(TTP) comparing letrozole 2.5 mg with megestrol acetate (MA) (AR/BC2) and aminoglutethimide (AG) (AR/BC3).

Methods: Tumor response and TTP (UICC criteria) were defined by independent, treatment-blinded peer review based on tumor imaging and tumor measurements. Median times were estimated by the Kaplan-Meier product-limit method. Treatments were compared by Cox proportional hazards regression.

Results: Duration of response (CR + PR) was significantly longer for letrozole 2.5 mg compared with MA (medians 33 and 18 mos respectively) but not with AG (median duration of response (MDR) 24 mos for letrozole, 15 mos for AG). In the trial against MA, MDR was 33 mos for patients with predominant soft tissue disease (19 mos MA), 27 mos for bone (18 mos MA), 33 mos for visceral (15 mos MA). In patients with lung metastases, MDR was not reached for letrozole (16 mos MA), and in liver metastases, was 33 mos for letrozole (13 mos MA). Median TTP in predominant soft tissue disease was 17 mos for letrozole, 8.6 mos for MA. In the trial against AG, MDR was 38 mos for letrozole 2.5 mg, 24 mos for AG in patients with visceral metastases. Median TTP in patients with predominant soft tissue disease was 11.3 mos for letrozole, 3.5 mos for AG.

Conclusion: Letrozole 2.5 mg appears to provide long duration of response, irrespective of the predominant site of disease.

47 POSTER

Serum hepatocyte growth factor (HGF) levels in patients with progressive metastatic breast cancer

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Purpose: Several studies have shown that HGF plays a crucial role in carcinogenesis and malignant progression. To investigate a possible impact of serum HGF levels on the clinical course, serum HGF levels in patients with metastatic breast cancer were examined.

Patients and Methods: Between September 1996 and January 1998, 80 patients with metastatic breast cancer were enrolled in this study. The sites of metastasis included soft tissues in 22 patients, bone in 37, lung and/or pleura in 30, liver in 19, brain in five, and ovarium in one. Twenty-two patients had multiple metastatic organs. Serum HGF levels were evaluated using ELISA kit.

Results: The average level of serum HGF in all the patients was 0.80 ± 0.52 ng/ml (average ± SD, 0.15–2.87). Circulating HGF levels in patients with liver metastasis (1.14 ± 0.67) were significantly higher than those without liver metastasis (0.69 ± 0.41). Significantly higher levels in serum HGF (1.0 ± 0.56) were also observed in patients with progressive disease compared with those with stable disease (0.53 ± 0.30). The patients with high HGF levels (more than 1.0 ng/ml) exhibited a significantly shorter survival rate than those with low HGF levels. Sequential monitoring revealed that circulating HGF levels significantly elevated in patients with progressive metastasis associated with disease progression.

Conclusion: Serum HGF level may be a useful indicator for the progression of metastatic lesions, existence of liver metastasis, and prognosis of patients with metastatic breast cancer.

48 POSTER

High-dose chemotherapy with peripheral blood stem cell transplantation as adjuvant therapy for primary breast cancer

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Twenty patients with breast cancer involving more than 10 regional lymph nodes were treated by high-dose chemotherapy (HD-CT) supported by peripheral blood stem cell plantation (PBSCT) as adjuvant therapy. After radical mastectomy, the combination chemotherapy with adriamycin 50 mg/m^2, cyclophosphamide 1,000 mg/m^2, vincristine 1.0 mg/m^2 and methotrexate 200 mg/m^2 with leucovorin rescue was started, and repeated every 3 weeks for 3 courses. G-CSF was also given. After the 2nd and 3rd courses, PBSCs were collected and cryo-preserved. Tamoxifen was also given to patients with breast cancer containing a high concentration of estrogen receptor, and radiation therapy for supraclavicular and parasternal lymph nodes was also combined. Finally, HD-CT with thio-TEPA 200 mg/m^2/day, etoposide 300 mg/m^2/day, and CPA 2,000 mg/m^2/day were administered for 3 consecutive days, and after 72 hours of final doses, frozen-thawed PBSCs were administered.

HD-CT with PBSCT was well tolerated, and recovery from myelosuppression of the HD-CT was rather quick and no serious side effects were observed. Seventeen patients remained in remission with a median follow-up of 40 months after mastectomy, and three relapsed at 13, 19 and 21 months after surgery. According to Kaplan-Meyer analysis, the probability of disease-free survival was significantly higher in patients treated by HDCT with PBSCT as compared with those treated by conventional chemotherapy in our division, showing 79.3% and 25.3%, respectively, at 5 years after mastectomy.

HD-CT with PBSCT as adjuvant therapy for primary breast cancer involving extensive lymph nodes may improve the supposed poor prognosis of such patients.

49 POSTER

Sequential administration of paclitaxel and doxorubicin followed by CMF in women with advanced breast cancer

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Purpose: The purpose of our study was to evaluate the activity of paclitaxel/doxorubicin combination in patients with advanced breast cancer but to avoid excessive cardiotoxicity.

