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# SASGO Abstracts 2023: Poster Presentation

## Symptom triad of primary cervical rhabdomyosarcomas as seen in a Nigerian tertiary hospital

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**Aim:** Carcinomas of the cervix, mostly squamous cells, are the most frequent histotypes of cervical cancers. Primary cervical rhabdomyosarcomas (PCR), on the other hand, is extremely rare with no standard management protocol and limited knowledge of its clinical presentation, pathology, and treatment options. We aim to conduct a retrospective review of all confirmed cases at our institution in the last 12 years.

**Methods:** Case notes and pathology reports of all women presenting with PCR from 1 January 2011 to 31 March 2023 were reviewed. Unconfirmed and referred cases were excluded.

**Results:** Only nine cases of PCR were found (all embryonal variants), under the period of investigation. The median age at presentation was 19 (range 3–40) years with three (33.3%) patients being children (< 18 years) at diagnosis. All patients presented with at least one protrusion per vaginam, bleeding, and discharge while women of reproductive age presented with procidentia and a characteristic slimy, foul-smelling discharge. The median duration of symptoms before hospital presentation was one month (four days to two months). Two (22%) patients had clinical staging using the Intergroup Rhabdomyosarcoma Study Group Clinical Classification System documented. Four patients were discussed at the multidisciplinary team meeting. Only two patients had immunohistochemistry done. Surgery was the most common treatment offered in eight (88.9%) cases combined with chemotherapy in half of them. One patient had radiotherapy. One patient had no form of treatment. In April 2023 (with a median follow-up of 36 months), six patients were alive with no clinical evidence of disease recurrence, one had died of disease, one died a maternal death, and the outcome of one patient could not be ascertained.

**Conclusion:** The increased frequency observed in the second half, non-staging of the tumour, and inadequate treatment modalities all call for concern. The triad of cervical mass with procidentia, slimy mucoid discharge, and vaginal bleeding in women of reproductive age should heighten the clinical suspicion for PCR. The prognosis/outcome and survival rate seem to be favourable.

## Patterns of protection against HPV types 5–10 years after bivalent and quadrivalent HPV vaccination

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**Aim:** Vaccine implementation trials VACCS1 and VACCS2 demonstrated successful school-based human papillomavirus (HPV) vaccination combined with maternal screening in South Africa. The current study is a follow-up trial, performed 5–10 years later, aiming to evaluate genital HPV deoxyribonucleic acid (DNA) status, self-reported sexual behaviour, and attitudes. Here we report and compare genital type-specific HPV infection rates of unvaccinated girls and vaccine recipients of one, two, or three doses of either the 2-valent (2vHPV) or 4-valent HPV (4vHPV) vaccine.

**Methods:** Previous invitees to VACCS1/VACCS2 were enrolled on the current trial. Self-collected vulvovaginal swab specimens were tested for 19 high-risk HPV (hrHPV) and 9 low-risk HPV (lrHPV) genotypes. The phylogenetic classification was done for hrHPV as α-9 (HPV16, 31, 35, 33, 58, 52) and α-7 (HPV18, 45, 59, 39, 68, 70), and for lrHPV type α-10 (HPV6, 11, 44, 40). Vaccine protection was defined per the World Health Organization (WHO) position paper in 2014.

**Results:** A total of 111 participants were enrolled. The mean age was 19.5 (range 16–22) years; 58 (52.3%) received 2vHPV, 44 (39.6%) received 4vHPV, and nine (8.1%) were unvaccinated. The mean age at vaccination was 11.0 (range 9–16) years. The majority, 75 (67.6%), were fully protected while 36 (32.4%) were insufficiently vaccinated/unvaccinated. HPV DNA was positive in 53 (47.7%) vulvovaginal samples, no HPV16/18 occurred, and five cases of HPV6 infection occurred – all in 2vHPV recipients. In 2vHPV recipients, 52 (89.7%) were α-9-negative, five (8.6%) had an infection with a single α-9 type, and one (1.7%) had multiple types; 48 (82.8%) were α-7-negative, eight (13.8%) had a single type, and two (3.4%) had multiple α-7 types. In 4vHPV recipients, 32 (72.7%) were α-9-negative, 12 (27.3%) had a single α-9 type, and 0% had multiple α-9 infections; 36 (81.8%) were α-7-negative, six (13.6%) had a single α-7 type, and two (4.5%) had multiple α-7 infections. Fully protected participants showed a lower positivity for α-9 and α-7 types than insufficiently vaccinated participants [12.0% (9/75) vs. 27.8% (10/36); 16.0% (12/75) vs. 22.2% (8/36)]. The prevalence of vaccine-targeted hrHPV types HPV16 and HPV18 in both 2vHPV and 4vHPV were 0%, while a cohort of

