Breast Cancer™ UPDATE

Conversations with Surgical Oncology Leaders

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2 audio tapes

Monograph

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How to use this supplement

This monograph supplements the audio program and contains edited comments, clinical trial schemas, graphics and references. **BreastCancerUpdate.com** includes a full transcription of the audio program and an easy-to-use representation of each page of this booklet, allowing users to link immediately to relevant full-text articles, abstracts, trial information and other web resources indicated throughout this guide in **red underlined text.** This regularly updated web site also features an extensive breast cancer bibliography, clinical trial links, a “breast cancer web tour” and an audio library with excerpts from interviews and meetings catalogued by topic.

Patrick Borgen, MD

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Edited comments by Dr Borgen

Sentinel node biopsy: The standard of care?

In experienced hands, sentinel node biopsy is absolutely a standard of care. The evidence is overwhelming. There are over 50 institutional series of 6,000 patients who had back-up axillary dissections. Sentinel node biopsy is actually more accurate than providing the pathologist 20 lymph nodes from an axillary dissection.

The question should not be whether sentinel node biopsy is an accepted standard of care, but rather, does each surgeon know how to do it, and is he or she comfortable accepting a sentinel lymph node biopsy result?

Patient selection is important — sentinel node biopsy is not for everyone. For example, if the tumor is very high in the tail of the axilla, sentinel node mapping can be problematic. Other examples of women who are not good candidates for sentinel node biopsy are patients with two cancers in one breast, clinically palpable nodes and those who have received neoadjuvant chemotherapy.

Parenchymal versus intradermal tracer injections for sentinel node biopsy

We started doing sentinel node biopsy with parenchymal injections of tracer in 1995, and in 1998 we began studying the intradermal injection. This became our standard of care in late 1999 because of the advantages to the intradermal injection.

First, the skin lymphatics drain much faster than the parenchymal lymphatics. Second, we can use a physician extender to inject the tracer — the surgeon doesn't have to go to nuclear medicine to do the injection. And third, we can use

two-thirds less radioactivity when injecting into the skin. The radioactivity in the lymph node is lower, and there is less radiation exposure to pathologists handling these nodes.

This intradermal technique is now being done widely. Kelly McMasters* from Louisville studied surgeons and found that the learning curve was far easier, and the success rate was much higher with intradermal injections of tracer than it was with intraparenchymal injections.

*McMasters KM. *Ann Surg* 2001;233(5):676-87.

AMERICAN COLLEGE OF SURGEONS Z-10 TRIAL: A PHASE III PROGNOSTIC STUDY OF SENTINEL NODE AND BONE MARROW MICROMETASTASES IN WOMEN WITH STAGE I OR IIA BREAST CANCER Open Protocol

Eligibility	**Stage I or IIA breast cancer amenable to lumpectomy**
Protocol	**Lumpectomy + SLND + may undergo bilateral iliac crest bone marrow aspiration**

+Sentinel Node → ACOS Z-11

All patients receive breast radiotherapy and systemic adjuvant therapy.

Patients with no sentinel node identified intraoperatively and patients with sentinel node metastasis identified by H & E who choose not to be registered to ACOSOG-Z0011 undergo ALND.

AMERICAN COLLEGE OF SURGEONS Z-11 TRIAL: A PHASE III RANDOMIZED STUDY OF AXILLARY LYMPH NODE DISSECTION IN WOMEN WITH STAGE I OR IIA BREAST CANCER WHO HAVE A POSITIVE SENTINEL NODE Open Protocol

Eligibility	**Positive sentinel node from ACOS Z-10 trial (Z-10 requires breast conservation therapy)**
ARM 1	**ALND (≥ level I and II) + whole breast radiation**
ARM 2	**Breast radiotherapy only as in ARM 1**

Patients in both arms may receive adjuvant systemic therapy at the discretion of the treating physician.

NSABP B-32 TRIAL: PHASE III RANDOMIZED STUDY OF SENTINEL NODE DISSECTION WITH OR WITHOUT CONVENTIONAL AXILLARY DISSECTION IN WOMEN WITH CLINICALLY NODE-NEGATIVE BREAST CANCER Open Protocol

Eligibility	**Sentinel node dissection with axillary dissection**
ARM 1	**Sentinel node resection with axillary dissection**
ARM 2	**Sentinel node examination**
+Sentinel node	**→ Axillary dissection**
–Sentinel node	**→ No axillary dissection**

All patients receive technetium Tc 99m sulfur colloid injected into normal breast tissue within 1 cm of the primary tumor or biopsy cavity, approximately 0.5-8 hours before surgery.

Patients also receive an injection of isosulfan blue dye around the tumor or biopsy cavity after a hot spot is identified with a gamma detector.

Intraoperative radiation therapy

We have an active research protocol looking at intraoperative radiation therapy to the quadrant of the breast with the cancer. This would be an enormous advantage if we can prove that it is as safe and efficacious, over six weeks of external beam radiation therapy. It is one-third as expensive, completed in 30 minutes rather than six weeks, and patients can start systemic therapy immediately. We are very enthusiastic about the idea of jointly doing surgery and radiation therapy.

Veronesi's group looked at their first 200 cases, using a different technology than we have in this country. Their early data shows local recurrence rates similar to rates with external beam therapy. Local recurrences overwhelmingly occur near the original cancer, so the idea of trying to not radiate the other three quadrants of the breast makes a lot of sense.

There also have been great improvements in systemic therapy, which affects the remainder of the breast. My early guess is that

intraoperative radiation therapy will be as effective as external beam and will be embraced rapidly once we work out the optimal technology.

