HIV, cancer, HPV & STI's

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HIV and cancer

- AIDS-defining malignancies:
  - Kaposi's sarcoma
  - Non Hodgkin lymphoma 1985
  - Cervical cancer 1993

HHV8
EBV
HPV

- Non AIDS-defining malignancies (NADM) is increasing
  - Linked with virus **HPV** (Anal), **HBV** and **HCV** (Liver), **EBV** (HL)
  - Linked with previous immunodeficiency and other factors

Background

- Before introduction of HAART, ADCs common, including Kaposi's sarcoma, NHL, and invasive cervical carcinoma
- Rate of ADCs significantly increased from early to late pre-HAART era and then significantly decreased following introduction of HAART
- Rates of nADCs stable during pre-HAART eras and then significantly increased following introduction of HAART

Crum-Cianflone N, et al. AIDS. 2009;23:41-50.

AIDS-Defining Cancer

SIR = Standardised Incidence Ratio

$$= \frac{\text{Nb cases of cancer in the HIV population}}{\text{Expected nb of cases in the general population, calculated with local cancer registry incidence}}$$

Cancer Incidence in AIDS Patients

- Study of cancer risk in AIDS patients from 1980-2006 (N=372,364)
- Predominantly male (79%), non-hispanic black (42%), MSM (42%)
- Median age of 36 years at the onset of AIDS

Cancer type	No. cases	SIR	95% CI
AIDS-defining cancers			
Kaposi sarcoma	3136	5321	5137 - 5511
Non-Hodgkin lymphoma	3345	32	31 - 33
Cervical cancer	101	5.6	5.5 - 6.8
Non-AIDS-defining cancers			
Anal cancer	219	27	24 - 31
Liver cancer	86	3.7	3.0 - 4.6
Lung cancer	531	3.0	2.8 - 3.3
Hodgkin lymphoma	184	9.1	7.7 - 11
All non-AIDS related cancers	2155	1.7	1.5 - 1.8

Cancer-related causes of death.

	Mortalité 2000	Mortalité 2005	Mortalité 2010	p-value[a]
Reported deaths	**964**	**1042**	**728**	
Cancer-related causes of death, n (%)	**269 (27.9%)**	**344 (33.0%)**	**262 (36.0%)**	**0.003**
AIDS-related, n (%)	**149 (15.5%)**	**134 (12.9%)**	**68 (9.3%)**	**0.024**
Non Hodgkin lymphoma	105 (10.9%)	103 (9.9%)	53 (7.3%) [b]	0.126
Kaposi sarcoma	40 (4.1%)	25 (2.4%)	11 (1.5%)	0.084
Cervical cancer	4 (0.4%)	6 (0.6%)	4 (0.5%)	0.848
Hepatitis-related, n (%)	**17 (1.8%)**	**37 (3.6%)**	**31 (4.3%)**	**0.028**
Hepatitis C	8 (0.8%)	27 (2.6%)	19 (2.6%)	0.021
Hepatitis B	7 (0.7%)	6 (0.6%)	10 (1.4%)	0.279
Hepatitis B and C	2 (0.2%)	4 (0.4%)	2 (0.3%)	0.732
Non AIDS/non hepatitis related, n (%)	**103 (10.7%)**	**173 (16.6%)**	**163 (22.4%)**	**<0.001**
Respiratory	50 (5.2%)	65 (6.2%)	78 (10.7%)	0.004
Lung	44 (4.6%)	53 (5.1%)	61 (8.4%)	0.040
Ear, nose and throat	6 (0.6%)	12 (1.2%)	17 (2.3%)	0.056
Digestive	6 (0.6%)	13 (1.2%)	10 (1.4%)	0.342
Pancreas	3 (0.3%)	11 (1.1%)	7 (1.0%)	0.282
Anal	6 (0.6%)	11 (1.1%)	13 (1.8%)	0.073
Skin	2 (0.2%)	10 (1.0%)	3 (0.4%)	0.065
Hodgkin's lymphoma	12 (1.2%)	9 (0.9%)	8 (1.1%)	0.473
Other hemopathies	5 (0.5%)	8 (0.8%)	7 (1.0%)	0.602
Breast	3 (0.3%)	7 (0.7%)	5 (0.7%)	0.647
Central nervous system	4 (0.4%)	6 (0.6%)	2 (0.3%)	0.530
Other and unknown[c]	12 (1.2%)	33 (3.2%)	27(3.7%)	0.029
Multiple[d]	-	-	3 (0.4%)	-

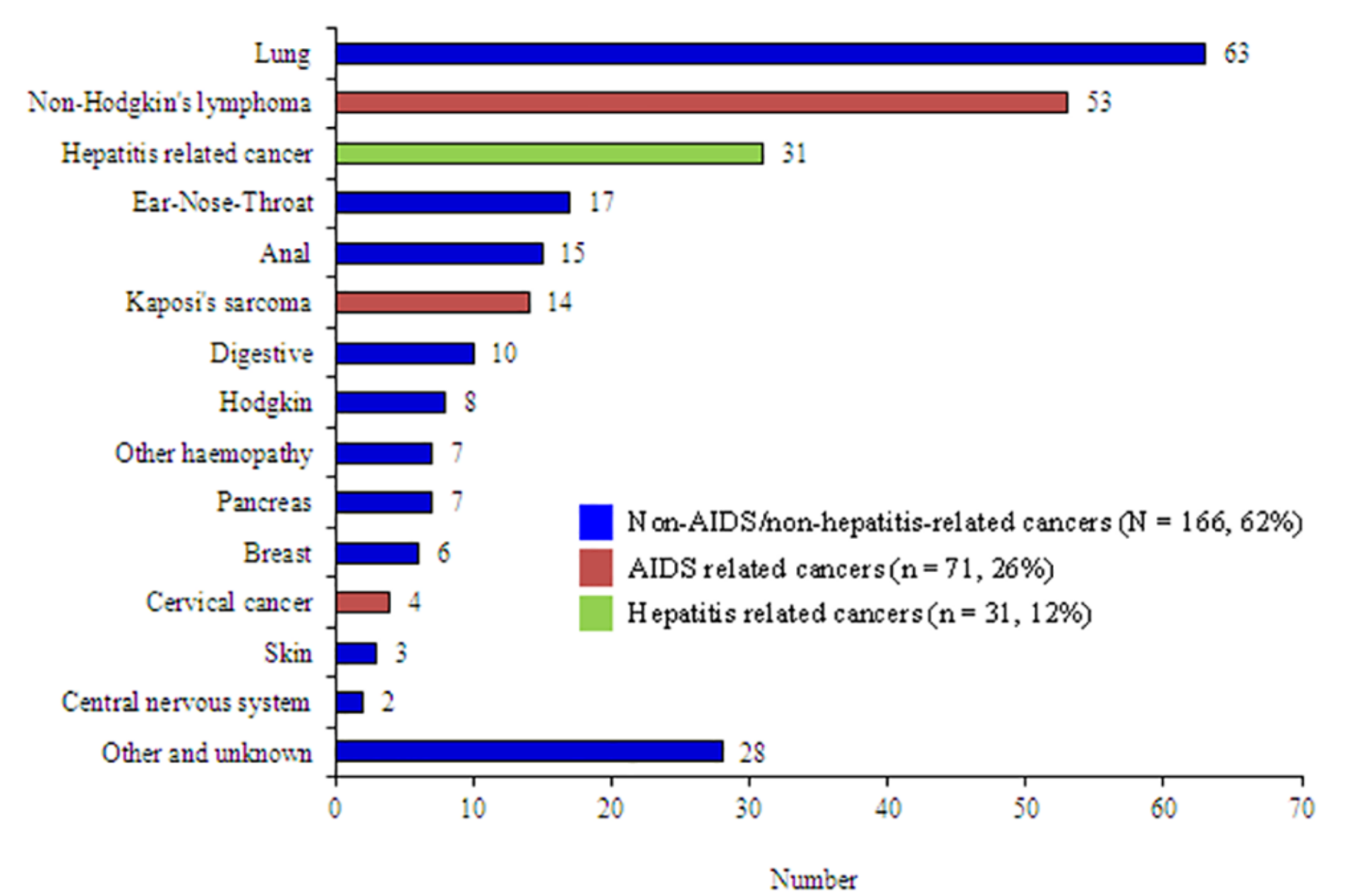
The Mortalité 2000, Mortalité 2005 and Mortalité 2010 surveys, France.

[a]Comparisons between 2000, 2005 and 2010 adjusted on age and gender

[b]including 3 patients with both non Hodgkin lymphoma and Kaposi sarcoma

[c]See Appendix for details

[d]Multiple: anus+prostate, anus+lung, lung+breast



Location of cancers (N = 268) among HIV-infected adults with underlying cause of death being cancer (N = 262), Mortalité 2010 survey, France.

Increased rates of nADCs. Why ?

- Increasing survival of patients with HIV might be associated with an increase of traditional cancer risk
- Aging of the HIV population
- Long-term toxicity of ART ?

Increased rates of nADCs. Why ?

