PR (OR = 0.43, 95% CI 0.24–0.78, $p = 0.005$) rate were protective (OR < 1) factors, while only axillary node positivity (OR = 8.05, 95% CI 4.29–15.0, $p < 0.0001$) and high MIB-1 rate (OR = 2.28. 95% CI 1.27–4.11, $p = 0.006$) represented the two statistically significant RFs for cancer recurrence. Size (OR = 1.25, 95% CI 0.70–2.25, $p = 0.44$), and CEA (OR=1.05, 95% CI 0.66–2.07, $p = 0.62$) and CA 15−3 (OR = 1.27, 95% CI 0.71–2.27, $p = 0.42$) baseline serum levels, were not significantly related to cancer recurrence.

Conclusions: In this population, axillary node negativity and ER positivity were the most sensitive RFs for cancer recurrence at long-term follow up, while MIB-1 labeling index and PR rates were weak RFs.

References

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344 Poster

Cell-cycle Phase Specific Markers' Expression in Breast Cancer

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Background: Cell-cycle phase specific markers have been identified to be of high prognostic relevance in breast cancer. Ki67 expression is traditionally the most widely justified method for the assessment of mitotic state of cancer cells. Although, its utilization to date lacks standardization.

Methods: A total of 387 breast carcinomas were analyzed for the immunohistochemical expression of Cyclin A (CYCA), Geminin, Histone H3F3 (HH3F3), MCM2, MCM6 and Polo-like kinase 1 (PLK1) based on tissue microarrays. A two dimensional score reflecting intensity and frequency of staining was established and evaluated semi-quantitatively (0−11). The data were tested for their prognostic utility and reflection of mitotic index and DNA content measured by FACS.

Results: CYCA (p = 0.004), Geminin (p = 0.002) and MCM2 (p = 0.020) were able to distinguish prognostic subgroups by themselves. A meta-score of all cycle-specific markers was established bearing robust prognostic power (p = 7.7E-5). All outperformed Ki67 for prediction of prognosis, but the latter reflected mitotic index in a more accurate way (p = 3.8E-29) than CYCA (p = 8.7E-4), HH3F3 (p = 0.039), MCM6 (p = 1.5E-8) or PLK1 (p = 8.0E-7). Among the investigated proteins CYCA reflected DNA index (p = 0.008).

Conclusion: Cell-cycle specific markers may add further prognostic information. Ki67 remains, however, the most promising marker related to mitotic activity, and Cyclin A expression could reflect aneupoidy.

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345 Poster

High Level of Ki67 (⩾10%) is Not a Adverse Prognostic Factor in Younger (<35years) Patients with a Hormone Receptor-positive Breast Cancer

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Background: Young age is regarded as an adverse prognostic factor in patients with breast cancer, especially in those with a hormone receptor (HR)-positive tumor. This study aims to investigate whether the high level of Ki67 is strong prognostic factor in younger (<35years) patients with hormone receptor (HR)-positive breast cancer.

Materials and Methods: Data from 1,023 HR positive breast cancer patients in the Seoul National University Hospital Breast Care Center (SNUHBCC) who underwent surgery between 2000 and 2003 were reviewed. Patients were classified into two groups according to the level of Ki67: low (<10%) and high(⩾10%).

Results: In an analysis of 1,023 patients form a single institution, an age of <35years (hazard ratio 2.62; 95% confidence interval [CI]: 1.58–4.35; P < 0.001) and high level (⩾10%) of Ki67 (hazard ratio 1.64; 95% CI: 1.09–2.47; P < 0.018) were found to be independent predictors of distant metastases.

According to the level of Ki67, distant metastasis free survival was not significantly differ in an age of <35years(Ki67 <10%, hazard ratio 1.66; 95% CI: 0.82–3.37; P = 0.158; Ki67⩾10%, hazard ratio 1.67; 95% CI: 0.71–3.90; P = 0.240, respectively).