Evaluating results of the ATAC adjuvant trial in postmenopausal women

The headline news from the ATAC trial is that anastrozole looks better than tamoxifen, and the combination does not look any different than tamoxifen. This confirms the findings in the stage IV setting showing that anastrozole was at least as good as, if not better, than tamoxifen and certainly had a more favorable side-effect profile.

We have been using aromatase inhibitors at Memorial Sloan-Kettering since 1995 when anastrozole was approved, and these agents are very well tolerated. They don't cause nearly the side effects that our patients on tamoxifen tell us about, and we've been enthusiastic about using them.

PROPOSED NSABP DCIS TRIAL: TAMOXIFEN VERSUS ARIMIDEX IN POSTMENOPAUSAL PATIENTS WITH DUCTAL CARCINOMA IN SITU

Eligibility	**Postmenopausal, DCIS, treated with lumpectomy & XRT**
ARM 1	**Tamoxifen 20 mg qd x 5 yrs**
ARM 2	**Arimidex 1 mg qd x 5 yrs**

Margolese R. **Rationale for proposed National Surgical Adjuvant Breast and Bowel Project (NSABP): DCIS Trial. Tamoxifen versus Arimidex® (anastrozole) in postmenopausal patients with ductal carcinoma in situ.** Poster, 2001 Miami Breast Cancer Conference. **Full-Text**

Future trials of aromatase inhibitors in DCIS

I'm confident that DCIS will be the first arena that we move into with the aromatase inhibitors beyond invasive breast cancer. The RTOG has a DCIS trial looking at women with small favorable lesions randomized to radiation or not. This trial requires that all women take tamoxifen. They couldn't

accrue enough patients, and ultimately they had to remove the tamoxifen requirement. This gets back to tamoxifen's image problem. I think that the community will embrace an aromatase inhibitor trial in DCIS. The prospect of an agent with a better side-effect profile than tamoxifen is very exciting in both the DCIS and the chemoprevention settings.

PROPOSED IBIS 2 TRIAL: INTERNATIONAL BREAST INTERVENTION STUDY 2

Eligibility	**Postmenopausal women at high risk for breast cancer or with DCIS**
ARM 1	**Tamoxifen 20 mg qd x 5 yrs**
ARM 2	**Arimidex 1 mg qd x 5 yrs**
ARM 3	**Placebo x 5 years**

Select publications

Vaidya JS et al. **Targeted intra-operative radiotherapy (Targit): An innovative method of treatment for early breast cancer.** *Ann Oncol* 2001;12(8):1075-80. **Abstract**

Aromatase inhibitors in DCIS and chemoprevention Chlebowski RT. Breast cancer risk reduction: Strategies for women at increased risk. *Annu Rev Med* 2002;53:519-40. **Abstract**

Fabian CJ et al. **Beyond tamoxifen new endpoints for breast cancer chemoprevention, new drugs for breast cancer prevention.** *Ann N Y Acad Sci* 2001;952:44-59. **Abstract**

Goss P. **Anti-aromatase agents in the treatment and prevention of breast cancer.** *Cancer Control* 2002;9(2 Suppl):2-8. **Full-Text**

Goss PE, Strasser K. **Aromatase inhibitors in the treatment and prevention of breast cancer.** J Clin Oncol 2001;19:881-94. **Abstract**

Ingle JN. **Aromatase inhibition and antiestrogen therapy in early breast cancer treatment and chemoprevention.** *Oncology (Huntingt)* 2001;15:28-34. **Abstract**

Lonning PE et al. **The potential for aromatase inhibition in breast cancer prevention.** *Clin Cancer Res* 2001;7(12 Suppl):4423s-4428s; discussion 4411s-4412s. **Abstract**

Powles TJ. **Breast cancer prevention.** *Oncologist* 2002;7(1):60-4. **Abstract**

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Edited comments by Professor Dixon

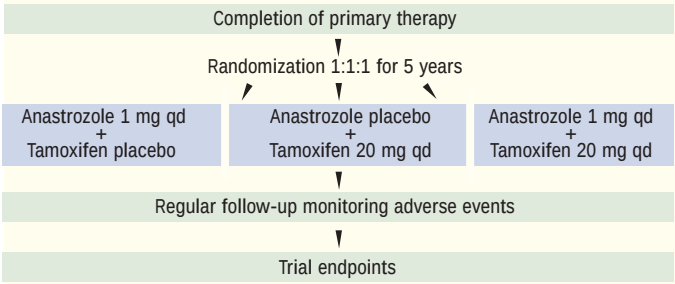
Background of ATAC Trial: Anastrozole vs Tamoxifen vs Combination

I've been convinced for quite some time that the aromatase inhibitors would be superior to tamoxifen in the adjuvant setting, because in the neoadjuvant situation we noticed that the rapidity and extent of responses to aromatase inhibitors were greater than with tamoxifen. So, I've had a feeling that these neoadjuvant findings would result in benefits in the adjuvant setting, which was proven in the early data from ATAC.

Aromatase inhibitors cut off proliferation in the tumor within days of starting treatment. This can have a major biological effect on the tumor even between the time of diagnosis and surgery. We've seen tumor shrinkage within a few weeks of starting an aromotase inhibitor. In the past, we've rushed to get patients to the operating room, and this does disrupt their lives.

Now we know that they can start anastrozole and cut down proliferation within the tumor and elsewhere in the body. When a woman takes that first tablet, she's on systemic treatment for breast cancer, and whether she has surgery in two days, two weeks or even two months is unlikely to have any impact on long-term outcome.

