

Il percorso sulla diagnosi del carcinoma anale

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Standardized Incidence Ratio (SIR) of AIDS-defining cancers in 99.309 pts with HIV/AIDS from French registry-linkage study in different cART periods (mean Follow-up 6.9 yrs)

Hleyhel M. et al. CID 2013

Cancer	Pre-cART (1992-96) SIR (95%CI)	Early cART (1997-2000) SIR (95%CI)	Intermediate (2001-2004) SIR (95%CI)	Late cART (2005-2009) SIR (95%CI)
KS All pts	787.0 (754-821)	388.1 (353 -425.)	408.6 (370-451)	304.5 (274-338)
MSM	1399.9 (1334 -1467)	534.5 (476-599)	531.6 (468-602)	414.1 (365-474)
NHL	116.7 (110-124)	33.6 (31-37)	15.4 (14-17)	9.1 (8-10)
Cervical cancer	12.2 (9-17)	9.3 (7-12)	5.4 (4-8)	5.4 (4-7)

M. Hleyhel et al. The risk for all AIDS-cancers continued to fall, including Kaposi's sarcoma and cervical cancer, but it remained higher than in the general population in late cART period.

Standardized Incidence Ratio (SIR) of NADCs in people with HIV/AIDS from registry-linkage studies in the cART era

Cancer	Grulich (2007) SIR (95%CI)	Engels (2008) SIR (95%CI)	Dal Maso (2009) SIR (95%CI)	Franceschi (2010) SIR (95%CI)
All NADCs		1.9 (1.8-2.1)		3.0 (2.6-3.6)
Hodgkin's lymphoma	11.0 (8.4-14.4)	6.7 (4.5-9.5)	21 (15-28)	28 (15-48)
Anal cancer	29 (22-38)	9.1 (5.1-15)	44 (22-79)	50 (18-109)
Liver cancer	5.2 (3.3-8.2)	3.1 (1.7-5.2)	6.4 (3.7-10.5)	6.1 (1.9-14.3)
Lung cancer	2.7 (1.9-3.9)	2.6 (2.1-3.2)	4.1 (2.9-5.5)	2.6 (1.3-4.6)

Cancer Trends among HIV and General Population (USA 1996-2010)

Age groups >50 yrs : 13% (1996-2000) vs 27% (2001-2010)

Robbins H.A et al. AIDS 2015

Non-AIDS-defining Cancer	Adjusted*-HIV Trend Annual changes % (95%CI)	General Population Trend Annual changes % (95%CI)
Anus	+ 3.4 (0.8,to 5.9)	+ 3.3 (1.4 -5.2)
Liver	+ 6.6 (2.7-10.7)	+ 5.6 (4.6 - 6.6)
Prostate	+ 2.9 (-0.3-6.3)	+ 0.1 (-0.2-0.3)
Hodgkin's Lymphoma	- 3.4 (-6.0,-0.7)	- 0.1 (-1.2-1.1)
Lung cancer	- 6.8 (-8.5- 5.0)	- 3.2 (-3.5-2.8)
Female Breast	- 1.6 (-5.6-2.6)	- 0.8 (-1.2,-0.5)
Colorectum	- 0.9 (-4.2-2,5)	- 0.7 (-1.1,-0.3)

*adjusted for registry, age, race/ethnicity, sex, HIV risk group, HIV/AIDS relative time

Summary to Contributions to Cancer Trends among HIV-infected Population (USA 1996-2010)

Robbins H.A et al. AIDS 2015

Cancer	Cancer Time Trend	Change in HIV Demographic	Change in General Population Trend	Change in SIR
Kaposi Sarcoma	Decreasing	yes	NA	yes
NHL	Decreasing	no	yes	yes
Cervix	Decreasing	no	yes	yes
ANUS	Increasing	no	yes	no
Hodgkin L.	Decreasing	no	no	yes
Liver	Increasing	yes	yes	no
Lung	Decreasing	yes	yes	yes
Prostate	Increasing	yes	no	no
Female Breast	No change	yes	yes	no
Colorectum	No change	yes	yes	no

