(OR 0.71; 95%CI 0.27–1.87), and no significant interactions between the COX-2 genotype and NSAID use were found.
Conclusions: In this exploratory study, NSAID use was associated with a reduced risk for BE, a premalignant lesion associated with progression to esophageal adenocarcinoma. This protective effect was not modulated by the common COX-2 T8473C polymorphism, suggesting further studies to define underlying biologic mechanisms of NSAID chemoprevention.

P27
Cancer chemopreventive potential of apple juice – Results of a short-term human intervention study with ileostomy patients

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Apples are widely consumed and a rich source of phytochemicals. Regular consumption of one or more apples/day was linked to reduced risk for lung- and colon cancer in various epidemiological studies. In addition, dietary intervention with turbid apple juice reduced adenoma formation in ApcMin/+ mice (Pan et al., in preparation), and DNA-damage, hyperproliferation, and aberrant crypt foci in the dimethylhydrazin-induced rat colon model (Barth et al., 2005). In the present study we determine whether apple juice polyphenols may reach the colon after oral intake of cloudy apple juice and retain chemopreventive properties after passage through the gastrointestinal tract. Eleven ileostomy volunteers consumed 1 l of cloudy apple juice after overnight fast. Ileostomy effluents were collected after 0 to 8 h and freeze-dried. A maximum of 33% of the ingested low molecular weight polyphenols were detected 1, 2, and 4 h after ingestion, in addition to 80% of the ingested oligomeric procyanidins (Kahle et al., 2005, 2007). Based on dried weights, polyphenol concentrations up to 10.2±1.6 mg/g bag contents (average ± standard error, n = 11) were recovered with a maximum after 4 h. We detected a transient increase in radical scavenging activity with a maximum at 4 h after apple juice consumption. Half maximum inhibitory concentrations for DPPH scavenging were significantly reduced by 65% from 0 h to 4 h (ANOVA with Student-Newman-Keuls Test for multiple comparison, $p < 0.05$). Concomitantly, potential to scavenge peroxyl radicals significantly increased from 2.9±0.3 to 4.5±0.5 ORAC units after 4 h (measured at 25 μg/ml). In contrast, potential to modulate carcinogen metabolism by inhibition of Cyp1A enzymatic activity and by induction of detoxifying mechanisms (measured as NAD(P)H:quinone reductase (QR) activity in Hepa1c1c7 cells) was highest at time point 0 h. After apple juice consumption, activities initially declined, and maximum preventive effects were then observed after 6 to 8 h. A similar trend was detected for the inhibition of aromatase (Cyp19) activity with strongest inhibitory effects at time 0 h, whereas Cox-1 activity was not affected. From these results we conclude that selected apple juice polyphenols, especially oligomeric procyanidins, may reach the colon and exert a local antioxidant effect. Modulation of additional chemopreventive mechanisms is likely.

P28
Endogenous IFN alpha during liver transition from quiescence to proliferation

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Background: Interferon alpha (IFNα) is used as main or adjuvant treatment in the therapy of viral infections and several types of cancer. This cytokine is a common therapy for chronic viral hepatitis and contributes to hepatocarcinogenesis prevention. However, the mechanism of IFNα antiproliferative activity in vivo is still obscure. The situation in the liver is complicated by the various types of cells revealing cell-specific response to IFNα, the expression of endogenous cytokine and specific intercellular communication during the transition of liver cells from quiescence to proliferation at preneoplasia. The aim of the study was to evaluate the production of endogenous IFNα during liver transition from quiescence to proliferation induced by partial hepatectomy at the rats.
Materials and Methods: The rats after 2/3 partial hepatectomy (PHE) and laparotomy (LAP) were used in 1, 3, 6 and 12 h post-surgery to model correspondingly G0–S transition and acute phase response, the latter being a constituent part of the former. The genes expression was assessed in liver samples, isolated Kupffer cells (KC) and hepatocytes by quantitative real-time RT-PCR and antiviral test.
Results: PHE induces 2-fold transient increase of IFNα mRNA content and liver antiviral activity at 1–3 h post surgery with subsequent normalization of the indices during 6–12 h period. LAP induces down regulation of IFNα mRNA content in comparison with intact animals. The antiviral activity after LAP was less than the detection limit. KCs and not hepatocytes in both models are responsible for IFNα expression.
Conclusions: The changes in IFNα expression may be essential for liver G0–S transition and acute phase response.

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Prevention of gynecological cancers

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Expression of proliferation biomarkers in female reproductive system malignancies

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Proliferative potential is known to be the integral characteristic enabling impartial estimation of tumor processes peculiarities and their prognosis. The realization of proliferative signals is provided by a complex mechanism through the interaction of several oncogenes and tumor supressor genes controlling cell cycle checkpoints and whose expression changes is a key event in cell malignant transformation.
Aim: To investigate the role of cooperative interactions between p53, p21WAF/CIP1 and p16INK4a in determination of proliferative activity in endometrial and ovarian tumors.
Materials and Methods: Operative material of 56 patients with endometrial adenocarcinoma (EC) and 41 patients with serous ovarian cancer (OC) aged 41–76 years. The