Other possible explanations:

- Confounding by shared lifestyle cancer risk factors

  Tobacco use

  – MSM have nearly double the rate of tobacco use compared to all U.S. men: 48% vs 29% (Stall 1999)

  – A role of HIV through its effect on immune deficiency

  Importance:

  – If immune deficiency is responsible, then reversing immune deficiency might decrease cancer risk

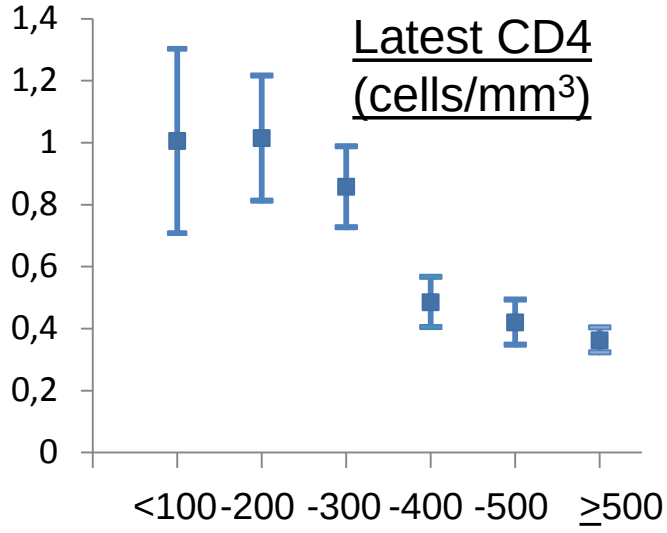
Characteristics of cancer immune control

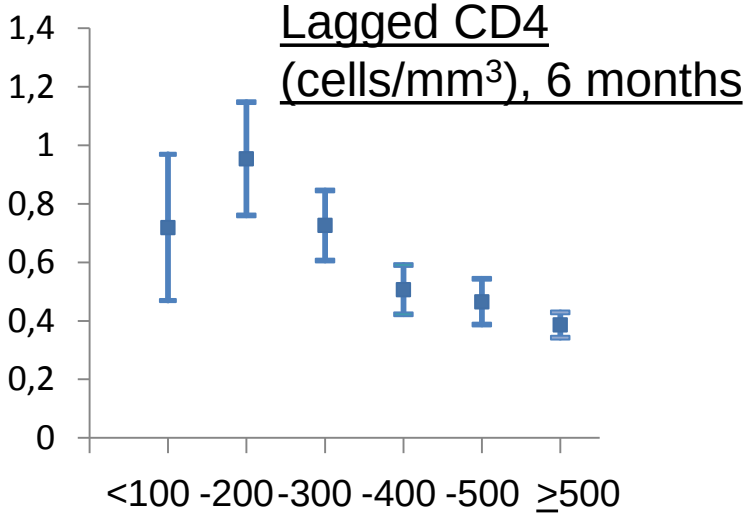
- CD4 cell count
- CTL function
- NK
- Immune memory Central/effector memory
- Level of immune activation:
  - PD-1, IL-10, Treg
- Immune system on pre-cancerous lesions

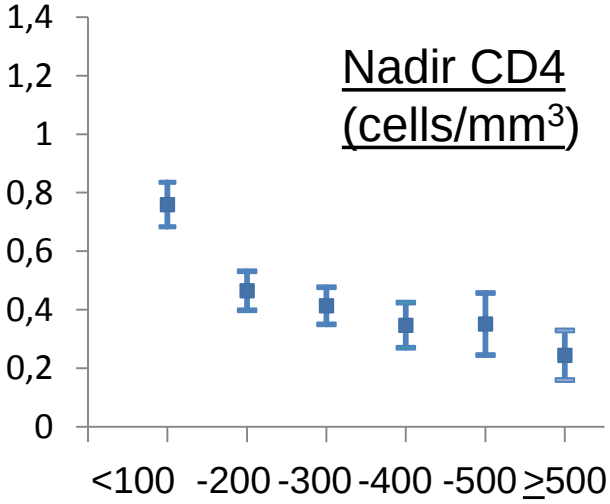
Cancers in HIV and transplant patients

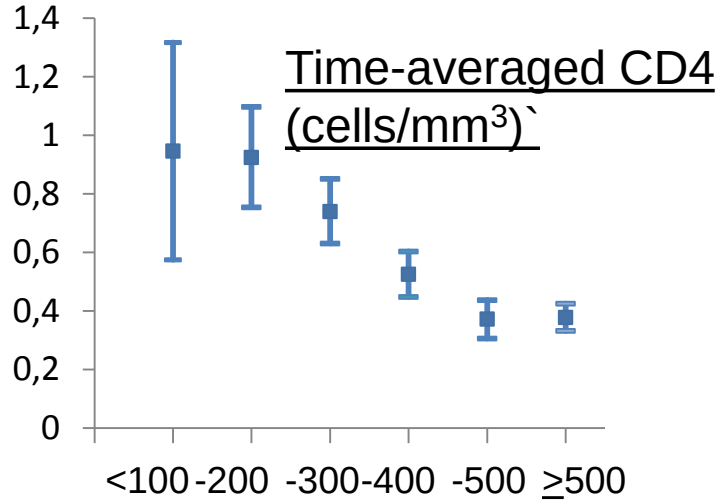
- The range of cancers occurring at increased rates is strikingly similar in the two groups
- Mostly those known or suspected to be caused by infective agents
- Impact of immunodeficiency on these cancers

Incidence of first NADM (with 95% CI) stratified by different indicators of immunosuppression



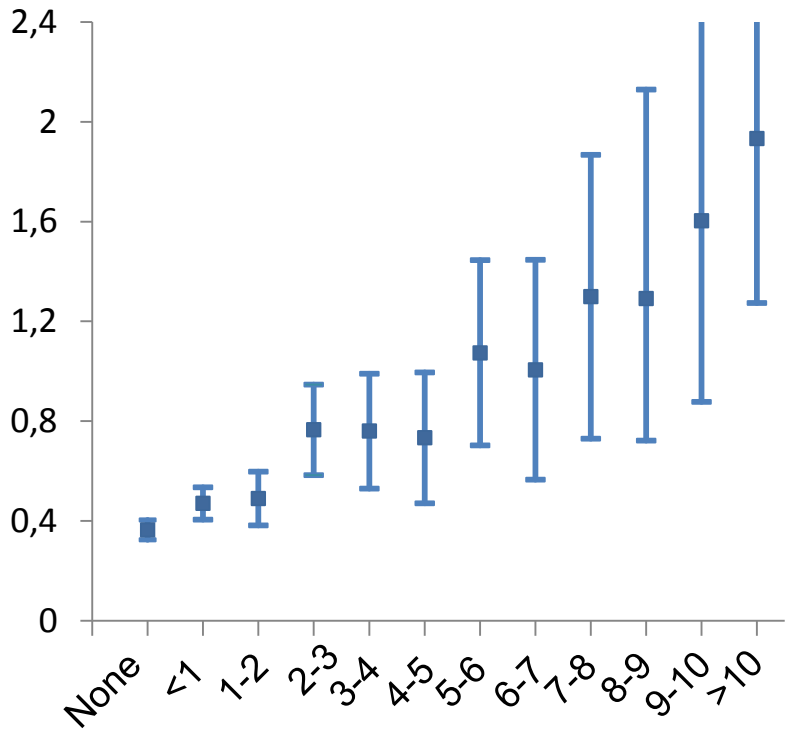






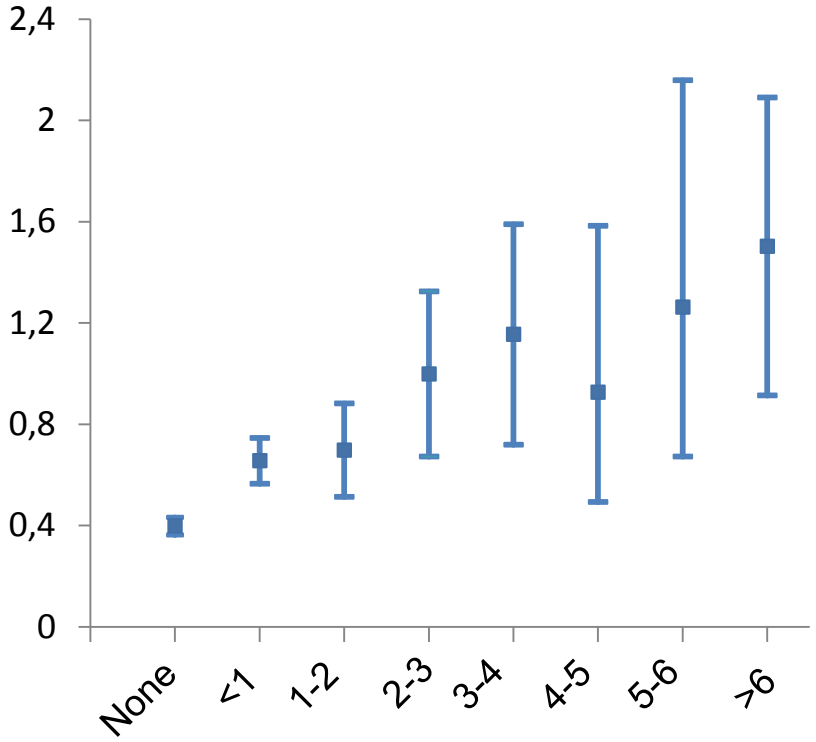
Incidence of first NADM (with 95% CI) stratified by duration of immunosuppression (years)

