The Effects of Neoadjuvant Anastrozole (Arimidex) on Tumor Volume in Postmenopausal Women with Breast Cancer: A Randomized, Double-Blind, Single-Center Study[1]

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ABSTRACT

Anastrozole, an orally active, nonsteroidal aromatase inhibitor, was evaluated in a randomized, double-blind, single-center study to determine its efficacy as neoadjuvant therapy in postmenopausal women with newly diagnosed, estrogen receptor-rich, locally advanced or large (>3 cm), operable breast cancers. Twenty-four eligible patients were recruited into the study and received either 1 mg ($n = 12$) or 10 mg ($n = 12$) of anastrozole daily over a 3-month period. Tumor volumes were estimated clinically, by using caliper measurements and ultrasound (at baseline and after 1, 2, and 3 months' treatment) and by mammography (at baseline and after 3 months). Tumor volume was also measured in surgical specimens. Twenty-one patients were classified as T_2, two patients as T_3, and one patient as T_{4B} at baseline. Three patients had clinical evidence of lymph node involvement. When considering the difference between the volume as measured by each assessment and the actual pathological volume, the interquartile range and the difference between the maximum and minimum values were smaller for ultrasound when compared with those measured with calipers and mammography. Therefore, of the three clinical assessments of tumor volume used in this study, the data suggest that ultrasound may be the most accurate. The median reductions in tumor volumes as measured by ultrasound for those patients with a measurable 12-week assessment were 80.5 and 69.6% for anastrozole (1 and 10 mg, respectively) after 12 weeks of treatment and 75.5% when both doses were grouped together. Moreover, of these patients, 11 of 12 given 1 mg and 7 of 11 given 10 mg of anastrozole were found on ultrasound to have a >50% reduction in tumor volume after 12 weeks of treatment. Of the 17 patients who would have required a mastectomy at initiation of treatment, 15 were suitable for breast conservation after anastrozole treatment. These results suggest that anastrozole is highly effective as neoadjuvant therapy in postmenopausal women with estrogen receptor-rich, large, operable breast cancer. Future studies comparing anastrozole with tamoxifen as a neoadjuvant treatment should be considered.

INTRODUCTION

Breast cancer is currently the most common malignancy to affect women in Europe and the United States; it is estimated that five million women will be diagnosed with the disease over the next 10 years (1). Although there have been substantial developments in breast cancer treatment, >50% of patients still die from metastatic disease (2). Locally advanced breast cancer, which may at one time have accounted for 15% of all breast cancer cases in the United States, has become less frequent as mammography has allowed earlier-stage disease to be diagnosed more accurately. However, locally advanced breast cancer may still account for up to 70% of breast cancer cases worldwide (3).

Currently, it is standard practice to offer adjuvant therapy to patients with surgically operable breast cancer. In cases of large, operable, locally advanced breast cancers, however, successful neoadjuvant (*i.e.*, preoperative) systemic therapy has the advantage of downstaging primary tumors, thus permitting a more conservative approach that requires less extensive surgery (4).

Although most studies have concentrated on chemotherapy as neoadjuvant treatment, a few groups have evaluated neoadjuvant endocrine therapy in hormone-sensitive, large, operable, locally advanced breast cancer (5–7). Substantial reductions in tumor volume over a 3-month period have been recorded with tamoxifen (8). The Edinburgh Breast Unit is indeed one group that has extensive experience of neoadjuvant systemic treatment for breast cancer (4).

Postmenopausal women treated with either tamoxifen or an aromatase inhibitor (either aminoglutethimide or 4-hydroxyandrostenedione) showed a significant reduction in tumor size (5). Tamoxifen has been used extensively as neoadjuvant therapy in locally advanced breast cancer in elderly patients (*i.e.*, ≥75 years old; Ref. 7). The amount of ER[3] protein expressed on cancer cells is related to the response to endocrine therapy in primary operable breast cancer; primary tumors with an ER

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[3] The abbreviations used are: ER, estrogen receptor; UICC, Union International Contre le Cancer; NSABP, National Surgical Adjuvant Breast and Bowel Project.

concentration of <20 fmol/mg cytosol protein are unlikely to respond to endocrine therapy (tamoxifen or an aromatase inhibitor) than those with higher ER values, 60% of which respond well (5).

