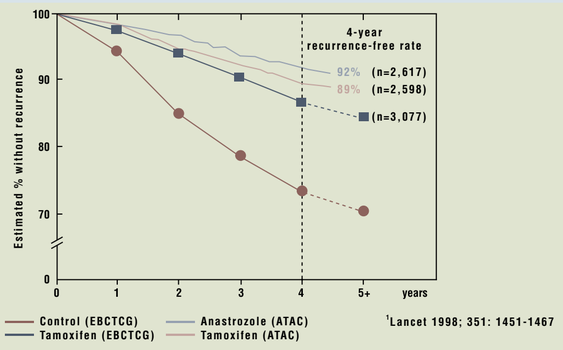
Anastrozole, Tamoxifen, Alone or in Combination (ATAC Trial)

On December 10, 2001, the initial results of the ATAC trial were presented at the San Antonio Breast Cancer Symposium and subsequently published in The Lancet on June 22, 2002. The study randomized more than 9,000 women to either tamoxifen, anastrozole or the combination. The US Food and Drug Administration granted a six-month priority review status, and on September 5, 2002, anastrozole was approved as adjuvant therapy for postmenopausal women with hormone receptor-positive breast cancer.

These groundbreaking data, updated at the San Antonio Breast Cancer Symposium with 47 months of follow-up, continue to demonstrate that in postmenopausal women with primary invasive breast cancer, the third-generation aromatase inhibitor anastrozole conferred an advantage over tamoxifen in terms of disease-free survival and rates of contralateral breast cancers. Importantly, the Kaplan-Meyer DFS curves are increasing in divergence with more follow-up.

FIGURE 1: COMPARISON OF ATAC DATA WITH EBCTCG 1995
OVERVIEW DATA[1]: ESTROGEN RECEPTOR-POSITIVE PATIENTS >50 YEARS



DERIVED FROM: Aman Buzdar, Presentation, 2002 San Antonio Breast Cancer Symposium

HAZARD RATIOS OF ANASTROZOLE COMPARED TO TAMOXIFEN IN UPDATED EFFICACY RESULTS OF THE ATAC TRIAL (MEDIAN FOLLOW-UP OF 47 MONTHS, 1373 EVENTS)

	Study population	Hormone receptor-positive subgroup
Probability of first event	HR = 0.86	HR = 0.82
Probability of recurrence	HR = 0.83	HR = 0.78
Incidence of new contralateral breast primaries	OR = 0.62	OR = 0.56

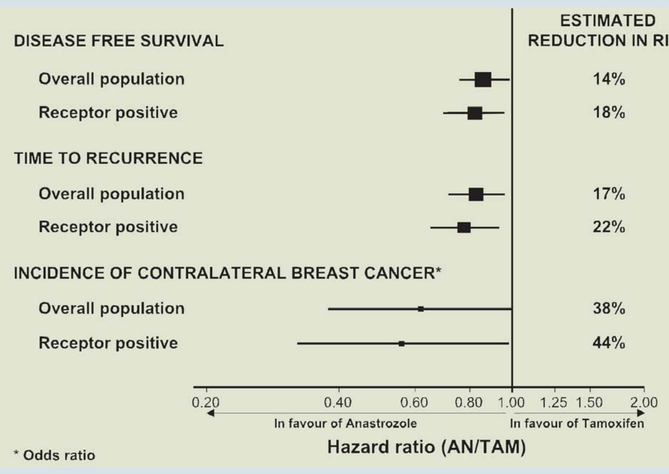
HR = Hazard ratio; OR = Odds ratio

DERIVED FROM: Buzdar A et al. *Breast Cancer Res Treat* 2002; Abstract 13.

FIRST EVENTS IN RECEPTOR-POSITIVE POPULATION

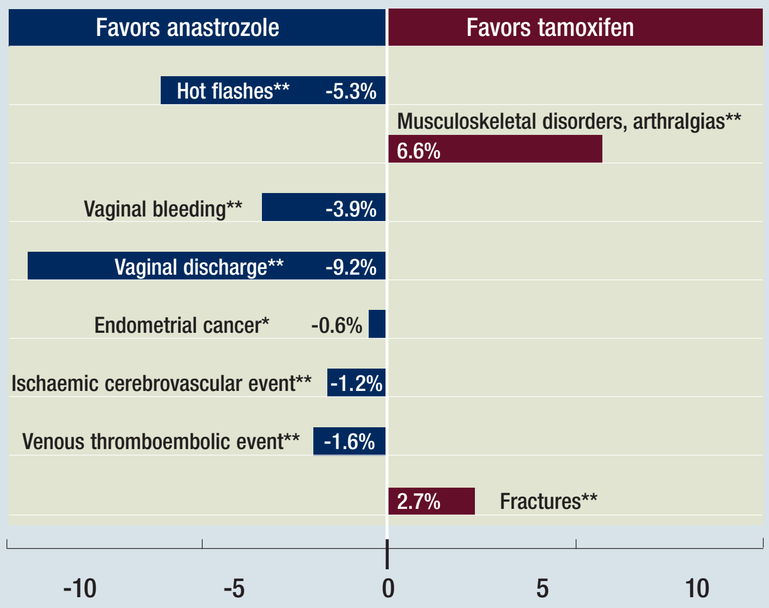
	Anastrozole n=2617 (%)	Tamoxifen n=2598 (%)
First event	290 (11.1)	345 (13.3)
Locoregional recurrence	49 (1.9)	62 (2.4)
Distant recurrence	133 (5.1)	158 (6.1)
Contralateral (invasive)	17 (0.6)	31 (1.2)
Contralateral (DCIS)	3 (0.1)	4 (0.2)
Death (non-breast cancer)	88 (3.4)	90 (3.5)

