INTERVIEW

Adam M Brufsky, MD, PhD

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Tracks 1-12

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: Would you comment on your recent update on the RIBBON 2 study evaluating chemotherapy with bevacizumab in the second-line setting presented at ASCO 2011 and the trend that was revealed toward an overall survival benefit for patients with triple-negative disease?

DR BRUFSKY: Based on the RIBBON 2 data (Brufsky 2010; [3.1]), I administer bevacizumab in the second-line setting for triple-negative disease even though it's not the approved setting.

The question is whether a signal for continued first-, second- and third-line therapy with bevacizumab exists, as it does with trastuzumab.

Bevacizumab has rare but severe side effects, such as pulmonary embolus and bowel perforation, which we must be mindful of. Other serious side effects can also occur, such as hypertension and proteinuria. In clinical practice we're struggling with where to place this agent. The ODAC has one perspective and the NCCN has another.

DR LOVE: In general, for what kind of patient would you likely administer chemotherapy and bevacizumab?

DR BRUFSKY: I consider it for patients with aggressive tumors for whom you would normally administer combination chemotherapy. If you're considering two cytotoxic agents, it's also reasonable to consider a cytotoxic agent with bevacizumab. Although I'm one of the principal investigators on one of the trials, I'm somewhat ambivalent because we're not convinced which patient subsets will experience a benefit.

Would I administer chemotherapy with bevacizumab in the first line? I may consider it in some situations. For a patient with bulkier disease, someone who is not at risk for hemorrhage or thrombosis and who has a decent performance status — for example, a young woman with bulky triple-negative disease that progresses within 12 to 18 months after adjuvant therapy — I would consider chemotherapy with bevacizumab in the first-line setting.

As I mentioned, I would also consider it for a patient with triple-negative disease who has completed first-line therapy — whether on a PARP trial, through the PARP expanded-access program or with another therapy. I would seriously consider second-line chemotherapy with bevacizumab in that setting.

The one setting in which I would not administer bevacizumab is in the case of a patient with ER-positive, slowly progressive disease with a long disease-free interval before metastasis. For a 65- or 68-year-old woman with a few

3.1

RIBBON 2 Study: Effect of Bevacizumab (Bev) on Efficacy of Second-Line Chemotherapy (CT)* in the Subset of Patients with Triple-Negative Breast Cancer

Efficacy	CT + bev (n = 112)	CT + placebo (n = 47)	Hazard ratio	*p*-value
Overall response rate	41%	18%	—	0.0078
Median progression-free survival	6.0 mo	2.7 mo	0.494	0.0006
Median interim overall survival	17.9 mo	12.6 mo	0.624	0.0534
Select adverse events†				
Neutropenia	18.8%	10.6%	—	—
Hypertension	10.7%	0%	—	—
Proteinuria	5.4%	0%	—	—

* Capecitabine, gemcitabine, paclitaxel, docetaxel, *nab* paclitaxel or vinorelbine
† No unanticipated side effects were observed except neutropenia.

Brufsky A et al. *Proc ASCO* 2011;**Abstract 1010**.

bony metastatic lesions who's experienced disease progression on one to three hormone therapies, I would administer chemotherapy — probably capecitabine — but not bevacizumab.

DR LOVE: What typical dose and schedule of capecitabine do you use?

DR BRUFSKY: It's interesting to note that nowadays a number of options are available for different doses and schedules. The label-indicated dose is too high, so many of us will start a patient like the one just described on three to four 500-mg tablets twice daily, which works out to a little less than 2 g/m^2 per day and is under the recommended dose. Additionally, the one-week-on, one-week-off schedule that was popularized in an unpublished abstract by investigators at Memorial Sloan-Kettering is becoming a more widely adopted practice.

Track 12

DR LOVE: Are you currently using the Onco*type* DX assay for patients with node-positive disease?

DR BRUFSKY: Yes. I use Onco*type* DX for postmenopausal patients with node-positive disease. Data from both ASCO and San Antonio suggest that certain subsets behave like node-negative disease (Dowsett 2010; Albain 2010). So for a patient with IHC-positive nodes or even simply one to three positive nodes, a strong estrogen receptor and a low Ki-67 level — five to 10 percent — I order an Onco*type* DX assay. It is reimbursed for postmenopausal women in my practice.

The challenge is for a premenopausal woman who receives an LHRH agonist and no chemotherapy for node-positive breast cancer. Suppose the patient is 45 years old and prefers not to go through chemotherapy. For premenopausal women with one to three positive nodes, no data exist with Onco*type* DX. However, one could argue that biology trumps anatomy so if you make her postmenopausal by administering an LHRH agonist, the Onco*type* DX assay should be predictive of her response to chemotherapy and/or hormone therapy. ■

SELECT PUBLICATIONS

Albain KS et al. **Prognostic and predictive value of the 21-gene Recurrence Score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial.** *Lancet Oncol* 2010;11(1):55-65.

Brufsky A et al. **Impact of bevacizumab (bev) on efficacy of second-line chemotherapy (CT) for triple-negative breast cancer: Analysis of RIBBON-2.** *Proc ASCO* 2011;**Abstract 1010**.

Cortazar J et al. **Relationship between OS and PFS in metastatic breast cancer (MBC): Review of FDA submission data.** *Proc ASCO* 2011;**Abstract 1035**.

Dowsett M et al. **Prediction of risk of distant recurrence using the 21-gene Recurrence Score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: A TransATAC study.** *J Clin Oncol* 2010;28(11):1829-34.

Hayes DF. **Bevacizumab treatment for solid tumors: Boon or bust?** *JAMA* 2011;305(5):506-8.