

prognosis (similar to grade 1) and one with a bad prognosis (similar to grade 3). We therefore also raised the question if a single proliferative factor, i.e. cyclin A, can be used for this purpose.

Material and Methods: In 219 consecutive premenopausal node negative patients, cyclin A was determined with immunohistochemistry on tissue microarray. High cyclin A was defined as the 7th decile of positive cells. Only 13% of the patients received adjuvant systemic therapy. Cox proportional hazards regression was used to model the impact of the prognostic factors on distant disease-free survival (DDFS). Due to non-proportional hazards, the analysis was restricted to the first five years after diagnosis, a time period during which 34 patients developed distant recurrences.

Results: Cyclin A was associated to DDFS in univariate analysis (hazard ratio (HR) 3.6, 95% confidence interval (CI): 1.8–7.1, $p < 0.001$). Corresponding HR:s were 2.7 for Ki67 (95% CI: 1.3–5.5, $p = 0.005$) and 2.7 for grade 3 vs 1+2 (95% CI: 1.3–5.2, $p = 0.004$). HER2, age, ER and progesterone receptor were also significant factors, whereas tumor size was not. Cyclin A could divide histological grade 2 into two groups with significantly different DDFS (HR: 15, 95% CI: 4.3–52, $p < 0.001$). In the grade 1 and 3 subgroups, cyclin A was not a prognostic factor. When subdividing according to ER status, cyclin A was a prognostic factor in the ER positive subgroup, but not in the ER negative (HR: 5.8, 95% CI: 2.2–16, $p < 0.001$) vs. 1.5 (95% CI: 0.6–3.9, $p = 0.44$). In multivariate analysis, cyclin A was an independent prognostic factor for DDFS (HR: 2.9, 95% CI: 1.2–7.0, $p = 0.018$), together with HER2 and age. Due to colinearity, histological grade and Ki67 were not included in the same model.

Conclusion: In this study cyclin A was an independent prognostic factor for premenopausal patients with node-negative breast cancer, but only in the ER positive subgroup. Similar to gene expression analyses, cyclin A can subdivide histological grade 2 breast cancer into two groups with different prognosis. Taken together, cyclin A may be an alternative or a complement to histological grade and Ki67 for prognostic considerations.

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Poster

Locoregional recurrences in triple-negative, node-negative early stage breast cancer treated with breast-conserving treatment

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Background: Breast conserving-surgery followed by whole breast radiotherapy is standard of care in patients (pts.) with early-stage breast cancer. It is unclear if loco-regional control after breast-conserving therapy is affected by the tumor's phenotype. The aim of this study was to assess whether triple negative phenotype (TN: ER-ve and PR-ve and Her2-ve) was associated with locoregional recurrences (LRR) in node-negative patients.

Materials and Methods: We studied a consecutive series of 754 patients with node-negative breast cancer treated with breast-conserving treatment at the Institut Curie between 1995 and 1998. All pts. underwent breast-conserving surgery and axillary lymph node dissection, followed by whole breast irradiation. 22% of patients received a tumor bed boost while 50% received regional lymph node irradiation. Adjuvant systemic treatment was delivered to 18%. ER and PR status were determined by immunohistochemistry (IHC). HER2/neu status was determined by IHC, and confirmed by FISH in uncertain cases. Cumulative locoregional recurrence and survival rates of TN tumors were compared to other tumors using a log-rank test. Multivariate Cox proportional hazard model was used to determine independent predictors of loco-regional recurrence.

Results: Among the 754 pts., 81 (10.7%) were TN. Compared to other tumors, TN phenotype was more likely associated with non-ductal/non-lobular subtypes, and less often with lobular cancers; it was significantly associated with pT2 tumors, grade III, lympho-vascular invasion, and high mitotic index. With a median follow-up of 11.7 years, the 10-year cumulative rates of LRR were 19.2% in TN tumors and 13.9% in other tumors, ($p = 0.11$). TN tumors tended to occur earlier than other tumors. On multivariate analysis, only age and grade were significant, independent predictors of LRR. Ten-year survival rates were 70.5% in TN tumors and 88.7% in others, respectively ($p < 0.0001$).