<200 cells/mm^3



RR /year: 1.05 (1.04, 1.06), p=0.0001

<100 cells/mm^3

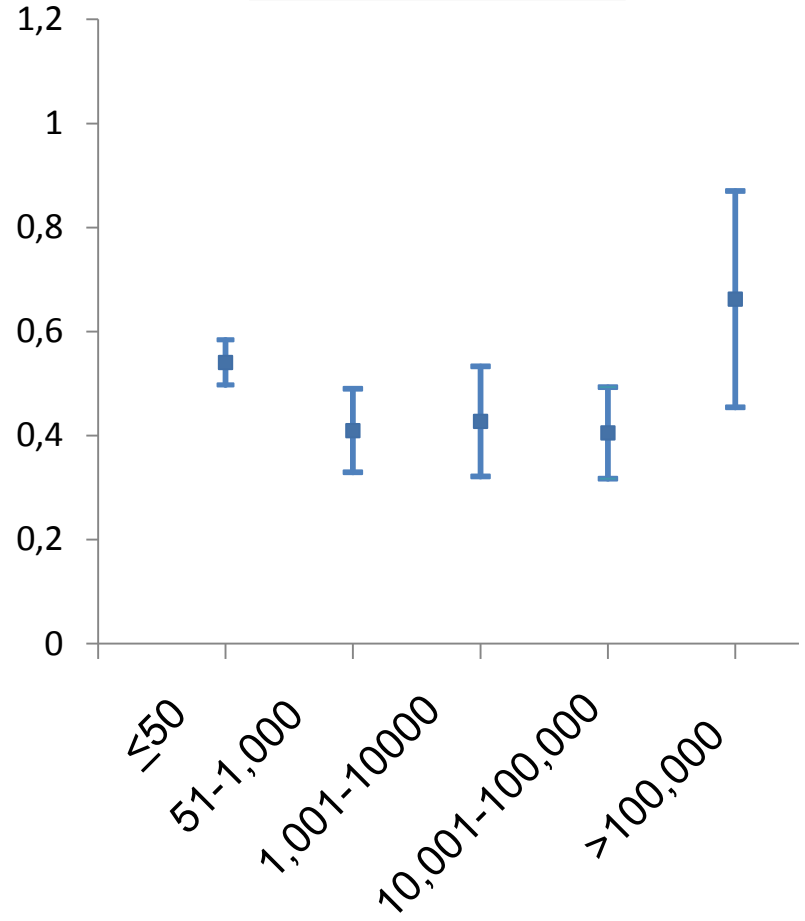


RR /year: 1.05 (1.03, 1.07), p=0.0001

Years, duration of immunosupression

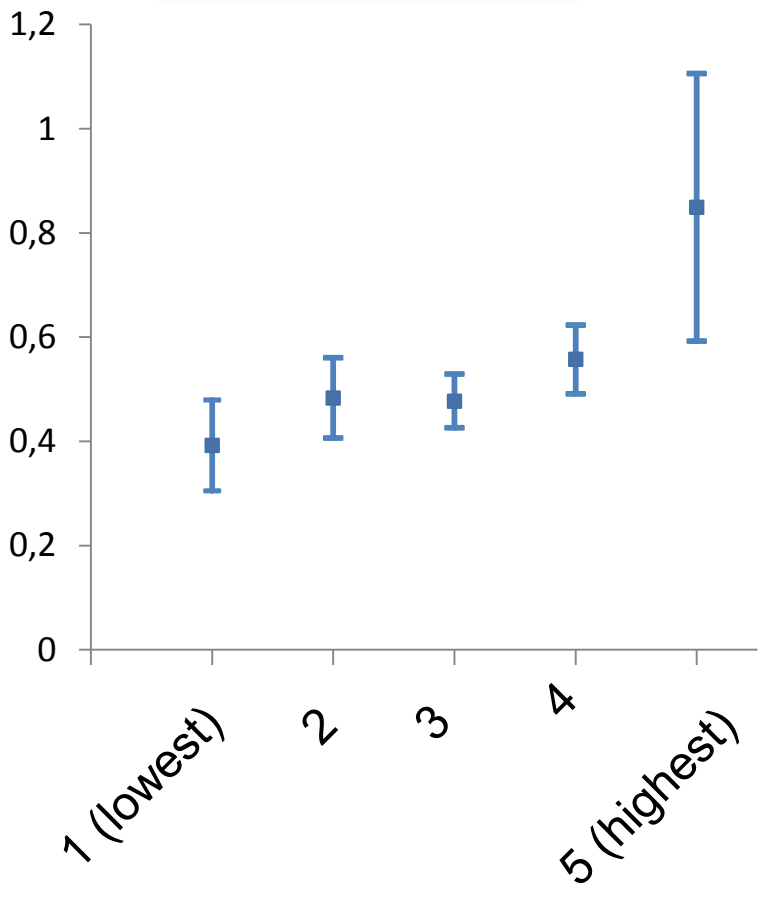
Incidence of first NADM (with 95% CI) stratified by indicators of viraemia

Latest HIV RNA



RR /log higher (log 10 copies/ml): 1.05 (0.99, 1.13), p=0.13

AUC for HIV RNA



RR /unit: 1.04 (1.00, 1.09), p=0.07

NADCs in HIV+ Patients compared to Cancer in HIV (-) Patients

- Occur at a younger age (?)
- Atypical pathology, higher tumor grade
- Diagnosed at more advanced stage
- More aggressive disease course
- Poorer outcomes
- Higher rate of relapse

Let’s concentrate on
Non AIDS-Defining Cancers

Hodgkin disease

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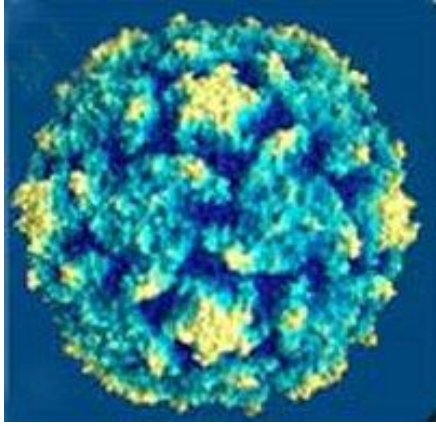
HIV and Hodgkin's Lymphoma



- Due to co-infection with EBV
  - Co-infection rates 75 to 100%, vs 20 to 50% in HIV- HL
- More aggressive disease
  - histology: mixed cellularity, lymphocyte depleted
  - B symptoms present (fevers, sweats, weight loss)
  - Extra-nodal disease common (75 to 90%)
  - Bone marrow involvement common (40 to 50%)
- Effect of HAART therapy on risk unclear, contradictory

Thompson 2004, Clifford 2005, Herida 2003, Spano 2008

Hepatocellular carcinoma

Cancer Incidence in AIDS Patients

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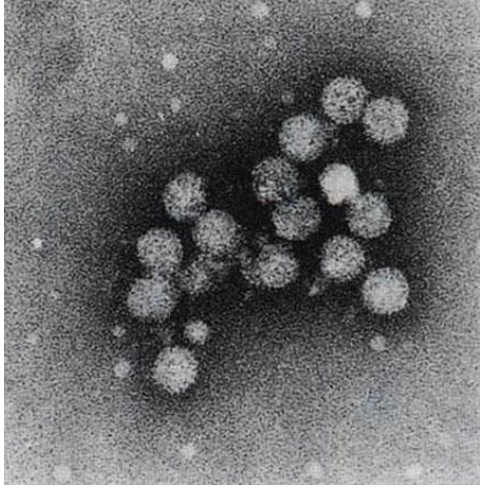
HIV and Liver Cancer



- Incidence rate 7 times higher in HIV +
- Due to Hepatitis B and C co-infection
- Lower risk in HIV patients on HAART (Only NADC)
- Higher risk of extrahepatic metastases, poorer outcome
- Treatment with transplantation complicated

Murillas 2005, Kramer 2005, Puoti 2004, Hessol 2007

Lung cancer

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Excess of risk of lung cancer in HIV

- Hypothesies for causal factors…
  - increased frequency of smoking in HIV population, but intensity and duration not different
  - HIV status seems probable, but the mechanisms remain unknown :
    - degree of immune deficiency
    - duration of immune deficiency
    - oncogenic role of HIV *per se*
    - other oncogenic virus
    - role of HAART

Lung Cancer

- Most frequent NADC in HAART era
- Incidence 2-4 fold higher than general population
  - SIRS between 2 and 3 and stable over time
- Diagnosed at younger age with advanced disease and primarily in smokers
- Adenocarcinoma is most frequent sub-type
- No clear screening strategy
- No argument to treat differently than non-HIV infected patients

Breast cancer

Breast cancer

- No higher incidence in HIV-positive women

- There might even be a **lower incidence**:
  - Significant decrease was recorded in Tanzania following HIV epidemics. Amir. *J Natl Med Assoc* 2000
  - Significant decrease in relative risk (observed cases/expected cases based incidence in general population). Frisch. *JAMA* 2001
  - Goedert Br J Cancer 2006

Why breast cancer could be less frequent in HIV women?

- Reduced incidence is also found in other immunosuppressed patients (suggesting that physiological immune response is a facilitating factor in breast carcinogenesis)
- Hormone production is reduced in HIV: oestradiol or testosterone
- CXCR4-tropic HIV is protective against breast cancer because
- Ritonavir has been studied in preclinical trials for its activity against breast cancer growth

Cancer screening – EACS

Problem	Patients	Procedure	Evidence of benefits	Screening interval	Additional Comments
Breast cancer	Women 50–70 yrs	Mammography	↓breast cancer mortality	1–3 years	
Cervical cancer	Sexually active women	Papanicolau test, HPV DNA test	↓cervical cancer mortality	1–3 years	Target age group should include at least the age range 30 to 59 years. Longer screening interval if prior screening tests repeatedly negative
Colorectal cancer	Persons 50–75 yrs	Fecal Occult Blood test	↓colorectal cancer mortality	1–3 years	Benefit is marginal

EACS guidelines 2011. Available at http://www.europeanaidsclinicalsociety.org/guidelinespdf/EACS-EuroGuidelines_FullVersion.pdf . Accessed March 2011.

