

# Infection à HPV et immunodépression - Suivi thérapeutique

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# **Infection à HPV et dysplasie chez les transplantés**

# Infection HPV chez les transplantées rénales

- Prévalence de l'infection à PVH:
  - Cervicale : 20 à 45 %
  - Génitale : 8 à 30 %
- Infection persistante
- Souvent multiple : 2 à 7 (génotypes PVH 16 et 18)
- Avec des génotypes rarement détectés dans la population générale

# Persistance de l'infection à HPV chez les transplantées rénales

133 femmes

- HPV positive = 39 femmes (29%)
  - Infection multiple = 18 femmes (46%)
  - HPV potentiellement oncogènes = 24 (61%)
  - Au moins un HPV non identifié = 24 (61%)
  - Persistance infection (5,6 ans en moyenne) = 14 (36%)
- 2/3 ont développé une NIC

# Néoplasies intra-épithéliales chez les transplantées rénales

- Prévalence
  - plus élevée dans les études cas-contrôles :
    - OR : 5.6 (95% CI, 1.1-38) à 8.5 (95% CI, 3.0-25),
- Durée moyenne d'apparition du CIN est de 3 ans après la transplantation

# Néoplasies intra-épithéliales chez les transplantées rénales

- Schneider *et al* (1983)

- 11 infections à PVH /132 femmes (8%), 6 NIC

Transplantation

HPV +

NIC



.....22 mois.....



16 mois



- Alloub *et al* (1989)

- Prévalence PVH tr/témoins : ns
- Prévalence PVH oncogènes 27% versus 6%  $p < 0.005$
- Prévalence NIC 49% versus 10%

# Cancers invasifs du col chez les transplantées rénales

- Cancers invasifs du col :
  - 2 cohortes (7035 et 2369 femmes)
    - Taux d'incidence st. **3.3** (95% CI, 1.7-5.8), 12 cas
    - Taux d'incidence st. **8.6** (95% CI, 5.7-13), 28 cas
  - Durée de suivi moyen : 5 à 6 ans

# **Infection à HPV et dysplasie du col au cours de l'infection à VIH**

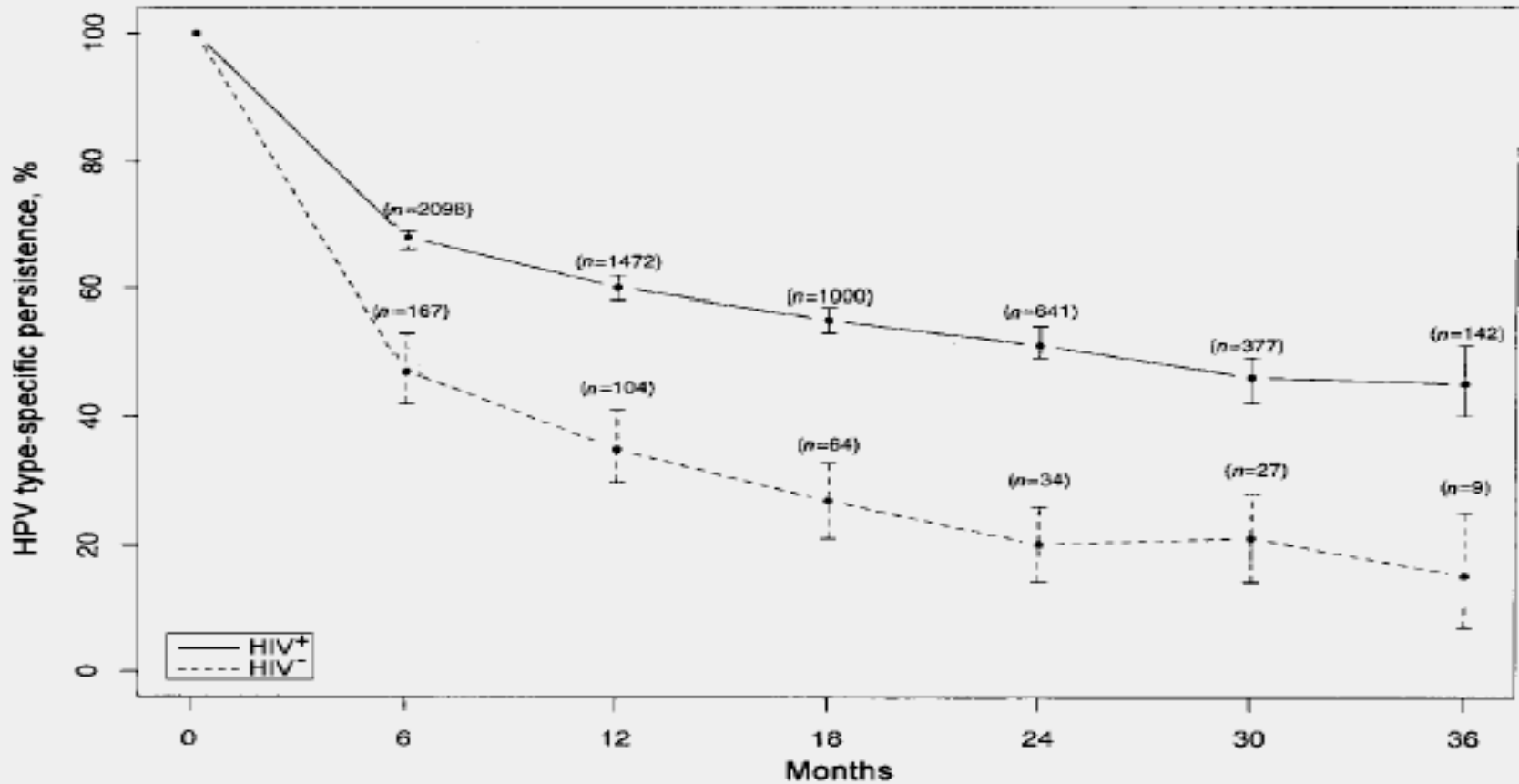
# Prevalence of HPV infection

- **Any HPV:**
  - 63% versus 27 %,
  - PR: 2.3 [95% CI, 2.0-2.8] (Jamieson *et al*, 2002)
- **High-risk HPV:**
  - 14% versus 3 %,
  - OR: 5.07 [95% CI, 2.98-8.63] (Palefsky *et al*, 1999).

# Characteristics of HPV infection

- **Multiple infection**
  - 38% versus 20 %,
  - PR: 1.9 [95% CI, 1.3-2.9] (Jamieson, 2002).
- **High HPV load**
  - 81% versus 63 %,
  - PR: 1.6 [95% CI, 1.1-2.2] (Jamieson, 2002).

# Persistence of HPV infection



# Risk factors for HPV infection

Immunosuppression ( $CD4 < 200/mm^3$ )

- ***In HIV positive women, lower CD4 cell count is strongly associated with***
  - ***HPV infection*** (OR 2.4 to 5.2 )
  - ***High-risk HPV types*** (OR 3.1; 95% CI, 2.0-4.7)
  - ***High HPV load*** (OR 5.9; 95% CI, 1.4-24.7)
  - ***Persistence of HPV DNA*** (OR 1.9; 95% CI, 1.5-2.3)