unvaccinated women (from a cervical cancer screening study) showed a 15% (21/140) HPV16 and 5% (7/140) HPV18 prevalence.

**Conclusion:** The high prevalence of HPV infection confirms early high-risk sexual behaviour. The absence of all vaccine-targeted types in vaccinated women is reassuring. Our data suggest better cross-protection against non-vaccine α-9 type for 2vHPV than 4vHPV, and cross-protection against both non-vaccine α-7 and α-9 types for fully vaccinated women compared with unprotected women.

## Histology results of women presenting with large warty vulva lesions

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**Aim:** Lower genital tract lesions are commonly found in South African women, especially in human immunodeficiency virus (HIV) infected patients. Here we describe the histological results of wart-like vulva lesions, clinically classified as Condylomata acuminata (C. acuminata), pre-invasive and invasive squamous lesions.

**Methods:** Women with large vulvovaginal warty lesions were recruited. At the first visit, a clinical examination was performed and biopsies were collected for histopathology. The treatment type was based on the size, number of lesions at the time of the treatment visit, and previous biopsy reports. Histopathology results of excised lesions were collected at the treatment visit.

**Results:** Included were 49 participants with a mean age of 34.2 years; 45 (91.8%) were HIV-positive. The worst grade histology of biopsies taken at the first visit showed C. acuminata in 34 (69.4%) women, vulvar intraepithelial neoplasia 1 (VIN1) in one (2.0%) case, VIN2 in seven (14.3%), VIN3 in four (8.2%), squamous cancer in two (4.1%), and one case of seborrheic keratosis. Lesions were removed surgically and histopathology results were collected in 40 women. The worst of the first-visit biopsy or treatment-visit result was regarded as the final histological diagnosis; these showed C. acuminata in 23 (46.9%), VIN1 in two (4.1%), VIN2 in another two (4.1%), VIN3 in 17 (34.7%), and squamous cancer in five (10.2%) women. All squamous cancer cases were HIV-positive women. In the four HIV-negative participants, the worst histology was VIN3 in one participant, while C. acuminata was diagnosed in the remaining three women.

**Conclusion:** Only 47% of women had C. acuminata as the worst diagnosis on histology. The histology of warty lesions that clinically resemble C. acuminata is essential to diagnose pre-invasive lesions or even invasive cancer. Among South African women who clinically and histologically have genital warts, pre-invasive and invasive lesions commonly coexist. It is imperative to obtain an excision biopsy of any suspicious warty vulva lesions in the era of HIV.

## The diagnostic accuracy of colposcopy for CIN2+ among HIV-positive and negative South African women

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**Aim:** We evaluated the performance of Reid's Colposcopic Index (RCI) versus colposcopic impression (CI) to diagnose histologically confirmed high-grade cervical intraepithelial neoplasia (CIN2+) lesions.

