



Key SABCS Presentations
Issue 7, 2011

The Efficacy of (Neo)Adjuvant Capecitabine-Containing Regimens in High-Risk Breast Cancer

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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 OBJECTIVES

- Recognize the rationale for employing a more intensive capecitabine-containing adjuvant regimen for patients with early TNBC.
- Compare and contrast the rate of pathologic complete response among patients with and without TNBC treated with neoadjuvant capecitabine, epirubicin and docetaxel.

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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: March 2011
Expiration date: March 2012

[**Click here for SABCS papers on HER2-negative breast cancer**](#)

In 2001 the first results from the ATAC trial demonstrated the superiority of an AI (anastrozole) over tamoxifen. One year later a CALGB study showed an advantage for dose-dense AC → paclitaxel, and not long after that US Oncology proved that TC was better than AC and along the way the NSABP presented data on the *Oncotype DX*[®] assay to help select patients for adjuvant chemo. However, since the presentation of those important yet modest research advances, one could make the argument that not a whole lot else positive has happened in adjuvant treatment for the 80 percent of patients with HER2-negative breast cancer.

2010 didn't do much to change this situation — at least that's my conclusion after watching Alan Coates' San Antonio "Year in Review" presentation on the management of early breast cancer. Of the 18 papers he discussed during this talk, none seem likely to lead to a meaningful change in the mortality of this disease. Perhaps the most provocative of the bunch highlighted by Dr Coates were the three neoadjuvant HER2-positive papers reviewed in a previous issue of this series. However, the HER2-negative papers that were "featured" made me long for a myeloma-like infusion of new agents that actually work.

Unfortunately, it's not totally clear that this is on the horizon, especially if the data sets coming out in San Antonio are any indication. What we saw there were mainly a few legacy studies evaluating adjuvant chemotherapy, including:

1. Findings from another [**CALGB trial**](#) suggesting similar outcomes with four and six cycles of dose-dense paclitaxel or AC.
2. [**Two trials**](#) testing the addition of capecitabine to anthracycline/taxane regimens demonstrating questionable or no benefit, although [**two other**](#) related data sets suggested a slightly greater advantage with cape in triple-negative disease.
3. Early [**tolerability data**](#) on "maintenance" capecitabine after an anthracycline and/or a taxane — a strategy that makes sense, but no definitive efficacy data exist yet.
4. Another [**early safety report**](#) in a trial evaluating bevacizumab/chemotherapy in the adjuvant setting, but the recent negative results of two adjuvant trials of bev in colon cancer have perhaps dampened enthusiasm for this approach.

It's a real disconnect to walk through the halls of San Antonio and see thousands of investigators presenting a seemingly endless array of data sets and still contemplate the fact that the current overall impact of this effort at a patient care level — especially in the most prevalent HER2-negative breast cancer subset — is relatively modest. It makes one wonder if we will soon see the payoff of this extensive investment in research and whether there is any way to change the trajectory of progress.

Next up on our final San Antonio issue of *5-Minute Journal Club*: Clinical trials in metastatic disease, including studies of combinations of biologic agents

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The Efficacy of (Neo)Adjuvant Capecitabine-Containing Regimens in High-Risk Breast Cancer

Presentations discussed in this issue

Lindman H et al. **Integration of capecitabine into anthracycline- and taxane-based adjuvant therapy for triple-negative early breast cancer: Final subgroup analysis of the FinXX study.** San Antonio Breast Cancer Symposium 2010; [Abstract PD01-02](#).

Steger GG et al. **Review of capecitabine for the treatment of triple-negative early breast cancer.** San Antonio Breast Cancer Symposium 2010; [Abstract PD01-03](#).

Slides from presentations at SABCS 2010 and transcribed comments from a recent interview with William J Gradishar, MD (1/4/11)

Integration of Capecitabine into Anthracycline- and Taxane-Based Adjuvant Therapy for Triple Negative Early Breast Cancer: Final Subgroup Analysis of the FinXX Study¹

Review of Capecitabine for the Treatment of Triple-Negative Early Breast Cancer²

¹**Lindman H et al.**
Proc SABCS 2010; Abstract PD01-02.