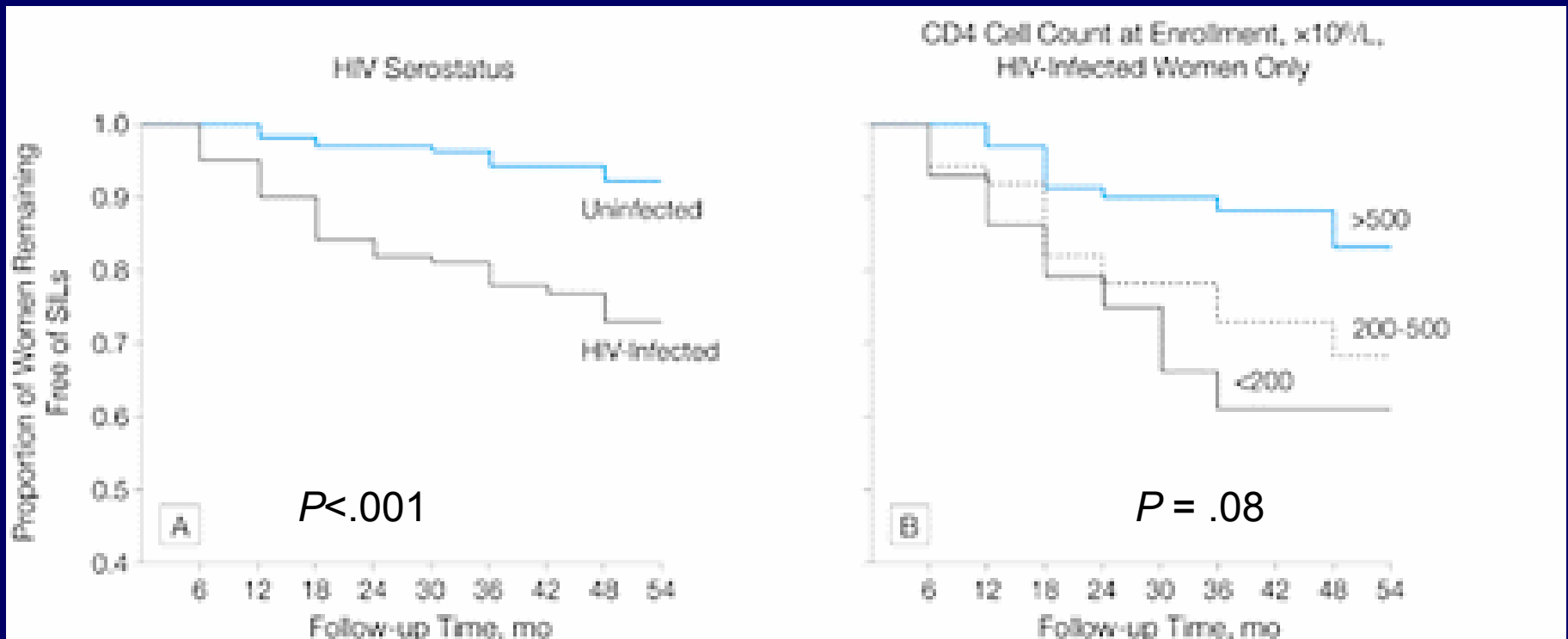
# Prevalence of cervical disease

	<b>HIV +</b>	<b>HIV -</b>	<i>p</i>
<b>Duerr</b> <i>et al</i> , 2001	39.9*	19.3	<0.001
<b>Massad</b> <i>et al</i> , 2000	38.3*	16.2	<0.001
<b>Six</b> <i>et al</i> , 1998	26.5	7.5	<0.05
<b>Wright</b> <i>et al</i> , 1994	20.1	4.2	<0.01

\* including ASCUS

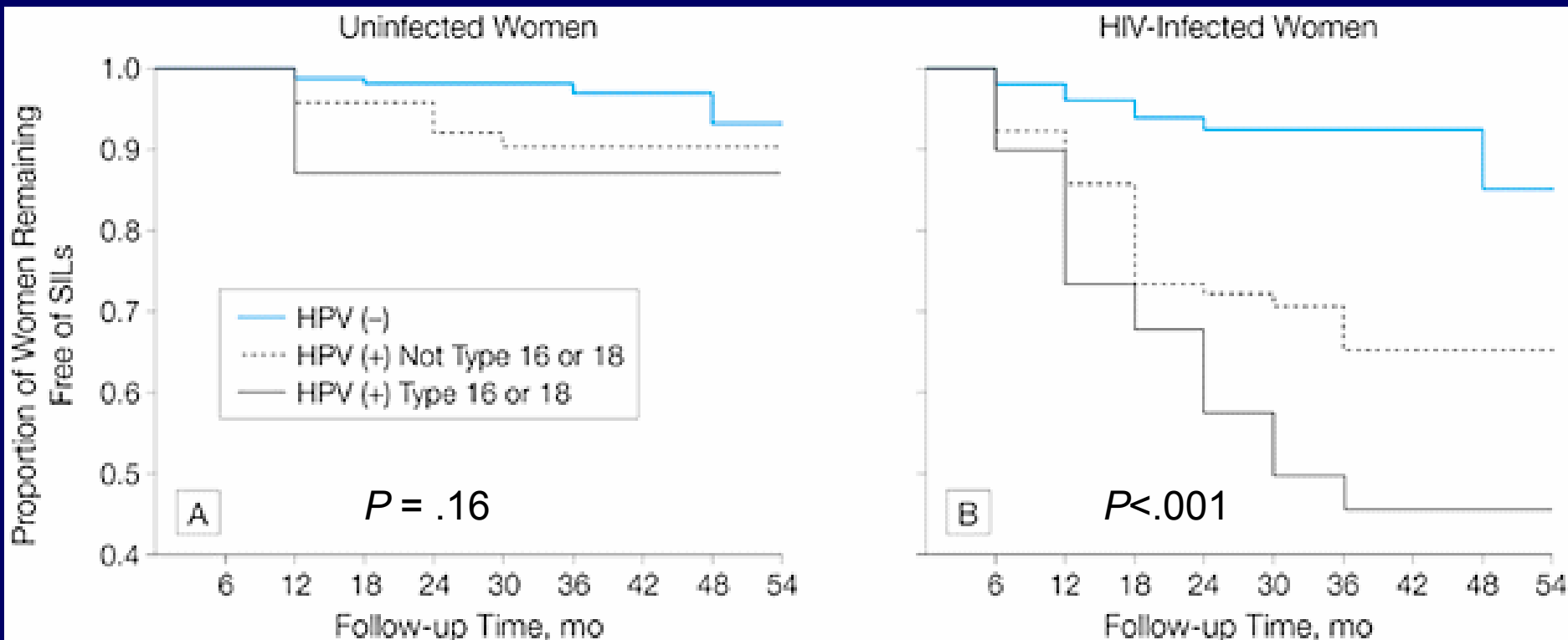
# Incidence of SIL

- 20% annual incidence
- Most low-grade SIL
- No association with CD4 cell count



# Incidence of cervical disease

- Significantly associated with HPV-DNA



# Risk factors for cervical disease

## 1/ Behavioral risk factors

### – No association was found with

- Age at first sexual intercourse,
- Number of sexual partners,
- Parity,
- Race or ethnicity

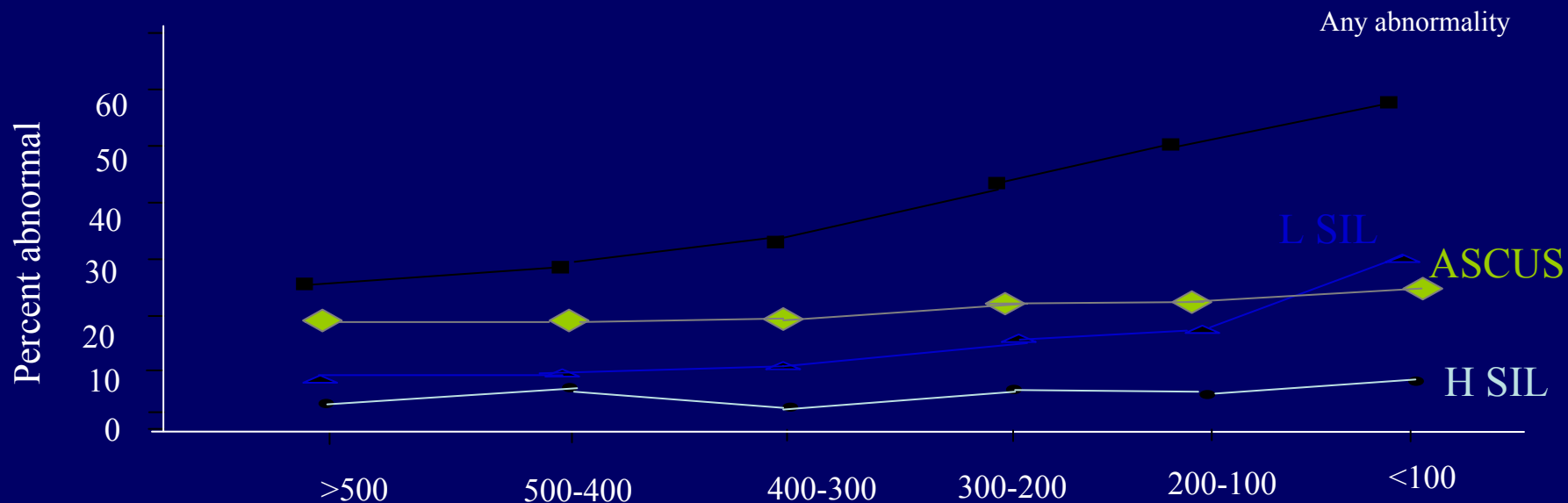
### – Current smoker $\pm$

### – Age $\pm$

# Risk factors for cervical disease

## 2/ immunosuppression

- Wright *et al*, *Obstet Gynecol*, 1994
  - mild association with ASCUS and L SIL
  - No association with H SIL
- Massad *et al*, *JAIDS*, 1999



# Risk factors for cervical disease

## 3/ HPV infection

– High-load HPV infection: aOR 16.8 [7.0-40.3]

Heard *et al*, Obstet Gynecol, 2000

– After adjustment for HPV infection, HIV infection increases

- moderately the risk of ASCUS
- Significantly the risk of SIL

Duerr *et al*, Am J Obstet Gynecol, 2001

# Natural history of cervical disease: 1/ regression

- **Before HAART**

- 29.5% at one year (Delmas *et al*, AIDS, 2000)

- **Upon HAART**

- 39% vs 12% (p=0.04) (Heard *et al*, AIDS, 1998)

- 35% vs 29% (OR 1,4[1.04-1.8]) (Minkoff *et al*, AIDS, 2001)

- L grade decrease after 1997 (Cubie *et al*, Sex Trans inf, 2000)

- No effect on CIN prevalence (Moore *et al*, AIDS, 1998)

# Natural history of cervical disease: 2/ progression

- **Before HAART**

- 55% vs 10% (Petry *et al*, Int J Cancer, 1994)