results of immunohistochemical reaction were evaluated using semiquantitive method via calculation of positively stained cells-labelling index (LI). Proliferative potential was defined through Ki-67 expression level (proliferative index – PI): PI $\leqslant$ 10.0% – low, PI > 10.0% – high proliferative activity.
Results: Current study has shown several similar molecular-and-biological features in female reproductive system neoplasias of different genesis (EC and OC), in particular, high proliferative activity (PI was 37.3±2.0 and 30.0±0.3%, respectively) and elevated p53 expression (LI = 46.1±0.5 and 40.3±0.3%, respectively). However some differences in p21WAF/CIP1 and p16INK4a expression have been noted: in EC and OC LI of p21WAF/CIP1 equaled 11.2±0.4 and 6.8±0.3% and LI of p16INK4a – 12.02±0.2 and 31.1±0.6%, respectively. Proliferative activity and p53 expression in EC and OC level rose along with increase in tumor histologic grade. But in EC p21WAF/CIP1 expression level went up while 16INK4a expression lowered, and in OC samples the opposite dependence was observed, i.e. decrease of p21WAF/CIP1 and significant elevation of p16INK4a expression. It is worth noting that aforesaid changes were the most expressed in G3 endometrial and ovarian tumors. Moreover it has been defined priority importance of Ki-67 and p53 expression for survival estimation in OC patients.
Conclusion: Expression of studied biomarkers in endometrial and ovarian neoplasias characterises different pathways of proliferative potential regulation and can be used for more accurate prognosis of these pathological processes.

P30
The study of prognostic significance of microvessel density for serous ovarian cancer patients

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Background: A variety of studies have shown the importance of angiogenesis for ovarian cancer metastasis and recurrence. But there are no consensus of opinion on microvessels quantity as possible prognostic factors for serous ovarian adenocarcinomas patients. Aim was to study the microvessel density (MVD), the expression of proliferative biomarker Ki-67 and such angiogenesis regulating proteins as p53, estrogen receptors (ER) with further comparison of these data with clinicopathologic characteristics of ovarian cancer patients.
Material and Methods: Operative material from 81 ovarian cancer patients aged 17–79 years. Tissue sections were immunohistochemically stained for Ki-67 using a monoclonal antibody MIB1, p53 – DO-7, ER – 1D5 and CD-34 – QBEnd 10. All monoclonal antibodies were produced by DakoCytomation, Denmark. The percentage of positively stained cells was calculated as labeling index (LI) and MVD – through the quantity of CD-34-positive microvessels per 1 mm2.
Results: It was established that MVD in ovarian serous carcinomas was very heterogeneous – 63.6±2.9 (10–128) vessels/mm2, showed a tendency to elevation along with increase in tumor histologic grade and hence was the highest (69.1±4.4 vessels/mm2) in G3 adenocarcinomas. The analogous expression patterns under increase in tumor grade were observed for Ki-67 and p53, but the opposite tendency – for ER expression. The connections between molecular-and-biological characteristics, morphological peculiarities and clinical course of ovarian cancer were shown. Thus it was demonstrated significantly increased MVD and negative correlation between MVD and p53 (r=-0.4), MVD and ER expression (r=-0.6) in patients with distant metastases compared to those without them. Similar increase in MVD in patients who lived less than 5 years compared to those who lived longer was determined.
Conclusion: The obtained data indicate that forming of tumor angiogenesis phenotype in ovarian serous carcinomas can be the result of low p53 and ER expression. Therefore parallel study of MVD, p53 and ER are important characteristics in serous ovarian cancer patients and can be used as prognostic markers of this pathological process.

P31
Expression of steroid hormones receptors in ovarian carcinomas

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Hormonal imbalance is proved to play a key role in ovarian cancer (OC) pathogenesis. Estrogens and progesterone through interaction with their respective receptors modulate such important events as cell differentiation, proliferation and death. OC patients are characterised by alterations either in gonadotropic and steroid hormones secretion or their receptors expression. Aim: To investigate estrogen (ER) and progesterone receptors (PR) expression and evaluate its possible prognostic significance in ovarian serous cancer patients. Materials and methods: Operative material of 81 ovarian cancer patients aged 16–79 years. The results of immunohistochemical reaction were evaluated using semiquantitive method via calculation of positively stained cells – labelling index (LI). ER and PR expression was considered negative when LI < 10.0%, low when 10.0% $\leqslant$ LI < 35.0%, moderate if 35.0% $\leqslant$ LI < 65.0% and high – LI $\geqslant$65.0%.
Results: Current study has shown the prevalence of ER+PR+ phenotype (54.0% of tumors), the presence of ER–PR– phenotype in 21% of cases, ER+PR– and ER–PR+ – in 14% and 11% of ovarian carcinomas, respectively. It also has been noted that ER and PR expression increased in OC patients of reproductive age compared to those during the period of menopause, decreased along with disease progression (i.e. 87.5% of I–II stage patients had ER+ and 75.0% – PR– phenotype unlike 66.1 and 67.9% in III–IV stage women, respectively). Moreover a tendency to reduction of ER and PR expression in patients with metastases compared to those without them has been observed. At the same time the loss of ER and PR expression along with an increase in tumor histologic grade has been detected: the majority of G1 tumors had high or moderate ER and PR expression (51.8±4.3% and 51.6±4.6% of cases, respectively) while most of G3 carcinomas had ER–PR– phenotype (31.6%) or low receptors expression. Kaplan-Meier data analysis showed better survival for ER+PR+ patients compared to women with other receptor phenotypes regardless of polychemiotherapy courses number.
Conclusion: Steroid hormones expression in ovarian neoplasias characterizes their biological and clinical peculiarities and can be used for more accurate prognosis of these pathological processes.