ATAC TRIAL DESIGN - POSTMENOPAUSAL WOMEN WITH INVASIVE BREAST CANCER



SUMMARY OF ATAC TRIAL OUTCOMES

9,366 evaluable patients

- At a median treatment duration of 2.5 years, anastrozole demonstrated superior efficacy and tolerability compared to tamoxifen
- Anastrozole was superior to tamoxifen in terms of disease-free survival in the overall population (relative reduction of 17%) and in estrogen receptor-positive patients (relative reduction of 22%)
- Anastrozole was superior to tamoxifen in terms of the incidence of contralateral breast cancer in the overall population (relative reduction of 58%)
- There were 156 patients with distant metastases in the anastrozole arm and 181 in the tamoxifen arm (not statistically different)
- There were only a total of five breast cancer deaths in the three treatment arms

Anastrozole was tolerated better than tamoxifen with respect to:

- Endometrial cancer
- Vaginal bleeding
- Vaginal discharge
- Ischaemic cerebrovascular events
- Venous thromboembolic events
- Hot flashes
- Weight gain

Tamoxifen was tolerated better than anastrozole with respect to:

- Musculoskeletal disorders (arthralgias)
- Fractures

Derived from a presentation by Michael Baum, 24th Annual San Antonio Breast Cancer Symposium

Baum M. **The ATAC (Arimidex, Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in postmenopausal (PM) women.** *Breast Cancer Res Treat* 2001; 69(3):**Abstract 8.**

Toxicity profile of anastrozole versus tamoxifen

Tamoxifen has many more side effects than we sometimes appreciate. Anastrozole was superior to tamoxifen in most of the quality of life endpoints; therefore, it is not only more effective, but also it causes fewer side effects.

The biggest long-term concerns about anastrozole are bone density and lipids. The available lipid data look reassuring. I don't see bone loss as a major long-term worry, because not only can we monitor this, but I also think that in the future we will be giving an aromatase inhibitor with a bisphosphonate. The other side effect we have observed with aromatase inhibitors is musculoskeletal symptoms — arthralgias, which are usually very mild but occasionally can be fairly severe.

ATAC showed a number of significant benefits to anastrozole versus tamoxifen. Vasomotor symptoms can be a problem in women taking tamoxifen, and the reduction in these symptoms with anastrozole was a pleasant surprise. Anastrozole also was associated with fewer thrombotic events and endometrial cancers. These are significant advantages over tamoxifen, in that these conditions can actually cause death.

Finally, it has always mystified clinicians that randomized trials of tamoxifen have not revealed weight gain, despite a large percentage of patients saying that it is associated with weight gain. Anastrozole caused less weight gain than tamoxifen in ATAC. This backs up the clinical impression that despite the trials, tamoxifen does affect weight.

We must attempt to prolong life, but we must also prolong good quality of life. We've now got another option in anastrozole.

Other aromatase inhibitors as adjuvant therapy

There are only adjuvant data for anastrozole and at the moment that is the drug we should use. All the aromatase inhibitors are slightly different, and there are slightly different effects on circulating estrogen levels. So, unless or until we obtain some data comparing the different drugs, then you've got to use the drug in this setting that has been tested, namely anastrozole. And of course, these agents currently are only for use in postmenopausal women.

Anastrozole in chemoprevention trials

The number of second breast cancers in the ATAC trial was significantly reduced with anastrozole, even beyond the nearly 50% reduction seen with tamoxifen. This is not surprising, because we know that estrogen is a carcinogen, which promotes the development of cancers. When you reduce estrogen, cells have less drive to proliferate and are much less likely to undergo carcinogenesis.

The next prevention study in the United Kingdom will compare placebo to tamoxifen to anastrozole in high-risk women. From the ATAC data we've seen already, we expect that anastrozole will dramatically decrease the number of breast cancers and should be superior to tamoxifen in the prevention setting.

Select publications

Pharmacokinetics of anastrozole and tamoxifen alone and in combination during adjuvant endocrine therapy for early breast cancer in postmenopausal women: A sub-protocol of the "Arimidex® and Tamoxifen Alone or in Combination" (ATAC) trial. *Br J Cancer* 2001;85(3):317-324. **Abstract**

Baum M. **The ATAC (Arimidex, Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in post-menopausal women.** *Breast Cancer Res Treat* 2001;69(3):**Abstract 8.**

Baum M et al. **Sequential power calculations in a recruitment phase of a multicentre trial — the experience of the 'Arimidex (anastrozole), tamoxifen alone or in combination' (ATAC) study.** *Proc ASCO* 2002;**Abstract 185.**

Brodie A. **Aromatase inhibitors in breast cancer.** *Trends Endocr Metab* 2002;13(2):61-65. **Abstract**

Buzdar AU. **Anastrozole (Arimidex) — an aromatase inhibitor for the adjuvant setting?** *Br J Cancer* 2001;85(2 suppl):6-10. **Abstract**

Duffy SRG et al. **The ATAC ('Arimidex,' tamoxifen, alone or in combination) early breast cancer (EBC) trial in postmenopausal (PM) patients: Endometrial sub-protocol results.** *Proc ASCO* 2002;**Abstract 158.**

Fallowfield L et al. **Assessing the quality of life (QOL) of postmenopausal (PM) women randomized into the ATAC ('Arimidex,' tamoxifen, alone or in combination) adjuvant breast cancer (BC) trial.** *Proc ASCO* 2002;**Abstract 159.**

Goss PE. **Preliminary data from ongoing adjuvant aromatase inhibitor trials.** *Clin Cancer Res* 2001;7(12 suppl):4397s-4401s. **Abstract**

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Edited comments by Dr Singletary

Risk assessment in clinical practice

I don't think surgeons use risk assessment on a routine basis. While they may be aware of the risk assessment tools, these are not being formally incorporated into practice or being routinely documented in the medical record. Any woman over age 35 should have a risk-factor history taken, and, if she appears to have elevated risk, she should be asked if she would like her five-year and lifetime risks calculated using the Gail model. Most women tend to overestimate their risk, so for many, risk assessment will provide some reassurance.

