EUROGIN 2022 ABSTRACTS

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#3690

P13-01 Human papillomavirus genotype specific concordance between physician-taken and self-collected cervical samples

13 - Self-sampling

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Background/Objectives: Human papillomavirus (HPV) self-sampling does increase participation in cervical cancer screening among unscreened or under-screened women and HPV genotype specific guidelines improve clinical management of high-risk (hr) HPV-positive women. We have demonstrated earlier good concordance for hr HPV DNA detection between self-collected and cervical samples collected by physician, but comparative data on HPV-genotype specific concordance between different self-collection methods is limited. Our study aim to 1) Assess the positivity rate for selected HPV-genotypes separately and in combination (HPV-genotypes grouped as 2 v", "4 v" and "9 v" based on HPV types targeted by prophylactic vaccines and the combined carcinogenic HPV types which excluded carcinogenic HPVs targeted by 2 v or 4 v and 9 v vaccines).2) Evaluate concordance in detecting HPV genotypes and in combination between self-taken and physician-taken samples using two sampling devices.

Methods: Study participants were recruited from the treatment units for premalignant lesions and cancer care units. Each participant collected at home the day before their appointment at the hospital two cervicovaginal specimens using a brush (Evalyn®Brush) and a swab (FLOQSwabsTM). Before the treatment, a physician took a cervical specimen using a brush, into PreservCyt® buffer for HPV testing. All specimens were tested using AnyplexTM II HPV28. We estimated HPV-genotype specific and combined positivity rate for each sampling method. Cohen's kappa (κ) was used to measure agreement of self- and physician-collected specimen regarding positivity to HPV-genotypes alone and combined. 95% confidence intervals (CI) were estimated using the bootstrap method provided in an ado file, kapci, written by Michael E. Reichenheim using Stata (version 15.0 StataCorp, College Station, TX, USA).

Results: 251 women were included in the final analysis. 43 women with normal or CIN1 diagnosis, 160 with CIN2+ diagnosis, 48 with cancer diagnosis. Of 48 histologically confirmed cervical cancers, 30 were squamous cell carcinomas,16 adenocarcinomas and 2 of other type. The overall HR HPV positive rate was 89.2%, 89.6% and 81.6% seperately for Physician sapmle, Evalyn Brush and FLOQSwab. The overall HR HPV, 2-valent vaccine types, 9-valent vaccine types, Non 2-valent HR HPV types and non 9-valent HR HPV types positive rate was 89.2%, 55.4%, 80.9%, 33.9%, 8.4% respectively. The kappa value for Evalyn brush on HPV16, HPV18, HPV31, HPV33, HPV52, any HR HPV type, 2-valent vaccine types, 9-valent vaccine types, non 2-valent vaccine HR types, non 9-valent vaccine HR types was 0.85, 0.81, 0.90, 0.94, 0.79, 0.81, 0.78, 0.80, 0.80 respectively. The kappa value for FLOQswab on HPV16, HPV18, HPV31, HPV33, HPV52, any HR HPV type, 2-valent vaccine types, 9-valent vaccine types, non 2-valent vaccine HR types, non 9-valent vaccine HR types was 0.74, 0.72, 0.90, 0.86, 0.62, 0.67, 0.61, 0.69, 0.60 respectively.

Conclusions: 1.Specimens collected by different sampling methods resulted in comparable positivity rates in detecting HPV genotypes alone and in combination; 2.Compared to swab-based devise, brush-based device has higher concordance with physician taken specimens for individual HPV and for HPV genotypes combined compared to swab based devise 3.Self-sampling can be used for detecting HPV genotypes, but device specific differences exist.

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#3711

P14-01 Optimization of an NGS-based HPV-14 protocol

14 - Genotyping

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Background/Objectives: High analytical sensitivity and specificity of the HPV assay is important for epidemiological research and vaccine surveillance. HPV genotyping is also increasingly used for clinical purposes and a better understanding in terms of risk management is warranted. HPV detection and genotyping can be done precisely, efficiently and with high resolution by next generation sequencing (NGS). The aim of this study was to optimize an NGS-based genotyping protocol previously developed in our laboratory.

Methods: Material used in optimization studies included HPV-positive cell lines, WHO international standards, in-house plasmids for 37 genotypes harbouring HPV L1 sequences, as well as material from the Equalis proficiency panel. The in-house WHO validated PCR-based Luminex hybridization assay, Anyplex II HPV28 (Seegene) and in-house E6/E7 type-specific PCR were included as comparable methods. The first step of the NGS workflow, equal to the Luminex assay, is the amplification of an L1 gene fragment with modified general primers (MGP), followed by an index PCR. The performance of different DNA polymerases was assessed. Samples were pooled and quantified prior to sequencing, which was conducted on an Illumina MiSeq platform generating 2x151bp paired-end reads. The obtained data was analysed with an in-house genotyping pipeline combining Cutadapt to remove adapters, primer sequences, and low-quality bases, and Bowtie2 for aligning reads to HPV reference genomes retrieved from the PaVE database. featureCounts function was used for counting the mapped reads.

Results: The presented NGS method is time and cost-efficient and shows high-quality results for the identification of single HPV types, with identical sensitivity as Luminex in dilution series. For samples containing multiple HPV types however, some inconsistency in type identifications was observed, likely associated with stochasticity in PCR target hybridization. To address positive/negative HPV type classifications, several cutoff parameters were applied. Due to variation in amplification efficiency for the different HPV types, implementation of individual HPV type-specific cutoffs is highly considered.

Conclusions: Method optimization has initially been performed on plasmids and cell lines and showed consistent results for samples containing one HPV type. Further improvement is needed for multiple genotype identifications and optimization with emulsion PCR is planned. For confirmation of performance and for further validation, we are currently in an application process for the use of clinical diagnostic biobank material. Results and findings including clinical material will be presented.

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#3715

P30-01 Long-term survival and recurrence in oropharyngeal squamous cell carcinoma in relation to subsites, HPV, and P16-status

30 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Long-term survival data in relation to subsites, human papillomavirus (HPV), and p16INK4a (p16) for patients with oropharyngeal squamous cell carcinoma (OPSCC) is still sparsely studied. P16 alone may be suboptimal surrogate marker for assessing an active HPV infection in tumour tissue. It has been suggested that p16- in combination with HPV DNA-status could predict clinical outcome better than p16 alone in OPSCC. Furthermore, reports have indicated atypical and late recurrences for patients with HPV and p16 positive OPSCC. Therefore, we assessed long-term survival and recurrence in relation to oropharyngeal subsite and HPV/p16-status.

Methods: A total of 529 patients with OPSCC, diagnosed in the period 2000-2010 in Stockholm and Gotland Region, treated with curative intent, with known HPV DNA- and p16-status, were included. HPV/p16-status and subsites were correlated to disease-free and overall survival (DFS and OS respectively).

Results: The overexpression of p16 (p16+) is associated with significantly better long-term DFS and OS in tonsillar and base of tongue squamous cell carcinomas (TSCC/BOTSCC), but not in patients with other OPSCC. Patients with HPVDNA+/p16+TSCC/BOTSCC presented better DFS and OS compared to those with HPVDNA-/p16- tumours, while those with HPVDNA-/p16+ cancer had an intermediate survival. Late recurrences were rare, and significantly more frequent in patients with p16- tumours and other OPSCC, while the prognosis after relapse was poor independent of HPVDNA+/-/p16+/- status and OPSCC subsite.

Conclusions: In conclusion, patients with p16+ OPSCC do not have more late recurrences than p16-, and a clear prognostic value of p16+ was only observed in TSCC/BOTSCC. Finally, the combination of HPVDNA and p16 provided superior prognostic information compared to p16 alone in TSCC/BOTSCC.

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#3718

P13-04 First-void urine and vaginal 13 In cervical cancer screening: feedback from a colposcopy referral population

13 - Self-sampling

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Background/Objectives: Cervical cancer (CC) is the seventh most common cancer in Europe. Almost all cases (99%) of CC are caused by oncogenic infections with high-risk human papillomavirus (hrHPV) strains. Many efforts have been made in several countries on hrHPV CC-related screening programs, although there is a great disparity between high- and low-income countries. First-void urine (FVU) is being more often positioned as the golden sample for HPV detection because it is non-invasive, has the ability to reach non-attendees of screening programs, and can overcome cultural barriers. The aim of the study was to evaluate sample preference as part of several studies in a colposcopy referral population.

Methods: Questionnaire data from the Predictors 5.1 study (United Kingdom)1, the VALHUDES study (Belgium, NCT03064087)2 and the Cocoss trial (Germany)3 were analyzed. The main goal of all studies was to investigate the clinical accuracy of hrHPV testing on FVU (Colli-Pee®) and vaginal self-sample (VSS) in a colposcopy referral populations. All participants were asked to fill out a questionnaire on their general experience and convenience on all different sampling methods. For comparison matters, only dry vaginal SS were compared between studies. Data are presented as mean ± SEM.

Results: In total, 1034 women aged 21 - 76 years consented their participation and provided all sample types. Self-collection was well accepted, with 48±4% of women indicating a preference for FVU over 39±4% who preferred a vaginal SS. On average, 77±9% of women indicated that FVU was "very easy to use" compared to 73±9% for VSS, and 76±8% and 60±1% of women indicated that they were confident that samples were taken correctly for FVU and VSS, respectively.

Conclusions: Here, we show that the majority of women enrolled in several European triage population preferred FVU over a vaginal SS, found that FVU was more easy-to-use and that they were confident that samples were taken correctly. This outcome highlights the potential of FVU to become the golden sample for detection of HPV infection and offers future perspective to screen non-attendees in low-income countries and regions where VSS is less well accepted.

References: 1Cadman, L., et. al., Cancer Epidemiology and Prevention Biomarkers (2021) 2De Pauw, H., et. al., Archives of Public Health (2021) 3Ertik, F. C., et. al., International journal of environmental research and public health (2021)

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#3722

P13-05 Home-based 13 of first-void urine for HR9 in cervical cancer screening: usability feedback from a Belgian colposcopy referral population

13 - Self-sampling

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Background/Objectives: Cervical cancer (CC) is the seventh most common cancer in Europe with 99% of cases caused by oncogenic infections with high-risk human papillomavirus (hrHPV) strains. Women with socio-economical disadvantages and lower education are often under-screened and hard-to-reach leading to an increased risk of developing CC. Successful CC screening programs strongly depend on the participation of the target population. Various barriers are known to contribute to lower participation such as physical discomfort, poor access to health services, time constraints and lack of knowledge. Here we report interim usability feedback results from the CASUS study (NCT04530201, Belgium) using first-void urine (FVU) as a liquid biopsy.

Methods: Women were asked to self-collect two FVU samples at home with the Colli-Pee® Small Volumes (10mL) variant (Novosanis, Belgium), prefilled with a non-toxic nucleic acid preservative the day prior to their colposcopy appointment. Afterwards, women completed a questionnaire indicating their usability feedback of the Colli-Pee® Small Volumes urine self-sampler. A specific Systems Usability Scale (SUS) score was incorporated in the questionnaires. A SUS score greater than 68 is considered good. Data are presented in relative percentages and as mean ± SEM.

Results: Up until the beginning of September 2021, a total of 280 women (25-64y) were enrolled and consented their participation in the CASUS study. The interim analysis includes data of 204 questionnaires with 197 valid SUS scores. Overall, 57% of women indicated to prefer FVU self-sampling over a physician taken PAP smear (37%) for their next CC screening. Additionally, 61% women indicated to prefer the use of Colli-Pee® Small Volumes over a urine cup whereby 95% of women experienced Colli-Pee® Small Volumes as easy to use and 97% who would use the device again. An average SUS score of 85.49 ± 15.60 was calculated.

Conclusions: The results of this study show that the majority of women would prefer a urine self-sample at home over a physician-taken PAP smear for their next CC screening. Moreover, Colli-Pee® Small Volumes was considered an easy-to-use and well-accepted self-sampling device for CC screening in a Belgian colposcopy referral population. From a future perspective, these results highlight the possibility of home-based urine self-sampling as a liquid biopsy in CC screening where hard-to-reach populations could be approached more easily.

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#3731

P13-06 Impact of vaginal self-samples resuspension volume on Human Papillomavirus (HPV) testing

13 - Self-sampling

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Background/Objectives: Validation of Human Papillomavirus (HPV) testing in combination with self-collection devices offers the possibility to improve cervical cancer (CC) screening coverage rates reaching women who do not attend screening programs. Moreover, the possibility of performing HPV testing on vaginal self-samples eluted in alternative media and resuspension volumes as compared to the methanol-based media, presently used routinely to perform cervical cytology (Pap Test) for the triage of women HPV-positive, may further reduce screening costs. This ongoing study aims to evaluate the performance of HPV detection on self-collected vaginal samples resuspended in two different non-alcohol-based media, eNat® and MSwab® (Copan), using two different resuspension volumes (2 ml and 5 ml).

Methods: Two self-collected vaginal samples (FLOQSwab®, Copan) and a clinician-taken cervical specimen (L-Shaped FLOQSwab®, Copan) were collected from 17 women referred to colposcopy at San Gerardo Hospital, ASST Monza. Cervical swabs were resuspended in 20 ml of ThinPrep®PreservCyt® (Hologic®), while vaginal samples were transported dry to the laboratory. In the laboratory, vaginal samples from 10 women were resuspended in 2 ml and 5 ml of eNat® respectively; vaginal samples from the remaining 7 women in 2 ml and 5 ml of MSwab®. Nucleic acids were extracted from 200 µL using Microlab Nimbus platform (Seegene) and HPV detection carried out with AnyplexTMII HR-HPV real-time assay (Seegene). HPV test results obtained from the 2 vaginal specimens/woman were then compared to those obtained from the cervical sample.

Results: Preliminary results showed HR-HPV positivity rates of 70.6% (12/17), 76.5% (13/17) and 64.7% (11/17) of women respectively in cervical swabs, vaginal self-samples resuspended in 2 ml and in 5 ml. Independently from the suspension medium used, the overall agreement rate between cervical and vaginal specimens resuspended in a volume of 2 ml was 94.12% (16/17), while the percentage of agreement between cervical and vaginal swabs resuspended in 5 ml was 82.35% (14/17).