HAART and chemotherapy

- Many patients will receive HAART and chemotherapy concurrently with high likelihood of drug interactions and overlapping toxicities
- Protease inhibitors and non-nucleoside reverse transcriptase inhibitors are substrates and potent inhibitors or inducers of cytochrome P450 system (CYP)
  - Many anti-neoplastic drugs also metabolized by CYP system leading to either drug accumulation and possible toxicity or decreased efficacy

Chemotherapy and HAART

Enzyme/ Transporter	HAART Inhibitors	HAART Inducers	Chemotherapy Substrates
CYP3A4	delavirdine, efavirenz, ritonavir, amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, saquinavir	nevirapine, efavirenz	paclitaxel, docetaxel, erlotinib, sunitinib, sorafenib, etoposide, vincristine, vinblastine, vinorelbine, cyclophosphamide
CYP2C9	efavirenz, ritonavir		cyclophosphamide
CYP2C19	efavirenz, amprenavir		cyclophosphamide, ifosfamide, thalidomide
CYP2D6	ritonavir		tamoxifen
CYP2B6	efavirenz, nelfanivir, ritonavir	nevirapine	cyclophosphamide, ifosfamide
CYP2E1	ritonavir		etoposide, dacarbazine
UGT1A1	atazanavir		irinotecan

Drug Transporters

Drugs	Transporter					
	ABCB1		ABCC1		ABCG2	
	Substrate	Inhibitor	Substrate	Inhibitor	Substrate	Inhibitor
NRTI						
Abacavir (ABC)	++		+	+	+++	
Didanosine (DDI)	NT		NT		NT	
Lamivudine (3TC)	+				+	
Stavudine (D4T)			+			
Zalcitabine (ddC)	NT		NT		NT	
Zidovudine (AZT)	+				+	
NtRTI						
Tenofovir disoproxil fumarate	+++		++	+/-	+++	
NNRTI						
Nevirapine						
Efavirenz	+			+		
PI						
Amprenavir				+		
Atazanavir		+		+	+	+
Indinavir				+		
Lopinavir		+		+		+
Nelfinavir	+	+		+	+	+
Ritonavir	+	+		+		+
Saquinavir	++	+		+		+
Tipranavir			+++			

NRTI: Nucleoside analog reverse transcriptase inhibitors. NtRTI: Nucleotide analog reverse transcriptase inhibitor
NNRTI: Non-nucleoside analog reverse transcriptase inhibitors. PI: Protease inhibitors.
+, ++, or +++ : weak, moderate, or strong substrate/inhibitor. NT: Non-toxic, could not be determined.

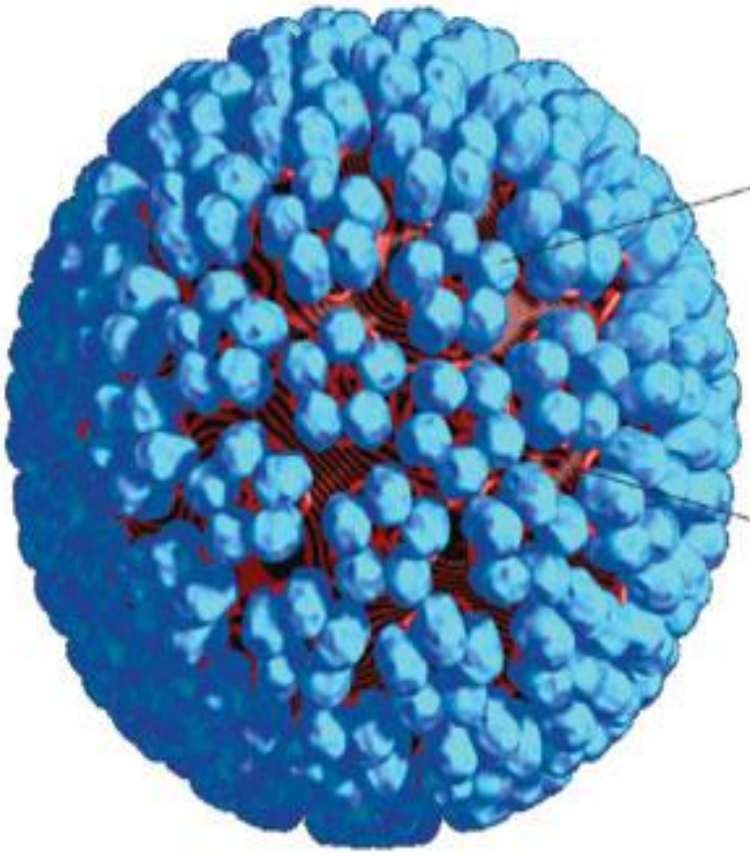
Chemotherapy Transporter Substrates		
ABCB1	**ABCC1**	**ABCG2**
Actinomycin D	Etoposide	Mitoxantrone
Doxorubicin	Teniposide	Methotrexate
Daunorubicin	Daunorubicin	Irinotecan
Docetaxel	Doxorubicin	Topotecan
Paclitaxel	Epirubicin	Imatinib
Epirubicin	Melphalan	Erlotinib
Idarubicin	Vincristine	Gefitinib
Vinblastine	Vinblastine	
Vincristine		
Etoposide		

HPV and cancer in HIV patients

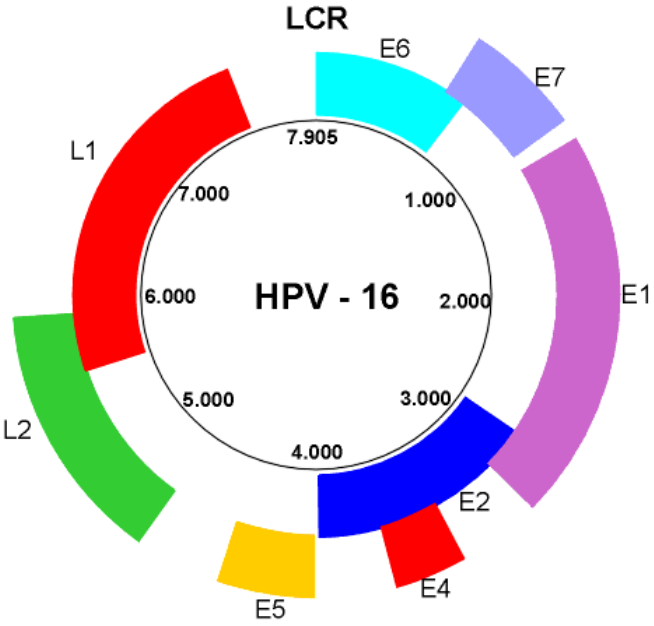
- HPV and HIV interactions
- The burden of HPV in HIV-infected patients

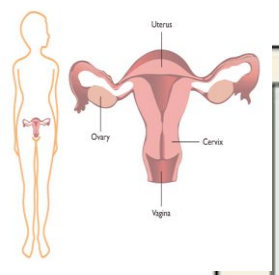
- Preventive and therapeutic strategies to reduce HPV infection and induced lesions in HIV-infected patients

Three-Dimensional Model of Human Papillomavirus



Published in The PRN Notebook, Volume 6, Number 3, September 2001 and The PRN Notebook Onli
Three-dimensional model of HPV created by Louis E. Henderson, Ph.D., Frederick Cancer Rese





Viral persistence and progression

Normal cervix

HPV-infected cervix

Precancerous lesion

Cancer

Clearance

Regression

Invasion

HPV

Persistent Infection

5-10% If HIV negative

20-30% If HIV positive

Precancer

Cancer

15 years

30 years

45 years

Pap tests

HPV vaccination

HPV test 1

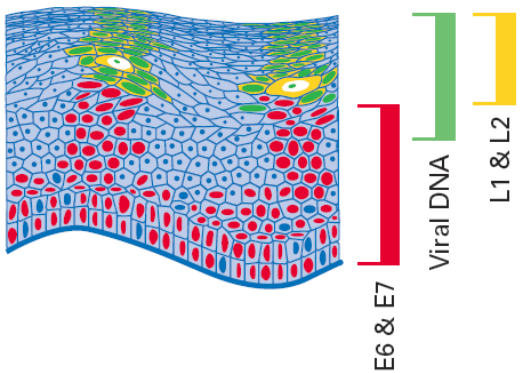
HPV test 2

Schiffman, M. et al. N Engl J Med 2005;353:2101-2104

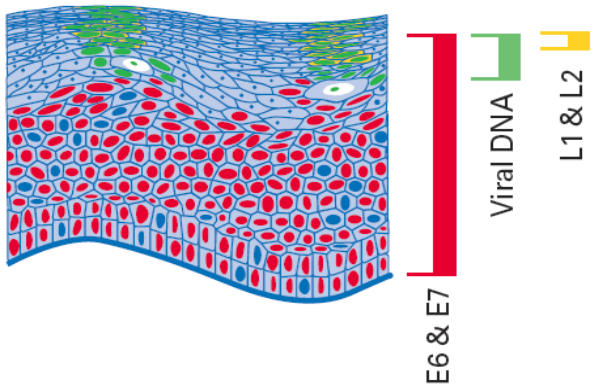
Cervical Intraepithelial Neoplasia

HISTOLOGY (BIOPSY)

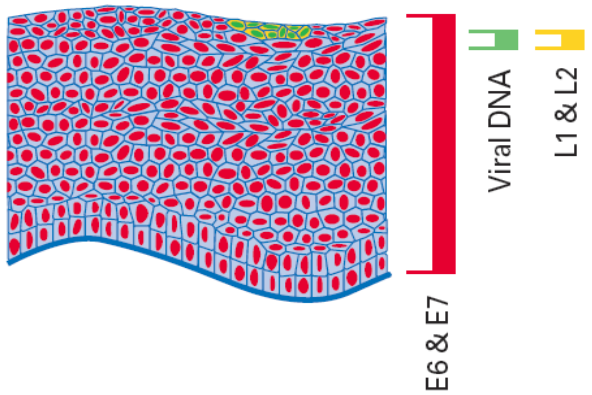
CIN I [and Warts]:
Mild dysplasia, lower one-third of epithelium
The full complement of HPV DNA and proteins (Early and Late) are produced. Infectious virus is produced in the mature squamous cell layer.