- **Upon HAART**

- Progression independent of the HIV treatment  
(Lillo *et al*, J Infect Dis, 2001)

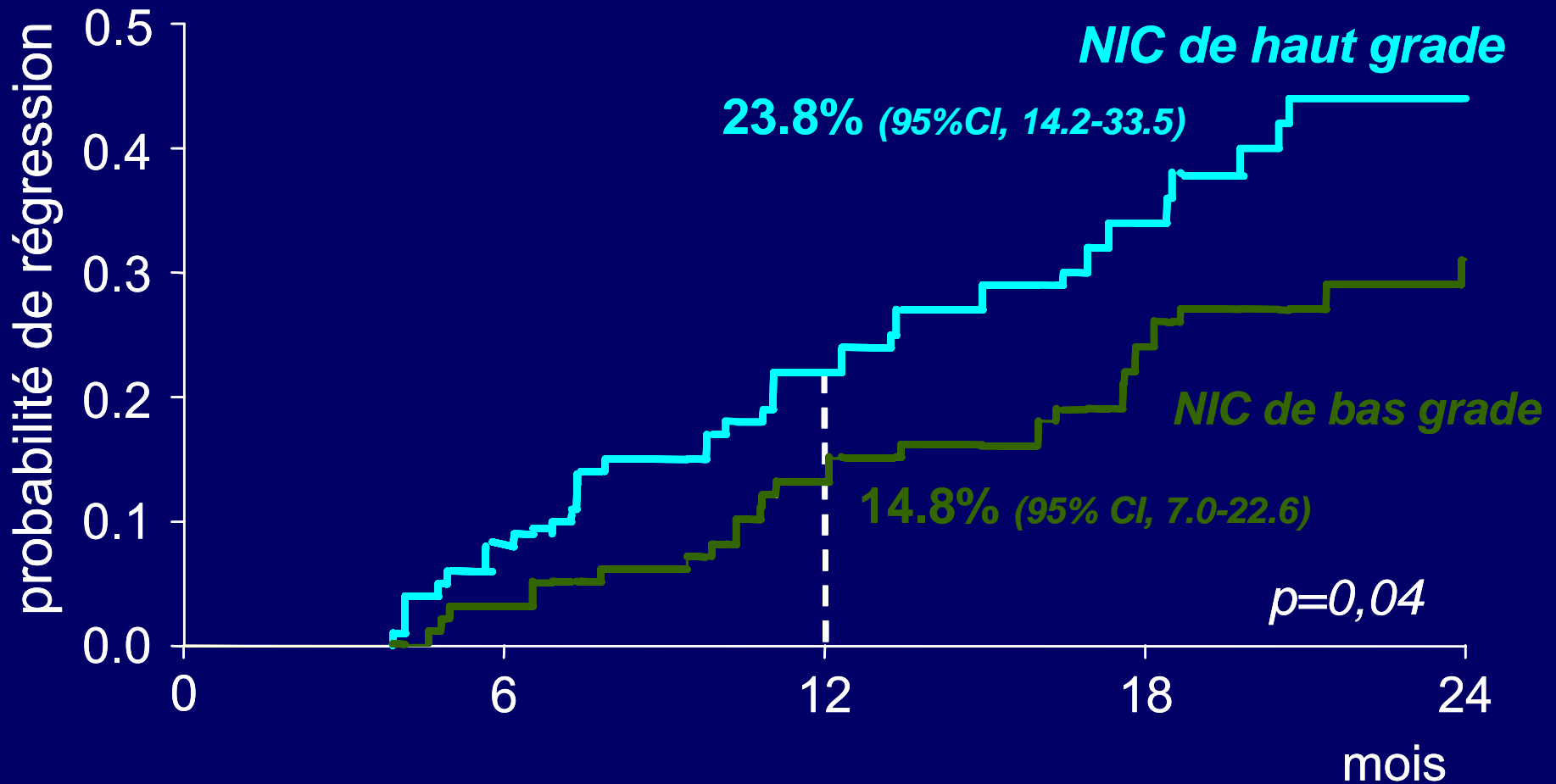
- Women on HAART were less likely to demonstrate progression (OR, 0.68; 95% CI, 0.52-0.88) (Minkoff *et al*, AIDS, 2001)

## *Highly active antiretroviral therapy enhances regression of cervical intraepithelial neoplasia in HIV-seropositive women*

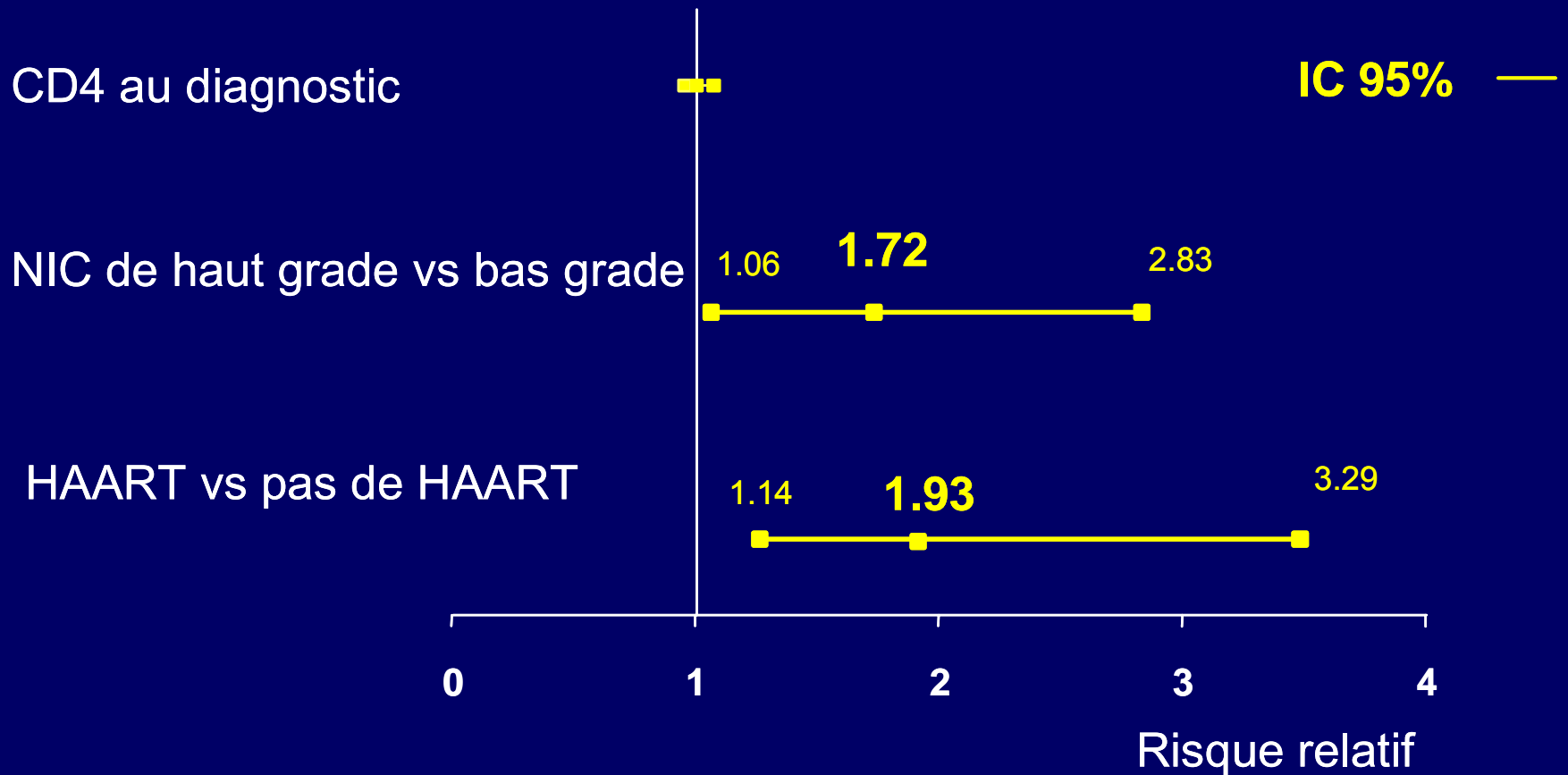
- 88 Lésions de bas grade et 80 lésions de haut grade suivies pendant une durée médiane de 18 mois,
- 96/168 (57%) femmes sous HAART
- Durée médiane du suivi sous HAART: 12,8 mois

