# 5 Minute JournalClub

***Key SABCS Presentations***

Issue 1, 2011

# Neoadjuvant Trastuzumab and Chemotherapy in the Management of Previously Untreated HER2-Positive Primary Breast Cancer

For more visit ResearchToPractice.com/5MJCSABCS2011

Research To Practice®

## 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

- Counsel patients receiving neoadjuvant trastuzumab-based therapy about the impact of pathologic complete response on longer-term clinical outcome.

## ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

## CREDIT DESIGNATION STATEMENT

Research To Practice designates this educational activity for a maximum of 0.25 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

## HOW TO USE THIS CME ACTIVITY

This CME activity contains slides and edited commentary. To receive credit, the participant should review the slide presentation, read the commentary and complete the Educational Assessment and Credit Form located at CME.ResearchToPractice.com.

## CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Harold J Burstein, MD, PhD
Associate Professor of Medicine
Harvard Medical School
Breast Oncology Center
Dana-Farber Cancer Institute
Boston, Massachusetts

No real or apparent conflicts of interest to disclose.

EDITOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: Abraxis BioScience Inc, a wholly owned subsidiary of Celgene Corporation, Allos Therapeutics, Amgen Inc, AstraZeneca Pharmaceuticals LP, Aureon Laboratories Inc, Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Cephalon Inc, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health Inc, Lilly USA LLC, Millennium Pharmaceuticals Inc, Myriad Genetics Inc, Novartis Pharmaceuticals Corporation, OSI Oncology, Sanofi-Aventis and Seattle Genetics.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

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

5 MinuteJournalClub

Key SABCS Presentations
Issue 1, 2011

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.

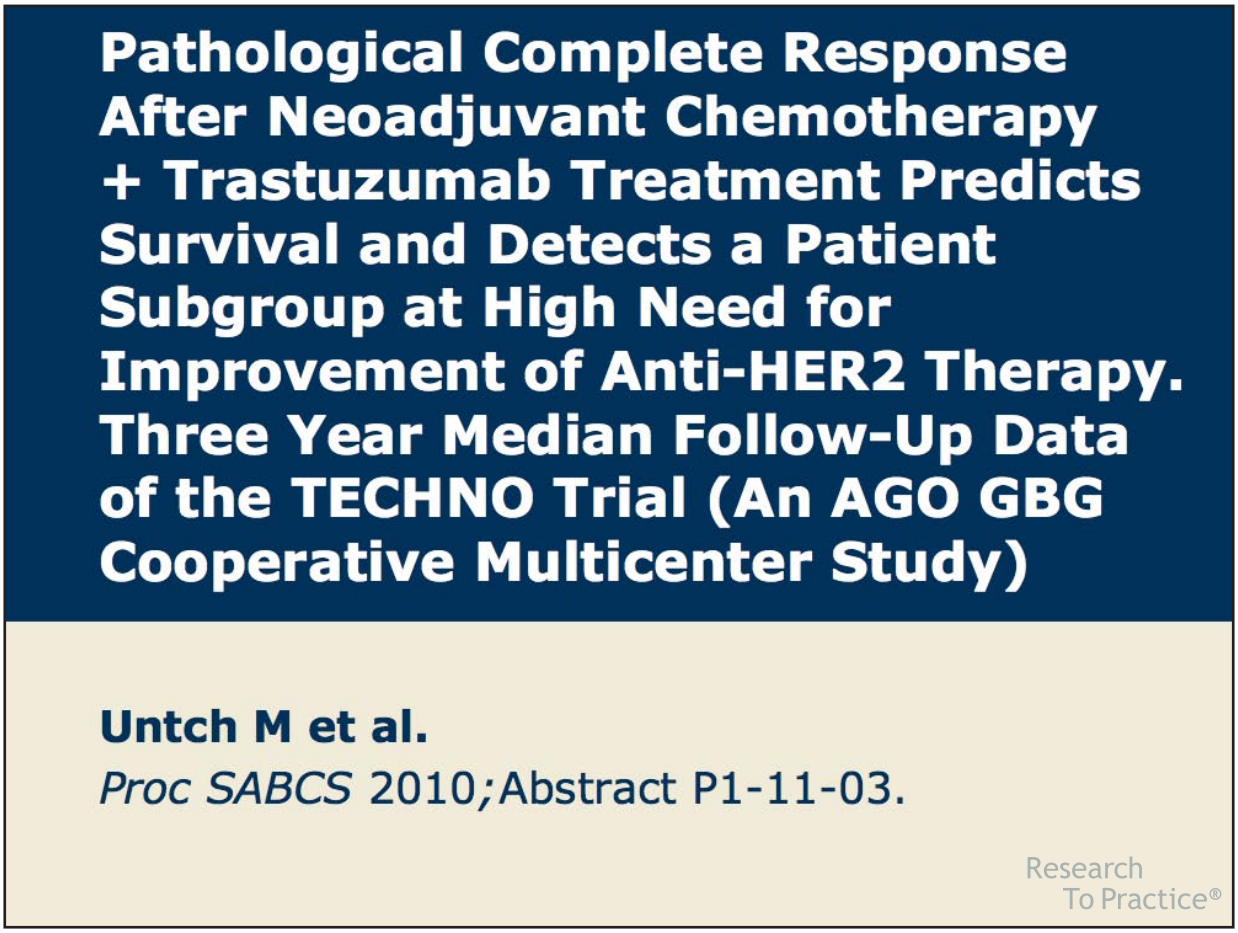
Neil Love, MD
**Research To Practice**
Miami, Florida

