

therapies. The relative reductions are smaller in the poorer prognostic groups; this may reflect failure to respond to adjuvant therapies.

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POSTER

Expression of ErbB family members and levels of phosphorylated ErbB2 in breast tumours

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Background: ErbB2 (Her2/Neu) receptor tyrosine kinase is overexpressed in 10–30% of human primary breast tumors depending on patient's age. The overexpression of ErbB2 in breast cancer correlates with a more aggressive phenotype and increased risk of metastases resulting in reduced survival. Recently, we have shown prognostic and predictive significance of ErbB2 overexpression as well as increased levels of phosphorylated (Y1248-P) ErbB2 in breast tumors. ErbB2 is known to be a preferred heterodimerisation partner for other ErbB family members, therefore the purpose of our study was to correlate ErbB2 phosphorylation with the expression patterns of ErbB1 (EGFR), ErbB2, ErbB3 and ErbB4.

Material and Methods: Quantitative expression levels of ErbB1, 2, 3 and 4 was measured by means of TaqMan Q-RT-PCR and quantitative levels of phosphorylated (Y1248-P) ErbB2 by means of a sandwich ELISA on membrane extracts from 70 well-characterized primary breast cancers. For ErbB1 quantification EGF binding assay was also performed. ER concentrations were assessed from tumor cytosolic extracts by commercial quantitative ER EIA kit.

Results: Increased Y1248-P ErbB2 content was found in ErbB2-overexpressing tumors (median 2.6 U/mg) as compared to low-ErbB2-expressing tumors (median 0.65 U/mg). ErbB2 phosphorylation significantly correlated with poor survival ($p=0.005$) and inversely correlated with ER status ($p=0$, $rs = -0.65$). Comparison of ErbB family expression on mRNA level with ErbB2 phosphorylation revealed significant correlation with ErbB2 ($p=0.0002$, $rs = 0.49$) and ErbB1 ($p=0.05$, $rs = 0.26$) and inverse correlation with ErbB4 ($p=0.0005$, $rs = -0.47$). Even better correlation was found between ErbB1 levels, detected by EGF binding assay, and ErbB2 ($p=0.08$, $rs = 0.43$). No correlation between Y1248-P ErbB2 content and ErbB3 mRNA levels was found.

Conclusions: Phosphorylation of ErbB2 is associated with poor prognosis and reduced ER content. Significant correlation of phosphorylated ErbB2 with ErbB2 and ErbB1 expression suggests the role of ErbB1/ErbB2 heterodimers in malignancy of tumors. Inverse correlation between phosphorylated ErbB2 and ErbB4 is in agreement with findings describing association of ErbB4 with good prognosis.

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POSTER

Bilateral breast cancer – prognostic significance of synchronous and metachronous bilateral breast cancer (BBC)

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Purpose: to evaluate the impact of the type of bilateral breast cancer and mutations of BRCA 1 and 2 genes on survival.

Material and methods: 131 patients treated at Institute of Oncology MCS Memorial in Gliwice between 1969–2002 developed bilateral breast cancer. There were 39 (29.7%) synchronous BBC, defined as tumor arising in both breast simultaneously or within a maximum 12 months interval and 92 (70.3%) metachronous BBC, defined as tumors of second breast diagnosed more than 12 months following ipsilateral breast cancer, in absence of distant metastases. The time interval between metachronous tumors ranged from 1.26 to 29.6 years (mean 7.3). BRCA 1 and 2 gene mutations analysis were performed in 92 patients with ASA-PCR technique. Survival distributions from the date of primary and opposite side tumors were compared in group of patients in synchronous and metachronous BBC and in patients with and without BRCA 1 and 2 genes mutations by the log-rank test.