Heard et al. AIDS 2002

# Probabilité de régression des NIC en fonction du grade



# Facteurs de risque de régression analyse multivariée



# Réponse immunitaire et virologique après 6 mois de HAART

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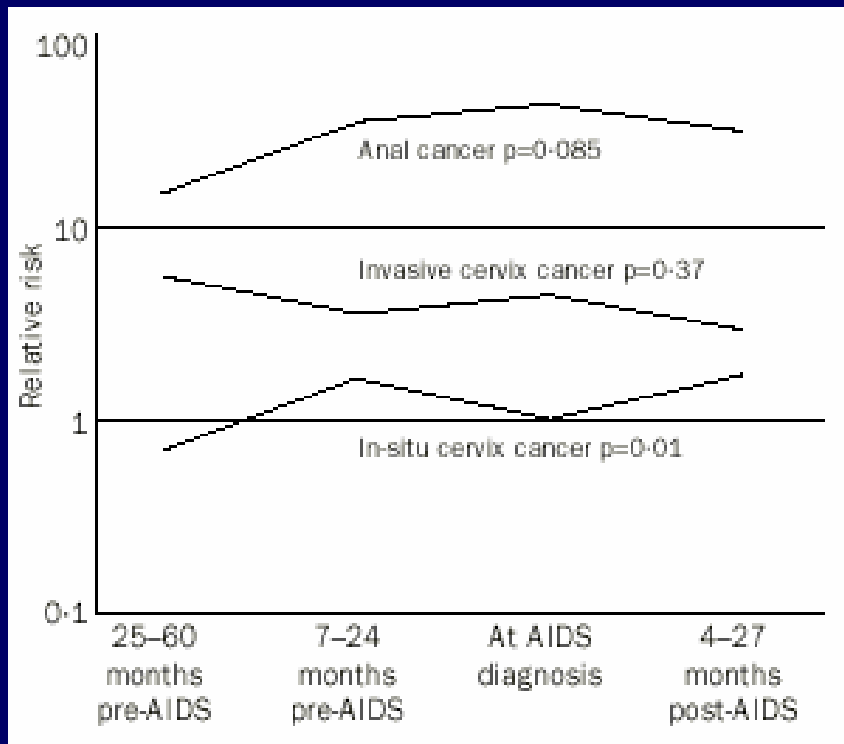
	régression de la lésion	Pas de régression	
CD4+ /mm <sup>3</sup> nb médián (IQR)	+ 112 (22-265)	+ 41(0-73)	p=0.057
Plasma HIV RNA log eq-copies/ml (IQR)	- 1.9 (0-4.4)	- 0.9 (0-3.4)	p= 0.3

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# Résultats des études disponibles

Réf.	Nombre de femmes	Objectifs de l'étude	Impact du HAART sur la NIC
Heard (1998)	49	Histoire naturelle des NIC après 5 mois de HAART	<b>positif *</b>
Orlando (1999)	15	Etude observationnelle de l'évolution des NIC de bas grade (régression/ progression)	aucun*
Del Mistro (1999)	119	Histoire naturelle des NIC chez des femmes traitées/non traitées	aucun
Lillo (2001)	163	Impact d'un court traitement sur la cytologie cervicale en cas d'infection par les PVH-HR	aucun
Minkoff (2001)	741	Impact du HAART sur la régression/ progression des lésions cytologiques à 6 mois	<b>positif*</b>
Luque (2001)	107	Effet du HAART sur l'infection et la maladie à PVH.	<b>positif</b>
Khanna (2001)	137	Effet du HAART sur la prévalence des NIC	<b>positif</b>
Robinson (2001)	54	Revue rétrospective – devenir des NIC après chirurgie.	<b>positif</b>
Wright (2002)	122	Efficacité du HAART sur la récurrence après chirurgie	aucun
Heard (2002)	168	Effet du HAART sur la régression des NIC	<b>positif *</b>
Moore (2002)	71	Prévalence des NIC avant et après 10 mois de HAART	aucun*
Keller (2002)	53	Revue rétrospective -Récurrence des NIC après chirurgie	<b>positif</b>

# Is HIV infection a risk factor for advanced cervical cancer ?



- CIN II-III/ in situ carcinoma = pre-aids defining event
- Invasive cervical cancer = AIDS-defining disease

J.J. Goedert *et al* Lancet 1998,

# Risk of ICC among women with HIV-infection

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Author	Years	Relative risk of ICC (95% CI)
Rabkin <i>et al</i>	1976-88	Decrease incidence
Frisch <i>et al</i>	1980-96	ICC : 5.4 (3.9-7.2) In Situ: 4.6 (4.3-5.0)
Serraino <i>et al</i>	1982-97	ICC : 12.8 (6.6-22.4)

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# Recurrent CIN after surgical treatment

- High rate of recurrence: 39% to 56%
- Regardless of
  - margin positive versus negative
  - CIN severity
  - Treatment: excision versus ablation
- Highly related with severe immunodeficiency
- High rate of VAIN after hysterectomy

# Effect of HAART + excisional therapy on CIN

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	Persistence/recurrence	
	Robinson <i>et al</i>	Wright <i>et al</i>
Ablation + HAART	3/17 = 18%	16/35 = 46%
Ablation without HAART	26/37 = 70% p<0.05	29/44=54 % ns

# Management of cervical lesions

## 1/ Screening tests

- Pap test :
  - 10-25 % false negative rates,
  - no decrease in sensitivity or specificity in HIV-positive women;
- Liquid-based media ?
- HPV testing in ASCUS,
- HPV-DNA testing as primary screening

# Management of cervical lesions

## 2/ Smears screening

- Complete gynecologic evaluation
- Pap test : 2/ year, then 1/year if normal
- More frequent if:
  - ✓ Previous abnormal
  - ✓ Known HPV infection
  - ✓ After surgical treatment
  - ✓ If symptomatic HIV ( $CD4 < 200/mm^3$ )


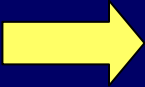
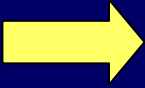

# Management of cervical lesions

## 3/ Colposcopy

- Indications :
  - ✓ Abnormal Pap smear,
  - ✓ Known HPV infection
  - ✓ After surgical treatment
  - ✓ If symptomatic HIV (CD4<200/mm<sup>3</sup>)
- Examine the entire lower genital tract,
- Biopsies obtained to confirm abnormalities.

# Management of cervical lesions

## (4)

- ASCUS  ◦ Colposcopy +biopsy twice a year
- Low-grade lesion  ◦ Colposcopy +biopsy once or twice a year
- High-grade lesions  ◦ Surgical treatment
- Invasive carcinoma  ◦ Surgery ± radiation

# **Infection à HPV et dysplasie anale au cours de l'infection à VIH**

# Infection à HPV et dysplasie anale

- Une pathologie probablement sous estimée et ignorée chez les homosexuels infectés par le VIH ?
- Augmentation du risque de cancer anal ?
- S'agit-il d'une infection sexuellement transmissible ou d'une infection opportuniste dans le cadre de l'infection à VIH ?
- Influence de la restauration immunitaire sous traitement antirétroviral combiné ?

# Prévalence de l'infection anale à HPV (1)

- Études chez l'homme homosexuel principalement
- Nombreuses études transversales
- Comparaisons infectés versus non infectés par le VIH
- Augmentation de la prévalence au cours de l'infection à VIH
- Corrélation avec  $CD4 < 500/mm^3$

# Prévalence de l'infection anale à HPV (2)

	VIH +	VIH -
PCR HPV +	n = 346	n = 262
Infection multiple	93%	61%
	73%	23%

Palefsky et al. J Infect Dis 98

	VIH +	VIH -
PCR HPV +	n = 322	n = 287
HPV faible risque	92%	66%
HPV haut risque	49%	36%
Infection multiple	56%	29%
	48%	19%

Critchlow et al. AIDS 98

# Prévalence des dysplasies anales

- Études chez l'homme homosexuel principalement
- Nombreuses études transversales
- Comparaisons infectés versus non infectés par le VIH
- Augmentation de la prévalence au cours de l'infection à VIH

	VIH +	VIH -
	n = 346	n = 262
ASIL	36%	7%
HSIL	5%	0,3%

# Facteurs de risque de dysplasie anale

- Infection à VIH : RR = 5,7 (IC95: 3,6 - 8,9)
- CD4
  - CD4 > 500 : RR = 3,8 (2,1 - 6,7)
  - CD4 = 200 – 500 : RR = 5,6 (3,4 - 9,0)
  - CD4 < 200 : RR = 7,3 (4,6 - 12)
- Hybride capture +
  - VIH + : RR = 8.8 (2,3 - 35)
  - VIH - : RR = 20 (5,5 - 71)

# Incidence et progression des dysplasies anales

- Incidence HSIL à 21 mois:
  - 24/158 (15 %) sujets infectés par le VIH
  - 8/147 (5 %) sujets non infectés par le VIH

Critchlow et al. AIDS 95

- Incidence HSIL à 2 ans et 4 ans
  - 277 séropositifs et 221 séronégatifs
  - 20 % et 49% chez sujets infectés par le VIH
  - 8 % et 17% chez sujets non infectés par le VIH

Palefsky et al. AIDS 98

# Facteurs de risques de progression

- Présence de HPV 16 et 18
- Persistance d'un haut niveau de détection d'HPV
- Progression de l'immunosuppression
- CD4 < 500

Palefsky et al. AIDS 98

# Cancer du canal anal et infection à VIH

- Incidence du cancer du col dans la population générale :
  - 8-10 / 100 000
- Incidence du cancer anal chez MSM VIH- :
  - 37 / 100 000
- Augmentation du risque de cancer anal chez MSM VIH+ d'un facteur 2  
(Goedert et al. Lancet 98)
- Cancer anal chez MSM stade SIDA / population générale:
  - Risque relatif = 84,1 (46,4 - 152)  
(Melbye et al. Lancet 94)
- Entre 1979 et 1985: ↗ incidence du cancer anal x 10 chez les hommes de 20 à 49 ans vivant à New York  
(Biggar et al. Int J Cancer 89)

L'infection à HPV anale est-elle  
seulement une IST ou peut-elle  
être une infection opportuniste ?

