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Special Report

19th Annual
Miami Breast Cancer Conference

Loews Miami Beach Hotel
Miami Beach, Florida

February 27 - March 2, 2002

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For a complete listing of the results of the Miami Breast Cancer Conference patterns of care study and interactive questions, go to BreastCancerUpdate.com. Patterns of care cases generally reflect samples of 20 physicians of the 200 in the study. Interactive questions reflect the fraction of 965 attendees responding.

Clinical decision-making in the absence of definitive research data

"Many of us were cautious about the use of tamoxifen in women with node-negative breast cancer in the 1980s and in premenopausal women until about 1995. Subsequently, the Breast Cancer Overview demonstrated that adjuvant tamoxifen was beneficial in those subsets. I am sure I had women die of breast cancer needlessly … if I had only possessed a crystal ball and given them tamoxifen. I feel bad about that, and it has worried me. On the other hand, I did not use high-dose chemotherapy outside the context of a clinical trial even though the data looked promising. Since the randomized trials failed to demonstrate a benefit, I feel good that I did not fast forward the clock and have patients die of leukemia or high-dose-related complications unless they had agreed to be part of a clinical trial. Admittedly, I am cautious and have been for years."

—Daniel Hayes, MD
University of Michigan
Interview for Breast Cancer Update

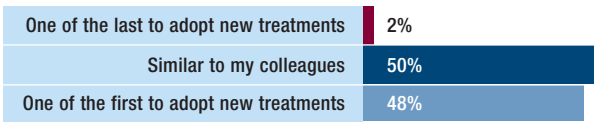
The management of patients with breast cancer has always been fraught with challenging decisions. For more than two decades, physicians and patients have struggled with choices in breast conservation, and the emergence of neoadjuvant regimens to downstage tumors has made these decisions even more complex. As noted by Dr Hayes, the controversies surrounding the use of systemic therapy are similarly challenging.

Part of this formidable task is the result of the rapid evolution of breast cancer clinical research, which constantly generates provocative but often inconclusive data. Dan Hayes recapitulates the dilemma — if we move too quickly, our patients may experience morbidity from unnecessary treatment; however, if we act too slowly, we may abrogate an opportunity for a potentially life-saving intervention.

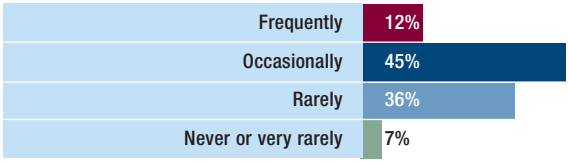
The Miami Breast Cancer Conference — now in its 19th year under the direction of Dr Daniel Osman — has always addressed these controversies directly. For years, using electronic keypad polling, we have posed questions about clinical scenarios and compared answers from attendees and faculty members. For 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 special supplement documents key results from this survey, answers to the interactive questions posed to the Miami Breast Cancer Conference (MBCC) attendees and select answers from our faculty. 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 MBCC, who by their presence at a 3-day breast cancer meeting are presumably more "up to speed." The following questions from the MBCC are particularly interesting in that regard:

MBCC attendees: Which statement best describes how you incorporate new clinical research results into your practice, relative to your colleagues?



MBCC attendees: How often do you encounter physicians in referral situations who practice outside the bounds of practice guidelines/standards of care?



These responses suggest that, as one might expect, Miami Breast Cancer Conference attendees view themselves as being proactive in the application of new research results. It is somewhat disconcerting to note that these physicians believe a significant number of their colleagues appear to practice outside the bounds of widely accepted practice standards. A casual perusal of the enclosed supplement also supports this notion. For instance, a small yet significant number of physicians prescribe aromatase inhibitors without ovarian suppression in premenopausal women — a practice that is not supported by research data.

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 supplement is intended to stimulate discussion on precisely that issue.

The final section of this report summarizes seven tumor panel cases presented by the MBCC to the meeting attendees. Drs Stephen Jones, Kathy Miller, Patrick Borgen, Richard Margolese, Frank Vicini and Eleftherios Mamounas (who also served as consultants to our patterns of care study) selected interesting cases from their own practices, and the audience and other faculty members contributed their viewpoints on how they would manage these patients.

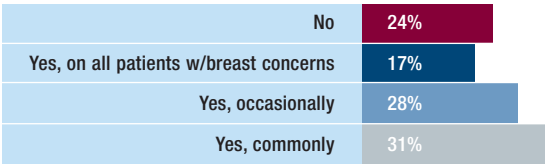
These cases typify the challenges encountered in breast cancer medicine. Even breast cancer research leaders struggle with the application of clinical trial results. Dr Margolese agonizes over a 70-old-woman who is BRCA1-positive, and he decides to follow her without intervention. Two years later, she develops a 6 cm, invasive breast tumor. Dr Jones' patient enrolls in a randomized clinical trial and experiences a prolonged complete response to capecitabine/docetaxel. Now, 5 years later, Dr Jones must decide whether or not to continue therapy. Dr Mamounas uses pre-op chemotherapy after fine needle aspiration of a breast and axillary mass, but now, after complete pathologic tumor response, there is no estrogen receptor data available. Dr Borgen employs neoadjuvant tamoxifen and, later, anastrozole. Then, he must decide whether this frail, elderly woman with severe cardiovascular disease should undergo definitive local surgery.

Seventeen years ago, in a small Boston café, Dr Craig Henderson made an amusing analogy that seems even more relevant today. He said, "Most people who are breast cancer mavens today would have been sitting on a little knoll debating the Talmud 1,500 years ago." The patterns of care data presented here confirms the diversity of viewpoints and proves that there is not yet a "Talmudic" truth when it comes to applying emerging research findings to breast cancer treatment decisions.

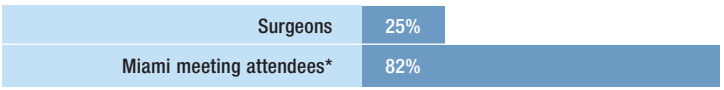
— Neil Love, MD
Editor, Breast Cancer Update

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 MBCC 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 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**

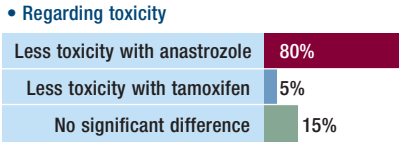
Port ER et al. **Patient reluctance toward tamoxifen use for breast cancer primary prevention.** *Ann Surg Oncol* 2001;8(7):580-5. **Abstract**

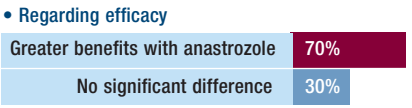
Rockhill B et al. **Validation of the Gail et al. model of breast cancer risk prediction and implications for chemoprevention.** *J Natl Cancer Inst* 2001;93(5):358-66. **Abstract**

Vogel VG. **Follow-up of the breast cancer prevention trial and the future of breast cancer prevention efforts.** *Clin Cancer Res* 2001;7(Suppl 12):4413s-18s. **Abstract**

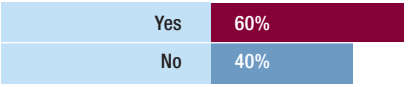
Implications of the ATAC Trial in Chemoprevention

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.

Select publications

Dowsett M. **Theoretical considerations for the ideal aromatase inhibitor.** *Breast Cancer Res Treat* 1998;49 Suppl 1:S39-44. **Abstract**

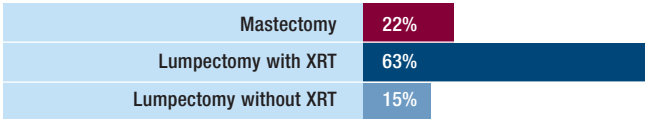
Goss PE, Strasser K. **Aromatase inhibitors in the treatment and prevention of breast cancer.** *J Clin Oncol* 2001;19(3):881-94. **Abstract**

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

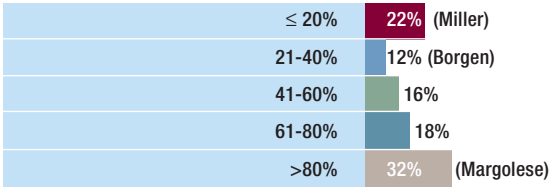
Santen RJ, Harvey HA. **Use of aromatase inhibitors in breast carcinoma.** *Endocr Relat Cancer* 1999;6(1):75-92. **Abstract**

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**

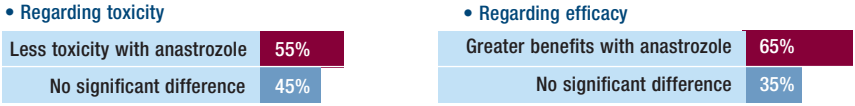
Mirza NQ et al. **Ductal carcinoma-in-situ: Long-term results of breast-conserving therapy.** *Ann Surg Oncol* 2000;7(9):656-64. **Abstract**

Skinner KA, Silverstein MJ. **The management of ductal carcinoma in situ of the breast.** *Endocr Relat Cancer* 2001;8(1):33-45. **Full-text**

Winchester DP et al. **The diagnosis and management of ductal carcinoma in-situ of the breast.** *CA Cancer J Clin* 2000;50(3):184-200. **Full-text**

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.**

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

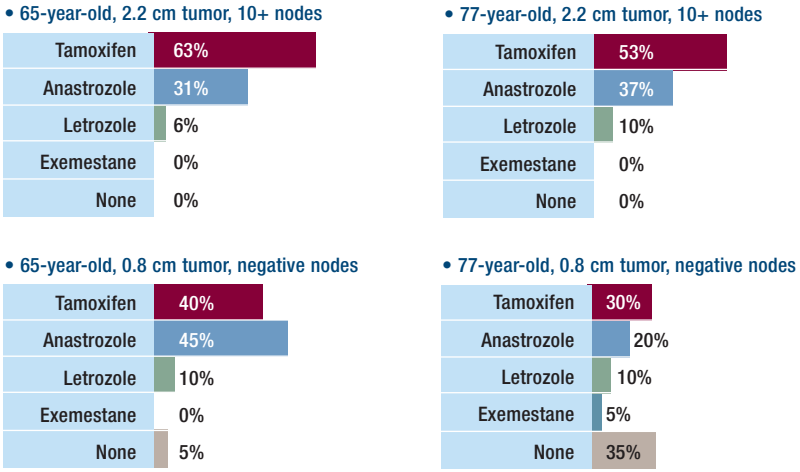
Fabian CJ, Kimler BF. **Beyond tamoxifen: New endpoints for breast cancer chemoprevention, new drugs for breast cancer prevention.** *Ann NY Acad Sci* 2001;952:44-59. **Abstract**

O'Regan RM, Jordan VC. **Tamoxifen to raloxifene and beyond.** *Semin Oncol* 2001;28(3):260-73. **Abstract**

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

Adjuvant Endocrine Therapy in Postmenopausal Women: Impact of the Early ATAC Trial Results

Oncologists: Which adjuvant endocrine therapy would you recommend for the following patients with ER-positive, HER2-negative breast cancer?



Commentary

Just a few weeks after the presentation of the early ATAC trial results, anastrozole was rapidly incorporated into the adjuvant setting. In some clinical situations, almost half of oncologists surveyed state that they are utilizing adjuvant anastrozole. While some physicians may propose letrozole or exemestane, the vast majority employing an adjuvant aromatase inhibitor prefer anastrozole.

Also note that while almost all of these women with ER-positive disease receive some form of endocrine therapy, a significant minority of oncologists would not prescribe endocrine therapy for elderly, low-risk women.

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.

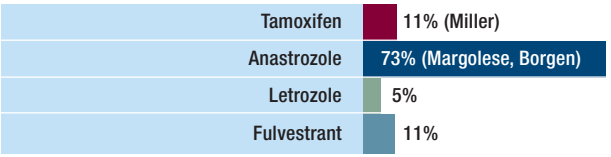
Buzdar AU. **Anastrozole (Arimidex) —- an aromatase inhibitor for the adjuvant setting?** *Br J Cancer* 2001;85(2 suppl):6-10. Abstract

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

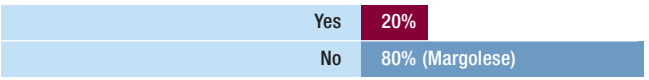
Adjuvant Endocrine Therapy: Current and Future Use of Aromatase Inhibitors

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. Faculty members Drs Richard Margolese and Patrick Borgen concur with this belief. Of note, nearly 20% believe anastrozole will almost completely replace tamoxifen in these patients this year.