**Methods:** This is a subset analysis of data collected during the DiaVACCS trial, a cervical cancer screening project. The main study included 1 104 participants (mean age 41.26, range 25–65 years); 465 were positive for human immunodeficiency virus (HIV) and 639 were HIV-negative. The disease profile of the main study showed positive cytology (≥ atypical squamous cells of undetermined significance [ASC-US]) in 39.9% of HIV-positive versus 17.0% HIV-negative women and high-risk human papillomavirus (HPV) deoxyribonucleic acid (DNA) in 41.2% versus 19.6%. The histological diagnosis of CIN2+ was suspected in 44.7% versus 23.5% and CIN3+ in 23.3% versus 10.2%, after adjustment for verification bias. Invasive cancer was diagnosed in 15 women, while verification bias adjustment suggested 20 cases (1.8% of the study population). In the current sub-analysis, RCI was calculated as negative (RCI 0–2), low-grade (RCI 3–4), and high-grade (RCI 5 +). CI was logged as negative, low-grade/uncertain, or high-grade. Directed punch biopsies (suspicious lesions) or blind punch biopsies (negative lesions) were taken. The worst biopsy or treatment result was regarded as the final histological diagnosis.

**Results:** This subset included 725 participants, the mean age was 40.7 years, and 46.8% (339/725) were HIV-positive and 53.2% (386/725) HIV-negative. In HIV-positive and negative groups, the RCI was high-grade in 35.1% (119/339) and 11.1% (43/386) ($p < 0.0001$), respectively. Similarly in HIV-positive and negative women, CI was high-grade in 30.1% (102/339) and 9.1% (35/386) ($p < 0.0001$), respectively. Histology confirmed CIN2+ in 49.9% (169/339) HIV-positive and 29.5% (114/386) HIV-negative women ($p < 0.0001$). CIN3+ was diagnosed in 26.8% (91/339) HIV-positive and 13.0% (50/386) HIV-negative participants ($p < 0.001$). For RCI to predict CIN2+ in the HIV-positive cohort, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 80.6%, 56.9%, 64.6%, and 75.0%; and for CI 82.4%, 56.3%, 61.8%, and 76.6%, respectively. For RCI in the HIV-negative cohort, these figures were 63.0%, 72.4%, 49.0%, and 82.3%; and for CI 63.9%, 70.2%, 47.5%, and 82.2%, respectively.

**Conclusion:** Colposcopy test performance differs significantly between HIV-positive and negative cohorts. The validity of colposcopy to identify possible CIN2 for biopsy is confirmed in HIV-positive women. Among HIV-negative women, the sensitivity of colposcopy is relatively low and blind biopsies are

warranted. RCI and CI performed equally in both HIV-positive and negative cohorts. In this study, using the RCI scoring system did not contribute significantly to the accuracy of predicting pre-invasive lesions.

## Screening for Lynch syndrome in patients with endometrial cancer presenting at the University of Pretoria Academic Hospitals

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**Aim:** The aim was to screen for Lynch syndrome in patients with endometrial cancer through immunohistochemistry (IHC) staining for the mismatch repair (MMR) proteins for MLH1, MSH2, MSH6, and PMS2.

**Methods:** Following ethical clearance, 163/2 019 newly diagnosed patients with endometrial cancer undergoing surgery at Kalafong and Steve Biko Academic Hospitals were recruited. Patients underwent surgical staging and their specimens were processed by the National Health Laboratory Service (NHLS). Tumour blocks were obtained from the uterine specimens and slides were prepared, which underwent staining for the MMR proteins with FLEX MoAHu MLH-1, FLEX MoAHu MSH-2, FLEX MoAHu MSH-6, and FLEX MoAHu PMS-2.

**Results: Over two years** (June 2019 to May 2021) 75 patients were recruited into the study. The average age was 68 years, with the youngest being 35 and the oldest 93. Of the participants, 88% were African, 11% Caucasian, and 1% Asian. The most common histology tumour types were endometrioid (48%) followed by carcinosarcoma (17%). The other histological types were serous (19%), adenosarcoma (5%), clear cell (4%), sarcomas (4%), and mixed (3%). Of the patients, 31 had all four proteins staining positive on IHC (MLH1+, PMS2+, MSH2+, MSH6+) followed by 37 patients who had negative staining of the MLH1 and PMS2 proteins only (MLH1-, PMS2-, MSH2+, MSH6+). One patient stained negative for the PMS2 protein only (MLH1+, PMS2-, MSH2+, MSH6+). One patient stained negative for MSH2 and MSH6 proteins (MLH1+, PMS2+, MSH2 -, MSH6-). Two patients stained positive for the MSH6 protein only (MLH1-, PMS2-, MSH2-, MSH6+), whilst three patients had all four proteins staining negative (MLH1-, PMS2-, MSH2-, MSH6-).

