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RANDOMIZED TRIAL BETWEEN SELECTIVE AROMATASE INHIBITOR FORMESTANE (®LENTARON) VS TAMOXIFEN AS FIRST-LINE HORMONAL THERAPY IN POSTMENOPAUSAL PATIENTS WITH ADVANCED BREAST CANCER: CONFIRMATION OF BIOEQUIVALENCE IN SURVIVAL

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409 patients were randomly allocated to receive either formestane (f) 250 mg i.m. fortnightly or tamoxifen (t) 30 mg orally o.d. in a multinational, prospective, open trial. The efficacy and tolerability results were previously reported in the Annals of Oncology 1994, Vol 5 (Supp 7) 519–524. Further analysis has been performed to confirm the survival data now that it has matured, including 218 additional visits from 67 patients. There was no difference between treatments in survival, (1062 (f) vs 1079 (t) days).

During the follow-up period of this trial, 84 patients, (48 (f), 36 (t)) achieved further response to other anticancer therapy, indicating that these patients remained responsive regardless of which endocrine therapy they received for first-line.

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WHICH PATIENTS DEVELOP AN EARLY LOCAL RECURRENCE AFTER BREAST CANCER?

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In a retrospective study of breast cancer patients, the disease course was examined in 137 pre- and postmenopausal patients with a local recurrence. Here especially the dependency of a recurrence-free interval on biological parameters of the primary tumor was investigated. It was found that in 23% of the cases the local recurrence expressed tumor generalization with the simultaneous occurrence of distant metastases. The average recurrence-free interval was 4 years, whereby more than half of the recurrences took place in the first two postoperative years. A statistically significant relationship to the recurrence-free interval could be demonstrated for the following parameters: Primary tumor size (P = 0.0003), node status (P = 0.0006) as well as the number (P = 0.0002) and level (P = 0.00001) of metastatically involved lymph nodes. The immunohistochemical estrogen and progesterone receptors (P = 0.0005) and the growth factor obtained with the monoclonal antibody Ki67 (P = 0.0005) also significantly correlated with the length of the recurrence-free interval. The type of operative primary therapy did not have an effect on recurrence-free survival. However, adjuvant therapy had a decisive influence—patients developed a local recurrence significantly later after adjuvant radiotherapy (P = 0.00001).

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INFUSIONAL 5-FLUOROURACIL (F) WITH EPIRUBICIN (E) AND CARBOPLATIN (ECARBOF) IN ADVANCED/METASTATIC BREAST CANCER (ABC)—CAN CARBO REPLACE CISPLATIN (C)?

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Infusional ECF is an active new schedule against ABC with a response rate of 84% in 43 patients (Jones *et al.*, *JCO* 1994; 12:1259–65). Cisplatin however is a major contributor to toxicity and usually requires inpatient treatment. We have investigated the substitution of carboplatin (AUC 5 iv 4-weekly) replacing C, in combination with E 50 mg/m^2 iv 4-weekly bolus and F 200 mg/m^2 daily. Fifty pts, with ABC median age 48 yrs (range 33–62 yrs) have been treated in a phase II trial. At a median follow-up of 9 mths (range 4–27 mths), there are 9 CR, 34 PR and 7 NC to give a RR of 86% (95% CI 70–97%) with responses in all sites. The median PFS is 11 mths and median survival is 17 mths. Grade 3/4 toxicities in the two non-randomised sequential studies were as follows: ECF v ECarboF: emesis 28% v 2%, alopecia 56% v 22%, lethargy 14% v 3%, plantar-palmar rash 26% v 6%, stomatitis 12% v 8%, neuropathy 2% v 0% and Hickman line complication 28% v 26%. These results suggest a regimen that is as active as ECF and has less toxicity.

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EFFECT OF ORAL CLODRONATE IN WOMEN WITH RECURRENT BREAST CANCER IN THE ABSENCE OF SKELETAL METASTASES

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Clodronate reduces morbidity in women with breast cancer and skeletal metastases. In this double blind controlled study, we examined the effect of clodronate on the incidence of skeletal metastases and morbidity in recurrent breast cancer without radiographic or scintigraphic evidence of skeletal disease.

In addition to anti-tumour therapy, 133 women received either clodronate 1600 mg daily by mouth (n = 66) or an identical placebo (n = 67). Fewer patients developed skeletal metastases during clodronate treatment (15 vs 19, NS) and the total number of skeletal metastases was significantly decreased (32 vs 63, $P < 0.005$). Treatment also reduced the number of hypercalcaemic episodes (10 vs 17) and vertebral deformities (35 vs 54). The latter effect was most marked in those with vertebral deformities at entry (41.9 vs 150.0 fractures/100 patient years, $P < 0.005$). The combined rate of all morbid skeletal events was reduced by 26% ($P < 0.01$). We conclude that oral clodronate reduces the progression of skeletal metastases in patients with recurrent breast cancer and may provide a useful adjunct in the management of these patients.

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ADVANCED BREAST CANCER: A PHASE II TRIAL WITH GEMCITABINE (GEM)

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A phase II study is being conducted to investigate the efficacy of the novel nucleoside analogue, GEM, in advanced breast cancer. At present, this condition is incurable and most current treatment is given with the expectation of palliating symptoms and improving quality of life. Female patients (pts) with progressive advanced or metastatic breast cancer which is not amenable to curative surgery or radiotherapy will be recruited to this 2 stage study. Inclusion criteria: life expectancy of at least 3 months; Karnofsky Performance status $\geq$60; WBC $\geq 3 \times 10^9$/L; Hb $\geq$ 10 g/dL; platelets $\geq 100 \times 10^9$/L. GEM (starting dose 1000 mg/m^2) was administered as a 30-min infusion once weekly for 3 weeks followed by a week of rest (1 cycle). To date, 33 pts have entered the study. There have been 6 PRs after treatment with GEM. In 13 other pts the disease stabilized. Toxicity was generally mild: no grade 4 WHO symptomatic toxicity was reported. Only 1 pt suffered grade 3 nausea and vomiting. Therefore, this study confirms that GEM is active in breast cancer. Further studies are warranted, particularly to evaluate the use of GEM in earlier stages of breast cancer and in combination with other cytotoxic drugs.

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TAXOL® (PACLITAXEL) AND FARMORUBICIN® (EPIRUBICIN) IN METASTATIC BREAST CANCER (MBC): PRELIMINARY RESULTS OF A PHASE I STUDY

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TAXOL® (T) (3 hour infusion) given immediately after FARMORUBICIN® (F) (IV bolus) every 3 weeks for MBC was explored in a phase I study:

Dose level	TAXOL® (mg/m^2)	FARMORUBICIN® (mg/m^2)	N pts	N cycles
1	110	50	3	14
2	135	50	4	19
3	175	50	6	37
4	200	50	6	29
5	200	60	3	4
6	225	50	3	6
			25	109