the program were compared with breast carcinomas detected in 313 female relatives outside the program and with a standard population documented in the local tumor registry.

Results: The acceptance rate for the surveillance program was 85%. Overall, 41 primary or secondary breast carcinomas were detected. The average detection rates were 89.6/1000 for mutation carriers, 47/1000 for high risk and 24.7/1000 for moderate risk women compared to 1/1000 in the local tumor registry. In a retrospective analysis these tumors were compared with tumors detected in relatives of these women outside the program and tumors documented in the local registry. Overall, 83% of the screen detected tumors were node negative and 85.4% were pre-invasive or smaller than 2 cm. In comparison, of the tumors detected in female relatives outside the program only 48% (p=0,0003) were node negative and 44% (p<0,0001) were pre-invasive or smaller than 2 cm. Of tumors gathered in the local tumor registry 56% (p=0,003) were node negative and 42% (p<0,0001) were pre-invasive or smaller than 2 cm.

Discussion: Prospective cancer detection rates in proven or suspected carriers of mutations in the BRCA1 or BRCA2 gene were significantly greater than expected in the average-risk population. A structured screening program including CBE, US, MG and MRI is effective in the early detection of breast carcinomas in this risk group and should be offered to these women as a matter of routine.

P4

The presence of hereditary BRCA1 gene mutations in women with familial breast cancer or familial ovarian cancer and the frequency of the occurrence of these tumours in their relatives

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In 48 women with familial breast cancer as well as in 22 women with familial ovarian cancer, the presence of patogenic mutations in BRCA1 gene were found in 35.4% or 54.6% of patients respectively. From the patients possessing mutations we created two groups: the CaM - probands with breast cancer and CaOv - with ovarian cancer. The probands with breast cancer were younger by a mean of 5 years, then the probands with ovarian cancer (p=0.048).

Methods: The PCR-SSCP procedure was used for seeking mutations in the BRCA1 gene. Fragments suspected of mutation presence were subjected to nucleotide sequencing.

Results: In the CaM group, which consisted of 17 women with breast cancer the following mutations in the BRCA1 gene were detected: 5382insC, T300G, 3819del5 and IVS20+60ins12. The probands of the CaM group, and their relatives, developed a total of 49 breast and ovarian cancers. Among all these tumours the breast cancers of probands made up 34.7%, the breast cancers of probands' relatives made up 57.1% and the ovarian cancers of probands and their relatives made up only 8.2%. The CaOv group consisted of 12 probands with ovarian cancers in whom we detected only 2 kinds of mutations: 5382insC and 185delAG. The probands of the CaOv group, and their relatives, developed a total of 38 ovarian and breast cancers. Among all these tumours the ovarian cancers of the probands made up 31.6%, the ovarian cancers of their relatives made up 34.2% and the breast cancers of the relatives 34.2% of tumours. In probands with breast or ovarian cancer the predominant mutation was the 5382insC – in the BRCA1 gene detected in 76.5%, and in 91.7%. Despite the predominant presence of the same mutation in probands from both groups the ratio of the number of breast cancers to the number of ovarian cancers in their relatives differed significantly (p=0.0003).

Conclusion: This data shows, that the presence of the 5382insC mutation in the BRCA1 gene is not always associated with the development of ovarian cancer. It is very likely that the development of ovarian cancer requires some additional factor, which is common among the familial ovarian cancer patients, and is almost inexistent among the familial breast cancer group of patients. On the other hand the development of ovarian cancer at a later age than breast cancer in probands suggests that there exist some factors, which slow down the development of ovarian cancer, or which accelerate the development of breast cancer.

P5

The analysis of genetic polymorphisms in CYP1B1 and COMT genes in breast and endometrial cancer patients

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Breast (BC) and endometrial (EC) cancer are known to be severe malignant diseases, characterized by unfavorable consequences for women's health. We focused our comparative study on the impact of genetic polymorphisms in CYP1B1 and COMT genes into the individual predisposition for the development BC or EC. CYP1B1 and COMT are two enzymes responsible for the synthesis and inactivation of catecholestrogens. Polymorphic forms of these enzymes were shown to differ in their enzymatic activities. Hence, inherited alterations in the activity of COMT and CYP1B1 hold the potential to define differences in cancer risk associated with estrogen-induced carcinogenesis. We analysed 3 polymorphisms in CYP1B1 gene: Arg48Gly, Ala119Ser, Val432Leu and Val158Met polymorphism in COMT gene. By using standard RFLP (restriction fragments length polymorphism) method we have analysed breast cancer patients (N=210), endometrial cancer patients (N=138) and control individuals (N=152). Neither for breast cancer nor for endometrial cancer we have found statistically significant association with COMT polymorphism. At the same time we have demonstrated that Arg48 CYP1B1 polymorphic form, characterised by Shimada et al., as a form with the highest activity for the 4-hydroxylation of the estrogens, is strongly