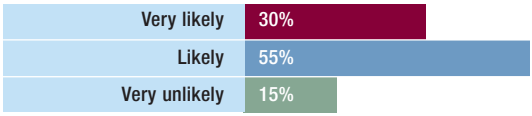
This viewpoint was confirmed in physicians' predictions for clinical practice three years from now, with nearly three-quarters stating that anastrozole will be the most commonly utilized adjuvant endocrine therapy. Interestingly, there is a lack of support of the other aromatase inhibitors as adjuvant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

Select publications

Nicholls H. **Aromatase inhibitors continue their ATAC on tamoxifen.** *Trends Mol Med* 2002;8(4):S12-3. **Abstract**

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.

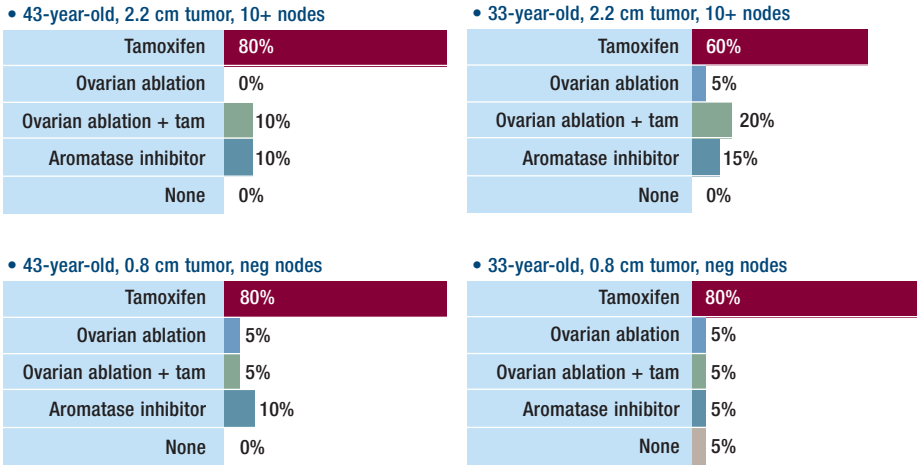
Select publications

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.**

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

Adjuvant Endocrine Therapy in Premenopausal Women

Oncologists: Which adjuvant endocrine therapy would you recommend for the following patients with ER-positive, HER2-negative breast cancer who continue to menstruate after receiving chemotherapy?



Commentary

Nearly all physicians would recommend some form of adjuvant endocrine therapy for premenopausal women with ER-positive cancers, and tamoxifen remains the common choice. Only a small fraction of physicians utilize LHRH agonists or surgical oophorectomy despite findings from an international meta-analysis demonstrating a significant survival advantage for this intervention. A small fraction of oncologists recommend aromatase inhibitors for premenopausal women; however, these agents are only indicated for postmenopausal women. The encouraging early results of the ATAC trial in postmenopausal patients has led to the development of new randomized clinical studies evaluating LHRH agonists plus aromatase inhibitors in premenopausal patients with ER-positive tumors. Until results from these studies are available, most clinical researchers generally do not advocate the nonprotocol use of this combined approach.

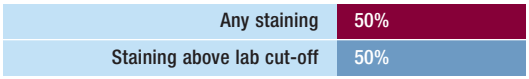
Select publications

Ovarian ablation for early breast cancer. Early Breast Cancer Trialists' Collaborative Group. *Cochrane Database Syst Rev.* 2000:CD000485. Abstract

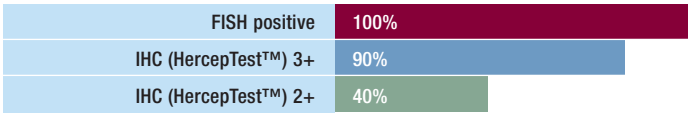
Davidson NE. **Ovarian ablation as adjuvant therapy for breast cancer.** *J Natl Cancer Inst Monogr* 2001;30:67-71. Abstract

Assessment of ER and HER2 Status

Oncologists: How do you define ER-positivity?



Oncologists: Which of the following lab results would you interpret as HER2-positive?



Oncologists: How often do you obtain FISH results on your patients?

Commentary

A widely quoted study by Harvey et al found that even those breast cancer patients with 1-2% of cells with weak tumor ER staining benefit from adjuvant hormonal therapy. Allred has questioned the quality control for the performance of this assay and assay interpretation by clinicians managing breast cancer patients. While half of responding oncologists treat breast cancers as ER-positive if they have any staining on immunohistochemistry, another half utilize a laboratory-defined cut-off for this definition.

A common algorithm for determining HER2 status, which is supported by the NCCN, accepts an immunohistochemistry score of 3+ as positive, but recommends FISH testing in tumors with an IHC score of 2+. This approach is reflected in data from the oncologists' survey. Only 35% commonly obtain FISH testing in their patients.

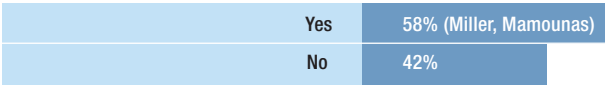
Select publications

Harvey JM et al. **Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer.** *J Clin Oncol* 1999;17:1474-81. **Abstract**

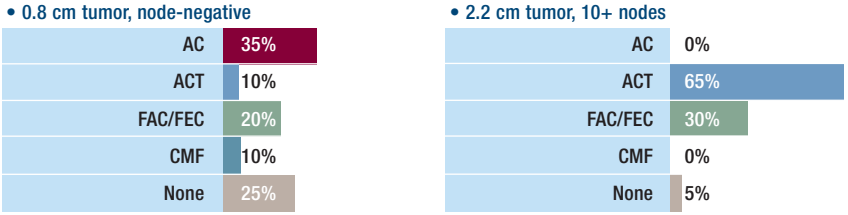
Perez EA et al. **HER2 testing in patients with breast cancer: Poor correlation between weak positivity by immunohistochemistry and gene amplification by fluorescence in situ hybridization.** *Mayo Clin Proc* 2002;77(2):148-54. **Abstract**

Choice of Adjuvant Chemotherapy

Miami meeting attendees: Do you think six cycles of FAC is more effective than four cycles of AC?



Oncologists: Which adjuvant chemotherapy regimen would you use in the following 43-year-old women with ER-negative, HER2-negative breast cancer?



Commentary

There was considerable discussion at the 2000 NIH Consensus Conference on the benefits of 4 cycles of AC chemotherapy compared to a longer duration. Dr Gabriel Hortobagyi argued that indirect evidence supported the use of a longer duration, but the Consensus statement reflected that there was inadequate data to make this a standard recommendation.

Although a large proportion of physicians (including Drs Miller and Mamounas) believe that 6 cycles of FAC is more effective than 4 cycles of AC, the addition of a taxane to the AC regimen was a more common treatment choice. Clearly, in the higher-risk patient, the vast majority of physicians believed AC chemotherapy to be inadequate treatment.

Select publications

National Institutes of Health Consensus Development Conference statement: Adjuvant therapy for breast cancer, November 1-3, 2000. *J Natl Cancer Inst Monogr* 2001;(30):5-15. **Abstract**

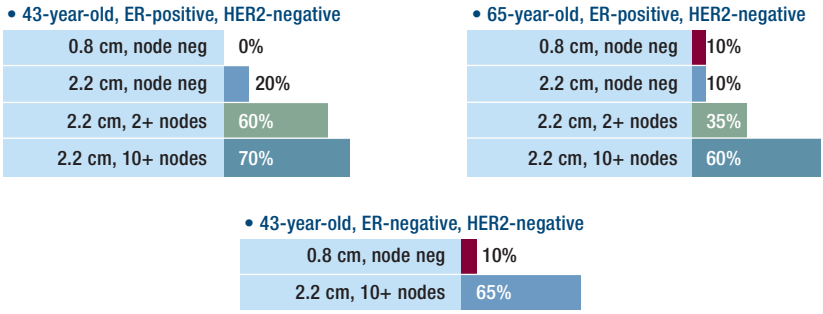
Aapro MS. **Adjuvant therapy of primary breast cancer: A review of key findings from the 7th international conference, St. Gallen, February 2001.** *Oncologist* 2001;6(4):376-85. **Abstract**

Hortobagyi GN. **Progress in systemic chemotherapy of primary breast cancer: An overview.** *J Natl Cancer Inst Monogr* 2001;(30):72-9. **Abstract**

Shulman LN. **What is the ideal duration of adjuvant therapy for primary breast cancer: Are four cycles of cyclophosphamide and doxorubicin enough?** *Curr Oncol Rep* 2001;3(6):523-8. **Abstract**

Use of Taxanes in the Adjuvant Setting

Oncologists: Would you use adjuvant taxanes in the following patients? (percent answering yes)



Commentary

Although the 2000 NIH Consensus Conference on adjuvant therapy of early breast cancer did not reach a consensus on the issue of adjuvant taxanes, community practitioners use adjuvant taxanes frequently, especially in women with high-risk tumors. The impact of age appears to be greatest in the women with intermediate risk, with 60% of oncologists treating a 43-year-old woman with a 2.2 cm tumor and 2+ nodes with taxanes, while only 35% would treat the 65-year-old with similar risk. The impact of ER status appears negligible, despite an unplanned retrospective subset analysis in a large Intergroup trial demonstrating less benefit of paclitaxel in women with ER-positive than ER-negative tumors.

Select publications

Mamounas EP, Sledge GW Jr. **Combined anthracycline-taxane regimens in the adjuvant setting.** *Semin Oncol* 2001;28(4 Suppl 12):24-31. **Abstract**

Nabholtz JM, Riva A. **The choice of adjuvant combination therapies with taxanes: Rationale and issues addressed in ongoing studies.** *Clin Breast Cancer* 2001;2 Suppl 1:S7-S14. **Abstract**

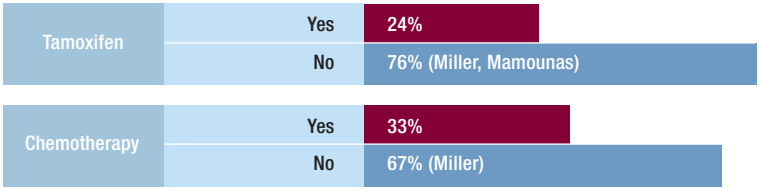
Norton L. **Theoretical concepts and the emerging role of taxanes in adjuvant therapy.** *Oncologist* 2001;6 Suppl 3:30-5. **Abstract**

Piccart MJ et al. **Taxanes in the adjuvant treatment of breast cancer: Why not yet?** *J Natl Cancer Inst Monogr* 2001;(30):88-95. **Abstract**

Sparano JA. **Taxanes for breast cancer: An evidence-based review of randomized phase II and phase III trials.** *Clin Breast Cancer* 2000:32-40. **Abstract**

HER2 Status in Determining Adjuvant Therapy

Miami meeting attendees: Should HER2 status be considered in deciding whether or not to use the following agents in the adjuvant setting?



Oncologists: Which adjuvant therapy would you give to a 43-year-old woman with a 0.8 cm, ER-positive, node negative breast cancer based on HER2 status?

	HER2 Status	
Chemotherapy	HER2-positive	HER2-negative
AC	25%	30%
ACT	10%	—
FAC	20%	—
No chemotherapy	45%	70%
Endocrine therapy		
Tamoxifen	70%	75%

Commentary

Most physicians state that they do not believe that decisions regarding whether to use adjuvant chemotherapy or endocrine therapy should be influenced by HER2 status of the patient's tumor. However, there is a significant tendency for oncologists to choose less aggressive or no cytotoxic therapy in patients who have HER2-negative as opposed to HER2-positive tumors. Anthracycline-based chemotherapy is routinely utilized in women with both HER2-positive and HER2-negative cancers as adjuvant therapy. Choice of endocrine therapy, particularly tamoxifen, is not influenced by HER2 status, which is consistent with the lack of conclusive evidence on this question in a variety of clinical trials.

