INTERVIEW

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Tracks 1-12

Select Excerpts from the Interview

Track 3

DR LOVE: You were part of an abstract presented recently at ASCO, "Time Trends in the Use of Adjuvant Chemotherapy and Outcomes in Women with T1a,b N0M0 Breast Cancer in the NCCN." Would you discuss the study?

DR BURSTEIN: During the past decade our threshold for administering chemotherapy for small tumors has decreased. Specifically in terms of triple-negative or HER2-positive disease, 10 years ago roughly 20% of patients with subcentimeter tumors were being offered chemotherapy and now it is closer to 65% or 70%. I believe this changed in response to both data and guideline updates. The data on trastuzumab came out in 2005 (Romond 2005), and with that many physicians started offering trastuzumab and chemotherapy to patients with small HER2-positive tumors.

In addition, in reviewing the risk associated with these smaller HER2-positive and triple-negative tumors it became evident that, although they were small tumors, they were biologically aggressive and probably carried more risk than we had anticipated. We started to consider trastuzumab and chemotherapy for 6- to 10-mm HER2-positive tumors or chemotherapy alone for triple-negative disease.

Did that change help patients fare better? The answer seems to be yes (Duarte Luis 2013; [1.1]). In terms of outcomes among women who did not receive chemotherapy for small tumors compared to patients who did, a clear benefit was evident among those who received chemotherapy even if the tumor was 6 to 10 millimeters in size. The recurrence risk for women who did not receive chemotherapy was approximately 15%, and among the patients who did receive chemotherapy it was closer to 10% or less. This suggests that the data and the guidelines were correct — we should be treating these smaller tumors with bad biology more aggressively to see better results.

1.1

Time Trends in the Use of Adjuvant Chemotherapy (CTX) and Outcomes in T1a,b NOMO Breast Cancer in the National Comprehensive Cancer Network

	No CTX or trastuzumab		CTX and/or trastuzumab	
Hormone receptor-positive, HER2-negative	**T1a**	**T1b**	**T1a**	**T1b**
5-year median distant relapse-free survival	97%	96%	100%	95%
5-year median overall survival	98%	97%	100%	98%
Hormone receptor-negative, HER2-negative				
5-year median distant relapse-free survival	90%	90%	95%	93%
5-year median overall survival	94%	91%	100%	96%
Hormone receptor-positive, HER2-positive				
5-year median distant relapse-free survival	93%	91%	100%	95%
5-year median overall survival	95%	95%	100%	99%
Hormone receptor-negative, HER2-positive				
5-year median distant relapse-free survival	89%	81%	89%	94%
5-year median overall survival	93%	100%	100%	95%

Duarte Luis IMV et al. *Proc ASCO* 2013;**Abstract 1006**.

Track 8

DR LOVE: Would you discuss your 62-year-old patient who received tamoxifen, trastuzumab and paclitaxel as first-line treatment for ER-positive, HER2-positive metastatic disease and then experienced progression on tamoxifen/trastuzumab?

DR BURSTEIN: You could consider switching from tamoxifen to fulvestrant. You could argue that her disease never progressed on first-line therapy and you could resume paclitaxel or consider a taxane with trastuzumab and pertuzumab, which is a relatively new option. You could argue that she's already had paclitaxel and trastuzumab and therefore she meets the criteria for getting the newly approved second-line agent T-DM1, or you could consider lapatinib/capecitabine, which is an all-oral regimen, or if the patient fits the population from the BOLERO-3 study, vinorelbine/trastuzumab with or without everolimus would also be a consideration. Thanks to shifts in the past

3 or 4 years, we now have a number of choices that allow patients to experience long runs of treatment with a biologic agent and no chemotherapy (1.2).

I like T-DM1 because the side-effect profile is favorable, and that's what I chose for this lady — it doesn't cause alopecia or other traditional chemotherapy-like side effects such as nausea, vomiting or low blood counts. The other interesting option would be pertuzumab/trastuzumab, without reintroduction of the chemotherapy, in the case of a patient with essentially asymptomatic radiologic progression. We typically limit our pertuzumab use to the FDA label at this juncture, however, which is first line with chemotherapy.

1.2

T-DM1 and the Promise of Antibody-Drug Conjugates

"The pharmacologic properties of trastuzumab emtansine that appear to have been confirmed by this trial [EMILIA] are impressive. Objective evidence of tumor shrinkage indicates, as previously reported in animal models, that HER2 receptor number and function remain intact in most patients in whom clinical resistance to trastuzumab has developed, allowing specific binding of the trastuzumab emtansine conjugate (T-DM1). The remarkable rate of breast-cancer regressions observed at sites of visceral metastases suggests, as originally hypothesized, that the cytotoxic maytansinoid portion of the conjugate is delivered intracellularly at sufficient concentrations to produce cell death (and consequent tumor shrinkage) consistent with mitotic catastrophe, rather than inducing the cytostasis commonly associated with single-agent trastuzumab. The beauty of T-DM1 is that conjugate formation does not preclude the antibody-dependent cellular cytotoxicity or HER2-neutralizing activity of the antibody; thus, T-DM1 retains the functions of trastuzumab and adds the effects of a potent cytotoxic drug."

Teicher BA, Doroshow JH. *N Engl J Med* 2012;367(19):1847-8.

Track 11

DR LOVE: How would you approach a patient with residual disease after neoadjuvant therapy for triple-negative, BRCA1 mutation-positive breast cancer?

DR BURSTEIN: Patients in this setting clearly need more chemotherapy. This is an area that continues to slowly accumulate data. A growing sentiment suggests that platinum-based chemotherapy agents might be particularly valuable in BRCA mutation carriers. The cleanest data come from a neoadjuvant study in Europe that accumulated large numbers of BRCA mutation carriers and reported high rates of complete pathologic response, in the range of 70% to 75%, with cisplatin-based chemotherapy (Byrski 2010).

Thus we are increasingly tempted to try platinum-based therapy for patients with BRCA-1 mutation-positive disease. Whether that's any better than a different alkylator or better than eribulin, ixabepilone or other chemotherapy or whether it improves the natural history remains unclear. But it has led to a resurgence and interest in our group in using platinum for patients with triple-negative breast cancer. I know that this also has been an area of substantial interest around the country. ■

SELECT PUBLICATIONS

Byrski T et al. **Pathologic complete response rates in young women with BRCA1-positive breast cancers after neoadjuvant chemotherapy.** *J Clin Oncol* 2010;28(3):375-9.

Romond EH et al. **Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer.** *N Engl J Med* 2005;353(16):1673-84.