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

5187 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.

5188 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 were mammography screening is insufficient.

5189 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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5190 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 sucpicious lesions via imaging modalities before they become palpable and their pathological assesment 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 51via MMG. Of 242 lesions, 237 were excised completely, 1 was excised partially and 4 was not excised at all (success rate: 97.9%).

Mean patient age at biopsy was 48.2 years, while malignancy detected 57 patients' mean age was 51.5 years.
59 malign lesions were detected in 242susceptible lesions (malignity rate: 24.4%) and high risk lesion (LCIS, atypical ductal/lobular hyperplasia, lobular neoplasia) in 11 (4.5%). Of 59malignancy, 19 were in situ and 40 invasive (inv) tumors.
Of 233 patients, 138 were between 35 and 49 years old. In these 138 women, 145susceptible lesions were detected [27 malign (18.6%), 7 high risk (4.8%)]. In these age group, microcalcifications (M) were the most detected lesion via MMG (84.9%) and mass via USG (89.2%).
Via imaging malign lesions of these age group were detected the most as M (55.6%), in situ tumors as M (75%) also, but inv tumors as mass (60%). If imaging presentation was M, malignancy or high risk lesion detection rate was 45% and if it was mass, the rate was 15.4%.
Of the 27 malign lesions, 12 were in situ tumors (44.4%) while 10 others (37.0%) were early stage inv breast ca (stage1, 2a&2b) (early stage breast ca rate was 81.5%).
This study shows, even in 35−49 year old women, although their breast is denser than the older age group, in nonpalpable lesions the malignity rate was 18.6%, comparable to all ages' malignity rate, and also early stage breast ca diagnosed via IGWLBB was as high as 81.5%. Then, since when M were detected via imaging, rate of detection of malign or high risk lesion was almost half of all M (45%), and since in situ tumors were detected the most as M (75%) and M are found the most easily via MMG, it's shown even in 35−49 year old women how important the MMG is in diagnosing breast ca at an earlier stage.

5191 POSTER

Allele-specific aberrations and two dimensional disparity of copy number alterations in breast cancer

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Background: The localization and identification of disease susceptibility genes is an active field in the forefront of medical genetics. Copy number variations (CNVs) usually occur when there is a genomic rearrangement in a segment of DNA during the cell division. Every diploid has two copies of a locus but in a cancer cell this may vary and leads to occurrence of copy number alterations (CNAs). We focus on the disparity of CNAs in tumor samples compared to blood samples in two directions (horizontal and vertical).
Material and Methods: We applied a visualization method to Illumina 109K SNPs array data on 112 individuals. Two outputs of Illumina, B allele frequency and log R ratio were derived from the BeadStudio Genotyping Module. Following analyses were performed in MATLAB®.
We applied a filter to blood (reference) data not only to remove the contaminations (unclear genotypes) but also divide into three regions of AA, AB and BB (around 0, 0.5 and 1). In second step, same SNP numbers were retrieved from tumor data for which the analysis performed. The distance between blood heterozygote and tumor was measured. If it was greater than the mean + standard deviation value then those tumor samples were chosen as departed from heterozygote to homozygote regions. Subsequently, for every SNP the frequencies of disparity of individuals were calculated and visualized for each chromosome with the A allele above and B allele frequencies below the X axis. SNPs with equal propensity to lose both alleles resulted a symmetric plot, while SNPs where one of the allele was preferentially lost, resulted in an asymmetric plot. Based on an arbitrary threshold, only the asymmetric SNPs were highlighted. Finally, genes involved in the asymmetric region were obtained.

Chromosome	SNPs	Uncontaminated	Asymmetric	Chromosome	SNPs	Uncontaminated	Asymmetric
1	9819	7416	4256	13	3093	2415	1349
2	8702	6765	3969	14	3420	2586	1485
3	7207	5686	3203	15	3307	2549	1544
4	6000	4734	2684	16	3388	2522	1482
5	6329	4990	2814	17	4079	3148	1825
6	6579	5147	2952	18	2570	2006	1209
7	5581	4349	2446	19	3520	2774	1699
8	4891	3949	2280	20	3007	2277	1330
9	4480	3504	2053	21	1381	1104	626
10	5240	3999	2313	22	1886	1407	765
11	5928	4659	2681	X	3430	2220	1370
12	5465	4128	2316				

Results: Table shows SNP numbers, uncontaminated (after filtering) and asymmetric SNPs involved in horizontal disparity.
Conclusions: These findings provide evidence which genes involve in breast cancer and studying in two directions helps in finding a statistically reliable statement about the behaviour of these groups of genes.

5192 POSTER

Early diagnosis and screening for breast cancer: a population-based study

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Background: The aim of this cross-sectional, population-based study is to inform the healthy women about breast cancer and to screen them as well as to present the relationship between the demographic and the clinical findings.
Methods: The present study was carried out between 1 January 2006 and 30 June 2008 in 111 health care centers located in Mersin, Turkey. 35 health teams were generated prior to the study. The teams were primarily trained for breast examinations and for screening methods to detect breast cancer. The study population was planned to include all of the female subjects who applied to the health care centers for any reason. Each subject was offered a detailed breast examination and a general examination as a screening method by the authorized health personnel.
Results: A total of 77,934 subjects were evaluated. General health examinations were performed in 66% (n = 51,706) of the participants. A suspected mass was detected in 6% of the examined participants. This constituted 3.6% of all subjects. The mean age, education and income levels of the subjects in the examined group were similar to those in the group refusing examination. The percentage of the subjects who declined an examination was 2-folds higher in the $\geqslant$60 year age group compared to <60 years (14.8 vs. 6.6%). The rate of those willing to be examined was lower among the subjects who were living outside the city center than of those living in the center (33% vs. 18%).
A breast mass was detected in 2838 subjects who had undergone a breast examination. The mean age of the subjects in whom a mass had been detected was 39.1 years, whereas it was 36.6 years for those with a normal breast examination ($p < 0.001$). While 15.1% of the subjects with suspicious examination findings were either high school or university graduates, this rate was higher in subjects with normal examination findings (23.7%; $p < 0.001$). Among the subjects in whom a mass had been detected, the rate of the subjects followed-up at the city center was 65%, whereas it was 35% for those in the other group.
Conclusion: For screening breast cancer, participation of elderly subjects, subjects living in rural areas and subjects with low educational as well as lower socio-economic levels should receive special attention.

5193 POSTER

Can adjuvant homeopathy improve the control of post-chemotherapy emesis in breast cancer patients? Results of a randomized placebo-controlled trial

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Background: Homeopathy used as an adjunct in the treatment of chemotherapy (CT)-induced emesis has rarely been evaluated.
Material and Methods: Patients with non-metastatic breast cancer treated with 6 courses of FAC 50, FEC 100 or TAC chemotherapy were randomized to Cocculine (C) or Placebo (P) in a multicentric comparative double-blind phase III study. Anti-emetic treatment was standardized (corticoids + ondansetron). Patients were evaluated after each course. The primary endpoint was nausea measured after the 1st CT course using the FLIE (Functional Living Index for Emesis) with 5-day recall. The planned sample size was 396 evaluable patients based on a minimum expected difference in mean of 0.5 ± 1.6 on a scale from 1 (a lot) to 7 (not at all) with 5% two-sided α error and 85% power. An intent-to-treat analysis was planned. Secondary evaluation criteria were: vomiting measured by the FLIE score, patient