of alkaline phosphatase, Pyr, DPyr and ICTP were significantly increased in 7/25 (28%), 21/25 (84%), 22/25 (88%) and 17/25 (68%) patients respectively ($p < 0.001$). Therpy significant reduced Pyr (84.4 ± 12.3 vs. 32.5 ± 7.6 nmol/mmol creatinin) and DPyr (16.7 ± 7.1 vs. 9.4 ± 3.7 nmol/mmol creatinin). There were no changes in osteocalcin and hydroxyproline levels. These results indicate that sequential measurement of Pyr and DPyr can be used to monitoring the results of therapy of bone metastases.

56 POSTER

A combination therapy with mitomycin-C, etoposide, doxifluridine and medroxyprogesterone acetate as second-line therapy for advanced breast cancer

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Purpose: To determine whether there is a effective therapy for the patients with advanced breast cancer refractory to doxorubicin-containing chemotherapy, we performed combination therapy of mitomycin C, etoposide, doxifluridine and medroxyprogesterone acetate as second-line therapy.

Method: Patients with breast cancer who failed to the previous CAF therapy were designated as those refractory to CAF therapy. A total of 32 patients were included in this trial from January, 1989 through December 1995.

Results: Observed responses included 6patients (18.7%) with complete response (CR) and 7 (21.9%) with partial response. Two (50%) out of 4 patients who had bone pain due to bone metastasis noted pain relief. CR and PR were obtained in 4 out of 12 patients who had not responsed to the previous CAF therapy. While grade III myelosuppression was observed in 3 patients, pther adverse effect were minimal.

Conclusion: It is suggested that this combination therapy may be recommended for advanced breast cancer patients as a second-line therapy.

57 POSTER

Mastectomy in addition to chemotheraphy improves relapse free survival in women with localy advanced breast cancer

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Purpose: The mainstay of treatment for localy advanced breast cancer (LABC) is chemotherapy (CT). Additional mastectomy improves relapse free survival (RFS) and overall survival (OS) in women with LABC.

Methods: We analysed 135 women with LABC in period from 1992 to 1997. Among them, 84 patients with mean age 51, 25 (min 38, max 65) had undergone mastectomy and postoperative RT in addition to CT while 51 patients with mean age 57, 6 (min 44, max 74) were treated with CT and radical RT. Mean follow up period for both groups of patients was 23 months (min 6, max 48 months for group with mastectomy and min 10, max 40 months for group without mastectomy). In these two groups we studied RFS and OS according to age, nodal status and tumour size.

Results: In the operated group of women (84) mean time to progression (TTP) was 20 months (min 6, max 36) and in nonoperated group of women (51) mean TIP was 14, 3 months (min 6, max 24). 2 years RFS was 22% and OS was 48% for operated group, while for nonoperated group 2 years RFS was 1% and OS was 42%.

Conclusion: LABC represents disease stage with a very poor prognosis. Although there was no statisticaly significant difference in OS among two analysed groups of patients, there was statisticaly significant difference in RFS depending on prognostic factors previously mentioned.

