the ability of immunohistochemical markers to predict survival in a large series TN breast cancer.

Materials and Methods: We identified 147 TN breast cancers among 625 consecutive invasive breast cancers by immunoprofiles for ER, PR and HER2 and compared clinicopathologic characteristics and patients' survival between TN and non-TN breast cancers. The TN cancers were further subclassified by staining for cytokeratin (CK) 5/6, epidermal growth factor receptor (EGFR), vimentin, c-Kit, p63, P-cadherin, CK8 and CK18. We then applied 4 different criteria to define basal-like phenotype in TN breast cancers (criteria 1: CK5/6+ only, criteria 2: CK5/6+ and/or EGFR+, criteria 3: CK5/6+ and/or EGFR+ and/or vimentin+, and criteria 4: one or more marker(s) positive among CK5/6, EGFR, vimentin, c-Kit, p63 and P-cadherin). Each of these criteria, as well as each individual marker, was then evaluated for prognostic significance by survival analysis.

Results: Among the 147 (23.5%) TN breast cancers, 138 (93.9%) patients received chemotherapy and median overall survival (OS) of TN patients was 64 months (range, 8–185 months). Compared with non-TN breast cancers, TN cancers showed larger tumor size and higher histologic grade, but fewer lymph node metastasis. In addition, patients with TN breast cancer had reduced OS within 6 years of diagnosis but not thereafter. Using immunohistochemical markers to define basal-like cancers among the TN breast cancers, we noted positive staining for CK5/6+ in 35.4%, EGFR+ in 16.3%, vimentin+ in 28.6%, c-Kit+ in 11.6%, p63+ in 8.0% and P-cadherin+ in 43.8%. Using the criteria outlined above, we defined 52 (35.4%) cases as basal-like by criteria 1, 65 (44.2%) by criteria 2, 82 (55.8%) by criteria 3 and 113 (76.9%) by criteria 4. Remarkably, basal-like phenotype defined by any of these criteria did not show survival difference from non-basal phenotype in TN breast cancers. Interestingly, however, luminal CKs, 8 and 18 were also commonly expressed in TN breast cancers (55.1% and 45.6%, respectively), and TN breast cancers expressing CK8 and/or CK18 showed reduced OS (p = 0.002) and disease-free survival (p = 0.011).

Conclusions: In our series, TN breast cancers showed poorer prognosis within 6 years of diagnosis than non-TN breast cancers. However, there was no survival difference between basal and non-basal phenotypes as defined by immunohistochemical profiles of 6 basal markers in TN breast cancers. By contrast, expression of luminal CKs appears to identify a more aggressive subgroup of TN breast cancers.

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Poster

Prognostic significance of triple-negative phenotype in breast cancer

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Background: Triple-negative breast cancers (TNBC) are defined as a lack of expression of estrogen, progesterone receptors and HER2. Recently gene expression analysis identified several breast cancer subtypes including basal-like, ER−/HER2+, luminal type and this transcriptionally basal type is compatible with histological TNBC. This TNBC subgroup accounts for 15% of all types of breast cancer and high relapse rate with poor prognosis. The aim of this study was to evaluate the clinico-pathological characteristics and prognosis in breast cancer patients who expressed triple-negative phenotype on immunohistochemistry and to compare this TNBC subgroup to the others.

Materials and Methods: Three hundred forty-eight patients who underwent curative breast cancer surgery from January 2000 to December 2005 were analyzed retrospectively. The IHC method was used to define ER, PR and HER2 expression status. HER2 was scored positive if 3+ result was found or amplified gene expression on FISH. According to this method, total patients were divided to three subgroups; Hormone receptor positive (HR+), HR negative/HER2 positive (HR−/HER2+) and TNBC.

Results: Sixty-seven cases (19.3%) of 348 patients showed triple-negative expression pattern and forty five cases (12.9%) showed HR−/HER2+ expression pattern and the others showed HR+ expression pattern. The TNBC subgroup was associated with a high tumor grade and high relapse rate. Other characteristics such as age, stage, lympho-vascular invasion, relapse site showed no difference between three subgroups. The 5YSR of HR+, HR−/HER2+ and TNBC subgroup were 94.0, 83.2 and 88.7% (p = 0.013) and 5 year DFS rate were 87.4, 75.1 and 79.7% (p = 0.011). In multivariate analysis, risk group by IHC was the only independent prognostic factor and TNBC phenotype showed the worst outcome (HR 3.85, 95% CI 1.41–10.52, p = 0.008).