Select publications

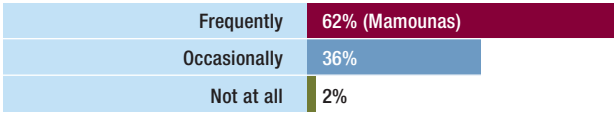
Piccart M et al. **The predictive value of HER2 in breast cancer.** *Oncology* 2001;61 Suppl 2:73-82. **Abstract**

Ravdin PM. **Is her2 of value in identifying patients who particularly benefit from anthracyclines during adjuvant therapy? A qualified yes.** *J Natl Cancer Inst Monogr* 2001;30:80-4. **Abstract**

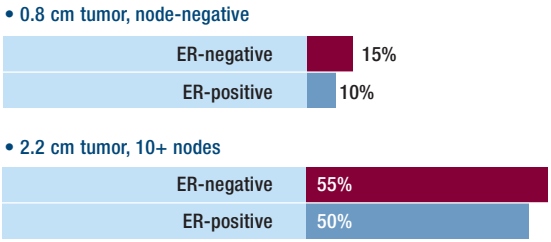
Sledge GW Jr. **Is HER-2/neu a predictor of anthracycline utility? No.** *J Natl Cancer Inst Monogr* 2001;30:85-7. **Abstract**

Use of Trastuzumab in the Adjuvant Setting

Miami meeting attendees: To what extent will trastuzumab be used as adjuvant therapy for patients with HER2-positive breast cancer 5 years from now?



Oncologists: Would you currently use adjuvant trastuzumab for the following 43-year-old patients with HER2-positive disease? (percent answering yes)



Commentary

The risks and benefits of adjuvant trastuzumab are currently under investigation in several large, randomized clinical trials. Most breast cancer research leaders believe that this intervention should only be utilized in a research setting. However, when presented with a young patient at high risk for recurrence because of multiple positive nodes, about half of physicians would use adjuvant trastuzumab if the tumor were HER2-positive. This practice seems to apply to patients with both ER-positive and ER-negative tumors. A small but significant number of physicians would also utilize trastuzumab in lower-risk women.

Select publications

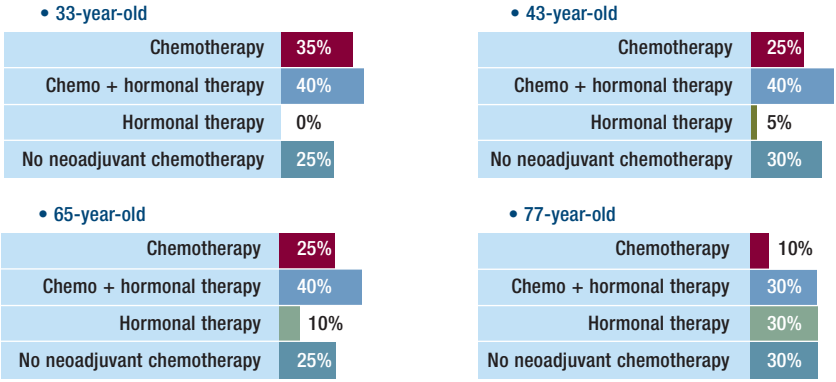
Leyland-Jones B, Smith I. **Role of Herceptin in primary breast cancer: Views from North America and Europe.** *Oncology* 2001;61 Suppl 2:83-91. **Abstract**

Nabholtz JM, Slamon D. **New adjuvant strategies for breast cancer: Meeting the challenge of integrating chemotherapy and trastuzumab (Herceptin).** *Semin Oncol* 2001;28(1 Suppl 3):1-12. **Abstract**

Slamon D, Pegram M. **Rationale for trastuzumab (Herceptin) in adjuvant breast cancer trials.** *Semin Oncol* 2001;28(1 Suppl 3):13-9. **Abstract**

Neoadjuvant Systemic Therapy

Oncologists: **The following patients with 2.8 centimeter, ER-positive, HER2-negative breast cancers desire breast-conserving surgery; however, their breasts are too small to allow a good cosmetic outcome with lumpectomy at the present time. Which neoadjuvant regimen would you use?**



(See next page for choice of hormonal therapy)

Commentary

A majority of oncologists would use neoadjuvant systemic therapy of some kind in these patients. Note the frequent use (40-75%) of neoadjuvant chemotherapy alone or in combination with hormonal therapy, regardless of the patient's age. The most commonly utilized neoadjuvant chemotherapy regimen is AC. Elderly patients are the only group in whom endocrine therapy alone is used to a significant extent.

Select publications

Aapro MS. **Neoadjuvant therapy in breast cancer: Can we define its role?** *Oncologist* 2001;6 Suppl 3:36-9. **Abstract**

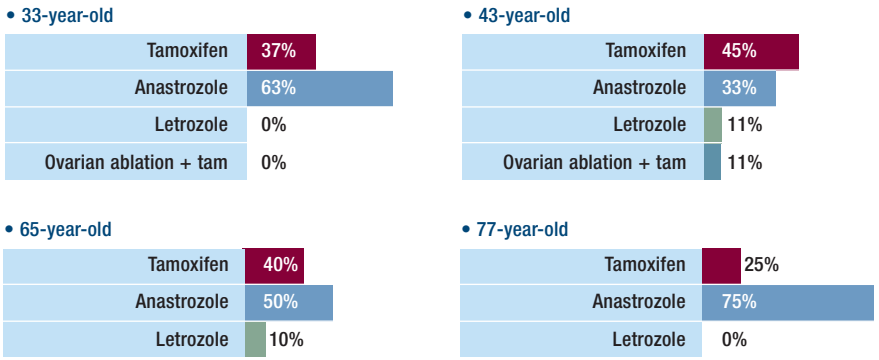
Gianni L et al. **Adjuvant and neoadjuvant treatment of breast cancer.** *Semin Oncol* 2001;28(1):13-29. **Abstract**

Mamounas EP, Fisher B. **Preoperative (neoadjuvant) chemotherapy in patients with breast cancer.** *Semin Oncol* 2001;28(4):389-99. **Abstract**

Smith IC, Miller ID. **Issues involved in research into the neoadjuvant treatment of breast cancer.** *Anticancer Drugs* 2001;12 Suppl 1:S25-9. **Abstract**

Neoadjuvant Endocrine Therapy

Oncologists: Of those using preoperative endocrine therapy, which therapy would you use in the following women with 2.8 cm, ER-positive, HER2-negative breast cancers?



Commentary

The inappropriate use of aromatase inhibitors in premenopausal women is most striking. These agents are indicated for postmenopausal women only. Also of note in postmenopausal women, aromatase inhibitors are used more often than tamoxifen, reflecting recently reported neoadjuvant studies indicating greater efficacy. Of the aromatase inhibitors, anastrozole is more widely utilized among oncologists than other agents.

Select publications

Cheung KL et al. **Preoperative endocrine therapy for breast cancer.** *Endocr Relat Cancer* 2000;7(3):131-41. **Full-text**

Dixon JM et al. **The effects of neoadjuvant anastrozole (Arimidex) on tumor volume in postmenopausal women with breast cancer: A randomized, double-blind, single-center study.** *Clin Cancer Res* 2000;6(6):2229-35. **Abstract**

Ellis MJ et al. **Letrozole is more effective neoadjuvant endocrine therapy than tamoxifen for ErbB-1- and/or ErbB-2-positive, estrogen receptor-positive primary breast cancer: Evidence from a phase III randomized trial.** *J Clin Oncol* 2001;19:3808-16. **Abstract**

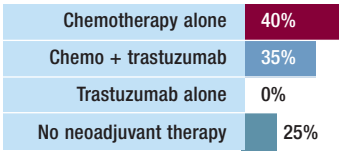
Geisler J et al. **Influence of neoadjuvant anastrozole (Arimidex) on intratumoral estrogen levels and proliferation markers in patients with locally advanced breast cancer.** *Clin Cancer Res* 2001;7:1230-6. **Abstract**

Milla-Santos A et al. **Anastrozole (A) as neoadjuvant (NEO) therapy for hormone-dependent locally advanced breast cancer (LABC) in postmenopausal (PM) patients (pts).** *Breast Cancer Res Treat* 2001;**Abstract 302.**

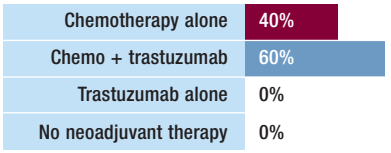
Neoadjuvant Chemotherapy and Trastuzumab

Oncologists: Would you utilize neoadjuvant chemotherapy and/or trastuzumab in the following women with ER-negative, HER2-positive breast cancers?

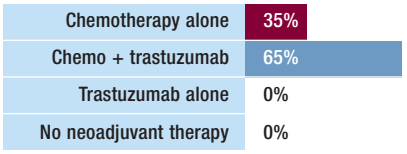
- 43-year-old, 2.2 cm tumor



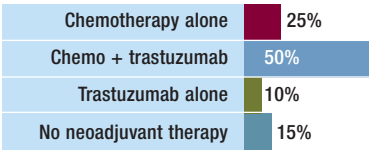
- 43-year-old, 6.5 cm tumor



- 43-year-old, inflammatory breast cancer



- 71-year-old, inflammatory breast cancer



Commentary

There are many ongoing randomized clinical trials of neoadjuvant chemotherapy with and without trastuzumab. A significant number of oncologists (35-65%) state that they would use trastuzumab in the neoadjuvant setting at the present time in a nonprotocol setting. Of the physicians using neoadjuvant trastuzumab and chemotherapy, 30-50% would use a cytotoxic regimen containing an anthracycline, despite concerns of cardiotoxicity with these agents in combination.

Select publications

Baselga J. **Current and planned clinical trials with trastuzumab (Herceptin).** *Semin Oncol* 2000;27 (5 Suppl 9):27-32. **Abstract**

Burstein HJ et al. **Preoperative trastuzumab (T) and paclitaxel (P) for HER2 overexpressing (HER2+) stage II/III breast cancer: Clinical, pathological and serological findings.** *Breast Cancer Res Treat* 2001;**Abstract 507.**

Carey LA et al. **Safety and efficacy of 4AC followed by paclitaxel plus trastuzumab in high risk breast cancer patients.** *Proc ASCO* 2001;**Abstract 1856.**

Stebbing JJ, Gaya A. **The evidence-based use of induction chemotherapy in breast cancer.** *Breast Cancer* 2001;8(1):23-37. **Abstract**

Treatment of the Premenopausal Patient with ER-positive, HER2-negative Metastatic Disease

What therapy would you utilize in a 43-year-old woman with asymptomatic bone metastases and ER-positive, HER2-negative disease?

Prior Treatment	Oncologists No prior adjuvant therapy	Miami attendees Prior adjuvant ACT
Chemo alone	—	5%
Chemo plus endocrine therapy	8%	25%
Endocrine therapy alone	92%	70%
Choice of Endocrine Therapy		
Tamoxifen	30%	28% (Miller)
Tamoxifen + ovarian ablation	—	40%
Ovarian ablation	5%	—
Aromatase inhibitor	40%	16%
Aromatase inhibitor + ovarian ablation	25%	16% (Jones)

Commentary

Almost all oncologists would give endocrine therapy to asymptomatic, ER-positive, premenopausal patients with bone metastases — primarily tamoxifen alone or combined with ovarian ablation/suppression or an aromatase inhibitor combined with ovarian ablation/suppression. It is noteworthy that 16-40% of oncologists would use single-agent aromatase inhibitors in premenopausal women, while 16-25% would use it in conjunction with ovarian ablation/suppression. Aromatase inhibitors are not indicated in the treatment of premenopausal women.

Select publications

Aebi S et al. **Is chemotherapy alone adequate for young women with oestrogen receptor-positive breast cancer?** *Lancet* 2000;355(9218):1869-74. **Abstract**

Buzdar AU. **Endocrine therapy in the treatment of metastatic breast cancer**. *Semin Oncol* 2001;28(3):291-304. **Abstract**

Cheung KL et al. **The combined use of goserelin and anastrozole as second-line endocrine therapy in premenopausal women with advanced breast cancer - a study of its clinical and endocrine effects.** *Proc ASCO* 2001;**Abstract 1937.**

Forward D et al. **Combined use of goserelin (Zoladex) and anastrozole (Arimidex) in premenopausal women with metastatic breast cancer (MBC).** *Proc ASCO* 2000;**Abstract 582.**

Hoffken K, Kath R. **The role of LH-RH analogues in the adjuvant and palliative treatment of breast cancer.** *Recent Results Cancer Res* 2000;153:61-70. **Abstract**

Treatment of the Premenopausal Patient with ER-positive, HER2-negative Metastatic Disease

What therapy would you utilize in a 43-year-old, very ill woman with visceral metastases and ER-positive, HER2-negative disease?