The earlier aromatase inhibitors, aminoglutethimide and formestane, were not widely used in the neoadjuvant setting because of either their nonselectivity or the need for i.m. injection. In contrast, the new aromatase inhibitor anastrozole is a potent and selective nonsteroidal aromatase inhibitor and is given p.o. Used in postmenopausal women, this new-generation aromatase inhibitor is well tolerated and significantly reduces estrogen levels (9). A combined analysis of two large, randomized trials in postmenopausal women with advanced breast cancer who had failed on tamoxifen therapy has shown that 1 mg of anastrozole significantly increases survival time compared with megestrol acetate at a mean follow-up of 31 months (10). Additional trials with anastrozole include comparisons with tamoxifen in postmenopausal women with advanced breast cancer and comparisons with tamoxifen alone or the combination of anastrozole and tamoxifen as adjuvant treatment for early breast cancer in postmenopausal women.

It is possible that a more complete estrogen blockade using a newer selective aromatase inhibitor might result in greater tumor shrinkage than with tamoxifen, because tamoxifen is a weak or partial estrogen agonist in some organs (11).

The aim of the current study was to investigate the effects of 1 mg of anastrozole (the clinically approved dose) and 10 mg of anastrozole once daily on tumor volume in the neoadjuvant setting in postmenopausal women with ER-rich, locally advanced or large (>3 cm), operable breast cancers. The inclusion of the 10-mg dose was for scientific reasons, to determine whether the data observed for 1 and 10 mg of anastrozole in the neoadjuvant setting mirrored that seen in the advanced breast cancer setting (10) and with respect to peripheral aromatase inhibition (9).

PATIENTS AND METHODS

Patient Selection

Postmenopausal women with invasive ER-rich (ER shown on initial core biopsy by histoscore to be >80, which is equivalent to >20 fmol/mg of cytosol protein; Ref. 12) breast cancers were enrolled in the study. Postmenopausal status was defined as those patients aged ≥50 years who had not menstruated in the last 12 months, or women of any age with follicle-stimulating hormone levels >40 IU/liter. Diagnosis of breast carcinoma was confirmed using fine-needle aspiration cytology. Only patients with operable breast cancers >3 cm (T_2, >3 cm; T_3, N_{0-1}, M_0) or locally advanced breast cancers (T_{4b}, N_{0-1}, M_0) were included.

Ethics committee approval was obtained, and the study was conducted in accordance with the Declaration of Helsinki. All of the patients in the study gave their written informed consent.

Patients were enrolled in the study between March 1997 and July 1998. Patients were screened for eligibility and to provide baseline assessments 4 weeks before randomization into the trial. This included a medical history, full physical examination, including a 12-lead electrocardiogram and laboratory determinations, an assessment of baseline evaluable disease clinically by calipers and ultrasound and also by mammogram, and a bone scan and chest X-ray to confirm the absence of overt metastases. For those assessments that could not be repeated at short intervals (*e.g.*, bone scan, chest X-ray, mammogram), these were accepted if performed within 12 weeks before randomization. Exclusion criteria included drug-induced menopause; liver function tests more than three times the upper limit of the reference range; other abnormal laboratory test results that would place the patient at risk or confound the results of the study; patients with a history of systemic malignancy other than breast cancer, with the exception of basal or squamous cell carcinoma of the skin, or cancer of the cervix that had been satisfactorily controlled; and patients with an expected survival time of <3 months from the start of the study.

Patients were not allowed to receive any other systemic treatment for breast cancer in addition to their trial therapy. If any additional systemic therapy for breast cancer was required, trial therapy was withdrawn.

Study Design

This was a randomized (1:1), double blind, single-center study in which patients received either 1 or 10 mg of anastrozole p.o. once daily for 12 weeks. A total of 24 patients were to be recruited for this trial. This number was based on feasibility rather than any formal statistical technique.

An open wedge biopsy was performed removing approximately 1 g of tumor for confirmation of ER status and to obtain tissue for estrogen synthesis and uptake studies. Patients were reviewed for surgical wound healing after 10 days of treatment. Physical examinations (including tumor caliper assessments and ultrasound measurements) and safety and tolerability assessments were carried out at the visits at 4, 8, and 12 weeks.

