# 5 Minute JournalClub

*Key SABCS Presentations*
Issue 7, 2011

# CIBOMA/2004-01/GEICAM 2003-11: Adjuvant Capecitabine Maintenance Therapy for Triple-Negative Early 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 OBJECTIVE

- Appraise the interim safety data for capecitabine maintenance therapy after standard adjuvant chemotherapy for triple-negative early breast cancer.

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**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 Onco*type* 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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# CIBOMA/2004-01/GEICAM 2003-11: Adjuvant Capecitabine Maintenance Therapy for Triple-Negative Early Breast Cancer

## Presentation discussed in this issue

Lluch A et al. **First safety data from a randomized Phase III (CIBOMA 2004-01/ GEICAM 2003-11) trial assessing adjuvant capecitabine maintenance therapy after standard chemotherapy for triple-negative early breast cancer.** San Antonio Breast Cancer Symposium 2010;**Abstract P5-10-15**.

## Slides from a presentation at SABCS 2010 and transcribed comments from recent interviews with William J Gradishar, MD (1/4/11) and Kathleen I Pritchard (12/30/10)

# Study Design

**Accrual: 816 (Open)**

**Eligibility**

- Operable node-positive (or node-negative with tumor diameter ≥1 cm)
- Centrally confirmed TNBC
- No evidence of metastatic disease
- 6-8 cycles of prior anthracycline and/or taxane-based chemo or 4 cycles of doxorubicin/cyclophosphamide (for node-negative disease) in the (neo)adjuvant setting

R

**Safety data reported for first 400 patients (pts)**

- **Capecitabine** 1,000 mg/m² BID d1-14 q3wks x 8
- **Observation**

Lluch A et al. *Proc SABCS* 2010;Abstract P5-10-15.

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# Treatment-Related Grade 3/4 Adverse Events*

| Outcome | Capecitabine (n = 207) | Observation (n = 193) |
|---|---|---|
| Hand-foot syndrome† | 17.4% | — |
| Diarrhea | 2.9% | — |
| Fatigue | 1.9% | — |
| Vomiting | 1.0% | — |
| Nail changes | 1.0% | — |
| Elevated bilirubin | 1.0% | — |
| Irregular menses | 0.5% | 7.8% |

* Grade 3/4 events occurring in ≥2 patients in either treatment arm;
† Grade 3 only

Lluch A et al. *Proc SABCS* 2010;Abstract P5-10-15.

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# Proportion of Cycles with Treatment Discontinuation Due to Toxicity

| Cycles, % | N = 1,440 |
|---|---|
| Toxicity | 12.2% |
| Hand-foot syndrome | 7.4% |
| Neutrophils/granulocytes | 1.2% |
| Diarrhea | 1.1% |
| Mucositis/stomatitis | 0.5% |
| Leukocytes | 0.4% |
| Fatigue | 0.3% |

Lluch A et al. *Proc SABCS* 2010;Abstract P5-10-15.

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# Selected Reasons for Discontinuation

| Rationale, n (%) | Capecitabine (n = 207) | Observation (n = 193) |
|---|---|---|
| Withdrawal request by pt | 16 (7.8%) | 2 (1.0%) |
| Unacceptable toxicity | 15 (7.2%) | 1 (0.5%) |
| Disease relapse | 5 (2.4%) | 7 (3.7%) |
| Tx interuption >3 wks | 4 (1.9%) | — |
| Death | 3 (1.4%) | 2 (1.0%) |
| Protocol deviation | 2 (1.0%) | 1 (0.5%) |
| Lost to follow-up | 1 (0.5%) | 1 (0.5%) |

Lluch A et al. *Proc SABCS* 2010;Abstract P5-10-15.

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# Author Conclusions

- The safety profile of adjuvant capecitabine as maintenance therapy is consistent with its known toxicity profile.
- More than 75% of patients are able to complete their treatment as planned, with approximately 15% of patients discontinuing due to toxicity or patient withdrawal.
- Ongoing recruitment with an accrual of 876 patients is planned.

Lluch A et al. *Proc SABCS* 2010;Abstract P5-10-15.



## Investigator Commentary: Maintenance Capecitabine After Adjuvant Chemotherapy for Triple-Negative Breast Cancer

The CIBOMA/GEICAM investigators demonstrated that administering maintenance capecitabine after standard adjuvant chemotherapy for patients with triple-negative early breast cancer was not associated with excessive capecitabine-associated side effects, and hand-foot syndrome and diarrhea were the most common adverse events. This was a preliminary report, and efficacy data are not yet available.

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

The Swiss have been investigating metronomic cyclophosphamide and methotrexate as maintenance therapy in the adjuvant setting. We were interested in joining the Swiss study, but we were unhappy about approaching patients to undergo a year of maintenance therapy.

I have used capecitabine a lot as a single agent for metastatic disease, and it may not be a "slam dunk" to administer it as maintenance therapy, even though it's orally administered. Patients must be carefully watched because they "soldier on" and do not always report symptoms. Using maintenance capecitabine will require careful management and watching the dose closely. However, if this approach turns out to be positive, then we will all be using maintenance therapy.

***Interview with Kathleen I Pritchard, MD, December 30, 2010***