58 POSTER

Improving results in the treatment of locally advanced T4 breast cancer

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Between 1990 and 1997 63 patients with T4 N1–3 M0 breast carcinoma were treated at our Institute. Storically, at first *from 1990 to 1995*, 43 patients aged from 36 to 71 years (median 51), PS 0–1, 20 premenopausal, with T4 breast carcinoma, following the tru-cut biopsy for the histology (31 infiltracting ductal, 8 infiltracting lobular, 4 mixed) and prognostic factors (ER15+/28−; PgR 12+/31−; 23G2, 20G3; Ki67 7+/36−) were treated with 3–5 cycles of primary standard chemotherapy (FEC 50, or HD-Epirubicin, or MMM). *Clinical response:* CR 1/43 (2.3%), PR > 50% 25/43 (58.1%), PR < 50% 15/43 (34.8%) and NC. 2/43 (4.6%). *Surgery* was performed in 41 pts (95.3%), 38 (88.3%) demolitive and 3 (7%) conservative. *Pathological response* was pTo 2/41 (4.8%), pT1 5/41 (12%), pT2 18/41 (44%), pT3 6/41 (14.6%) while 10 (24%) remained pT4. Lymphnodes were involved in 100% of cases, 1–3: 11 (27%); 4–10: 17 (41%), >10: 13 (32%). At median *Follow-up* of 57 months (27–93) the median DFS is 21 months (3–75) and OS 37 months (10–75). 33 pts (76.7%) relapsed and 10 (23.3%) are disease-free. 25 pts (58%) died and 18 (42%) are still alive. Relapses were directly proportional to the LN number (1–3: 64%; 4–10: 82%; >10: 85%), while survival inversely (64%, 35%, 31% respectively).

Afterwards *from 1996* we initiate a study to evaluate the effectiveness and the toxicity of a combination of Lonidamine (450 mg/die), CDDP (50 mg/mq), Epirubicin (100 mg/mq), Vinorelbine (25 mg/mq), day 1–21. Until now we treated 20 T4 pts in age from 39 to 68 years (median 50), 11 premenopausal, PS 0–1, 17 infiltracting ductal, 3 infiltracting lobular, ER11+/9−; PgR 7+/13−; 18G2, 2G3; Ki67 9+/11−. *Clinical response:* CR: 7/20 (35%); PR > 50%: 13/20 (65%). *Surgery* was feasible in 100% of 18 evaluable cases, 12 demolitive (67%) and 6 conservative (33%). *Pathological response:* pTo 2/18 (11%); pT1 5/18 (28%); pT2 8/18 (44%); pT3 1/18 (6%); pT4 2/18 (11%); pLN0: 4/18 (22%); pLN 1–3: 5/18 (28%); pLN 4–10: 6 (33%); pLN > 10: 3/18 (17%).

Conclusions: the L-PEV regimen is more active than the first that we used, in terms of global clinical response (100% vs 60%), clinical CR (35% vs 2.3%) and patholocical CR (11% vs 4.8%) of the primary and nodes (pLN0 22% vs 0%). Since in the our first trial relapses and survival were strictly correlated to the pathological status of LN, the high activity of L-PEV also at nodal level may better the outcome of these patients.

59 POSTER

Continuous infusion of adriamycin + cyclophosphamide + 5-fluorouracil in disseminated breast cancer

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Purpose: The aim of this study is to improve the treatment efficacy of the patients suffering from disseminated breast cancer by increasing the dose of chemodrags using a continuous infusion.

Methods: The program includes three chemotherapeutic agents: adriamycin in a dose of 20 mg/m2/24 hours, from 1 to 5 days i.v. as a 120-hour continuous infusion, 5-fluorouracil in a dose of 500 mg/m2 on the 1-st and the 8-th days i.v. and cyclophosphamide in a dose of 600 mg/m2 on the 1-st and the 8-th days i.v. Continuous infusion is performed through a catheter plased in v. subclavia. The treatment according to this program has been performing at Chemotherapy Department since 1995. A total of 21 women aged 38–64 have been treated. There were 6 women in premenopause, 15 patients in postmenopause. Performance status (ECOG) was 0–2. All the patients were histologically diagnosed as having breast cancer. The localization of metastases was the following: periferal lymphatic nodes – 14, lungs – 4, bones – 8, intracutaneous – 5. Each patient reseived 2 or more courses of chemotherapy. The total number of courses was 50.

Results: Complete regression was observed in 6 cases (28.6%), parcial regression in 10 (47.6%), no change 4 patients (19.0%), progression 1 case (4.8%). Complication included leukopenia. I–II gr.-20 courses, III–IV gr.-6 courses; anemia I–II gr.-4 courses, stomatitis I–II gr. 15 courses, III gr.-2 courses, nausea/vomiting I–II gr.-12 courses, III gr.-2 courses, alopecia – practically in all the patients.