Prior Treatment	Oncologists Prior adjuvant ACT
Chemo alone	55%
Chemo plus endocrine therapy	30%
Endocrine therapy alone	15%
Choice of Endocrine Therapy	
Tamoxifen	22%
Aromatase inhibitor	56%
Aromatase inhibitor + ovarian ablation	22%

Commentary

In very ill women with visceral metastases, 80% of oncologists would utilize chemotherapy alone or combined with endocrine therapy.

Whether or not endocrine therapy alone is adequate in an asymptomatic patient with visceral metastases is a topic of controversy. Research leaders often note that endocrine therapy usually takes somewhat longer than chemotherapy to elicit a tumor response, so that clinical judgment involves assessing whether the patient is stable enough to wait for a response to endocrine treatment. In the adjuvant setting, chemotherapy and endocrine therapy have been proven to have an additive or synergistic effect.

Select publications

Ingle JN et al. **Evaluation of tamoxifen plus letrozole with assessment of pharmacokinetic interaction in postmenopausal women with metastatic breast cancer.** *Clin Cancer Res* 1999;5(7):1642-9. **Abstract**

Jordan C. **Historical perspective on hormonal therapy of advanced breast cancer.** *Clin Ther* 2002;24 Suppl A:A3-A16. **Abstract**

Klijn JG et al. **Combined tamoxifen and luteinizing hormone-releasing hormone (LHRH) agonist versus LHRH agonist alone in premenopausal advanced breast cancer: A meta-analysis of four randomized trials.** *J Clin Oncol* 2001;19(2):343-53. **Abstract**

Michaud LB et al. **Combination endocrine therapy in the management of breast cancer.** *Oncologist* 2001;6(6):538-46. **Abstract**

Treatment of Premenopausal Patients with ER-negative, HER2-negative Metastatic Disease

What therapy would you utilize in the following 43-year-old women with ER-negative, HER2-negative metastatic breast cancer, who received prior adjuvant ACT?

	bone mets — asymptomatic	visceral mets — very ill	
	Oncologists	Oncologists	Miami meeting attendees
Taxane	22%	5%	5%
Capecitabine	10%	5%	15%
Capecitabine/taxane	17%	20%	56%
Vinorelbine	33%	20%	9%
Vinorelbine/gemcitabine	11%	10%	—
Gemcitabine	—	10%	—
Adriamycin/taxane	—	10%	—
Other combinations	7%	20%	15%

Commentary

With an increasing fraction of breast cancer patients receiving taxane-based adjuvant systemic therapy, the dilemma of the patient presenting shortly thereafter with metastatic disease is becoming more common. There is considerable variation in choice of chemotherapy regimen in this situation. About one year after the initial results of the capecitabine/docetaxel study were first reported — demonstrating a survival advantage and a relatively favorable side-effect profile — more than half of attendees to the Miami meeting would choose this regimen, but relatively few physicians in practice follow this approach.

Select publications

Crown J. **Nonanthracycline-containing docetaxel-based combinations in metastatic breast cancer.** *Oncologist* 2001;6 Suppl 3:17-21. **Abstract**

Domenech GH, Vogel CL. **A review of vinorelbine in the treatment of breast cancer.** *Clin Breast Cancer* 2001 Jul;2(2):113-28. **Abstract**

Miles D. **Survival benefit with Xeloda (capecitabine)/docetaxel vs docetaxel: Analysis of post-study therapy.** *Breast Cancer Res Treat* 2001;**Abstract 442.**

Seidman AD. **The evolving role of gemcitabine in the management of breast cancer.** *Oncology* 2001;60(3):189-98. **Abstract**

Vukelja SJ et al. **Xeloda (capecitabine) plus docetaxel combination therapy in locally advanced/metastatic breast cancer: Latest results.** *Breast Cancer Res Treat* 2001;**Abstract 352.**

Treatment of Postmenopausal Patients with ER-negative, HER2-negative Metastatic Disease

What therapy would you utilize in the following 63-year-old women with ER-negative, HER2-negative metastatic breast cancer, who received prior adjuvant ACT?

	bone mets — asymptomatic	bone mets — multiple sites, moderate pain
	Oncologists	Miami meeting attendees
Taxane	41%	6%
Capecitabine	6%	71% (Miller, Jones)
Capecitabine/taxane	—	13%
Capecitabine/vinorelbine	8%	—
Vinorelbine	24%	6%
Vinorelbine/gemcitabine	12%	—
Other	9%	4%

	visceral mets very ill	
	Oncologists	Miami meeting attendees
Adriamycin/taxane	5%	—
Taxane	20%	—
Capecitabine	5%	40%
Capecitabine/taxane	20%	55%
Capecitabine/vinorelbine	5%	—
Vinorelbine	15%	5%
Vinorelbine/gemcitabine	5%	—
Gemcitabine	10%	—
Other combinations	15%	—

Commentary

The older patient relapsing after taxane-based adjuvant systemic therapy is commonly treated with capecitabine, either alone or in combination with a taxane. Over one-half of the oncologists attending the 2002 Miami Breast Cancer Conference would treat a 63-year-old woman with visceral metastases with the combination of capecitabine/docetaxel. Another agent commonly utilized in this situation is vinorelbine.

Select publications

Maher JF, Villalona-Calero MA. **Taxanes and capecitabine in combination: Rationale and clinical results.** *Clin Breast Cancer* 2002;2(4):287-93. **Abstract**

Single-Agent Versus Combination Chemotherapy in Metastatic Disease

Oncologists: Would you utilize single-agent or combination chemotherapy in the following women with ER-negative, HER2-negative metastatic breast cancer who received prior adjuvant ACT?

	43-year-old, asymptomatic bone metastases	43-year-old, very ill visceral metastases
Single-agent chemo	65%	40%
Combination chemo	35%	60%

	63-year-old, asymptomatic bone metastases	63-year-old, very ill visceral metastases
Single-agent chemo	80%	50%
Combination chemo	20%	50%

Commentary

Proponents of sequential single-agent chemotherapy in metastatic breast cancer believe there is no survival advantage for combination chemotherapy, and that patients are exposed to less toxicity with single agents.

Oncologists are more likely to use combination chemotherapy for patients with rapidly progressing, visceral metastases in whom a rapid response to therapy is critical. Since earlier and more effective disease control may translate into a better quality of life, some breast cancer research leaders use combination regimens earlier in the metastatic setting. If clinical trial results with newer, rationally derived, synergistic and relatively less toxic combinations demonstrate progression-free and overall survival advantages, more oncologists may adopt these combinations. Most recently, a survival advantage was observed for capecitabine/docetaxel in a trial comparing it to docetaxel alone.

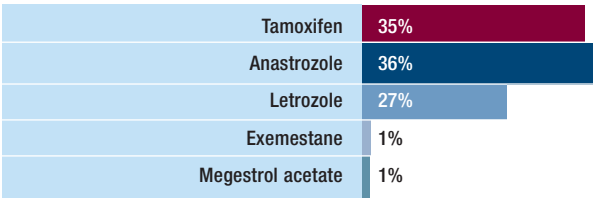
In this survey, three-quarters of oncologists reported that 60% or more of their patients receive combination chemotherapy at some point in the treatment of their metastatic disease.

Select publications

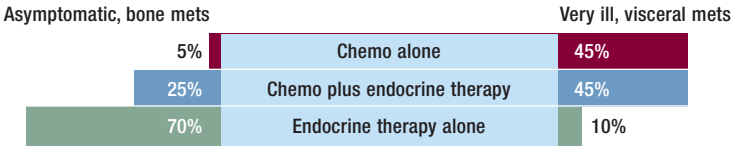
Sledge GW Jr et al. **Phase III trial of doxorubicin versus paclitaxel versus doxorubicin plus paclitaxel as first-line therapy for metastatic breast cancer: An Intergroup trial.** *Proc ASCO* 1997;**Abstract 2.**

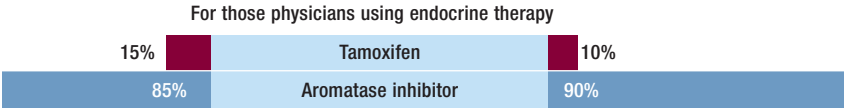
Treatment of Postmenopausal Patients with ER-positive, HER2-negative Metastatic Disease

Miami meeting attendees: What is your usual first-line hormonal agent for a 65-year-old breast cancer patient with ER-positive, HER2-negative bone metastases, who has not received adjuvant endocrine therapy?



Oncologists: What therapy would you utilize in the following 63-year-old, ER-positive, HER2-negative patients with metastatic disease who received prior adjuvant ACT?





Commentary

A number of clinical trials have demonstrated improved efficacy and less toxicity with the third-generation aromatase inhibitors compared to tamoxifen as first-line therapy for metastatic breast cancer. Currently, two-thirds of oncologists use aromatase inhibitors as first-line therapy with anastrozole and letrozole utilized about equally. About half of oncologists use a combination of chemotherapy and hormonal therapy in the highly symptomatic patient with visceral disease.

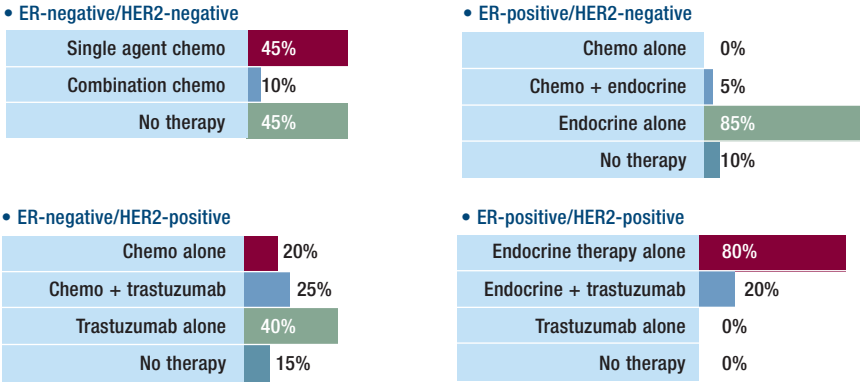
Select publications

Mouridsen H et al. **Superior efficacy of letrozole versus tamoxifen as first-line therapy for postmenopausal women with advanced breast cancer: Results of a phase III study of the International Letrozole Breast Cancer Group.** *J Clin Oncol* 2001;19(10):2596-606. **Abstract**

Nabholtz JM et al. **Anastrozole is superior to tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women: Results of a North American multicenter randomized trial. Arimidex Study Group.** *J Clin Oncol* 2000;18(22):3758-67. **Abstract**

Treatment of the Elderly Patient with Metastatic Breast Cancer

Oncologists: How would you treat the following 78-year-old women with asymptomatic bone metastases, who received no prior adjuvant therapy?



Commentary

Oncologists are reluctant to expose elderly patients to the morbidity associated with chemotherapy. Depending on the ER and HER2 status, 5-55% of oncologists would treat a 78-year-old woman with chemotherapy, most often employing single-agent therapy. In ER-positive patients 90-100% of physicians would utilize endocrine therapy, and nearly all would use an aromatase inhibitor. In ER-negative, HER2-positive patients, nearly two-thirds of oncologists would use trastuzumab, alone or in combination with chemotherapy; however, they were still more likely to use endocrine therapy in the ER-positive, HER2-positive patient. Research leaders believe HER2 overexpression may confer only partial resistance to endocrine therapies, and this effect may be more evident with tamoxifen rather than the aromatase inhibitors.

Select publications

Balducci L. **The geriatric cancer patient: Equal benefit from equal treatment.** *Cancer Control* 2001;8(2 Suppl):1-25. **Full-Text**

Du X, Goodwin JS. **Patterns of use of chemotherapy for breast cancer in older women: Findings from Medicare claims data.** *J Clin Oncol* 2001;19:1455-61. **Abstract**

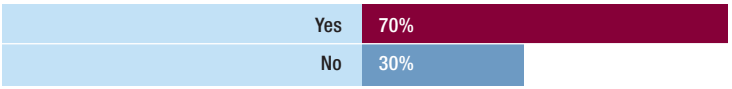
Hurria A et al. **Factors influencing treatment patterns of breast cancer (BC) patients (Pts) age 75 and older.** *Proc ASCO* 2001;**Abstract 1577.**

Kimmick GG, Muss HB. **Systemic therapy for older women with breast cancer.** *Oncology (Huntingt)* 2001;15(3):280-91. **Abstract**

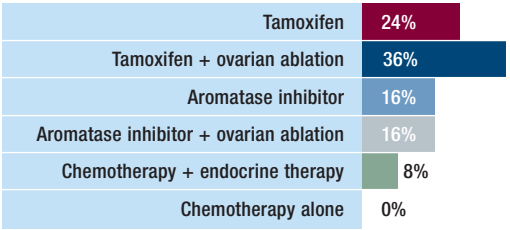
Lichtman SM, Villani G. **Chemotherapy in the elderly: Pharmacologic considerations.** *Cancer Control* 2000;7(6):548-56. **Full-Text**

Combined Use of Aromatase Inhibitors and Ovarian Ablation for Metastatic Breast Cancer

Oncologists: Have you utilized an aromatase inhibitor in combination with ovarian ablation?