Si oui, quel est le risque de  
dysplasies anales associées ?

# HIV-infected Intravenous Drug Users are at High Risk of Anal Squamous Intraepithelial Lesions Related to HPV Infection

**C. Piketty<sup>1\*</sup>, T.M. Darragh<sup>2</sup>, M. Da Costa<sup>2</sup>, P. Bruneval<sup>1</sup>, I. Heard<sup>1</sup>, M.D. Kazatchkine<sup>1</sup>, J.M. Palefsky<sup>2</sup>**

<sup>1</sup>Hôpital Européen Georges Pompidou, Paris, France.

<sup>2</sup>Univ. of California, San Francisco.

# OBJECTIVE

- **Several studies have shown the risk of anal cancer to be elevated among men with history of homosexual and bisexual activity**
- **Recent reports have shown that HIV-positive homosexual men have higher rates of anal squamous intraepithelial lesions (SIL) and HPV infection, than HIV-negative men**
- **To date, the prevalence of anal SIL and HPV infection has not been evaluated in HIV-infected intravenous drug users (IVDUs) in the absence of receptive anal intercourse**

# METHODS (1)

- **117 HIV-infected patients including :**
  - **67 homosexual males**
  - **50 IVDU males**
- **Subjects were interviewed by self administered questionnaire regarding medical history, sexual practices and substance use**
- **All included IVDUs reported never having had sex with men**

# **METHODS (2)**

- **A complete anal examination was conducted that included insertion of Dacron™ swabs for anal cytology and HPV DNA testing and anoscopy**
- **In case of abnormal cytology consenting subjects underwent anal biopsy**
- **If both cytologic and histologic results were available for analysis, a subject's diagnosis was categorized in terms of the most severe result**

# **METHODS (Anal cytology and biopsy)**

- **Anal cytology samples were processed by the ThinPrep™ process**
- **Anal cytology and histology were evaluated without knowledge of clinical status of the subject**
- **Anal cytology and histology results were classified as normal, ASCUS, LSIL, or HSIL using current criteria for evaluation**

# **METHODS (HPV testing)**

- **To obtain a sample for HPV testing, a Dacron™ swab was inserted into the anal canal and immediately rinsed in a vial of PreservCyt™ solution**
- **HPV DNA was detected and typed by L1 consensus PCR**
- **Type specific probing was performed for the following HPV types individually:**
- **6, 11, 16, 18, 26, 31, 32, 33, 35, 39, 40, 45, 51, 52, 53, 54, 56, 58, 59, 61, 66, 68, 69, 70, 73, Pap 155, Pap 291, and AE2**

# RESULTS

## (Characteristics of the population)

	Homosexual males N = 67	IVDUs N = 50	p
Age, y $\pm$ SE	41.6 $\pm$ 1.2	38.1 $\pm$ 0.5	0.01
AIDS	18 / 67 (27 %)	15 / 50 (30 %)	ns
ARV treatment	61 / 67 (91 %)	42 / 50 (84 %)	ns
PI treatment	46 / 67 (69 %)	30 / 50 (60 %)	ns
CD4 cell count ( $\times 10^6$ / L $\pm$ SE)	317 $\pm$ 16	244 $\pm$ 21	0.005
HIV-RNA (Log / mL $\pm$ SE)	3.05 $\pm$ 0.15	3.40 $\pm$ 0.2	ns

# RESULTS (histology and / or cytology)

Anal lesion status		Men who have sex with men N = 67	Injection drug user men N = 50	p*
Normal		19 (28%)	32 (64%)	0.0002
Abnormal				
	ASCUS	3 (5 %)	1 (2 %)	0.14
	LSIL	33 (49 %)	8 (16 %)	
	HSIL	12 (18 %)	9 (18 %)	
Total		67 (100%)	50 (100%)	

\*Fisher's exact test

# Proportion with anal HPV infection stratified by HIV risk group

	Men who have sex with men N = 67	Injection drug user men N = 50	p*
<b>HPV positive</b>	<b>57 (85 %)</b>	<b>23 (46 %)</b>	< 0.0001
More than one HPV type	<b>35/57 (61%)</b>	<b>6/23 (26%)</b>	0.006
At least three different HPV types	<b>25/57 (44%)</b>	<b>2/23 (8%)</b>	0.003
At least one high-risk type	<b>37/57 (65 %)</b>	<b>10/23 (44 %)</b>	0.08
Low risk types alone	<b>20/57 (35 %)</b>	<b>10/23 (44 %)</b>	0.08
Unidentified types	<b>6/57 (10%)</b>	<b>6/23 (26 %)</b>	0.5
<b>Among patients with at least one high risk type</b>			
≥ 2 high risk types	<b>24/37 (65%)</b>	<b>1/10 (10%)</b>	0.003
PCR intensity of high risk types ≥ 2	<b>33/37 (89%)</b>	<b>9/10 (90%)</b>	1

# RESULTS (High risk types)

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	Homosexual males	IVDUs	p
HPV 16	17 / 57 (30 %)	5 / 23 (22 %)	ns
HPV 18	9 / 57 (16 %)	1 / 23 (4 %)	ns
HPV 31	7 / 57 (12 %)	0	ns
HPV 45	6 / 57 (11 %)	1 / 23 (4 %)	ns

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Multiple HPV infection was usual among homosexual group  
The percentages represent the percentages of only the HPV+ men

# Risk factors for anal SIL: Univariate analysis

Variables	Men who have sex with men group			Injection drug user group		
	Anal histology and/or cytology		Odds ratio (95% confidence interval); p value	Anal histology and/or cytology		Odds ratio (95% confidence interval); p value
	Abnormal	Normal		Abnormal	Normal	
Age < 35 years	12/48	7/19	0.6 (0.2 - 1.8); 0.3	4/18	6/32	1.2 (0.3 - 5.1); 0.7
Current smoking	28/48	12/19	0.9 (0.3 - 3.1); 0.9	16/18	31/32	0.3 (0.2 - 3.0); 0.3
Age at first intercourse < 16 years	11/48	6/18	0.6 (0.2 - 1.9); 0.4	10/18	16/32	1.2 (0.4 - 3.9); 0.7
Lifetime sexual partners ≥ 40	34/48	12/18	1.2 (0.4 - 3.8); 0.7	10/18	15/32	1.4 (0.4 - 4.5); 0.6
More than 10 lifetime episodes of receptive anal intercourse	42/48	10/18	<b>5.6 (1.6 - 19.8); 0.007</b>	–	–	NA
History of anogenital warts	23/48	6/19	1.9 (0.6 - 6.1); 0.2	5/18	4/32	2.7 (0.6 - 11.7); 0.2
History of gonorrhea, syphilis or anogenital herpes	29/48	10/19	1.4 (0.5 - 4.0); 0.6	4/18	11/32	0.5 (0.1 - 2.1); 0.4
CD4+ cell count < 250 x 10 <sup>6</sup> / L	15/48	6/19	0.9 (0.3 - 3.1); 0.9	13/18	10/32	<b>5.7 (1.6 - 20.4); 0.007</b>
Nadir CD4+ cell count < 100 x 10 <sup>6</sup> / L	16/48	5/19	1.4 (0.4 - 4.6); 0.6	14/18	11/32	<b>6.7 (1.8 - 25.2); 0.005</b>
Plasma HIV-RNA > 1.7 log /mL	38/48	12/19	2.2 (0.7 - 7.1); 0.2	17/18	21/32	<b>8.9 (1.1 - 76.0); 0.04</b>
Prior AIDS defining event	15/48	3/19	2.4 (0.6 - 9.6); 0.2	9/18	6/32	<b>4.3 (1.2 - 15.6); 0.02</b>
Current antiretroviral treatment	44/48	17/19	1.3 (0.2 - 7.7); 0.8	15/18	27/32	0.9 (0.2 - 4.4); 0.9
Current protease inhibitor treatment	33/48	13/19	1.0 (0.3 - 3.2); 0.9	12/18	18/32	1.6 (0.5 - 5.1); 0.5
Presence of HPV	45/48	12/19	<b>8.7 (1.9 - 39.0); 0.004</b>	13/18	10/32	<b>5.7 (1.6 - 20.4); 0.007</b>
Presence of high risk HPV type in patients with positive HPV detection	30/45	7/12	1.4 (0.4 - 5.3); 0.6	6/13	4/10	1.2 (0.2 - 6.8); 0.8