Conclusions: These preliminary data demonstrated a good agreement in HPV detection between cervical and vaginal self-collected samples independently from the resuspension medium and/or volume used, supporting the possibility of introducing alternative safer and more cost-effective media for the implementation of vaginal self-sampling in CC screening programs. Studies on a larger set of samples could confirm these findings.

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#3753

P18-01 A biomarker panel from genome-wide 18 to predict early oropharyngeal cancer

18 - Methylation

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Background/Objectives: As oropharyngeal cancer (OPC) associated with human papillomavirus (HPV) increases in men, the need for a screening test to diagnose OPC early is crucial. Prognosis is favorable though recurrence is likely and metastatic OPC is often incurable regardless of HPV status. We previously reported that methylation of the host tumor suppressor gene, EPB41L3, and the HPV16 genome assessed from oral gargles in pretreatment, male OPC cases (n=228) was significantly ($p<0.0001$) higher among cases compared to controls and predicted cases with an AUC of 0.82. However, prediction in early OPC cases alone (T1-T2, N0-N1; small tumors with a single ipsilateral node <3cm)was lower (AUC=0.78), indicating the need for additional biomarkers to improve screening performance.

Methods: Therefore, this study agnostically identified oral cell CpG sites differentially methylated among early OPC cases. DNA was extracted from oral gargles of 228 OPC cases (92 early cases) and 142 frequency matched healthy controls and processed for genome-wide methylation using the MethylationEPIC BeadChip (Illumina) array. Ten fold cross validation was used to independently compare detection at individual CpG sites and select sites for modeling. Selected sites were combined with our prior methylation data, which included three CpG sites (438, 427 and 425) in the EPB41L3 gene. Due to strong association with cancer, oral HPV16 status was considered as a binary variable (positive/negative). Lasso regression identified CpG sites strongly associated with early OPC. Receiver operator characteristic (ROC) curves with area under the curve (AUC) and optimized sensitivity and specificity cut points were generated. As a final step, the panel was validated utilizing bootstrap re-sampling.

Results: Analyses revealed 14 markers significantly associated with early OPC, including one EPB41L3 CpG site (438) and oral HPV16 status. Together this panel trained the model and was able to predict early OPC compared to controls with an AUC of 0.970. In the bootstrap validation set, the AUC was 0.930, indicating adequate internal validity. OPC, a still rare event, requires high specificity from a biomarker panel to minimize identification of false positives. A specificity of 99.1% was achieved with a sensitivity of 70.1%. Allowing specificity to drop to 98.1% resulted in a substantial gain in sensitivity to 78.0%.

Conclusions: Our data suggest this panel can detect OPC early. Internal validation showed high predictability, however external validation of this panel is needed. A panel of biomarkers to diagnose OPC earlier is needed to prevent complex treatment of OPC and associated co-morbidities, while reducing risk of recurrence.

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#3772

P26-01 Cervical cancer diagnosed after the detection of protein P16 in an iliac adenopathy

26 - Cervical neoplasia

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Background/Objectives: The p16 protein is overexpressed in HPV-associated tumours and there appears to be a higher expression in more severe lesions. We report a case of cervical cancer suspected after the biopsy of an iliac adenopathy which was positive for p16.

Methods: Case report based on the information collected from the clinical records of the patient.

Results: A 44-year-old woman went to the emergency room with asthenia, anorexia, weight loss and fever. The patient mentioned these symptoms had begun a month prior. She denied gynecological symptoms. On physical examination she had multiple inguinal adenopathies and one supraclavicular. A computerized tomography was performed and detected multiple peri-aortic and iliac adenophaties. A biopsy of an iliac adenopathy revealed a squamous cell carcinoma which was strongly positive for p16, suggesting the primary origin of the metastasis to be a cervical cancer. The gynecological observation showed an apparently normal cervix and the gynecologic ultrasound was normal. The cytology revealed a HSIL. Colposcopy showed in the posterior lip a red lesion with irregular margins, areas of ulceration and exophytic lesions with atypical vascularization, that stained with acetic acid. Biopsies of the lesion confirmed the suspicion of a cervical cancer. Although the supraclavicular adenopathy was palpable, it did not show on the PET scan. The patient is currently under chemoradiotherapy.

Conclusions: p16 immunostaining can be an important aid in determining the probable primary tumour site in the context of metastatic squamous cell carcinoma. When positive, and in the appropriate clinical and imagiological context, it should raise the suspicion of a cervical primary.

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#3776

P10-02 Cervical cancer screening: preliminary results of 22 aces in the region of Lisbon and Tejo valley

10 - HPV screening

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Background/Objectives: The implementation of organized screening programs would allow early diagnosis. Abnormalities found on screening need follow-up, diagnosis and treatment, to prevent the development of cancer or to treat cancer at an early stage. Despite the high coverage of HPV vaccines in Portugal, introduced in 2008 in the National Immunization Plan for girls and more recently (2020) for boys, an organized screening based on the HPV test was implemented for cervical cancer at the national level. AIM We intend to verify the prevalence of HPV HR types in the first organized screening program in the region of Lisbon and Tejo Valley.

Methods: A total of 7793 women (age range 29-66 years) were screened with HPV HR test as the main method for cervical cancer screening, between December 2018 and August 2021. Samples were collected from 22 ACES (Public Health Centers). Clinical algorithms refer all HPV16 or HPV18 positive women for colposcopy and all samples with other HR HPV types were forwarded to cytological evaluation, owing to the type of cell abnormalities women could be referred for colposcopy.

Results: The percentage of women negative for HPV HR types is 88,49% (n=6897) while women positive for at least one HR HRV type is 11,02% (n=859). 20,37%. The number of women that test positive for HPV16 and/or HPV18 is 175 (20.37%) and positive for others HR HPVs types (HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV59, HPV66, HPV68) is 684 (79,63%). As expected HPV infection tends to decrease with age. Women with HR HPVs who underwent reflex cytology, 55,26% (n=205) were negative, 21,58 (n=80) had ASCUS, 2,96% (n=11) ASC-H, 0,81% (n=3) AGC, 15,90% (n=59) LSIL, 3,23% (n=12) HSIL and 0,27% (n=1) CPC. In terms of HPV prevalence, HPV68 (17,69%) is the most prevalent, follow by HPV16 (14,67%), HPV31 (12,92%), HPV 52 (11,64%) and HPV51 (10,36%), all other HPV detected as a prevalence less than 10% (HPV18 has a prevalence of 6,29%).

Conclusions: HPV 16 is usually the most prevalent HPV detected in screening programs, the fact that in our study HPV68 is the most prevalent may be related to the introduction of the vaccine in the National Vaccination Plan since women that were vaccinated are already being screened. The collection of more data is being carried out to give more strength to the data already obtained, namely: HPV vaccination, age of menarche, type of contraception.

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#3783

P28-01 Anal cytology and molecular findings from HIV positive and negative MSM in Ireland

28 - Anal neoplasia

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Background/Objectives: Almost 90% of anal cancers globally are attributable to HPV infection. While rare amongst the general population, men who have sex with men (MSM), particularly HIV positive MSM, are far more at risk for the development of anal cancer. This research aimed to describe the anal cytology and molecular findings from HIV positive and negative MSM in Ireland.

Methods: 252 MSM participants were recruited to this study. Anal swabs were collected from participants and placed in PreservCyt. hrHPV DNA testing was performed using the Cobas HPV test on the Cobas 4800 Platform (Roche diagnostics). HPV mRNA testing was performed using the Aptima HPV assay (Hologic). Samples also underwent anal pap staining for cytological analysis. Samples that tested positive for the presence of hrHPV DNA underwent further analysis using P16/Ki67 dual staining. 148 participants underwent repeat testing at 1 year.

Results: 234 participants had valid baseline samples for HPV16 DNA analysis. 52 (22%) tested positive for HPV16 DNA. 232 had valid baseline samples for HPV18 DNA analysis of which 22 (9%) tested positive. 238 participants had valid baseline samples for other hrHPV DNA analysis of which 139 (58%) tested positive. HIV positivity was statistically significantly associated with the presence of other hrHPV DNA on multivariate analysis (OR 2.87, 95% CI 1.34 - 6.14, p=0.007). Overall, 240 participants had valid baseline samples for any hrHPV DNA analysis, of which 153 (64%) tested positive for at least one hrHPV type. HIV positivity was statistically significantly associated with the presence of any hrHPV DNA on multivariate analysis (OR 2.71, 95% CI 1.29 - 5.70, p=0.008). 252 participants had valid baseline samples for hrHPV mRNA analysis, of which 101 (40%) tested positive. Current smoking was statistically significantly associated with hrHPV mRNA positivity on multivariate analysis (OR 2.02, 95% CI 1.11 - 3.68, p=0.022). 245 samples were valid for cytological analysis. 110 (45%) were reported as normal, 81 (33%) were reported as AIN1 (LSIL), 46 (19%) were reported as AIN2 (HSIL) and 8 (3%) were reported as AIN3 (HSIL). Receptive anal intercourse (RAI) was statistically significantly associated with the presence of HSIL (OR 8.81, 95% CI 1.91 - 40.65, p=0.005). 145 returned valid P16-Ki67 dual staining results. 50 (34%) of these samples were positive for P16/Ki-67 dual staining. Being originally from Ireland was significantly associated with lower rates of dual staining positivity on multivariate analysis (OR 0.25, 95% CI 0.10 - 0.60, p=0.002). At 1 year follow up, hr HPV mRNA persistence was seen in 60% of participants (29/48). HPV16 DNA persistence was seen in 77% (17/22), HPV18 DNA persistence was seen in 44% (4/9), and other hrHPV DNA in 77% (58/75). Overall, persistence of any hrHPV DNA was seen in 79% (63/80). HSIL persistence was present in 22% (7/32), with AIN3 persis

Conclusions: This study demonstrates the molecular burden of hrHPV infection and persistence of hrHPV infection in this high risk group in an Irish context for the first time. It also demonstrates the burden of cytological HPV disease in this high risk cohort. In light of recent data showing the benefit of treating anal cancer precursor lesions in HIV positive MSM, this study supports calls for the consideration of the currently unmet need in Ireland for anal cancer screening in this high risk population.

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#3598

P14-03 Incidence of high-risk HPV genotypes in the Wielkopolska region

14 - Genotyping

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Background/Objectives: Human papillomavirus infection is one of the most common sexually transmitted infections. Persistent infection with high-risk HPV (hrHPV) is the direct cause of most cervical intraepithelial neoplasia and invasive cervical cancers. Temporary guidelines of the Polish Society of Gynecologists and Obstetricians recommend the usage of exclusively validated liquid media, tests for 14 hrHPV and the p16 / Ki67 test. Furthermore, current data indicate that genotypes 16 and 18 are assumed to be responsible for about 70% of cervical cancer cases. We aim to assess the most common hrHPV genotypes in the population of women from the Wielkopolska region.

Methods: We obtained material from 1200 women registered to Specialist Medical Practice in 2008 - 2021. The probe for the molecular test was collected with a combi brush and passed to the independent, standardized laboratory. HPV detection was done using PCR followed by DNA enzyme immunoassay and genotyping with a reverse hybridization line probe assay. Sequence analysis was performed to characterize HPV - positive samples with unknown HPV genotypes. The molecular test detected DNA of 41 HPV genotypes.

Results: The age range of the study group is from 18 to 85. We found that 52.4% of patients received HPV - positive test results. We detected that the following high-risk HPV types are the most common: 16, 52, 31, 51, 56 and 18. Of all HPV-positive patients, one-third have genotype 16. The frequency of genotypes 52 and 31 was the same and amounted to 11%. The frequency of genotypes 51, 56 and 18 accounted for 8.4%, 8.4% and 7.8%, respectively.

Conclusions: To our knowledge, this study is the most extensive assessment of high-risk HPV genotypes in Poland. Our results suggest that type-specific high-risk HPV DNA - based screening should focus on HPV types 16, 52, 31, 51, 56 and 18. It coincides with the Polish Society of Colposcopy and Cervical Pathophysiology recommendations. Moreover, such an analysis may indicate the potential groups with the highest risk of precancerous lesions and determine a new vaccination trend against specific HPV genotypes.

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#3599

P05-01 Level of L1 HPV serum antibodies after vaccination against HPV - a pilot study

05 - Immunology

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Background/Objectives: Cervical intraepithelial neoplasia (CIN) and cervical cancer are significant health problems globally. Vaccinations against HPV, which belong to the primary prevention of the development of precancerous lesions, significantly reduced the incidence of HPV-related changes in Australia and the United States. After treating CIN lesions or condylomata, some patients decide to vaccinate against HPV to develop L1 HPV antibodies for protection against re-infection.

Methods: We provide a pilot study in which we obtained material from women registered in Specialist Medical Practice in 2021. The experimental group constitutes patients who received three doses of vaccination against HPV after a diagnosis of either HPV infection or squamous intraepithelial lesions (SIL). In the Department of Immunology, we collected blood to the serum collected tubes (S-Monovette, Sarstedt), put centrifuge at 2.000 rpm for 20 minutes. ELISA microtiter plate was coated with recombinant VLP derived from HPV Type: 6, 11, 16 and 18. After stopping the reaction, we read the optical density (OD) at 450 and 620 nm. We set the seropositive cut points determined by calculated formulation from the manufacture at OD>0,303.

Results: There were nine times more women with positive HPV tests in the experimental group than in the control 1 group. In contrast, no significant dependency between group and HPV test results was found in the experimental group vs control 2 group. Antibody level was higher in the experimental group than in both control groups. Antibody level divided by cut-off value (0.303) was also significantly higher in experimental group than both in control 1 group ($p < 0.001$) and control 2 group ($p < 0.001$). Women with LSIL diagnosis and women with HSIL or cancer diagnosis did not differ significantly in antibody level and antibody level divided by cut-off value.

