standard CCR with weekly Cisplatin plus 3D conformal pelvic radiotherapy followed by brachytherapy (BT) and group B (received the standard CCR and BT). The primary end point: the assessment of response rate and local control. The secondary end points: assessment of the 2 years overall survival (OS) and progression free survival (PFS).

Results The median age was 54 years old and a range of 44 years old with a performance status (0, 1). The majority of patients had squamous cell carcinoma (88.24% group A vs. 94.12% group B) and most of the patients were FIGO stage IIIC, IVA and IIB (41.18%, 32.35% and 20.59% in group A vs. 32.35%, 17.65% and 17.65% in group B respectively). CT abdomen and pelvis done at time of diagnosis showed pathological enlarged lymph nodes in 64.71% and 58.82% of patients in group A and B respectively. After NAC, 97.06% of the patients achieved partial response with a reduction of tumor volume by 76.07% and only 2.94% had stable disease. Higher partial response in groups A (55.88% in group A vs. 32.35% in group B, p value 0.151) and higher overall response rate (ORR) in group A (79.41% vs.70.59%) while local control was higher in group B (91.18% vs. 97.06%, p value 0.614). The 2 years PFS was 91% in group A and 97.1% in group B and OS of 100% as all the patients remain alive till the end of the 2 years follow up.

Conclusion The addition of NAC to the standard CCR achieved a higher partial response rate and ORR with a reasonable local control of the disease. This can facilitate the CCR plane and subsequently the brachytherapy planning parameters in locally advanced cases with no inferiority of the PFS and OS compared to the standard.

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378 MUCOADHESIVE BILAYER VAGINAL TABLET AS A POTENTIAL ADJUVANT TREATMENT FOR CERVICAL CANCER

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Introduction/Background Cervical cancer (CC) is described as cancer that occurs in the cells located in the cervix. Each year, more than 500,000 women are diagnosed with CC and the disease results in over 300,000 deaths across the world. Infection by high-risk oncogenic subtypes of human papillomavirus (HPV); HPV16 and HPV18, is the cause for almost all cases of CC. In developed countries, CC incidence and mortality have more than halved over the past 30 years as they were able to establish successful national HPV screening and vaccination programs. However, this disease remains persistent and has become one of the leading causes of death among women in developing (low to middle-income) countries; mostly in African countries. Adapting to low resources, developing countries have practiced a feasible and cost-effective solutions with the screen and treat approach instead. Screening usually involves visual inspection with acetic acid (VIA) or Lugol’s iodine (VILI) that gives immediate results, facilitating instantaneous treatment strategies and prevents loss to follow-up. Treatments include loop electrosurgical excision procedure (LEEP), cryotherapy or cold-knife conization. This research proposes the development of a self-administered chemotherapeutic vaginal tablet formulation that would complement these current treatment strategies.

Methodology The bilayer tablets were prepared one layer at a time, using a single punch direct compression machine. Tablets were then evaluated using the pharmacopeial guideline that include tablet uniformity, hardness, friability and content uniformity. Swelling test was performed by simple immersion of the tablets in dissolution medium for 24 hours, the tablet’s weight before and after were recorded. The drug release profile was evaluated in vitro drug dissolution test using the USP paddle method in 2% aqueous sodium dodecyl sulphate (SDS) solution; maintained at 100rpm, 37±1°C and in sink conditions. All samples were measured spectroscopically. Cell viability after treatment with the drugs was determined using the MTT assay on Ca-ski cells.

Results Results showed that the tablet of this combination are uniform and durable in compliance to pharmacopeial standards, a swelling study shows promising potential for mucoadhesion and has an extended in vitro drug release profile over 72 hours. In vitro cell culture with Ca-Ski cells however, did not show a synergistic effect but only a small additive effect was observed.

Conclusion A vaginal tablet offers an easy application and direct localized access to the cervix; adjacent to the cancerous tissue. The advantages of vaginal drug delivery include (i) bypassing hepatic first pass-effect; (ii) low systemic drug exposure; and (iii) higher bioavailability. A bilayer tablet provides an opportunity to deliver two active pharmaceutical ingredients (API) simultaneously for a synergistic pharmacological effect. Additionally, the different layers physically avoid chemical incompatibilities. Chitosan and polyacrylic acid are the polymers employed for their mucoadhesive property. These polymers also provide an extended and a controlled drug release rate.

5-fluorouracil (5FU) a drug developed and used for the treatment of cancer for more than 50 years was selected as the primary API. Cell studies showed the first combination formulated; 5FU and disulfiram did not show a synergistic effect. Other API will be investigated in combination with 5FU in order to achieve the synergistic effect desired.

Disclosures The authors declare no conflict of interests.

383 CHANGES IN THE PROTEOME OF CERVICOVAGINAL FLUID DURING HPV INFECTION IN HPV-VACCINATED WOMEN

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Methodology This study was approved by the Institute Research Medical Ethics Committee. The study involved 62 patients vaccinated against HPV, aged 19 to 45 years. The
patients were divided into 2 groups: group 1 - HPV-positive (n = 14) and group 2 - HPV-negative (n = 48). CVF proteomic analysis was carried out by the bottom-up method (HPLC-MS/MS) on an Agilent 1100/7 TI LTQ-FT Ultra mass spectrometer (Thermo Electron, Germany). The search for protein identification and semiquantitative analysis was carried out against the UniProt Knowledgebase (UniProtKB, version 16.05.2014) using the MaxQuant software, version 1.1.1.2.

