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

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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

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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

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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

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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

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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

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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

biochemical toxicity were controllable or tolerable, and several side effects were mild and tolerable. The combined chemoendocrine therapy with MIT is useful for anthracycline-resistant advanced or recurrent breast cancer.

PP-8-29 Initial Characteristics and Outcome of Infiltrating Lobular Carcinomas (ILC): A Retrospective Study about 737 Patients

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From January 1980 to September 1991, 737 women have been treated for an ILC at Institut Bergonié. Among them, 102 patients had metastatic recurrence and were compared with 224 patients treated for an infiltrating carcinoma of an other histologic type (non ILC) which were matched according to the year of diagnosis and to the TNM classification. The results show a difference between the two groups according to age of patients: women with ILC were older than those with non ILC (55 and 58 years old respectively, $p = 0.05$). Furthermore, ILC were more often N_0 than non ILC at initial examination (48% vs 34%, $p = 0.03$). At last, as expected from literature, a difference was noted for the histological Scarff-Bloom-Richardson grading: ILC are more often grade II and less often grade III than non ILC. On the contrary, no difference was observed about menopausal status, onset of the tumor (97% of breast cancer were found during clinical examination), clinical and histological size, tumor growth and hormonal receptor status. Treatment was the same in the two groups. Overall survival (median survival of four years) and survival after the first metastasis were not different in the two groups. Half of the patients have had a metastatic disease in the first 21 months. Metastatic localisations were the same in the two groups but we found lung metastasis more often for the non ILC (42% vs 19%, $p = 0.00006$). On the contrary, we noted peritoneal metastasis more often for the ILC (22% vs 6%, $p = 0.0001$). In conclusion, despite ILC are rather rare tumors (10% of non ILC), it is noteworthy to recognize their characteristics in order to improve their treatment.

PP-8-30 MRF (Mitomycin, Folinic Acid and 5FU) for Metastatic Breast Cancer — A Prospective Pilot Study

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From 6/1994–2/1996 20 patients with metastatic breast cancer were treated with Mitomycin C, Folinic acid and 5FU. 18 pts. were evaluable. The median age was 53.6 years. 16 pts had been pretreated with chemotherapy, 12 pts with hormontherapy. 4 pts were pre- and 14 pts postmenopausal.

The following regimen was used: Mitomycin C at 8 mg/m2 D1, Folinic acid at 200 mg/m2 D1–5 and 5FU at 375 mg/m2 D1–5 every 4 weeks. A total of 43 courses had been given (2.3/patient).

Tumour response (according to WHO criteria): CR 1/18 (5.56%); PR 4/18 (22.22%) pts., NC 6/18 (33.33%) pts., PD 7/18 (38.89%) pts. Progession-free survival (Kaplan-Meier) was 4.64 months (PR 5.29; NC 4.01 months). Survival after therapy (K-M) was 5.69 months (PR 7.89; NC 7.31; PD 4.40 months).

Side effects of this treatment modality were moderate (WHO criteria): only 2 pts showed anemia grade II, grade III leucopenia occured in 1 patient, grade III thrombopenia in 1 pts, vomiting/nausea grade II in 4 pts.

PP-8-31 Intra-Arterial Liver Chemoinfusion in Patients with Metastatic Breast Cancer

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From 8/1989–10/1995 48 patients with rapidly progressive liver metastases of breast cancer received palliative intra-arterial chemoinfusions (IAC). 36 pts. had been pretreated with systemic chemotherapy. 34 pts. had received previous hormonal treatments.

Using the Seldinger technique and digital subtraction angiography the catheter was placed with its tip in the proper hepatic artery (77.08%), right hepatic artery (16.67%), common hepatic artery (4.17%) and in celiac axis in 2.08%. A total of 99 treatment courses has been performed (2.1 courses/patient). The chemotherapeutic regimen consisted of *4-Epirubicin* at 90 mg/m^2 over 2 hours, *Folinic acid* at 120 mg/m^2 over 30 minutes and *5-FU* at 1.5 g/m^2 over 20 hours. *Results:* A CR was achieved in 2/48 pts. (4.17%), PR in 20/48 pts. (41.67%), MR in 9/48 pts. (18.7%), NC in 7/48 pts (14.58%). 20.83% of the patients (10/48 pts.) showed PD.