When we look at the option of chemoprevention with tamoxifen, we need to always weigh the benefits versus side effects. Certainly for young women at high risk, tamoxifen has far more benefits than risks. Many women have heard about the side effects but do not understand the results of the P-1 trial showing the 49% reduction in breast cancer risk.

The role of ductal lavage in a clinical risk management strategy

Ductal lavage is a fairly simple technique that is not very time-consuming and can be incorporated in a surgical or medical practice without any difficulty. We actually have our research nurse perform our ductal lavage procedures. It's well tolerated by the patients, and we have not had any patients complain of discomfort.

Ductal lavage can be offered to patients if the cytologic information would help them in their risk management decision-making process. It may help patients who are considering tamoxifen but unsure about whether to take it. Lavage provides a physician and patient with more information

to round out the risk profile. The presence of atypical cells may be enough to encourage a woman to take tamoxifen or consider participating in a chemoprevention study. These ductal lavage findings may help put the side effects of tamoxifen into perspective. Not finding atypical cells does not necessarily decrease their risk, as we do not know the meaning of a negative ductal lavage.

The Risk Assessment Working Group developed a risk management strategy, dividing patients into three risk categories: average risk, elevated or high risk, and very high risk. The algorithm targets the moderate to very high risk groups and addresses the issue of where ductal lavage would be incorporated. Essentially, it would be for women in whom information from the ductal lavage would influence their decision-making.

Risk Assessment Working Group

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Modified Risk Management Strategy

RISK STATUS	MANAGEMENT
VERY HIGH RISK Personal history of breast cancer, DCIS or LCIS Personal history of cellular atypia or ADH/ALH and a first-degree affected relative with breast cancer Known or suspected BRCA 1/2 mutation carriers	CBE (complete breast exam) every 6 months and annual mammography Genetic counseling (mutation carriers) Consider chemoprevention* Consider prophylactic surgery (mutation carriers & LCIS)* ** Consider ductal lavage if the presence of atypia would alter decision-making*
ELEVATED OR HIGH RISK ADH/ALH or cellular atypia 5-year Gail risk > 1.7% 2 or more second-degree premenopausal affected relatives On combined HRT for > 10 years	Annual CBE and annual mammography beginning at age 40 HRT counseling (combination HRT patients) Consider chemoprevention* ** Consider ductal lavage if the presence of atypia would alter decision-making*
AVERAGE RISK All other categories excluded	Annual CBE and annual mammography beginning at age 40 Reassess risk every 2-3 years

This algorithm was first presented at the 2002 Miami Breast Cancer Conference Risk Assessment Symposium. It now is available as a webcast online at www.cancerconf.com.

Recently published management algorithms:

Morrow M et al. **Evaluation and management of the woman with an abnormal ductal lavage.** *J Am Coll Surg* 2002; 194(5): 648-656. No abstract available.

O'Shaughnessy JA et al. **Ductal lavage and the clinical management of women at high risk for breast carcinoma.** *Cancer* 2002:94(2):292-298. **Abstract**

Relationship between atypical cytology and atypical ductal hyperplasia

A finding of atypia on ductal lavage may put a woman at the same risk as finding atypical hyperplasia on a tissue biopsy — four- to five-fold increased risk.

If we look at the P-1 data, women with atypical ductal hyperplasia received the most benefit from tamoxifen, with an 86% reduction in breast cancer risk. We cannot say that atypical cytology is the same as atypical ductal hyperplasia, but there may be some relationship.

The best data we have is from Carol Fabian's fine-needle aspiration study* in which she did four quadrant periareolar aspirations. She showed that women with atypical cells had a 15% risk of breast cancer within a short time, especially in those patients who also had an elevated Gail risk. We cannot say that atypical cytology is equivalent to atypical hyperplasia on a tissue biopsy, but it seems to be in the same ballpark figure of increased risk.

*Fabian CJ et al. *J Natl Cancer Inst* 20001;92(15):1217-27. **Abstract**

Incorporating the ATAC outcomes into clinical practice

We are now going to use anastrozole at MD Anderson as first-line adjuvant endocrine therapy for postmenopausal women with node-positive, estrogen receptor-positive disease. We think that the side effects may be slightly less than tamoxifen, and there was a modest disease-free survival advantage. This decision was reached among our medical oncologists, surgical oncologists and radiation oncologists.

I think anastrozole will eventually also move into the node-negative setting and perhaps also be used in clinical trials of ductal carcinoma *in situ*. Anastrozole has a good safety profile, and I believe that surgeons will be very comfortable prescribing this agent.

2002 Miami Breast Cancer Conference Patterns of Care Study

Editor's Note:

The management of patients with breast cancer has always been fraught with challenging decisions. For more than two decades, physicians and patients have struggled with choices in breast conservation, and the emergence of sentinel node biopsy, new adjuvant endocrine therapies, chemoprevention strategies and neoadjuvant regimens has made these decisions even more complex.

The Miami Breast Cancer Conference – now in its 19th year under the direction of Dr Daniel Osman – has always addressed these controversies directly. For years, using electronic keypad polling, we have posed management questions about clinical scenarios and compared answers from attendees and faculty members.

