Disease progression/dissemination was registered within mean 8 months (range 1 to 32 months). Local progression was noted in 22 patients, visceral metastases were seen first in 6 patients and bone metastases in one patient.

PP-8-23 Oral Clodronate for Bone Metastases in Breast Cancer

M. Projević*, S. Filipović, S. Veselinović, M. Burić. *Clinic of oncology-University Clinical center-Niš*

Pains due to osteolytic bone lesions may cause severe morbidity in breast cancer patients. Biphosphonates as supportive therapy were used in a group of 20 breast cancer patients with bone involvement. All patients were normocalcemic and were treated on outpatient basis. Clodronate was administered orally in a dose of 1600 mg/day for three months. All patients received Concommitant chemotherapy and/or hormonotherapy due to advanced/disseminated breast cancer. 15 of them received additional local radiotherapy.

Analgesio requirements, standard symptom scores and laboratory test were performed initially, monthly throughout and after treatment completion. X-ray were done initially and after treatment completion. Decrease in bone pain was noted in 12/20 patients with no change in disease status; in 6/8 patients without pain decrease progression of bone involvement was registered after treatment completion.

PP-8-24 The Effect of Vorozole on Tissue Aromatase Activity in Advanced Breast Cancer

P.Chr. de Jong*, J. vd Ven, J.W.R. Nortier, J.H.H. Thijssen, P.H.Th.J. Slee, M.A. Blankenstein. *Department of Endocrinology, University Hospital Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands*

In about 60% of breast cancers estrogens have a growth stimulating effect. Intratumoral estrogen levels depend largely on local production. The enzyme aromatase is considered to be the key enzyme in this respect. We have previously shown that Vorozole is an extremely potent inhibitor of peripheral aromatase activity (Cancer Research 53, 4563–4566, 1993). In the present study its effect on local, in situ, aromatase activity was evaluated. Ten breast cancer patients were treated with Vorozole, 2.5 mg daily, during the week preceding mastectomy. Intratumoral aromatase activity was measured and compared to the values of nine untreated patients. Median aromatase activity was eightfold lower in the treated patients compared to non-treated patients (0.85 vs 7.19 fmol/mg protein/2 h; $p = 0.0002$). These results suggest that Vorozole exerts its antitumoral effect largely through in situ aromatase inhibition in tumor tissue.

PP-8-25 The Clinical Relevance of Static Disease for 6 Months on Endocrine Therapy in Patients with Breast Cancer

J.F.R. Robertson*, P. Willsher, K.L. Cheung, R.W. Blamey. *City Hospital, Nottingham, UK*

This study assessed the value of static diseases (SD) in 255 breast cancer patients who received both first and second-line endocrine therapy.

Patients were categorised for therapeutic remission, complete or partial remission (CR or PR) or SD after 6 months (UICC 6/12). Patients who showed disease progression $\leq$ 6 months were categorised as PD.

UICC 6/12	1st Line therapy		2nd Line therapy	
	n	Md surv (wks)	n	Md surv (wks)
CR	23	140	7	140
PR	48	115	20	180+
SD	88	88	105	106
PD	63	38	118	43

There was no significant difference in survival between patients with SD and either PR or CR for first or second line treatments. All 3 categories survived significantly longer than patients with PD (between $p = 0.005$ and $p < 0.0001$). SD for 6 months appears a clinically useful criterion of therapeutic remission. It emphasises that the clinically important distinction should be made between non-progression (OR + SD) and progression (PD) — the latter being the clinically relevant indication to institute a change of therapy.

PP-8-26 Breast Cancer Bone Metastases Specifically Express Parathyroid Hormone Related Protein (PTHrP) and its Receptor

S.E. Downey*, J.A. Hoyland [1], A.J. Freemont [1], N.J. Bundred. *Dept. of Surgery, University Hospital of South Manchester;* [1] *Dept. of Osteoarticular Pathology, University of Manchester*

