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ADJUVANT TAMOXIFEN TREATMENT IN POSTMENOPAUSAL PATIENTS WITH OPERABLE BREAST CANCER

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Summary—Between November 1, 1976 and December 31, 1981, 826 post-menopausal females with operable breast cancer were included into a trial comparing tamoxifen 40 mg daily for 2 years with no endocrine treatment. Patients without axillary lymph node metastases and tumors <30 mm received no other treatment whilst those with more advanced disease were in addition superrandomised to receive postoperative irradiation or 12 courses of CMF.

With a mean follow-up of 44 months tamoxifen significantly reduced the incidence of recurrence. There was no significant interaction between the effect of tamoxifen and any other treatment or prognostic subgroup.

INTRODUCTION

Adjuvant treatment with tamoxifen increases a recurrence-free survival of postmenopausal women with carcinoma of the breast [1, 2, 3].

This report serves to give a brief summary of the present status of our currently ongoing studies evaluating the usefulness of post-operative adjuvant tamoxifen treatment alone or in conjuction with other adjuvant therapy forms in postmenopausal females with carcinoma of the breast.

EXPERIMENTAL

Between November 1, 1976 and December 31, 1981, 826 eligible postmenopausal females were randomly allocated into one of the treatment regimens which did or did not include tamoxifen. The dose of tamoxifen was 40 mg daily during 2 years. The patients were stratified at randomisation and at analysis according to the extent of the disease. Consequently, 2 groups of patients were obtained out of which 1 subset was defined as favourable (not involved axillary lymph nodes and the tumour size equal or less than 30 mm) and the other as unfavourable (involved axillary lymph nodes and/or tumours larger than 30 mm). The patients were, of course, also stratified according to the other types of treatment. Unfavourable stage patients were all included into a trial comparing adjuvant chemotherapy given as CMF with postoperative radiation treatment. Favourable stage patients were treated either with modified radical mastectomy or partial mastectomy and radiation treatment to the breast, following which they were randomised to tamoxifen during 2 years or no further treatment. The numbers of patients in each of the above mentioned subsets are given in Table 1.

All entered patients have been followed up and are included in the analysis whether the planned treatment was given or not. The mean time of follow-up is 44 months ranging between 12 and 75 months. Estrogen-receptor (ER) data were available for 79% of the patients. Differences between the treatment groups were analyzed using the log-rank test allowing for treatment subsets.

RESULTS AND DISCUSSION

The recurrence free survival is given in Fig. 1. Recurrence or death have occurred in 76 of the tamoxifen treated patients and in 89 of the patients belonging to the control group. The difference between the groups does not yet reach the level of statistical significance ($P = 0.07$).

An analysis of the relative recurrence rate in the tamoxifen treated patients (the recurrence rate of control patients was put at 1.0) showed that there was a lower frequency recurrence in the tamoxifen group during the first 3 years of the study (relative recurrence rate 0.61, $P = 0.01$) with a little difference between the prognostic group in this respect (Table 2). During the following years, this ratio was reversed and the recurrence rate of the tamoxifen treated patients was almost significantly higher than that of controls (relative recurrence rate 1.82, $P = 0.06$).

Table 1. Numbers of patients in treatment subsets

Subset	Tamoxifen group	Control group
Favourable	257	264
Modif. radical mastectomy	230	234
Partial mastectomy	27	30
Unfavourable	159	146
Cytotoxic chemotherapy	73	74
Radiotherapy	86	72
Total	416	410

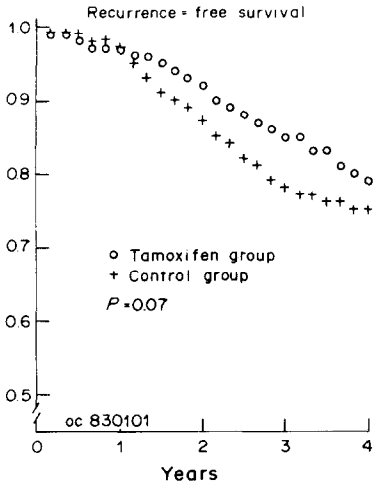

Fig. 1. Recurrence-free survival in the total material of patients.

In conclusion, the present results confirm the previous findings of others and ourselves [1, 2, 3] that adjuvant tamoxifen treatment during 1 or 2 years postoperatively prolongs the recurrence free survival rate of females with breast cancer. Whether or not this type of adjuvant treatment will have any impact on the overall survival remains to be seen. However, findings summarized in the Table 2 might indicate that tamoxifen treatment for 2 years only postponed recurrence in some cases. As demonstrated by Jordan *et al.*[4], a short term administration of tamoxifen at the time when DMBA induced mammary carcinomas begin to appear in rats only postpones the outgrowth of tumours, whereas a continuous administration of the drug largely prevents their occurrence. Since breast cancer disease in humans is frequently associated with long natural history, 1 or 2 years of treatment may indeed be regarded as a short term administration.

Table 2. Relative recurrence rates (Control patients = 1.0) for tamoxifen treated patients by prognostic group and period of follow-up.

	Follow-up period		
Prognostic group	1–3	>3	All years
Favourable	0.70	2.10	0.92
Unfavourable	0.57	1.59	0.67
Total	0.61	1.82	0.75

Currently ongoing trials are aiming at determining an optimal length of tamoxifen treatment as well as finding more favourable combinations with other types of adjuvant therapy.

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