At the last visit (week 12), a mammogram and, if it was believed clinically appropriate, a bone scan, chest X-ray, and electrocardiogram were also performed. Tumors were then excised by breast-conserving surgery or by mastectomy if appropriate. The excised tumor was measured in three dimensions to assess the actual tumor volume by pathology, and samples were removed for histology. The protocol required patients to be withdrawn from the study and undergo surgery earlier if there was any evidence of disease progression. Surgery also was performed earlier if a patient had responded well to the treatment (*i.e.*, if the clinician predicted that there would be insufficient tissue remaining by the 12-week end point to provide adequate amounts of tumor tissue for assessment of all of the parameters).

Clinical Efficacy of Anastrozole

Measurement of Tumor Volume. The percentage change in tumor volume (V) from baseline was used to assess the response to treatment. Tumor volumes obtained using caliper and mammography assessments were calculated by measuring the average diameter (D) of the tumor (an average of four diameters using calipers or two diameters with mammography) and using the following formula (13):

$$V = \frac{D^3 \times \pi}{6} \quad \text{(A)}$$

Table 1 Patient demographics and baseline tumor characteristics

	Anastrozole	
	1 mg/day (n = 12)	10 mg/day (n = 12)
Age (yr)[a]	74.1 ± 8.7	68.8 ± 8.9
Weight (kg)[a]	69.6 ± 9.6	77.5 ± 14.2
Height (cm)[a]	156.3 ± 12.2	157.8 ± 11.7
Tumor stage[b]		
T_2	11 (91.7)	10 (83.3)
T_3	0 (0)	2 (16.7)
T_{4B}	1 (8.3)	0 (0)
Lymph node metastases	2 (16.7)	1 (8.3)
Tumor volume assessment (cm^3)		
Caliper		
Median	23.7	27.3
Maximum	42.4	161.0
Minimum	12.4	10.9
Ultrasound		
Median	4.8	4.9
Maximum	9.9	14.3
Minimum	2.4	1.4
Mammography		
Median	7.3	8.4
Maximum	25.5	47.7
Minimum	1.4	0.7

[a] Mean ± SD.
[b] No. of patients, with percentage in parens.

Tumor volume was also calculated using D, the average of four diameters obtained with ultrasound, and using the following formula (13):

$$V = \frac{D^2 \times d \times \pi}{6} \quad \text{(B)}$$

where d is the depth or thickness.

Tolerability and Safety Assessments. All of the adverse events were recorded, irrespective of their being related to the trial therapy.

Analysis of the Results

The data on tumor volumes were not subject to any formal statistical analysis. The study was not sized to show a difference between the dose of anastrozole and the effect on tumor volume. Tumor volumes (actual volume and percentage reduction from baseline) were summarized using the median, minimum, maximum, and total number of patients for those eligible patients by the treatment received. The difference at 12 weeks between the tumor volumes as estimated by calipers, mammography, ultrasound, and the actual pathological volume were summarized by treatment received for all of those eligible patients who had a measurable 12-week assessment.

For completeness, data on changes in the product of two diagonal clinical measurements 90° apart were calculated before and after treatment, and the percentage reduction was determined. This is the approach outlined by the UICC for measuring tumors.

Adverse event data were summarized by treatment received for all of the randomized patients who took trial treatment.

Table 2 Tumor volume after 12 weeks of anastrozole treatment

	Anastrozole			
	1 mg/day		10 mg/day	
Assessment method	Tumor volume (cm^3)	% Reduction from baseline	Tumor volume (cm^3)	% Reduction from baseline
Caliper				
n	12	12	11	11
Median	2.0	89.3	0.1	99.6
Maximum	7.9	100.0	50.1	100.0
Minimum	0.0	74.0	0.0	−8.8
Ultrasound				
n	12	12	11	11
Median	0.9	80.5	1.4	69.6
Maximum	2.5	95.7	5.1	97.6
Minimum	0.3	6.3	0.1	−16.8
Mammography				
n	12	12	11	11
Median	1.8	73.6	5.6	69.3
Maximum	5.6	98.8	22.5	100.0
Minimum	0.1	37.0	0.0	8.1

