = gemcitabine; TAC = docetaxel/doxorubicin/cyclophosphamide

Swain SM et al. *Proc ASCO* 2012;**Abstract LBA1000**.

Tracks 10-12

Case discussion

A 38-year-old woman with a 6-cm, ER-positive, PR-negative, HER2-positive infiltrating ductal carcinoma with a 3-cm, biopsy-proven breast cancer metastasis in the liver experiences a near-complete response with docetaxel/carboplatin/trastuzumab (TCH)

DR BRUFSKY: This patient was young and desired aggressive therapy. A number of people may consider administering paclitaxel/trastuzumab but I administered TCH, which is my "go-to regimen." To digress somewhat to the adjuvant treatment of HER2-positive breast cancer, I know there's been a lot of debate about AC followed by docetaxel/trastuzumab versus TCH. I was an involved participant in the adjuvant BCIRG 006 trial that compared these regimens. I used to administer AC followed by docetaxel/trastuzumab somewhat frequently.

In my view the recurrence rate is numerically higher with TCH than with AC followed by docetaxel/trastuzumab, but when you evaluate the overall picture and other potential complications associated with the latter regimen, everything evens out (Slamon 2011; [3.2]). We have to evaluate the big picture, not simply the breast cancer.

This patient actually attained a near-complete response in both the breast and the liver with TCH. This has occurred within the last month, and now we're trying to figure out the best next approach for her. The first question was, "Do we remove the primary breast tumor?" She opted to do so, so we performed a mastectomy. We also discussed options — laparoscopic resection, radiofrequency ablation, cryotherapy, observation, et cetera — for the mass in her liver, and we opted to observe.

The next question was what to do next. The options for a premenopausal patient such as this one would be an LHRH agonist or tamoxifen. I chose tamoxifen and I'm continuing the trastuzumab. But the big issue now is, does she receive pertuzumab? I'd love to be able to administer trastuzumab, pertuzumab and tamoxifen, but we don't have data on this approach. ■

3.2

BCIRG 006: A Phase III Trial Evaluating AC → Docetaxel, AC → Docetaxel/ Trastuzumab and Docetaxel/Carboplatin/Trastuzumab in the Adjuvant Treatment of HER2-Amplified Early Breast Cancer

Outcome	AC → T (n = 1,073)	AC → TH (n = 1,074)	TCH (n = 1,075)
Estimated 5-year disease-free survival	75%	84%	81%
Hazard ratio, *p*-value	—	0.64, <0.001	0.75, 0.04
Estimated 5-year overall survival	87%	92%	91%
Hazard ratio, *p*-value	—	0.63, <0.001	0.77, 0.04
Cardiac-related adverse events	**AC → T**	**AC → TH**	**TCH**
Cardiac-related death	0%	0%	0%
Grade 3 or 4 congestive heart failure	0.7%	2.0%	0.4%
>10% relative reduction in LVEF	11.2%	18.6%	9.4%

AC = doxorubicin/cyclophosphamide; T = docetaxel; H = trastuzumab; TCH = docetaxel/carboplatin/ trastuzumab

Slamon D et al. *N Engl J Med* 2011;365(14):1273–83.

SELECT PUBLICATIONS

Abbott DE et al. **Resection of liver metastases from breast cancer: Estrogen receptor status and response to chemotherapy before metastasectomy define outcome.** *Surgery* 2012;151(5):710–6.

Duan XF et al. **Outcome of patients with liver-only metastases from breast cancer after mastectomy: A retrospective analysis.** *J Cancer Res Clin Oncol* 2011;137(9):1363–70.

Rocque G et al. **Adjuvant therapy for HER2+ breast cancer: Practice, perception, and toxicity.** *Breast Cancer Res Treat* 2012;131(2):713–21.

Ruiterkamp J, Ernst MF. **The role of surgery in metastatic breast cancer.** *Eur J Cancer* 2011;47(Suppl 3):6–22.

Slamon D et al. **Adjuvant trastuzumab in HER2-positive breast cancer.** *N Engl J Med* 2011;365(14):1273–83.

Sparano JA et al. **Weekly paclitaxel in the adjuvant treatment of breast cancer.** *N Engl J Med* 2008;358(16):1663–71.

Swain SM et al. **NSABP B-38: Definitive analysis of a randomized adjuvant trial comparing dose-dense (DD) AC → paclitaxel (P) plus gemcitabine (G) with DD AC → P and with docetaxel, doxorubicin, and cyclophosphamide (TAC) in women with operable, node-positive breast cancer.** *Proc ASCO* 2012;**Abstract LBA1000**.