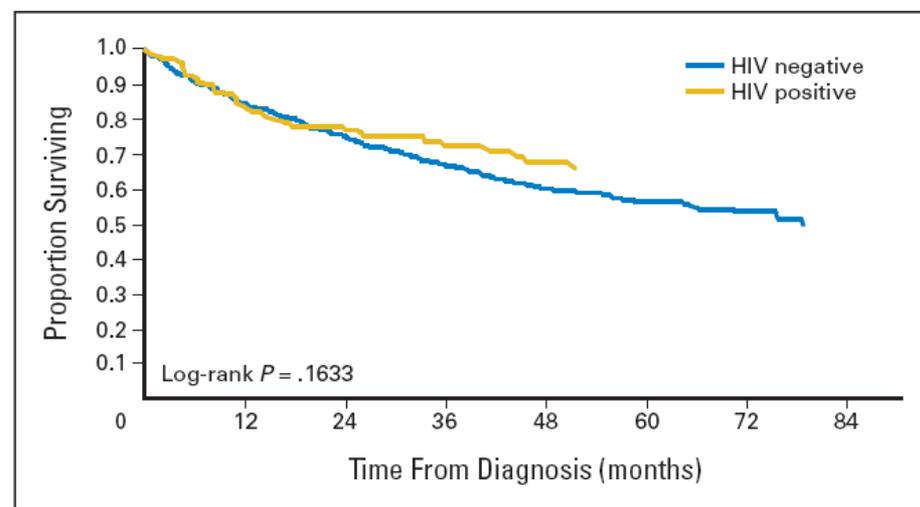
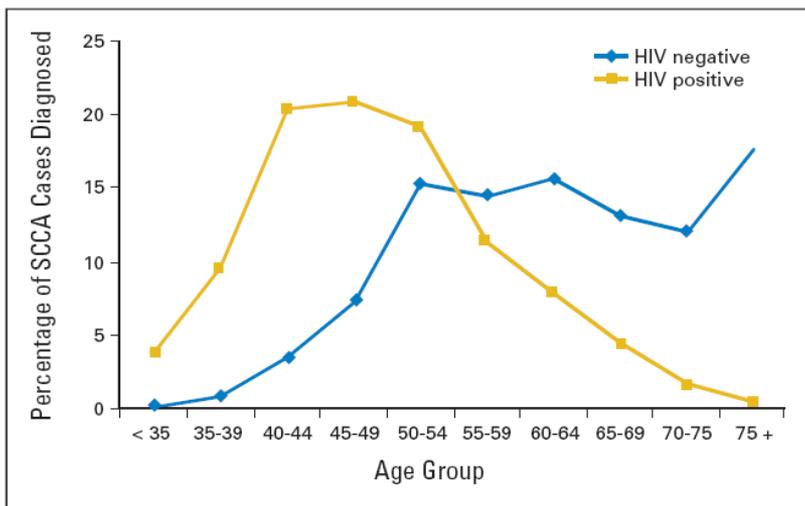
Overall Survival (OS) in the pre- and post-cART era of the most common HIV-related cancers (Prospective studies)

	OS pre-cART	OS post-cART
Kaposi Sarcoma	13 mos (median)	57- 100 % (3-yr)
NHL DLCL	6-8 mos (median)	60-80 % (5-yr)
Hodgkin Disease	45% (2-yr)	76-81 % (5 yr)
ANAL Cancer	20-34 % (5-yr)	64-71 % (5-yr)
HCC	6-8 mos (median)	35 mos (median)

Message: Safer and better tolerated cART regimens, reduced infectious morbidity, improved supportive care strategies and incremental refinements in cancer treatment have all contributed to improvement in overall survival.

Human Immunodeficiency Virus–Associated Squamous Cell Cancer of the Anus: Epidemiology and Outcomes in the Highly Active Antiretroviral Therapy Era

Elizabeth Y. Chiao, Thomas P. Giordano, Peter Richardson, and Hashem B. El-Serag



HIV-positive pts treated with CRT and combination antiretroviral therapy have the same outcome as HIV-uninfected pts (2-yr OS 76 vs 77%)

Tabella 3 - Programmi di Screening oncologici adattati/specifici per la popolazione HIV-positiva.

