(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.

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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.

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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.

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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.

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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