Conclusion: This retrospective study with long follow-up confirms that, in pts. with node-negative breast cancer of whom only 18% had received adjuvant systemic treatment, TN phenotype was associated with a worse survival than other tumors. However, this study did not find a significant increase in locoregional recurrences in TN tumors, whereas age and grade were significant predictors of LRR. It suggests that breast-conserving treatment can be carried out in pts. with TN tumors.

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Down regulation of Heat Shock Protein 70 (HSP70) predicts responsiveness to neoadjuvant aromatase inhibitors in post-menopausal hormonal receptors expressing breast cancer

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Introduction: Aromatase inhibitor is an effective endocrine therapy in breast cancer patients expressing endocrine receptors. Our group has demonstrated changes in protein expression profile using proteomic approach before, ten proteins were found to have potential impact as predictors for AI responsiveness or resistance. In the present study, we test the change in expression profile of heat shock protein70 (HSP70), carbonic anhydrase 1 (CA1) and GDI in larger cohort of patients using immunohistochemical (IHC) staining.

Methods: Eligible post-menopausal breast cancer patients were recruited. Pre- and post-treatment tumour tissues were obtained and IHC staining was performed for targeted proteins. The changes of expression profile were compared to clinical response to determine the correlations.

Results: Total 32 patients, with both pre- and post-treatment carcinoma samples available, were recruited. Majority of patients responded to treatment (16 patients with PR, 14 with SD and 2 with PD). Increment in tumour size was observed in 4 patients (2 PD and 2 SD patients). Down-regulation of HSP70 was significantly associated with clinical responsiveness of AI treatment, $p = 0.014$; and change of proliferative index, Ki67, $p = 0.042$. Patients with pre-treatment high HSP level and proliferative index using Ki67 assay, were associated significantly with downregulation of HSP after treatment.

Conclusions: With the use of AI as neoadjuvant treatment, downregulation of HSP is associated with observed clinical response. Pre-treatment high HSP and Ki67 levels predict treatment response via their significant correlation with HSP downregulation. Therefore, pre-treatment HSP and Ki67 can be potential surrogate markers for AI treatment.

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Small breast tumours with adverse prognosis

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Background: Tumours less than 10 millimetres are often node negative, of grade 1 and have an excellent prognosis. However, even a tumour of a few millimetres would sometimes be mortal. We wanted to assess risk factors for dissemination of very small breast cancers.

Materials and Methods: The patient registry and pathology database were used to identify all patients with breast tumours less than 10 millimetres that were diagnosed 1985 to 2008 in the Kalmar county and their outcome. Multivariate analyses were carried out.

Results: 220 pts with tumours less than 10 mm were identified. 118 were grade 1, 73 grade 2 and 32 grade 3. HER2 was amplified and/or IHC 3+ in 36 cases. One or more lymph nodes were positive in 10 pts. Lymphovascular invasion (LVI) occurred in 13 cases. DCIS grade 3 of an extension of 15 mm or more accompanied 65 of the tumours.

During a median observation period of 9 years 20 pts, 9%, had distant metastasis. In the multivariate analysis HER2 positivity and the coexistence of extensive DCIS grade 3 were the only significant parameters, $p < 0.001$ and < 0.006 resp.

Conclusion: Tumours less than 10 millimetres with extensive DCIS grade 3 and HER2 positivity have an increased risk of dissemination.

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Poster

A straightforward but not piecewise relationship between age and lymph node status in Chinese breast cancer patients

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Purpose: To investigate the relationship between age and axillary lymph node (LN) involvement in Chinese breast cancer patients, and to replicate a recently identified piecewise relationship between age and LN involvement.

Patients and Methods: A dataset, consisting of 3,715 patients (with complete information on study variables) with operable breast cancer consecutively surgically treated between 1996 and 2006, was derived from the database of Shanghai Cancer Hospital. Univariate and multivariate logistic regression were employed to analyze the relationship between age and LN. We subsequently performed a similar analysis on another dataset