For our 2002 meeting, we took this process to a new level and obtained an unrestricted educational grant to allow a nationally recognized polling firm, ReedHaldyMcIntosh, to survey 200 randomly selected medical oncologists and surgeons in December 2001 about dozens of controversial breast cancer management issues, which included many specific case scenarios.

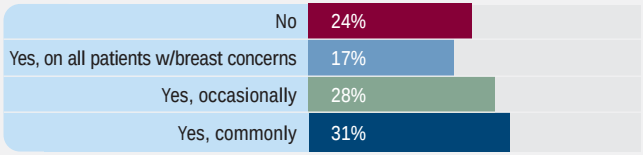
This issue of Breast Cancer Update documents key results from this survey and answers to the interactive questions posed to the Miami Breast Cancer Conference (MBCC) attendees. The comprehensive results are available on the BreastCancerUpdate.com website. It is interesting to compare the responses from the physicians in this national survey to those attending the conference, who by their presence at a three-day breast cancer meeting are presumably more focused on breast cancer in their practices.

When one considers the enormous investment in breast cancer clinical research, it is surprising how little attention is committed to defining whether these advances are being actualized in clinical practice. In part, this survey was intended to stimulate discussion on precisely that issue.

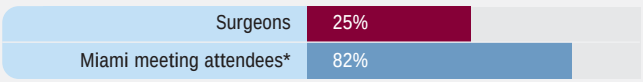
— Neil Love, MD

Breast Cancer Risk Assessment and Chemoprevention

Surgeons: Do you use the Gail model in your practice?



Physicians starting at least one high-risk woman on tamoxifen for chemoprevention in the past year



** 48% of these physicians started six or more patients on tamoxifen for chemoprevention in the past year.*

Commentary

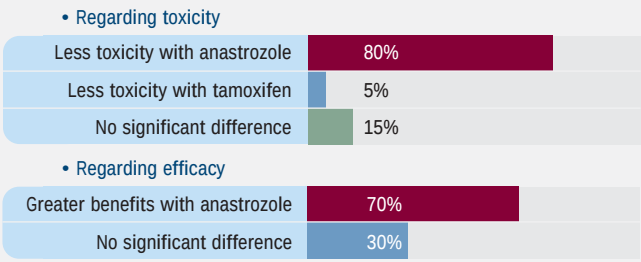
The 1998 publication of the NSABP P-1 prevention trial led to considerable discussion in the breast cancer research community about the need to routinely employ quantitative risk assessment in women over the age of 35. The P-1 study utilized the Gail model and established a 1.67% five-year breast cancer risk as a key entry criterion. This is also being incorporated into the current NSAPB prevention trial, protocol P-2, comparing tamoxifen to raloxifene. The patterns of care study demonstrated that 76% of surgeons are currently utilizing the Gail model to assess breast cancer risk in their patients; however, only 25% of these physicians have initiated tamoxifen for chemoprevention in any patient in the past year. The number of physicians prescribing tamoxifen for chemoprevention increases dramatically in physicians attending the Miami Breast Cancer Conference.

Select publications

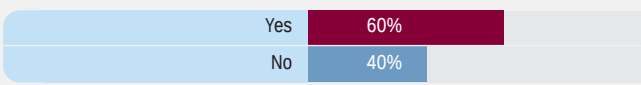
Fisher B et al. **Tamoxifen for prevention of breast cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study.** *J Natl Cancer Inst* 1998;90(18):1371-88. **Abstract**

Implications of the ATAC Trial in Chemoprevention

Surgeons: What results would you expect from a randomized clinical trial comparing tamoxifen to anastrozole in high-risk postmenopausal women?



Surgeons: Based on the ATAC data, would you currently use anastrozole or another aromatase inhibitor in a high-risk postmenopausal woman?

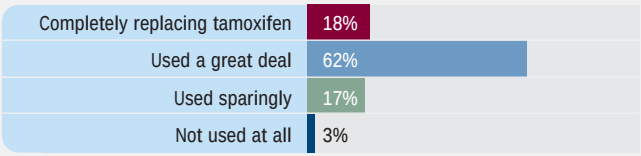


Commentary

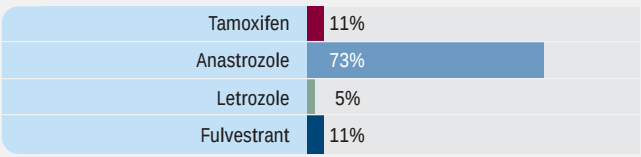
The primary rationale for utilizing tamoxifen in high-risk women in clinical trials, such as NSABP P-1, was the reduction in contralateral breast cancer observed with adjuvant tamoxifen in patients with invasive breast cancer. The preliminary results of the ATAC trial demonstrated 56% fewer second breast cancers in women randomized to anastrozole compared to tamoxifen. Based on these early findings, most surgeons surveyed believe that a randomized trial comparing anastrozole to tamoxifen in high-risk postmenopausal women would demonstrate both greater efficacy and less toxicity for anastrozole. Sixty percent of surgeons would use anastrozole in these women at the present time, for which there is no FDA indication, but breast cancer researchers almost uniformly believe that aromatase inhibitors should only be utilized in high-risk patients as part of a clinical trial. In the United Kingdom, a massive trial is being planned to evaluate the use of anastrozole in high-risk patients. The final design of this IBIS II trial is awaiting the presentation of IBIS I study results comparing tamoxifen to placebo.

Adjuvant Endocrine Therapy: Current and Future Use of Aromatase Inhibitors

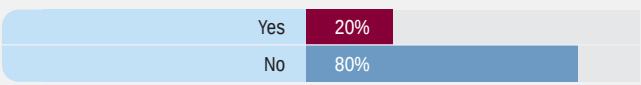
Miami meeting attendees: How is anastrozole utilized as adjuvant therapy in postmenopausal patients at the current time?



