of patients, and febrile neutropenia was observed in 5.6% of patients. The most common grade 3/4 non-hematologic adverse event was hand-foot syndrome, observed in 11.3% of patients. The median relative dose intensities of FEC, T, and X were 0.982, 0.968, and 0.933, respectively. Patients with HR-negative tumors had significantly higher pCR rate than HR-positive tumors (35.3% vs. 10.5%, p = 0.03). HER2 status was not significantly correlated with pCR rate. Patients with Ki67 expression >20% revealed significantly higher pCR rate than <20% (23.5% vs. 8%, p = 0.02). In HR+negative subgroup, Ki67 expression were significantly correlated with pCR (p = 0.02).

Conclusions: Our data indicate that the sequential combination of XT followed by FEC is a well-tolerated, effective preoperative treatment for stage II/III breast cancer and HR status and Ki67 expression are useful predictive biomarkers.

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Estrogen receptor-negative tumour and positive family history for breast cancer highly modify the risk of second contra-lateral breast cancer

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Background: A recent study reported an increased risk of contra-lateral estrogen-negative breast cancer after a first primary estrogen-negative breast cancer. Our study aims to confirm this result and to evaluate how the risk of second breast cancer occurrence is affected by family history of breast cancer and anti-estrogen treatment.

Patients and Methods: We included in the study all 4152 women diagnosed with breast cancer between 1994–2007, using data from the population-based Geneva Cancer Registry. We compared the incidence of second breast cancer among patients according to estrogen receptor (ER) status with that expected in the general population by age-period Standardized Incidence Ratios (SIRs).

Results: Among the cohort, 63 women developed second breast cancer. Patients with ER-positive first tumors had a decreased risk of second breast cancer occurrence (SIR: 0.67, 95% CI: 0.48–0.90), whereas patients with ER-negative primary tumors had an increased risk (SIR: 1.98, 95% CI: 1.19–3.09) limited to ER-negative second tumors (SIR: 7.94, 95% CI: 3.81–14.60). Patients with positive family history had an 8-fold (SIR: 7.67, 95% CI: 2.49–17.90) higher risk of ER-negative second tumor, which increased to nearly 50-fold (SIR: 46.18, 95% CI: 12.58–118.22) when the first tumor was ER-negative. Treatment with anti-estrogen decreased the risk of second ER-positive tumors but not ER-negative tumors.

Conclusions: The risk of second ER-negative breast cancer is very high after a first ER-negative tumor, in particular among women with strong family history. Surveillance and prevention of second cancer occurrence should consider both ER status of the first tumor and family history.

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The effect of lymphovascular invasion (LVI) on survival

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The ONCOPOOL database (n = 17,000) is compiled from primary operable (⩽5 cm) breast cancers in women aged ⩽70, from 12 European Breast Units, treated by first line operative treatment and entered in 1990−99 inclusive.

Method: LVI was regularly measured in 4 units (n = 5195) on H & E staining. Scoring was to definite positive or negative. 20% were LVI+.

Results:

- Relation to Nottingham Prognostic Index (NPI). A highly significant rank order from 7% LVI+ lying in Excellent NPI group to 60% and 62% in the Poor and Very Poor groups.
- Overall survival by both LN stage and LVI (Table 1): survival by LN status was moved down one stage by LVI+ positivity.
- LVI positivity lowers survival within all Nottingham Prognostic Index (NPI) groups: Cox Analysis entering NPI and LVI shows both to have p values of <0.000 with hazard ratios of 1: 7 and 1: 6 respectively.

Table 1

LN group	Stage	LVI	n LN/LVI		10 yr OS (%)	LVI+ .v. Neg
1	LN Neg	Neg	2359	1	86±1	p < 0.000
2	LN Neg	Pos	429	2	78±3	
	LN 1 Pos	Neg	413		80±2	p = 0.025
3	LN 1 Pos	Pos	245	3	73±4	
	LN 2−3 Pos	Neg	307		72±3	p = 0.025
4	LN 2−3 Pos	Pos	266	4	65±4	
	LN 4+ Pos	Neg	574		69±2	p < 0.000
5	LN 4+ Pos	Pos	508	5	44±3	

Conclusion: LVI is an important additional independent variable to NPI for survival.

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P-cadherin, Osteopontin and MIB1 as prognostic factors for loco-regional relapse in breast cancer

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Introduction: Loco-regional relapse in breast cancer is considered to be an independent predictor of subsequent metastization and death. As a consequence, one of the current pathways of research stands on the discovery of new risk factors for local relapse due to the significant discrepancy in prognosis of patients with identical staging and similar pattern of known molecular markers.

Three new molecular markers have been associated in previous studies to worst outcomes in breast cancer patients: P-cadherin has been identified as an independent prognostic factor in breast cancer; Osteopontin in breast cancer stroma has been related with the expression of genes associated with worst prognosis; Proliferation index (MIB1) is also considered to be inversely related with survival. The purpose of this work was to study the value of these three markers as possible determinants factors for loco-regional relapse in breast cancer.

Material and Methods: We retrospectively analyzed the clinical records of 1432 patients treated at our institution between January 1998 and June 2008. The case group consisted of 101 patients (7%) with local relapse as first new related event. The control group, consisted of 92 patients, from the same series with a disease free survival longer than 10 years.

Clinical data and classical pathological factors were retrieved for cases and controls. We performed Tissue MicroArrays and Immunohistochemistry for estrogen and progesterone receptors, HER2, Ck-5, P-cadherin, Osteopontin and MIB1.

Results: The average time to recurrence was 41 months; the mean survival after relapse was 33 months and the 5-year survival was 55%. On multivariate analysis tumour size, nodal status, histological grade and P-cadherin showed independent prognostic value for disease-free survival. None of the studied markers had a significant association with local relapse.

The aberrant expression of P-cadherin was related to higher histological grades and estrogen-receptor negativity; Osteopontin expressing tumours had more advanced disease at diagnosis and the MIB-1 was associated with tumours negative for estrogen receptors.

Conclusion: P-cadherin is a promising marker for loco-regional disease prognosis and a putative novel therapeutic target. Its real biological value is still undetermined and further studies are required.

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Cyclin A − an alternative to gene expression profiling for subdividing histological grade 2 breast cancer into groups with different prognosis

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Background: Ki67 has recently been included in the St Gallen guidelines as a prognostic factor, but the role of other proliferation markers, such as cyclin A, is still under debate. We investigated the prognostic importance of cyclin A, and if this was dependent on estrogen receptor (ER) status. Gene expression profiles, consisting mainly of genes associated to proliferation can subdivide histological grade 2 into two groups, one with a good