Methods: We administered 4 cycles of doxorubicin/paclitaxel followed by 6 cycles of standard CMF regimen. Study medication consisted of doxorubicin 60 mg/m^2 as a 15-minute intravenous infusion followed by paclitaxel 175 mg/m^2 as a 3-hour infusion.

Results: The main toxicity of doxorubicin/paclitaxel treatment phase was neutropenia (WHO grade 3/4, 58%) but we observed only one cardiac adverse event. Toxicities of the CMF treatment phase were not significant. Of 24 patients evaluable for response, two (8%) had complete response and 11 (46%) achieved partial response. Ten additional patients (42%) had stable disease. The median time to progression was 12 months and the median overall survival was 18.5 months.

Conclusion: The sequential administration of doxorubicin and paclitaxel followed by CMF appeared active and well tolerated in patients with metastatic breast cancer.

50 POSTER

A randomised clinical trial of primary chemotherapy (PC) with taxol + epirubicin (TE) V. 5-FU + epirubicin + cyclophosphamide (FEC) in stage III_A breast cancer: A preliminary report

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Introduction: The possible contribution of (PC) in the management of breast cancer has been investigated since 1980 following the hypothesis that (PC) might alternate cancer cell behavior.

Aim: The aim of this study was to determine the incidence of satisfactory response to (PC) treatment and prolongation of disease free survival and overall survival rates using a new combination (TE) as compared to the standard approach (FEC).

Material and Patients: In this trial 30 patients 35–70 yeasrs of age (mean 52) with stage III_A breast cancer were included. Of these 11 were pre and 19 post-menopausal and they were randomised in two groups. Arm A (TE, n = 16) and arm B (FEC, n = 14). Two cases from each arm were not evaluable. Patients in both arms received 3 courses of pre-operative chemotherapy at a dose of 200 mg/m^2 Taxol + 75 mg/m^2 Epirubicin and 5-FU 600 mg/m^2 + Epirubicin 75 mg/m^2 + Cyclophosphamide 600 mg/m^2 every three weeks respectively. Following modified radical mastectomy they had 3 additional courses of chemotherapy. All patients received a course of radiation therapy and 20 mg Tamoxifen daily regardless of receptor status.

Results: 1) Clinical response rates: Arm A: CR 4 (28.5%), PR 9 (64.5%), SD 1 (7%). Overall response rate 93%. Arm B: CR 1 (9%), PR 5 (45.5%), SD 4 (36.5%), PD 1 (9%) overall response rate 54%. 2) Pathological complete response rates: Arm A: 4 (28.5%) Arm B: 0 (0%).

Conclusion: The preliminary results of this trial demonstrate that combination of Taxol + Epirubicin seems to have a better activity in clinical and pathological response rates. However conformation of these observations

and evaluation of disease free survivals interval and overall survival rates require further investigation and longer follow-up.

51 POSTER

Sequential doxorubicine (DOX) and docetaxel (DOC) as neoadjuvant chemotherapy in locally advanced breast cancer (LABC): A pilot study

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DOX is the best single agent for treatment of breast cancer and plays an important role for adjuvant treatment. Many observations showed that taxanes, especially DOC, still could remain active in DOX resistant cases. It is therefore logical to try to combine these 2 agents. Instead of giving them simultaneously at reduced dosis, we gave full dosage of both sequentially to patients with LABC. Between 06/97 and 12/97, 8 patients (stage IIIb), received first 2 cycles of DOX 75 mg/m^2 (q3w), followed by 2 cycles DOC 100 mg/m^2 (1 hour infusion, q3w). Clinical, biochemical and radiological evaluation of response were performed after the 2nd and 4th cycle. Thereafter, loco-regional treatment was administered and systemic treatment was planned in function of observed response. All patients had objective regression, according to the UICC criteria (2CR, 6PR). In 1 pt. we found no invasive tumor after surgery, only DCIS. Evaluation of early response after 2 cycles proved very difficult because of poor sensitivity and specificity of clinical examination and mammography. There were no serious complications. Dose reduction during 2nd course of DOC (75%) was only necessary because of mucositis (1) and myalgia (1). We conclude that a high response rate can be achieved within 12 weeks with the proposed regimen. Because of the poor reliability of clinical and radiological evaluation, new techniques like MRI or PET-scan deserve consideration. This regimen could also be compared to others for inducing response in LABC. Further research should also focus on optimizing loco-regional and maintenance systemic treatment.

52 POSTER

Neoadjuvant hormonal therapy in locally advanced breast cancer

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Background: Management of locally advanced breast cancer (LABC) it's not consensual. In post-menopausal women, particularly in the elderly, primary hormonal therapy (HT) is an option, to convert an inoperable tumour into operable.

Objective: To evaluate the influence of a neoadjuvant HT protocol in local control of the disease (tumour downstaging and HR status).