SUMMARY I — UPDATED ANALYSIS



SOURCE: Presentation, A Buzdar, San Antonio Breast Cancer Symposium 2002. Reproduced with permission.

SIGNIFICANT DIFFERENCES IN PRE-DEFINED ADVERSE EVENTS



DERIVED FROM: Sainsbury R on behalf of the ATAC Trialists' Group. **Beneficial side-effect profile of anastrozole compared with tamoxifen confirmed by additional 7 months of exposure data: a safety update from the 'Arimidex', Tamoxifen, Alone or in Combination (ATAC) trial.** *Breast Cancer Res Treat* 2002;Abstract 633.

UPDATED DATA FROM THE ATAC TRIAL

The new ATAC trial data gives me comfort and a sense of vindication that we waited a year before starting to make therapeutic recommendations. Last year, I publicly supported the ASCO technology assessment. Last year I needed persuasion to use adjuvant anastrozole. It was a nice option if tamoxifen could not be tolerated or was contraindicated. I could not live with the uncertainty.

This year, however, with the updated efficacy and safety data, I've turned. Now, my default therapy for receptor-positive postmenopausal women is anastrozole unless contraindicated. We have another year of follow-up in the ATAC trial, and I am impressed by the separation of the curves. The safety update is also comforting. The fracture rate isn't racing away, the relative risks are stable and the other safety profile issues strongly continue to favor anastrozole.

—Michael Baum, ChM, FRCS

IMPLICATIONS OF THE ATAC TRIAL IN CLINICAL PRACTICE

The results of the ATAC trial are quite compelling. Even if you assume for the sake of argument that the curves will come together with further followup, the safety profile of anastrozole is still clearly better than tamoxifen. I cannot prevent endometrial cancer short of removing the uterus, but I can prevent or treat osteoporosis and fractures. Since the safety profile of anastrozole is better than tamoxifen and it is therapeutically superior, I have a problem not offering anastrozole to my postmenopausal patients — not as a neutral choice but as a better choice. I do discuss with my patients the enormous amount of clinical experience we have with tamoxifen, but if my sister developed breast cancer today, I would certainly recommend anastrozole as opposed to tamoxifen.

—Gabriel N Hortobagyi, MD

Until now, I had not changed my clinical practice based on the early ATAC results. I was waiting to see more data and whether or not the curves were coming together. However, at 47 months, the divergence of the curves shows a three-percent advantage for anastrozole. There will not be three-percent events in either arm over the next year; therefore, the anastrozole advantage will continue to be the same or greater in the next year.

I will now tell patients that there are two options. One option, tamoxifen, seems less efficacious in the short term, but we know its short- and long-term toxicities. With anastrozole, the time to relapse is substantially improved at the four-year point, but we really don't have any long-term safety or efficacy data. The FDA did, however, find adequate evidence to allow approval of the drug in the adjuvant setting. There is a risk with either therapy, and some patients will want the new therapy with the potential to be better.

— Peter Ravdin, MD, PhD

USE OF OTHER AROMATASE INHIBITORS IN THE ADJUVANT SETTING

I do not use the other aromatase inhibitors in the adjuvant setting, because there are no adjuvant data. While we have to extrapolate in a number of situations, I do not see an advantage for the other aromatase inhibitors from the existing data. It is possible that some time in the future, someone will show a distinct advantage of one of these other agents, but at this point, the data were generated with anastrozole, so I use anastrozole.

—Gabriel N Hortobagyi, MD

SELECT PUBLICATIONS

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

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Sainsbury R on behalf of the ATAC Trialists' Group. **Beneficial side-effect profile of anastrozole compared with tamoxifen confirmed by additional 7 months of exposure data: a safety update from the 'Arimidex', Tamoxifen, Alone or in Combination (ATAC) trial.** *Breast Cancer Res Treat* 2002;Abstract 633.

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