



Key SABCS Presentations
Issue 1, 2011

First Results of the NeoALTTO (BIG 01-06/EGF 106903) Neoadjuvant Study of Lapatinib, Trastuzumab or the Combination and Paclitaxel for Women with HER2-Positive Primary Breast Cancer

CME INFORMATION

OVERVIEW OF ACTIVITY

The annual San Antonio Breast Cancer Symposium (SABCS) is unmatched in its significance with regard to the advancement of breast cancer treatment. It is targeted by many members of the clinical research community as the optimal forum in which to unveil new clinical data. This creates an environment each year in which published results from a plethora of ongoing clinical trials lead to the emergence of many new therapeutic agents and changes in the indications for existing treatments across all breast cancer subtypes. In order to offer optimal patient care — including the option of clinical trial participation — the practicing medical oncologist must be well informed of the rapidly evolving data sets in breast cancer. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets from the latest SABCS meeting, including expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for breast cancer.

LEARNING OBJECTIVE

- Compare and contrast response rate and tolerability of trastuzumab- and lapatinib-based neoadjuvant therapy versus the combination approach in the treatment of HER2-positive primary breast cancer.

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This program is supported by educational grants from AstraZeneca Pharmaceuticals LP, Genentech BioOncology, Genomic Health Inc, Novartis Pharmaceuticals Corporation and Sanofi-Aventis.

Last review date: January 2011
Expiration date: January 2012

To go directly to slides and commentary, [click here](#).

Sometimes the cavernous San Antonio conference hall can be so devoid of attendees that you feel like you could throw a Frisbee® and not hit anyone. But on Friday, December 10, 2010 at 9 AM, even the spillover video simulcast section was standing room only. The occasion was the presentation of three highly anticipated neoadjuvant trials for patients with HER2-positive tumors. To begin this memorable session, Duke's Neil Spector gave a superb review of anti-HER2 treatment, which he ended with a photo of himself wired up in a hospital gown taken shortly after a heart transplant. (He implored the audience to sign their organ donor cards.) Eric Winer finished things off with an enlightening and thought-provoking follow-up discussion that he told me had him up until 3 AM the night before changing slides. In between, there was plenty to warrant the massive crowd.

To start off this series of eight weekly reports from San Antonio, here's the bottom line on these historic neoadjuvant HER2 data sets.

1. **[German GeparQuinto study: More path CRs with trastuzumab/chemo than lapatinib/chemo](#)**

In the first reported head-to-head comparison of these two commonly used anti-HER2 agents, Michael Untch demonstrated that the antibody won out over the TKI with a pCR rate (in breast and nodes) of 31.3 percent versus 21.7 percent. A second study reported at SABCS (see below) also showed an advantage to trastuzumab over lapatinib but was not considered statistically significant. Although it may not matter in the long run, much debate has focused on whether this interesting finding is related to an inherent difference in the antitumor efficacy of these agents or the fact that some patients randomly assigned to lapatinib ended up receiving less drug as a result of discontinuation of therapy due to toxicity.

2. **[Neo-ALTTO trial: More pCRs with chemo/trastuzumab/lapatinib than with chemo plus either anti-HER2 agent alone](#)**

In a parallel trial design to the ongoing 8,000-plus-patient international adjuvant trial, this much-awaited neoadjuvant study evaluated chemo with trastuzumab, lapatinib or the combination, and as reported by José Baselga, the dual anti-HER2 arm doubled the pCR rate to 46.9 percent. Although few, if any, investigators are suggesting this approach outside a protocol setting, perhaps this is a first glimpse at where we'll end up in the next few years.

3. [NEOSPHERE study: Chemo/trastuzumab versus chemo/pertuzumab versus chemo/trastuzumab/pertuzumab versus trastuzumab/pertuzumab](#)

Luca Gianni (protégé of the legendary Gianni Bonadonna) surprised the multitudes with this study that demonstrated the best pCR rate (39.3 percent) when both antibodies were combined with chemo. However, he also reported an 11.2 percent pCR rate when pertuzumab and trastuzumab were used together without chemo. Pertuzumab — a yet-unavailable agent that inhibits HER2 dimerization — is about to be studied in the adjuvant setting, adding even more hope and potential for the future.