Miami meeting attendees: In three years, what will be the most common adjuvant endocrine therapy of postmenopausal women?



Miami meeting attendees: Do you believe that the other aromatase inhibitors (letrozole, exemestane) can be used interchangeably with anastrozole as adjuvant therapy?



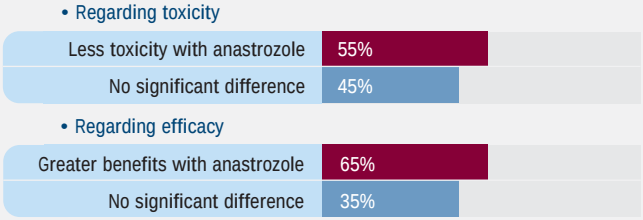
Commentary

Almost two-thirds of the Miami Breast Cancer Conference attendees believe that in 2002, anastrozole will be utilized a great deal as adjuvant endocrine therapy for postmenopausal breast cancer patients. Of note, nearly 20% believe anastrozole has almost completely replaced tamoxifen in these patients.

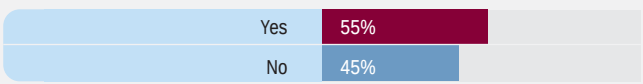
This viewpoint was confirmed in physicians' predictions for clinical practice three years from now, with nearly three-quarters stating that anastrozole will be the most commonly utilized adjuvant endocrine therapy. Interestingly, there is a lack of support of the other aromatase inhibitors as adjuvant therapy. This is likely to continue until compelling, randomized clinical trial data become available for these agents.

Implications of the ATAC Trial in the Systemic Therapy of DCIS

Surgeons: What results would you expect from a trial comparing tamoxifen to anastrozole in women with DCIS?



Surgeons: Would you currently use anastrozole or another aromatase inhibitor in a postmenopausal woman with DCIS?



Commentary

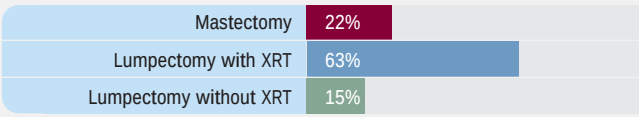
Based on the encouraging initial ATAC trial results with regard to both toxicity and second breast cancers, the NSABP is planning a randomized trial in DCIS patients comparing anastrozole to tamoxifen. The IBIS II trial in the United Kingdom will also evaluate anastrozole in DCIS patients. More than half of the surgeons surveyed believe that a randomized trial comparing tamoxifen to anastrozole in women with DCIS would yield both greater benefits and less toxicity with anastrozole. More than half of the surgeons surveyed would currently utilize an aromatase inhibitor based on the ATAC data, for which there is no FDA indication. In contrast, breast cancer researchers almost uniformly believe that aromatase inhibitors should only be given to DCIS patients enrolled in a clinical trial.

Select publications

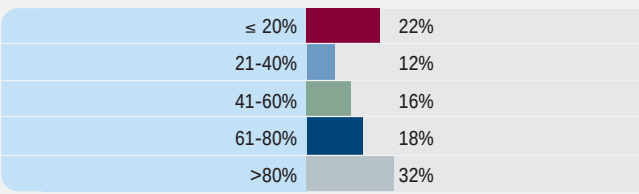
Baum M. **The ATAC (Arimidex, Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in post-menopausal women.** *Breast Cancer Res Treat* 2001;69(3):**Abstract 8.**

Local and Systemic Therapy of DCIS

Surgeons: What percent of your DCIS patients do you treat with the following:



Miami meeting attendees: What fraction of your patients with DCIS receives tamoxifen?



Commentary

Most patients with DCIS are being treated with lumpectomy and radiation as local therapy. While there is considerable controversy about selection of patients for breast-conserving therapy without radiation, only about one in seven women receive this local treatment approach.

There is significant variation in the use of tamoxifen for DCIS patients. Although NSABP B-24 demonstrated approximately a 50% reduction in the rates of all breast cancer events with the use of tamoxifen in DCIS patients, some physicians believe the potential toxicities outweigh the absolute benefits of therapy in many patients with this low-risk lesion.

Select publications

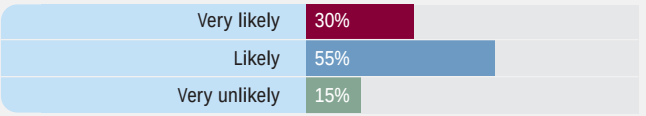
Bordeleau L et al. **A comparison of four treatment strategies for ductal carcinoma in situ using decision analysis.** *Cancer* 2001;92(1):23-9. **Abstract**

Fisher B et al. **Prevention of invasive breast cancer in women with ductal carcinoma in situ: An update of the National Surgical Adjuvant Breast and Bowel Project experience.** *Semin Oncol* 2001;28(4):400-18. **Abstract**

Mirza NQ et al. **Ductal carcinoma-in-situ: Long-term results of breast-conserving therapy.** *Ann Surg Oncol* 2000;7(9):656-64. **Abstract**

Surgeons and Aromatase Inhibitors in the Adjuvant Setting

Surgeons: If the ATAC data are widely accepted and anastrozole generally replaces tamoxifen as adjuvant endocrine therapy for postmenopausal women, which of the following best describes how likely it is that surgeons will prescribe anastrozole?



Surgeons: How would you manage the following 65-year-old woman with ER-positive invasive breast cancer?