Conclusion: The total effect of the program was considered to be rather high – 76.2%. Toxicity was acceptable. Long-term results are being studied.

60 POSTER

Sonomammography an objective tool for assessment of chemotherapeutic response in locally advanced breast cancer

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Purpose: Primary chemotheraphy in locally advanced breast cancer (LABC) produces objective clinical response. In a prospective study the role of sonomammography has been evaluated as a tool for monitoring the objective tumour response following primary chemotherapy.

Methods: Patients with LABC were treated with Primary Chemotherapy. Ultrasonography was done using 7.5 MHz probe before commencing each

cycle. Mastectomy was done in responders. The sonographic changes were recorded and correlated with histological changes.

Results: Fourteen cases were evaluated. Nine patients showed response in form of reduction in tumour size, improved tumour margin definition, decreased echogencity of tumour, more homogenous internal echos and reduction of skin oedema.

Conclusions: Sonomammography can be used as a readily available cost effective tool for assessment of tumour response following primary chemotherapy in patients with LABC.

61 POSTER

Activity of chemotherapy based on Navelbine in pre-treated metastatic breast cancer patients

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Purpose: To evaluate the activity and hematologic toxicity of Navelbine-based combinations in metastatic breast cancer patients previously treated with one or more line of chemotherapy.

Materials: From March 1996 through January 1997, 34 metastatic breast cancer patients were included in the study. The age ranged from 31 to 73 (mean 47). According to ECOG scale, their performance status was 0–2. All the patients had two-dimension measurable or assessable tumor lesions. The sites of metastases were lymph nodes (16 patients), bones (15), lungs (12), skin (8), breast (7), liver (4), kidney (1). The number of metastatic sites was 1 in 9 (26.5%) patients, 2 in 14 (41.2%) and 3 in 11 (32.3%), metastases in the internals occurring in 50% of the cases (in 17 of 34 patients). Twenty-two of the 34 patients had previously received one line of chemotherapy, 12 patients – two lines. The mean number of previous courses of multidrug chemotherapy for one patient was 5 (range 1 to 8). Get the start of Navelbine treatment all patients had a disease progression.

Methods: Twenty-three patients were administered combination chemotherapy: Navelbine 25 mg/m2 day 1 and 8 plus Doxorubicin 50 mg/m2 day 1, every 21 days. Eleven patients were given Navelbine 39 mg/m2 day 1 and 5 plus 5-Fluorouracil 750 mg/m2 days 1 through 5, every 21 days.

Results: We evaluated 122 courses with Navelbine. Leucopenia occurred in 88 (72.1%) courses, but only in 24 (19.6%) courses it was grade III–IV toxicity. Grade III anemia developed only after 1 (0.8%) course. Grade III thrombocytopenia was observed in none of the patients. Navelbine dose had to be decreased due to hematologic toxicity in 13 (10.7%). No treatment-related fatal outcomes were registered. Partial response occurred in 11 (32.4%) patients. 17 (50.0%) stabilizations of disease and 6 (17.6%) progressions were observed. 9 patients (26.5%) are still alive in follow-up time of 9 to 17 months. The median survival was 9.8 months. The one-year survival rate is 36.9%.

Conclusion: Navelbine-based chemotherapy combinations are satisfactorily tolerated and are moderately active in the 2nd or 3rd lines of metastatic breast cancer therapy.

62 POSTER

Vinorelbine (VNR) + 5-fluorouracil continuous infusion (5-FU c.i.) in pretreated advanced breast cancer – Adria Medica Group

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The results in terms of objective response in pretreated advanced breast cancer are generally not over 30–40%, and the median duration of the response is about 5 months. From March 1997 we investigated the therapeutic effect and the tolerability of a combination of VNR + 5-FU c.i. as second line in patients with metastatic breast cancer.