# Neoadjuvant Trastuzumab and Chemotherapy in the Management of Previously Untreated HER2-Positive Primary Breast Cancer

## Presentation discussed in this issue

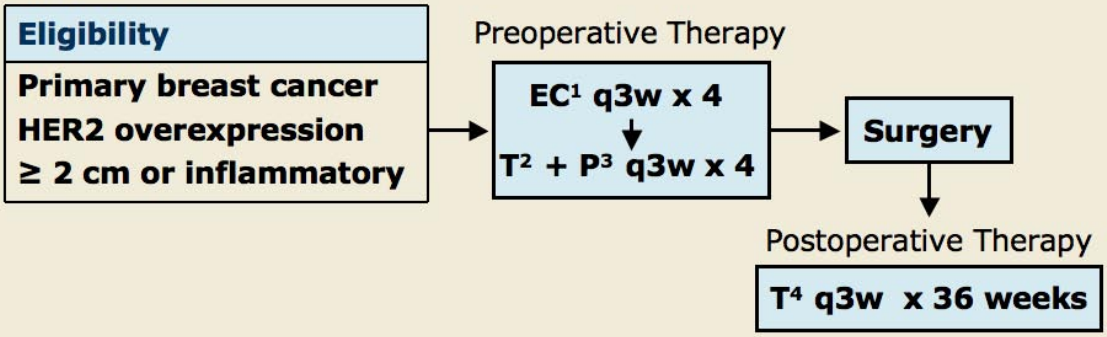
Untch M et al. **Pathological complete response after neoadjuvant chemotherapy + trastuzumab treatment predicts survival and detects a patient subgroup at high need for improvement of anti-HER2 therapy. Three year median follow-up data of the TECHNO trial.** San Antonio Breast Cancer Symposium 2010;**Abstract P1-11-03**.

## Slides from a presentation at SABCS 2010 and transcribed comments from a recent interview with Harold J Burstein, MD, PhD (12/22/10)



# Study Schema

Enrolled = 217




[1] Epirubicin 90 mg/m$^2$ + Cyclophosphamide 600 mg/m$^2$ (C 1-4)
[2] Trastuzumab 8 mg/kg loading dose (C 5) followed by 6 mg/kg q3wks (C 6-8)
[3] Paclitaxel 175 mg/m$^2$ (C 5-8)
[4] Trastuzumab 8 mg/kg loading dose (C 9) followed by 6 mg/kg q3wks (C 10-21)

Untch M et al. *Proc SABCS* 2010;Abstract P1-11-03.