Conclusions: The study aims to assess the level of anti-HPV (L1 HPV) antibodies in healthy patients and with diagnosed cervix pathology after vaccination. Further research will be necessary to enlarge the research group. The introduction of tests detecting L1 HPV antibodies may facilitate the evaluation of the effectiveness of vaccine programs. The analysis of specific types of immune disorders in patients diagnosed with HPV-related changes will facilitate the identification of groups of women with the highest risk of developing HSIL and, consequently, cervical cancer.

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#3603

P13-03 Introduction of 13 in cervical cancer prevention screening program based on papillomavirus (HPV) test in the Italian Veneto region (ULSS 9 Scaligera): Resilience during SARS-Cov-2 Pandemic

13 - Self-sampling

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Background/Objectives: Vaginal self-sampling is a recently introduced approach to screen Papilloma virus (HPV) infection for cervical cancer prevention. This method is more convenient for patients compared to the established PAP test, since women can independently collect the sample at home. Several studies show that vaginal self-sampling is widely accepted by women across different cultural, religious, and socio-economic backgrounds and numerous countries are progressively introducing it in their screening programs. Veneto Region (Azienda Zero) developed a project to test vaginal self-sampling as a screening method for cervical cancer screening to increase participation in the non-respondent population. This study evaluates the outcomes of the first round of screening, considering the impact of the concurrent SARS-CoV-2 pandemic.

Methods: 9939 women between 30 and 64 years old in AULSS 9 Scaligera (including the province of Verona) were invited between January 10th 2021 and July 31st 2021 to a home self-sampling-based screening. The target population included respondent, non-respondent and women never invited for the cervical cancer screening. The self-sampling kit was sent to participants' addresses. It included a Copan Self Vaginal FLOQSwabs® REF#552C.80, instructions for use specifically designed for self-sampling and an acceptability questionnaire. After collection, women returned the sample to a local hospital or pharmacy. From there, samples were sent to the laboratory for analysis (Fracastoro Hospital, San Bonifacio). Dry swabs were eluted in 5mL of PreservCyt media and processed with Cobas 4800 (Roche diagnostics).

Results: 28% of invited women from ULSS 9 participated to the screening. Among these, 31% participated to a cervical cancer screening (HPV test or PAP test) for the first time and 8.5% tested HPV positive. From the questionnaire it emerged that 85% of participants prefer self-sampling at home compared to point-of care (POC) sampling and 77% scored self-sampling 4/5 on a 1 to 5 scale. Among women who refused to participate to the screening but filled the questionnaire, 40% would adhere to the program if offered self-sampling in POC.

Conclusions: Self-sampling-based HPV screening in ULSS 9 showed a good rate of participation, increasing the number of first-time participants to cervical cancer screening programs and demonstrating women's preference toward self-sampling at home. While SARS-CoV-2 pandemic halted most cervical cancer screening programs in Italy, this study demonstrates how self-sampling promotes cervical cancer screening resilience, maintaining a good participation rate despite lack of healthcare personnel and logistical difficulties.

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#3629

P27-03 Characterization of patients with vulvar lichen sclerosus et atrophicus and association to vulvar carcinoma: a retrospective single center analysis

27 - Vulvar diseases and neoplasia

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Background/Objectives: Lichen sclerosus (LS) is a benign, cutaneous, chronic inflammatory (autoimmunological) disease. The HPV independent or differentiated vulvar intraepithelial neoplasia (dVIN) accounts as a precursor lesion of vulvar squamous cell carcinoma and is often associated with lichen sclerosus. Although association between lichen sclerosus and vulvar carcinoma has long been recognized, there is a lack of evidence in literature.

Methods: This retrospective study examined pseudonymized data of 499 women diagnosed with vulvar pathology between 2008 and 2020 at the Department of Obstetrics and Gynecology of Hannover Medical School (MHH). Data were further stratified with respect to time of onset, location of disease, accompanying disease, HPV status and progression of disease into vulvar squamous cell carcinoma (VSCC).

Results: In total, 56 patients were diagnosed with vulvar lichen sclerosus et atrophicus. The median of onset of disease was 60.3 years of age (78.6% postmenopausal). The incidence of vulvar cancer in women diagnosed with lichen sclerosus was 48.2%, namely 27 women with lichen sclerosus developed a VSCC during patient's treatment. 25 patients reported a diagnosis of VIN in their self-reported history (44.6%). In 17 patients who developed vulvar carcinoma in course, lichen sclerosus and VIN were confirmed histologically (62.9%). 33.4% of VSCC were HPV negative, in 63% HPV status was not done.

Conclusions: Lichen sclerosus is an underestimated disease. The association between lichen sclerosus and vulvar cancer is well known, but further studies are missing to close the lack of data. In our retrospective study we showed a strong correlation between vulvar lichen sclerosus et atrophicus and VSCC. VIN and postmenopausal status at time of lichen sclerosus diagnosis tent to be important predisposing factors for development of a VSCC. Our results highlight the importance to diagnose Lichen sclerosus et atrophicus early to ensure adequate follow-up and prevent progression to VSCC.

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#3630

P30-04 Level of cytotoxic T cells populations in head and neck squamous cell carcinoma microenvironment as a predictor of patient prognosis

30 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Head and neck squamous cell carcinomas (HNSCC) belong to a group of diverse tumors, which can be induced by infection of human papillomavirus (HPV) or by tobacco and / or alcohol consumption. The viral etiology of HNSCC relates to the better clinical outcome reflecting the different immune system response. Recently, spatial analysis of the tumor microenvironment has enabled in situ analysis of infiltrating immune cells.

Methods: Here, we retrospectively analyzed 97 tissue samples of oral and oropharyngeal carcinomas with the known etiology using multispectral fluorescent immunohistochemistry based on OpalTM chemistry. To evaluate the immune cell infiltration in tumor and stroma compartments we designed 4 panels of 5 - 6 antibodies each. We mainly focused on quantification of CD4+, CD8+, and FOXP3+ T lymphocytes as well as on their subpopulations expressing PD1, CTLA4, or ICOS molecules. The cell counts were compared according to the tumor etiology and univariate and multivariate survival analyses were performed.

Results: More CD4 + and CD8 + T cells were detected in both compartments of HPV + tumors, which may be explained by the presence of viral antigens. Higher prevalence of PD1 + T cells both in the parenchyma and the stroma of HPV+ tumors points to T cell activation rather than exhaustion status. The higher prevalence of ICOS+ Tregs and CTLA4 +CD4 + T cells in the HPV - group agrees with poor prognosis of these patients and may also explain their poor immune response. Additionally, we observed significantly higher VEGF production in both compartments of HPV- tumors. To evaluate the influence of TIL infiltration on patients' prognosis we used Cox models. We fitted 38 models (19 for the parenchyma and 19 for the stroma) for OS and DSS analyses. We also tested modesl for the whole tumour and models where HPV status was not included. The detailed results will be presented.

Conclusions: We confirmed the HPV status as a main predictor of patients' prognosis but the number of PD1+CD8+ T cells, and the number of CD8+ T cells, all T cells and CD8+/FOXP3+ ratio were independent factors influencing the overall and / or disease specific survival.

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#3632

P14-04 Distribution of Human Papilloma Virus (HPV) genotypes in cervical samples of Latin American women, in the framework of the ESTAMPA study

14 - Genotyping

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Background/Objectives: Persistent infection with high-risk human papillomavirus (HR-HPV) is the leading cause of cervical cancer (CC). While the proportion of CC associated with HPV16 and 18 is greater than 70% and similar throughout the world, the relative importance of the other types of HR-HPV differs according to geographic region. The aim was to analyze the genotype-specific distribution of HPV in cervical samples with different histological diagnoses, within the framework of ESTAMPA trial ("EStudio multicéntrico de TAMizaje y triage de cáncer cervicouterino con pruebas del PApillomavirus") ongoing in nine Latin American countries.

Methods: A cross sectional study was carried out in a sub-cohort of 1,114 women, being HPV positive by screening tests (HC2, Qiagen and Cobas 4800 assay, Roche), at recruitment. Four groups of clinical categories by histological diagnosis were analyzed: 1) cervical intraepithelial neoplasia grade 1 or minus (≤CIN1) (n=728); 2) CIN2 (n=115); 3) CIN3 (n=188), and 4) CC (n=83). Samples were selected by convenience in order to achieve a similar number of samples in each of the diagnostic categories. Type-specific genotyping was carried out by two PCR strategies combined with reverse hybridization: a) BSGP5 +/GP6+ bio and b) PGMY09/11 (CHUV), which can identify 37 low risk (LR) and HR-genotypes. Each genotype was counted independently.

Results: The most common genotype in all clinical categories was HPV16, varying between ≤ CIN1 (17%) and CIN2 (20.9%), but increasing in CIN3 (53.2%) and CC (65.1%) ($p < 0.001$). A great diversity of LR and HR-HPV was observed in ≤ CIN1 and CIN2; while in CIN3 and CC, the viral spectrum was more restricted, with a clear predominance of HR-HPV (98.4% and 97.6%, respectively) ($p < 0.001$); among them stand out, in addition to HPV16, HPV31 (13.3%), HPV52 (11.7%) and HPV58 (9.0%) in CIN3 and HPV45 (8.4%), HPV18 (7.2%) and HPV52/58 (4.8%) in CC, although without statistical significance.

Conclusions: Our results confirm the relevance of HPV16 in the whole clinical spectrum of cervical lesions, with a strong rise of its proportion in CIN3+; particularly, in CC, the top ranked HPV types are the seven HR-HPVs which are components of the nonavalent vaccine (HPV16, 18, 31, 33, 45, 52, and 58), being dominant HPV16, HPV18, HPV45. These baseline data on the distribution of HPV genotypes in women from Latin America in the context of screening will be valuable to predict how vaccination and screening based on the HPV test will specifically influence the prevention of CC in our region (Grants IARC-PRI; PICT 0364-2016 and INC, Argentina)

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#3635

P09-03 Evaluation of the clinical detection of the Human Papilloma Virus (HPV) using a validated platform: first interlaboratory study in Argentina

09 - HPV testing

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Background/Objectives: The detection of high risk HPV (HR-HPV) DNA as a primary screening test is being gradually implemented by the Ministry of Health from Argentina, as part of a comprehensive strategy for the prevention of cervical cancer. There are different diagnostic platforms for the detection of HR- HPV validated for clinical use. In order to evaluate the performance of the laboratories and their competence, it is necessary to participate in external quality assessment programs. Since the participation in international programs is expensive and the panels are complex to import, a local program is of great interest for Argentina, with the possibility to be extended to other countries of the region. Our aim was to organize a first interlaboratory study to analize the competence of laboratories that use a clinical validated platform.

Methods: A panel consisting of 6 vials containing cervicovaginal cells in Preservcyt medium with different concentrations of HPV16, HPV18 and other HR-HPV, was developed; it included samples with single genotype or several (coinfections). The panel was tested 10 times to analyze its homogeneity; the acceptance criterion, considering 1 logs = 3.3 Cp (crossing point), was: trimmed mean of Cp±0.25 logs in 90% of the repetitions. Panels were sent to 13 laboratories that routinely use the HPV COBAS 4800 test (ROCHE). The Kappa (K) index was estimated to analyze the concordance in genotypes identification. To analyze the precision at different levels of detection, the mean of the reported Cps for each detected genotype in each of the vials by all the participants, was calculated; the acceptance criterion was trimmed mean of Cp±0.5 logs.

Results: The 6 batches of samples showed Cps within the acceptance criterion of reproducibility. There was agreement in 77/78 results of the reported HR-HPV genotypes (K = 0.98). The 96.6% of the reported Cp were in an acceptable range and random deviations were detected in 14/117 (12.0%), without a trend for any of the participants.

Conclusions: The call was successful; all participating laboratories submitted their results in a timely manner and proved to be competent for the detection of HR-HPV, showing similar levels of analytical sensitivity. This first study constitutes the starting point for the establishment of an external quality assurance program, which will allow the continuous monitoring of the HPV tests performance in Argentina.

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#3646

P41-01 A diagnose of advanced cervical cancer during longterm infertility treatment - removal of cervical tumor above 4 cm

41 - Fertility and HPV

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Background/Objectives: In 1974 profesor Harald zur Hausen had proved, that persistent infection with high-risk human papillomavirus is the direct cause of cervical intraepithelial neoplasia and invasive cervical cancer. In 2006 the first prophylactic vaccine against human papillomavirus was registered. Although, despite the knowledge of this pathomechanism, invasive cervical cancer still claim the lives of many women worldwide. Every year we loose about 300,000 patients.

Methods: A 32-years-old woman presented for a routine visit to the gynecologist. The physical examination suggested cervical cancer. Pap smear come back with High-Grade Squamous Intraepithelial Lesions result. The patient was qualified for a colposcopic examination - transformation zone type 3, Reid Colposcopy Index with result 8 points. A punch biopsy and endocervical curretage was performed. The result of the histopathological examination confirmed the diagnosis of cervical cancer. By analyzing the results, the diagnosis of cervical cancer stage IB2 was made.

Results: The patient was qualified for a radically modified hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic lymphadenectomy. In the postoperative material, a cerivdal tumor of the size 45x39x20 mm was found. The margins were negative. In one of the removed lymph nodes a metastatic tumor was described, also invasion of lymph vessels was confirmed after the histopathologic examination. The preliminary diagnosis of stage IB2 cervical cancer was confirmed. The patient was qualified for adjuvant chemo-radiotherapy. She underwent five cycles of cisplatin in the dose of 40mg/m2 each and radiation - teleradiotherapy (50,4 Gy), radiation boost (9 Gy) and hight dose rate brachytherapy (18 Gy).

Conclusions: The presented case report of a patient treated for many years due to primary infertility may be an example of oversight, which can occur during specialist treatment with the omission of obligatory, preventive examinations. Correctly used knowledge concluded in Jeorjos Papanicolau and prof. Teresa Koprowska publications in the 1920s and the achievements of the 1970s, make it possible to diagnose and to treat pre-cancerous lesions.