**Conclusion:** Patients with the presence of all four proteins had no IHC evidence of an MMR deficiency and needed no further investigation. Patients who had a loss of MHL1 and PMS2 proteins only, loss of all four proteins (MLH1-, PMS2-, MSH2-, MSH6-), and loss of three proteins (MLH1-, PMS2-, MSH2-, MSH6+) needed further testing for MLH1 promoter hypermethylation. Only those with absent MHL1 promoter hypermethylation were considered at risk of Lynch syndrome and referred for genetic testing. One patient who stained negative for the PMS2 protein only and the other who stained negative for both the MSH2 and MSH6 proteins screened positive for Lynch syndrome and were referred for genetic testing.

## Molar pregnancy: a 15-year experience at a single tertiary institution

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**Aim:** This descriptive study provides a detailed analysis of all patients diagnosed with molar pregnancy at the Groote Schuur Hospital (GSH) from January 2004 to December 2019.

**Methods:** This was a retrospective descriptive study of all women who were referred and followed up at the molar clinic at GSH with confirmed histological diagnosis of molar pregnancy from 2004 to 2019. Subjects were identified from the molar clinic register and folders were retrieved for those meeting the inclusion criteria. Analysis was done by simple frequencies and rates using Statistical Package for the Social Sciences (SPSS) software. Subgroup analyses were performed by chi-square and t-tests.

**Results:** There were 554 057 deliveries and 235 cases of molar pregnancies during the period. The incidence of molar pregnancy was 0.42/1 000 deliveries and that of persistent trophoblastic disease was 0.03/1 000 deliveries. Women aged 20–40 years and multiparous women constituted 78.7% and 59.8% of patients, respectively. Most patients (51.3%) were diagnosed in their second trimester. The most common presenting complaint was vaginal bleeding (37.4%) and the most common complication was hyperthyroidism (16.6%). Of the patients, 26 (11.2%) required a blood transfusion, 10 patients (4.2%) required a second evacuation, and only four patients (1.7%) required a hysterectomy due to excessive haemorrhage. Patients with molar pregnancy normalised their human chorionic gonadotropin (hCG) at 12 weeks post-evacuation. There were 47 cases of persistent disease, of which 42 cases were referred for chemotherapy. The remaining five cases did not require chemotherapy as they achieved spontaneous regression after the second evacuation. Suction evacuation was performed in 97.4% of cases. Regarding follow-up, 44.3% of patients defaulted post-evacuation surveillance and care.

**Conclusion:** As the incidence of molar pregnancy in our centre continues to decline, we must take the necessary steps to improve the follow-up protocols for patients with this condition. Doing so will avoid a loss to follow-up. The majority of our patients have uncomplicated disease. Telemedicine or early down-referral once hCG normalises seems to be a safe and reasonable compromise as our study proves that malignant sequelae are low and that follow-up programs for these patients are resource-intensive and place an undue economic, social, and emotional burden on them.

## Cervical cancer patient sample biobanking optimisation towards drug sensitivity screening with a HTS platform in South Africa

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**Aim:** Cervical cancer (CvCa) is the fourth most common cancer worldwide, occurring more frequently in low- and middle-income countries (LMIC) such as South Africa where it appears to be in second position after breast cancer. The standard of care for patients with advanced CvCa includes platinum-based chemotherapy and platinum resistance is one of the key factors for the lower survival rates in gynaecological cancers. Due to the high heterogeneity between cancers, individual and precise therapy is of great importance. We aim to obtain primary patient samples for biobanking from collaborating with state cancer clinics for use in a drug sensitivity screening pipeline developed at the Council for Scientific and Industrial Research (CSIR) for CvCa patients who have relapsed or are resistant to therapy.