Results None of the vaccinated women showed cervical pathology by cytology. In 6 cases, a biopsy of the cervix was performed in the presence of HPV carcinogenic risk together with mild changes in the cervix epithelium during colposcopy. The histological diagnosis in all cases (n = 6) corresponded to CIN1.

In total, more than 419 different proteins were detected in CVF samples. The level of 34 CVF proteins were significantly different in HPV positive group compared to HPV negative patients (p<0.05). Among them, 9 proteins were involved in the innate immunity processes (APOB, FABP5, GRN, HP, MUC5AC, OLFM4, PKPI, QSOX1, S100A8). The level of 34 CVF proteins were significantly different in HPV positive group compared to HPV negative patients (p<0.05). Among them, 9 proteins were involved in the innate immunity processes (APOB, FABP5, GRN, HP, MUC5AC, OLFM4, PKPI, QSOX1, S100A8). The level of 34 CVF proteins were significantly different in HPV positive group compared to HPV negative patients (p<0.05). Among them, 9 proteins were involved in the innate immunity processes (APOB, FABP5, GRN, HP, MUC5AC, OLFM4, PKPI, QSOX1, S100A8).

Conclusion A high incidence of HPV was revealed in Russian women previously vaccinated against HPV (23%). CIN 1 was detected in 6 HPV-positive vaccinated women (43%) with normal cytology (NILM). Proteomic analysis of CVF can be proposed as a non-invasive method for detecting biomarkers for early diagnosis of CIN. This work was supported by RSF grant No. 18-75-10097.

Disclosures Nothing to disclose.

426  THE ROLE OF Ki-67, P16 AND BCL-2 IN THE MANAGEMENT OF CERVICAL NEOPLASIA

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Introduction/Background Cervical cancer, a common gynaecological tumor, has a high mortality and it seriously threatens the health of the women. The biomarkers of cell proliferation and apoptosis indicate the early carcinogenesis and are useful for future patient monitoring. HPV persistent infection causes overexpression of P16, but this could be also in normal tissue. P16 is important and useful for cervical cancer screening, but combined with another biomarker - Ki-67, which is a marker of cell proliferation. In normal tissues, the simultaneous expression of P16 and Ki-67 is less likely to occur. Bcl-2 is an intracellular membrane protein which prevents apoptotic cell death and it can be used as a biomarker, too.

Methodology We selected a number of 40 paraffin embedded specimens of cervical tissue from patients diagnosed with cervical pathology, who were admitted in our department from 1st of January 2018 till 31th of December 2019. The specimens groups were formed by L-SIL (10), H-SIL (10), squamous cervical carcinoma – SCC (10) and nontumoral cervical tissue (10) as control group. For all the specimens were performed the histopathological exam and the immunohistochemistry for Ki-67, P16 protein and Bcl-2 protein. Expression of Ki 67, P16 protein and Bcl-2 was detected and the diagnostic values were analyzed.

Results Positive rates of Ki 67 and P16 expression in H-SIL and SCC groups were significantly higher than those in L-SIL and control group. In our study the expression’s intensity of P16 and Ki-67 was positively correlated with the degree of cervical lesions. The immunostaining for Bcl-2 is highly expressed in cervical cancer tissue, compared with nontumoral cervical tissue. The difference is not well expressed compared to H-SIL and L-SIL.

Conclusion Cervical cancer is the malignant tumor with a known etiology, so that prophylactic measures could be taken. The combination of P16 and Ki-67 can identify patients with high risk of SCC and reduce the rate of misdiagnosis. This is of high value for the differential diagnosis between SCC and H-SIL. Bcl-2 is an important regulator of apoptosis. The relationships of tumor genesis with anti-apoptotic genes and pro-apoptotic genes have been confirmed. Combined with other biomarkers, Bcl-2 could be usefull in assessing the patients’ prognosis.

Disclosures I have nothing to disclose.

430  PREOPERATIVE MEASUREMENT OF TUMOR VOLUME IN EARLY CYSTIC CANCER. IS IT RELIABLE?

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Introduction/Background Maximum diameter-based tumour measurement is the standard method to asses tumour size and staging pre and postoperatively. Traditionally, clinically estimation of tumour size was the preferred preoperative measuring tool.

Nowadays, thanks to the availability of advanced imaging techniques, preoperative staging could be done more precisely. Several studies have analysed the correlation between the tumour size measured with MRI and ultrasound and final pathology findings.

In this study we analyse not only the correlation of diameter-based tumour size, but also the correlation of tumour volume estimation.

Methodology A secondary analysis of the SUCCOR study was performed (European patients with FIGO 2009 stage IB1 cervical cancer that underwent radical hysterectomy from January 1st, 2013 to December 31st, 2014). Patients with previous conization were excluded. Patients with at least 3 different tumour measurements both in MRI or ultrasound and in the final pathology report were included. The 3 diameters measured to calculate the volume were defined as: cranio-caudal diameter (dc); anteroposterior diameter (dap) and the largest lateral diameter (dl).

Tumour volume estimation was calculated using the ellipsoid formula (V = dcc x dap x dl x π/6). Intraclass Correlation Coefficient (ICC) was applied to study the correlation of diameter-based tumour size and volume tumour estimation between MRI and pathology report and Ultrasound and pathology report.

Results 693 patients were included in the final analysis of SUCCOR study. 137 of them had both preoperative MRI with 3 different measures (Anteroposterior, Cranio-caudal and largest lateral diameter) and pathology report. 81 patients had the 3 diameters measured preoperatively by ultrasound.

When performing a preoperative MRI, the ICC between MRI and final pathology for maximum diameter size was 0.71 (0.61–0.78) and for tumour volume 0.53 (0.38–0.64).