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#3647

P01-01 Effective treatment of cervical pathology in pregnant woman during COVID-19 pandemic

01 - HPV disease and COVID-19

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Background/Objectives: In the beginning of 2020 the whole world was paralysed by SARS-CoV-2 pandemic. The functioning of public health care system has been subordinated to fight against a previously unknown virus. Despite that, other health problems did not disappear.

Methods: In 2020 a patient presented for a routine gynecological visit. After abnormal Pap-smear (ASC-H) and positive HPV 16 test a biopsy was performed. The histopathology examination did not confirm any pathology. The patient qualified for LEEP-conization. Again, the histopathology results were correct. Parallel to the diagnostic process, the patient was vaccinated against human papilloma virus. The subsequent pap smear came in with result LSIL. The molecular test confirmed persistent HPV infection. She reffered to the gynecologist to perform another colposcopy, biopsy and endocervical curretage. Histopathology report described adenocarcinoma in situ. In the meantime the patient suffered from COVID-19. After quarantine, the patient was admitted to hospital to undergo surgical conization of cervix. The postoperative histopathological report confirmed, that the tumor was removed radically with clean margins. Oncological supervision was recommended. In December 2020 a schedule visit was planned. The patient reffered with a positive pregnancy test. Analyzing the patient's medical history, she was in the risk group of developing cervical insufficiency. During this visit the cervical lenght was about 30 mm. As part of the prevention of miscarriage and premature birth resulting from earlier treatment of the cervix, progestagen supplementation was joined. Next follow up visits showed no pathology till the 18 week of pregnancy. The cervix shortened to 20 mm. Because of that, the patient was admitted to the hospital. Mycoplasma and Ureaplasma infection was ruled out. During the stay, the cervix did not shorten, so the physicians did not decide for cervical cerclage. The patient was discharged from hospital in good condition, with stable cervix lenght. During pregnancy, colposcopic examinations were performed in which no abnormalities were found.

Results: In 38 weeks of pregnancy, the patient was referred to hospital for elective caesarean section. The male newborn with a weight of 3200 g was given 10 points in Apgar score.

Conclusions: The presented situation shows, that even during pandemic preventive examinations should not be missed. Early treatment of pre-cancerous lesions is significant to prevent cervical cancer.

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#3662

P23-01 Classification of high-grade CIN by KI-67 status - Significant constituent element in prognosis of personally tailored management

23 - Diagnostic procedures / management

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Background/Objectives: Histological assessment of cervical biopsies is a "gold standard" to confirm cervical intraepitelial neoplasia (CIN)and its grading, but misinterpretation may occur due to intra- and interobserver variability. High-grade cervical intraepithelial neoplasia (CIN2 and CIN3) is a heterogeneous condition and with different potential for cancer progression. These difficulties mean that patients as well may be over-treated for CIN lesions, which will naturally regress ,as undertreated . Biomarker Ki-67 indicative for a cellular proliferation could improve diagnostic accuracy and quality and could personalize management in women with high-grade CIN.1.

Methods: A cross-sectional study that enrolled a total of 110 women aged 18-65 with abnormal cytology referred for colposcopy to Reference Colposcopy Centre in Riga East Clinical University Hospital in July 2016-July 2017. Histological evaluation of cervical biopsy samples taken under colposcopy control was performed to each patient and all specimens were examined for Ki67 expression through IHC tecnique. The cumulative score of immunohistochemical expression Ki-67 (score 0 - 3), referred to as the "immunoscore' (IS), in the corresponding cervical scrape were evaluated.

Results: In the total group of CIN2/3 lesions(79 cases), 5 lesions were classified as IS group 0 - 2 (6.0%), 24 lesions as IS group 3 - 4 (30.4%) and 50 lesions as IS group 5 - 6 (63.6%),confirming heterogeneity within high-grade CIN lesions. Increasing Ki-67 expression was associated with increasing CIN grade($p<0.05$).

Conclusions: We have found a significant heterogenity in the expression of Ki-67 in high-grade CIN lesions .Additional use of Ki-67 biomarker with classical histology interpretation complete each other to reach the higher accuracy on diagnosis of high -grade CIN ,might help detect the prognosis and more personalised management so preventing overtreatment, especially in young women.

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#3533

P40-01 The effect of implementation of an organised cervical cancer screening programme on cervical cancer incidence and mortality in Poland

40 - Public health

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Background/Objectives: The Organised Cervical Cancer Screening Programme (OCCSP) was launched in 2006/2007 in Poland and provides cytology sampling once in a 3 years interval for each insured Polish women between 25 and 59 years old. We have aimed to evaluate cervical cancer (CC) incidence and mortality trends to assess the potential effect of OCCSP implementation.

Methods: Data on number of CC cases and deaths in 1980-2018 were retrieved from the Polish National Cancer Registry and data on female population was generated from the Central Statistical Office of Poland. Standardized incidence rates (SIRs) and standardized mortality rates (SMRs) per 100,000 women were calculated using the world standard population. To identify the influence of screening on specific age groups three trend analyses were performed: for women aged 0+ (whole population), 25-59 (screening age) and 60+ (post-screening age). Joinpoint regression analysis was performed with the maximum number of 3 joinpoints to search for the point in time when trends had changed. Significance level of <.05 was set as indicating statistically significant difference.

Results: Trends for SIR (Figure1): The SIRs were highest throughout the study period for women 60+. The annual percentage change (APC) was 1.2% in 1980-1985 (p=.324) and -2.0% in the subsequent period (pinf.001). The significant downward trend was observed in cohort aged 25-59 years in 1991-2007 (APC=-1.7%, pinf.001) and was accelerated after 2007 (APC=-5.6%, pinf.001). Similar result was obtained for the whole female population, where the trend identified in the period of 1987-2007 (APC=-1.7%, pinf.001) was hastened afterwards (APC=-4.4%, pinf.001). Trends for SMR (Figure 2): Insignificant SMR trend among women aged 60+ in 1980-1991 (APC=-0.4%, p=.247) was declining in subsequent period and slopes differed for 1991-2004 and 2004-2018 (APC=-2.8%, p inf .001 and APC=-0.8%, p=.002, respectively). For women aged 25-59 the downward trend noticed in 1980-1993 (APC=-0.9%, p=.001) was accelerated afterwards (APC=-1.9%, pinf.001 and APC=-5.2%, pinf.001 in 1993-2007 and 2007-2018, respectively). Similar pattern can be observed for women of all ages.

Conclusions: The implementation of the OCCSP in Poland seemed to have an impact on accelerating the downward trend for CC incidence and mortality among women in screening age of 25-59 years and in entire female population. However, the modelled trend on CC incidence in elderly women (60+) was not influenced by the OCCSP commencement and trend on CC mortality in this group was slowed down after the start of screening programme. The prolongation of screening age should be discussed in Poland to protect women 60+ who are at higher risk of CC incidence and death.

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#3539

P30-03 Geographic distribution and 9 methodologies of studies reporting HPV attributable fraction In advanced stage head and neck cancers: results of the "Alarm' systematic literature review

30 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Human papilloma virus (HPV) is a potentially preventable causative factor of head and neck cancer (HNC) particularly in the oropharynx. In light of the challenges in the management of advanced stage [locally-regionally advanced (LA) and recurrent/metastatic (RM)] HNC and lack of information on HNC attributable to HPV, we systematically reviewed available literature to provide updated information on the proportion of HPV+ cases (i.e., HPV attributable fraction; HPV AF) in advanced stage HNC worldwide. Here, we present exploratory outcomes of regional diversities in data availability and distribution of HPV detection methods.

Methods: We searched on clinicaltrials.gov for interventional studies (IS; i.e., phase I-III trials) as well as MEDLINE (via Pubmed) and Embase databases for non-interventional studies (NIS) of advanced stage HNC published between January 1, 2010 and December 31, 2020. NCT numbers retrieved for IS were further searched on MEDLINE and Embase databases and ASCO/ESMO journals of congresses for abstracts/articles with available results. Studies were selected if initiated from January 1, 2010 onwards and had available HPV prevalence data among patients with LA and/or RM HNC, including oropharynx among head and neck subsites.

Results: A total of 81 studies (62 IS and 19 NIS) were included, contributing data from 53 countries for 9,607 cases of advanced stage HNC. Overall, 61 studies were single-country studies conducted in Northern America, Europe and Eastern Asia, five were multiple-country single-continent studies and the rest were multiple-country multiple-continent studies. In total, 44 studies included data from the USA, 16 from Germany, 15 from France, 13 from Spain, 12 from Italy, and 11 each from Belgium, Canada and the United Kingdom. HPV status was reported to be assessed solely based on p16 expression in 58.0% of the studies, another method in 8.0% and multiple methods in 8.6%, while the method of assessment was not specified in the remaining 24.7% of the studies. The distribution of HPV detection methods was similar when examined separately for IS and NIS.

Conclusions: Our results indicate there is considerable inconsistency in the availability of data on HPV prevalence in the last decade across countries and continents, suggesting further efforts for a better representation of all regions are needed. Additionally, though HPV detection was primarily based on p16 expression, methodological heterogeneity as well as literature gaps were observed, highlighting the necessity for implementing a consistent testing methodology to accurately and consistently assess HPV burden.

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#3519

P30-02 Trans-oral robotic surgery for oropharyngeal squamous cell carcinoma, Guy's hospital institutional experience

30 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Trans-oral robotic surgery (TORS) has become established in the treatment of early oropharyngeal squamous cell carcinomas (SCC) and may play a key role in treatment de-intensification strategies in HPV related malignancy. Our centre instituted TORS as part of the OPSCC treatment paradigm in 2018 and report our experience.

Methods: This is a prospective case series of all patients who underwent trans-oral robotic surgery for primary treatment of head and neck malignancy between January 2018 and October 2021 at Guy's Hospital (London UK). All patients underwent comprehensive evaluation, staging (AJCC 7th edition) and multidisciplinary meeting (MDM) review. Primary TORS was offered to patients following MDM discussion and adjuvant radiotherapy (RT) or chemoradiotherapy (CRT) was given according to protocol. Specimen margins were analysed as per PATHOS protocol. Patients treated as part of ongoing clinical trials and "off trial" were included for analysis. Functional swallow outcomes were assessed via the MD Anderson Dysphagia Index (MDADI).

Results: 33 patients were treated from March 2018 to October 2021. The cancer location was 51.5% (17 patients) of tonsil, 27.3% of tongue base (9 patients), 15.2% of glosso-tonsillar sulcus and 6% of posterior pharyngeal wall. For the majority of patient (91%), the tumor was HPV positive. 82% of patients had an adjuvant treatment in which 22 patients received radiotherapy and 5 patients had chemoradiotherapy. The 6 other patients were treated only surgically. 6 patients (18%) had a post-operative bleeding but only two of them had to be managed surgically. The Mean MDADI functional outcome post-operative score at least 6 weeks after surgery was 73 with a minimum of 33 and a maximum of 100. 2 patient remained long term gastrostomy dependant, one had RT adjuvant treatment and the other one was a salvage case with free flap reconstruction.

Conclusions: Transoral robotic surgery is a safe and effective treatment method for oropharyngeal squamous cell carcinoma. To date oncological outcomes in our institution are promising. TORS for oropharyngeal SCC has good functional outcomes with an acceptable risk level but this study is limited by a small population. Further investigations with a comparison of functional outcomes in patient treated with standard chemoradiotherapy should be evaluated and the oncological outcomes reported after sufficient follow up.

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#3501

P14-02 High-risk HPV types using next generation sequence (NGS) in European and Latin women with negative and positive cytology: preliminary results from ELEVATE study

14 - Genotyping

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Background/Objectives: The main etiological factor of cervical cancer (CC) and its precursor lesions is a persistent human papillomavirus (HPV) infection. High-risk HPV (hr-HPV)-induced carcinogenesis is mainly related to E6/E7 integration in human DNA that causes transformation of the host cells. This virus can be classified into several levels: genus, species, type, subtype, and variants, which can be divided into lineages and sub-strains according to the percentage of genetic similarity. This project is part of an international collaboration entitled ELEVATE of which the main objective is to develop a new point-of-care screening device based on self-sampling. The new test will be able to detect 14 hr-HPV types and protein biomarker expression.

Methods: In order to develop the HPV DNA test and detect well-conserved target regions, hr-HPV genotyping was performed using Ampliseq manually and Ion Torrent S5 technologies in 1000 samples collected in Brazil, Ecuador, Belgium, and Portugal (300 normal samples, 300 low-grade lesions, and 400 high-grade lesions). Through NGS of the E6/E7 genes, it will be possible to genotype all 14 hr-HPV individually and also HPV co-infections. The genotyping was performed with a workflow developed in the Galaxy platform, in which the alignment was made against the 14 hr-HPV genotypes.

Results: To date, 106, 123, 89, and 68 samples from the Brazilian, Ecuadorian, Belgian, and Portuguese participants respectively have been sequenced. These samples correspond to 218 high-grade lesions, 119 low-grade lesions, and 49 normal samples. All 14 genotypes were present in at least one sample. Considering only positive samples, in all countries, the majority of the samples had HPV coinfections (except for Ecuador: HPV 59 and HPV 16, and co-infections were found in the same number of samples). HPV 16 was most prevalent in Brazil and Portugal, versus HPV 31 in Belgium. Also were analyzed all the HPV types even those the types present in coinfection separately. It is possible to note that some trends persist. We found a high prevalence of HPV 52 in Portugal, which is important since it is not targeted by present vaccines. We also analyzed the types according to cytology results, in samples with high-grade lesions the most common HPV types until now are HPV negative and HPV 16.

Conclusions: It is still necessary to finish the analyses of the 1000 samples to confirm the genotypes frequency tendencies. Also, we will make other bioinformatic analyses like phylogenetic tree and lineages/sub-lineages classification.