Miami meeting attendees: What therapy would you recommend for a 43-year-old premenopausal woman with ER-positive, HER2-negative, asymptomatic bone metastases who received no adjuvant therapy?



Commentary

Clinical data have demonstrated an advantage for LHRH agonists plus tamoxifen when compared to LHRH agonists alone in premenopausal patients with metastatic disease. Unfortunately, there are no data comparing the combination to tamoxifen alone. Among oncologists surveyed, over one-third would treat a premenopausal woman with an LHRH agonist/tamoxifen regimen, and one-quarter would utilize tamoxifen alone. Interestingly, nearly 20% would combine an aromatase inhibitor with ovarian ablation to treat a 43-year-old patient with asymptomatic bone metastases — a maneuver that has been utilized by 70% of oncologists in certain patients at some point in their practice.

Select publications

Celio L et al. **Premenopausal breast cancer patients treated with a gonadotropin-releasing hormone analog alone or in combination with an aromatase inhibitor: A comparative endocrine study.** *Anticancer Res* 1999;19:2261-8. **Abstract**

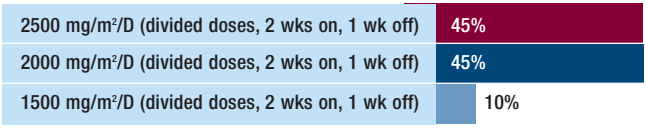
Cheung KL et al. **The combined use of goserelin and anastrozole as second-line endocrine therapy in premenopausal women with advanced breast cancer — a study of its clinical and endocrine effects.** *Proc ASCO* 2001;**Abstract 1937.**

Forward D et al. **Combined use of goserelin (Zoladex) and anastrozole (Arimidex) in premenopausal women with metastatic breast cancer (MBC).** *Proc ASCO* 2000;**Abstract 582.**

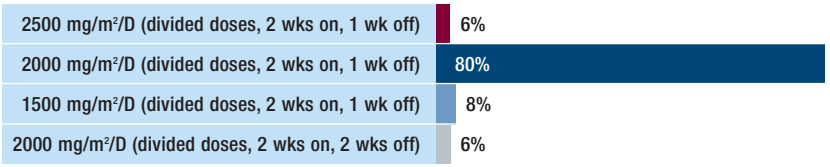
Ingle JN et al. **Combination hormonal therapy involving aromatase inhibitors in the management of women with breast cancer.** *Endocr Relat Cancer* 1999;6:265-9. **Abstract**

Dosing and Scheduling of Capecitabine

Oncologists: What dosing schedule for capecitabine do you generally use for a 55-year-old patient?



Oncologists: What dosing schedule for capecitabine do you generally use for a 75-year-old patient?



Commentary

While 2500 mg/m²/day is the approved dose for capecitabine, retrospective studies have demonstrated no decrement in response associated with reducing the dose to 2000 mg/m²/day. While nearly half of respondents would start a 55-year-old woman at full-dose capecitabine, three-quarters would reduce this to 2000 mg/m²/day for a 75-year-old woman. A current adjuvant capecitabine trial in elderly women will utilize this reduced dose. The primary dose-limiting toxicity for capecitabine use is hand-foot syndrome.

Select publications

Fujimoto-Ouchi K et al. **Schedule dependency of antitumor activity in combination therapy with capecitabine/5'-deoxy-5-fluorouridine and docetaxel in breast cancer models.** *Clin Cancer Res* 2001;7(4):1079-86. **Abstract**

Michaud LB et al. **Improved therapeutic index with lower-dose capecitabine in metastatic breast cancer (MBC) patients (Pts).** *Proc ASCO* 2000; **Abstract 402.**

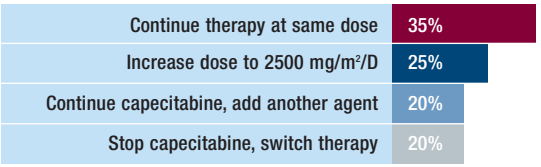
O'Shaughnessy J. **Clinical experience of capecitabine in metastatic breast cancer.** *Eur J Cancer* 2002;38 Suppl 2:10-4. **Abstract**

O'Shaughnessy J et al. **A retrospective evaluation of the impact of dose reduction in patients treated with Xeloda (capecitabine).** *Proc ASCO* 2000; **Abstract 400.**

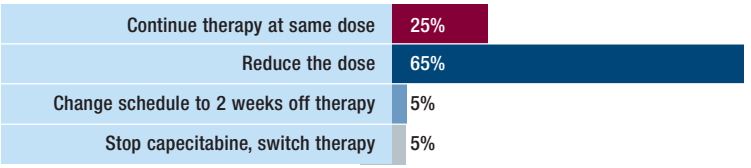
Dosing and Scheduling of Capecitabine

Oncologists: A 55-year-old, asymptomatic woman with lung metastases was started on capecitabine at 2000 mg/m²/day given in two divided doses for 2 weeks on, then one week off.

Scenario 1: After 3 cycles, there is no change in the lesions and no side effects of therapy. What would you generally do?



Scenario 2: After 3 cycles, there is an objective response in the lung lesions, but the patient complains of mild pain and redness in her hands and feet. What would you generally do?



Commentary

In a patient who is tolerating capecitabine but not responding, 25% of oncologists would dose-escalate. Although stable disease in the asymptomatic patient with metastases is widely viewed as a positive effect of therapy, about two-thirds of oncologists would make some change in such a patient.

In the patient developing mild symptoms of hand-foot syndrome, early intervention with dose reductions or changes in schedule are usually recommended by research leaders, who also emphasize the importance of educating patients to notify physicians about these symptoms. Two-thirds of the oncologists report that less than half of their patients on capecitabine develop side effects requiring some type of intervention.

Select publications

O'Shaughnessy J. **Clinical experience of capecitabine in metastatic breast cancer.** *Eur J Cancer* 2002;38 Suppl 2:10-4. Abstract

Tumor Markers in Clinical Practice

Miami meeting attendees: Do you use tumor markers for follow-up in the following situations?

	metastatic	node-positive primary
Never/rarely	51%	63%
Occasionally/commonly	49%	37%

Commentary

Over one-third of physicians surveyed utilize tumor markers to detect recurrence after primary therapy in patients with node-positive disease. Although there is one well-designed study, which demonstrated that CA 27.29 could predict recurrence 5.3 months before other symptoms or tests, the 2000 update to the American Society of Clinical Oncology guidelines for the use of tumor markers does not recommend their routine use in this setting, because the clinical benefit and options for therapy are not significantly impacted. Another consideration in determining whether or not to use tumor markers in this situation is the psychological effect on the patient of rising tumor levels.

One-half of physicians reported the use of tumor markers in following a patient with metastatic breast cancer. The ASCO guidelines do not support the routine use of CEA to monitor response to treatment; however, CEA may be useful in determining treatment failure for patients without readily measurable disease or those with elevated CA 15-3 and/or CA 27.29.

Select publications

Bast RC Jr et al. **2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: Clinical practice guidelines of the American Society of Clinical Oncology**. *J Clin Oncol* 2001;19(6):1865-78. **Abstract**

Cheung KL et al. **Tumour marker measurements in the diagnosis and monitoring of breast cancer.** *Cancer Treat Rev* 2000;26(2):91-102. **Abstract**

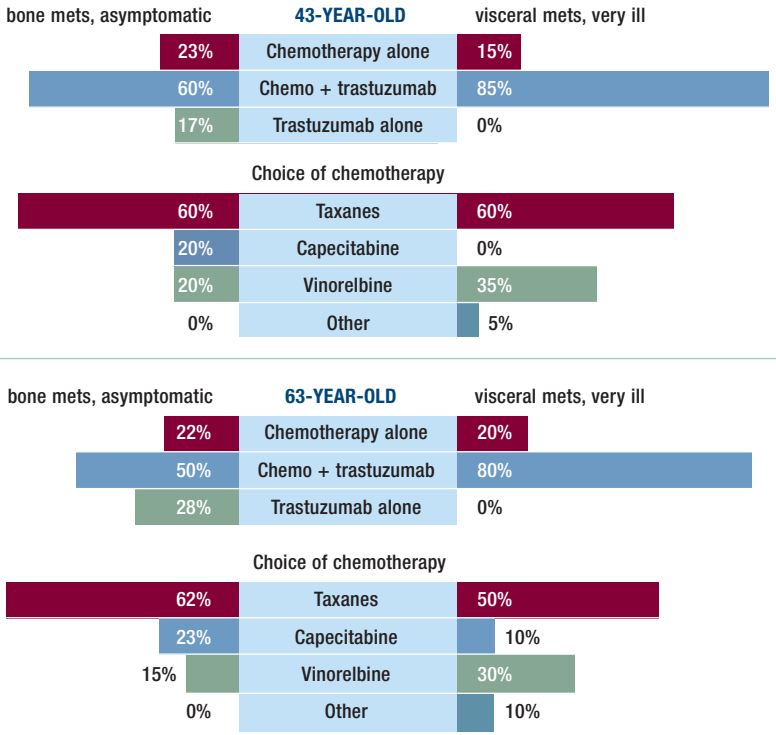
Duffy MJ. **Clinical uses of tumor markers: A critical review.** *Crit Rev Clin Lab Sci* 2001;38(3):225-62. **Abstract**

Nicolini A, Carpi A. **Postoperative follow-up of breast cancer patients: Overview and progress in the use of tumor markers.** *Tumour Biol* 2000;21(4):235-48. **Abstract**

Sakorafas GH et al. **Follow-up after primary treatment for breast cancer.** *Acta Oncol* 2000;39(8):935-40. **Abstract**

Treatment of Patients with ER-negative, HER2-positive Metastatic Disease and Metastases

Oncologists: How would you treat the following patients with metastatic disease?



Commentary

Virtually all breast cancer clinical investigators consider trastuzumab a baseline to first-line therapy for women with HER2-positive metastatic disease, as do the NCCN guidelines. However, a small but significant fraction of oncologists do not follow this practice. Based on encouraging reports from Vogel and others, a significant fraction of oncologists uses trastuzumab monotherapy in the patient with metastases confined to bone. Reflecting the pivotal randomized trial data from Slamon et al demonstrating a survival advantage with the addition of trastuzumab to paclitaxel, taxanes are most commonly the agents combined with trastuzumab. However, physicians also utilize vinorelbine and capecitabine in this situation.

Select publications

Slamon DJ et al. **Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2.** *N Engl J Med* 2001;344(11):783-92. Abstract

Vogel CL et al. **Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing breast cancer.** *J Clin Oncol* 2002;20(30):719-26. Abstract

Trastuzumab Use in the Patient with HER2-positive, ER-positive Metastatic Disease

Oncologists: Which therapy would you utilize at first relapse in the following women with ER-positive, HER2-positive disease with bone metastases?

	Hormonal therapy alone	Hormonal therapy plus trastuzumab
43-year-old	45%	15%
63-year-old	40%	20%
78-year-old	80%	20%

Commentary

When treating patients with ER-positive, HER2-positive metastatic disease with bone metastases, 40-80% of oncologists would utilize hormonal therapy alone as first-line treatment. A significant minority would use hormonal therapy plus trastuzumab in these women.

In the 43- and 63-year-old women, approximately 40% of oncologists would combine chemotherapy with either trastuzumab or endocrine therapy.

