In 3 pts TBI was repeated during the follow-up period. Radiation therapy was well tolerated. Partial or minor responses were obtained in 29 cases, even after failed chemotherapy. Disease stabilization occurred in 3, and progression in 1 pts. Median 2-years survival was 36%. This data confirms the value of HBI and TBI in the management of metastatic breast cancer.

PP-8-12 Unclear Value of Salvage Chemotherapy After Failure to First-Line 5-Fluorouracil, Epirubicin, Cyclophosphamide (FEC) Regimen for Metastatic Breast Cancer

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The clinical benefit of salvage chemotherapy following failure of a first-line regimen was retrospectively analyzed in 140 metastatic breast cancer patients all homogeneously treated with first-line FEC and followed until death by a single institution. Pt characteristics: median age 54.5 yr. (range, 29–71 yr.); median ECOG PS 0 (0–3); median DFI 22 mos. (0–164); dominant site: soft tissue 13 (9%), bone 43 (31%), viscera 84 (60%). After disease progression, 72/140 (51%) pts received at least 1 line of salvage CT. Overall response (CR + PR), response rate (RR) and time to treatment failure (TTF) of FEC and all subsequent salvage regimens was:

Treatment	Total	CR + PR	RR (%)	Median TTF in months
I CT (FEC)	140	57	40.7	7.5
II CT line	72	7	9.7	2.6
III CT line	24	1	4.2	1.7
IV CT line	10	1	10.0	0.9
V CT line	3	0	0.0	1.9
VI CT line	1	0	0.0	–

Only a very small fraction of pts receiving first-line FEC can objectively respond to subsequent CT regimens. The advantages of salvage CT are unclear and must be weighed against the inconvenience, cost, and morbidity of treatment.

PP-8-13 Chemoradiotherapy in Complex Treatment of Locally Advanced Breast Cancer

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On purpose to compare the efficacy of two chemotherapy regimens, the complex treatment method was applied to 121 patients with locally advanced breast cancer (LABC). Radiotherapy was given before operation with CMF to 61 patients or VAM to 60 patients. All women were operated on with mastectomy. Chemotherapy was continued after operation. Whole course of treatment consisted of 6 cycles of CMF or VAM respectively. Hormonotherapy was administered in patients with ER+ tumours. Androgens or prednisone were given in premenopausal patients after ovariectomy. Postmenopausal women were treated with tamoxifen for two years. While comparing results we couldn't find any difference in survival rate in patients treated with CMF or VAM. 5-year overall survival was 62.79% in VAM group and 66.26% in CMF group. Disease-free survival was 48.08 and 50.67% respectively. Our finding suggest that CMF regimen is of the same efficacy as VAM in treatment of patients with LABC and can be successfully used in treatment of patients with LABC.

PP-8-14 Five-Year Results of a Multimodal Management of Stage III B Breast Cancer

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Stage III B breast cancer carries a high incidence of local and/or distant metastases reaching even 70% and with a 5-year overall survival of 20%. The present study was initiated to verify the effectiveness of a combined modality approach which includes primary chemotherapy, surgery, radiation and adjuvant therapy, in improving prognosis. Forty-four pts in age from 36 to 71 years (median 51), PS 0–1, 21 premenopausal, with T_4 N_{1-3} M_0 breast carcinoma, following the tru-cut biopsy for the histology and prognostic factors, were treated by 3–5 cycles of q 21 or q 14 FEC 50 or 120-100 mg/m^2 Epirubicin or MMM. 13 pts were ER$^+$, 9 PgR$^+$, 9 Ki-67 L.I.$^+$, 24 G_2, 20 G_3, 32 infiltrating ductal, 8 lobular, 4 mixed. *Clinical response:* of 42 evaluable pts 1 (2.4%) reached a CR, 25 (59.5%) a PR > 50%, 14 (33.3%) a PR < 50% and 2 (4.8%) a NC. *Surgery* was performed in 40 pts (95.2%), radical in 37 pts (92.5%) and conservative in 3 pts (7.5%). Moreover all pts received radiation and adjuvant chemotherapy. *Pathological response* (40 pts) was pT_0 in 2 pts (5%), pT_1 in 5 (12.5%), pT_2 in 17 (42.5%), pT_3 in 6 (15%) and pT_4 in 10 (25%). Lymph nodes were involved in 40/40 pts, 1–3 in 11 pts (27.5%), 4–10 in 16 pts (40%), > 10 in 13 (32.5%). Response (CR + PR > 50%) not significantly correlate with ER status (50% ER$^+$, 66.6% ER$^-$). Of 42 pts, 23 relapsed (54.8%) (3 local, 9 distant, 11 mixed) and 12 of these (28.6%) died. None of the pts who achieved a CR relapsed while no significant difference in relapsing was found between those with PR > 50% and with less than PR. Kaplan-Meier 60 months overall and disease-specific-survival were 38.26% and 31.74% respectively. Since our study demonstrates the efficacy of the primary chemotherapy in making technically resectable the 95.2% of pts, the combined modality approach, even if could improve the outlook of many pts, it do not significantly betters the poor prognosis of these patients suggesting that more effective systemic therapies, including high-dose chemotherapy with PBPC need to be evaluated.