Methods: We used a prospective non-randomised study between Jan/93 and May/94, which included 28 pts. An initial evaluation was made through clinical examination, ultrasonography and incisional biopsy with HR determination. The neoadjuvant HT consisted in a minimum of two months therapy with Tamoxifen (20 mg/day). In all pts, a clinical and/or ultrasonographic revaluation was made. A radical mastectomy was then proposed, with a new HR determination. The treatment was completed with adjuvant Radiotherapy and HT. The median Follow-up was 50 months (range: 11–62).

Results: The median age was 72 years (range: 52–86). *Initial evaluation*: Twenty-two (79%) pts were in stage III-B and six (21%) pts in stage III-A. In 27 pts, ductal invasive Ca was found and lobular invasive Ca in one. The ER were positive in 24 (86%) pts and PR n 18 (64%) pts. Ultrasonography was used to study tumour size and axillary lymph nodes. *Post-HT evaluation*: Clinical and/or ultrasonographic response was observed in 20 (71%) pts, with two complete remissions. No relevant side effects were found. *Postoperative evaluation*: Tumour downstaging occurred in 22 (79%) dts; in three other pts, there was a significant decrease in tumour size. HR status changed in 10 (36%) pts.

Conclusions: 1- Neoadjuvant HT can play an important role in LABC management, mainly in the elderly. 2- Tamoxifen had a good response rate (71%) and was well tolerated. 3- Correlation between clinical and pathologic responses occurred in 22 (79%) pts.

53 POSTER

Photodynamic therapy versus laser induced thermotherapy in the treatment of local recurrences and skin secondaries of breast cancer

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Aim: The effect of photodynamic therapy (PDT) and Laser induced thermotherapy (LITT) as palliative methods in otherwise pretreated patients on locoregional recurrences should be investigated.

Material and Methods: The PDT was currently performed on 6 women using the Photosan 3 (HPD) as a photosensitizer, the irradiation was performed with laser light at a wavelength of 630 nm 48 h, 72 h and 196 h after photosensitization. – In 10 women with locally advanced breast cancer and pretreatment with surgery (primary and secondary mastectomy, m. latiss. dorsi-flap), irradiation and chemotherapy, an interstitial laser application was performed percutaneously into the center of the diseased tissue. The laser used was a Nd:YAG laser with a wavelength of 1064 nm. Heat expansion was controlled digitally and monitored by ultrasound and colour coded duplex sonography (CCDS), respectively.

Results: All patients are scheduled for long-time follow-up. The initial results of PDT are promising. – LITT enabled the precise coagulation of the tumour without ulceration or destruction of the skin, although these areas had been pretreated by radiotherapy up to 60 Gy, before.

Conclusion: PDT and LITT are safe and minimal invasive methods for palliative treatment of subcutaneous local recurrences of breast cancer.

54 POSTER

Diagnostic problems of evaluating bone metastasis from breast cancer by proliferative activity: Comparison of findings between bone scintigraphy and MRI and their relationship to prognosis

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Purpose: Bone metastases from breast cancer are frequently observed, however, diagnosis and treatment are difficult in many cases. We evaluated the relationship between diagnosis of bone metastases of breast cancer and clinicopathological factors.

Methods: We enrolled 51 breast cancer patients with vertebral matastases diagnosed by plain radiography, bone scintigraphy or MRI. Diagnosis of bone metastases was classified into the following groups: the A group: those who showed similar findings in plain radiography, bone scintigraphy and MRI; the C group: those who showed no abnormalities in radiography or scintigraphy, and their lesions were diagnosed by MRI.

Results: Twenty-four of 51 patients were included in the A group, while 14 were included in the C group. Regarding the relationship with clinicopathological factors, a significant number of patients with ER-negative tumors demonstrating a high level of DNA polymerase α, short disease-free intervals (DFI) and metastases to other organs were included in the C group. Prognoses of patients were apparently poor in the C group.

Conclusion: Bone scintigraphy sufficiently reflects foci in patients with ER positive or low proliferative tumors, while false negative bone scintigraphy is likely in patients with ER negative or highly proliferative tumors. MRI was useful in diagnosing such patients. Therefore, consideration of malignancy such as proliferative activity and ER is thought to be necessary during postoperative follow-up of breast cancer patients.

55 POSTER

Changes in biochemical markers of bone turnover in breast cancer patients with bone metastases

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The understanding and the monitoring of metastatic bone disease remains unsatisfactory. this study we compared several markers of bone turnover in 25 breast cancer patients with bone metastases, aged 48–70 years. All patients were treated with pamidronate 60 mg i.v. every month in addition to standard endocrine or chemotherapy. Blood or urine measurements included total and bone alkaline phosphatase, osteocalcin (BGP), hydroxyproline, pyridinoline (Pyr), deoxypyridinoline (DPyr) and ICTP were performed baseline, 1, 3 and 6 months after starting therapy. The mean values