Ki 67 or Bax, Bcl-2 and the morphological growth pattern or patient clinical profile.
Conclusion: The histogenesis and morphogenesis of these neoplasms demonstrated wide spectrum of histologic features depends on their biologic behavior. Salivary gland neoplasms are clinically diverse group of neoplasms and the frequency of these neoplasm outcomes is probably not recognized when analyzing short term survival results in patients to whom the disease has a long natural history.

102 Large melanoma of skin: level of invasion or tumour volume what is superior?

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Background: The main prognostic factors for malignant melanoma are Breslow and Clark criteria, ulceration, growth patterns and localization of tumour [Balch, 2001; Cascinelli et al., 2009]. But, on the other hand, the exophytic nodular part of large melanoma often is ignored. Purpose: to access prognostic significance of nodular melanoma tumour burden in comparison with its Clark level of invasion.
Material and Methods: 107 patients of 28−70 years of age (M – 35, F – 72) with melanoma T4N0M0 were enrolled in the retrospective study. The tumour volume of exophytic nodular part of melanoma was calculated in vivo by formulas for spherical and hemispherical patterns after measurement of tumour's thickness and base. All patients underwent surgery – wide local excision of melanoma. Survival analysis estimated by using the Kaplan-Meier method and the log-rank test. Spearman and Kendall's correlation coefficients (τ) were used for comparison of prognostic signification between Clark's levels and tumour mass.
Results: The 5-year overall survival rates in 15 patients with nodular melanoma 5−10 mm of thickness (or tumour volume about 0.5 cm^3) were 86.6%; in 40 patients with nodular melanoma 11−20 mm (tumour volume 0.5−4.0 cm^3) − 52.5%; in 33 patients with nodular melanoma 21−30 mm (tumour volume 4.1–14.0 cm^3) − 36.4%; and nobody of 19 patients with tumour more than 31 mm thickness (>14.0 cm^3) lived out 5 years. Equation, which shows dependence of survival rate of patients on tumour volume, was made on the base of regressive analysis of received data. It estimates that in case of large melanoma tumour volume is significantly superior ($\tau = 0.67$) in prognosis of patients' overall survival than Clark's levels of invasion ($\tau = 0.10$).
Conclusion. The assessment of tumour volume in the nodular exophytic part of melanoma could be the additional diagnostic and prognostic criterion, which will determine the strategies of patient's treatment.

103 KRAS mutational spectra in routine diagnostic analysis of metastatic colorectal cancer

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Background: *KRAS* tumour mutational status is now widely recognized as a predictive biomarker in patients with colorectal cancer (CRC). Large clinical trials have shown that only CRCs with wild-type *KRAS* respond to epidermal growth factor receptor (EGFR) targeted antibody treatment. Seven different DNA base pair substitutions within codons 12 and 13, each leading to an amino acid substitution in the protein, are the most frequently observed genetic events within *KRAS* gene in CRC. Therefore, analysis of these hotspot clustered mutations is compulsory before treatment and for large routine diagnostic tests reliable frequency and types of *KRAS* mutations have yet to be established.
Material and Methods: Formalin-fixed paraffin-embedded tissue blocks were collected and DNA was extracted from tissue sections from 259 cases of metastatic CRC. Mutation analysis of *KRAS* codons 12 and 13 was performed by allele-specific real-time polymerase chain reaction.
Results: *KRAS* point mutations in codons 12 and 13 were present in 96 cases (37.07%) of 259 analyzed CRCs. All seven tested mutation types were observed; among them the frequencies of mutations in codon 12 were GAT (p.G12D, 11.58%), GTT (p.G12V, 10.42%), GCT (p.G12A, 4.25%), TGT (p.G12C, 3.47%), CGT (p.G12R, 1.16%), AGT (p.G12S, 1.16%) and the only one in codon 13 was GAC (p.G13D, 5.02%). Furthermore, the rate of transversions (52.08%) was found to be higher than the transitions' rate (47.92%). All the transitions were of the G>A type (the most prevalent alteration in our study) affecting the first base of codon 12 or predominantly the second base of both codons. Two types of transversions (G>T, G>C) occurred only in codon 12, mainly at the second base.
Conclusions: According to the previous studies G12V and G12R mutations may predispose to more aggressive biological behavior in advanced CRC. Though, G12D and G12S mutants have less aggressive transforming phenotypes. In addition, G>A nucleotide substitutions score the second place among the point mutations in human cancers in the Human Gene Mutational Database for all human somatic missense mutations and in our study they represent the most common alterations. Since the performed analysis detected all tested *KRAS* mutation types, which may have different impacts on the outcome of CRC patients, we want to emphasize as a conclusion the need for defining individual mutational spectra for developing therapeutic strategies targeting *KRAS* mutations in clinical practice.