**Methods:** The HeLa cell line (derived from human CvCa) was used to screen drug sensitivity to bleomycin sulfate, metformin, mitomycin C, and delavirdine mesylate printed to 96 well plates ranging from 1 000 nm to 1 nm in triplicate. A 0.1% dimethyl sulfoxide (DMSO) was used as the negative control and 100 µm benzethonium chloride as the positive control with cells seeded at 15 000 cells/well into the 96 well plates. Dose-response data from the enzymatic cell viability assay was measured with PrestoBlue and showed consistency following the incubation of the cancerous cell line with the drugs for 72 hours. Fluorescence readings were used to determine relative cell viability and the readings were normalised for benzethonium chloride.

**Results:** A drug sensitivity score (DSS) < 20 was considered as low sensitivity, 20–40 moderate, and > 40 highly sensitive. Therefore, HeLa was the most sensitive to mitomycin, a chemotherapeutic deoxyribonucleic acid (DNA) alkylating agent that selectively inhibits the synthesis of DNA.

**Conclusion:** We found the platform would apply to primary patient CvCa cells and the future aim is to ensure quality patient samples are biobanked for use with the HTS drug-screening pipeline to characterise tumour heterogeneity that can provide cancer patient benefits to those who have exhausted all potential, standard treatments. Preliminary data on the cancer cell lines indicate that this platform will be invaluable to clinicians.

## Evaluation of the Medically Necessary Time Sensitive triage score during and beyond the local COVID-19 pandemic at a tertiary hospital in Pretoria, South Africa

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**Aim:** This study aimed to evaluate and describe the Medically Necessary Time Sensitive (MeNTS) scoring system in triaging gynaecological oncology surgery during and beyond the COVID-19 pandemic.

**Methods:** This was a retrospective, cross-sectional study including 209 patients who either had surgery (151) or were postponed (58) between 26 March and 30 September 2020 at an academic hospital in South Africa. The MeNTS score was used to independently score each patient three times by two observers.

**Results:** The mean age of the participants was 46.6 ± 15 years and the cumulative mean MeNTS score was 51.0 ± 5.1. Over two-thirds of the cases had surgery. There was no significant difference between the first and second observers' cumulative scores (51.0 vs. 51.1, $p = 0.77$). The cumulative score among those who had surgery was significantly lower than for those whose surgeries were postponed (49.8 vs. 54.1, $p < 0.0001$). The intra-observer and inter-observer reliability were 0.78 and 0.74, respectively. After adjusting for confounding variables, those with low MeNTS scores were about five times more likely to have surgery than those with high scores (Adj. OR = 4.67, 95% CI: 1.92–11.4, $p < 0.001$). Patients with malignant diagnoses were also five times more likely to be operated on than those with benign diagnoses (Adj. OR = 5.03, 95% CI: 1.73–14.6, $p < 0.001$). The area under the curve (AUC) was 0.85, suggesting an excellent discriminatory power between those who were operated and those who were postponed.

**Conclusion:** The study provided some insight into the potential usefulness of the MeNTS score in prioritising patients for surgery in the gynaecological oncology subspecialty. The score performed well across a range of gynaecological conditions and procedures with good intra- and inter-observer consistency and reliability. This is a prioritisation tool that is dynamically adaptable to accommodate changes in resource availability and operating theatre capacity.

## Extended genotyping as triage of HPV-positive screened women in low- to middle-income countries

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**Introduction:** Cervix cancer screening with human papillomavirus (HPV) testing is widely accepted. The ideal triage test of screen-positive women should identify those at the highest risk of high-grade cervical intraepithelial neoplasia (CIN2+) and avoid overtreatment of those with lesions (< CIN2).

We evaluated extended genotyping on the Xpert® HPV platform as a triage test.

**Methods:** A total of 1 063 women, aged 25–65 years, with no screening in the preceding five years, were screened and genotyped with an Xpert® HPV test. The 14 targeted HPV types are detected in five fluorescent channels: HPV16, HPV18/45, HPV31/33/35/52/58, HPV51/59, and HPV39/56/66/68. Biopsies were performed on all HPV-positive women.

