INTERVIEW

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Tracks 1-9

Track 1 Clinical needs for a new generation of genomic assays in BC

Track 2 Perspective on the utility of the Onco*type* DX assay in node-negative and node-positive early BC

Track 3 Clinical utility of the MammaPrint® assay in BC

Track 4 Potential role of mTOR inhibitors in reversing resistance to endocrine therapy

Track 5 **Case 4 discussion:** A 69-year-old woman presents with a 4-mm, moderately differentiated, ER/PR-positive, HER2-positive, node-negative breast tumor and Ki-67 of 15%

Track 6 T-DM1: Proof of concept for antibody-drug conjugates with reduced toxicity in HER2-positive BC

Track 7 Adjuvant trastuzumab monotherapy for patients with HER2-positive BC who are not candidates for chemotherapy

Track 8 Lessons learned and remaining questions from the NEOSPHERE and Neo-ALTTO studies of dual HER2 blockade

Track 9 Future treatment strategies for early and advanced HER2-positive BC

Select Excerpts from the Interview

Track 2

DR LOVE: What is your perspective on the utility of the Onco*type* DX assay in node-negative and node-positive breast cancer?

DR ANDRE: We have enough evidence to consider that Recurrence Score (RS) can identify a group of patients with ER-positive, node-negative disease who do not derive a large benefit from adjuvant chemotherapy. The RS has such a strong prognostic value in node-negative disease that you don't need to add chemotherapy for patients with a low RS — the rate of metastasis is below 10% at 10 years.

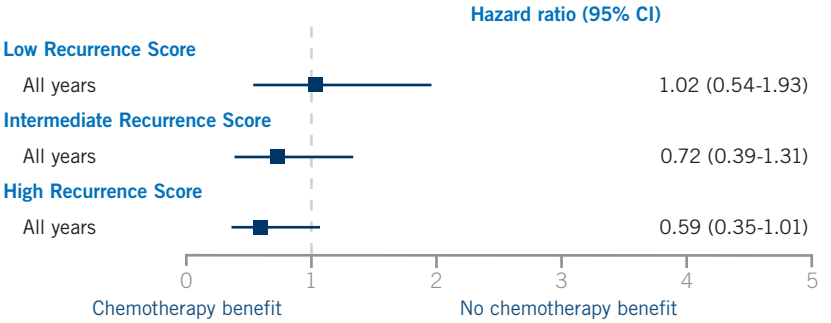
The picture is less clear in node-positive disease. A study by Kathy Albain reported that patients with a low RS do not derive a large benefit from anthracycline-based chemotherapy (Albain 2010; [4.1]). Still, node-positive

disease has its pitfalls, the first being that no one has yet shown the predictive value of RS for a taxane.

Second, the amount of evidence is minimal for RS in the node-positive setting. That said, I'm aware that the RxPONDER trial is now open to address the value of the RS in node-positive disease (4.2). This is important in distinguishing between the prediction of the value of adjuvant chemotherapy and the prognostic value of the RS.

4.1

Disease-Free Survival Hazard Ratios for Tamoxifen Alone versus CAF-T According to Recurrence Risk Group



Albain KS et al. *Lancet Oncol* 2010;11(1):55–65.

4.2

Phase III Randomized Clinical Trial of Adjuvant Endocrine Therapy with or without Chemotherapy in Node-Positive Breast Cancer

Protocol IDs: SWOG-S1007; RxPONDER

Target Accrual: 4,000

Eligibility
- Node-positive (1 to 3 nodes) breast cancer
- ER/PR-positive, HER2-negative
- Recurrence Score by Oncotype DX ≤25

R

- Endocrine therapy x 5 to 10 years
- Adjuvant chemotherapy based on patient and/or physician preference followed by endocrine therapy x 5 to 10 years

www.clinicaltrials.gov. Identifier NCT01272037, November 2011.

Tracks 8-9

DR LOVE: What are your thoughts on the NEOSPHERE study evaluating pertuzumab with trastuzumab and Neo-ALTTO trial data (trastuzumab and lapatinib) on dual anti-HER2 blockade?

DR ANDRE: The data show that with dual blockade in the neoadjuvant setting, an increase occurs in the pathologic complete response (pCR) rate (Baselga 2010; Gianni 2010; [4.3]). This means that targeting different parts of the same HER2 receptor could increase the efficacy of trastuzumab.

Many unknowns exist, such as the extent to which the improvement in pCR rates translates into improvement in progression-free survival, overall survival, et cetera. This should be answered by several ongoing adjuvant trials, including the ALTTO trial, which is evaluating trastuzumab versus trastuzumab/lapatinib versus lapatinib.

DR LOVE: Where do you see pertuzumab fitting into your treatment strategy for patients with early and advanced HER2-positive breast cancer?

DR ANDRE: Pertuzumab should be further developed in the setting of relapse after treatment with trastuzumab because, in the neoadjuvant setting, we have evidence that adding pertuzumab to trastuzumab improves pCR (4.3). ■

4.3

NEOSPHERE Study: Pathologic Complete Response (pCR) in the Breast and Lymph Node Status of Patients Receiving Neoadjuvant Trastuzumab and/or Pertuzumab

	TH (n = 107)	THP (n = 107)	HP (n = 107)	TP (n = 96)
pCR in breast	29.0%	45.8%	16.8%	24.0%
pCR in breast and node-negative at surgery	21.5%	39.3%	11.2%	17.7%
pCR in breast and node-positive at surgery	7.5%	6.5%	5.6%	6.3%

T = docetaxel; H = trastuzumab; P = pertuzumab

Gianni L et al. San Antonio Breast Cancer Symposium 2010;**Abstract S3-2**.

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.

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**.

Gianni L et al. **Neoadjuvant pertuzumab (P) and trastuzumab (H): Antitumor and safety analysis of a randomized Phase II study ('NeoSphere').** San Antonio Breast Cancer Symposium 2010;**Abstract S3-2**.

Gonzalez-Angulo AM et al. **SWOG S1007: A phase III, randomized clinical trial of standard adjuvant endocrine therapy with or without chemotherapy in patients with one to three positive nodes, hormone receptor (HR)-positive, and HER2-negative breast cancer with recurrence score (RS) of 25 or less.** *Proc ASCO* 2011;**Abstract TPS104**.