Of course, it will be some time before we know how these neoadjuvant strategies pan out in the long term, but in another important and encouraging paper by the Germans ([the TECHNO trial](#)), pCR after neoadjuvant trastuzumab/chemo was highly correlated with longer-term disease-free and overall survival. If that finding holds true, then SABCS 2010 will forever be remembered as a harbinger of what is to come in the management of HER2-positive disease.

Next up in this series: The big disappointment of San Antonio — the AZURE trial demonstrates no adjuvant benefit with zoledronic acid.

Neil Love, MD

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Miami, Florida

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First Results of the NeoALTTO (BIG 01-06/EGF 106903) Neoadjuvant Study of Lapatinib, Trastuzumab or the Combination and Paclitaxel for Women with HER2-Positive Primary Breast Cancer

Presentation discussed in this issue

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 HER 2-positive primary breast cancer.** San Antonio Breast Cancer Symposium 2010; **Abstract S3-3**.

Slides from a presentation at SABCS 2010 and transcribed comments from a recent interview with Eric P Winer, MD (12/11/10)

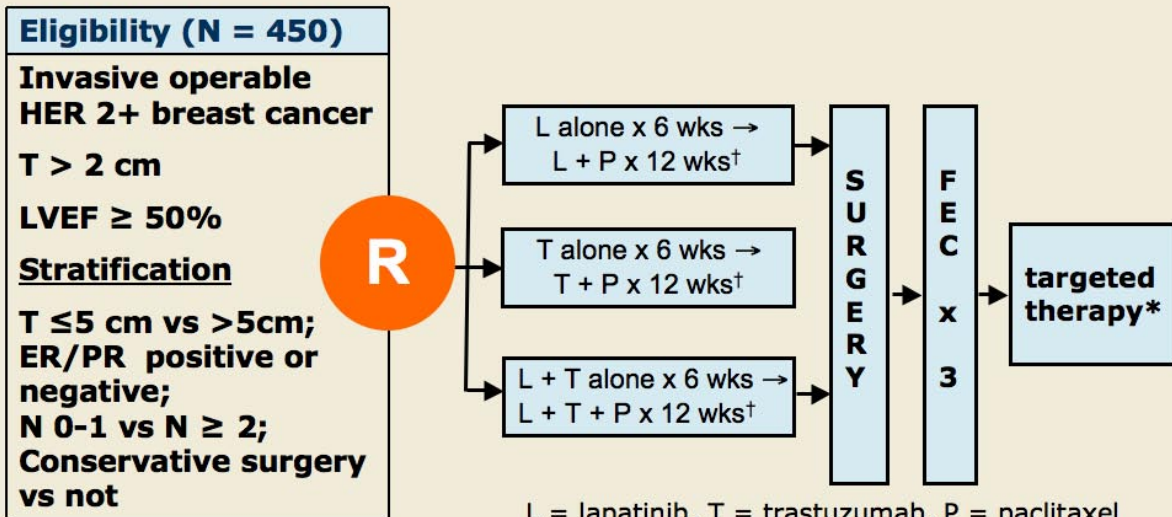
First Results of the NeoALTTO Trial (BIG 01-06/EGF 106903): A Phase III, Randomized, Open-Label, Neoadjuvant Study of Lapatinib, Trastuzumab, and Their Combination Plus Paclitaxel in Women with HER2-Positive Primary Breast Cancer

Baselga J et al.

Proc SABCS 2010;Abstract S3-3.

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Neo ALTTO (BIG 01-06/EGF 106903) Study Design



† Neoadjuvant therapy consisted of 6 wks of anti-HER2 therapy alone (biologic window) followed by 12 wks of the same anti-HER2 therapy with weekly paclitaxel; total neoadjuvant therapy duration of 18 wks

* Same anti-HER2 therapy as in the neoadjuvant phase for an additional 34 wks

Baselga J et al. *Proc SABCS 2010*;Abstract S3-3.