²**Steger GG et al.**
Proc SABCS 2010; Abstract PD01-03.

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Integration of Capecitabine into Anthracycline- and Taxane-Based Adjuvant Therapy for Triple Negative Early Breast Cancer: Final Subgroup Analysis of the FinXX Study

Lindman H et al.

Proc SABCS 2010;Abstract PD01-02.

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FinXX Study Design

Accrual: 1,500 (Closed)

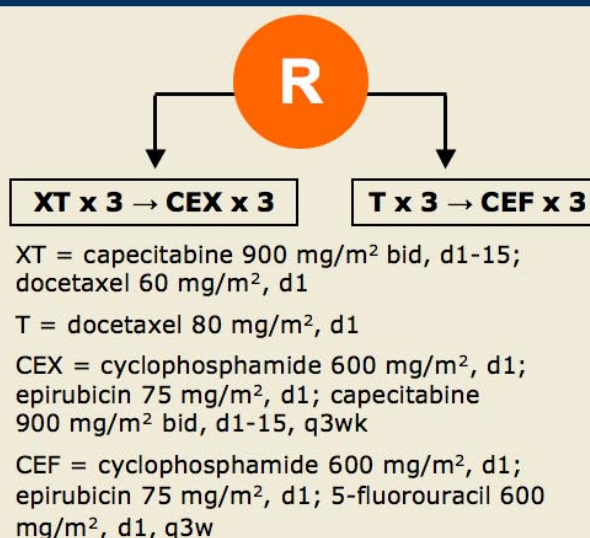
Eligibility

Age 18 to 65 years
Histologically confirmed invasive, node-positive breast cancer or node-negative if tumor >20 mm and PR-negative
WHO PS 0-1
No previous neoadjuvant chemotherapy

Primary objective: To perform a 5-year exploratory analysis of a subgroup of patients from the FinXX study with triple-negative early breast cancer (TNBC)

Lindman H et al. *Proc SABCS 2010;Abstract PD01-02.*

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5-Year Survival in TNBC (n = 202)

	XT → CEX (n = 93)	T → CEF (n = 109)	HR (95% CI); p-value
Relapse-free survival	84.5%	70.3%	0.48 (0.26-0.88); 0.018
Distant disease-free survival	84.5%	70.9%	0.51 (0.28-0.95); 0.035
Overall survival	89.1%	75.6%	0.42 (0.20-0.87); 0.019
Deaths	10.8%	23.9%	NR
Deaths due to breast cancer	7.5%	22.9%	NR

HR, hazard ratio

Lindman H et al. *Proc SABCS 2010*;Abstract PD01-02.

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Author Conclusions

- The FinXX trial was the first to report the efficacy of capecitabine in combination with anthracycline/taxane-containing therapy in the adjuvant treatment of early breast cancer.¹
- The final 5-year subgroup analyses of TNBC, a population with a high unmet need, reported significant benefits in all endpoints for patients receiving the capecitabine-containing regimen XT → CEX compared to the standard arm T → CEF.²
 - Relapse-free survival, 84.5% vs 70.3%
 - Distant disease-free survival, 84.5% vs 70.9%
 - Overall survival, 89.1% vs 75.6%
- The estimated risk reduction of relapse or death in patients with TNBC was around 50% in patients receiving XT → CEX.²
- The findings from this subgroup analysis are exploratory and must be confirmed in other studies.²

¹ Joensuu H et al. *Lancet Oncol* 2009;10:1145-51; ² Lindman H et al. *Proc SABCS 2010*;Abstract PD01-02.

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Review of Capecitabine for the Treatment of Triple-Negative Early Breast Cancer

Steger GG et al.

Proc SABCS 2010;Abstract PD01-03.