Select publications

Buzdar AU. **Endocrine therapy in the treatment of metastatic breast cancer.** *Semin Oncol* 2001;28(3):291-304. **Abstract**

Hortobagyi GN. **Overview of treatment results with trastuzumab (Herceptin) in metastatic breast cancer.** *Semin Oncol* 2001;28(6 Suppl 18):43-7. **Abstract**

Leyland-Jones B. **Trastuzumab: Hopes and realities.** *Lancet Oncol* 2002;3(3):137-44. **Abstract**

McKeage K, Perry CM. **Trastuzumab: A review of its use in the treatment of metastatic breast cancer overexpressing HER2.** *Drugs* 2002;62(1):209-43. **Abstract**

Mouridsen H et al. **Superior efficacy of letrozole versus tamoxifen as first-line therapy for postmenopausal women with advanced breast cancer: Results of a phase III study of the International Letrozole Breast Cancer Group.** *J Clin Oncol* 2001;19(10):2596-606. **Abstract**

Nabholtz JM et al. **Anastrozole is superior to tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women: Results of a North American multicenter randomized trial. Arimidex Study Group.** *J Clin Oncol* 2000;18(22):3758-67. **Abstract**

Robertson JF. **Estrogen receptor downregulators: New antihormonal therapy for advanced breast cancer.** *Clin Ther* 2002;24 Suppl A:A17-30. **Abstract**

Winer EP, Burstein HJ. **New combinations with Herceptin in metastatic breast cancer.** *Oncology* 2001;61 Suppl 2:50-7. **Abstract**

Chemotherapy and Trastuzumab in the Metastatic Setting

Oncologists: Which therapy would you utilize in the following patients with ER-negative, HER2-positive asymptomatic bone metastases who have not received prior adjuvant therapy?

Therapy	43-year-old	63-year-old	78-year-old
Chemotherapy alone	25%	35%	20%
Chemo + trastuzumab	50%	30%	25%
Trastuzumab alone	15%	20%	40%
No therapy	10%	15%	15%

Commentary

As patients age, the use of chemotherapy decreases, and the use of single-agent trastuzumab in asymptomatic patients increases from 15% to 40% for the 43- and 78-year-old women, respectively. Twenty-five percent (25%) to 35% of physicians would utilize a single-agent chemotherapy in these HER2-positive patients. Of the chemotherapy selected, approximately half would utilize a taxane. A subset of physicians would utilize more convenient and tolerable agents such as capecitabine or vinorelbine especially in the 78-year-old woman.

Select publications

Baselga J. **Herceptin alone or in combination with chemotherapy in the treatment of HER2-positive metastatic breast cancer: Pivotal trials.** *Oncology* 2001;61 Suppl 2:14-21. **Abstract**

Burstein HJ et al. **Clinical activity of trastuzumab and vinorelbine in women with HER2-overexpressing metastatic breast cancer.** *J Clin Oncol* 2001;19(10):2722-30. **Abstract**

Esteva FJ et al. **Phase II study of weekly docetaxel and trastuzumab for patients with HER-2-overexpressing metastatic breast cancer.** *J Clin Oncol* 2002;20(7):1800-8. **Abstract**

Miller KD et al. **Gemcitabine, paclitaxel, and trastuzumab in metastatic breast cancer.** *Oncology (Huntingt)* 2001;15(2 Suppl 3):38-40. **Abstract**

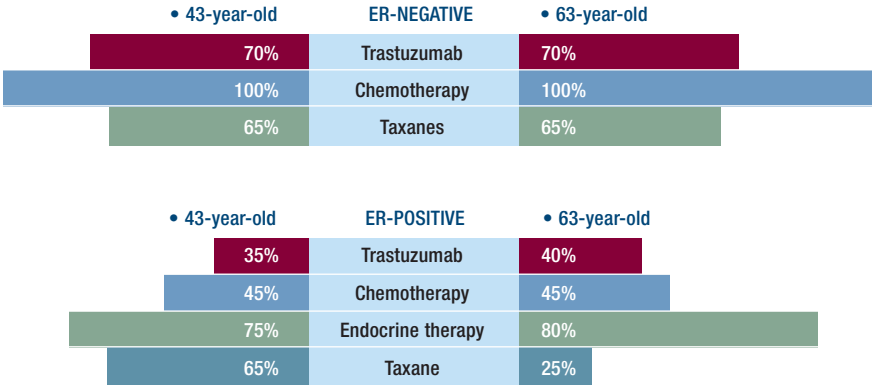
Pegram MD. **Docetaxel and Herceptin: Foundation for future strategies.** *Oncologist* 2001;6 Suppl 3:22-5. **Abstract**

Seidman AD et al. **Weekly trastuzumab and paclitaxel therapy for metastatic breast cancer with analysis of efficacy by HER2 immunophenotype and gene amplification.** *J Clin Oncol* 2001;19(10):2587-95. **Abstract**

Slamon DJ et al. **Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2.** *N Engl J Med* 2001;344(11):783-92. **Abstract**

Management of the Patient with HER2-positive Breast Cancer

Oncologists: How would you treat the following women with HER2-positive disease, bone metastases and multiple sites of moderate pain who have not received adjuvant therapy?



Commentary

Although trastuzumab is considered standard baseline therapy for patients with HER2-positive metastatic disease by most breast cancer researchers and the NCCN guidelines, about one-third of oncologists do not routinely follow this practice. Management of patients with ER-positive, HER2-positive disease is controversial. Current clinical trials are evaluating the use of anastrozole plus trastuzumab in postmenopausal patients, and there is a theoretical rationale to combine these two non-cross-resistant and potentially complementary antitumor approaches. Until the results of these trials are available, many physicians will initiate endocrine treatment and utilize trastuzumab at the time of progression, but about one-third of oncologists are combining trastuzumab and endocrine therapy.

Select publications

Knoop AS et al. **Value of epidermal growth factor receptor, HER2, p53, and steroid receptors in predicting the efficacy of tamoxifen in high-risk postmenopausal breast cancer patients.** *J Clin Oncol* 2001;19(14):3376-84. **Abstract**

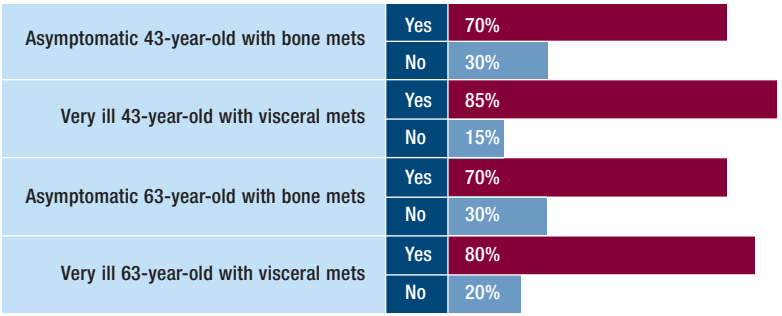
Lipton A et al. **Elevated serum Her-2/neu level predicts decreased response to hormone therapy in metastatic breast cancer.** *J Clin Oncol* 2002;20(6):1467-72. **Abstract**

Winer EP, Burstein HJ. **New combinations with Herceptin in metastatic breast cancer.** *Oncology* 2001;61 Suppl 2:50-7. **Abstract**

Yamauchi H et al. **When is a tumor marker ready for prime time? A case study of c-erbB-2 as a predictive factor in breast cancer.** *J Clin Oncol* 2001;19(8):2334-56. **Abstract**

Trastuzumab in the Metastatic Setting

Oncologists: Would you use trastuzumab in the following women with ER-negative, HER2-positive metastatic disease, who have received adjuvant ACT?



Commentary

The use of trastuzumab in the metastatic setting appears to be slightly greater in symptomatic than asymptomatic disease and greater in women who have received adjuvant ACT than those who received no adjuvant therapy. This effect is independent of the patient's age.

Select publications

Bell R. **Ongoing trials with trastuzumab in metastatic breast cancer**. *Ann Oncol* 2001;12 Suppl 1:S69-73. **Abstract**

Cobleigh M et al. **Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease.** *J Clin Oncol* 1999;17(9):2639-48. **Abstract**

Cook-Bruns N. **Retrospective analysis of the safety of Herceptin immunotherapy in metastatic breast cancer.** *Oncology* 2001;61 Suppl 2:58-66. **Abstract**

Slamon DJ et al. **Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2.** *N Engl J Med* 2001;344(11):783-92. **Abstract**

Vogel CL et al. **Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing metastatic breast cancer**. *J Clin Oncol* 2002;20(3):719-26. **Abstract**

Winer EP, Burstein HJ. **New combinations with Herceptin in metastatic breast cancer.** *Oncology* 2001;61 Suppl 2:50-7. **Abstract**

Duration of Chemotherapy and Trastuzumab in Metastatic Disease

A 57-year-old patient with HER2-positive breast cancer is treated with trastuzumab/paclitaxel on first relapse for bone metastases. After 4 months, she has had a good response and is doing well. Which of the following best describes how long you would normally continue trastuzumab?

	Oncologists	Miami meeting attendees
Continue after progression; add another chemo agent	40%	51% (Miller, Jones)
Continue indefinitely as long as patient was doing well clinically; add multiple chemo agents	30%	20%
Continue until progression, then stop	20%	27%
Stop before progression	10%	2%

Commentary

Although no definitive data exist on the optimal duration of trastuzumab therapy for metastatic disease, most oncologists and attendees polled at the 2002 Miami Breast Cancer Conference continue trastuzumab after disease progression and add another chemotherapeutic agent. Several current clinical trials are evaluating the optimal duration for trastuzumab, specifically whether to continue treatment beyond progression.

Select publications

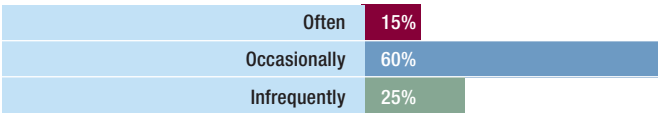
Bell R. **Duration of therapy in metastatic breast cancer: Management using Herceptin.** *Anticancer Drugs* 2001;12(7):561-8. Abstract

Hortobagyi GN. **Optimal duration of therapy with trastuzumab.** *Semin Oncol* 2001;28(5 Suppl 16): 33-40. Abstract

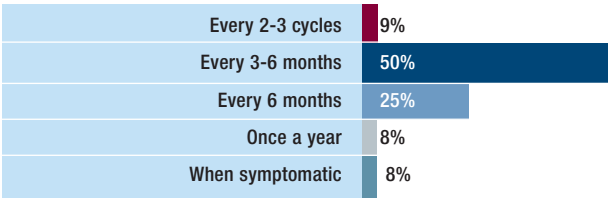
Leyland-Jones B. **Trastuzumab: Hopes and realities.** *Lancet Oncol* 2002;3(3):137-44. Abstract

Trastuzumab and Cardiotoxicity

Oncologists: How often is cardiotoxicity a major concern when considering the use of trastuzumab for metastatic disease?



Oncologists: What is your routine interval of cardiac monitoring in patients who receive trastuzumab?



Commentary

In the trastuzumab pivotal trials, cardiac dysfunction (CD) was observed, particularly in patients treated with anthracyclines. The pathophysiologic basis for trastuzumab-associated CD remains unclear. Formal safety analyses have been introduced into large randomized trials conducted by the NSABP, Intergroup and other cooperative groups.

While many believe that the risk of trastuzumab-associated CD is justifiable in the metastatic setting, three-quarters of oncologists in the survey report occasional-to-frequent concerns about cardiotoxicity when utilizing trastuzumab in patients with metastatic disease. Sixty percent (60%) of oncologists report routine monitoring of cardiac functioning. The MUGA scan is used by all oncologists, although this procedure may not be able to identify CD before significant cardiac damage has occurred. Other methods to monitor cardiac functioning are being evaluated in clinical trials.

Select publications

Seidman A et al. **Cardiac dysfunction in the trastuzumab clinical trials experience.** *J Clin Oncol* 2002;20(5):1215-21. **Abstract**

Chien KR. **Myocyte survival pathways and cardiomyopathy: Implications for trastuzumab cardiotoxicity.** *Semin Oncol* 2000;27(6 Suppl 11):9-14. **Abstract**

Gerber B et al. **Effectiveness of Trastuzumab (Herceptin) in a patient with locally recurrent breast cancer after cardiac failure caused by severe cytotoxic pretreatment.** *Oncology* 2001;61(4):271-4. **Abstract**

Sparano JA. **Cardiac toxicity of trastuzumab (Herceptin): Implications for the design of adjuvant trials.** *Semin Oncol* 2001;28(1 Suppl 3):20-7. **Abstract**

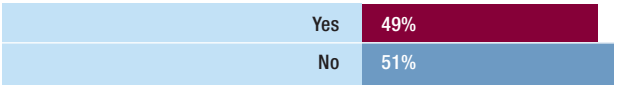
Sentinel Lymph Node Biopsy (SLNB)

Miami meeting attendees:

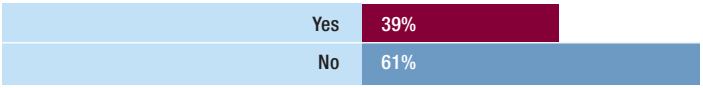
What technique do you utilize in performing sentinel lymph node biopsies?