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#3505

P26-02 Conservative treatment for cervical adenocarcinoma in situ: long term results

26 - Cervical neoplasia

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Background/Objectives: To evaluate the effectiveness of conservative treatment for cervical adenocarcinoma in situ (AIS). A retrospective study of Italian women with histologically confirmed AIS on cervical Loop Electrosurgical Excision Procedure (LEEP) specimen who were treated conservatively between 2008 and 2020. The main outcome investigated was the risk of recurrence defined as a subsequent finding of recurrent AIS or invasive adenocarcinoma in a long-term follow-up. All patients underwent colposcopy with endocervical curettage (ECC) and cytology every 6 months for the first two years after initial surgery and then annual cytology.

Methods: A retrospective study of Italian women with histologically confirmed AIS on cervical Loop Electrosurgical Excision Procedure (LEEP) specimen who were treated conservatively between 2008 and 2020. The main outcome investigated was the risk of recurrence defined as a subsequent finding of recurrent AIS or invasive adenocarcinoma in a long-term follow-up. All patients underwent colposcopy with endocervical curettage (ECC) and cytology every 6 months for the first two years after initial surgery and then annual cytology.

Results: Thirty women aged 26-51 years withhistologically proven AIS on excisional specimen with negative margins, negative apex, and negative endocervical curettage were included. The median follow-up was 5.4 years. One woman had a recurrence of AIS after eight years of follow-up and underwent total hysterectomy. No invasive cervical disease was detected during surveillance.

Conclusions: Women with cervical AIS can be managed conservatively by an excisional procedure, provided that the margins are free and a close and long-term follow-up is guaranteed.

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#3512

P09-02 Performance of full and extended 14 assays using a new high-risk HPV multiplex panel

09 - HPV testing

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Background/Objectives: The development of extended (beyond HPV16/18) and full genotyping HPV assays has resulted in a demand for external control panels that can confirm assay performance across multiple high-risk genotypes. To address this need, we have designed and developed third-party HPV multiplex panels for use with HPV genotyping assays. These panels are designed to facilitate in-house assay verification, provide known positive material for personnel training and assist with routine Quality Control Assurance. Our controls are developed using full-length viral genomes grown in cell culture, which provide 100% clinical sample equivalence and are inactivated to meet Clinical Lab Biosafety requirements. The objective of this study is to confirm prototype panel performance and sample usability using extended and full genotyping assay workflows.

Methods: Microbix designed HPV16/18/45, HPV39/51/52, HPV31/33/66 whole-genome, inactivated HPV liquid multiplex samples formulated in PreservCyt®, which mimic diagnostic targets found in infected patient specimens. All samples were tested using the ELITe Panel (EliTech Group), OnclarityTM HPV assay (BD), and the AnyplexTM II HPV28 Detection Assay (Seegene) to ensure sample compatibility with partial, extended, and full genotyping assays, respectively.

Results: All samples showed acceptable performance when tested on the ELITe Panel, OnclarityTM HPV Assay, and AnyplexTM II HPV28 Detection Assay.

Conclusions: We have successfully designed high-risk HPV multiplex panels to support assay verification/validation, personnel training, and quality assurance. The samples exhibited acceptable performance using multiple Original Equipment Manufacturer platforms, demonstrating their potential use as cross-platform-compatible quality controls, verification panels and External Quality Assessment samples. Finally, our unique manufacturing process, which utilizes full-length viral genomes, provides a universal total nucleic acid (DNA/RNA) control compatible with any molecular assay target region.

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#3499

P27-02 HPV induced alterations in vulvar pathology

27 - Vulvar diseases and neoplasia

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Background/Objectives: Human Papilloma Viruses have been the subject of numerous studies related to cervical cancer. But the tropism of these viruses for the squamous epithelium does not stop at the cervical level. Histologically similar lesions can be identified in other epithelia. Precursor lesions of squamous cell carcinoma can be divided into two major groups, depending on the association with HPV infection. The new WHO classification (2020) emphasizes the importance of human papillomavirus (HPV) infection in the development of vulvar squamous cell carcinoma, thus reflecting on patient management. Our review studies the correlation between clinical data, HPV status, histological features and molecular markers in vulvar squamous lesions.

Methods: We selected cases diagnosed with vulvar lesions and recorded clinicopathologic variables, as well as immunohistochemical test results. All slides were reviewed and classified according to the new WHO classification.

Results: Of a total of 21 cases, the HPV-associated ones showed distinctive morphology that suggested their nature even before the p16 staining

Conclusions: A clear distinction of the place of origin of the tumor is often difficult to achieve both clinically and by imaging techniques, especially in advanced diffuse lesions, exceeding the limits of anatomical structures. Vulvar squamous lesions represent a heterogenous group of tumours, some with adverse outcome and although their recognition can be difficult, refinement of diagnosis and prognostication based on a systematic evidence review has great value in a better personalized treatment for these patients.

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#3316

P36-01 Health impact and cost-effectiveness analysis of gender-neutral 9-valent human papillomavirus vaccination in Taiwan

36 - Economics and modelling

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Background/Objectives: Human papillomavirus (HPV) can cause cancers and HPV diseases in both genders. Most prevalent HPV cancer in women is cervical cancer while the most prevalent HPV cancer in men is head and neck (H&N) cancer globally. Many countries have transitioned from female-only vaccination (FOV) to gender-neutral vaccination (GNV), directly protecting men against HPV infection and diseases and possibly further reducing HPV-related diseases in women. Since December 2018, the Taiwanese government has provided the two-dose regimen of the bivalent HPV vaccine (2vHPV) free of charge to 13-year old girls as part of the National Immunization Program (NIP). The 9-valent HPV vaccine (9vHPV) provides additional benefits through direct protection against seven additional HPV types. This study assesses the health impact and cost-effectiveness of 9vHPV GNV vs. 2vHPV FOV strategies in Taiwan.

Methods: Using Taiwanese data, a validated dynamic transmission model was used to simulate the natural history of HPV infections and estimate the cost associated with HPV-related diseases. HPV-associated health outcomes included cervical lesions (CIN-1/2/3), cervical, vaginal, vulvar, H&N, anal, and penile cancers as well as genital warts (GWs) and recurrent respiratory papillomatosis (RRP). Costs, quality-adjusted life-years (QALY), and incremental cost-effectiveness ratio (ICER) were estimated. The model assumed lifelong duration of vaccine protection, herd immunity, a discount rate of 3% for costs and QALYs.

Results: Compared to 2vHPV FOV strategy, 9vHPV GNV strategy would prevent more cases of HPV-related diseases and cancers (15,860 cervical cancer, 271,753 CIN-1/2/3, 132 vaginal, 822 vulvar, 13,885 H&N, 775 anal and 181 penile cancer, 1,708,978 GWs, and 9,873 RRP) and death (8,899 cervical cancer, 54 vaginal, 357 vulvar, 8,799 H&N, 364 anal and 102 penile cancer, and 438 RRP). 9vHPV GNV strategy resulted in a 11% reduction in disease management cost as compared to 2vHPV FOV strategy. The ICER of 9vHPV GNV strategy vs. 2vHPV FOV strategy was NTD 391,360 /QALY.

Conclusions: A 9vHPV GNV strategy for 13-year old girls and boys would have additional public health and economic impact and would be highly cost-effective as compared to the current 2vHPV FOV strategy, relative to per capita GDP, which is estimated at NTD 833,447 for Taiwan. The 9vHPV GNV approach would not only help to accelerate the timeline in achieving cervical cancer elimination goal but also to reduce the incidence HPV related H&N cancer. Since Taiwanese data were used in this analysis, the results can be used as a fundamental reference to better evaluate cancer prevention policy in the future.

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#3336

P13-02 Self-sampling as a cervical screening among HIV-positive women in Moscow region

13 - Self-sampling

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Background/Objectives: HIV-infected women are monitored in AIDS centers in the Russian Federation. Unfortunately, the AIDS Centers in the Russian Federation do not diagnose HPV-associated diseases. HIV-infected women are forced to go to general medical facilities for cervical screening, which they often do not do for a number of reasons (stigma, lack of free time, disclosure of the diagnosis). Objective: to study the effectiveness of using self-sampling at the first stage of cervical screening of HIV-infected women in Moscow region.

Methods: 100 HIV-infected women from Moscow region were examined from February 2020 to May 2021. All women were tested for HPV-test with the determination of 14 types of HPV HCR (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68). Test material: smear of epithelial cells of the vagina and cervical canal. All women completed the questionnaire (results were assessed on a ten-point scale, where hard = 0 and easy = 10).

Results: Among the 100 HIV-women mostly young people (37.74± 6.3 y-s, Me - 38, min - 19, max - 57, 95%CL: 37.7-38.9). Route of HIV infection: 72.6% - sexual route, 23% - when using intravenous psychoactive substances, 4.4% - could not answer. HIV-women have CD4+- lymphocytes 617.7 ± 258.4 cells / μl. 96.4% of women received ART. In 43% cases (95%CL: 33.3 - 52.7) of HIV-infected women were diagnosed HPV of using self-sampling. In 36% cases (95%CL: 26.6 - 45.4) were diagnosed HPV in cervix. Results of the questionnaire: ease of taking a smear - 9.4, accessibility of understanding and ease of following instructions - 9.5, comfort of using the kit - 8.9 and only 15% of respondents would prefer a traditional visit to a gynecologist.

Conclusions: self-sampling is easy and comfortable to use for HIV-infected women. self-sampling efficiently detects HPV infection in a situation of limited funding. Using self-sampling at the AIDS center is the only way to increase participation in cervical screening for HIV-infected women in the Moscow region of the Russian Federation.

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#3348

P09-01 Does the prevalence and genotype distribution of HPV oncologic potential change over time?

09 - HPV testing

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Background/Objectives: The distribution of HPV oncogenic potential is changing due to virus mutations, seroprevalence for a specific virus, or alternations in our immune response to the virus.There are more than 118 detected types of HPV in anogenital region. Clinical experience has shown their different oncogenic potential. So, they are classified as:high-risk16,18,31,33,39,45,51,52,56,58,59,68,73,82, probably high-risk 26,53,66, and low-risk 6,11,40,42,43,44,54,61,70 (1). Within the group of high-risk types, HPV types 16 and 18 are the most oncogenic ones since the risk of progression and cancer development for these two types is twice as high as for other types from this group (2).

Methods: Statistical Hi kvadrat test

Results: Oncogenic HPV potential also depends on geographic region, race or ethnicity, religion ....The first research on oncogenic potential and geographic tropism in south-eastern Serbia was performed in 2017.Types 56 and 58 were then found to be predominant as specific tropism for this region. Further research conducted until 2000 have shown changes in oncogenic distribution in relation to the year of the research. Each year a new type is identified in the top 10, and then it disappears in the years to come. In our region these types are 56 , 54 , 59 , 39. If we rule out these types, then a regularity in oncogenic potential distribution can be observed.Top 7 HPV types according to their oncogenic potential are as follows: 16, 31, 58,33, 18, 45 and 51.

Conclusions: Understanding of oncogenic potential distribution is important for: the assessment of oncogenic risk and the need for personalized, more aggressive diagnostic and therapeutic approach; triage of HPV positive tests and cytology-negative HPV + tests: the assessment and selection of the most effective vaccine in one geographic region

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#3349

P08-01 Design and objective of GLUCANCIN study: efficacy of intravaginal carboxymethyl-B-glucan and polycarbophil on low-grade cervical lesions

08 - Immunotherapy - Immuno-oncology - New treatments

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Background/Objectives: Human papillomavirus (HPV) infection represents a significant source of morbidity and mortality worldwide. High-risk oncogenic HPVs cause 99.7% of cervical cancers. Most of these infections are transitory and only if they are persistent and caused by a high-risk oncogenic HPV are they an important risk factor for the development of cervical intraepithelial lesions and invasive cervical cancer. Immunity plays a key factor in eliminating HPV infection. HPV evasion of these immune defense mechanisms is critical for the persistence of the infection and leads to the development of preneoplastic lesions and ultimately to cervical cancer. Medical treatments represent a therapeutic strategy to avoid the evasion mechanisms of HPV. One of these most promising treatments is beta-glucans that seem capable of affecting the course of HPV infection.

Methods: Multicentric, Interventional, longitudinal, prospective, open-label trial with a control group with randomized, consecutive recruitment for each group, to evaluate the safety and efficacy of carboxymethyl-beta-glucan and polycarbophil as a treatment for low-grade CIN associated with HR-HPV infection. n=200. Unvaccinated women aged 30-50 with LSIL/CIN1 histological results on cervical biopsy preceded by HR-HPV+ test were randomized into 2 groups: A) Carboxymethyl-ß-glucan (Colpofix®) once/day for 3 months B) Control group: no treatment (usual clinical practice).

Results: There are more than 6000 studies that have described the effects of glucans. Recent studies focusing on their influence on cytotoxic and helper T cells, APCs, inflammatory pathways, and oxidative burst (using reactive oxygen species to kill cells) have revealed that they may also have some anti-cancer properties. Carboxymethyl ß-glucan gel treatment has been studied in 4 different studies on affected individuals by CIN1 or/and HPV+. These case-control studies demonstrated that it has an anti-cervical cancer role in CIN1 regression vs wait and see statistically significant. These studies suggested that, in addition to the anticancer effects of beta-glucans, they also have some effects on infection by HPV, the main cause of cervical cancer.

Conclusions: Data from this ongoing study will indicate if ß-glucans have a therapeutic effect on the Regression of Low-grade Cervical Intraepithelial Lesions on the different genotypes. Given a new approach different from wait and see and would represent a significant advance in the management of HPV-positive patients.

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#3258

P10-01 Pilot screening of cervical cancer 9 in the Republic of Karakalpakistan

10 - HPV screening

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Background/Objectives: Detection of HPV associated precancerous diseases of the cervix and cervical cancer in ecologically unfavorable regions of the Republic of Karakalpakstan.

Methods: The first UNFPA-WHO pilot project on HPV-based cervical cancer screening is underway with funding from the Government of Japan, technical assistance from WHO, IARC and UNFPA, and some support from the French Embassy. The pilot screening project was approved by the Ministry of Health of the Republic, covering 10 districts, mainly near the Aral Sea: Khojeyli, Kanlykul, Shumanay, Chimbay, Karauzyak, Kungrad, Kegeili, Muynak, Buzatau, Nukus district. The age of women is 30-55, the number of women is 50,000 (100%).