# Risk factors for anal SIL: Multivariate analysis

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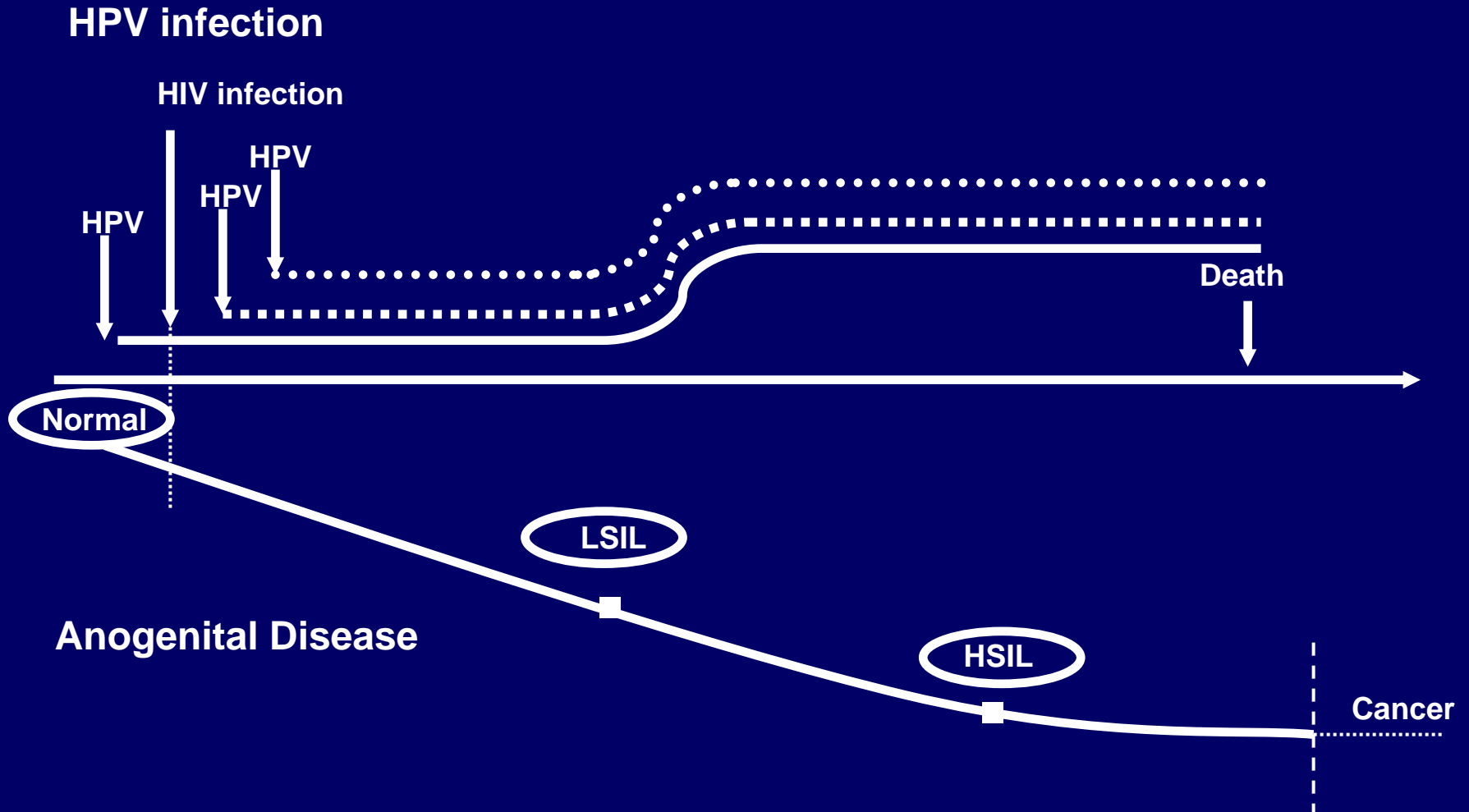
Parameters	Odds ratio (95% confidence interval); p value	
	Homosexual group	IVDU group
More than 10 receptive intercourses	<b>4.6 (1.2 - 17.8); 0.02</b>	
CD4+ cell count < 250 x 10 <sup>6</sup> / L		<b>5.1 (1.1 - 25.8); 0.04</b>
Plasma HIV-RNA > 1.7 log /mL		<b>16.4 (1.2 - 228.2); 0.03</b>
Prior AIDS defining event		<b>5.2 (1.1 - 26.9); 0.04</b>
Presence of HPV	<b>6.0 (1.2 - 30.2); 0.03</b>	<b>9.5 (1.7 - 52.4); 0.01</b>

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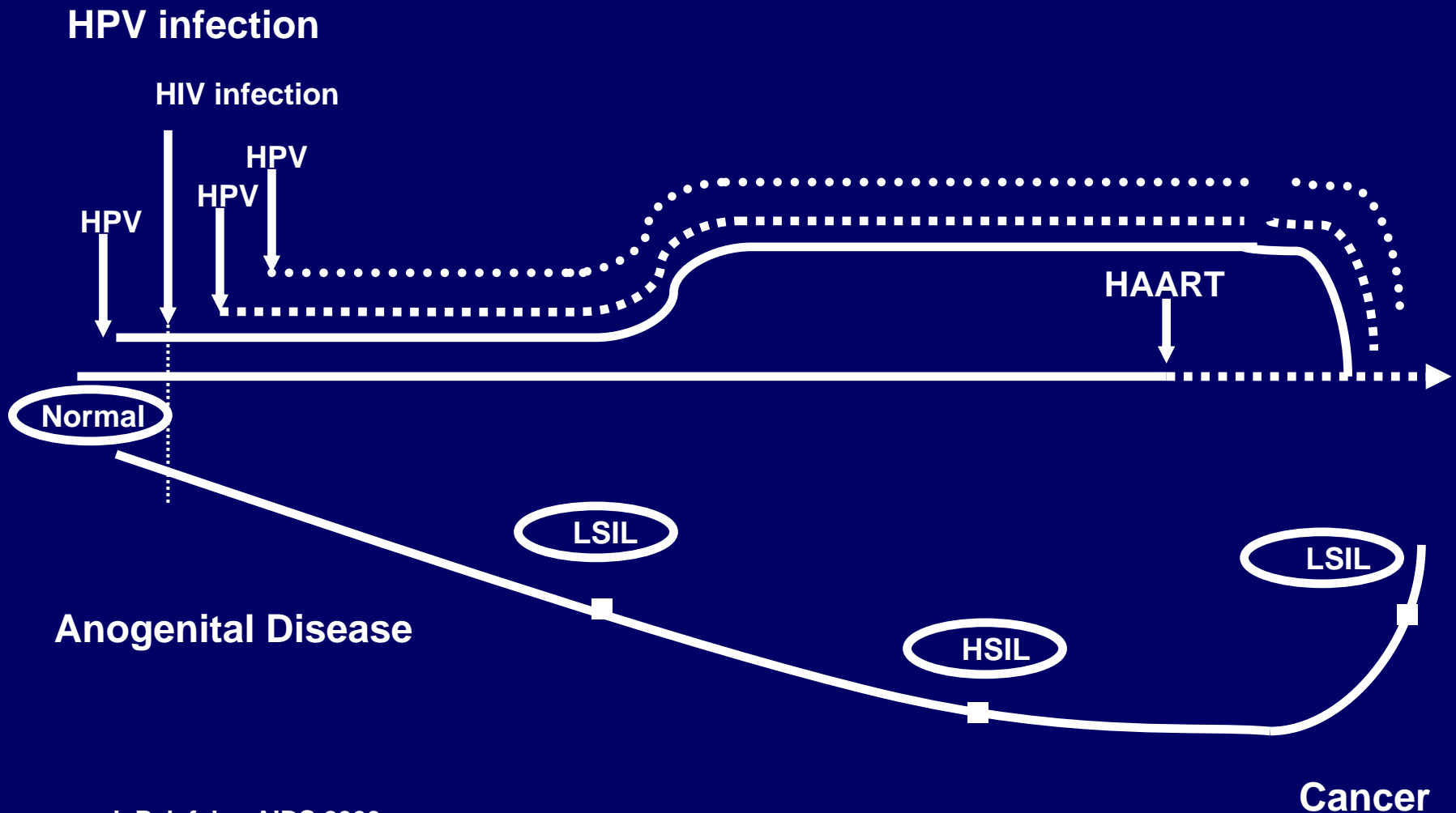


La restauration immunitaire sous  
trithérapie antirétrovirale a-t-elle un  
impact de la sur  
l'infection à HPV, les dysplasies et  
les néoplasie anales

