

to include racial information to help provide insight into the potential impact of race and ethnicity on treatment outcomes.

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POSTER

# **Multifactorial CNS relapse susceptibility in HER-2-positive breast cancer patients: first results from a population-based registry study**

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**Background:** A series of retrospective studies have reported a higher incidence of central nervous system (CNS) metastases in HER-2-positive (HER-2+) metastatic breast cancer. Trastuzumab, which does not cross the blood-brain barrier, has been associated with this increased risk.

**Materials and Methods:** The aim of this study was to evaluate incidence, survival and risk factors of CNS metastases in the incident breast cancer population systematically collected by the Tumor Registry of Parma Province over the 4-year period, 2004–2007. Study endpoints were: any distant metastasis as first event; CNS metastasis as first event; CNS metastasis at any time. Associations between CNS metastases and HER-2 status in the entire population and between trastuzumab and CNS metastases in HER-2+ patients (pts) were estimated. A multivariate analysis was performed to test the effect of covariates.

**Results:** We evaluated the total resident population (n = 1500) of breast cancer pts diagnosed during the period 2004–2007 in Parma Province. Two-hundred and twenty-five pts (15%) were HER-2+ (IHC 3+/FISH amplified). Of these, 100 pts were treated with adjuvant trastuzumab-based therapy. At a median follow-up of 36 months from the diagnosis, the incidence of CNS relapse was 3% (1.3% as first recurrence). The median time to death from the diagnosis of CNS metastases was 25 months. Among the HER-2+ pts, there was a significant association between trastuzumab and subsequent CNS metastases ( $P = 0.02$ ). However, in multivariate analysis, HER-2 status regardless of trastuzumab therapy was found to be the only independent predictive factor for CNS metastases (either as first or as subsequent recurrences;  $P < 0.001$ ).

**Conclusions:** This is the first population-based registry study analyzing CNS metastases in breast cancer in relation to tumor biological features, systemic treatment, and clinical outcome. Based on our results, HER-2 status independently distinguishes pts with a higher risk of CNS metastases. It is however presumable that, in some cases, improvements in systemic control and overall survival associated with trastuzumab-based therapy lead to an “unmasking” of CNS relapse that would otherwise have remained clinically silent prior to a patient's death.

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POSTER

# **A breast cancer fingerprint in peripheral blood – a novel method for early diagnosis**

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**Background:** Existing technology for detecting breast cancer has its limitation, especially among women with dense breast tissue. To reduce mortality early detection is crucial in order to start treatment before the disease becomes metastatic. We here propose a novel method for early detection of breast cancer using blood as clinical sample. Blood samples are easily available, minimally invasive and can be sampled at low cost.

**Material and Methods:** A total of 130 blood samples were analyzed using high density oligonucleotide microarrays from Applied Biosystems. Blood samples were collected from women participating in the national mammography screening program that were called in for a second look after a first suspect mammogram. Further clinical examination revealed that 67 subjects had breast cancer, while 54 had no malignant findings. In addition 9 samples from healthy controls were included. Partial Least Square Regression (PLSR) in combination with a 20-fold double cross validation (CV) approach was used to identify differentially expressed genes between cases and controls, and to estimate their prediction efficiency.

**Results:** We have identified a gene signature consisting of 689 probes that predict cancer patients from controls with an accuracy of 81% ( $\pm 7\%$ ). Functional enrichment analysis of the genes in the signature suggests that a defense response is provoked in breast cancer patients. Furthermore, genes involved in lipid- and steroid metabolism seem to be differentially

expressed between cases and controls. A 96 probe TaqMan based diagnostic tool BCtect® is developed partly based on these results and will be launched in Europe in 2009.

**Conclusion:** Our results indicate that the blood transcriptome of breast cancer patients carries biological relevant information about breast tumor growth. The genes identified possibly reflect a crosstalk between the growing tumor and the immune system of the host. We believe that this tool can constitute a supplement to existing diagnostic technology, but also offer a breast cancer test in areas where mammography screening is insufficient.

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POSTER

# **M0 breast cancer patients exhibited a decreasing incidence of metastases but no improvement in prognosis after metastases since 1978 in Bayern: report from Munich Cancer Registry**

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**Background:** The course of breast cancer may be changing over time, related to detection and treatment. We explored trends in metastasis in breast cancer patients without metastasis at diagnosis (M0).

**Patients and Methods:** Data of 28,687 M0 patients with primary breast cancer diagnosed between 1978 and 2003 in Bayern were obtained from the first (general) hospital-based, later population-based, Munich Cancer Registry, which uniquely documents metastases during follow up. Time to metastasis and survival following metastases were determined for the most common sites of metastases, and were assessed per time period (1978–1984 vs 1985–1994 vs 1995–2003) with follow-up until October 2008. Cox regression was performed to identify the following determinants associated with time to metastases and survival: period of diagnosis, age, pT, pN, differentiation grade, receptor status, histological grade, site of metastasis and time to metastasis.

**Results:** In the recent decade the incidence of metastases among M0 patients decreased markedly, however survival after metastases did not improve (HR 1.00 vs 1.18 vs 1.19,  $p < 0.001$ ). Furthermore, within 5 years following diagnosis, the actuarial rate for time to metastases became shorter in the last decade (35% vs 43% vs 24%,  $p < 0.001$ ). The proportion of bone metastases decreased whereas liver and CNS metastases occurred more often. Skin and lymph node metastases showed best prognosis until 10 years follow up. Time to and survival after metastases was worse for patients with ER or PR negative tumours.

**Discussion and Conclusions:** In recent decades, development of metastases in M0 breast cancer seems to have been increasingly prevented, probably due to both stage migration by screening and developments in systemic therapy. However, if metastases occur shortly after diagnosis of M0 patients, they appear sooner, which might be mainly determined by more aggressive tumours following initial treatment. Potential improvements in treatment of M0-patients who developed metastases seem to be nullified by a worse pattern of metastases, with the shift to liver and CZS.

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POSTER

# **Importance of breast cancer screening in women aged between 35 and 49 years old**

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Today 1 in every 8 women has breast cancer (ca) in the world. Its early detection and treatment are the most important factors affecting breast ca mortality. Therefore to detect the suspicious lesions via imaging modalities before they become palpable and their pathological assessment have recently gained importance a lot. Imaging guided wire localization breast biopsy (IGWLBB) is one of the techniques used to get pathological diagnosis of these nonpalpable lesions. And with these study we aimed to show even in 35–49 year old women how important the mammography (MMG) is to detect breast ca at an earlier stage.

From August 2006 to June 2007, 233 patients underwent 242 IGWLBB to nonpalpable lesions. 9 patients had 2 simultaneous localizations: 4 to ipsilateral breast, 5 to contralateral breast. 191 localizations were guided sonographically (USG) and 51 via MMG. Of 242 lesions, 237 were excised completely, 1 was excised partially and 4 was not excised at all (success rate: 97.9%).