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Methods

- **Objective:**
 - To assess the potential benefit of capecitabine in patients with triple-negative breast cancer (TNBC) treated on the ABCSG-24 and FinXX trials.
- **Patient eligibility:**
 - Neoadjuvant ABCSG-24: Operable breast cancer except T4d with or without nodal involvement (*Proc ECCO-ESMO 2009;Abstract 4BA*)
 - Adjuvant FinXX: Invasive breast cancer at medium to high risk of recurrence (*Lancet Oncol 2009;10:1145*)
- **Treatments:**
 - ABCSG-24: Neoadjuvant epirubicin (E) and docetaxel (T) with or without capecitabine (X)
 - FinXX: Adjuvant T → cyclophosphamide/epirubicin/5-fluorouracil (CEF) or XT → CEX

Steger GG et al. *Proc SABCS 2010;Abstract PD01-03.*

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Primary Efficacy Analysis

Pathologic Complete Response (pCR) Rate			
ABCSG-24 study	ET + X	ET	p-value
All patients (n = 255, 257)	24.3%	16.0%	0.02
Patients with TNBC (n = 29, 19)	47.5%	31.2%	NS

3-Year Relapse-Free Survival (RFS)			
FinXX study	XT → CEX	T → CEF	p-value
All patients (n = 747, 753)	92.5%	88.9%	0.02

NS, not significant

Steger GG et al. *Proc SABCS 2010*;Abstract PD01-03.

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TNBC Subgroup Analysis

ABCSG-24 study	TNBC (n = 122)	Non-TNBC (n = 348)	Odds ratio (95% CI)	p-value
pCR, all patients	39.3%	10.9%	5.29 (3.22-8.68)	<0.0001
pCR, ET + X group	47.5%	13.2%	5.95 (3.05 -11.59)	<0.0001
pCR, ET group	31.2%	8.6%	4.80 (2.25-10.23)	<0.0001

FinXX study	TNBC	Non-TNBC	Hazard ratio (95% CI)	p-value
RFS, all patients	81.7%	92.2%	0.43 (0.29-0.63)	<0.001

- Within the TNBC subgroup of patients in the FinXX study, 3-year RFS was significantly longer in the capecitabine-containing arm (n = 93) than in the control arm (n = 109): 87.7% vs 76.6% (HR: 0.43, p = 0.024)

Steger GG et al. *Proc SABCS 2010*;Abstract PD01-03.

Author Conclusions

- Patients with TNBC have a high unmet therapeutic need with generally worse prognosis than patients with non-TNBC.
- Initial data with capecitabine in early breast cancer are promising, with the randomized Phase III ABCSG-24 and FinXX trials demonstrating significant improvements in pCR and RFS, respectively, with the addition of capecitabine to standard (neo)adjuvant regimens.
- Subgroup analyses from these studies report additional benefit of capecitabine therapy in patients with TNBC.
- An ongoing study (CIBOMA collaborative group Phase III trial) is evaluating capecitabine as maintenance therapy after adjuvant anthracycline/taxane for patients with TNBC.
 - First study utilizing capecitabine to specifically target patients with early TNBC
 - Interim safety data also presented at SABCS 2010 (Lluch A et al. *Proc SABCS 2010*;Abstract P5-10-15)

Steger GG et al. *Proc SABCS 2010*;Abstract PD01-03.

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Investigator Commentary: Incorporation of Capecitabine into Adjuvant Therapy for High-Risk Early BC

In the subgroup analysis of FinXX, patients with triple-negative breast cancer (TNBC) who received adjuvant XT → CEX experienced an improvement in overall survival, distant disease-free survival and relapse-free survival compared to those who received T → CEF. Several studies have suggested that patients with TNBC may benefit from a more intense therapeutic approach.

In the review of capecitabine for the treatment of early breast cancer in ABCSG-24 and FinXX, they demonstrated, not surprisingly, that patients with TNBC experienced worse outcomes. They also suggested that the patients with TNBC who received capecitabine-containing regimens had better outcomes that were equivalent to patients with non-TNBC.

Interview with William J Gradishar, MD, January 4, 2011

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