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Study Endpoints

- Primary endpoint:
 - Pathologic complete response in the breast (pCR)
- Secondary endpoints:
 - pCR rate in breast AND lymph nodes [total pCR (tpCR)]
 - Safety and tolerability
 - Objective response rate at week 6 (end of biological window)
 - % of patients with node-negative disease at surgery
 - Rate of conversion to breast conserving surgery
 - Rate of conversion to breast surgery in those with non-operable disease at presentation
 - Disease free survival (DFS) and overall survival (OS)

Baselga J et al. *Proc SABCS 2010*;Abstract S3-3.

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Efficacy: pCR and tpCR

Response	L (N = 154)	T (N = 149)	L + T (N = 152)
pCR (no invasive cancer in the breast)	24.7%	29.5%	51.3%
	p-value: 0.34 (L vs T); 0.0001 (L +T vs T)		
Response	L (N = 150)	T (N = 145)	L + T (N = 145)
tpCR (no invasive cancer in the breast or LNs)*	20.0%	27.6%	46.9%
	p - value: 0.13 (L vs T); 0.001 (L+T vs T)		

* Excludes 15 patients with non-evaluable nodal status

Baselga J et al. *Proc SABCS 2010*;Abstract S3-3.

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Efficacy: Overall Clinical Response at 6 Weeks and at Surgery

Response	L (N = 154)	T (N = 149)	L + T (N = 152)
Week 6	52.6%	30.2%	67.1%
	p-value: <0.001 (L vs T); <0.001 (L +T vs T)		
Surgery	74.0%	70.5%	80.3%
	p-value: 0.49 (L vs T); 0.049 (L+T vs T)		

Baselga J et al. *Proc SABCS 2010*;Abstract S3-3.

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Efficacy: % with Conservative Surgery and % Node Negative

Response	L (N = 154)	T (N = 149)	L + T (N = 152)
Conservative Surgery	42.9%	38.9%	41.4%
	<i>p</i> -value: >0.5 (L vs T); >0.5 (L +T vs T)		
Response	L (N = 150)	T (N = 143)	L + T (N = 147)
Node-Negative*	48%	56.6%	69.0%
	<i>p</i> -value: 0.14 (L vs T); 0.03(L+T vs T)		

* Excludes 15 patients with non-evaluable nodal status

Baselga J et al. *Proc SABCS 2010*;Abstract S3-3.

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Conclusions

- pCR rate with L + T was significantly higher than with T (51.3% vs 29.5%).
- The overall response rate at 6 weeks was higher for both arms containing lapatinib vs the trastuzumab arm.
- Increased but manageable toxicity (diarrhea and liver enzyme alterations) was observed in the arms containing lapatinib (data not shown).
- Dual blockage of HER2 is a valid concept.
- Correlation between pCR and DFS and OS is pending events and follow-up.
- Accrual is continuing to the ALTTO trial, which includes T → L, L, T, and L + T in the adjuvant setting (NCT00490139).

Baselga J et al. *Proc SABCS 2010*;Abstract S3-3;www.clinicaltrials.gov.

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Investigator Commentary: NEO-ALTTO Neoadjuvant Study in HER2-Positive Breast Cancer

This study was meant to complement the ALTTO adjuvant study, for which we will likely have results in a few years. In NEO-ALTTO the pCR rates in the breast for trastuzumab versus lapatinib were not statistically different, although a trend appeared to favor trastuzumab. However, lapatinib could not be administered as planned in approximately one third of patients, which necessitated dose reductions.

The remarkable observation from this study was the substantial improvement in pCR with the combination of trastuzumab/lapatinib compared to either lapatinib or trastuzumab. These findings are consistent with both preclinical data and data from the study published by Dr Blackwell in the *Journal of Clinical Oncology* earlier in 2010, which demonstrated that in a HER2-positive, refractory setting, the combination of trastuzumab and lapatinib compared to lapatinib alone resulted in an improvement in progression-free and overall survival. I hope the results of NEO-ALTTO will correlate with an improvement outcome for the combination regimen in the ALTTO trial.

Comments from Eric P Winer, MD, December 11, 2010

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