Results: Mean age of diagnosis of cancer in SBBC and MBBC group was 52 and 46 ($p=0.002$). The proportion of early stage tumors T0–1 was significantly higher in opposite side tumors compared to the first primary tumor in both groups ($p<0.0001$). The mean tumor diameter of first primary and contra lateral breast tumors were 3.6 and 2.4 cm ($p<0.00001$). BRCA 1 and 2 mutations were recognized in 25 patients (27.6%). All but two mutations were detected in MBBC ($p=0.006$). Median follow-up from the diagnosis of primary and BBC was 9.34 and 3.78 years. Five year DFS for SBBC and MBBC were 67 and 93% respectively (log-rank $p=0.005$).

MFS were 76 and 97% (log-rank $p=0.07$), RFS were 77 and 95% (log-rank $p=0.03$). If the same analysis was performed since the date of the second breast tumor DFS, MFS and RFS in both groups did not reach statistical significance. Differences in 5-year survival-DFS, MFS, RFS in BBC patients with and without BRCA 1 and 2 mutations did not reach statistical significance.

Conclusion:

1. A close follow-up policy based on clinical examination and annual mammography enables detection the second breast cancer at an earlier stage than the primary one.
2. Patients with metachronous bilateral breast cancer (MBBC) have better survival characteristics in comparison with SBBC patients.
3. BRCA 1 and 2 gene mutations do not have the adverse impact on survival in bilateral breast cancer.

BBC – bilateral breast cancer; MBBC – metachronous bilateral breast cancer; SBBC – synchronous bilateral breast cancer; DFS – disease free survival; MFS – meta free survival; RFS – Recidiva free survival.

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POSTER

Women under age 50 with an ER-positive breast cancer are more likely to have positive lymph nodes if PR is not expressed

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Background: Women with an ER-positive breast cancer have a better prognosis if PR is also expressed and this prognostic significance is independent of treatment. This study examines qualitative and quantitative PR-expression in women with a primary invasive ER-positive breast cancer, in predicting axillary lymph node involvement.

Patients and Methods: 1008 consecutive women with a complete axillary clearance for a primary operable invasive breast cancer were evaluated retrospectively between Jan 2000 and Jun 2003 in the Multidisciplinary Breast Centre, UZ-KULeuven. We excluded those with a lobular type breast cancer, those with ER-negative breast cancer and those who received neoadjuvant therapy or the sentinel lymph node procedure only for axillary staging. The following variables were tested in an uni- and multivariate analysis: tumour diameter (less or more than 20 mm) and grade, histologic type, quantitative steroid hormone receptor status, hormone replacement therapy, menopausal status and family history of breast cancer. Age at diagnosis is stratified as less or more than 50 years. Immunohistochemical stains for ER (6F11/2) and PR (312) were categorised using the H-score; ≤ 50 was defined as ER/PR negative.

Results: Univariate analysis shows that tumor grade, size and PR status are significantly related with lymph node status in patients less than 50 years of age. Selected PR<200 versus PR>200 and size > 20 mm versus size ≤ 20 mm were determined by ROC curve. Multivariate analysis also demonstrates grade, tumor size and PR status as independent predictors for lymph node positivity in women under age 50.

Univariate Analysis: (correlation between predicting variables and LN metastasis)

Variables	P-value		
category	All patients	50 years	≥ 50 years
No of patients (%)	1008	282 (28%)	726 (72%)
PR (≤ 200 vs > 200)	0.035*	0.010*	0.170
ER (≤ 200 vs > 200)	0.225	0.118	0.776
Histology	0.428	0.523	0.679
Grade (I/II vs III)	0.000*	0.001*	0.000*
Size (≤ 20 vs > 20 mm)	0.000*	0.000*	0.000*
HRT (– vs +)	0.761	0.807	0.603
Family History (– vs +)	0.907	0.730	0.543
BMI	0.761	0.393	0.241

Multivariate analysis in patents under age 50:

	Odds ratio	95% Confidence Interval
PR (<200/300 vs >200/300)	1.9	1.15–3.30
Grade (3 vs 1.2)	5.3	1.86–15.30
Size (>20mm vs <20mm)	4.4	2.55–7.66

Conclusion: PR expression and its quantitative value, tumour grade and size are all independent predictors for axillary lymph node involvement in women under age 50 with an ER-positive breast cancer.