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

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**

Derossis AM et al. **A trend analysis of the relative value of blue dye and isotope localization in 2,000 consecutive cases of sentinel node biopsy for breast cancer.** *J Am Coll Surg* 2001;193(5):473-8. **Abstract**

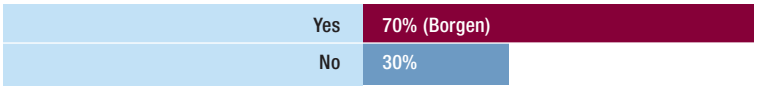
Hansen NM. **Blue versus hot: Learning the techniques with dye and isotopes.** *Ann Surg Oncol* 2001;8(9 Suppl):64S-66S. **Abstract**

Lucci A Jr et al. **National practice patterns of sentinel lymph node dissection for breast carcinoma.** *J Am Coll Surg* 2001;192(4):453-8. **Abstract**

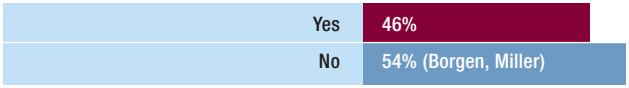
When Is Sentinel Lymph Node Biopsy (SLNB) Appropriate?

Miami meeting attendees:

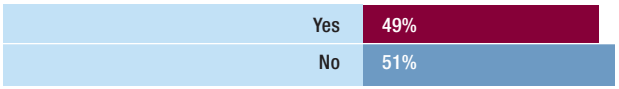
Is SLNB currently the standard of care for patients with clinical T1NO disease?



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**

Pendas S et al. **Sentinel node biopsy in ductal carcinoma in situ patients.** *Ann Surg Oncol* 2000;7:15-20. **Abstract**

Stearns V et al. **Sentinel lymphadenectomy after neoadjuvant chemotherapy for breast cancer may reliably represent the axilla except for inflammatory breast cancer.** *Ann Surg Oncol* 2002;9(3):235-42. **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**

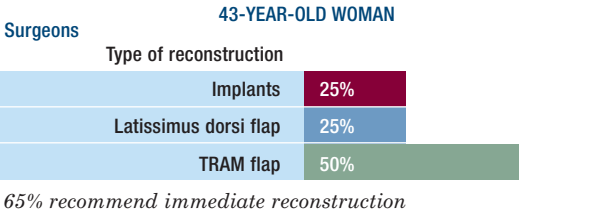
Pierce LJ. **Treatment guidelines and techniques in delivery of postmastectomy radiotherapy in management of operable breast cancer.** *J Natl Cancer Inst Monogr* 2001;30:117-124. **Abstract**

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**

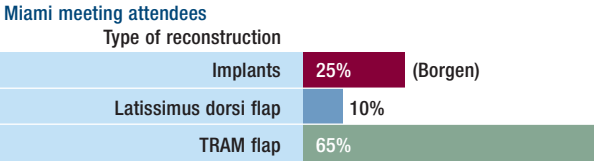
Vallis KA et al. **Assessment of coronary heart disease morbidity and mortality after radiation therapy for early breast cancer.** *J Clin Oncol* 2002;20(4):1036-42. **Abstract**

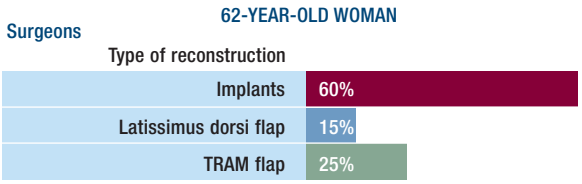
Type and Timing of Breast Reconstruction

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?



65% recommend immediate reconstruction





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.

Select publications

Morrow et al. **Factors influencing the use of breast reconstruction postmastectomy: A national cancer database study.** *J Am Coll Surg* 2001:1(192);1-8. **Abstract**

Tran NV et al. **Comparison of immediate and delayed free TRAM flap breast reconstruction in patients receiving postmastectomy radiation therapy.** *Plast Reconstr Surg* 2001;108(1):78-82. **Abstract**

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% (Borgen)

- 78-year-old woman with DCIS recurrence

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

- 43-year-old woman with invasive cancer recurrence

Local therapy	Surgeons
Re-excision	16%
Mastectomy	84% (Borgen)

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.

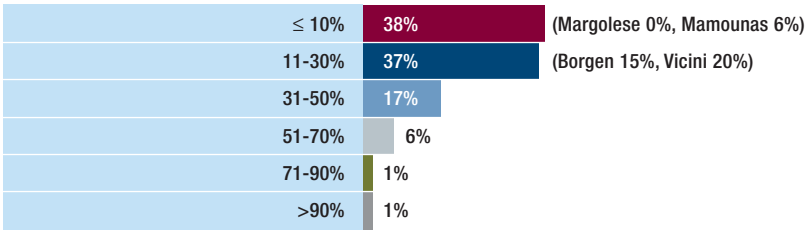
Select publications

Harms W et al. **Results of chest wall reirradiation using pulsed-dose-rate (PDR) brachytherapy molds for breast cancer local recurrences.** *Int J Radiat Oncol Biol Phys* 2001;49(1):205-10. **Abstract**

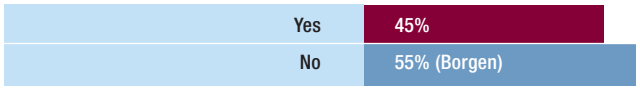
McCormick B et al. **Local regional recurrence and salvage surgery. American College of Radiology. ACR Appropriateness Criteria.** *Radiology* 2000;215 Suppl:1181-92. **Abstract**

Local Management of Primary Breast Cancer

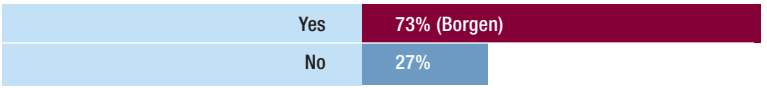
How many of your breast cancer patients when presented with the option of breast conservation choose to have a mastectomy?



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.

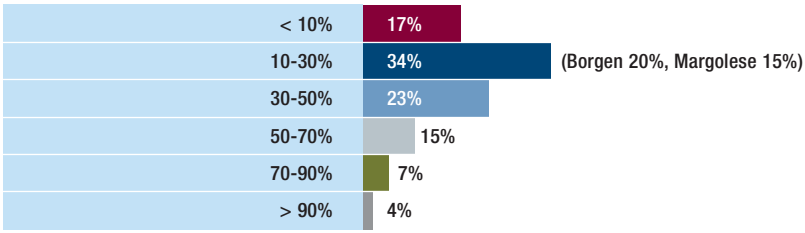
Select publications

Margolese RG, Lasry JC. **Ambulatory surgery for breast cancer patients.** *Ann Surg Oncol* 2000;7(3):181-7. **Abstract**

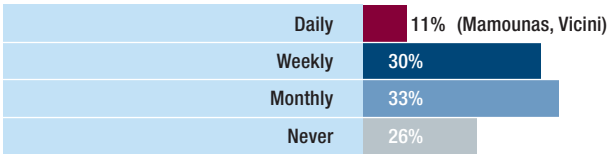
Morrow M et al. **Factors predicting the use of breast-conserving therapy in stage I and II breast carcinoma.** *J Clin Oncol* 2001;19(8):2254-62. **Abstract**

Use of Alternative Medicine / the Internet

How many of your patients do you believe utilize some form of complementary or alternative medicine?



How often do you use the Internet to access medical information related to your practice?



Commentary

While Miami meeting attendees estimate that less than half of their breast cancer patients utilize some form of complementary or alternative medicine, many surveys suggest that the actual number seeking this type of treatment is much higher. It has been pointed out that often physicians are not aware that patients are seeking these therapies.

Virtually all Miami meeting attendees utilize email, and almost half use the Internet regularly to access medical information to assist in patient care.

Select publications

Burstein HJ et al. **Use of alternative medicine by women with early-stage breast cancer.** *N Engl J Med* 1999;340:1733-9. **Abstract**

Cassileth BR et al. **Alternative medicine use worldwide: The International Union Against Cancer survey.** *Cancer* 2001;91:1390-3. **Abstract**

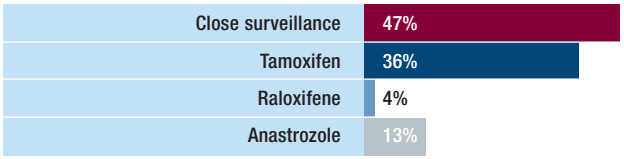
Lee MM et al. **Alternative therapies used by women with breast cancer in four ethnic populations.** *J Natl Cancer Inst* 2000;92:42-7. **Abstract**

Meric F et al. **Breast cancer on the world wide web: Cross-sectional survey of quality of information and popularity of websites.** *BMJ* 2002;324(7337):577-81. **Abstract**

Richardson MA et al. **Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology.** *J Clin Oncol* 2000;18:2505-14. **Abstract**

Miami Breast Cancer Conference
Tumor Board Case 1: Richard Margolese, MD
A high-risk patient a with BRCA1 mutation

The patient is a 70-year-old woman with a history of severe coronary artery disease and bypass surgery for which she is on multiple medications. She has 3 daughters with breast cancer and is known to carry a BRCA1 mutation. How would you manage this patient?



Commentary

A series of actual cases from the faculty were presented to the attendees at the Miami Breast Cancer Conference, and the audience voted as to how they would have managed similar patients.

Half of the meeting attendees recommended close surveillance for Dr Margolese's patient, and about one-third would recommend tamoxifen. Faculty panelists also favored close monitoring, primarily because in postmenopausal women the risks of thromboembolic disease and endometrial cancer with tamoxifen may outweigh the benefit. A subgroup analysis of the NSABP P-1 trial suggested that tamoxifen does not result in a benefit for BRCA1 patients, but there were few patients in this analysis.

The IBIS II trial will evaluate the role of anastrozole in this setting based on the promising contralateral breast cancer risk reduction and the more favorable toxicity profile encountered with anastrozole in the ATAC trial. The NSABP STAR trial is currently evaluating the role of raloxifene compared to tamoxifen in high-risk women.

FOLLOW-UP: Dr Margolese reported that two years after evaluation, the patient presented with a 6 cm invasive breast cancer, which was treated with mastectomy.

Select publications

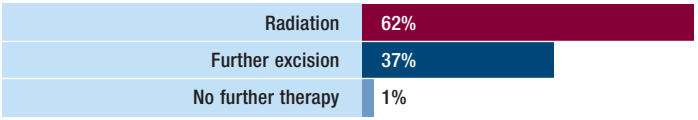
Duffy SW, Nixon RM. **Estimates of the likely prophylactic effect of tamoxifen in women with high risk BRCA1 and BRCA2 mutations**. *Br J Cancer* 2002;86(2):218-21. **Abstract**

King MC et al. **Tamoxifen and breast cancer incidence among women with inherited mutations in BRCA1 and BRCA2: National Surgical Adjuvant Breast and Bowel Project (NSABP-P1) Breast Cancer Prevention Trial.** *JAMA* 2001;286(18):2251-6. **Abstract**

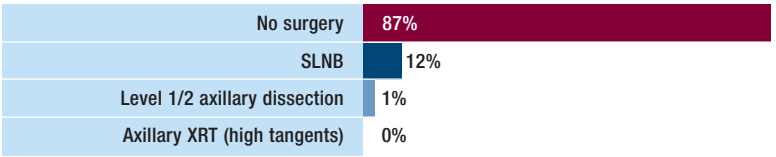
Miami Breast Cancer Conference Tumor Board Case 2: Frank Vicini, MD

A young woman with DCIS

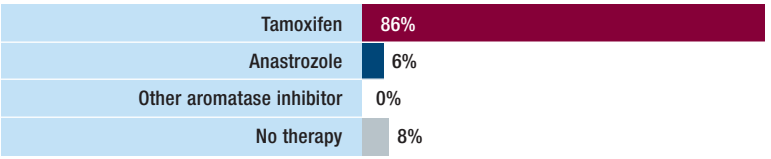
The patient is a 45-year-old premenopausal woman with a 3 cm, grade 3 DCIS, which was excised with clear but very close margins (less than 1 mm). She has small breasts but wants breast conservation and is very concerned about cosmesis. What is your recommendation for local therapy?



