



# Research To Practice: Adjuvant Endocrine Therapy

Extensive resources are allocated for the evaluation of breast cancer treatments. In contrast, minimal investments are made to determine how these therapeutic strategies are implemented in clinical practice. Continuing medical education not only informs clinicians about emerging research results but also evaluates, through needs assessment, the implementation of research results by physicians in practice. Data from the *Breast Cancer Update Patterns of Care Study*, a survey conducted in September 2005 of breast cancer investigators and randomly selected medical oncologists in the United States, are presented here. One of the key facets of this initiative was the use of adjuvant hormonal therapy. In postmenopausal women, the adjuvant trials evaluating the aromatase inhibitors as initial therapy and following two to three or five years of adjuvant tamoxifen have had a dramatic impact on the clinical use of adjuvant endocrine therapy. In premenopausal women, controversy continues with regard to the use of ovarian ablation/suppression.

## THE ROLE OF ADJUVANT AROMATASE INHIBITORS IN POSTMENOPAUSAL WOMEN

Based on data from various adjuvant endocrine therapy trials, I believe it is unreasonable to withhold aromatase inhibitors from postmenopausal women with hormone receptor-positive disease. ATAC is still the definitive adjuvant trial in terms of comparing tamoxifen to an aromatase inhibitor, and the data are very compelling. An aromatase inhibitor is now my drug of choice, and that changed in just the past years.

As for switching patients from tamoxifen to an aromatase inhibitor, I discuss this with every postmenopausal patient on tamoxifen. We don't know the optimal time to switch, and we don't know the optimal duration of various endocrine therapies. While we know that five years of tamoxifen is as good as or better than 10 years, the optimal duration of aromatase inhibitors is unknown at this time.

— *I Craig Henderson, MD.*  
*Breast Cancer Update 2005 (2)*

If you start with tamoxifen, after two and a half, three or five years, more patients will have relapsed than on an aromatase inhibitor. A substantial number of those patients will be irretrievable — they have incurable disease — and so you're banking on the fact that you'll be able to capture more patients later, but we don't have any data for that. That's just speculation. While I believe sequencing therapy may be better, ultimately, I still don't see any reason not to start with the most effective therapy. An aromatase inhibitor followed by tamoxifen or a nonsteroidal aromatase inhibitor makes more sense to me. We have to wait to see the data from the BIG FEMTA trial, which includes an arm with letrozole as initial treatment followed by tamoxifen.

— *Rowan T Chlebowski, MD, PhD.*  
*Breast Cancer Update 2005 (7)*

I believe a clear, consistent story is emerging without a lot of conflicts and conundrums: Adjuvant aromatase inhibitors are better than tamoxifen. Whether the aromatase inhibitors are used at the time of initial diagnosis, after two to three years or five years of tamoxifen, there is a favorable impact on local, distant and even contralateral breast cancer recurrences.

The unresolved questions are: Should you use a little tamoxifen, maybe two years and then cross over? Should you only use an aromatase inhibitor right off the bat and maybe even think of continuing beyond five years? The trial that will provide the most information in this regard is the BIG FEMTA/BIG 1-98 trial.

— *Debu Tripathy, MD.*  
*Breast Cancer Update 2005 (5)*

## 2004 ASCO TECH ASSESSMENT ON THE USE OF ADJUVANT AROMATASE INHIBITORS

Based on results from multiple large randomized trials, adjuvant therapy for postmenopausal women with hormone receptor-positive breast cancer should include an aromatase inhibitor in order to lower the risk of tumor recurrence. Neither the optimal timing nor duration of aromatase inhibitor therapy is established. Aromatase inhibitors are appropriate as initial treatment for women with contraindications to tamoxifen. For all other postmenopausal women, treatment options include 5 years of aromatase inhibitors treatment or sequential therapy consisting of tamoxifen (for either 2 to 3 years or 5 years) followed by aromatase inhibitors for 2 to 3, or 5 years.

— *Eric P Winer, MD et al.*  
*J Clin Oncol 2005;23:619-29.*

## ADJUVANT ENDOCRINE THERAPY IN PREMENOPAUSAL WOMEN

I have combined an LHRH agonist with an aromatase inhibitor in premenopausal women, but it's rare because for women who are at high enough risk for that therapy — multiple positive nodes or even node-positive, HER2-positive breast cancer — I generally recommend oophorectomy, and then I'm comfortable with an aromatase inhibitor.

— *Joyce O'Shaughnessy, MD.*  
*Patterns of Care 2004 (2)*

### CHOICE OF AROMATASE INHIBITORS AS ADJUVANT THERAPY

When you use an aromatase inhibitor in each of the following settings, what percentage of this use is with each of the following agents?