# Modèle de progression avant HAART



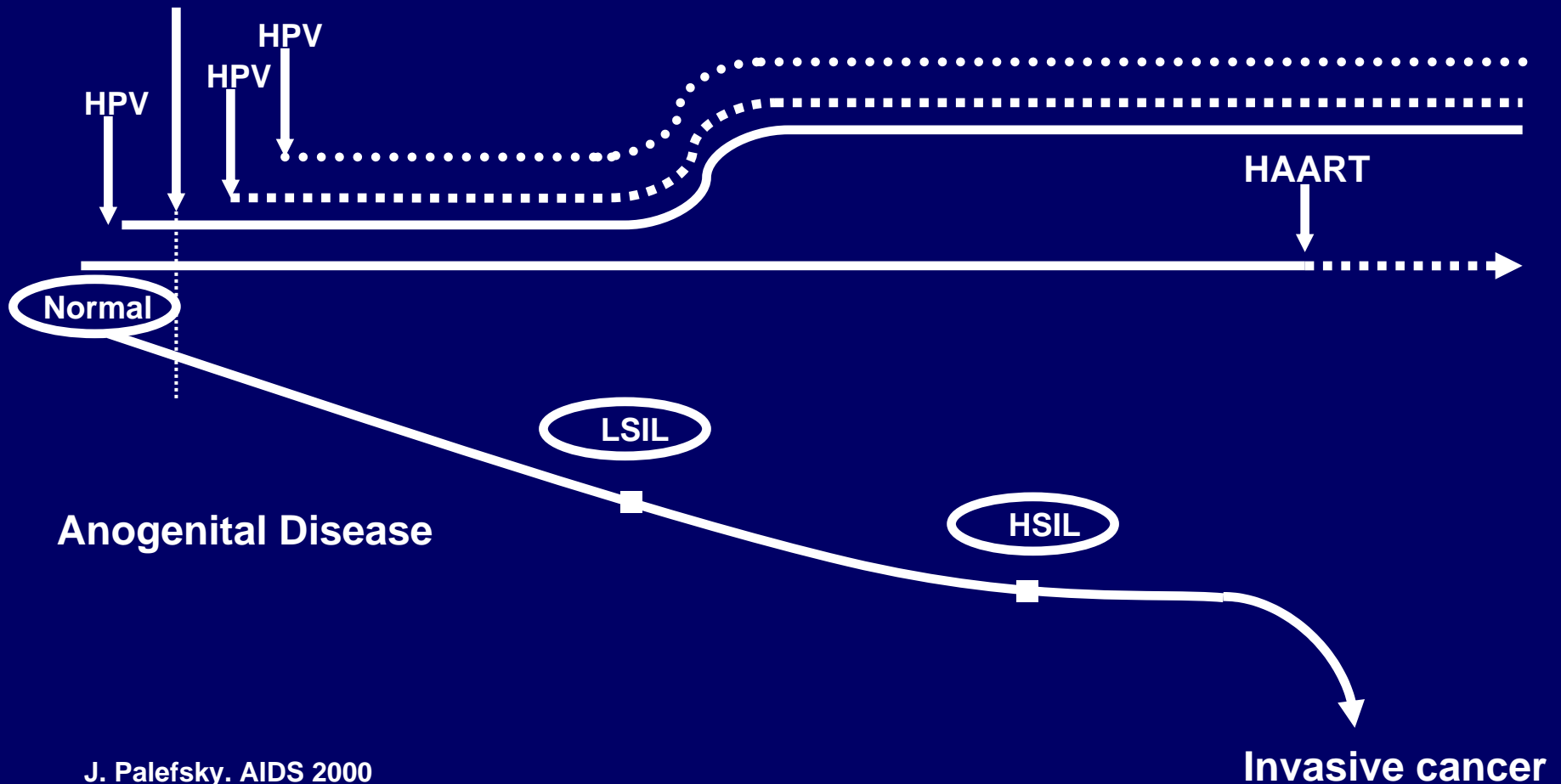
# Modèle de progression après HAART (a)



# Modèle de progression après HAART (b)

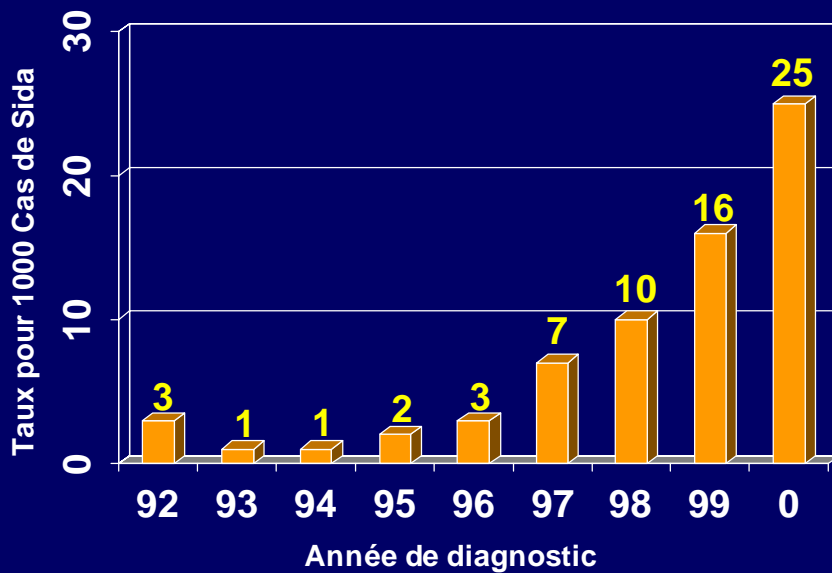
HPV infection

HIV infection



# HPV, HAART et cancer anal

Nombre de cas de cancer anal parmi les cas de SIDA à San Diego 1992 - 2000



	Pre HAART	Post HAART
Durée de l'infection VIH	29 mois	84 mois
Cancer anal	8 (21%)	21 (79%)
Cancer anal in situ	3 (28%)	8 (72%)

# HAART et infection à HPV anale

- Étude longitudinale
- 98 patients sous HAART
- Suivi 48 mois avant HAART et 6 mois après
- Évolution de l'infection à HPV :
  - Hybrid Capture + chez 4/5 (80%) patients négatifs avant HAART
  - Low Risk type + chez 8/26 (31%) patients négatifs avant HAART
  - High Risk type + chez 5/10 (50%) patients négatifs avant HAART
  - Hybrid Capture négative chez 2/79 (3%) patients positifs avant HAART

# HAART et dysplasie anale

- Évolution des dysplasies :
  - 7/38 ASCUS/LSIL (18%) : progression à 6 mois
  - 8/38 ASCUS/LSIL (21%) : régression à 6 mois
  - 2/12 NORMAL (17%) : progression à 6 mois
  - 12/28 HSIL (43%) : régression
  - 16/28 HSIL (57%) : stable
- Pas d'association entre régression et réponse immunitaire

# High Prevalence of Anal Squamous Intraepithelial Lesions Related to HPV Infection Despite Immune Restoration Under HAART

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# METHODS

- 46 HIV-infected protease inhibitor-experienced homosexual males were enrolled in a cross-sectional study.
- A complete anal examination was conducted that included insertion of Dacron™ swabs for anal cytology and HPV DNA testing and anoscopy.
- In case of abnormal cytology consenting subjects underwent anal biopsy.
- If both cytologic and histologic results were available for analysis, a subject's diagnosis was categorized in terms of the most severe result .

# Characteristics of the population

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Age, y $\pm$ SE	41.2 $\pm$ 1.4
AIDS	16 / 46 (35 %)
Duration of ARV treatment, m $\pm$ SE (range)	57.3 $\pm$ 4.6 (3 – 149)
Duration of PI treatment, m $\pm$ SE (range)	30.8 $\pm$ 10.1 (3 – 53)
CD4 cell count ( $\times 10^6$ / L $\pm$ SE)	294.5 $\pm$ 18.9
Nadir of CD4 cell count ( $\times 10^6$ / L $\pm$ SE)	121.4 $\pm$ 18.3
HIV-RNA (Log / mL $\pm$ SE)	2.9 $\pm$ 0.18

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# RESULTS (histology and / or cytology)

<b>Abnormal</b>		<b>33 (72 %)</b>
	<b>ASCUS</b>	<b>3 (7 %)</b>
	<b>LSIL</b>	<b>19 (41 %)</b>
	<b>HSIL</b>	<b>11 (24 %)</b>

**ASCUS : atypical squamous cell of indetermined significance**

**HSIL : high-grade squamous intraepithelial lesion**

**LSIL : low grade squamous intraepithelial lesion**

# RESULTS (HPV testing)

<b>HPV positive</b>	<b>37 (80 %)</b>
<b>More than one HPV type</b>	<b>21/37 (57%)</b>
<b>At least one High-risk type</b>	<b>22 / 37 (60 %)</b>
<b>Low-risk types alone</b>	<b>15 (40 %)</b>
<b>Number of different HPV types (mean <math>\pm</math> SE)</b>	<b>2.4 <math>\pm</math> 0.3</b>
<b>Number of high risk types (mean <math>\pm</math> SE)</b>	<b>1.9 <math>\pm</math> 0.2</b>

**High-risk types included types 16, 18, 31, 45, 33, 35, 39, 51, 52, 56, 58, 59, 68, 70, 73**  
**Low-risk types included types 6,11, 26, 40, 53, 54, 55, 61, 66, Pap 155, Pap 291, AE2**

# Anal SIL and HPV infection according to baseline CD4 cell counts

	CD4 < 250	CD4 ≥ 250	p
Presence of anal SIL	12/18 (67%)	21/28 (75%)	0.78
Presence of HSIL	4/18 (22%)	7/28 (25%)	0.9
Presence of HPV infection	15/18 (83%)	22/28 (79%)	0.9
Presence of high risk type	15/22 (68%)	7/15 (47%)	0.3

# Anal SIL and HPV infection according to increase in CD4 cell count

	↗ CD4 < 100	↗ CD4 ≥ 100	p
Presence of ASIL	7/13 (54%)	26/33 (79%)	0.1
Presence of HSIL	4/13 (31%)	7/33 (21%)	0.7
Presence of HPV infection	10/13 (77%)	27/33 (82%)	0.7
Presence of high risk type	5/10 (50%)	17/27 (63%)	0.7
Number of different HPV types	1.8 ± 0.4	2.6 ± 0.3	0.1

# Conclusion

- Nécessité d'un dépistage systématique des dysplasies anales
  - Peu ou pas de prise de conscience en France ?
- Nécessité de nouvelles études longitudinales pour mieux préciser l'impact de la restauration immunitaire sous HAART ainsi que la prévalence et l'incidence chez les hétérosexuels infectés par le VIH
- Quel traitement optimal ?

