Research To Practice: Adjuvant Endocrine Therapy

Extensive resources have been allocated to evaluate new breast cancer treatment interventions; however, relatively minimal investment has been made to determine how these advances are implemented in practice. Continuing medical education has the potential to be a useful component in the clinical research continuum, not only by informing clinicians about available trials and emerging research findings, but also by performing outcomes assessments to evaluate how research advances are being implemented in clinical practice. The data presented here from the Breast Cancer Update Patterns of Care Study are from a national telephone survey initiated in 2004 of 150 randomly selected United States-based medical oncologists.

One of the key aspects of this initiative was the use of hormonal therapy. The most important databases currently affecting nonprocotol use of adjuvant endocrine therapy were derived from trials of aromatase inhibitors in postmenopausal patients, both as initial therapy and after two to three, or five years of tamoxifen. In premenopausal women, controversy continues with regard to the use of ovarian ablation/suppression, particularly in women who continue to menstruate after receiving adjuvant chemotherapy.

CHOICE OF ADJUVANT ENDOCRINE THERAPY BASED ON TUMOR SIZE AND NODAL/HER2 STATUS

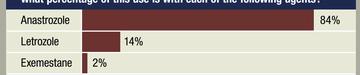
Which endocrine therapy would you most likely recommend to a 65-year-old woman with an ER-positive tumor?

Therapy	2.2-cm, N2+ HER2-neg	2.2-cm, N- HER2-neg	0.8-cm, N- HER2-neg	2.2-cm, N10+ HER2-pos
Tamoxifen	34%	33%	43%	23%
Anastrozole	59%	61%	45%	75%
Letrozole	7%	6%	2%	2%
Exemestane	—	—	—	—

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004;1(1).

USE OF ADJUVANT AROMATASE INHIBITORS FOR INITIAL THERAPY

When you use an aromatase inhibitor as initial adjuvant therapy, what percentage of this use is with each of the following agents?



SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004;1(1).

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-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?

	No side effects with tamoxifen	Complains of 20-pound weight gain	Complains of moderate hot flashes
Continue tamoxifen	45%	17%	16%
Stop tamoxifen	—	—	—
Stop tamoxifen and switch to anastrozole	12%	35%	36%
Stop tamoxifen and switch to letrozole	11%	16%	12%
Stop tamoxifen and switch to exemestane	32%	32%	36%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004;1(2).

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-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
Continue tamoxifen	—	—	—
Start anastrozole	16%	14%	4%
Start letrozole	77%	58%	19%
Start exemestane	1%	—	—
Use no further hormonal therapy	6%	28%	77%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004;1(2).

ADJUVANT ENDOCRINE THERAPY IN PREMENOPAUSAL WOMEN

Which endocrine therapy would you recommend for a woman in average health with a 1.2-cm, ER-positive, HER2-negative, Grade II tumor and negative lymph nodes?

	Age 35	Age 45
Tamoxifen	73%	76%
LHRH agonist or ovarian ablation	2%	2%
Tamoxifen + LHRH agonist or ovarian ablation	14%	9%
Aromatase inhibitor + LHRH agonist or ovarian ablation	4%	4%
Other	5%	7%
Would not recommend endocrine therapy	2%	2%

SOURCE: *Breast Cancer Update* Patterns of Care Study, 2004;1(2).

SELECT PUBLICATIONS

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Colleoni M et al. **Randomized comparison of adjuvant tamoxifen (Tam) versus no hormonal treatment for premenopausal women with node-positive (N+), early stage breast cancer: First results of International Breast Cancer Study Group Trial 13-93.** *Proc ASCO* 2004;Abstract 532.

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Coombes RC et al. **The Intergroup Exemestane Study: A randomized trial in postmenopausal patients with early breast cancer who remain disease-free after two to three years of tamoxifen — Updated survival analysis.** *Breast Cancer Res Treat* 2004;Abstract 3.

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AROMATASE INHIBITORS AS INITIAL ADJUVANT THERAPY IN POSTMENOPAUSAL WOMEN

What we are seeing in this survey is the trend to switch from tamoxifen to aromatase inhibitors as initial adjuvant therapy. Clearly, the transition has been quick because of the clear efficacy of the aromatase inhibitors. The current aromatase inhibitor trials in postmenopausal women demonstrate approximately a 25 to 50 percent relative reduction in the risk of recurrence with aromatase inhibitors compared to tamoxifen, which translates into a two to five percent absolute difference in overall events, including local and distant recurrences and new contralateral lesions. Efficacy drives oncologists' opinions and, in this survey, most are going with the more efficacious treatment; however, some physicians will still utilize tamoxifen.

I generally lean toward aromatase inhibitors, and I think patients are receptive to that decision. Many patients come in asking about them. Aromatase inhibitors already have a reputation, among both patients and physicians, as not only more effective but also less toxic. All of the studies comparing adjuvant aromatase inhibitors to tamoxifen are reporting compositely better tolerability with the aromatase inhibitors.

The side effects of vaginal discharge, vaginal bleeding, hot flashes and uterine cancer are more common with tamoxifen, whereas arthralgias and myalgias are more common with aromatase inhibitors. As women become older — late sixties, seventies and eighties — the risk of deep vein thrombosis and stroke while on tamoxifen becomes significant, and this is clearly not observed with aromatase inhibitors.

— Debu Tripathy, MD

With the majority of postmenopausal patients, I tend to use an aromatase inhibitor, generally anastrozole, in the adjuvant setting. If a contraindication or resistance to using an aromatase inhibitor exists, my second option is tamoxifen. I'm surprised that so many postmenopausal women are currently receiving an aromatase inhibitor as first-line adjuvant hormonal therapy. That is a huge shift from what we saw just a couple years ago.

— Robert W Carlson, MD

SEQUENCING AROMATASE INHIBITORS AFTER ADJUVANT TAMOXIFEN

I discuss aromatase inhibitors with all truly menopausal patients I see in the adjuvant setting. Depending on the patient's situation, I will discuss starting with an aromatase inhibitor, switching to one at two to three years, or completing tamoxifen at four and a half years and then switching to letrozole. The conversation comes up for virtually all menopausal patients, and in most cases I urge them to consider switching.

— Clifford Hudis, MD

Some physicians believe that an ideal approach to adjuvant endocrine therapy is to start with tamoxifen and then switch to an aromatase inhibitor. The problem with that approach is, what are you going to tell the woman who was on tamoxifen in the first five years and relapsed because she wasn't on anastrozole in those first five years?

And what are you going to tell the woman who had a deep vein thrombosis or a stroke in those first five years, who wouldn't have had a deep vein thrombosis or a stroke had she been on anastrozole? Admittedly, the woman who doesn't have a fracture will be happy, but if she's going to receive anastrozole later on, she might have a fracture later on.

— Gershon Locker, MD

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