CIN 2:
Moderate dysplasia,
lower two-thirds of epithelium
More extensive production of E6 and E7 proteins and less extensive production of viral DNA and late proteins than CIN 1.



CIN 3:
Severe dysplasia,
total involvement of epithelium
Very high level of production of E6 and E7, and little production of late proteins or viral DNA.

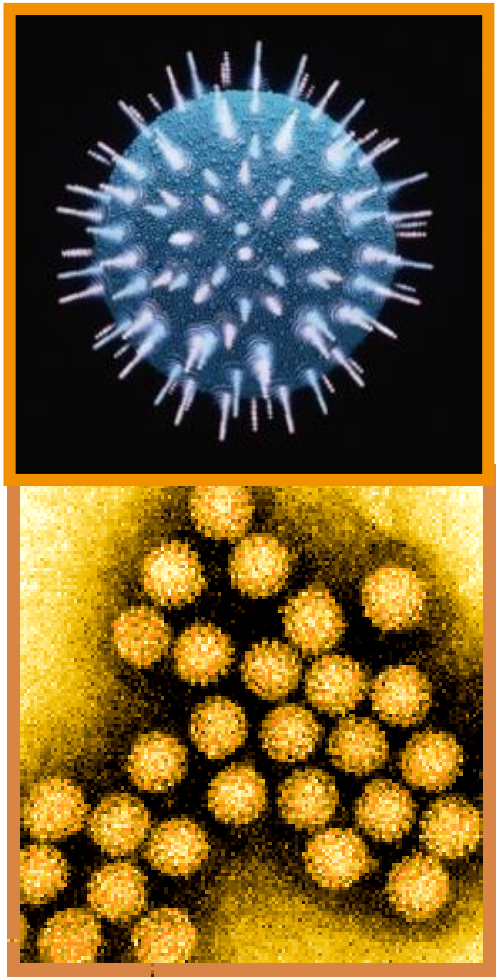


LG-SIL Squamous Intraepithelial Lesions **HG- SIL**

CYTOLOGY (Smear)

HPV-induced cancers

- Cervix
- Anus
- Vagina
- Vulva
- Penis



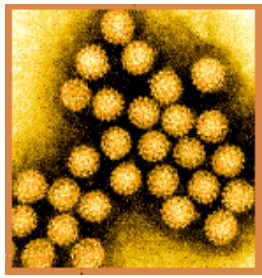
- Oro-pharyngal

70% **sk HPV genotypes:**

16, 18, 31, 33, 35, 39, 45, **51, 52**, 56, **58**, 59, 68

HPV and HIV interactions

- HIV increases HPV infection and HPV-induced lesions



➢ Molecular level

In vitro and ex vivo:

Adding HIV proteins or cytokines

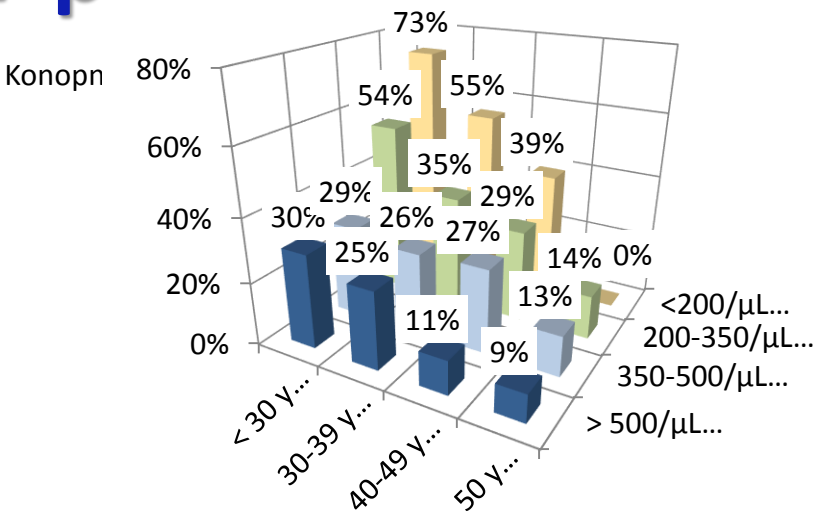
- Increases epithelial tight junction disruption
- Enhances the expression of E6 E7 oncoproteins

Vernon. Virus Res 1993

Tugizov. Virology 2013

➢ Clinical level

Infection by HPV and HPV-induced lesions in the cervix in HIV-positive women



- High risk HPV

	HIV+		HIV-
▪ Prevalence :	43 %	vs.	12%
▪ Incidence:	13.4%	vs.	5 % women year

- Cervical dysplasia
  - Prevalence of abnormal cytology 38% vs. 16% [1]
  - Prevalence in Belgium All **28%** [2] vs. 5.9%
    HSIL **3%** [2] vs. 1.2%
  - Incidence of abnormal cytology 20% vs. 5% after 30 months [3]
  - Incidence in Belgium All **6% women year** [2]
    HSIL **1.4% women year**

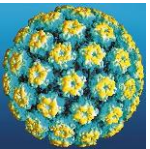
- After conisation:
  Normal cytology after conisation 33% vs. 66% [17]

[1] Massad. *J Acq Imm Defic Syndr* 1999.
[2] Konopnicki D. PhD June 2014
[3] Ellebrock. *JAMA* 2000.
[4] Gilles C. *Gynecologic Obstetric* 2005.

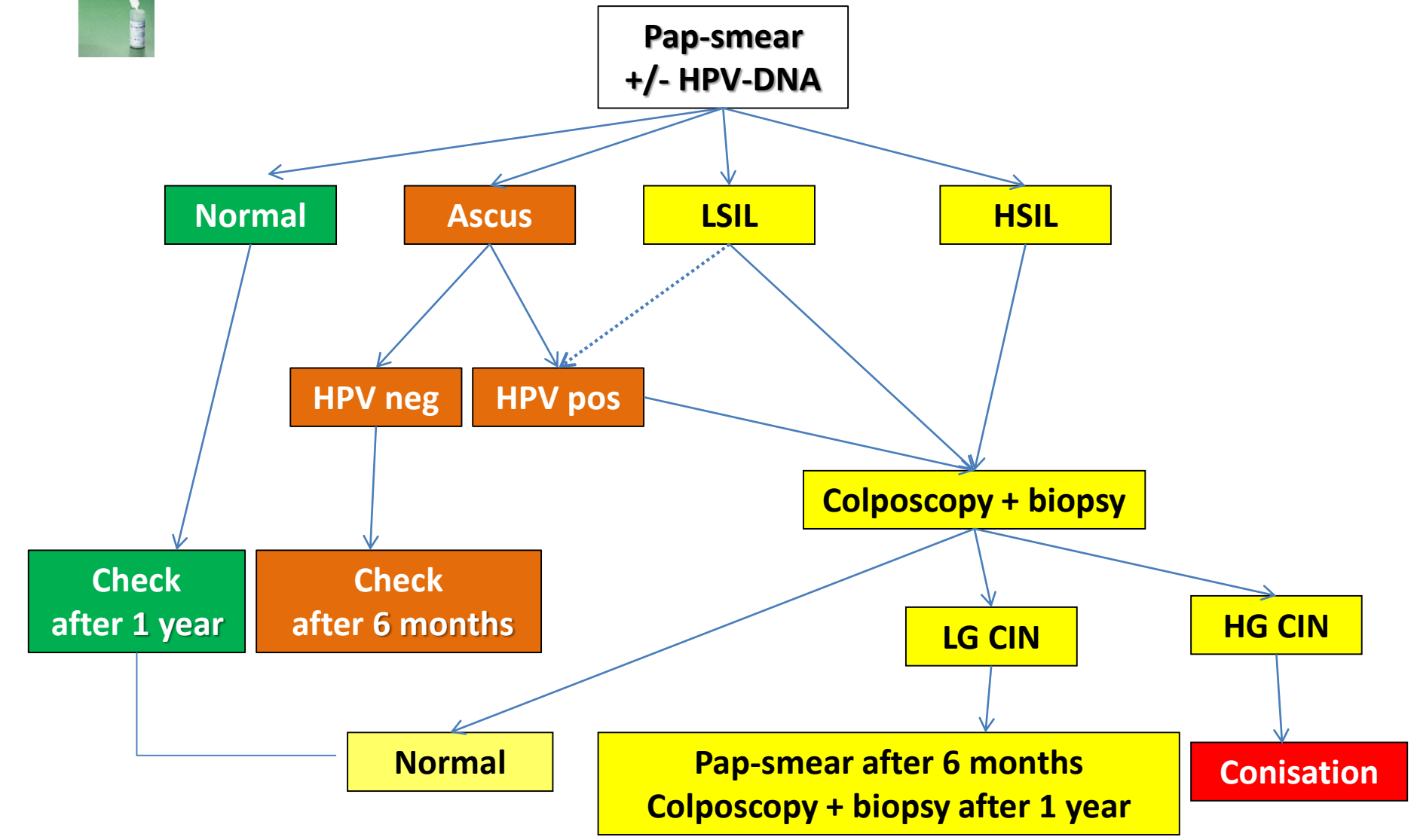
The burden of HPV infections and induced lesions in HIV-positive patients