RESULTS

Patient Characteristics. Twenty-six patients were enrolled in the study: 13 patients were randomized to receive the 1-mg dose of anastrozole and 13 patients received the 10-mg dose. At initial wedge biopsy, two of these patients had fine-needle aspirations suggesting that they had tumors rich in ERs. However, their histoscore values on the open wedge biopsy were below the cutoff of 80, indicating that they were not eligible for the study, and, therefore, they were not included in the summaries of tumor volume. One of these patients was withdrawn from the study after 4 weeks of treatment, and the other continued on treatment and had surgery according to protocol after 3 months. Because these two patients did take anastrozole (although, in the case of one of the patients, only for a short time), they have consequently been included in the analysis of tolerability. Patient characteristics for the eligible patients are shown in Table 1; the demography was comparable between the two treatment groups. Twenty-one patients were classified as T_2 at baseline, two patients were T_3, and one patient was T_{4B} (Table 1). Three patients had clinical evidence of lymph node involvement. At the outset of the study, on the basis of tumor volume compared with breast volume or disease stage, 17 patients would have required mastectomy according to our unit protocol. The mean tumor volumes at baseline for the two treatment groups are also given in Table 1. One patient eligible for the study withdrew because of adverse events (headaches, depression, and tiredness).

Clinical Efficacy of Anastrozole. The median reduction from baseline in tumor volume after 12 weeks of treatment with 1 mg/day of anastrozole was calculated to be 89.3% using calliper measurements (n = 12), 80.5% using ultrasound (n = 12), and 73.6% using mammography (n = 12), as shown in Table 2. With 10 mg/day of anastrozole, the median reduction from baseline in tumor volume was calculated to be 99.6% using calipers (n = 11), 69.6% using ultrasound (n = 11), and 69.3%