# Efficacy Results

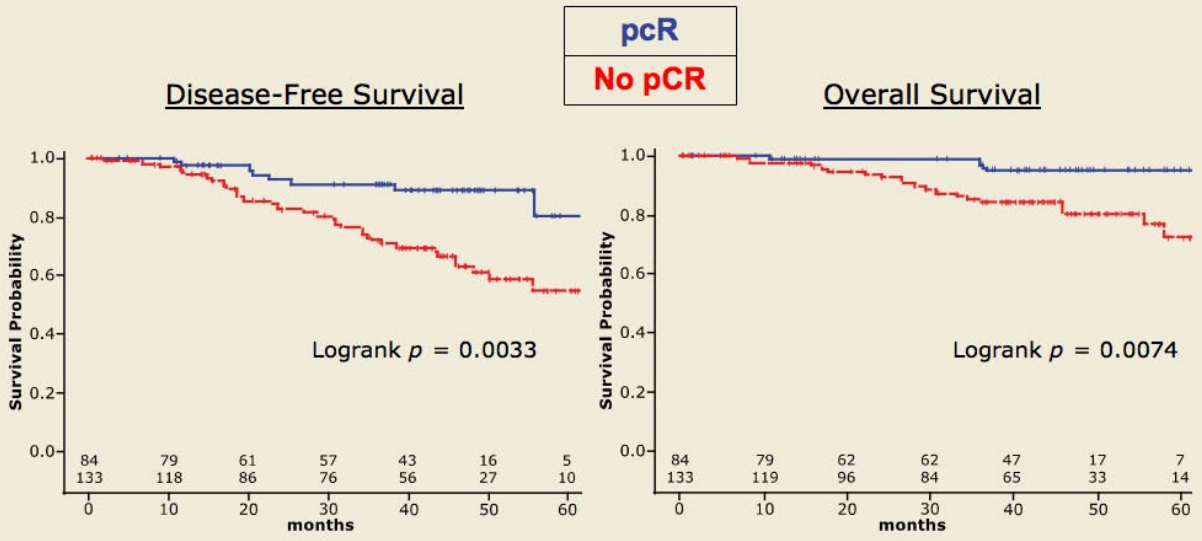
Enrolled = 217

| | |
|---|---|
| pCR (no invasive tumor in breast and axillary nodes) | 39% |
| Breast conservation rate | 64% |

| | Patients with pCR | Patients without pCR | *p*-value |
|---|---|---|---|
| 3-year overall survival | 96% | 86% | 0.025 |
| 3-year disease-free survival | 88% | 73% | 0.01 |

Untch M et al. *Proc SABCS* 2010;Abstract P1-11-03.

# pCR is Prognostic for Disease-Free and Overall Survival




With permission from Untch M et al. *Proc SABCS 2010*; Abstract P1-11-03.



# Multivariate Analysis of Efficacy Results by Baseline Factors and pCR

| | Disease-Free Survival (DFS) | | Overall Survival (OS) | |
|---|---|---|---|---|
| | Hazard Ratio | *p*-value | Hazard Ratio | *p*-value |
| Age (< 40 vs ≥ 40) | 1.03 | 0.925 | 6.94 | 0.059 |
| Initial T stage (T 1-3 vs T4) | 1.90 | 0.084 | 1.83 | 0.205 |
| ER/PR status (negative vs positive) | 1.14 | 0.672 | 2.67 | 0.034 |
| pCR (yes vs no) | 2.49 | 0.013 | 4.91 | 0.012 |

In multivariate analysis, pCR remained a significant prognostic factor for DFS and OS.

Untch M et al. *Proc SABCS* 2010;Abstract P1-11-03.

# Cardiac Safety Results

| | |
|---|---|
| Cardiac events | 8/217 (3.7%) |
| Decrease in left ventricular ejection fraction | 6/217 (2.8%) |
| Clinical congestive heart failure (CHF) | 2/217 (0.9%) |

Untch M et al. *Proc SABCS* 2010;Abstract P1-11-03.

Research To Practice®

# Conclusions

- Neoadjuvant combination of trastuzumab and chemotherapy results in a high pathologic CR rate in the breast and lymph nodes of 39% and breast conservation rate of 64%.
- Symptomatic CHF rate <1%.
- Patients without a pCR have an increased risk for relapse and death and are therefore candidates for further improvement of anti-HER2 directed adjuvant therapy.

Untch M et al. *Proc SABCS* 2010;Abstract P1-11-03.

Research To Practice®

## Investigator Commentary: Pathologic Complete Response with Trastuzumab-Based Neoadjuvant Therapy Predicts Survival in the TECHNO Study

TECHNO was another European neoadjuvant study for patients with HER2-positive breast cancer, of which several were presented at San Antonio 2010. Notably, this study has longer-term follow-up, which is important because in addition to evaluating short-term endpoints, such as pathologic complete response (pCR) in the breast, the investigators were also able to evaluate longer-term endpoints, such as disease-free and overall survival.

In this study, women who received trastuzumab-based neoadjuvant therapy and achieved a pCR fared better in the long term than those who did not achieve a pCR. That's not a big surprise in the sense that many other studies have demonstrated that women who experience a pCR to other types of therapy fare better in the long run, but it is a nice confirmation that the same trends will be observed in women who receive trastuzumab-based therapy.

***Interview with Harold J Burstein, MD, PhD, December 22, 2010***