of serum versus tumour levels of IGFBP-3. It is possible that future characterisation of breast tumours may include fibronectin and IGFBP-3 production, so that clinical response to agents targeting the EGF pathway may be predicted, resulting in a more targeted use of such therapies.

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167 POSTER

HER2 polymorphism and the risk of breast and ovarian cancer

D. Pinto[1], A. Vasconcelos[1], S. Costa[1], D. Pereira[2], H. Rodrigues[2], C. Lopes[1], R. Medeiros[1]. [1]*Portuguese Institute of oncology, Molecular Oncology, Porto, Portugal;* [2]*Portuguese Institute of oncology, Medical Oncoloy, Porto, Portugal*

Introduction: Breast cancer is a major public health problem around the world, and its carcinogenesis is not yet well understood. The Human Epidermal growth factor Receptor-2 (HER2) seems to play an important role in the development of this neoplasia, and genetic alterations in this gene, such as point mutations and polymorphisms have been detected in breast cancer patients, as well as ovarian cancer patients. The aim of our study was to analyze the frequency of a single nucleotide polymorphism in the HER2 gene in a southern European population.

Materials and Methods: The study included 152 patients with breast cancer, 139 ovarian cancer patients and a control group of 146 healthy donors. DNA extracted from peripheral blood was submitted to PCR-RFLP, in order to identify the possible HER2 genotypes; Ile/Ile, Ile/Val and Val/Val. The restriction fragments were analyzed in a 3% agarose gel, stained with ethidium bromide.

Results: A twofold increase in risk of breast cancer was found among women who are carriers of a Val allele genotype – Ile/Val and Val/Val genotypes (OR = 2.00; 95% CI: 1.23–3.25; p=0.005). As for the ovarian patients, we also found an increased risk in ovarian cancer, with an OR of 1.59 (95% CI: 0.96–2.63).

Discussion: Our results indicate an association between the presence of the Val allele in the HER2 polymorphism and the risk of breast and ovarian cancer. Further studies are needed to evaluate the role of this polymorphism in the behavior of breast and ovarian cancer.

168 POSTER

DNA diagnosis of hereditary breast and ovarian cancer in Latvia

O. Sinicka[1], A. Stengrevics[2], D. Smite[1], J. Eglitis[2], L. Tihomirova[1]. [1]*Biomedical Research and Study Centre of University, Riga, Latvia;* [2]*Latvian Oncology Center, Riga, Latvia*

Background: Breast cancer is the leading cancer site in Latvian women and ranks as the first highest cause of cancer-related death. Since the discovery of BRCA1 and BRCA2 genes, the mutation analysis of these genes is widely used for the identification of women with a high risk of breast and ovarian cancer and developing management strategies. The BRCA1 and BRCA2 mutation spectrum and frequencies vary significantly in different populations and geographic regions. Therefore the criteria for BRCA1/2 genetic testing should be optimised for each population.

The objective of this study was to develop effective BRCA1 gene mutation detection strategy in Latvia based on characterisation of mutation profile in breast and ovarian cancer patients.

Material and methods: Mutation analysis of entire BRCA1 gene was performed in DNA from 75 breast cancer patients and 30 ovarian cancer patients from Latvian Oncology Center selected by early onset of disease or family history of breast/ovarian cancer. Most of patients tested have insignificant cancer history in family. The analysis was performed by SSCP/HDA in polyacrylamide gels and automatic direct sequencing (ABI PRISM 310) of variants detected. The screening for recurrent mutations was performed as well in early onset breast/ovarian cancer patients unselected for family history.

Results: 5 different deleterious mutations have been detected by the analysis of entire BRCA1 gene. Three of mutations detected were recurrent. Missense-mutations, registered in BIC database as unclassified variants and common polymorphisms, have been found in this study as well. High proportion of mutation carriers were found in this study regardless insignificant cancer histories in families of patients tested. Altogether 20 mutation carriers were detected by the analysis entire BRCA1 gene and 28 by the screening for recurrent mutations.