	0.8 cm, node-neg	2.2 cm, 1+ node
Refer to medical oncologist	50%	85%
Start tamoxifen and refer to medical oncologist	—	5%
Start anastrozole and refer to medical oncologist	20%	5%
Manage primarily without adjuvant therapy	5%	—
Manage primarily with tamoxifen	5%	—
Manage primarily with anastrozole	20%	5%

Commentary

With the increased use of chemotherapy in women with invasive breast cancer, many surgeons routinely refer patients for evaluation by a medical oncologist. However, it is also a common practice for surgeons to initiate adjuvant endocrine therapy with tamoxifen.

The patterns of care survey demonstrates that this practice is also likely to occur with adjuvant aromatase inhibitors in postmenopausal patients. Surgeons are more likely to initiate adjuvant endocrine therapy in lower-risk patients, who are less likely to receive adjuvant chemotherapy. Almost one-third of surgeons would manage an older patient with a small, node-negative tumor without referral to a medical oncologist.

Select publications

Baum M. **The ATAC (Arimidex, Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in post-menopausal women.** *Breast Cancer Res Treat* 2001;69(3):**Abstract 8.**

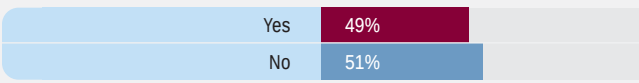
Sentinel Lymph Node Biopsy (SLNB)

Miami meeting attendees:

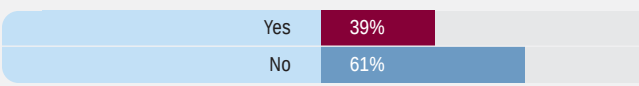
What technique do you utilize in performing sentinel lymph node biopsies?

	Surgeons	Miami meeting attendees
Dye	8%	14%
Radioisotope	8%	7%
Both	84%	79%

Is SLNB a good option for a woman with a 2 cm lesion high in the upper-outer quadrant in the tail of Spence?



Have you done SLNB in a woman with DCIS?



Commentary

Sentinel lymph node biopsy (SLNB) has been shown to be accurate using a variety of techniques and a variety of dyes and tracers. Most surgeons performing sentinel node biopsies utilize both dye and radioisotopes to identify the sentinel node.

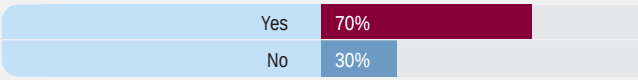
Overall, surgeons report that about two-thirds of the SLNBs performed are negative, sparing the patient the need for axillary dissection. SLNB is now being utilized in some patients with DCIS, and more than one-third of surgeons have done an SLNB in a DCIS patient.

Select publications

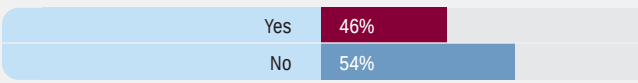
Cox CE. **Lymphatic mapping in breast cancer: Combination technique.** *Ann Surg Oncol* 2001;8(9 Suppl):67S-70S. **Abstract**

When Is Sentinel Lymph Node Biopsy (SLNB) Appropriate?

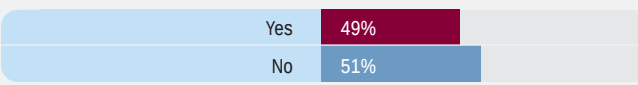
Miami meeting attendees: Is SLNB currently the standard of care for patients with clinical T1NO disease?



Is SLNB useful after neoadjuvant chemotherapy?



Is SLNB a good option for a woman with 2 lesions in different quadrants (upper-outer and lower-inner) of the breast?



Commentary

More than two-thirds of the surgeons believe that SLNB is now the standard of care, although both the American College of Surgeons and the NSABP have current clinical trials addressing this question. However, there is considerable controversy about the role of SLNB in several groups of patients, including patients who have undergone neoadjuvant therapy and those with more than one lesion in the same breast.

Select publications

Haid A et al. **Is sentinel lymph node biopsy reliable and indicated after preoperative chemotherapy in patients with breast carcinoma?** *Cancer* 2001;92:1080-4. **Abstract**

Julian TB et al. **Sentinel lymph node biopsy after neoadjuvant chemotherapy for breast cancer.** *Am J Surg* 2001;182(4):407-10. **Abstract**

Klauber-DeMore N et al. **Sentinel lymph node biopsy: Is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion?** *Ann Surg Oncol* 2000;7(9):636-42. **Abstract**

Postmastectomy Radiation Therapy

Would you recommend postmastectomy radiation therapy for the following patients with 4.2 cm tumors? (percent answering yes)

	Surgeons	Miami meeting attendees
43-year-old with neg nodes	25%	n/a
65-year-old with neg nodes	20%	n/a
43-year-old with 3+ nodes	75%	67%
65-year-old with 3+ nodes	65%	n/a
43-year-old with 5+ nodes	80%	85%
65-year-old with 5+ nodes	80%	n/a
78-year-old with 5+ nodes	75%	71%

Commentary

The 2000 NIH Consensus Conference and the NCCN guidelines indicate that postmastectomy radiation therapy is standard for women with four or more positive axillary lymph nodes. A small but significant fraction of physicians do not follow this practice, and many respondents indicate that they recommend radiation therapy for women with three positive nodes. Age does not seem to be an important factor in this decision. Patients with one to three positive nodes are currently being studied in a large Intergroup randomized clinical trial.