Results: Interim analysis: from August to October 2021, 17,662 (35%) were tested,915 (5.6%) of which HPV positive, 15,908 (90.1%)- HPV negative By randomization 1/1, a triage of VIA was performed - 438 (37.9%) / colposcopy - 364 (47.8%), invalid and erroneous tests - 0.4%, by the end of the project 32,338 (65%) should be tested. 92 (10%) referred to oncologist, pathological conclusion: CIN I - 5 (0.5%), CIN II - 14 (1.5%), CIN III - 6 (0.7%), Cancer in situ - 6 (0.7%).

Conclusions: The completion of the pilot screening is scheduled for late February 2022. Upon successful completion of the project, a national cervical cancer screening program will be developed.

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#3241

P34-01 Prevalence of different types of HPV HCR in cervix and anus among HIV-positive women in Moscow region

34 - Sexually transmitted diseases and HIV infection

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Background/Objectives: HIV-infected women have a higher risk of HPV infection than HIV-negative women, and a higher risk of persistence and malignancy. A number of researchers recommend screening for HPV-associated anus disease in HIV-infected women, regardless of the results of a cervical examination. Unfortunately AIDS Centers in the Russian Federation do not have funding for diagnostics of HPV-associated diseases. Objective: to study the prevalence of human papillomavirus of high carcinogenic risk (HPV HCR) in cervix and anus among HIV-infected women in Moscow region.

Methods: 101 HIV-infected women from Moscow region were examined from August 2018 to July 2019. All women were tested for HPV-test with the determination of 14 types of HPV HCR (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) in cervix and anus.

Results: Among the 101 HIV-women mostly young people (38.99±6.52 y-s, min-26, max-58, median-58) predominated. In 60.4% cases (95%CL: 50.9 - 69.9) of HIV-infected women were diagnosed with HPV HCR. At the same time the frequency of HPV detection differed in the studied anatomical locus: in 50.8% of cases HPV was detected simultaneously in the cervix and anus, in 21.3% - only cervix and in 27.9% - only anus. All 14 HPV HCR types were diagnosed. Prevalence of different types of HPV HCR among HIV-positive women significantly depending by anatomical locus (tab.1). In cervix, 33 and 52 types of HPV were in the lead (20.5% and 18.2%, respectively). In anus - 16 and 51 types of HPV (31% and 27%, respectively). In 67.7% (95%CL: 51.3 - 84.2) HIV-women with HPV-infection the types of HPV were recorded, which were absent them in cervix during the simultaneous examination of the two studied loci in anus. At the same time, in the anus in 38.7% cases, the number of identified HPV types was greater than that found during examination of the cervical canal.

Conclusions: High incidence of HPV detection was revealed in the group of HIV-infected women from the Moscow region. All 14 HPV HCR types were diagnosed in all studied anatomical locus. The results obtained demonstrate the necessity to introduce screening for HPV-associated diseases at the AIDS centers in the Moscow region of the Russian Federation.

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#3137

P27-01 Clinical characteristics and risk factors of invasiveness and recurrence in the patients with extramammary Paget's disease of the vulva

27 - Vulvar diseases and neoplasia

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Background/Objectives: Extramammary Paget's disease (EMPD) of vulva is a rare and slow growing disease. Studies about EMPD had not been established, and especially, studies on Asians are still lacking. We aimed to identify clinical features of patients with EMPD of the vulva in Korea, and evaluate the risk factors of invasiveness and recurrence.

Methods: We conducted retrospective analysis of the patients with EMPD of vulva who underwent surgical treatment in Asan medical center from 2005 to 2020. Clinical characteristics, histopathologic results, surgical complications, and recurrence were reviewed. The differences between the patients' clinical and histopathologic factors were examined using Chi-square and Fisher's exact tests. All statistical analyses were conducted using SPSS 20.0 software (Chicago, USA).

Results: Forty-seven patients with EMPD of vulva were treated with wide excision or radical vulvectomy in Asan medical center. The mean age at the time of initial diagnosis was 64.3 (range 44-80) years. Among them, 17 (36.2%) patients had invasive diseases, and seven (14.9%) patients experienced recurrence. Median duration of recurrence was 67.2 (range 32.8-160.0) months. Vulvar lesion size on physical examination was significantly associated with invasiveness (p=0.01). Margin status, adnexal involvement, and lesion sized was not significantly associated with recurrence (all p>0.05).

Conclusions: Vulvar lesion size on physical examination was significantly associated with invasive disease in the patients with EMPD of vulva. Margin status during surgery was not significantly associated with recurrence.

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#3076

P15-01 Investigating survival after penile cancer: A nationwide study of Human Papillomavirus (HPV) and P16 as prognostic markers In penile cancer

15 - Molecular markers

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Background/Objectives: Human papillomavirus (HPV) positivity and expression of p16 have been suggested as potential prognostic markers in penile cancer. However, the majority of previous studies are limited by small sample sizes, lack of adjustment for other prognostic factors, and shorter follow-up. In this nationwide study, we will investigate the prognostic significance of HPV DNA status and p16 expression for survival after penile cancer in a large cohort of patients.

Methods: In the nationwide Danish Pathology register, we identified all cases of penile squamous cell carcinomas (SCC) in Denmark during 1995-2017. We restricted our retrieval of material to the six largest centers in the study period. Since 2009, treatment of penile cancer has been centralized at two centers (Rigshospitalet, Copenhagen and Aarhus University Hospital). Archived tumor material will be retrieved from all cases, and the diagnosis reviewed by a pathologist. HPV DNA testing of the tumor material will be performed using INNO LiPA HPV Genotyping Extra test, and p16 staining will be performed using the CINtec histology kit at a central laboratory. P16 slides will be evaluated and scored by two pathologists independently, and tumors with >70% tumor staining cells will be considered positive. From nationwide registries, we will obtain information on deaths and recurrences in the study population during up to 26 years. We will estimate the overall, disease-specific and disease-free survival after penile SCC according to HPV status and p16 expression. We will use Cox proportional hazards regression to investigate whether HPV and p16 have independent prognostic value after adjusting for other known prognostic factors, including cancer stage at diagnosis.

Results: Altogether,we identified 936 cases of penile SCC at the included pathology departments during 1995-2017, corresponding to approximately 82% of all cases in Denmark. Cases were diagnosed at pathology departments at: Aarhus University Hospital (N=350), Rigshospitalet, Copenhagen (N=320), Odense University Hospital (N=96), Aalborg University Hospital (N=67), Herlev Hospital (N=73), and Vejle, Lillebælt Hospital (N=30). 21.9% of cases were diagnosed during 1995-2002, 35.8% during 2003-2010, and 42.3% during 2011-2017. According to records, surgical specimens are available in 811 cases (86%), and biopsies in 80 cases (9%). In 45 cases (5%), the type of available tumor material is to be determined, as the tumor material is yet not retrieved from the archives.

Conclusions: Data collection for the study is ongoing. A more detailed description of the study design, final number of included cases and patient characteristics will be presented.

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#3097

P03-01- Estimating the prevalence of non-cervical human papillomavirus infection in mainland China: The design of PROGRESS-Plus study

03 - Epidemiology and natural history

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Background/Objectives: Evidence indicated that human papillomavirus (HPV) infection may increase risks of anogenital warts, oral warts, and a varying proportion of several cancers among men and women. The prevalence of cervical HPV infection has been extensively reported in women worldwide. Much less has been reported on the disease burden of non-cervical HPV infection in women and men, especially in China. Thus, a study named PROGRESS (PRevalence of Oral hpv infection, a Global aSSessment)-Plus will be conducted in mainland China to estimate the prevalence of HPV oral infection in women, and of HPV oral and anogenital infection in men. This abstract describes the design of the PROGRESS-Plus study.

Methods: PROGRESS-Plus is a national, multi-site, cross-sectional study in China, conducted from 2020-2023.

Results: Approximately 4,742 participants (2,371 women and 2,371 men) aged 18-60 years will be recruited from 6 regions in China through 12 study sites during 2021 Nov-2022 Nov for oral/anogenital sample collection. HPV DNA detection and genotype identification will be performed using the SPF10 LiPA assay at a central laboratory. The HPV infection rates will be reported overall as well as by HPV genotype, age, and geographic region. The risk factors (e.g. demographics and sexual behaviors) associated with oral and anogenital HPV infection will be surveyed among study participants.

Conclusions: Results from the PROGRESS Plus study will fill important evidence gaps in the oral HPV burden in the Chinese general population and the anogenital HPV burden among men. This evidence can raise public awareness of HPV infection and help health care providers, policymakers, public health professionals, and health care consumers make decisions for gender-neutral HPV vaccination. In addition, the approaches established in the PROGRESS Plus study could provide a methodological framework for future epidemiologic research related to sexually transmitted diseases and other health outcomes in mainland China.

References: NA

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#3649

P03-02- Incidence trends for HPV-associated anal squamous cell carcinoma in the United States, 1999 to 2018

03 - Epidemiology and natural history

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Background/Objectives: Human papillomavirus (HPV) vaccines can prevent HPV-associated anal cancer; new promising trial data also suggest a role for screening and treatment for anal cancer among HIV-infected populations. HPV-associated anal cancer cases have increased in the past two decades in the United States (US), with an average annual burden of 7,000 cases.

Methods: Using population-based cancer registries covering approximately 97% of the US population, we calculated age-adjusted incidence rates for HPV-associated anal squamous cell cancers (SCC) using SEER*Stat (version 8.3.9). All cancers were malignant, microscopically confirmed, and restricted to the following ICD-O-3 histology codes for SCC: 8050-8084, 8120-8131. We also examined incidence trends from 1999 to 2018 using average annual percentage change (AAPC). AAPC was calculated using a weighted average of the slope coefficients of the underlying joinpoint regression line with the weights equal to the length of each segment over the interval using the Joinpoint regression program (version 4.9.0.0).

Results: Overall, an average of 5,346 incident cases (rate of 1.66 per 100,000 persons) of HPV-associated anal SCCs were diagnosed over the 20-year period. Incidence rates were higher among females (2.03) than males (1.24), higher among non-Hispanic persons (1.71) than Hispanic persons (1.27), and higher among White persons (1.72) than Black persons (1.60). By age, rates were highest in the older age groups: 50-59 (3.98), 60-69 (5.12), 70-79 (5.22), and >80 (5.12) years. From 1999 to 2018, incidence increased by 2.5% annually, most notably among persons aged 60-69 (AAPC: 4.2) and 50-59 (AAPC: 3.9) years. Incidence also increased among both sexes (female AAPC: 2.9; male AAPC: 1.9), ethnicity groups (non-Hispanics AAPC: 2.7; Hispanic AAPC: 0.8), and among White (AAPC: 2.6), Black (AAPC: 2.3), and American Indian and Alaska Native (AAPC: 1.6) people. Conversely, incidence declined by 1.7% each year among persons aged 30-39 years and remained stable among persons aged 20-29 (AAPC: 1.5; 95% CI: -0.6, 3.7) and 40-49 (AAPC: 0.2; 95% CI: -0.4, 0.7) years.

Conclusions: HPV-associated anal SCC incidence continues to increase overall and among both sexes, ethnicity groups, and most races and age groups; however, incidence declined among persons aged 30-39 years. Ongoing surveillance using population-based registries is needed to monitor trends in the US. Improving HPV vaccine coverage and increased anal cancer screening and treatment among HIV-positive populations could prevent many HPV-associated anal cancers in the future.

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#3293

P08-03- Phase 3 recurrent/metastatic cervical carcinoma trial: subgroup efficacy analysis of Cemiplimab versus individual investigator's choice chemotherapy.

08 - Immunotherapy - Immuno-oncology - New treatments

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Background/Objectives: There is no standard-of-care regimen in the second-line setting for women with recurrent/metastatic (R/M) cervical carcinoma. Cemiplimab was recently shown to significantly improve overall survival (OS) compared with investigator's choice (IC) chemotherapy in patients with R/M cervical cancer after first-line platinum-based chemotherapy (NCT03257267; ESMO-VP-2021). We present a pre-planned exploratory subgroup analysis comparing Cemiplimab to individual IC chemotherapy options.

Methods: EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9 is an open-label, randomised (1:1), multi-centre, Phase 3 clinical trial of anti-programmed cell death (PD)-1 cemiplimab vs IC single-agent chemotherapy in R/M cervical cancer that has progressed after first-line platinum-based treatment. The selection of single-agent chemotherapy by the investigator (gemcitabine, pemetrexed, vinorelbine, topotecan or irinotecan) was not protocol-defined, but the regimen had to be chosen prior to randomisation. Adult females (age ≥18 years) were enrolled regardless of PD-ligand 1 expression and received cemiplimab 350 mg intravenously every 3 weeks or IC chemotherapy for up to 96 weeks; and were stratified by histology (squamous cell carcinoma/ adenocarcinoma or adenosquamous), geographic region (North America/Asia /rest of world), prior bevacizumab, and ECOG performance status (0/1). Primary endpoint was OS. Additional endpoints included progression-free survival (PFS), objective response rate (ORR), duration of response, quality of life and safety. Data cutoff was 4 January 2021.

Results: A total of 608 patients were randomised: 304 to cemiplimab and 304 to IC chemotherapy (gemcitabine, n=121; premetrexed, n=111; vinorelbine, n=32; topotecan, n=21; irinotecan, n=19) across geographic regions and histologies. Median duration of study follow-up (range) was 4.8 months (0.0–25.9) for the overall population. At second interim analysis, the trial was stopped early for efficacy. OS demonstrated improvements with cemiplimab vs each IC chemotherapy treatment—HR (95% CI) vs: pemetrexed, 0.71 (0.52–0.98); topotecan, 0.78 (0.31–1.96); irinotecan, 0.69 (0.28–1.70); gemcitabine, 0.76 (0.54–1.06); vinorelbine, 0.77 (0.40–1.48)—similar to those observed with cemiplimab vs pooled IC chemotherapy. Results were similar with PFS—HR (95% CI) vs: pemetrexed, 0.70 (0.52–0.94); topotecan, 0.90 (0.43–1.90); irinotecan, 0.77 (0.34–1.72); gemcitabine, 0.73 (0.54–0.97); vinorelbine, 1.21 (0.70–2.09). ORR were consistently higher with cemiplimab— % vs: pemetrexed, 16.0 vs 6.3; topotecan, 15.0 vs 4.8; irinotecan, 23.1 vs 15.8; gemcitabine, 17.6 vs 5.0; vinorelbine, 9.7 vs 6.3.