Conclusion: Both TNBC subgroup and HR−/HER2+ subgroup showed significantly worse prognosis than HR+ subgroup and there was no significant difference between these two subgroups. In multivariate analysis, TNBC showed the significant prognostic variable in breast cancer

and to overcome these characteristics of TNBC, it is need to find another powerful molecular targeted agents or new cytotoxic drugs.

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Poster

Activated Leukocyte Cell Adhesion Molecule (ALCAM/CD166) predicts response to adjuvant chemotherapy in breast cancer

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Background: Activated Leukocyte Cell Adhesion Molecule (also known as ALCAM or CD 166 and MEMD) functions as cell surface immunoglobulin and is recently reported as possible prognostic marker in breast cancer. Its predictive value regarding adjuvant chemotherapy has not yet been evaluated.

Material and Methods: To evaluate ALCAM expression levels in the primary tumor tissue ALCAM mRNA expression was analyzed by cDNA microarray analysis in 162 patients (100 of them received adjuvant chemotherapy) and ALCAM protein expression was analyzed by Western Blot analysis in 160 patients (among them 87 received adjuvant chemotherapy). Both results were obtained in 133 cases. A strong positive correlation between protein and mRNA expression (p < 0.001) was observed.

Results: Using statistical analysis a stratified subgroup analysis showed positive correlation of high ALCAM mRNA expression with longer overall survival (OAS; p = 0.0012) in patients treated with adjuvant chemotherapy regimens (n = 100). In contrast, patients with high ALCAM mRNA expression who did not receive chemotherapy tended to have a worse prognosis than those with low ALCAM mRNA levels. Similar but statistically weaker correlations were found regarding ALCAM protein expression data. The predictive impact of ALCAM mRNA expression in chemotherapy treated patients was corroborated by multivariate Cox regression analysis also including histopathological markers like histological grading, nodal involvement, ER status, clinical stage and the logarithmic values of ALCAM mRNA expression (p = 0.001 for OAS).

Conclusion: High ALCAM expression levels in primary breast cancer might be a suitable marker for prediction of response to adjuvant chemotherapy.

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Poster

Urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1 for tumor-biological risk assessment in node-negative breast cancer patients – The multicenter trial NNBC 3-Europe

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Background: Various groups started clinical trials aimed at a feasible way to improve risk-assessment by testing biological parameters based on RNA or protein level. Current ASCO guidelines allow the use of biological risk assessment by the invasion factors uPA/PAI-1 (Harris et al. 2007). In 2003 we launched the NNBC 3-Europe trial with the following questions:
1. Is risk-assessment by the invasion markers uPA and its inhibitor PAI-1 more effective than by clinico-pathological factors (St. Gallen 2005) with regard to identification of low-risk patients?
2. Is adjuvant chemotherapy using an anthracycline-taxane sequence (FEC-Docetaxel) superior to standard FEC in high-risk patients?

Study Design: Risk assessment was performed either by St. Gallen 2005 or by the invasion markers uPA/PAI-1. In low-risk patients, no adjuvant chemotherapy is given. High-risk patients receive adjuvant chemotherapy according to randomisation: FEC-Doc versus FEC. Adjuvant endocrine therapy is given according to current AGO guidelines.

Results: To date, 109 centres participate, 2308 patients have been registered. Overall, in 811 patients chemotherapy could be avoided, 687 were randomized to receive FEC-Doc, 683 to FEC. Biological risk assessment was performed in 1710 patients. Using both, grading and uPA/PAI-1 results, the low-risk group comprised 39% of the patients.

Discussion: The NNBC-3 Europe trial shows that risk assessment based on biological testing of fresh frozen tumor material is feasible. The study is planned to recruit 5.700 patients and it is performed in cooperation