associated with clinical outcome in these heavily treated pts, whereas the absence of CIP-1 expression seems to be associated with good prognosis.

P37 Multivariate prognostic index with emphasis on proliferation adds specificity to standard prognostic factors in operable breast cancer

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The selection of breast cancer patients for systemic adjuvant therapy stands on multiple clinico-pathological factors with proven prognostic value. Although the toxicity of the standard forms of adjuvant therapy is not great, the question more often asked is, which patients could be left without the therapy. For patients with obviously high risk of recurrence, the standard forms of adjuvant therapy certainly are not sufficiently effective, and consequently more aggressive chemotherapy protocols are under evaluation. There is an urgent need for standardized, easily accomplished model according to which the patients could be selected for appropriate treatment, taking together the individual risk-benefit profile.

We re-evaluated the prognosis of 230 breast cancer patients (mean age 59, SD13), with median follow-up of 6.6 years; all invasive tumors, ductal 85%, lobular 9%, other 6%, N+ 34%, N– 66%, Gr1 22%, Gr2 55%, Gr3 23%, estrogen receptor status positive 87%, negative 13%. The patients were divided in groups of low and high risk of mortality according to three different prognostic models: the former clinical model M1 (stage), the present model M2 (stage, grade and estrogen receptor status), and model M3 based on multivariate prognostic index (MPI) of Baak et al. (1985) (tumor size, lymph node status, mitotic activity index). 68 patients were actually given adjuvant systemic therapy. All three models unanimously suggested 73 patients to have low risk and 62 patients to have high risk. Among the rest of the patients (95) the models diverged.

The disease-specific survival at the end of the follow-up among the patients in the low risk group by each model was 87%, 90%, 88% in M1, M2, M3 respectively. Corresponding figures in the high risk group were 75%, 79%, 72%. The models showed quite similar power as prognostic models, but M2 was the most sensitive (0.83) and M3 the most specific (0.64). When premenopausal patients were analyzed separately, M3 showed high efficiency in identifying patients with high risk, the absolute difference in survival in the low and high risk groups being 44%, meanwhile the difference by grouping according to M1 and M2 was 31% and 27%, respectively.

The results speak in favor of using the present clinico-pathological factors which appeared to construct a sensitive model, in decision making about adjuvant therapy. The multivariate model, in which mitotic activity is stressed, helps to create different prognostic categories with higher specificity.

P38 Immunohistochemical detection of tumor cells in lymph nodes and bone marrow aspirates in node negative (N0) breast cancer (BC)

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Simultaneous immunohistochemical (IHC) examination of axillary lymph nodes and bone marrow aspirates from patients (pts.) with nodal negative BC have not been published yet.

Pts. & Methods: 180 pts. with pT1-2 N0 M0 BC were subjected to bone marrow aspiration. Lymph nodes as well as bone marrow aspirates were retrospectively examined for tumor cells using a cytokeratin antibody and ABC-technique. The immunohistochemical results were correlated with the histological findings and other prognostic factors (ER, PR, S-Phase, Ploidy, Ki-67, EGF-R, HER-2/neu, p53, Cathepsin-D and pS 2. The mean follow up time was 56 ± 18 months.

Results: Totally in 58 of 180 pts. (32%) tumor cells were detected in lymph nodes (12.7%; N1a-IHC) and/or bone marrow aspirates (27.7%; M1-IHC).

	Lymph nodes	
Bone marrow	N0-IHC (n = 157)	N1a-IHC (n = 23)
M0 (n = 130)	122 (67.8%)	8 (4.4%)
M1-IHC (n = 50)	35 (19.4%)	15 (8.3%)

Disease free survival and overall survival showed a prognostic disadvantage for women with tumor cell detection in any site and number compared to women without any tumor cells ($p < 0.05$). Differences between IHC-positive and IHC-negative pts. were found in tumor size, grading, vessel invasion, ER, S-phase, Cathepsin D. By multivariate analysis tumour size and grading, but not the detection of tumor cells, were confirmed as independend prognostic factors in node negative BC.

Conclusion: In 32.2% of all conventionally as pT1-2 N0 M0 staged breast cancer pts. tumor cells are detectable in axillary lymph nodes and/or bone marrow aspirates. A prognostical disadvantage of tumor cell detection has been proven, but they do not represent independent prognostic factors.