Conclusions: Improvements in OS, PFS and ORR with cemiplimab trended consistently with the results for the overall population regardless of IC chemotherapy drug.

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#3334

P11-01 Understanding facilitators and barriers for follow-up after an abnormal cervical cancer-screening exam among women living in remote areas of Romania: a qualitative study

11 - Screening for women difficult to reach

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Background/Objectives: As of 2020 in Europe, Romania has the second highest incidence and mortality rates of cervical cancer, after Montenegro. In efforts to address cervical cancer in the country, the Romanian government established a national cervical cancer-screening programme in 2012. The programme provides free testing as well as free treatment in the event of cervical pre-cancer diagnosis for women 25-64 years old with health insurance who are referred from a programme-registered general practitioner. Participation in screening, re-testing and follow-up of detected precancerous lesions is suboptimal, thus reducing the overall effectiveness of the programme. The overall aim of the study is to examine facilitators and barriers to cervical cancer screening follow-up after an abnormal cervical cancer-screening exam among underserved women living in remote areas of Romania.

Methods: We will conduct an exploratory qualitative study using semi-structured interviews. Data analysis will be based on the thematic analysis outlined by Braun and Clarke. We will use QSR International's NVivo 12 as the qualitative data analysis software for both data management and analysis.

Results: Preliminary findings to be updated. The initial coding framework for our analysis will be inductively derived from the data. In this sense, our approach will include bottom-up development of analytic categories and themes. We will use QSR International's NVivo 12 as the qualitative data analysis software for both data management and analysis.

Conclusions: Study findings will inform recommendations for the Romania national policy for the cervical cancer prevention programme, with a particular focus on underserved women living in remote areas with limited access to health care services.

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#3803

P13-07 Validity of a new urine collection media in stabilizing RNA for HPV-MRNA detection

13 - Self-sampling

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Background/Objectives: Numerous recent studies have recommended the use of urine samples as an alternative to vaginal swabs and cervical samples for HPV DNA detection in regular screening programmes1,2. Urine sample collection is simple and non-invasive when compared to alternative methods that are currently in use

Methods: I In this study, we evaluated two urine preservation media for the detection of HPV mRNA. One of the media, UCM, is included in the Colli-Pee urinary self-sampling device developed for HPV DNA detection (Novosanis). The second medium, UAS, is included in Colli-Pee urine collection device under development for HPV mRNA detection. To evaluate the performance of the two media, a spike RNA from cervical adenocarcinoma (HeLa-S3, ThemoFisher) or combined in vitro transcripts of IC, HPV16, HPV18 and HPV45, prediluted in normal saline (0.9%), was used in the ratios recommended by the manufacturer for each medium. The in vitro transcripts used contain template DNA in addition to the transcribed RNA. Test samples, each containing 20 ng of either HeLa RNA or the in vitro transcribed RNA, were prepared from each medium. To test the capability of these media in preserving RNA and DNA, the test samples were incubated (in triplicate) at different temperatures and for different lengths of time. These include incubations at room temperature (RT) for 48 hr, at RT for 8 days, or at 37°C for 8 hr followed by an overnight incubation at RT. The integrity of RNA and DNA in the samples was assessed by real-time RT-PCR using Papilloplex®HR-HPV mRNA Detection Kit and the obtained Ct-values for the different targets were statistically compared for significant differences.

Results: The UAS medium was found to be good at preserving both RNA and DNA as no significant change in the detected Ct-value of all tested targets in HeLa-S3 cells and in vitro transcribed targets between the fresh samples and those incubated for 48 hr at RT, 8 days at RT or 8 hr at 37°C. The UCM medium which was designed to preserve DNA was found to be good at preserving DNA under all the tested conditions where no significant loss in the amount of detected DNA was observed in any of the tested in vitro transcription samples. This medium, however, was found not suitable for preserving RNA since no RNA could be detected even the samples incubated for 48 hr at RT.

Conclusions: UAS medium is capable of stabilising both RNA and DNA and is potentially suitable for collection of urine samples required for HPV mRNA/DNA detection. UCM medium is suitable for preserving urine samples for DNA detection.

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#3693

P15-02 Association of CßS, p22Phox, NOS3 and GSTM1 genes with cervical cancer or precursor lesions

15 - Molecular markers

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Background/Objectives: HPV is the leading necessary cause of cervical cancer, a malignant tumour that initiates in the cells of the cervix and later may spread to other parts of the body. CβS, p22Phox, NOS3 and GSTM1 are genes involved in several events crucial to tumour formation and biology, such as the body's response to oxidative stress. The purpose of this study was to understand the role of the variants 844Ins68 (CβS), C242T (p22Phox), 27-bp VNTR 4b/a (NOS3) and GSTM1-0/1 (GSTM1) in the development of HPV caused cervical cancer or precursor lesions.

Methods: The genotyping was made by PCR in the CßS and NOS3 genes, by PCR-RFLP in the p22Phox gene and by PCR-multiplex in the GSTM1 gene.

Results: Results show an association of the -/+ genotype of the CßS gene (p = 0.036; OR = 0.219 [0.047-1.018]), the CC genotype of the p22Phox gene (p = 0.012; OR = 2.057 [1.166-3.63]), the 4b4b genotype of the NOS3 gene (p = 0.042; OR = 2.032 [1.019-4.052]) and the GSTM1-1(p = 0.047; OR = 0.594 [0.355-0.994]) of the GSTM1 gene with the disease.

Conclusions: Altogether, results demonstrate the relevance of mechanisms related with ROS formation and oxidative stress response in the onset of cervical cancer or precursor lesions.

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#3384

P26-03 Cervical adenocarcinoma: review of the last 5 years in a tertiary center

26 - Cervical neoplasia

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Background/Objectives: Cervical cancer is a leading cause of mortality among women. In 2020, an estimated 604 000 women were diagnosed with cervical cancer worldwide and about 342 000 women died from the disease. Despite the implementation of screening and vaccination programs against HPV, cervical cancer is still considered a public health problem today. The epidermoid cancers are more prevalent, but the incidence of adenocarcinoma has increased over the past few years, especially in young women. This study aimed to describe the cases of cervical adenocarcinoma in the last 5 years in our center.

Methods: Were review 12 women diagnosed with cervical adenocarcinoma from january 2017 to october 2021.

Results: Were analyzed twelve cases of adenocarcinoma: 4 cases of adenocarcinoma in situ (33,3%) and 8 invasive (66,7%). The average age at diagnosis was 47,3 years (min-max 31-75) with an average age at coital age 17 years. The average number of partners was 2.75 however 4 women did not respond. Regarding the age group, 66.7% were of reproductive age, with 75% of them using hormonal contraception. Regarding personal history, the patients were healthy, except one with a history of drug abuse and HCV infection. Smoking habits were described by 1/3 of the patients and only 8% had complied with the HPV vaccination schedule. Seventy-five percent of patients were referred to the center with altered cytology (ASCUS=4; AGC=3; HSIL=2) and twenty five percent were referred due to abnormal uterine hemorrhage/coitorrhagia. Two of the patients with a final diagnosis of adenocarcinoma invasive reported that it was the first cytology ever performed. HPV typing was performed in only seven patients: in six cases (86%) HPV 16 was present and one (14%) was negative for HPV. On colposcopic examination, grade 1 findings were found in 16% (n=2), grade 2 in 66% (n=8), and frank suspicion of invasion in 16% (n=2). The final histological diagnosis was obtained by directed biopsy in 10 patients and 2 by large loop excision of the transformation zone (LLETZ). Sixty-three percent of invasive adenocarcinomas were diagnosed at stage I of FIGO (IA 2:1, IB1:2;IB3:2); 12.5% in stage II (IIB:1), 12.5% in stage III (IIIC2: 1) and 12.5% in stage IV (IVB: 1). Regarding treatment, two women opted, informedly, for conservative treatment (LLETZ), five (42%) after EZT were submitted to hysterectomy (33% radical hysterectomy with bilateral anexectomy and bilateral pelvic lymphadenectomy and 16% total hysterectomy); three patients underwent chemotherapy plus radiotherapy (CRT) and one patient is currently pregnant (diagnosis at 29 weeks) with indication for CRT after cesarean section.

Conclusions: Although the sample was small, we can gain that the incidence of adenocarcinomas in our unit was slightly higher than the reduction in the literature (31% vs 25%) with a strong association with HPV 18. Thus constituting a real challenge for the clinic, being urgente the need to implemente more studies aimed at facilitating the diagnosis and approach of this entity.

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#3727

P26-04 Efficacy of a multi-ingredient Coriolus versicolor-based vaginal gel in high-risk HPV infected patients: results of 6 different studies

26 - Cervical neoplasia

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Background/Objectives: To evaluate the consistency of the efficacy of a multi-ingredient Coriolus versicolor-based vaginal gel, Papilocare®, on high-risk human papillomavirus (HR-HPV) clearance in 6 different studies.

Methods: Results from 4 independent observational studies (6 month-treatment period with Papilocare®) were compared to results from a randomized, open, parallel, controlled trial (Paloma: NCT04002154) and an observational, multicenter, prospective, one-cohort study (PapilOBS: NCT04199260). Vigo study: Prospective one-cohort. Secondary endpoint (SE), HPV clearance in 25 patients infected by HPV 16 and/or 18. Coruña study: Retrospective one-cohort. Primary endpoint (PE), HPV clearance assessed in 57 medical patients' records. Hospitalet study: Retrospective one-cohort. PE, Composite efficacy variable (patients with normal cytology and/or HPV clearance) in 91 HR-HPV patients. Roma study: Retrospective controlled. PE, HR-HPV clearance in 183 patients. Paloma trial: SE, HR-HPV clearance in 65 patients. PapilOBS study: SE, HR-HPV clearance in 176 patients.

Results: 48% of patients cleared 16-/18 -HPV in Vigo study. 58% of reduction was observed in the number of HR-HPV patients (Coruña) and 72.5% normalized cytology and/or cleared HR-HPV (Hospitalet). 67% HR-HPV clearance was observed (treated group) vs 37.2% (control group), in the Roma study. In the Paloma trial, HR-HPV clearance reached 63% (treated group) vs 40% (control group). 57.4% HR-HPV clearance was observed in the PapilOBS study.

Conclusions: Papilocare® has shown significant consistent rates of efficacy with a 64% of HR-HPV clearance in average in 6 different studies involving 597 patients which reinforce its beneficial effect for HR-HPV patients.

Results in different studies

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#3712

P32-01 Vulvar Condylomata Acuminata: new local synergistic treatments

32 - Genital warts

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Background/Objectives: Condylomata acuminata or genital warts are the clinical expression of low oncogenic risk (No. 6 and 11) human papillomavirus (HPV) infection. Genital infection by HPV is one of the most common sexually transmitted infections. However, condylomata acuminata are not included in surveillance systems in most countries, so worldwide epidemiological data is limited. The lack of a single effective treatment and the high post-treatment relapse rate, as new lesions appear in treated or untreated areas makes the management difficult. We present the clinical case of a young woman, presenting multiple vulvar condylomatous lesions previously evaluated and treated.

Methods: A 26-year-old patient visiting our office in CIMEG MADRID in August 2020 due to presenting multiple vulvar condylomatous lesions that had already been evaluated and treated in a dermatology center using local cryotherapy and sinecatechins (Veregen) ointment twice a day at home; she decided to seek out another medical opinion. In our unit, after adequate physical and colposcopy examination we decided to start local therapy with ErYag Laser (Fotona laser) with a wavelength of 2940nm together with a Coriolus versicolor-based external genital gel as an adjunct to local laser therapy. The gel was prescribed as co-adjuvant treatment and it was administered for 6 weeks at home to help re- hydrate, epithelialize and repair the area. At the end of the 6th week, a second local vulvar laser session was performed, and the Coriolus versicolor-based external genital gel was prescribed as co-adjuvant treatment again for a total of 6 months.

Results: After the 2nd laser session and 42 days of treatment, the patient was re-evaluated and fewer lesions were observed. The last evaluation was performed after 6 months of treatment and no the vulvoscopy was normal and no esions were observed macroscopically. Currently the patient is asymptomatic, with completed healed lesions.

Conclusions: The combination of Laser Therapy with the Coriolus versicolor-based external genital gel was suitable for this patient with a satisfactory evolution, showing total elimination of the lesions and absence of recurrences after 6 months of treatment.

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#3400

P40-02 Motivation for the HPV vaccine uptake among parents of vaccinated children in NOVI SAD (SERBIA): results from the initial findings

40 - Public health

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Background/Objectives: Current estimates indicate that Serbia ranks third in the morbidity rate and fourth in the death rate from cervical cancer in Europe. Every year in Serbia around 634 women die from cervical cancer. The HPV vaccine, has been available in Serbia since 2008, recommended, but not "free of charge". To determine motivation for the HPV vaccination of children, a cross-sectional survey was conducted among parents during November, 2021. Within the project in the City of Novi Sad, the HPV vaccine was offered "free of charge" for children aged 12-18 years, regardless of gender.

Methods: The Institute of Public Health of Vojvodina collected data at the vaccination point in collaboration with the Health Care Centre of Novi Sad, using an anonymous survey questionnaire. The questionnaire consisted of parents' sociodemographic data, age and sex of children and 17 motives (positive parental attitude towards HPV vaccination) as possible reasons for deciding to vaccinate children. Chi-squared test or Fisher's exact test was for categorical and Wilcoxon rank-sum test for nonparametric data and significance levels are considered $p<0.05$.