The estimated mean progression-free survival (Kaplan-Meier) for local disease was 7.61 months (10.78 months for CR; 9.95 months for PR; 5.47 months for MR and 6.7 months for NC). The estimated mean survival (K-M) after IAC was 9.75 months (12.82 months for CR, 25.59 months for PR, 11.96 months for MR, 6.10 months for NC and 4.47 months for PD).

Side effects were well tolerated: only moderate myelosuppression and gastrointestinal toxicity. There were only five patient with Grade III thrombopenia, 10 pts grade III/IV leucopenia, 5 pts grade III anemia, no patients with grade III/IV infection and 14 patients with grade III vomiting. 19 patients had epigastral pain and in 7 pts (14.58%) stomach/duodenal ulcers were observed.

PP-8-32 EGR-R in Locally Advanced and Inflammatory Breast Carcinomas

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Aim: To investigate the prognostic role of EGF-R in locally advanced (LA) breast cancer (BC), its relation to other prognostic factors and SRs. *Patients:* A group of 40 LA BC pts consisted of clinical stages IIIa, IIIb and IV (11, 22 and 7 pts, respectively, the latter one having the minimal distant disease). Ten pts had inflammatory BC. All BCs were histologically confirmed and assayed for ER, PR and EGF-R in cytosol. The pts were then treated by primary breast irradiation (preoperative or radical), or CMF chemotherapy, alone or combined with breast irradiation. None of the pts received the endocrine therapy during the primary treatment. *Results:* In a whole group, there was no correlation of the EGF-R with the age, menopausal status, and SRs. In higher clinical stages a decreasing tendency of the ER, and an increasing tendency of the EGF-R were noted. Significantly lower ER, and a trend towards a higher EGF-R content, was found in inflammatory BC. No influence of ER, PR or EGF-R was found on the local response. However, EGF-RØ, PR + tumors gave complete or partial regression frequently, than EGF-RØ, PRØ ones (90% vs. 57%). *Conclusion:* Our results showed a certain degree of correlation between EGF-R and clinical stage, biological aggressiveness, and estrogen dependency, in LA BC. Their predictive significance for the local response could not be directly confirmed. It remains to be elucidated whether EGF-R content could be predictive for the overall disease response.

PP-8-33 Chemotherapy for Metastatic Breast Cancer: Ten Years Experience

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Since 1984 to 1994, 795 patients (pts) with breast cancer were admitted to our Department. Among these, 789 were treated with surgery, 6 were inoperable. After the elective therapy (according to the 1986/92 Consensus-Conferences guidelines) pts were followed up. During the last ten years, 184/795 pts (23%) went into progression. Sites of first event: 39 (28.5%) local relapse; 98 (71.5) systemic: 47 (48%) bones; 51 (52%) visceral or soft tissues. Twenty pts (20.4%) showed multiple synchronous metastases. Menopausal state: post-104 pts (75%); pre-33 pts (25%). Surgery and local radiotherapy were performed in all 39 pts with local relapse; among these, only 5 were treated with chemotherapy. Bone metastases were treated with palliative radiotherapy in 21/47; 26/47 pts were treated with hormonotherapy or supportive care. Visceral metastases (51 pts) were treated with chemotherapy as following: 18 (35%) with classic 6 CMF cycles; 13 (25%) with 6 CNF cycles; 9 (18%) with 6 FEC cycles; 5 (10%) with 3 HD-EPI (120 mg/sqm) cycles; 6 (12%) with different polychemotherapic schedules. We report responses and time to progression of the most representative groups:

Treatment	n° pts	PR	NC	PD	TTP mo. (range)
CMF	18	7 (39)	5 (28)	6 (33)	16 (1–78)
CNF	13	6 (46)	3 (23)	4 (31)	23 (2–84)
FEC	9	4 (44)	2 (23)	3 (33)	15 (6–48)

We obtained comparable responses using the three schedules; the introduction of Novantrone or Anthracycline allowed to obtain a better percentage of PR and a longer Time To Progression.