CD4 cell count decreases
HIV Viral load increases

- **HPV Infection**
  - Prevalence and incidence of HPV infection are higher.
  - **HPV viral load are higher. More infections with multiple genotypes.**
  - Clearance is decreased and recurrence of latent infection are frequent.
  - Persistent infection is significantly higher.
- **Dysplastic lesions**
  - Prevalence and incidence of dysplasic lesions are higher.
  - Spontaneous regression are less frequent.
  - Recurrence after treatment are more frequent.
- **Cancer**
  - Incidence 6-10 times higher for the cervix
  - Incidence 40-90 times higher for the anus



Cervical screening in developed countries



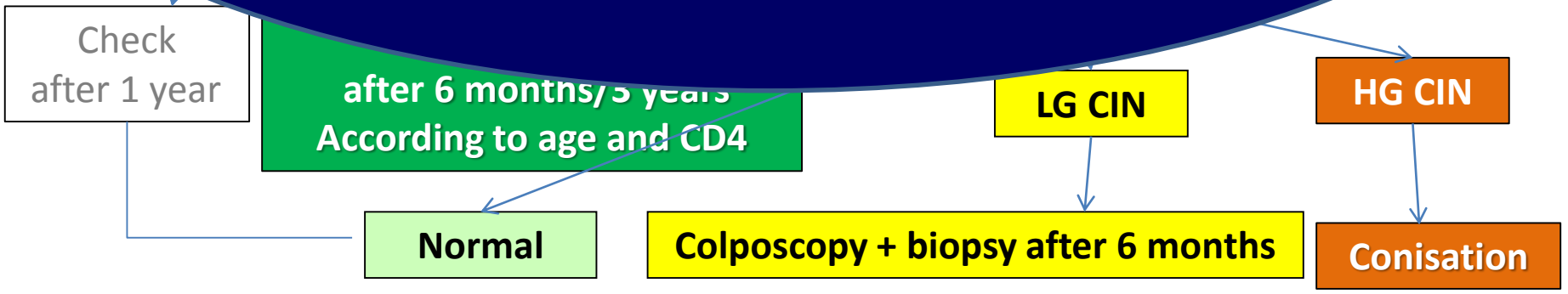
Cervical screening in developed countries

Could this be applied to HIV-positive women?

- Under 30 years HPV prevalence is too high
- HPV testing is **cost-effective** in HIV-women
- It has a good **Negative Predictive Value** for women with CD4>500/µL.

These women could be screened at longer interval.

Harris. *JAMA* 2005. Keller *JAMA* 2012

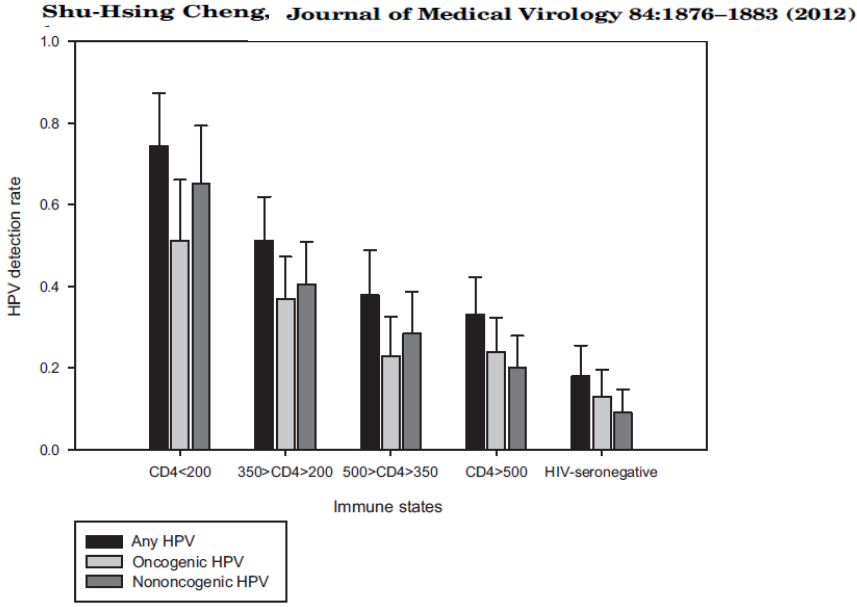


Screen and treat approach in limited resource setting

Cervical Cancer Prevention in HIV-infected women using the « see and treat » approach: Testing for HRHPV; results after 2 hours which allows treatment the very same day in

- South Africa — Kuhn and al. *AIDS* 2010
- Botswana — Ramogola-Masire D. *J Acqui Immune Def Syndr* 2012
- India — Joshi S. *AIDS* 2013

Infection by HPV and HPV-induced lesions in HIV-positive MSM



- HPV Prevalence :
  - all HPV **93%** (vs.64%)
  - **HR HPV** **74%** (vs.37%)
  - Plateau from young to 50-60 years old

- **Prevalence HGAIN**
  - **43-52%**
  - **In Belgium 25%** (Libois A. EACS 2013)
  - **Risk increases with age**
    - **40-49 years** **OR 3.09**
    - **>50** **OR 4.78**

    Compared to <40 years

- **Incidence of HGAIN** (HR anuscopy) :

  8.5-15.4% **patients year**

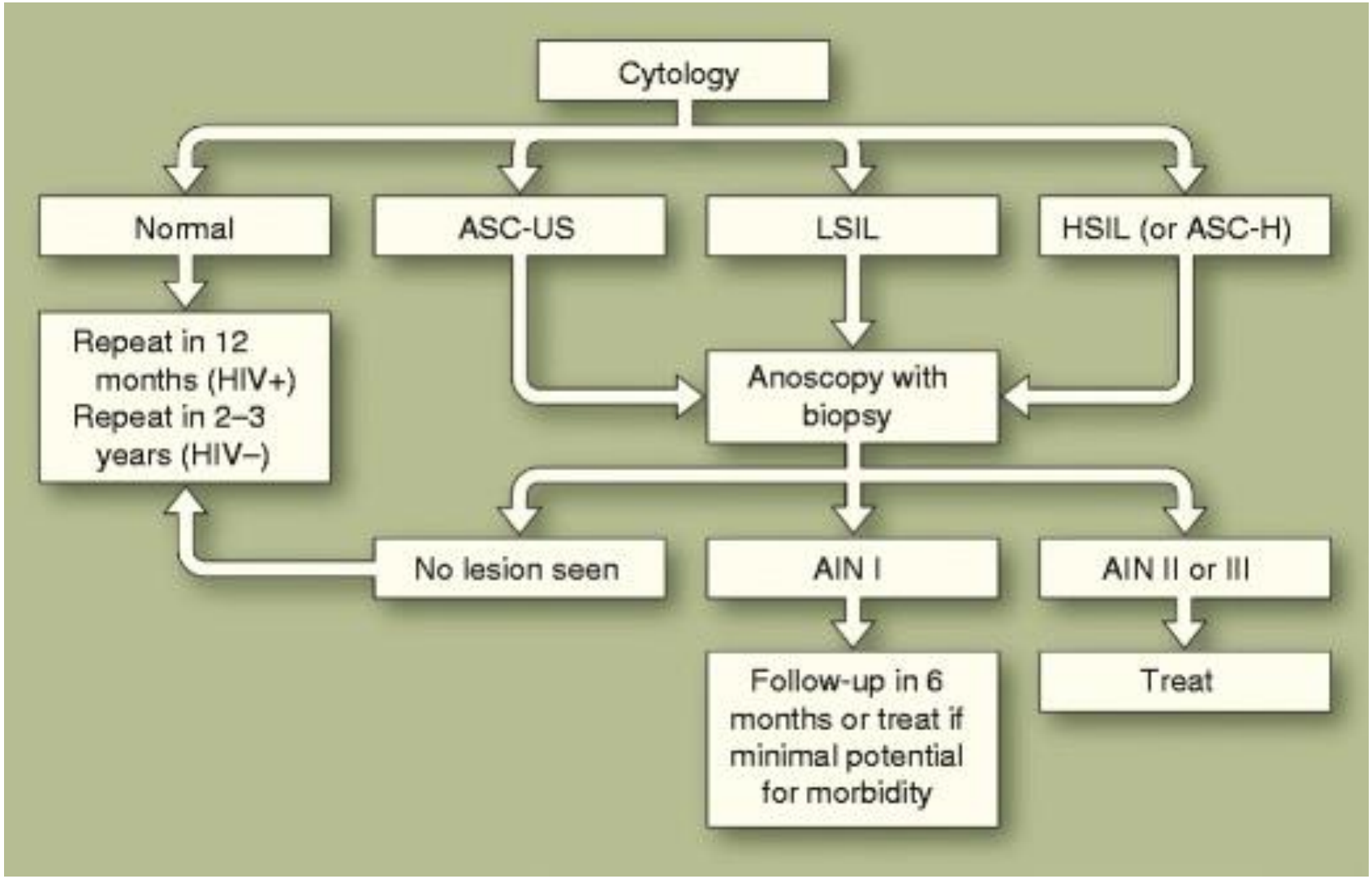
  vs. 3.3-6% patients year in HIV-neg MSM

Machalek and al. The lancet oncol. 2012

Anal screening in HIV patients

should be implemented… *but questions remain for HIV-patients:*

Anal screening in HIV patients



Park I and Palefsky J. *Curr Infect Dis Rep* (2010)

Does cART prevent HPV infections or HPV- induced lesions?