P39 Prognostic value of plasminogenaktivator inhibitor type 1 and 2 in primary breast cancer

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Introduktion: Elevated concentrations of urokinase-type plasminogenaktivator (uPA) and his inhibitor PAI-1 in cytosolic extracts obtained from breast cancer patients are associated with a poor prognosis. Data about the prognostic value of another uPA inhibitor PAI-2 are incomplete. In order to substantiate the prognostic value of PAI-1 and PAI-2 in primary tumor we have measured the concentrations in the cytosol from 252 breast cancers.

Material and Methods: We used ELISA to test PAI-1 and PAI-2 in tumor extracts. The relation of this data to know prognostic factors and other variables such s-phase fraction and ploidy was studied. Disease-free and overall survival were analyzed according to Cox's proportional hazard model.

Results: The median PAI-1 value was 20.3 μg/g protein and for PAI-2 1.63 μg/g protein. Ductal invasive breast cancer has a greater concentration of PAI-1 than lobular invasive cancers. No differences was found for PAI-2. Patients with negative lymph node status had significantly higher PAI-2 values than those with affected lymph nodes ($p = 0.015$). After a median observation of 32 months in the univariate analysis showed that high levels of PAI-1 are correlated with short DFS (RR:1.56; 95% CI; $p = 0.005$) and OAS (RR: 186; $p = 0.001$).

Summary: The present study indicates that PAI-1 is an independent prognostic factor and high PAI-2 concentrations exercise a protective function in tumor metastasis via the lymphatic system.

P40 Prognostic factors predictive of lymph node status in breast cancer

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In T1 tumours the incidence of lymph node metastases ranges from 21 to 35%. The Authors developed a case-control study to individualize a predictive factor of positive nodes. One hundred thirty one patients with T1a-b breast cancer were studied. All underwent axillary dissection and the pathologic status of the nodes was T1a: 29 N–, 9 N+ and; T1b: 103 N–, 33 N+. The factors evaluated were necrosis, p53, CerbB2, Bcl2, NM23 and Mib1. All of these were categorized in three levels but necrosis and the worst category in terms of prognosis were compared with the others two. The percentage of each worst factor is reported: T1a p53 (14% N– vs 12.5% N+); CerbB2 (54% N– vs 14% N+); Bcl2 (90% N– vs 71% N+); NM23 (0% N– vs 33% N+) and Mib1 (0% N– vs 12.5% N+); necrosis (80% N– vs 90% N+). T1b: p53 (4% N– vs 17% N+); CerbB2 (10% N– vs 20% N+); Bcl2 (39% N– vs 54% N+); NM23 (35% N– vs 43% N+); Mib1 (2% N– vs 0% N+); necrosis (91% N– vs 92% N+). The only statistically significant factor was p53 (<0.05) but only in the T1b category. The Authors concluded that these factors are not able to predict the axillary lymph node status.

P41 Urokinase plasminogen activator and cathepsin D in micrometastatic cells of patients with primary breast cancer

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Proteases in tumor tissue may play an important role in metastasis and invasion. This study evaluated the prognostic relevance of urokinase plasminogen activator (UPA) and cathepsin D detection in disseminated tumour cells in bone marrow.

Bone marrow was sampled intraoperatively from both iliac crests in 280 patients with primary breast cancer. Interphase cells were enhanced and stained immunocytologically. Three antibodies were used: 2E11, detecting tumor associated glycoprotein (TAG 12, which is typically expressed by almost all breast cancer cells), anti-UPA and anti-cathepsin D antibodies.

87 women (31%) developed distant metastatic disease after a median follow-up of 68 months. Patients without tumor cell detection in bone marrow had a significantly longer metastasis-free interval (MFI = 70 months, $p < 0.001$) as well as a significantly longer survival time (median 72 months). Women with cathepsin D positive tumor cells in bone marrow (n = 27; 10%) had a significantly shorter MFI (38 months) compared with cathepsin D negative women (64.5 months; $P = 0.003$). Patients with UPA-positive tumor cells in bone marrow (n = 98; 35%) had a significantly shorter MFI (44 months) compared with UPA-negative patients (MFI = 60 months; $p < 0.001$). The worst prognosis was