study of intermittent pamidronate 120 mg infusions in 30 patients with bone metastases from breast cancer, we measured a variety of resorption markers including the peptide-bound N-telopeptide (Ntx) and C-telopeptide (Crosslaps) fragments of type 1 collagen, free deoxy-pyridinoline (Fdpd), and urinary calcium excretion (uCa). Response, measured by a pain score assessing the intensity of pain, analgesic consumption and performance status, was related to both the initial rate of bone resorption and the ability of pamidronate to normalise the rate of resorption. 14/20 (70%) of patients with Ntx levels $\leq$ 2x upper limit of normal achieved a subjective response compared with only 1/9 (11%) with Ntx > 2x normal ($p = < 0.01$). In those patients in whom the rate of bone resorption, as measured by Ntx, returned to normal, the subjective response rate was 66% but response was not seen in patients with persistently raised Ntx ($p = < 0.01$). Similar findings were found for Crosslaps and Fdpd but not with uCa.

PP-8-18 Long-Term Palliation of Metastatic Bone Pain with Intermittent Pamidronate

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Pamidronate provides useful palliation in around one half of patients. Within this group of responders some patients experience repeated responses to treatment with control of their disease for many months. 52 women with painful, progressing, heavily pretreated bone metastases received pamidronate 120 mg as a 2 hour infusion. No new systemic treatments were allowed but endocrine therapy was continued to avoid a withdrawal response. Patients reporting clinical benefit were retreated on demand for worsening symptoms. The characteristics of the 14 patients (27%) who received $\geq$ 3 treatments have been assessed. They had a median age of 52 (range 36–75) years, median DFI of 32 (range 2–168) months, median time from 1st bone metastasis of 21 (range 2–96) months and 11 had disease confined to the skeleton. Bone resorption as measured by Ntx was > 2x normal in only 2 (14%) of these long term responders and normalised in 13 (93%) patients. Between 3 and 7 treatments (median 3) were received every 2–27 (median 11) weeks. Pamidronate was subsequently discontinued for clinically important skeletal (n = 8) or extraskeletal (n = 2) progression after a median of 47 (range 16–82+) weeks. 4 patients remain on treatment. Single infusions of pamidronate are of clinical value in patients with slowly progressive disease with only modest increases in the rate of bone resorption. For patients with more aggressive disease, more potent bisphosphonates or combined anticancer and bisphosphonate treatment may be required.

PP-8-19 Combination of Intraarterial Chemotherapy with Endocrine Therapy in the Treatment of Liver Metastases of Breast Cancer

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Between 1986 and 1995, we had treated 17 patients with liver metastases of breast cancer with a combination of intraarterial chemotherapy followed by endocrine therapy. Of 17 patients, 9 were treated with one shot intraarterial chemoembolization through hepatic artery using 40–50 mg/body of Farmorubicin and Lipiodol and the other 8 were treated with hepatic infusion chemotherapy using 20–30 mg/body of Farmorubicin every two weeks. All patients were followed by oral administration of 800–1200 mg/day of medroxy-progesterone acetate. The results were as follows: 1. The response rate between two groups was not substantially changed (44.4% in the former group versus 50.6% in the latter group). 2. A median duration of response was 25 months (range 4–45) and 8.7+ months (range 3–25+) 3. At two years, the survival rates were 44.4% and 25.0%. In former group, 5-year survival rate was 22.2%. These date suggest that this combination therapy is effective against liver metastases of breast cancer. Further studies are now in progress.

PP-8-20 Epirubicin (E) + Navelbine (NVB) as First Line Chemotherapy in Advanced Breast Cancer (ABC) Patients (PTS): A Multicentric Phase II Study

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We are performing a multicenter phase II study in ABC patients to evaluate the activity and the toxicity of the combination regimen EPI + NVB as first line chemotherapy. *Treatment:* EPI 90 mg/sqm i.v. bolus day 1, NVB 25 mg/sqm i.v. day 1 and 8 every 21 days. The treatment is administered on day 1 if WBC $\geq$ 3,500 and/or ANC $\geq$ 500 u/L and PLT $\geq$ 100,000 u/L. The dose of NVB on day 8 is as follows: G2 neutropenia: 25% dose reduction, G3 neutropenia: 50%, G4 neutropenia: NVB omitted. In case of: G4 neutropenia lasting more than 72 hours or febrile neutropenia G-CSF is administered until recovery and a 25% dose reduction is applied in the subsequent courses. *Patient characteristics:* so far 31 pts have been enrolled: median age 64 years (range 39–72), PS0 = 15, PS1 = 6, PS2 = 9. A total of 121 courses have been administered, with a median of 5 courses (range 1–7) for each patient. *Toxicities:* Neutropenia G3 21.1%, G4 70.4%; Thrombocytopenia G3 1.6%; Anemia G4 0.8%; Emesis G3 2.4%; Mucositis G3 4.9%; Diarrhoea G3 1.6%. The median duration of G4 neutropenia is 5 days (range 2–7). The doses on day 1 were reduced at 75% in 30.5% of the courses while the treatment was delayed in 14.8%. On day 8 NVB was omitted in 14.8% of the courses and reduced at 75% or 50% in 23.1% and 8% respectively; G-CSF was administered in 15.7% of the courses. Seven episodes of febrile neutropenia occurred. *Results:* 25 pts are evaluable for response: the overall response rate is 68% (95% C.I. 46.5%–85%) with 3 CR, 14 PR, 6 SD and 2 PD. 5 pts are not evaluable: 4 pts too early, 1 pt worsening PS. *Conclusions:* EPI + NVB is a very active combination regimen in ABC; however, considering the high percentage of neutropenia on day 8 requiring NVB dose reduction, we have modified the original schedule and NVB is now aministered on day 1 and 5. The study is ongoing.

PP-8-21 Response to Neoadjuvant Chemotheraphy in Locally Advanced Breast Cancer

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During 1993–1995 22 patients with locally advanced breast cancer (T2–4, N0–2, M0) were treated by the following regimen: two to three cycles of chemotheraphy with FAC schedule + mastectomy. Then almost all patients underwennt postoperative radiotheraphy to regional lymph nodes. Preoperative radiotheraphy was performed in four patients. Nine patients (40.9%) underwent ovariectomy. Adjuvant chemotherapy was continued in all cases for total 6 cycles. Patients with ER positive or unknown tumors then continued hormonetheraphy with Tamoxifen.

The median age of patients was 51 year (33–66). Cytology was diagnostic in 86% and information was as following: 5 patients (23%) had pourly differentiated tumours (G3) and 17 patients (77%) – moderately differentiated tumours (G2).

During the follow-up two patients (9%) died from metastatic dissemination, 14 patients (63%) were alive and free from any mts, 8 patients (36.4%) had further progression of disease. The median disease free survival was twenty one month.

Our experience suggest that neoadjuvant chemotheraphy combined with other treatment modalities is rather effective and possible to prolong disease free survival in locally advanced breast cancer patient group.

PP-8-22 Metastatic Dissemination in the Inflammatory Breast Cancer (IBC)

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The occurrence of inflammatory breast cancer is of 1 to 4% among all breast cancer. Most patients experience metastatic dissemination within first two years after diagnosis is made. At ou Institute 30 IBC patients were treated with chemotherapy III cycle (CAF regimen: ADR 50 mg/sqm day 1, iv, 5-FU 500 mg/sqm iv., day 1, and Cyclophosphamide 500 mg/sqm iv del, every 4 weeks), then all received radiotherapy, and after another III chemotherapy cycles.