Conclusions: Young age (<35 years) and high level (⩾10%) of Ki67 were adverse prognostic factors in patients with HR-positive breast cancer. However, high level of Ki67 was not a strong predictor of distant metastasis in the young age (<35 years) patients.

Table 1. Multivariate analysis for prognostic factor associated with distant metastasis free survival among HR+ breast cancer according to the level of Ki67

	p	HR	95.0% CI of HR	
			LL	UL
Ki67 <10%				
Age of <35 years (vs ⩾35 years)	0.158	1.66	0.82	3.38
Tumor size >2 cm (vs ⩽2 cm)	0.001	2.65	1.47	4.80
Node positive (vs negative)	0.000	4.39	2.33	8.25
Histological Grade3 (vs G1 or G2)	0.262	1.36	0.79	2.32
Ki67⩾10%				
Age of <35years (vs ⩾35years)	0.240	1.67	0.71	3.90
Tumor size >2 cm (vs ⩽2 cm)	0.043	3.52	1.04	11.91
Node positive (vs negative)	0.002	4.32	1.73	10.79
Histological Grade3 (vs G1 or G2)	0.882	1.06	0.49	2.27

346 Poster

Comparison of Molecular Subtyping with BluePrint and MammaPrint to Local IHC/FISH Based Subtype Classification According to St Gallen 2011 in 133 Breast Cancer Patients

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Background: Molecular subtypes in breast cancer are increasingly important in guiding adjuvant treatment decisions. We compared (locally assessed) molecular subtyping as defined by St Gallen treatment recommendations 2011 with three microarray based assays: BluePrint which classifies samples into Luminal, Basal and HER2 types, MammaPrint which classifies Luminal patients into High Risk Luminal B and Low Risk Luminal A, and TargetPrint which measures mRNA levels of Estrogen Receptor (ER), Progesterone Receptor (PR) and Her2neu (Her2).

Material and Methods: BluePrint, MammaPrint and TargetPrint were performed on fresh tumor samples from 133 breast cancer patients (T1−4, N0−2) between Dec 2008 and Jul 2011 at 11 institutions in US and Europe.

ER, PR, Her2 (n = 130) and Ki-67 (n = 79) IHC/FISH assessments were performed according to local practice at each institution. FISH was performed on 11 Her2neu samples if Her2 2+.

For 86 patients St Gallen subtype classification is possible.

Results: Concordance of TargetPrint with IHC/FISH is 97% for ER, 78% for PR and 95% for Her2.

Concordance of BluePrint with IHC/FISH subtyping is 88% for Luminal type and 93% for both Her2 and Basal type.

BluePrint	Subtyping according to St Gallen with local PA assessments					
	Luminal A (HR+, Her2−, Ki67 <14%)	Luminal B/Her2− (HR+, Her2−, Ki67 high)	Luminal B/Her2+ (HR+, Her2+)	Her2+ (HR−, Her2+)	Basal (HR−, Her2−)	Total
Luminal A-type	26	9	0	0	0	35
Luminal B-type	12	18	1	1	1	33
HER2-type	0	0	4	2	0	6
Basal-type	0	3	1	1	7	12
Total	38	30	6	4	8	86

Of 35 MammaPrint Low Risk (BluePrint Luminal A) 26 are Luminal A according to St Gallen definition (HR+, Her2−, Ki67 <14%) and 9 are Luminal B according to St Gallen definition (HR+, Ki67 high or Her2+).

Of 31 MammaPrint High Risk (BluePrint Luminal B) 12 are Luminal A according to St Gallen definition (HR+, Her2−, Ki67 <14%) and 19 are Luminal B according to St Gallen definition (HR+, Ki67 high or Her2+).

Resulting in a concordance of Ki67 and MammaPrint of 68%.

Conclusions: There is high concordance between IHC/FISH and TargetPrint. There is fair concordance with subtyping according to St Gallen and BluePrint. Concordance between MammaPrint and Ki67 is poor.

Implementation of TargetPrint, BluePrint and MammaPrint may improve the clinical management of breast cancer patients.