Results: 136 parents of vaccinated children aged 12-18 participated in the survey. The average age of the parents was 45 years, and 80% were female. The percentage of vaccinated girls in respect to boys was 88%. Out of the total number of vaccinated children, 25% were 15 years old. The strongest motive (29.4%) for vaccination in the entire group was the attitude that "It is better to immunize child than expose them to risk possible infection". Around 26% of parents that were healthcare workers selected answer that strongest motive for vaccination was recommendation from a paediatrician, while parents from other professions selected the affirmation that it is better to immunize child than to expose them to risk of possible HPV infection (24.7%). Also, paediatrician's recommendation was more frequently selected motive among health professionals compared with other professions (78.3% vs 50.7%, $p=0.02$). Recommendation given from friends or family members was motive for 64.4% of parents from other professions compared with 34.8% of health professionals ($p=0.01$). Motive related to the fact that vaccine is "free of charge" during the period of this project was selected in similar percentage by both groups of parents ($p= 0.942$).

Conclusions: This project is ongoing.In order to better understand the main reasons for acceptance of HPV vaccine additional research is needed. Until then, it is crucial to raise awareness of infection consequences and establish public dialogs in media as well as among pediatric professionals.

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#3531

P41-02 Fertility in women with cervical cancer and precancerous lesions in relation to cervical screening: a Swedish nationwide matched-cohort study

41 - Fertility and HPV

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Background/Objectives: Previous studies have shown that HPV infections and cervical treatment are associated with poorer obstetric and neonatal outcomes. It implies that the reproductivity of women with cervical cancer and precancerous lesions might be impaired. However, on the other hand, cervical screening might have potential positive impact on women's fertility through early detection enabling less-aggressive treatments. Using live birth as an indicator of fertility, this study aims to investigate the potential impact of cervical screening on women's fertility.

Methods: We performed a matched-cohort study using the Swedish national population and healthcare registers. Women with cervical precancerous lesions (n=32,614), screen-detected invasive cervical cancer (n=863), and symptom-detected invasive cervical cancer (n=488) were each matched to 5 women without these diseases at the diagnostic date, who have the same birth year and parity (n=169,816). They were followed until they give a live birth or other censored events. Kaplan-Meier and Cox regression analyses were performed.

Results: After adjustment of country of birth and educational level, the hazard ratios (HRs) of giving live birth for women with cervical precancerous lesions, screen-detected cancer, and symptom-detected cancer were 1.14 (95% CI, 1.11 - 1.16), 0.62 (95% CI, 0.52 - 0.73), and 0.16 (95% CI, 0.11 - 0.24), respectively, compared to women without known disease. Among nulliparous women, the corresponding adjusted HRs of giving live birth were 1.24 (95% CI, 1.21 - 1.28), 0.87 (95% CI, 0.69 - 1.10), and 0.20 (95% CI, 0.12 - 0.33), respectively.

Conclusions: Being diagnosed with cervical precancerous lesions through screening and most likely treated is not associated with lower incidence of giving live birth compared to the healthy population. Being diagnosed with invasive cervical cancer through screening therefore undergone less-aggressive treatment is associated with higher incidence of giving live birth compared to being diagnosed symptomatically. These indicate the potential positive impact of cervical screening on women's fertility.

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P06-01 Quadrivalent and 9-valent human papillomavirus vaccine immunogenicity and safety in Indian studies

06 - HPV prophylactic vaccines

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Background/Objectives: Efficacy, immunogenicity, and safety of quadrivalent human papillomavirus (qHPV; HPV6/11/16/18) vaccine and 9-valent HPV (9vHPV; HPV6/11/16/18/31/33/45/52/58) vaccine have been demonstrated. We report outcomes in Indian participants from three vaccine clinical trials. Objectives: Evaluate qHPV vaccine immunogenicity and safety in Indian girls (9-15 years) from an open-label, single-arm study (V501-029 [NCT00380367]; N=110), qHPV vaccine safety in Indian females (9-45 years) from a post-marketing safety surveillance study (V501-125; N=188), and 9vHPV vaccine immunogenicity and safety in a subgroup (n=225) of Indian girls (9-15 years), boys (9-15 years), and women (16-26 years) from a global study (V503-002 [NCT00943722]).

Methods: In V501-029 and V503-002, HPV vaccines were administered as three doses (Day 1, Month 2, Month 6). Vaccine HPV-type serum antibodies (Day 1, Month 7) were tested using competitive Luminex immunoassay; immunogenicity was analyzed in the per-protocol population. Injection-site adverse events (AEs), systemic AEs, and serious AEs (SAEs) were assessed. In V501-125, participants received qHPV vaccine during routine care and were actively surveilled for SAEs occurring within 30 days post-qHPV vaccination.

Results: Robust anti-HPV 6, 11, 16, and 18 responses were induced in V501-029; ≥97% of participants seroconverted at Month 7 for each HPV type. In V503-002, anti-HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 responses were robust; ≥98% of Indian participants seroconverted at Month 7 for each HPV type. In the V501-029 study, 58% of participants reported AEs (injection-site, 46%; systemic, 32%; mostly mild/moderate in intensity). In the V503-002 study, 70%, 58%, and 56% of Indian girls, boys, and women, respectively, reported AEs (injection-site, 56%-66%; systemic, 13%-28%; mostly mild/moderate in intensity). Across these two studies, no deaths, vaccine-related SAEs, or discontinuations due to AEs were reported. In V501-125, no SAE was reported.

Conclusions: In Indian populations, qHPV and 9vHPV vaccines elicited robust antibody responses and were generally well tolerated.

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#3413

P14-05 Prevalence and genotype distribution of high-risk HPV infection in ten-year period in Vojvodina, Serbia

14 - Genotyping

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Background/Objectives: Human papillomavirus (HPV) infection is the leading risk factor for cervical cancer development. Among women in Serbia, cervical cancer is the 5th most frequent cancer and the 2nd most frequent cancer in women 15-44 years of age. The incidence rate of cervical cancer in Serbia is approximately twice as high as the average incidence rate in Europe (10.7/100,000). This study aimed to determine the prevalence and distribution of different high-risk (HR) HPV genotypes according to age among women in Vojvodina, northern province of Serbia.

Methods: From January 2012 to November 2021, a total of 7974 women from 14 to 80 years of age, with an abnormal Pap test and normal cytology results with suspicious colposcopic findings, were included in the study. Extraction of HPV DNA was performed using SaMag STD DNA Extraction Kit on SaMag-12 Automatic Nucleic Acids Extraction System. Twelve HR HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59) were determined by the HPV High Risk Typing Real-TM kit on the SaCycler-96 Real Time PCR System.

Results: The overall prevalence of HR HPV was 43.3% (3455/7974). We observed that 62% of women had a single infection, while 38% had multiple HR HPV infections. The results showed that members of the alpha-9 HPV species, particularly HPV 16 (25.2%), HPV 31 (18.9%), and HPV 39 (6.9%), were the most prevalent HPV genotypes in our province. Additionally, 6.9% of the single infections were caused by HPV 51, a member of the alpha-5 HPV species. Other HR HPV genotypes were found in 42.1% of the single infections. HR HPV 16 was the most prevalent genotype overall, 30.2% (1042/3455). The age-specific distribution of single HR HPV infection was as follows: 14-20 (57.4%), 21-30 (55.0%), 31-40 (45.8%), 41-50 (37.6%), 51-60 (34.3%), and the older than 61 years (44.1%).

Conclusions: The high prevalence and presence of vaccine HPV types, particularly type 16, indicates the need for a large-scale immunization program in our province in order to decrease the prevalence of HPV infections and future cervical cancer incidence. Determination of the contribution of HR HPV genotypes causing cervical cancerogenesis is valuable as a starting point for the implementation of a vaccination program and as a critical step in the algorithm of cancer diagnosis and treatment of individual patients.

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#3287

P08- 04 Design and objective of Glucanvir study: efficacy of an intravaginal treatment with carboxymethyl-ß-glucan and polycarbophil in high risk-HPV clearance

08 - Immunotherapy - Immuno-oncology - New treatments

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Background/Objectives: Human papillomavirus (HPV) infection represents a significant source of morbidity and mortality worldwide. High-risk oncogenic HPVs cause 99.7% of cervical cancers. Most of these infections are transitory and only if they are persistent and caused by a high-risk oncogenic HPV are they an important risk factor for the development of cervical intraepithelial lesions and invasive cervical cancer. Immunity plays a key factor in eliminating HPV infection. HPV evasion of these immune defense mechanisms is critical for the persistence of the infection and leads to the development of preneoplastic lesions and ultimately to cervical cancer. Medical treatments represents a therapeutic strategy to avoid the evasion mechanisms of HPV. One of these most promising treatments is beta-glucans that seem capable of affecting the course of HPV infection.

Methods: monocentric, interventional, longitudinal, prospective, open label trial with a control group with randomized, consecutive recruitment for each group, to evaluate the safety and efficacy of an intravaginal treatment with carboxymethyl-ß-glucan and polycarbophil in the learance of High-risk Human Papillomavirus Infection in women without cytological alterations. n=200.Unvaccinated HPV+ women aged 30-40 with normal cytology were randomized into 2 groups: A) Carboxymethyl-ß-glucan (Colpofix®) 1 application / day x 20 days, rest 10. Repeat 20 x 3 cycles. B) Control group: no treatment (usual clinical practice).

Results: There are more than 6000 studies that have described the effects of glucans. Recent studies focusing on their influence on cytotoxic and helper T cells, antigen presenting cells (APCs), inflammatory pathways, and oxidative burst (using reactive oxygen species to kill cells) have revealed that they may also have some anti-cancer properties. Carboxymethyl ß-glucan gel treatment has been studied in 4 different studies on affected individuals by CIN1 or/and HPV+. These case-control studies demonstrated that it has an anti-cervical cancer role in CIN1 regression versus wait and see statistically significant. These studies suggested that, in addition to the anticancer effects of beta-glucans, they also have some effects on infection by HPV, the main cause of cervical cancer.

Conclusions: Data from this ongoing study will indicate if ß-glucans has a therapeutic effect upon the clearance of HPV infection on the different genotypes. Given a new approach different from wait and see and would represent a significant advancement in the management of HPV positive patients.

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P15-03 Transcriptome analysis in vulvar squamous cell cancer

15 - Molecular markers

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Background/Objectives: To date, therapeutic strategies in vulvar squamous cell carcinoma (VSCC) are lacking molecular pathological information and targeted therapy hasn´t been approved in the treatment of VSCC, yet. Two etiological pathways are widely accepted: HPV induced vs. HPV independent, associated with chronic skin disease, often harboring TP53 mutations (mut). The aim of this analysis was to analyze RNA expression patterns for subtype stratification on VSCC samples that can be integrated in to the previously performed whole exome sequencing data for detection of prognostic markers and potential therapeutic targets.

Methods: We performed multiplex gene expression analysis (NanoString) with 770 genes, in 24 prior next generation sequenced samples. Integrative data analysis was performed

Results: 98 genes were differentially expressed in TP53mut vs. HPV+ VSCC, in the TP53mut cohort, 56 genes were upregulated and 42 were downregulated in comparison to HPV+ tumors. In the TP53mut subgroup Dickkopf-1 (DKK1: log2 FC: 3.69) and cell cycle regulators CCND1 (log2FC: 2.68), CCND2 (log2FC: 1.82), CCNA1 (log2FC: 3.22) and CDK6 (log2FC: 2.25) were observed to be highly upregulated compared to HPV+ VSCC. Within the TP53mutgroup a distinct cluster was identified which correlated to a significant worse overall survival (p=0.017).In the HPV+ subgroup genes involved in G1/S transition like CDKN2A, CCNE2, CDKN1C, CDKN2C, as well as S/G2 and G2/M phase regulators CDK2, Wee1, CDC25C, CDC7 and mini chromosome maintenance complex genes (MCM2/4/5/7) were particularly often upregulated. Also, genes involved in DNA repair like BRCA2, BRIP1, FANCA, FANCC, RFC4, PCNA, POLE2, RFC3, and EZH2 were upregulated compared to TP53mut tumors.None of the HPV+ tumors showed upregulation of cell cycle regulator cyclin D1, this were exclusively upregulated in TP53mut tumors.

Conclusions: RNA expression profiles show distinct regulation of selective candidate genes with regard to the known VSCC subtypes and potentially enable further subclassification in the TP53mut group. For HPV+ VSCC upregulation of cell cycle regulators was predominantly shown.

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#3932

P02-01 HPV E6/E7mRNA association with Interleukin - 10 592C/A variant in group of Macedonian women

02 - Viral and molecular biology

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Background/Objectives: Interleukin 10 (IL-10) is an immunosuppressive cytokine and its genetic variant could have an indirect impact on viral biology and HPV E6/E7 mRNA expression as well. In the study, we evaluate the association between IL10 -592 C/A polymorphism and HPV E6/E7 mRNA expression in a group of women from R North Macedonia.

Methods: Using commertial tests we analyzed 272 women's cervical samples for HPV E6/E7 mRNA and HPV DNA presence respectively. The cases were stratified into three groups: double-positive (n=108, positive for both tests), negative (n=51, negative for HPV E6/E7 mRNA and HPV DNA positive), and the control group (n=113, negative for both tests). The IL10-592 C/A polymorphism was analyzed using polymerase chain reaction-restriction fragment length polymorphism.

Results: The CC genotype and the C allele frequencies of IL10-592C/A were significantly higher in double-positive (59.3% and 78.2%) compared to negative group (39.2% and 65.7%), (p=0.01, CI=0.44;0.22-0.87- dominant model; and p=0.01, CI =0.53; 0.3-0.8) respectively and compared to negative and control groups together

Conclusions: The CC genotype and C allele of IL10-592 showed to be associated with HPV E6/E7 mRNA but not with HPV DNA positivity, which could mean this polymorphism could affect the course of the infection only after HPV onset and it is not associated with susceptibility to HPV.