104 HPV infection in epithelial ovarian cells of women at high risk of developing ovarian cancer

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Background: The causal role of high-risk (HR) HPV has been well established for cervical and other anogenital cancers but our understanding of the role of HPV in ovarian cancer etiology is controversial. Attempts to identify molecular risk factors for ovarian cancer in women at high risk of developing ovarian cancer which include family history of ovarian or/and breast cancer as well as personal history of breast cancer lead to the discovery that their ovarian epithelial cells are characterized by cross-linking-agent-induced chromosomal instability analogous to Fanconi Anemia phenotype and therefore can be susceptible to environmental risk factors including HPV infection.
The objective of the study is to investigate the frequency of HR HPV in women at high risk of developing ovarian cancer.
Materials and Methods: 20 ovarian samples were obtained from women undergoing risk reducing oophorectomy because of significantly elevated risk of developing ovarian cancer. The patients considered to be at high risk for ovarian cancer are defined as women with two or more first degree relatives with ovarian and/or breast cancer, or a personal history of breast cancer and a first-degree relative with breast and/or ovarian cancer. HPV testing was performed using polymerase chain reaction (PCR) with type-specific primers for E6 fragment of high-risk HPV type 16, 18 and 33. Real-time quantitative PCR was performed with ABI 7500 Fast Real-time PCR system and SYBR-Green master mix to calculate HPV copy number. Immunohistochemistry by using polyclonal anti-HPV 16 E6/18 E6 antibody (clone SC-460, Santa Cruz Biothechnology) to detect the E6 expression in the ovarian sections was performed..
Results: In the tissues derived from women at high risk of developing ovarian cancer, 30% of the samples were positive for HPV-16, 35% positive for HPV-18 and 10% positive for HPV-33. About 20% of the studied samples had a mixed infection. HPV copy number varied from 0.04 to 851 copies/reaction in HPV-16 positive samples and from 0.27 to 2793.51 copies/reaction in HPV-18 positive samples. By immunohistochemistry we determined that E6 HPV16/18 protein is expressed in follicular and surface ovarian epithelium. It is necessary to note that some vessel endothelium of the ovaries was focal positive for E6 protein.
Conclusion: Our study suggests that HR-HPVs ascending from the cervix to the ovaries might have a role in susceptibility of ovarian surface epithelium to neoplastic changes in women at high risk of developing ovarian cancer. Our broader goal is to define tools and methods to better understand the environmental risk factors that account for ovarian cancer risk and to translate these mechanisms into strategies for early ovarian cancer prevention.

105 Role of IL-1RN VNTR polymorphism in host immune susceptibility to viral associated neoplasias

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Background: A common 86bp VNTR polymorphism within intron 2 of the IL-1 receptor antagonist (IL-1RN) gene seems to be associated with the balance between host immunity and viral infections. Several authors have referred that the Il-1RN A2 allele is responsible for shorter immune responses to viral infections and therefore might be associated with increased risk of viral associated cancers development.
Methods: We have developed a cross-sectional study to analyse the role of this 86bp VNTR polymorphism on the development of viral associated neoplasias: cervical and nasopharyngeal carcinoma. Genotyping of Il-1RN VNTR polymorphism was performed by PCR in DNA extracted from peripheral blood samples from both healthy individuals (n = 446), individuals with cervical lesions (n = 346) and nasopharyngeal carcinoma (n = 122) from the Northern Region of Portugal.
Results: Our study revealed that the IL-1RN A2 allele was significantly increased in both patients with cervical and nasopharyngeal carcinoma when compared with healthy individuals. Statistical analysis revealed that it is associated with increased risk for both invasive cervical cancer ($p = 0.027$; OR = 1.84) and undifferentiated type of nasopharyngeal carcinoma ($p < 0.001$; OR = 3.73).