TUMORE	POPOLAZIONE	PROCEDURE SCREENING	TEMPISTICA SCREENING	RACCOMANDAZIONE (Forza/Evidenza)	RIFERIMENTI BIBLIOGRAFICI
Cervice uterina	Donne sessualmente attive. Lo screening deve iniziare entro un anno dall'inizio dell'attività sessuale o alla diagnosi di HIV.	- PAP test convenzionale - - PAP test su base liquida § -solo Pap test o Co-testing (Pap test+HPV test) - Colposcopia	Età < 30 aa: il secondo° esame a 12 mesi; - ogni 3 aa se 3 Pap test annuali negativi. Età ≥ 30 aa: il secondo° esame a 12 mesi; - ogni 3 aa se 3 Pap test annuali negativi o se Co-test negativo°° - Co-test annuale se Pap test normale ed HPV test positivo Se Pap test patologico o HPV test positivo per ceppi alto rischio	[BII] [BII] [BII] [BII] [BII] [BII] [AII]	[27,30] [27,30,31] [27,28,30]
Ano	- MSM; - Tutti con storia di condilomi ano- genitali; - Donne con istologia genitale patologica ∞ ∞ ∞ ∞ ∞ ∞ ∞ ∞ MSM*	- PAP test convenzionale - PAP test su base liquida Anoscopia ad alta risoluzione	*Annuale, se 2 esami consecutivi neg Se Pap test patologico	[AIII] [AII]	[4,32,33] [33]
Fegato	- HCV coinfetti con cirrosi; - Tutti HBV con viremia rilevabile -Tutti HBV/HCV aviremici se con cirrosi -Tutti HCV aviremici (post-DAA) con pregresso epatocarcinoma	Ecografia addome +/- α-fetoproteina	Ogni 6-12 mesi -Ogni 6 mesi §§	[AI] [AI] [AI]	[4,27-32,34] [34,35] [35,36]

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HPV-related precancerous screening in HIV infected MSM accessing the Infectious Diseases Clinic of Modena

Carlotta Rogati, MD

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UNIVERSITÀ DEGLI STUDI
DI MODENA E REGGIO EMILIA

Background

- **Squamous cell carcinoma of anus (SCCA)** is strongly associated with Human Papilloma Virus (HPV) infection and in particular with high-risk HPV genotypes (**HR-HPV**)¹
- At the present SCCA is one of the most frequent **non-AIDS defining malignancies** in HIV patients, especially MSM¹
- The relative risk of anal cancer among HIV seropositive MSM is 59-fold higher than in the general population²
- According to **international** and **national** guidelines MSM patients with HIV infection should yearly undergo an anal pap test with cytology. Then, an **High-Resolution Anoscopy (HRA)** is suggested with positive cytology.³

¹Hidalgo-Tentorio et al. Risk factors for infection by oncogenic human papillomaviruses in HIV-positive MSM patients in the ART era (2010-2016). *Medicine* 2017 96:39

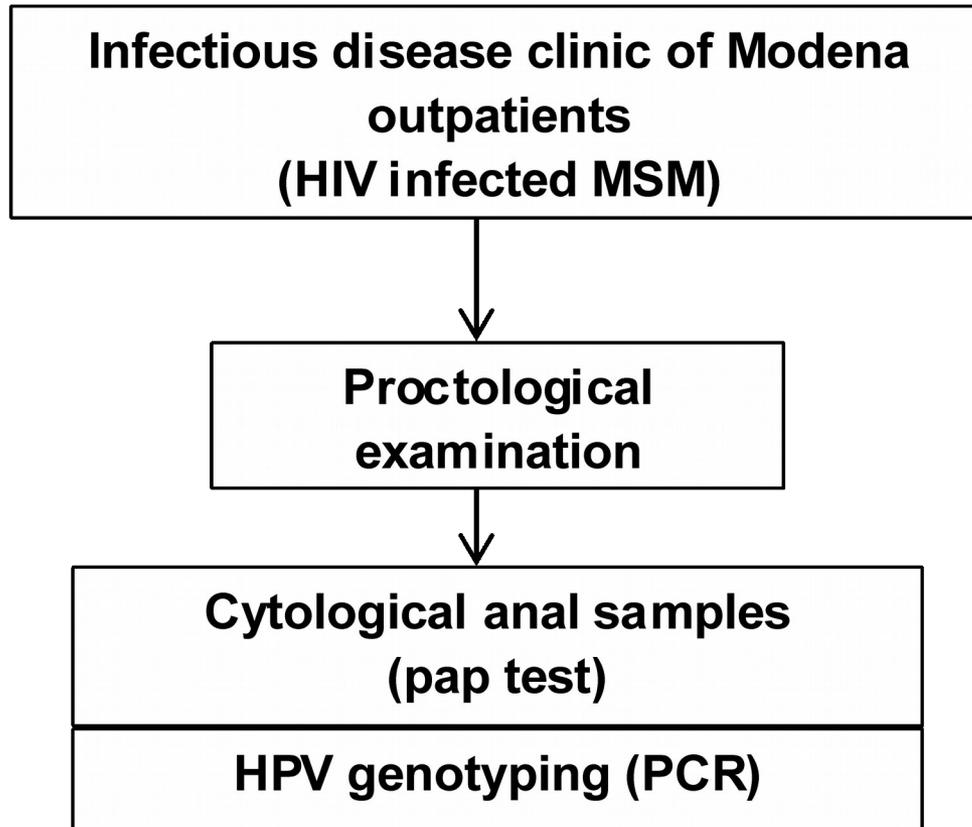
²Piketty C. et al. Marked increase in the incidence of invasive anal cancer among HIV-infected patients despite treatment with combination antiretroviral therapy, *AIDS* 2008, vol. 22, 1203-11