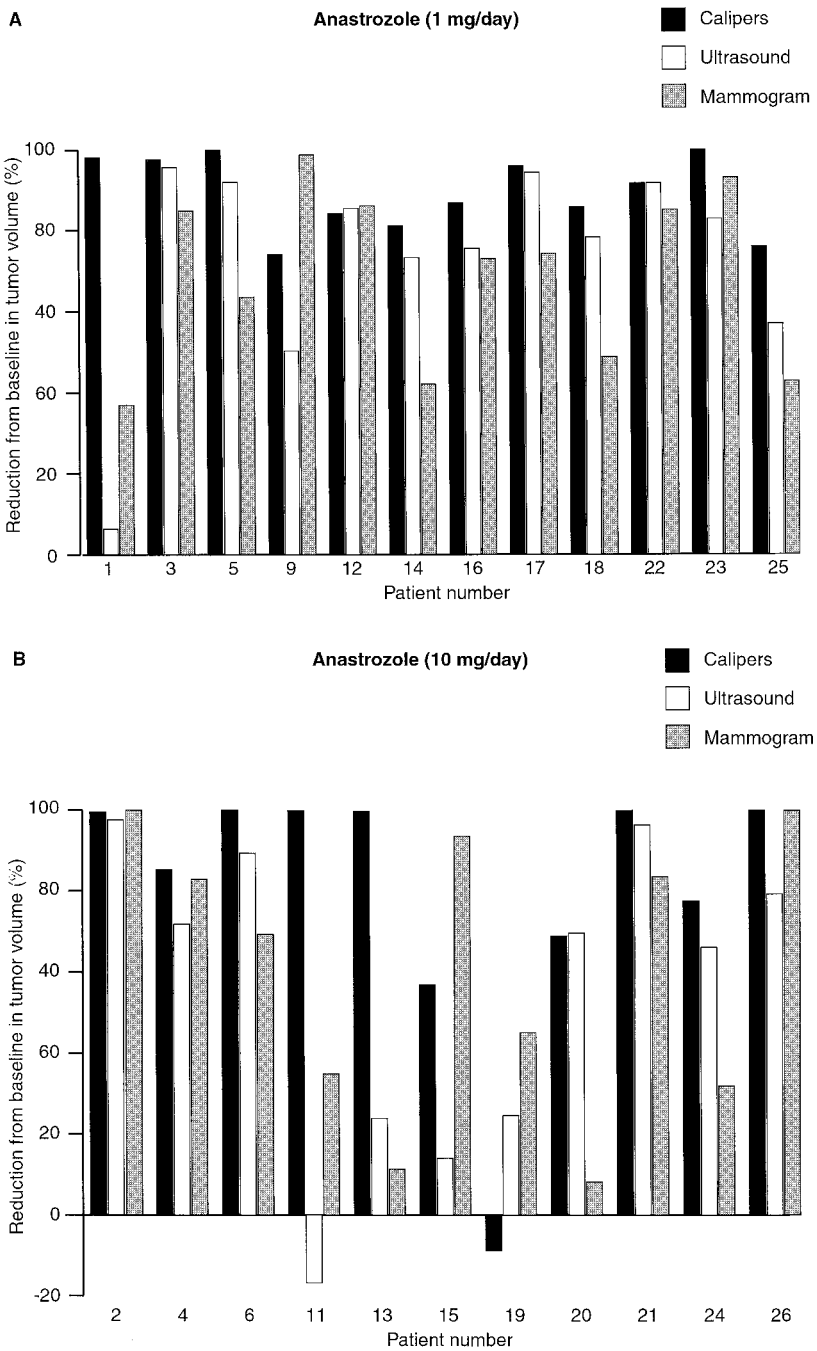

Fig. 1 The reduction from baseline in tumor volume at week 12 as measured by calipers, ultrasound, and mammography in patients administered either (*a*) 1 mg/day or (*b*) 10 mg/day of anastrozole.

using mammography measurements ($n = 11$). For ultrasound assessments, the median reduction from baseline when subjects receiving 1 and 10 mg anastrozole were grouped together was 75.5%. The actual tumor volumes as measured by the three assessment methods are also presented in Table 2.

Figure 1 shows the individual percentage reductions from baseline in tumor volumes of patients after 12 weeks of anastrozole treatment. In all but two patients (patients 11 and 19), all three of the methods of assessment showed a reduction in tumor volume. Patient 11 showed an increase in tumor volume using ultrasound, and patient 19 showed an increase in tumor volume using calipers.

Irrespective of the assessment used, many patients showed a >75% reduction in tumor volume: 11 of 12 (calipers), 5 of 12 (mammogram), and 8 of 12 (ultrasound) after treatment with 1 mg of anastrozole and 8 of 11 (calipers), 5 of 11 (mammogram), and 4 of 11 (ultrasound) after treatment with 10 mg of anastrozole (Table 3). No patient showed a progression in disease, regardless of the measurement used.

Fifteen of the 17 patients who would have been expected to

Table 3 Tumor shrinkage in response to treatment with anastrozole treatment for 12 weeks

Change from baseline after 12 weeks of treatment	Caliper		Ultrasound		Mammogram	
	Anastrozole, 1 mg/day (n = 12)	Anastrozole, 10 mg/day (n = 11)	Anastrozole, 1 mg/day (n = 12)	Anastrozole, 10 mg/day (n = 11)	Anastrozole, 1 mg/day (n = 12)	Anastrozole, 10 mg/day (n = 11)
100% decrease (*i.e.*, lesions disappeared)	2	3	0	0	0	2
>75 to <100% decrease	9	5	8	4	5	3
50–75% decrease	1	2	3	3	3	1
<50% decrease to 25% increase	0	1	1	4	4	5
>25% increase	0	0	0	0	0	0

Table 4 Difference between assessment and surgical specimen tumor volumes for all of the patients who had a measurable 12-week assessment (measured at 12 weeks), treated with anastrozole, irrespective of dose

	Caliper	Ultrasound	Mammography
n	23	23	23
Median	−0.24	−0.12	−1.33
Q1[a]	−4.88	−0.67	−2.80
Q3	0.44	0.79	−0.35
Maximum	6.15	4.39	5.69
Minimum	−42.60	−1.89	−14.91

[a] Q1, lower quartile (25% of data); Q3, upper quartile (75% of data).

require a mastectomy at the outset of the study were suitable for breast conservation after treatment with anastrozole. The other seven patients who completed the study had their tumors removed by local excision as planned. The two patients who enrolled in the study and were ineligible also were suitable for breast conservation.

Measurement Techniques. The tumor volumes calculated using calipers, ultrasound, and mammography were all similar to the actual tumor volume measured by pathology at week 12 (Table 4). The data do suggest, however, that on the basis of descriptive assessment, ultrasound is the most accurate measure of tumor volume because the interquartile range (the difference between the presented lower and upper quartiles) and the difference between the maximum and minimum values were smaller with ultrasound measurements than with those of calipers and mammography.

Confirmation that ultrasound is the most accurate measure of tumor volume can be seen using scatter plots of the tumor volumes calculated by each method (calipers, ultrasound, and mammography) *versus* the pathological tumor volume (Fig. 2). Ultrasound measurements were closest to the pathological volume, with no outliers being seen, compared with calipers and mammography, in which four and one outliers were seen, respectively.