The schedule is the following:

5-FU	700 mg/m^2 i.v./day	for 5 days	every 3 weeks
VNR	25 mg/m^2 i.v. bolus	day 1 and 6	every 3 weeks

In December 1997 n.27 patients were enrolled and 19 were valuable. Median age 55 years, 4 pts were premenopausal and 23 postmenopausal. Recettorial state: positive 15 patients, negative 5 and 7 unknown. 14 patients had received prior chemotherapy in adjuvant setting, 23 for advanced disease, 13 for both. The site of metastatic disease were visceral + bone 13, bone 6, visceral and soft tissue 21 pts, WHO PS was 0 in 6 pts, 1 in 18 and 2 in 3 pts. There were 8 PR and 6 SD. The median duration of the response was 5 months. 5 pts progressed on treatment.

Toxicity: Grade 1: leukopoenia in 7 pts and grade 3 in 1 pt. Grade 2: mucositis in 4 pts and grade 3 in 1 pt. Grade 3: diarrhea in 1 pt. Grade 4: vomiting in 1 pt. The study is ongoing.

63 POSTER

Treatment of liver-metastases in patients with breast cancer

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Purpose: Treatment of liver metastases with anthracyclines or antimetabolites leads to few responses and does probably not prolong survival significantly. Therefore the effectiveness of taxanes was tested in these patients.

Methods: Breast cancer patients with only liver metastases as first side of relapse were treated with 200 mg/m2 taxol as monotherapy or in combination with epirubicine (60 mg/m2) (in the latter combination the dose of taxol was reduced to 175 mg/m2). Response was categorized according to the WHO-criteria.

Results: 18 patients were treated between 1994 and 1996 with 200 mg/m2 taxol. One patient achieved a complete remission (CR), 4 patients a partial remission (PR), giving an overall response rate of 30%. Mean duration of response was 5 months and mean survival was 20 months.

10 patients received the combination chemotherapy since 1996. While only one patient achieved a complete remission, 5 patients had a PR, giving a response rate of 60%. Mean duration of response was 8 months. Mean survival could not be calculated since 6 patients are still alive.

Conclusion: In previous studies mean survival of patients with liver metastases was reported to be in the range of 12 months. Using taxol, 6 of the 14 patients survived more than 24 months and the remaining 14 patients are still living. That could be considered as an improvement. According to the still preliminary data the combination with epirubicine could be even more effective.

64 POSTER

Primary medical treatment of locally advanced disease reveals causes of failure of adjuvant chemotherapy

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Hypothesis: The sequestered cell – a cell remote from the circulation at the time of treatment – is a major cause of failure of chemotherapy. The effectiveness of systemic therapy may be improved in tumours that shrink slowly (grades I and II) by protracting the treatment to allow time for revascularization of poorly nourished areas.

Methods: New primary breast cancers were treated by sequential single agent therapy (chemotherapy and hormones). Timing was regulated by the rate of shrinkage of individual tumours. The existence of poorly nourished tissue around the margins of ulcerated tumours was demonstrated by thermographic scanning. Sites of recurrent nodules after early healing of these tumours were compared photographically to the original areas of poor circulation.

Results: Despite improved early local control, nearly all tumours eventually regrew. In ulcerated tumours close correspondence was seen between areas of poor circulation and sites of local recurrence.

Conclusions: The demonstrable failure in ulcerated tumours will be repeated on a microscopic scale in smaller, non-ulcerated tumours. If shrinkage, with accompanying improvement of the local circulation, does not occur during treatment, then systemic therapy is unlikely to succeed. Tumours that shrink slowly will do better if treatment time is extended. However, total extinction is rare and therefore surgery should follow when possible.

65 POSTER

Comparative study of taxol (T) and Cisplatin© versus Taxotere (Tx) and vinorelbine (V) in metastatic breast cancer (MBC). Preliminary results

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Introduction: Taxanes have shown important activity as rescue treatment in metastatic breast cancer refractary to anthracycline therapy. In this trial