³Società Italiana di Malattie Infettive e Tropicali. Linee Guida Italiane sull'utilizzo della Terapia Antiretrovirale e la gestione diagnostico-clinica delle persone con infezione da HIV-1. 2017 Edition

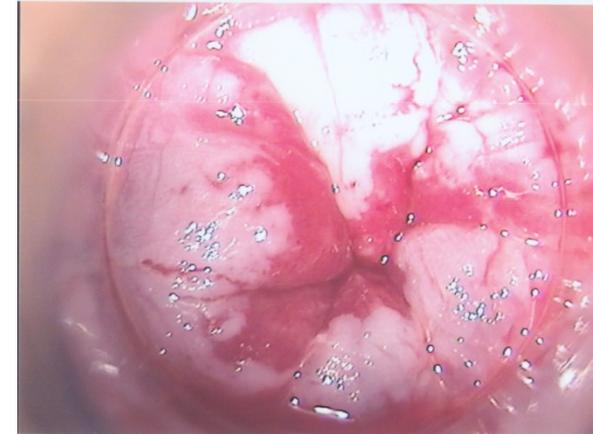
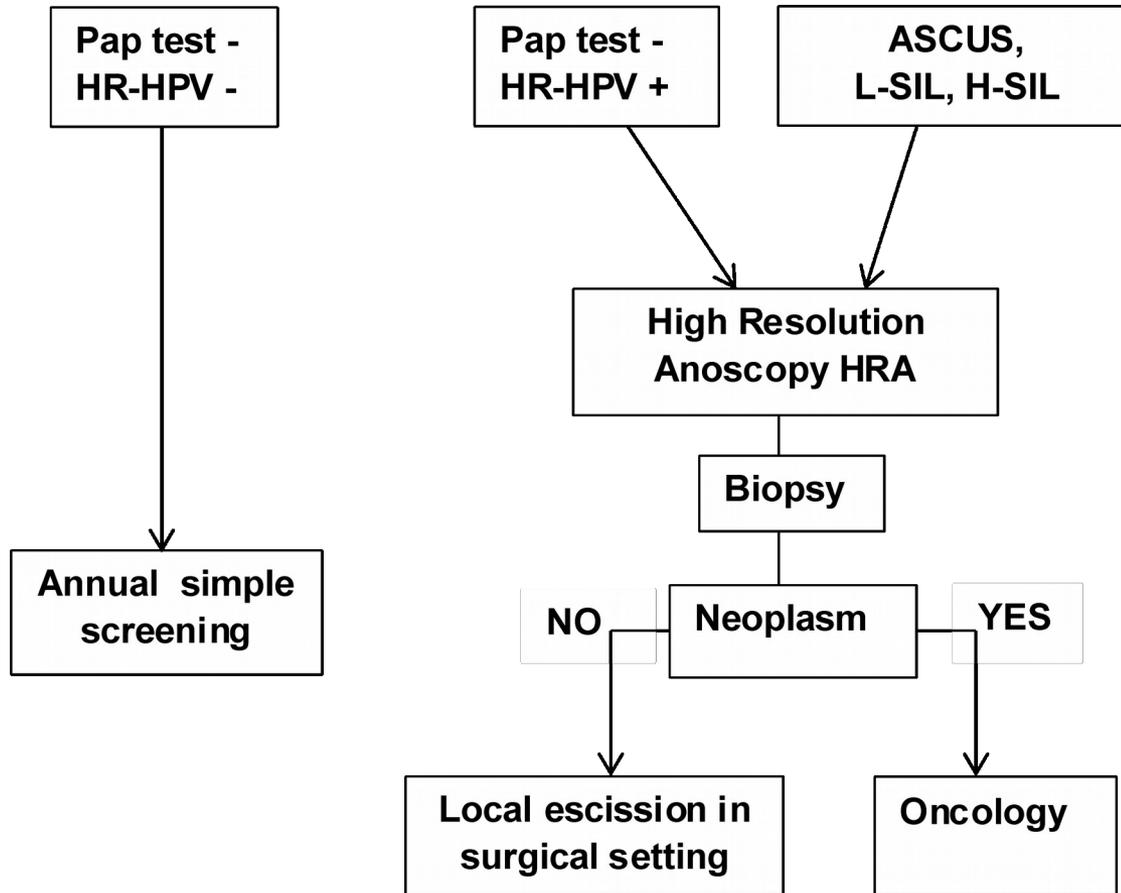
Aims of the study