Select publications

Arriagada R. **Radiotherapy for breast cancer.** *N Engl J Med* 2002;346(11):862-4. **Abstract**

Hurkmans CW et al. **Reduction of cardiac and lung complication probabilities after breast irradiation using conformal radiotherapy with or without intensity modulation.** *Radiother Oncol* 2002;62(2):163-71. **Abstract**

Pierce LJ. **Treatment guidelines and techniques in delivery of postmastectomy radiotherapy in management of operable breast cancer.** *J Natl Cancer Inst Monogr* 2001;30:117-124. **Abstract**

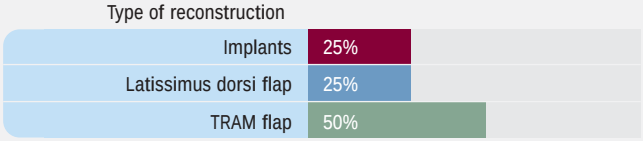
Recht A et al. **Postmastectomy radiotherapy: Clinical practice guidelines of the American Society of Clinical Oncology.** *J Clin Oncol* 2001;19(5):1539-69. **Abstract**

Type and Timing of Breast Reconstruction

The following patients have 2 cm, poorly differentiated, ER-negative, infiltrating ductal carcinoma and wish to undergo mastectomy and reconstruction. What type and timing of breast reconstruction would you generally recommend?

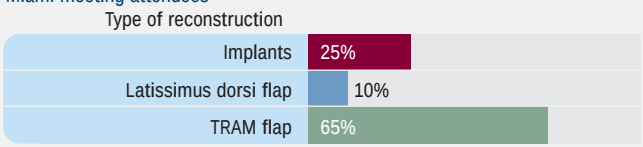
43-YEAR-OLD WOMAN

Surgeons



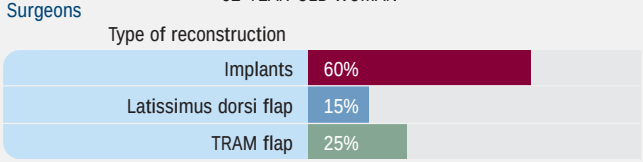
65% recommend immediate reconstruction

Miami meeting attendees



62-YEAR-OLD WOMAN

Surgeons



50% recommend immediate reconstruction

Commentary

While at least half of the surgeons (in the community and attending the Miami meeting) would perform reconstruction with a TRAM flap in a 43-year-old woman, significantly fewer would do so in a 62-year-old woman, with more surgeons opting to use breast implants for reconstruction. About half of the surgeons recommend immediate as opposed to delayed reconstruction.

Therapy for Local Recurrence

The following patients had an 0.8 cm, cribriform DCIS excised with 1 cm margins and were treated with radiation and tamoxifen. What would you recommend for a local recurrence one year after the initial therapy?

- 43-year-old woman with DCIS recurrence

Local therapy	Surgeons	Miami meeting attendees
Re-excision	30%	55%
Mastectomy	70%	45%

- 78-year-old woman with DCIS recurrence

Local therapy	Surgeons	Miami meeting attendees
Re-excision	60%	68%
Mastectomy	40%	32%

- 43-year-old woman with invasive cancer recurrence

Local therapy	Surgeons
Re-excision	16%
Mastectomy	84%

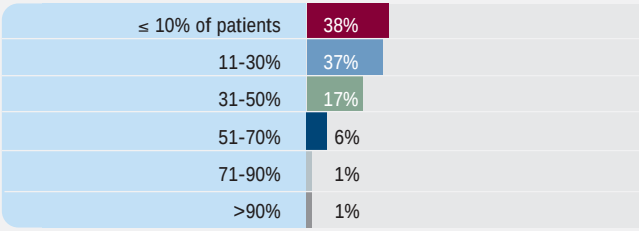
Commentary

There is a significant divergence of opinion for the preferred surgical approach to the patient with a local recurrence of DCIS. Surgeons consistently prefer mastectomy when the recurrence is invasive.

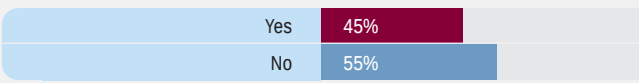
Systemic therapy in this situation is controversial, and the NSABP is considering a trial to evaluate the combination of docetaxel and capecitabine for patients with invasive recurrences. In the patient who recurs while on tamoxifen, most surgeons would continue some type of endocrine therapy. In the elderly patient, nearly a third of surgeons would prefer an aromatase inhibitor over tamoxifen.

Local Management of Primary Breast Cancer

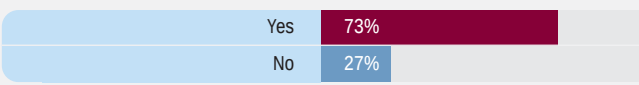
How many of your breast cancer patients when presented with the option of breast conservation choose to have a mastectomy?



Do you ever perform modified radical mastectomy on an outpatient basis?



Do you ever perform skin-sparing mastectomy?



Commentary

Patterns of care studies have demonstrated significant variation in the use of lumpectomy. Various factors have been attributed to this observation including physician bias towards mastectomy. Many academic-based breast surgeons have breast conservation rates in excess of 80%, and both Miami meeting attendees and faculty believe that women clearly prefer breast conservation.

Outpatient breast cancer surgery has received a mixed reception in community practice. About half of surgeons attending the Miami meeting have performed an outpatient mastectomy, and about two-thirds of attendees have performed outpatient axillary dissection. Skin-sparing surgery is now widely accepted as a cosmetically superior procedure with broad indications; however, about one-quarter of surgeons attending the Miami meeting do not perform this procedure.

Breast Cancer™
UPDATE

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This program was supported by educational grants from AstraZeneca Pharmaceuticals, LP, and Cytyc Health Corporation.

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