Bidimensional Measurements. Changes in the product of the bidimensional measurements are shown in Table 5. These groups equate to the UICC criteria for complete response, partial response, and no change, but because they were not maintained for 1 month (because surgery followed the last assessment), they are not equivalent to UICC criteria.

Changes in Clinical Node Status. The tumor, node, metastases status before and after treatment and the pathological nodal status for each patient are shown in Table 6. This study did not demonstrate any consistent effect on nodal status, with the majority of patients (19 of 23) remaining clinically node negative throughout the study, although in 7 of these cases nodal status was found to be positive on pathological evaluation. The three patients who were N_1 at the start of treatment were pathologically node-positive after therapy, although one was clinically downstaged to N_0. One patient had an increased clinical nodal status from N_0 to N_1, but pathological examination showed no nodal involvement.

Tolerability. In general, treatment was well tolerated in this study. There were no serious adverse events, and only one patient withdrew because of adverse events (headaches, depression, and tiredness).

DISCUSSION

This is the first study to investigate the potential of anastrozole as a neoadjuvant therapy. Using ultrasound, we found that, of those eligible patients who had a measurable 12-week assessment, 11 of 12 patients given 1 mg and 7 of 11 patients given 10 mg of anastrozole had a >50% reduction in tumor volume after 12 weeks of treatment. Without neoadjuvant treatment, 17 patients would have required a mastectomy, but this was only necessary in 2 patients after anastrozole treatment.

In clinical trials, both chemotherapy (many studies with different regimens) and endocrine therapy (tamoxifen and letrozole), when used as neoadjuvant therapy before surgery, have been shown to reduce tumor size (3, 6, 7, 14, 15). Although chemotherapy can be used irrespective of estrogen status, studies of neoadjuvant therapy have demonstrated clearly that endocrine therapy is most effective in tumors that are ER-rich; hence, for the current study, this was a prerequisite to trial entry (5). This small exploratory trial in selected patients with ER-rich tumors highlights the effectiveness of endocrine therapy in the form of the nonsteroidal aromatase inhibitors. Anastrozole was highly effective (in terms of breast conservation) in tumor downstaging in this selected group of postmenopausal women, thereby offering the clinician an additional tool for chemotherapy in the neoadjuvant setting. Generally, endocrine therapy is preferred in postmenopausal women because it is better tolerated than chemotherapy, and these data confirm that, in addition to good tolerability, anastrozole is highly effective in reducing tumor size. This study did not demonstrate any consistent effect on nodal status.

The role of neoadjuvant treatment in breast cancer remains to be fully determined. In line with data from other studies, this

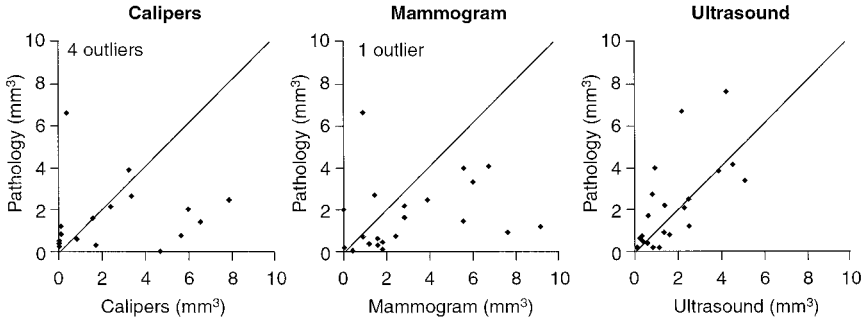

Fig. 2 Relationship between pathological and calliper (*left*), mammography (*middle*), and ultrasound (*right*) tumor volumes (mm^3) for all of the patients.

Table 5 Bidimensional measurements

Change from baseline in product of bidimensional measurements	Clinical		Ultrasound		Mammogram	
	Anastrozole, 1 mg/day (n = 12)	Anastrozole, 10 mg/day (n = 11)	Anastrozole, 1 mg/day (n = 12)	Anastrozole, 10 mg/day (n = 11)	Anastrozole, 1 mg/day (n = 12)	Anastrozole, 10 mg/day (n = 11)
100% decrease	2	3	0	0	0	2
>50% decrease	10	6	9	7	8	4
<50% decrease to 25% increase	0	2	3	4	4	5

study confirms that neoadjuvant treatment can be useful in increasing the rate of breast conservation in women who would have previously required more radical surgery, including mastectomy. With the exception of the NSABP B-18 trial,[4] however, there have been no trials of sufficient size and statistical power to determine the long-term outcome after neoadjuvant treatment. In the NSABP B-18 trial, there was no difference in disease-free survival or overall survival at a median of 5 years' follow-up (16).