- To retrospectively establish the **prevalence of HPV infection**, the **distribution of HPV genotypes** and the **prevalence of pre-cancer lesions** in Modena HIV+ MSM cohort **from Dec 2015 to Jan 2018**
- To evaluate epidemiological and viro-immunological risk factors associated with HPV infections/lesions

Methods: annual anal pap test and HPV typing by PCR



Methods: High Resolution Anoscopy (HRA) is proposed in selected cases



ASCUS: Atypical Squamous Cells of Undetermined Significance
L-SIL: Low-grade Squamous Intraepithelial Lesion
H-SIL: High-grade Squamous Intraepithelial Lesion

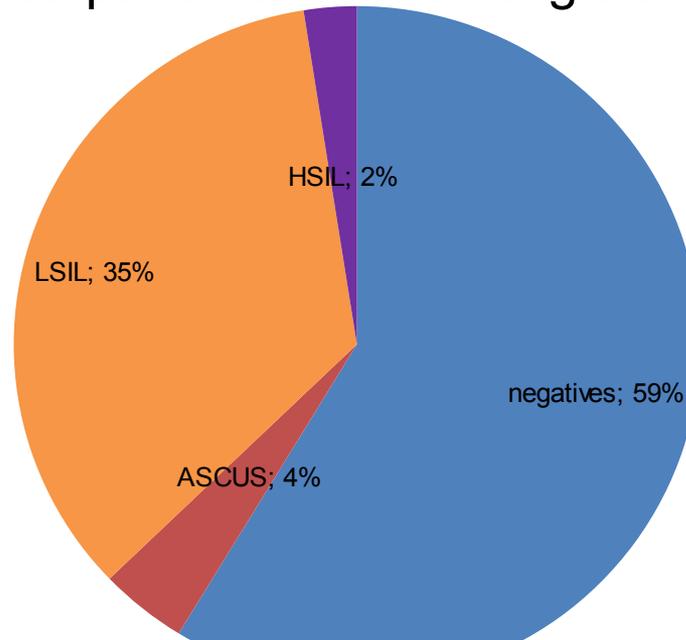
Results: 121 patients enrolled

Characteristics	Number of patients n=121
Age \pm SD	47.2 \pm 11
<30 y, n, %	6 (4.9)
30-50 y, n, %	71 (58.7)
>50 y, n, %	44 (36.4)
Previous Syphilis, %	53 (43.8)
Previous Hepatitis A, %	18 (14.8)
Previous Condylomatosis, %	33 (27.2)
Previous AIDS-defining events, %	15 (12.3)
Coinfections (HBV, HCV), %	8 (6.6)
Nadir CD4, cells/ μ L \pm SD	326 \pm 199
Nadir CD4<200/ μ L, %	30 (24.8)
HIV NR, months \pm SD	75 \pm 134
Current CD4 count, cells/ μ L \pm SD	793 \pm 297
CD4<200/μL, %	2 (1.6)
Current VL, copies/mL \pm SD	19 \pm 122
VL>40 copies/mL, %	4 (3.3)
CD4/CD8 ratio < 0.8, %	53 (43.8)