	Anastrozole		Letrozole		Exemestane	
	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)
Initial adjuvant therapy	86%	86%	11%	11%	3%	3%
After 2 to 3 years of adjuvant tamoxifen	17%	37%	12%	18%	71%	45%
After 5 years of adjuvant tamoxifen	5%	19%	90%	73%	5%	8%

Legend: Breast cancer specialists (n = 45) (light blue), General oncologists (n = 50) (light green)

SOURCE: *Breast Cancer Update Patterns of Care Survey*, September 2005.

### CHOICE OF ADJUVANT ENDOCRINE THERAPY IN POSTMENOPAUSAL WOMEN

Which endocrine therapy would you be most likely to recommend to a 55-year-old postmenopausal woman with each of the following tumors?

	1.2-cm, ER+/PR+, HER2-, N-		1.2-cm, ER+/PR+, HER2-, 3N+		1.2-cm, ER+/PR-, HER2-, 3N+	
	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)
Anastrozole	63%	72%	78%	80%	92%	83%
Letrozole	5%	—	4%	—	4%	—
Exemestane	—	2%	—	—	—	2%
Tam x 5y	5%	4%	—	4%	—	4%
Tam x 2-3y → AI	25%	16%	16%	8%	4%	9%
Tam x 5y → AI	2%	6%	2%	8%	—	2%

Tam = tamoxifen; AI = aromatase inhibitor; N = node

Legend: Breast cancer specialists (n = 45) (light blue), General oncologists (n = 50) (light green)

SOURCE: *Breast Cancer Update Patterns of Care Survey*, September 2005.

### SEQUENCING ADJUVANT THERAPY AFTER FIVE YEARS OF TAMOXIFEN

The patient is a 65-year-old woman in average health with a 1.2-cm, ER/PR-positive, HER2-negative, Grade II tumor and three positive lymph nodes who has completed five years of tamoxifen therapy. How would you manage this patient's endocrine therapy?

	Has just completed 5 years of tamoxifen		Completed 5 years of tamoxifen 1 year ago		Completed 5 years of tamoxifen 3 years ago	
	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)
Continue tamoxifen	—	2%	—	—	—	—
Start anastrozole	2%	16%	2%	12%	—	6%
Start letrozole	98%	78%	88%	62%	20%	18%
Start exemestane	—	2%	—	2%	—	2%
Use no further hormonal therapy	—	2%	10%	24%	80%	74%

Legend: Breast cancer specialists (n = 45) (light blue), General oncologists (n = 50) (light green)

SOURCE: *Breast Cancer Update Patterns of Care Survey*, September 2005.

### SWITCHING ADJUVANT THERAPY AFTER TWO TO THREE YEARS OF TAMOXIFEN

The patient is a 65-year-old woman in average health with a 1.2-cm, ER/PR-positive, HER2-negative, Grade II tumor and three positive lymph nodes on tamoxifen for two years. How would you manage this patient's endocrine therapy?

	Tolerability of tamoxifen					
	No side effects with tamoxifen		Complains of 20-pound weight gain		Complains of moderate hot flashes	
	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)
Continue tamoxifen	5%	24%	2%	4%	5%	8%
Stop tamoxifen	—	—	—	2%	—	—
Stop tamoxifen and switch to exemestane	72%	38%	70%	40%	67%	36%
Stop tamoxifen and switch to anastrozole	14%	26%	19%	40%	21%	44%
Stop tamoxifen and switch to letrozole	9%	12%	9%	14%	7%	12%

Legend: Breast cancer specialists (n = 45) (light blue), General oncologists (n = 50) (light green)

SOURCE: *Breast Cancer Update Patterns of Care Survey*, September 2005.

### CHOICE OF ENDOCRINE THERAPY IN PREMENOPAUSAL WOMEN

Which endocrine therapy would you be most likely to recommend to a 35-year-old premenopausal woman with each of the following tumors?

	1.2-cm, ER+/PR+, HER2-, 3N+		1.2-cm, ER+/PR-, HER2-, 3N+		1.2-cm, ER+/PR+, HER2+, 3N+	
	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)	Breast cancer specialists (n = 45)	General oncologists (n = 50)
Tam x 5y	47%	52%	47%	50%	37%	46%
Tam x 5y → AI	9%	10%	7%	10%	9%	12%
Tam x 2-3y → AI	—	4%	—	4%	—	4%
Tam + LHRH or OA	20%	20%	11%	20%	12%	26%
AI + LHRH or OA	22%	6%	33%	6%	33%	6%
Other	2%	6%	2%	4%	9%	4%
None	—	2%	—	6%	—	2%

N = node; Tam = tamoxifen; AI = aromatase inhibitor; LHRH = LHRH agonist; OA = ovarian ablation

Legend: Breast cancer specialists (n = 45) (light blue), General oncologists (n = 50) (light green)

SOURCE: *Breast Cancer Update Patterns of Care Survey*, September 2005.

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