**Conclusion:** These findings suggest that *CCR2−64I* polymorphism has a protective role in the evolution from SIL to ICC.

**947** POSTER

**Molecular defects in endometrial carcinomas: microsatellite instability (MSI), PTEN and beta-catenin gene mutations.**

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**Background:** In order to better understand the molecular pathogenesis of sporadic endometrial carcinomas, we assessed the frequency of incidence of microsatellite instability (MSI) and mutations in PTEN and beta-catenin gene and analyzed detected defects in relation to each other and to clinico-pathological features of endometrial carcinomas.
**Material and methods:** Material included DNA from 59 endometrial carcinomas, all but two are endometrioid type, and from blood lymphocytes of the same patients. Mutations were assessed in all nine exons of PTEN gene and in exon 3 of beta-catenin gene by PCR-SSCP and sequencing methods. The analysis of MSI was carried out using eight DNA microsatellite markers by PCR with fluorescent-labelled primers and electrophoresis in polyacrylamide gel.
**Results:** In 30 carcinomas (50.8%) mutations were found in PTEN gene and in 9 tumors (15%) in beta-catenin gene. Microsatellite instability (MSI+) was identified in 19 carcinomas (32.2%). The remaining 40 tumors (67.8%) was stable DNA (MSI−). In 17 cases (28.3%), in the studied microsatellites a loss of heterozygosity (LOH) was also revealed. The following relations were observed between the detected defects. In MSI+ tumors, PTEN mutations occurred significantly more frequently than in MSI− tumors (73.7% vs 40%, $\alpha = 0.0094$) but, except for one, none of PTEN mutations was characteristic for MSI. In contrast, no significant differences were found in frequency of incidence of beta-catenin gene mutations in MSI+ and MSI− tumors (15.8% vs 15.0%, $\alpha = 0.785$). Interesingly, mutations in beta-catenin gene most frequently coexisted with mutations in PTEN (7/9; 77.8%). PTEN and beta-catenin gene mutations as well as MSI were more frequent in early clinical stages as compare to advanced tumors, although these differences did not reach statistical significance. However, statistically significant, reverse correlations were observed between the frequency of PTEN gene mutations or MSI and the grade of morphological differentiation of the tumors (G3 vs G2+G1, $\alpha = 0.033$ and 0.023, respectively) and the age of women (before vs after age of 60, $\alpha = 0.044$ and $\alpha = 0.065$, respectively).
**Conclusions:** The results of this study suggest that most frequently occurring mutations in PTEN gene may play crucial role in endometrial carcinoma pathogenesis. The coexistence with them or absence of mutations in beta-catenin gene or MSI may reflect the heterogeneity of molecular mechanisms of development of endometrial carcinoma.

**948** POSTER

**Fc-gamma, RIIa-131RH polymorphism is associated with decreased risk for the development of cervical lesions**

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**Background:** The infection by HPV is the necessary cause for the development of cervical cancer and the clinical course of the disease is mainly influenced by immunological responses. The IgG response is associated with both squamous intraepithelial lesions (SIL) and cervical (CC) cancer, and it is barely induced in the preclinical infection. The Fcã receptors of the IgG play an important role, coupling the humoral and cellular immune responses, and their described polymorphisms may influence the immune responses due to the higher or lower affinity of the receptor for the IgG molecule.
**Material and methods:** The FcãRIIa H/R polymorphism was analysed in 310 individuals: 200 women with cervical lesions and 110 healthy women, by PCR-RFLP.
**Results:** In this preliminary study, we observed statistically significant differences between the heterozygous genotype HR in cases and controls (OR = 0.535, CI95% [0.326−0.876], p = 0.012) and this difference is highly stronger when we compare women with SIL lesions and the healthy group, regarding the HR genotype (p = 0.00012; OR = 0.143, 95% CI [0.048−0.425]).
**Conclusions:** Our results suggest that the presence of the FcãRIIa HR genotype has a protective role for the development of pathologies of the uterine cervix, especially in the case of SIL.

**949** POSTER

**Antiangiogenesis as new treatment modality in ovarian cancer: a phase Ib, open label, safety and pharmacokinetics (PK) study of escalating doses of PTK787/ZK222584 (PTK/ZK) in combination with paclitaxel and carboplatin in patients (pts) with stage IC to IV epithelial ovarian cancer**

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**Background:** Vascular endothelial growth factors (VEGFs) and VEGF receptors (VEGFRs) are important mediators of tumor growth and metastasis and their expression is associated with poor prognosis in epithelial ovarian cancer. PTK/ZK is a novel, oral, angiogenesis and lymphangiogenesis inhibitor that blocks tyrosine kinase signaling from all known VEGFRs.
**Methods:** An open-label, multicenter, phase-IB, dose-escalation study evaluated PTK/ZK with chemotherapy as first line-therapy in pts with stage IC-IV epithelial ovarian cancer. Paclitaxel was administered as a 3-hour infusion on day 1 of each 21-day cycle at 175 mg/m$^2$. Carboplatin was given immediately after paclitaxel as a 30-min IV infusion to an AUC of 5 mg min/mL. PTK/ZK was given daily from day 3−21 of each cycle. Cohorts of 3 to 6 pts received doses of PTK/ZK at 250, 500, 750, 1,000 or 1,250 mg/day. MTD and DLT of PTK/ZK were assessed; PK of PTK/ZK, carboplatin and paclitaxel was characterized.
**Results:** 19 pts were evaluated; 16 for DLT; 18 for PK. No DLTs or PTK/ZK-related SAEs were reported. One pt discontinued due to AEs. Grade 1−2 hypertension was the most common AE. Steady-state PTK/ZK plasma levels were constant between cycle 1−2. PTK/ZK has no impact on systemic exposure of free platinum. Paclitaxel exposure was not affected at the biologically active dose of 1,250 mg/day PTK/ZK. Additional data are being collected at the 1,250 mg dose level.
**Conclusion:** PTK/ZK with paclitaxel and carboplatin is feasible and shows acceptable safety. Updated data will be presented.

**950** POSTER

**The prognostic significance of c-erbB-2, p53 and bcl-2 immunoexpression in patients with epithelial ovarian cancer treated with paclitaxel and platinum**

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**Background:** Several oncogenes and oncosuppressor genes have been implicated in epithelial ovarian carcinogenesis, but their clinical significance is not clear and several conflicting data are found in various studies.
**Material and methods:** We investigated the immunohistochemical expression of c-erbB-2, p53 and bcl-2 proteins in a cohort of 95 patients with advanced epithelial ovarian cancer (stage IIc-IV), who participated in a phase III randomized clinical trial and were treated by either paclitaxel plus carboplatin or paclitaxel plus carboplatin alternating with cisplatin. The immunohistochemical expression profiles were correlated with conventional prognostic parameters, remission status after first line chemotherapy and overall survival at uni- and multivariate levels.
**Results:** Positive immunostaining for c-erbB-2, p53 and bcl-2 proteins was found in 68%, 71% and 69% of the cases respectively. In multivariate analysis, age (<63 vs.⩾63 years, p = 0.016), remission status after first line chemotherapy (patients in complete remission vs. all others, p < 0.001) and p-53 expression (negative vs. positive, p < 0.001) were found to be the only significant prognostic factors independently associated with overall survival.
**Conclusions:** p-53 status along with age and complete remission status after first line chemotherapy appear to be independent prognostic factors for overall survival in patients with epithelial ovarian cancer. Surprisingly, p53 positive expression was correlated with improved survival.