Results

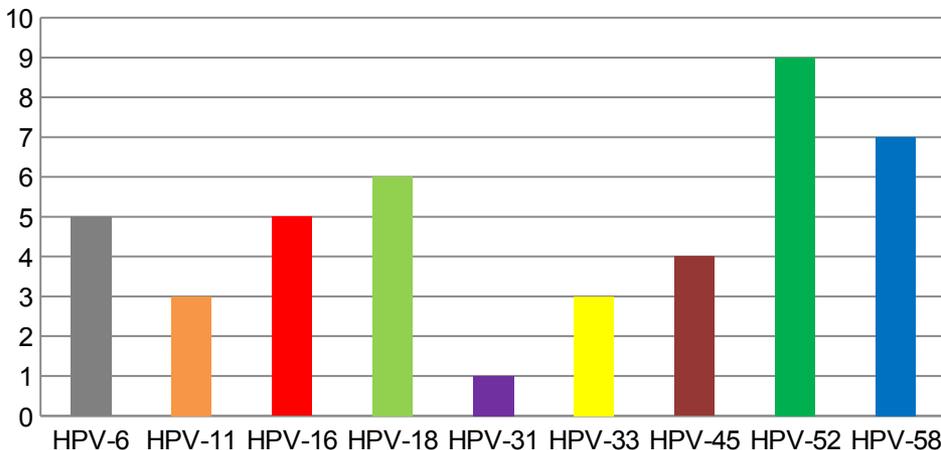
- 50 out of 121 swabs (41.3%) resulted positive to cytological analysis for HPV-related lesions
- HPV genotype known in 72 (59.5%) patients
- HR-HPV genotype were detected in 67% of analyzed samples
- Among negatives pap-test (71), 42 resulted positive for at least one HPV genotype (59%)
- 65.2% of the screened outpatients resulted eligible to HRA (pap-test+/HR-HPV+)

