INTERVIEW

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Tracks 1-10

Track 1 GEPARQUINTO GBG 44 study: Lapatinib versus trastuzumab with neoadjuvant anthracycline/taxane-based chemotherapy in HER2-positive early BC

Track 2 Pathologic complete response rates with chemotherapy/trastuzumab versus chemotherapy/lapatinib in the neoadjuvant setting

Track 3 Perspective on the efficacy and tolerability of trastuzumab versus lapatinib in HER2-positive early BC

Track 4 Potential clinical implications of the NeoALTTO trial for adjuvant therapy in HER2-positive BC

Track 5 NeoSphere: A randomized Phase II study of neoadjuvant pertuzumab and trastuzumab

Track 6 GEPARQUINTO GBG 44 study: Neoadjuvant chemotherapy with or without bevacizumab for HER2-negative early BC

Track 7 Translational investigations to identify predictive biomarkers for biological agents in BC

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DR LOVE: Your German Breast Group (GBG) GEPARQUINTO GBG 44 study has an ambitious design that stratifies patients to neoadjuvant chemotherapy with or without differing biologic agents based on HER2 status. Would you discuss the results you reported at SABCS 2010 for patients with HER2-positive disease?

PROF UNTCH: The HER2-positive component of the GEPARQUINTO study evaluated 620 patients with HER2-positive early breast cancer. Patients were randomly assigned to 24 weeks of either trastuzumab or lapatinib with neoadjuvant chemotherapy with epirubicin/cyclophosphamide followed by four cycles of docetaxel.

This was the first clinical trial to compare chemotherapy/trastuzumab to chemotherapy/lapatinib. According to NSABP criteria, the pathologic complete response (pCR) rate was 50 percent with chemotherapy/trastuzumab and 35 percent with chemotherapy/lapatinib, which was unexpectedly lower than what was hypothesized at the beginning of this study (Untch 2010; [3.1]).

In the intent-to-treat analysis, 23 percent of patients on the chemotherapy/lapatinib arm had treatment discontinued, mainly because of Grade III or higher diarrhea, compared to a 13 percent rate of discontinuation in patients who received chemotherapy/trastuzumab.

This was the first time that lapatinib has been administered with anthracyclines and docetaxel, and we had to learn how to cope with the side effects of this combination. We learned that it was necessary to reduce the dose of lapatinib from 1,250 mg per day to 1,000 mg per day to avoid diarrhea, and we also learned to add G-CSF to avoid febrile neutropenia from lapatinib and docetaxel. These are important lessons learned from this trial, and we now discuss with patients which side effects to expect and how to deal with them.

The total cardiac failure rate on study with epirubicin/cyclophosphamide/trastuzumab was less than 0.5 percent. This experience is in line with previous experiences in Europe.

DR LOVE: What about the results reported by your colleague Dr von Minckwitz for patients with HER2-negative disease?

PROF UNTCH: We expected to see a signal with the addition of bevacizumab to neoadjuvant chemotherapy in the HER2-negative population, but the addition of bevacizumab to chemotherapy did not significantly increase the pCR rate overall (von Minckwitz 2010). The only subgroup of patients who seemed to benefit from the combination of chemotherapy and bevacizumab were the patients with triple-negative disease. We eagerly await further data

3.1

GEPARQUINTO GBG 44 Trial: Efficacy of Trastuzumab versus Lapatinib in Combination with Neoadjuvant Anthracycline/Taxane-Based Chemotherapy in HER2-Positive Early Breast Cancer

	T + EC-doc	L + EC-doc	*p*-value
pCR[1]	50.4%	35.2%	<0.05
pCR[2]	45.0%	29.9%	<0.05
pCR[3]	31.3%	21.7%	<0.05
Breast conservation rate	65.6%	56.0%	—

[1] No invasive residual cancer in breast only; [2] No invasive residual cancer in breast and nodes; [3] No invasive or noninvasive residual cancer in breast and nodes based on central pathology report review

T = trastuzumab; E = epirubicin; C = cyclophosphamide; doc = docetaxel; L = lapatinib; pCR = pathologic complete response

Untch M et al. San Antonio Breast Cancer Symposium 2010;**Abstract S3-1**.

on the use of chemotherapy/bevacizumab from the ongoing NSABP-B-40 and BEATRICE trials in early breast cancer.

Track 4

DR LOVE: What is your take on the neoadjuvant Phase III NeoALTTO trial, which evaluated lapatinib, trastuzumab and the combination with paclitaxel in patients with HER2-positive primary breast cancer?

PROF UNTCH: The concept of dual receptor targeting with lapatinib and trastuzumab is to attack the tumor cell from the outside with trastuzumab and from the inside with lapatinib. This principle was shown in the NeoALTTO trial, in which the authors reported an extremely nice synergistic effect (Baselga 2010; [3.2]). All of us wonder if this will also be the case with the more than 8,000-patient ALTTO study in the adjuvant setting. I would await additional results with dual receptor combination inhibitors before using that approach outside of a protocol in the adjuvant or neoadjuvant setting. ■

3.2

NeoALTTO: Pathologic Complete Response (pCR) Rates in a Phase III Neoadjuvant Trial of Lapatinib (L), Trastuzumab (T) and the Combination with Paclitaxel (P) in HER2-Positive Primary Breast Cancer

Response	**P + L** (n = 154)	**P + T** (n = 149)	**P + L + T** (n = 152)
pCR[1]	24.7%	29.5%	51.3%
	p-value: 0.34 (L vs T); 0.0001 (L + T vs T)		
	P + L (n = 150)	**P + T** (n = 145)	**P + L + T** (n = 145)
Total pCR[2]	20.0%	27.6%	46.9%
	p-value: 0.13 (L vs T); 0.001 (L + T vs T)		

[1] No invasive cancer in the breast; [2] No invasive cancer in the breast and lymph nodes (excludes 15 patients with nonevaluable nodal status)

Baselga J et al. San Antonio Breast Cancer Symposium 2010;**Abstract S3-3**.

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**.

Chang HR. **Trastuzumab-based neoadjuvant therapy in patients with HER2-positive breast cancer.** *Cancer* 2010;116(12):2856-67.

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**.

Von Minckwitz G et al. **Neoadjuvant chemotherapy with or without bevacizumab: Primary efficacy endpoint analysis of the GEPARQUINTO study (GBG 44).** San Antonio Breast Cancer Symposium 2010;**Abstract S4-6**.