**Results:** A total of 454 participants were positive for human immunodeficiency virus (HIV), women living with HIV (WLWH), and 609 were HIV-negative (Table I). The overall HPV prevalence was 34.0%. The prevalence was significantly higher in WLWH compared to HIV-negative women (48.9% vs. 22.8%). This was consistent across all channels. CIN2+ prevalence among all participants was 32.74% ($n$ = 348), 44.93% ($n$ = 204) among WLWH, and 23.65% ($n$ = 144) among HIV-negative participants (Table II). The absolute risk (PPV) of CIN2+ for channels 1 and 2, channel 3, and channels 4 and 5 were 81.12%, 62.50%, and 30.77%, respectively. The corresponding PPV for WLWH were 87.10%, 68.97%, and 31.03%, respectively; and for HIV-negative women 70.00%, 51.02%, and 30.43%, respectively.

**Conclusion:** Extended genotyping identified women who tested positive in the first 3 channels to be at the highest risk for CIN2+. These women could be directly referred for treatment. Women testing positive for channels 4 and 5 should either be subjected to a second triage test or followed up.

**Table I:** GeneXpert HPV results

| | WLWH ($n$ = 454) | | HIV-negative (or unknown) ($n$ = 609) | | $p$-value | Total ($n$ = 1 063) |
|---|---|---|---|---|---|---|
| | $n$ | % | $n$ | % | | |
| Any HR-HPV-positive | 222 | 48.9 | 139 | 22.8 | $p < 0.0001$ | 361 (33.96%) |
| HPV 16 | 47 | 10.4 | 25 | 4.1 | $p < 0.0001$ | 72 (6.77%) |
| HPV 18/45 | 56 | 12.3 | 25 | 4.1 | $p < 0.0001$ | 81 (7.61%) |
| HPV 31/33/35/52/58 | 130 | 28.6 | 61 | 10.0 | $p < 0.0001$ | 191 (17.96%) |
| HPV 51/59 | 31 | 6.8 | 17 | 2.8 | $p = 0.0019$ | 48 (4.51%) |
| HPV 39/56/66/68 | 46 | 10.1 | 18 | 3.0 | $p < 0.0001$ | 64 (6.02) |
| Invalid | 13 | 2.9 | 17 | 2.8 | $p = 0.9227$ | 30 (2.82%) |
| HR-HPV-negative | 232 | 51.1 | 470 | 77.2 | $p < 0.0001$ | 702 (66.03%) |

**Table II:** Performance of extended genotyping for the detection of CIN2+ lesions

| | PPV % | NPV % | Positive likelihood ratio | Negative likelihood ratio |
|---|---|---|---|---|
| **All women ($n$ = 1063)** | | | | |
| HPV 16 & 18/45 | 81.12 | 74.78 | 8.25 | 0.70 |
| HPV 31/33/35/52/58 | 62.50 | 71.63 | 3.43 | 0.82 |
| HPV 51/59 & 39/56/66/68 | 30.77 | 67.16 | 1 | 1 |
| All HR-HPV | 65.56 | 82.10 | 3.88 | 0.45 |
| **HIV-negative or unknown ($n$ = 609)** | | | | |
| HPV 16 & 18/45 | 70.00 | 80.50 | 8.0 | 0.78 |
| HPV 31/33/35/52/58 | 51.02 | 78.75 | 3.4 | 0.87 |
| HPV 51/59 & 39/56/66/68 | 30.43 | 76.62 | 1.7 | 0.98 |
| All HR-HPV | 54.92 | 84.19 | 3.92 | 0.60 |
| **WLWH ($n$ = 454)** | | | | |
| HPV 16 & 18/45 | 87.10 | 65.93 | 13.3 | 0.62 |
| HPV 31/33/35/52/58 | 68.97 | 60.76 | 2.6 | 0.80 |
| HPV 51/59 & 39/56/66/68 | 31.03 | 54.12 | 0.5 | 1.04 |
| All HR-HPV | 71.77 | 77.96 | 3.08 | 0.34 |