Conclusions: Breast cancer diagnosed before the age 48 is suggestive for DNA testing to be offered to patients in Latvia, regardless cancer history in the family. The identification of three founder mutations in Latvian population allows rapid and cost-effective detection of mutation carriers. Further study of founder mutations could be useful for understanding the role of these mutations in the incidence of breast and ovarian cancer in order to provide individual risk assessment and to design better therapeutic strategies.

169 POSTER

Are lobular carcinomas more often steroid receptor positive?

P. Neven, H.J. Huang, M. Drijkoningen, R. Paridaens, F. Amant, P. Berteloot, I. Vergote, M. Christiaens. *UZ-Leuven, Multidisciplinary Breast Centre, B-3000 Leuven, Belgium*

Background: Invasive lobular carcinomas (LC) and invasive ductal carcinomas (DC) differ with respect to their expression of a variety of molecular tumour markers including oestrogen (ER) and progesterone receptor (PR) expression. LC are generally referred to be more likely ER and PR positive compared to DC. We analysed whether tumour grade affects differences in ER/PR expression by histologic tumour types.

Patients and Methods: Charts from 1472 consecutive female patients diagnosed with primary operable invasive breast cancer (Jan. 2000–May 2003) were reviewed, excluding those who received neoadjuvant therapy. The highest tumour grade was retained for each case and each tumour was classified according to its histological type as LC or non-lobular carcinoma (non-LC). Immunohistochemical stains for ER (antibody 6F11/2) and PR (antibody 312) were categorised using the H-score as follows: <50/300 negative; ∗ 50/300 positive.

Results: 204 (13.8%) of invasive tumours were classified as LC. LCs were more frequently ER/PR positive than non-LCs ($p<0.001$ – table 1). The great majority of LCs (85.3%) were grade 2 where only 40% of non-LC were classified as grade 2. When we only classified grade 2 tumours by receptor state, there was no difference in incidence of ER/PR positivety between LC and non-LC (table 2); differences however, were significant for grade 3 lesions.

Table 1

Type	ER-positive	PR-positive
LC (n=204)	92.7%	79.5%
non-LC (n=1268)	80.0%	62.4%

Table 2

Type	ER-positive	PR-positive
Gr 2 LC (n=174)	94.3%	79.9%
Gr 2 non-LC (n=508)	94.7%	76.0%
Gr 3 LC (n=25)	76.0%	72.0%
Gr 3 non-LC (n=535)	59.1%	42.9%

Conclusion: Regarding the frequency of positive steroid receptors in invasive breast cancer, grade 2 LCs do not differ from grade 2 non-LCs. The difference for ER/PR positivety between both histologic tumour types lies in grade 3 lesions; grade 3 LCs are more often ER/PR-positive than grade 3 non-LCs.

170 POSTER

The progesterone receptor has a prognostic value in oestrogen receptor negative breast cancers

H.J. Huang, P. Neven, M. Drijkoningen, R. Paridaens, P. Berteloot, F. Amant, I. Vergote, M. Christiaens. *On behalf of all members, Multidisciplinary Breast Centre (MBC), UZ-KULeuven, Leuven, Belgium*

Background: Considering oestrogen (ER) and progesterone receptor (PR) expression in breast cancers, the ER-negative (−ve) PR-positive (+ve) phenotype is the least common variant. Some believe that non-expression of ER in the presence of PR is a laboratory error whereas others consider this as a separate category. The aim of this study is to analyse whether prognostic factors are differently expressed in ER−ve breast cancers with or without PR expression.

Patients and methods: Charts from 1358 women who underwent primary breast surgery and complete axillary clearance for invasive breast cancer between Jan 2000 and June 2003 (excluding those who had neoadjuvant therapy and those with sentinel lymph node only) were examined. We compared age, mean tumor size, histologic type, incidence of grade 3 lesions, axillary lymph node status, HER-2/neu expression [immunohistochemical (IHC) measurement] and menopausal status between ER−ve PR+ve and ER−ve PR−ve tumours. Steroid receptors were measured by IHC using the H-score and defined negative with a score of less than 50/300.