Tumor volume is thought to be a useful indicator of response to treatment in patients with breast cancer. The results obtained with tumor volume in this study very closely reflect those with bidimensional measurements. However, a problem with bidimensional measurement is that it does not take into account tumor shape. In this study we chose to measure tumor volume by three methods—calipers, ultrasound, and mammography—during the 12-week treatment period and compared these measurements with final volume, as assessed by the pathologist after surgery.

The results obtained in the present study, based on a comparison of the interquartile ranges and scatter plots, indicate that ultrasound is the most accurate of the methods studied for assessing actual tumor volume. This is in agreement with the study by Forouhi *et al.* (13), which concluded that ultrasound is the most practical and accurate method of measuring breast tumor volume and monitoring response to primary systemic treatment; however, this conclusion does require confirmation in larger studies specifically designed to address this issue. Other studies have investigated various methods of measuring breast tumor size, although not in the context of monitoring response to primary systemic treatment (17–20). In one study (17), ultrasound was shown to be the most accurate technique of measuring tumor size compared with mammography and clinical

Table 6 TNM clinical stage before and after treatment and pathological nodal status

Patient no.	TNM[a] stage before treatment	TNM stage after treatment	Nodal status (pathology assessment)
1	$T_2N_0M_0$	$T_1N_0M_0$	0/5
2	$T_2N_0M_0$	$T_1N_0M_0$	1/4
3	$T_2N_0M_0$	$T_1N_0M_0$	4/5
4	$T_3N_0M_0$	$T_2N_0M_0$	2/5
5	$T_2N_1M_0$	$T_1N_0M_0$	1/7
6	$T_2N_0M_0$	$T_1N_0M_0$	0/5
9	$T_2N_0M_0$	$T_2N_1M_0$	0/4
11	$T_2N_0M_0$	$T_1N_0M_0$	2/3
12	$T_2N_0M_0$	$T_1N_0M_0$	0/4
13	$T_2N_0M_0$	$T_1N_0M_0$	0/2
14	$T_2N_0M_0$	$T_1N_0M_0$	2/7
15	$T_2N_0M_0$	$T_2N_0M_0$	0/5
16	$T_2N_0M_0$	$T_1N_0M_0$	0/5
17	$T_2N_0M_0$	$T_1N_0M_0$	0/4
18	$T_2N_0M_0$	$T_1N_0M_0$	0/7
19	$T_2N_0M_0$	$T_2N_0M_0$	1/18[b]
20	$T_3N_1M_0$	$T_2N_1M_0$	17/22[b]
21	$T_2N_0M_0$	$T_0N_0M_0$	3/6
22	$T_2N_0M_0$	$T_1N_0M_0$	0/4
23	$T_2N_0M_0$	$T_0N_0M_0$	0/5
24	$T_2N_0M_0$	$T_2N_0M_0$	0/4
25	$T_{4b}N_1M_0$[c]	$T_2N_1M_0$	3/4
26	$T_2N_0M_0$	$T_0N_0M_0$	0/3

[a] TNM, tumor, node, metastasis.
[b] Patients underwent mastectomy plus axillary clearance (all of the other patients had wide local excision and axillary node sampling).
[c] Peau d'orange.

[4] Patients with T_{1-3}, N_0 disease randomized either to surgery followed by four courses of doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) or to four courses of doxorubicin and cyclophosphamide followed by surgery.

measurements, but another study (18) described them as having the same degree of accuracy. However, other studies concluded that ultrasound is a useful adjunct to mammography in detecting tumor size, particularly in the diagnosis of breast cancer (19, 20). Ultrasound has the advantage that it is painless, easily performed, and has a low level of intraobserver error. It has now become our standard method of assessing response to primary systemic therapy.

In conclusion, our data from this small study suggest that anastrozole is highly effective as neoadjuvant therapy in postmenopausal women with ER-rich, large, operable breast cancers, as assessed by tumor volume. The study also showed that of the three noninvasive methods used to measure tumor volume, ultrasound is the most accurate. Additional studies with larger numbers of patients are required to confirm these findings. Future studies comparing anastrozole with tamoxifen as a neoadjuvant treatment are planned.

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