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E20. Neoadjuvant endocrine therapy in breast cancer

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Neoadjuvant endocrine therapy given to patients with large operable or locally advanced breast cancers has the advantage that it can reduce tumour volumes making inoperable tumours operable or patients who would have required mastectomy suitable for breast-conserving surgery. Early studies of patients treated sequentially in Edinburgh suggested that responses with neoadjuvant aromatase inhibitors were superior to those seen with tamoxifen (Table 1). It was also evident that patients treated with tamoxifen had a lower rate of conversion to breast-conserving surgery than those given letrozole a subsequent randomised trial described below.

Trial P024 compared four months of neoadjuvant letrozle with tamoxifen in 324 patients and demonstrated significanty better clinical responses, ultrasound

Table 1
Median tumour volume reduction in series of patients with locally advanced breast cancer who received neoadjuvant endocrine therapy in the Edinburgh Breast Unit[a]

Agent	Number of patients	Patients with >50% reduction, *n* (%)	Patients with <50% reduction or <25% increase, *n* (%)	Patients with >25% increase, *n* (%)
Tamoxifen	65	30 (46)	34 (52)	1 (2)
Letrozole	36	32 (89)	3 (8)	1 (3)
Anastrozole	23	18 (78)	5 (22)	0
Exemestane	12	10 (83)	2 (17)	0

[a] Tumour volume changes (reduction or increase) were assessed by ultrasound measurements during the 3-month treatment period.

Table 2
Primary and secondary efficacy end-point results of trial P024 comparing 4 months of neoadjuvant letrozole versus tamoxifen (all study patients)

Efficacy end-points	Letrozole (*n* = 154) (%)	Tamoxifen (*n* = 170) (%)	*P* value
Primary end-point			
Clinical response (palpation)	55	36	<0.001
Complete	10	4	
Partial	45	32	
Secondary end-points			
Ultrasound response	35	25	0.042
Complete	3	1	
Partial	32	24	
Mammographic response	34	16	<0.001
Complete	4	0	
Partial	30	16	
Breast-conserving surgery	45	35	0.022

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Table 3
Comparing ER scores 8 *vs.* 6 and 7

ER score allred	No. of Pts	No. of responders	% Response	Median % reduction in tumour volume	
				Clin	USS
8	60	48	80	76+	67+
6 + 7	23	17	74	63	48

+$P < 0.005$ comparing ER scores 8 *vs.* 6 and 7.
ER, oestrogen receptor; Pts, patients; USS, ultrasound scan; Clin, clinical assessment.

reponses, mamographic responses and rates of converion to breast-conserving surgery with letrozle than for tamoxifen treatment (Table 2). The major factor predicting response to aromatase inhibors is the oestrogen receptor (ER) status. New data from Edinburgh confirms our previous observations that the reponse rate, in particular the median reducion in tumour volume, is greater for ER 8 tumours than ER 6 and 7 tumours when assessed using the ALLRED scale (Table 3). In the P024 study patients with tumours which were ER or PgR positive and were erbB1 or erbB2 positive were significantly more likely to respond to letrozole (88%) than tamoxifen (21%), $p = 0.004$. A recently completed study (IMPACT) compared neoadjuvant anastrozole alone, tamoxifen alone or the two combined in 330 postmenopausal women with ER-positive disease. The results of this study were somewhat disappointng in that the reponse rates in all three arms were similar. The only end-point which was significanty in favour of anastrozole was the number of patients whose tumours initially required mastectomy, but who subsequently could be treated by breast-conserving surgery. Although there was a suggestion in this study that patients whose tumours were erbB2-positive were more likely to respond to anastrozole, the difference was not significant. What was evident in this study was that there were biological differences between the drugs with regard to their effect on proliferation. By two weeks, anastrozole reduced proliferation to a greater degree than tamoxifen alone or the two agents combined. These are important data and they mirror those of the Anmidex, tamoxifen, alone or in combination (ATAC) study. This study sugests that an analysis of biological end-points two weeks after starting on the drug predicts for long-term adjuvant efficacy and warrants further investigation.