She undergoes further excision and no more tumor is found. How would you approach the axilla?



She undergoes a sentinel lymph node biopsy, which is negative. Which systemic therapy would you recommend?



Commentary

For the initial presentation, most of the respondents recommended radiation therapy without further surgery. This is consistent with data from the NSABP suggesting that as long as margins are clear, no further surgery is needed. Dr Vicini's patient was sent for further surgery, primarily because of her young age. Most respondents would not use axillary staging in this patient, but this woman had a negative sentinel node biopsy. Most of the respondents recommended tamoxifen, which is what the patient received.

Select publications

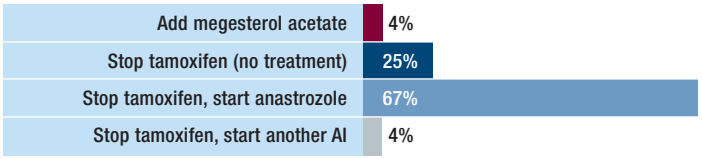
Fisher B et al. **Prevention of invasive breast cancer in women with ductal carcinoma in situ: An update of the national surgical adjuvant breast and bowel project experience.** *Semin Oncol* 2001;28(4):400-18. **Abstract**

Skinner KA, Silverstein MJ. **The management of ductal carcinoma in situ of the breast.** *Endocr Relat Cancer* 2001;8(1):33-45. **Full-text**

Miami Breast Cancer Conference
Tumor Board Case 3: Patrick Borgen, MD

A patient with invasive disease at low risk for recurrence

The patient is a 59-year-old postmenopausal woman with an 0.8 cm invasive breast cancer. The pathology is poorly differentiated, ER-positive, HER2-negative. After 4 months of adjuvant tamoxifen, she developed a 12-pound weight gain and severe hot flashes. How would you treat her?



Commentary

Even before the preliminary results from the ATAC trial were presented, many oncologists were substituting aromatase inhibitors for tamoxifen in women with increased risk for thromboembolism or difficulty tolerating tamoxifen. Most attendees recommended substituting anastrozole in this patient. In fact, Dr Borgen made this change and the patient, who was being treated with antidepressants, was able to lose the gained weight and go off antidepressant medication. She has essentially no symptoms at this time on anastrozole.

While hot flashes have clearly been associated with tamoxifen, the NSABP P-1 quality of life study did not find any significant association between tamoxifen and weight gain, depression or sexual function (side effects sometimes attributed to tamoxifen). Early results from the ATAC trial indicate that anastrozole is associated with both less episodes of hot flashes and weight gain than tamoxifen.

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.**

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

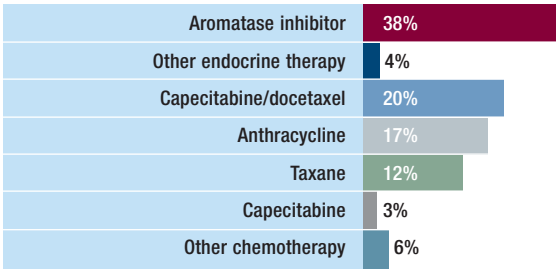
Demissie S et al. **Adjuvant tamoxifen: Predictors of use, side effects, and discontinuation in older women.** *J Clin Oncol* 2001;19(2):322-8. **Abstract**

Ganz P. **Impact of tamoxifen adjuvant therapy on symptoms, functioning, and quality of life.** *J Natl Cancer Inst Monogr* 2001;30:130-134. **Abstract**

Miami Breast Cancer Conference Tumor Board Case 4: Kathy Miller, MD

A patient with ER+ visceral metastases

The patient is a 62-year-old woman diagnosed 30 months ago with a 1.4 cm, stage I, ER-positive breast cancer. She underwent a modified radical mastectomy and had negative axillary nodes. She was treated with tamoxifen. Now on tamoxifen, she develops mild back pain. A chest X-ray reveals multiple pulmonary nodules; the largest one is 2 cm. A CT reveals 3 small liver lesions. FNA of a lung lesion confirms metastatic breast cancer. She is asymptomatic. What is your suggested treatment?



Commentary

There is considerable debate about the management of women with ER-positive breast cancer metastatic to visceral organs. Most research leaders recommend a trial of endocrine therapy, unless the patient is extremely symptomatic. Another strategy is to start both chemotherapy and endocrine therapy and discontinue the chemotherapy after the patient has a response and continue the hormone therapy. This woman was asymptomatic, and most of the audience favored using an aromatase inhibitor. In fact, Dr Miller's patient was treated with anastrozole and had a two-year complete response to this treatment.

Select publications

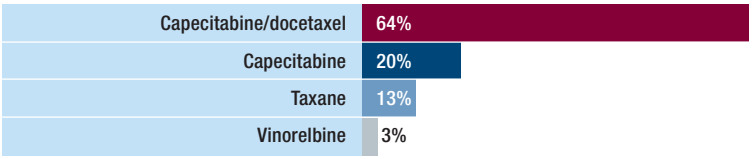
Mouridsen H et al. **Superior efficacy of letrozole versus tamoxifen as first-line therapy for postmenopausal women with advanced breast cancer: Results of a phase III study of the International Letrozole Breast Cancer Group.** *J Clin Oncol* 2001;19(10):2596-606. **Abstract**

Nabholtz JM et al. **Anastrozole is superior to tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women: Results of North American multicenter randomized trial. Arimidex Study Group.** *J Clin Oncol* 2000;18(22):3758-67. **Abstract**

Miami Breast Cancer Conference
Tumor Board Case 5: Stephen Jones, MD

A patient with rapidly recurring metastatic breast cancer

The patient is a 58-year-old woman treated 9 months ago for a 3 cm, ER-negative, PR-negative, infiltrating ductal carcinoma. She underwent lumpectomy, axillary dissection and radiotherapy and had 20 positive lymph nodes. She was treated with high-dose chemotherapy (including induction AC) with bone marrow transplantation. She now presents 9 months later with multiple bilateral bulky cervical, supraclavicular and mediastinal lymph nodes. What is your treatment recommendation?



She was treated with capecitabine/docetaxel and had a complete response but developed hand-foot syndrome. The capecitabine was discontinued, and the patient remains in remission. Would you stop the docetaxel?

Commentary

Two-thirds of the attendees would utilize combination chemotherapy with capecitabine/docetaxel (X-T), which has been demonstrated in a randomized trial to improve survival compared to docetaxel alone. The short disease-free interval in this patient and the rapid appearance of bulky metastases after high-dose chemotherapy suggests a poor prognosis.

This patient was treated several years ago as part of the X-T trial. She was randomized to receive the combination of capecitabine/docetaxel. After 4 courses of therapy, she had a complete tumor response. The patient developed hand-foot syndrome but delayed reporting it to Dr Jones. By the time she presented, she had grade 3 toxicity. The capecitabine dose was decreased, and eventually the drug was discontinued. The patient has been maintained on low-dose docetaxel. She continues in complete remission. In view of the minimal treatment-related morbidity, the unanimous opinion of the faculty was to continue docetaxel.

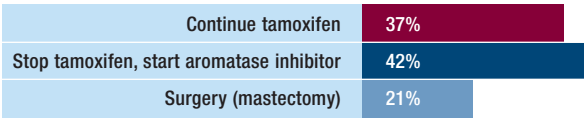
Select publications

Vukelja SJ et al. **Xeloda (capecitabine) plus docetaxel combination therapy in locally advanced/metastatic breast cancer: Latest results.** *Breast Cancer Res Treat* 2001;**Abstract 352.**

Miami Breast Cancer Conference Tumor Board Case 6: Patrick Borgen, MD

An elderly woman with a tumor too large for breast conservation

The patient is a 73-year-old woman who had coronary bypass at age 68 and is now on multiple cardiovascular medications. She has claudication upon climbing one flight of stairs. She presented 6 months ago with a 4 cm breast mass. Core biopsy revealed intraductal carcinoma, strongly ER-positive. She has small breasts and has been on neoadjuvant tamoxifen for 6 months. The tumor is now 2.5 cm, but she is still not a good candidate for excision and radiotherapy. What is your recommendation?



Commentary

Aromatase inhibitors have been reported to have greater response rates in the neoadjuvant setting than tamoxifen, and almost half of the attendees would switch this patient to an aromatase inhibitor. The faculty was split in terms of management, noting that mastectomy carries some risk in this older patient with cardiovascular disease. Dr Borgen switched the patient to anastrozole, and the tumor has further decreased in size. Breast-conserving surgery is being considered at this time.

Select publications

Dixon JM et al. **The effects of neoadjuvant anastrozole (Arimidex) on tumor volume in postmenopausal women with breast cancer: A randomized, double-blind, single-center study.** *Clin Cancer Res* 2000;6(6):2229-35. **Abstract**

Ellis MJ. **Preoperative endocrine therapy for older women with breast cancer: Renewed interest in an old idea.** *Cancer Control* 2000;7(6):557. **Full Text**

Ellis MJ et al. **Letrozole is more effective neoadjuvant endocrine therapy than tamoxifen for ErbB-1- and/or ErbB-2-positive, estrogen receptor-positive primary breast cancer: Evidence from a phase III randomized trial.** *J Clin Oncol* 2001;19:3808-16. **Abstract**

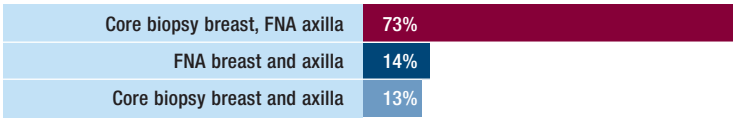
Mandelblatt JS et al. **Measuring and predicting surgeons' practice styles for breast cancer treatment in older women.** *Med Care* 2001;39(3):228-42. **Abstract**

Milla-Santos A et al. **Anastrozole (A) as neoadjuvant (NEO) therapy for hormone-dependent locally advanced breast cancer (LABC) in postmenopausal (PM) patients (pts).** *Breast Cancer Res Treat* 2001;**Abstract 302.**

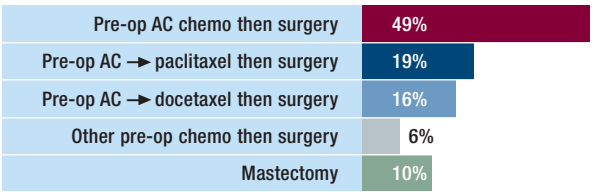
Miami Breast Cancer Conference Tumor Board Case 7: Eleftherios Mamounas, MD

A young woman with a tumor too large for breast conservation

The patient is a 50-year-old woman with a 4.5 cm right breast mass in the lower-outer quadrant and a 3 cm ipsilateral axillary node. She wishes to have breast conservation, which is not currently possible due to her small breast size. What is your diagnostic recommendation?



The patient had an FNA of the breast and axilla, both of which show adenocarcinoma. What is your treatment recommendation?



Commentary

One of the disadvantages of FNA is the difficulty of performing adequate estrogen and progesterone receptor assays. Most of the attendees would use AC neoadjuvant chemotherapy, which was studied by the NSABP and found to downstage most patients without compromising long-term outcome. Dr Mamounas offered this patient participation in a randomized clinical trial, protocol NSABP B-27. The patient accepted and was randomized to AC followed by docetaxel given preoperatively. The patient had a complete tumor response, which was documented during breast-conserving surgery and axillary dissection. The patient is now doing well and is free of cancer. No estrogen receptor information is available to guide future therapy.

Select publications

NSABP. **The effect of primary tumor response of adding sequential Taxotere to Adriamycin and cyclophosphamide: Preliminary results from NSABP Protocol B-27.** *Breast Cancer Res Treat* 2001;**Abstract 5.**

Smith IC et al. **Neoadjuvant chemotherapy in breast cancer: Significantly enhanced response with docetaxel.** *J Clin Oncol* 2002;20(6):1456-66. **Abstract**

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