PTHrP, an osteolytic factor secreted by osteoblasts and tumour cells, is reported to predispose to bone metastasis. To determine whether expression of PTHrP or its receptor specifically enhance tumour cell survival in bone, we studied their expression in primary breast cancers (n = 107) and breast cancer metastases in bone (n = 33) and lung (n = 15). In situ hybridisation was used to identify the mRNA for both PTHrP and its receptor. Tumours were scored by 2 independent observers using the product of intensity of signal (1–3) and number of positive tumour cells ($1 < 20\%$, $20\% < 2 < 80\%$, $3 > 80\%$). Levels of PTHrP and its receptor mRNA were significantly higher in bone metastases than in primary breast carcinomas (protein: $p = 0.0379$; receptor: $p = 0.0008$) but significantly lower in lung metastases (protein: $p = 0.0027$; receptor: $p = 0.0003$). Osteoblasts in bone metastases over-expressed PTHrP mRNA compared to normal bone.

Overexpression of both PTHrP and its receptor in breast cancer cells produces site specific metastases in bone due to autocrine/paracrine growth stimulation by PTHrP.

PP-8-27 Analysis of Factors that Improve Quality-of-Life of Patients with Advanced or Recurrent Breast Cancer

K. Shimozuma*, H. Sonoo, K. Ichihara [1]. *Division of Breast and Thyroid Surgery, Kurashiki, Japan;* [1] *Dept. of Clinical Pathology, Kawasaki Medical School, Kurashiki, Japan*

Objective: The objectives of this study were (1) to examine the relationship between therapeutic efficacy and improvement of quality-of-life (QOL) of patients with advanced or recurrent breast cancer, (2) to reveal pre-treatment factors that improve their QOL by multiple regression analysis, and (3) to examine relationship between kinetic patterns of QOL scores over time and types of therapy. *Methods:* Monthly during the treatments, the QOL scores of 26 patients were assessed by the QOL questionnaire developed by the Ministry of Welfare in Japan (QOL-ACD). *Results:* (1) Therapeutic efficacy correlated well with the improvement of QOL (especially in activity, psychological and physical aspects). (2) Pre-treatment factors that improve their QOL were smaller numbers of previous therapies, shorter disease-free interval, lack of cutaneous or pleural metastases, and hospitalization. More precise analyses revealed that chemoendocrine or endocrine therapy incorporating medroxyprogesterone acetate (MPA) significantly improved psychological aspect of QOL. (3) The analysis of kinetic patterns revealed that chemoendocrine therapy tended to improve QOL quickly after initiation of the treatment although chemotherapy alone tended to deteriorate it quickly. *Conclusions:* To improve QOL of patients with advanced or recurrent breast cancer, we should attempt to obtain higher efficacy of treatments in the earlier period of their clinical course. Endocrine therapy incorporating MPA can improve psychological aspect of QOL.

PP-8-28 Usefulness of a Combination Chemoendocrine Therapy of Mitoxantrone, Doxifluridine and Medroxyprogesterone Acetate for Anthracycline-Resistant Advanced or Metastatic Breast Cancer

Y. Iino* [1], T. Yokoe [2], H. Takei [1], J. Horiguchi [1], M. Maemura [1], S. Ohwada [1], Y. Morishita [1]. [1] *2nd Dept. of Surgery, Gunma University School of Medicine, Maebashi, Gunma, Japan;* [2] *Emergency and Critical Care Medicine, Gunma University School of Medicine, Maebashi, Gunma, Japan*

Thirty-four patients with anthracycline-resistant advanced or recurrent breast cancer were treated with a combination chemoendocrine therapy of mitoxantrone (MIT), doxifluridine (5′-DFUR) and medroxyprogesterone acetate (MPA). Out of 34 patients, 28 were evaluable for efficacy of this combination therapy, and 30 including 2 incomplete cases were assessed for toxicity. Adriamycin (ADM) was pretreated in 12 patients, 4′-epi-ADM in 6, and THP-ADM in 12. In the eligible patients, 7.0 mg/m^2 of MIT were administered intravenously every 4-week, and 600 mg of MPA and 600 mg of 5′-DFUR were given orally every day. The median follow-up period was 31.5 weeks (range 2–90). Eleven (39.3%) out of 28 patients showed partial response. One (7.7%) out of 13 soft tissues, 8 (36.4%) out of 22 bone metastase and 3 (15.8%) out of 19 viscera responded to this treatment. The median duration of response was 31 + weeks (range 12–82). Hematological and