

**CONCLUSIONS:** Diffuse full thickness p16 expression in lesion with high and intermediate-risk HPVs appears a good marker of persistent high risk HPV infection and might be useful to discriminate in equivocal cases HSIL from LSIL and to select LSIL with higher risk of neoplastic progression.

#### P 747

##### **KI-67 EXPRESSION IN THE INVASION FRONT AS AN ADDITIONAL INDEPENDENT SIGNIFICANT PROGNOSTIC FACTOR INFLUENCING RECCURENCE IN EARLY STAGE CERVICAL CARCINOMAS**

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**INTRODUCTION:** The attempts to determine the prognostic significance of biological markers and their relation to human papillomavirus (HPV) infection in cervical cancer have yielded controversial results.

**AIMS:** The aims of this retrospective study were to correlate alterations of cell proliferation, growth, differentiation and apoptosis regulatory proteins in early stage cervical carcinomas with HPV infection, histopathological and clinical parameters, and to estimate their prognostic significance.

**METHODS:** Expression of Ki-67, p53, mdm-2, bcl-2, c-erbB-2, EGFR protein, as well as estrogen and progesterone receptors was evaluated by immunohistochemistry in operative specimens of 83 patients with early stage cervical carcinoma. The results were assessed semiquantitatively in the surface area, center and invasion front of each tumor as a percentage of the immunostained cells and/or intensity of immunostaining for each protein. The presence of HPV was assessed by conventional in situ hybridization (ISH) technique and catalyzed reporter deposition signal amplification ISH using mixed biotinylated probes to identify types 6/11, 16/18 and 31/33 or 31/33/51.

**RESULTS:** In our case series 73 patients had a tumor limited to the uterine cervix less than 4 cm in diameter (pT1b1), while 10 patients had larger neoplasms belonging to pT1b2 category. Pelvic lymph node involvement was found in 20 patients. During the follow-up period (range, 65 -181, mean, 121 months) recurrences were observed in 9 patients. The 5, 10 and 15-year disease-free survival rate was 92.7%, 90.8% and 86.6%, respectively. Among the 18 variables pelvic lymph node involvement ( $P=0.0008$ ), tumor diameter ( $P=0.035$ ), depth of stromal invasion ( $P=0.029$ ), histotype ( $P=0.0009$ ), grade ( $P=0.056$ ), HPV DNA presence ( $P=0.056$ ), HPV type ( $P=0.043$ ), as well as bcl-2 ( $P=0.035$ ), mdm-2 ( $P=0.051$ ), EGFR ( $P<0.0001$ ), and Ki-67 ( $P=0.031$ ) expression in the tumor's invasion front were identified as important predictive indicators of recurrence in the univariate analysis. Independent significant prognostic factors for disease-free survival in multivariate analysis were the histotype, HPV DNA presence and Ki-67 expression.

**CONCLUSIONS:** The invasive front of carcinomas proved to be the most important area for tumor prognosis. In addition to the detection of HPV presence and morphological parameters, Ki-67 evaluation could be used in selecting appropriate therapeutical approaches in patients with early stage cervical cancer.

#### P 748

##### **HUMAN PAPILLOMA VIRUSES DO NOT PLAY AN AETIOLOGICAL ROLE IN ADENOSARCOMAS OF THE UTERINE CERVIX**

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Primary adenosarcomas of the uterine cervix are exceedingly uncommon neoplasms. Although high-risk human papilloma virus (HPV) types have been linked to cervical carcinosarcomas, with demonstration of integrated virus in the nuclei of the malignant epithelial and sarcomatoid components, their role in the histogenesis of adenosarcomas is unclear. The aim of this study was to determine if HPVs play an aetiological role in cervical adenosarcomas. The HPV status of 7 adenosarcomas of the cervix was investigated by non-isotopic in situ hybridisation (NISH) and polymerase chain reaction (PCR). NISH was carried out using digoxigenin labelled probes to HPV types 6, 11, 16, 18, 31 and 33. PCR employed GP5+/GP6+ primers to the HPV L1 gene. Neither the benign epithelial components nor the malignant stromal components of the 7 neoplasms harboured nuclear NISH signals for the HPV types investigated. Amplimers of the HPV L1 gene could also not be detected by PCR in any of the tumours studied. HPVs do not appear to play an aetiological role in the pathogenesis of uterine cervical adenosarcomas. This suggests that a different histogenetic pathway for this rare tumour type must exist.

#### P 749

##### **THE USEFULNESS OF HYBRID CAPTURE II (HC2) AS SCREENING OPTION IN LOW-RESOURCE SETTINGS OF LATIN AMERICA.**

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**Objective:** Hybrid Capture II (HC2) to detect high-risk HPV (hr-HPV) in our ongoing multi-centre trial was performed and compared to other optional testing screening tools [cytology (conventional and liquid-based {LBC}), screening colposcopy, Visual Inspection with acetic acid (VIA), Visual Inspection with Lugol's Iodine (VILI): conventional and self-sampling], for cervical cancer in Brazil and Argentina, in order to test the potential use of HC2 as a primary option for cervical screening. **Purpose:** A cohort of 12,107 women attending four clinics (Campinas, São Paulo, Porto Alegre, and Buenos Aires) are randomised into the 8 diagnostic arms. Women testing positive with any of the tests are referred for colposcopy, and cervical biopsies are used as the gold standard to assess performance characteristics (SE, SP, PPV, NPV, ROC) of the HC2 test. **Methods:** All cases with cytological abnormalities were referred to colposcopy and biopsies were taken according clinical evaluation. The HC2 protocol was performed according to the instructions of the manufacturer (Digene Co., Gaithersburg, MD, USA). In estimation of the viral load, samples with relative light units