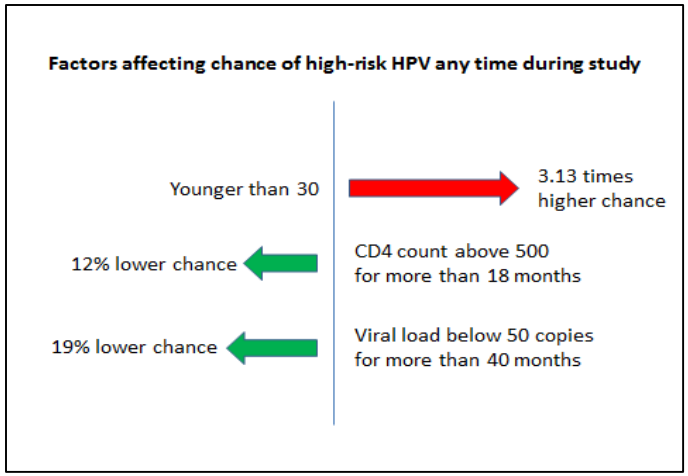
…more recently

FEMALE

Cohort of 652 women, 38 years,
successfully treated for HIV,
FU 61 months

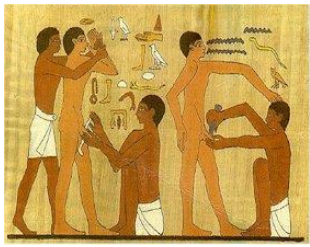
Sustained viral suppression and higher CD4 T cell reduces the risk of persistent HRHPV and of cytological abnormalities

Konopnicki D. *JID 2013*



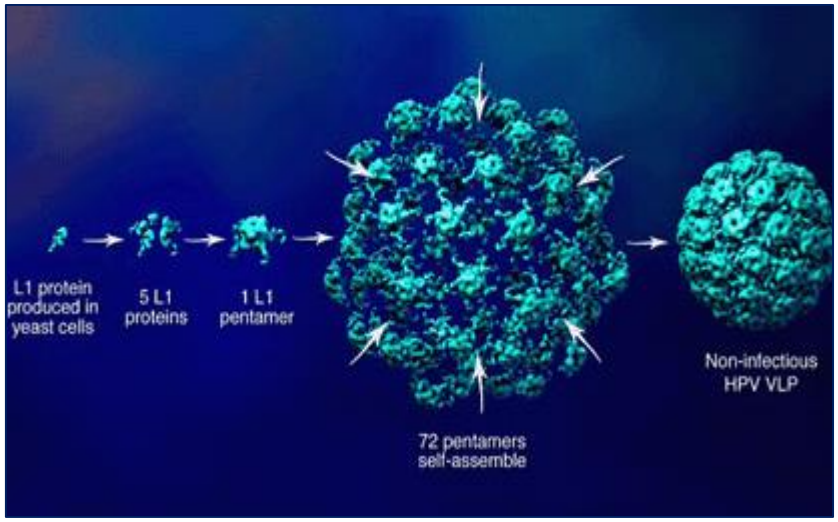
What about HPV prevention?

Condom and circumcision



- **Condoms** confer partial protection in HIV-negative couples both hetero- and homosexual . *What about HIV patients?*
- **Circumcision** decreases the prevalence and incidence of HRHPV in HIV-positive heterosexual men. Although it decreases also the prevalence in female partners when HIV- negative, *data in HIV-positive women and MSM are too scarce to draw similar conclusions*.

Preventive Vaccine



Quadrivalent (HPV4)

Gardasil®Merck:

L1 from HPV 6, 11, 16 and 18

Approval for EMA & FDA: 2006

0, 2 and months 6

Bivalent (HPV2)

Cervarix®GSK:

L1 from HPV 16 and 18 + ASO4

Approval for EMA & FDA:2007/9

0, 1 and 6 months

Preventive vaccine in HIV+patients

Quadrivalent vaccine 4 studies

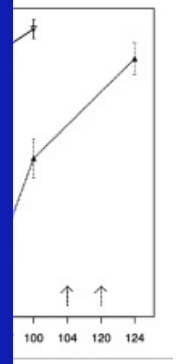
Levin. *J AIDS.* 2010
Wilkin. *JID* 2010
Kahn J. XIX International AIDS Conference. Washington 2012. WEAB0202
Kojic E. XIX International AIDS Conference. Washington 2012. WEAB0203

Studies on clinical efficacy ?

Phase IV 2010-2015:
Thailand, Brazil, USA

Gardasil vs Cervarix
in women 15-25 years

ongoing



-
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lso
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Biv

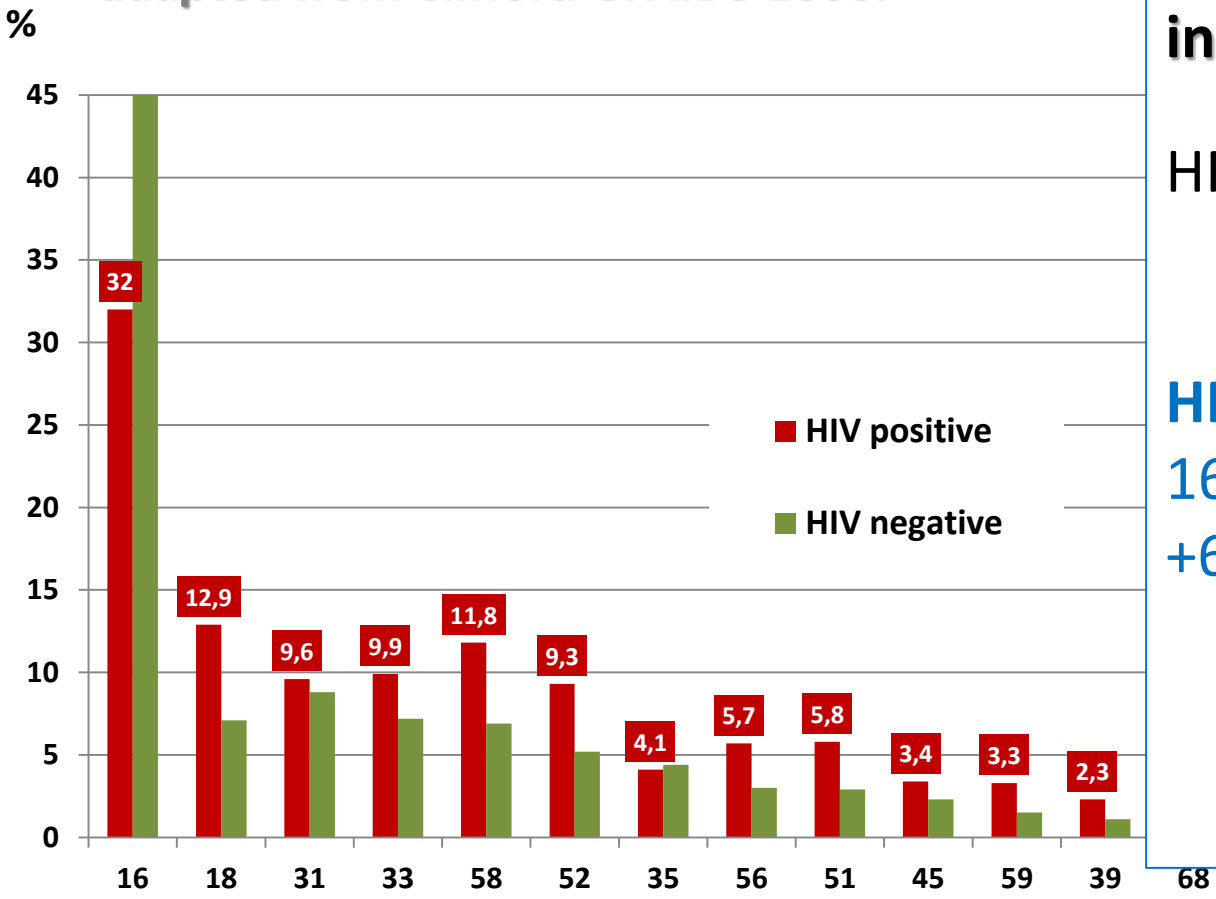
ne. 2013

- ***Good Immunogenicity***
- ***Good Safety, no deleterious effect on CD4 nor VL***
- ***Cellular immunity:*** HPV16/18 specific CD4+T cells response was substantially increased from month 2 to 12 in more than 82%

...an issue in HIV-positive patients

HPV genotype distribution in HG CIN in HIV positive and negative women

adapted from Clifford G. *AIDS* 2006.



Prevalence of HPV vaccine type in HGAIN in MSM in USA

HPV 2/4v 56.4%

HPV 9-v 89%
16/18/31/33/45/52/58 +6/11

Sahasrabudhe V. *JID 2013*

Proportion of women infected with HRHPV genotypes that could be covered by the different vaccines

Prevalence of women of whom all or a part of HRHPV types are covered by	Current HPV vaccines including HRHPV 16 /18	Ninevalent HPV vaccine including HRHPV 16/18/31/33/45/52/58
Among all women (n=126)	27%	**77%**
Among women with abnormal cytology (n=48)	28%	**82.5%**

Konopnicki D.
14th EACS Conference, October 16-19th 2013, Brussels. Poster PE 17/13

Ninevalent vaccine

- Gardasil 9®Merck
  - 6, 11
  - 16,18
  - 31, 33, 45, 52, 58
- Study phase III comparing Gardasil9 to Gardasil
  - N= 14,000 females 16-26 years
  - Efficacy for prevention of CIN2+, VIN2+or VAN2+ (induced by HPV31/33/45/52/58) : **97%**
- Safety similar
- Approved by FDA in Dec 2014 and EMA in march 2015
- 13$ more per dose: cost effective

Is vaccination indicated in patients with high grade lesions as secondary prophylaxis?