Cytological+ Histological results

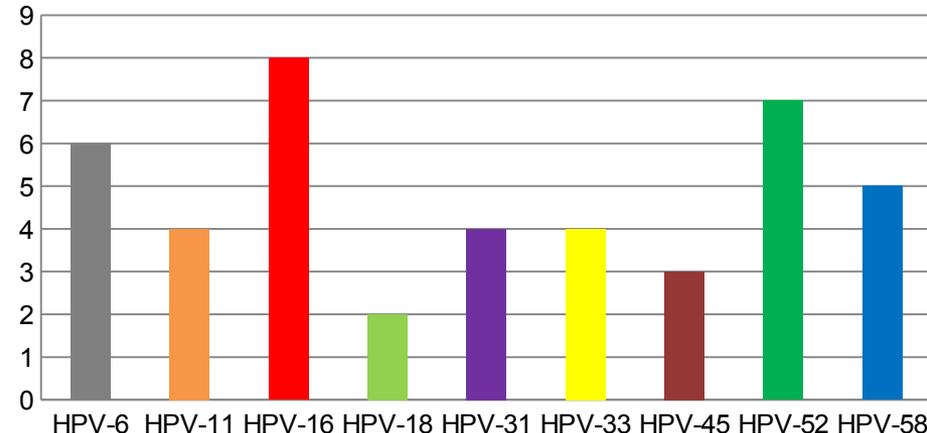


Results: HPV Genotypes

Normal histology/citology



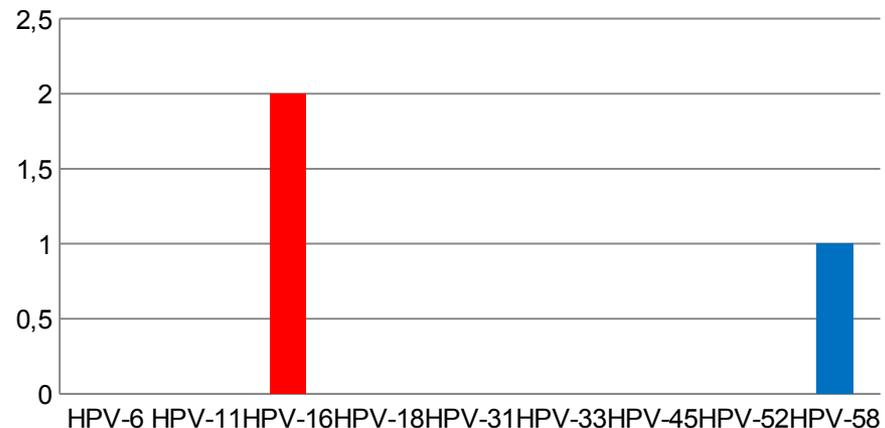
LSIL (AIN1)



- **HPV-16** is the most frequent genotype in L-SIL e H-SIL

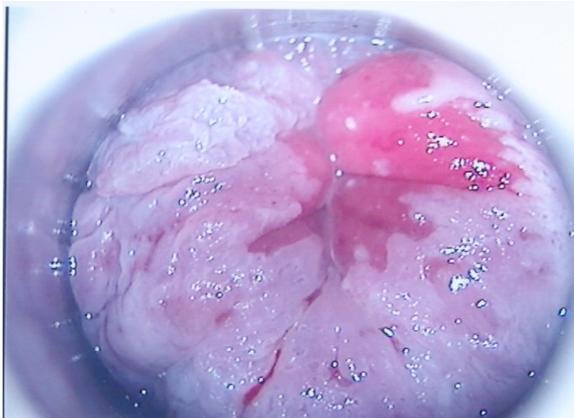
- **HPV-52** e **HPV-58** are the most frequent in negative pap tests

HSIL (AIN2/3/CIS)



Results: HRA

- 19 patients performed HRA and biopsies and 14/19 (73.7%) resulted positive for HPV-related alterations
- HRA was determinant for H-SIL diagnosis in two cases (one case detected for the first time)
- In a patient previously diagnosed and treated for H-SIL an anal CIS was diagnosed within 4-months-follow up thanks to HRA
- In a patient previously positive for L-SIL (due to HPV-16) an anal CIS was diagnosed within 6-months-follow up thanks to HRA



An extensive HSIL

Results: Univariate analysis: risk factors for HPV infections/lesions

Characteristics	Total (121)	Positive pap test (50)	HR HPV genotype (48)	HSIL (3)
Condylomatosis, n (%)	33 (27.2%)	22 (44%)	9 (18.7%)	2 (67%)
Previous Syphilis, n (%)	53 (43.8%)	26 (52%)	26 (54.1%)	0 (0%)
Previous Hepatitis A, n (%)	18 (14.8%)	10 (20%)	2 (4.2%)	0 (0%)
AIDS, n (%)	15 (12.3%)	5 (10%)	8 (16.6%)	1 (33%)
Coinfections, n (%)	8 (6.6%)	3 (3.6%)	3 (6.2%)	1 (33%)
Mean nadir CD4	326	337	329	170
HIV NR, mean months	75	79.8	55.6	82
Mean current CD4 count	793	844	698	345
CD4/CD8 ratio < 0.8, n (%)	53 (43.8%)	25 (50%)	24 (50%)	2 (67%)
Mean age	47,2	47	47,6	61

Condylomatosis: p = 0.0006

Conclusions

- Our results show similar rates of HPV-related lesions to those reported in literature ^{1,2}
- The importance of HR-HPV genotyping in subjects with no evident lesions at a first level evaluation (pap test)
- In our population the occurrence of HPV-related infections **does not correlate with immuno-virological characteristics**
- **Limits:**
 - Sample size
 - **HRA eligibility** (we started HPV genotyping later than the first pap tests)
 - No data on number of different sexual partners

¹ Iribarren-Diaz M, Ocampo-Hermida A et al. Preliminary results of a screening program for anal cancer and its precursors for HIV-infected men who have sex with men in Vigo-Spain. Rev Esp Enferm Dig 2017;109(4):242-249

² Hidalgo-Tentorio et al. Risk factors for infection by oncogenic human papillomaviruses in HIV-positive MSM patients in the ART era (2010-2016). Medicine 2017 96:39



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