PP-8-15 Phase II Studies with Rivizor® (Vorozole) in Advanced Breast Cancer

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Rivizor® (vorozole) is an orally active, potent and selective, non-steroidal aromatase inhibitor. In DMBA-induced rat mammary tumors the reduction in tumor growth with vorozole was equal to oophorectomy. *In vivo* peripheral aromatization in postmenopausal women was inhibited by at least 93%.

Four phase II trials were performed with vorozole in a total of 114 patients. Patients had ER +ve or ER-unknown tumours, measurable disease, and failed prior tamoxifen as adjuvant or as first-line therapy for advanced disease. Previous adjuvant chemotherapy was allowed. Performance status had to be 0–2. Vorozole was given at a dose of 2.5 mg OD p.o. until progression. Response was assessed by UICC criteria every 2 months. 114 patients were evaluable for toxicity and 107 patients were evaluable for response. 29 patients responded to vorozole (26%, 5 CR, 24 PR), for a median duration of 11.7 months (min 8.6–max. 15). Responses occurred more frequently in soft tissue disease. Serum oestradiol was suppressed significantly (90%). Vorozole did not affect adrenal function as assessed by ACTH stimulation test; there were no effects on androgens, progesterone or TSH. Vorozole was very well tolerated; toxicities were mild and consisted mainly of hot flushes, nausea and anorexia.

A phase III programme comparing vorozole to aminoglutethimide and megestrol acetate is ongoing.

PP-8-16 Detection of Liver Metastases in Advanced Breast Cancer

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The routine use of imaging tests to identify liver metastases is disputed and in some centres imaging is only performed in those patients with abnormal liver function tests (LFTs) — AST, ALT and GGT. We have reviewed 65 consecutive patients with advanced breast cancer who had both liver ultrasound scans and LFTs performed. In 43 patients the scan was performed as part of routine restaging and in 22 because of a suspicion of liver involvement due to either clinical features (n = 15) or abnormal LFTs (n = 7). 29 scans (45%) were diagnostic of liver metastases, with 25 showing multiple lesions and 4 a single metastasis. LFTs were abnormal in 21 (positive predictive value = 0.72) but 8 patients (31%) with liver metastases had normal LFTs. Conversely in 36 patients with a normal scan, LFTs were normal in only 18 (negative predictive value = 0.5). The median survival from detection of liver metastases was 5 (range 0.1–34) months. We believe ultrasound scans should be part of routine restaging of patients with advanced breast cancer prior to any change in systemic therapy and that imaging of the liver should not be restricted to patients with abnormal LFTs or clinical features of liver involvement.

PP-8-17 Biochemical Markers of Bone Resorption Predict Response to Bisphosphonate Treatment

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Around one half of patients experience symptomatic response with pain relief following intravenous pamidronate but the mechanisms which underly a lack of response are unknown. In a randomised placebo-controlled

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.