Women (HIV-negative)

- 2 randomised studies: Joura E. *BMJ* 2012.Woo Dae Kang. *Gynecol Oncol* 2013
- Decreased in recurrent lesions
  1. **- 65%** 2 years after treatment of CIN2-3 and vaccination

     -35% 2 years after treatment of condyloma and vaccination
  2. **2.5%** had recurrent CIN 2-3 among women vaccinated **vs 7.2%** in non vaccinated women

MSM (HIV-negative)

- 2 retrospective studies: Swedish K. *CID* 2012 & *PLOS ONE* 2014
- Limitations++ in methodology
- Decrease in recurrence in HGAIN or anal condyloma after treatment and vaccination

Should we vaccinate HIV-positive patients?

- High burden of disease
- Good immune efficacy and tolerability
- **The answer should be « Yes »!**

- We propose to vaccinate
  - **Girls and boys**
  - Young women and men **up to 26 years**
  - **When treating high grade lesions**

Conclusion: in HIV-infected patients (1)

- Infection with HPV and HPV-related cancerous lesions are more frequent and severe in HIV-infected patients.

- HPV infection (and in particular its clearance) favours the acquisition of HIV.

- **Preventive vaccines against HPV are safe and immunogenic: they should be implemented in HIV-infected children and adults.**

Conclusion: in HIV-infected patients (2)

- HPV testing for primary cervical screening could become the gold standard in both developed and in developing countries in women after 30 years.

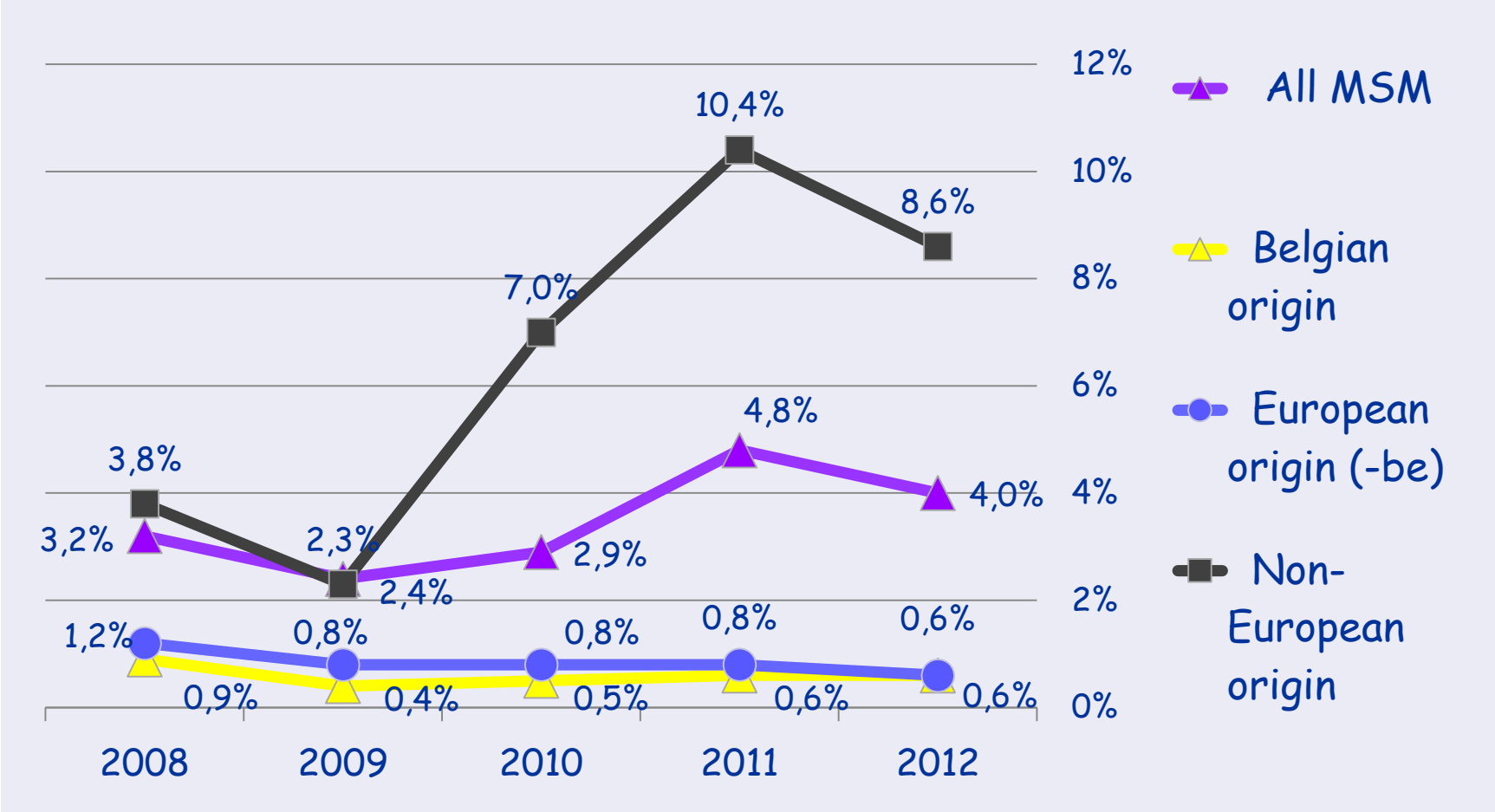
- **cART decreases infection by HRHPV and induced lesions but favourable impact appears after several years.**

- Therapeutic vaccines are in developpment

Few words on other sexually transmitted diseases in HIV patients

1. STI’s are HIV indicator diseases

HIV PREVALENCE in MSM



STI prevalences were stable :

8% for Syphilis, 4,8% for Chlamydia, 2,8% for Gonnorrhea, 0,8% for Hepatitis C.

Results – HIV diagnoses per Indicator Condition

	HIV test	HIV +	Prevalence (95%CI)	
Total	3588	66	1.84	(1.42-2.34)
STI	764	31	4.06	(2.78-5.71)
Malignant lymphoma	344	1	0.29	(0.01-1.61)
Cervical or anal dysplasia	542	2	0.37	(0.04-1.32)
Herpes Zoster <65yo	207	6	2.89	(1.07-6.21)
Hepatitis B/C	1099	4	0.36	(0.10-0.93)
On-going mononucleosis-like illness	441	17	3.85	(2.26-6.10)
Leuko/thrombocytopaenia	94	3	3.19	(0.66-9.04)
Seborrheic dermatitis/exanthema	97	2	2.06	(0.25-7.24)

HIV in Europe

HIV in Europe: Brussels data

HIV prevalence for each of the diseases tested with 95% CI, using the exact binomial method

	N° enrolled	N° test HIV positive	Prevalence (95%CI)	CD4 median	VL (log) median
Total indicator disease	**3588**	**66**	**1.84** (1.42-2.34)	**400**	**4.79**
A. Sexually transmitted	**764**	**31**	**4.06** (2.78-5.71)	**457**	**4.86**
Male	**538**	**29**	**5.39 %**		
Female	**226**	**2**	**0.88 %**		
- Gonorrhoea	**74**	**3**	**4.05** (0.85-5.14)		
- Syphilis	**80**	**8**	**10.00** (4.41-18.8)		
- Ulcer	**73**	**1**	**1.37** (0.03-7.40)		
- Chlamydia	**176**	**5**	**2.84** (0.09-6.50)		
- Unspecified	**373**	**16**	**4.29** (2.47-6.88)		
B. Malignant lymphoma	**344**	**1**	**0.29** (0.006-1.61)	**unk**	**unk**
C. Cervical or anal dysplasia or cancer	**542**	**2**	**0.37** (0.04-1.32)	**308**	**5.06**
- Cervical cancer/dysplasia	**460**	**0**	**0.00** (0.00-0.80)		
- Anal cancer/dysplasia	**69**	**2**	**2.90** (0.35-10.1)	**308**	**5.06**
- Unspecified (female only)	**13**	**0**	**0.00** (0.00-24.7)		
D. Herpes zoster	**207**	**6**	**2.89** (1.07-6.21)	**198**	**3.76**

2. Higher risk of neurosyphilis in HIV patients: consider LP!

3. Syphilis, Chlamydia, Gono, HCV, HBV and HPV are the most prevalent but do not forget:

- Trichomonas vaginalis
- Gardnerella vaginalis
- Mycoplasma genitalium
- and many others…


thank you
danke
рахмат
謝謝
ngiyabonga
teşekkür ederim
gracias
merci
obrigado
bedankt
dziękuję
спасибо
Баярлалаа
go raibh maith agat
mochchakkeram
sukriya
kop khun krap
terima kasih
grazie
arigatō
dakujem
takk
tack
dank je
tapadh leat
mersi
barka
welalin
spas
kia ora
mahalo
taafetai lava
vinaka
спасибі
blagodaram
misaotra
matondo
paldies
grazzi
хвала
asante
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nanni
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maururu
hvala
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