# Dépistage et prise en charge des lésions anales

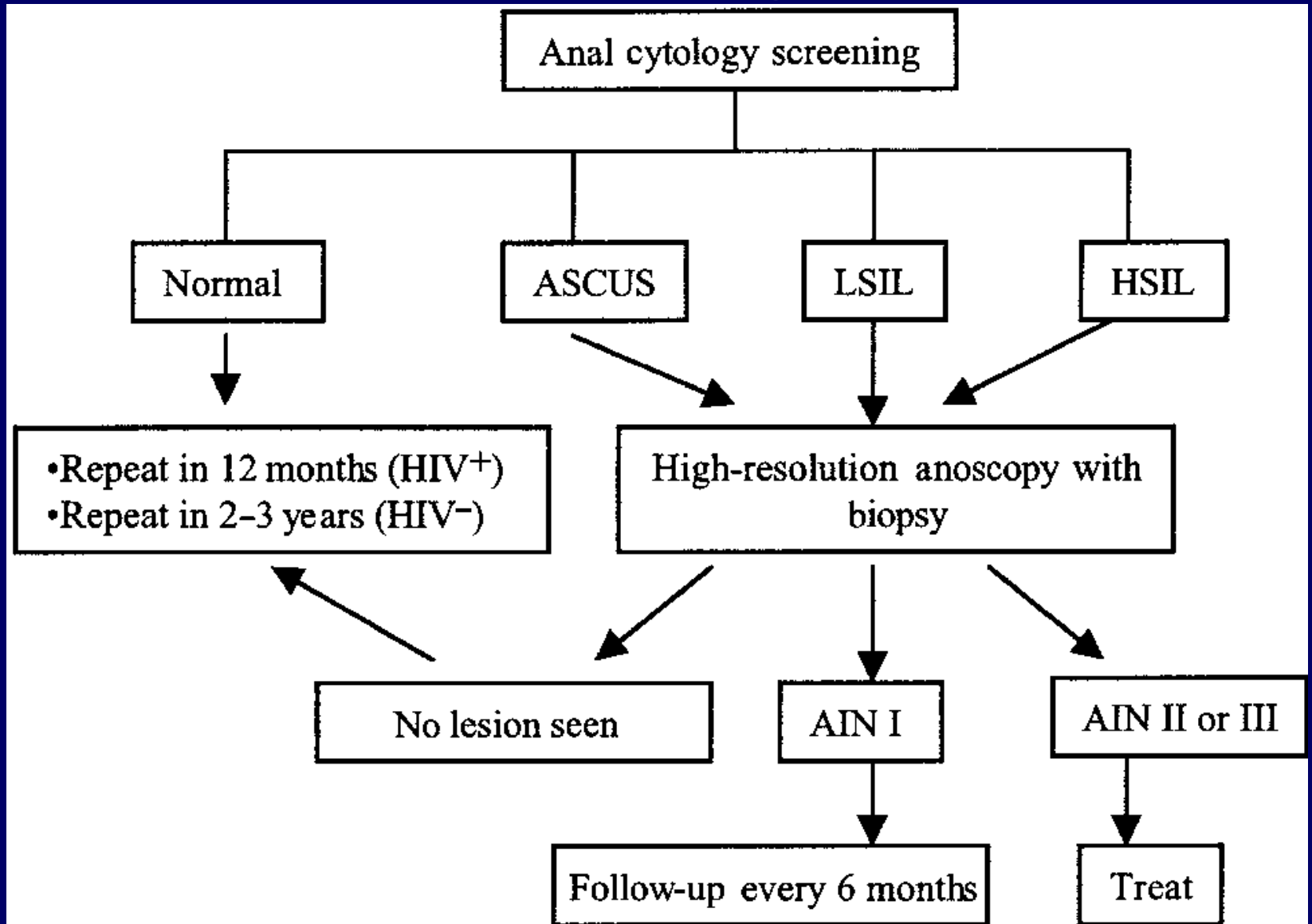
Quelle population ?

- Homosexuels ,  $CD4 < 500/mm^3$
- Autres groupes de transmission du VIH ?
- Femmes ?

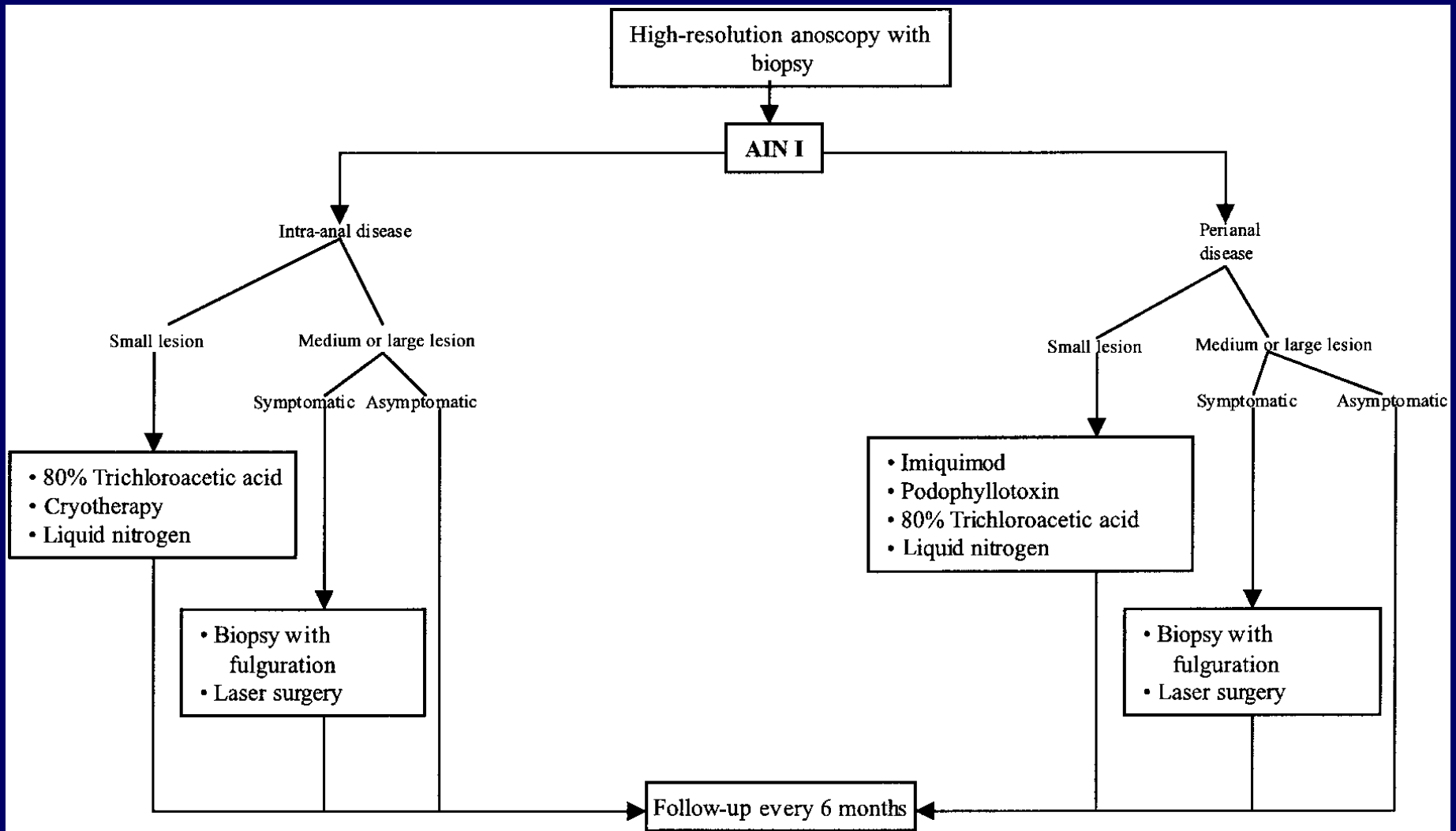
Quel dépistage ?

- Clinique
- Cytologie puis histologie si cytologie anormale
- Détection HPV si ASCUS

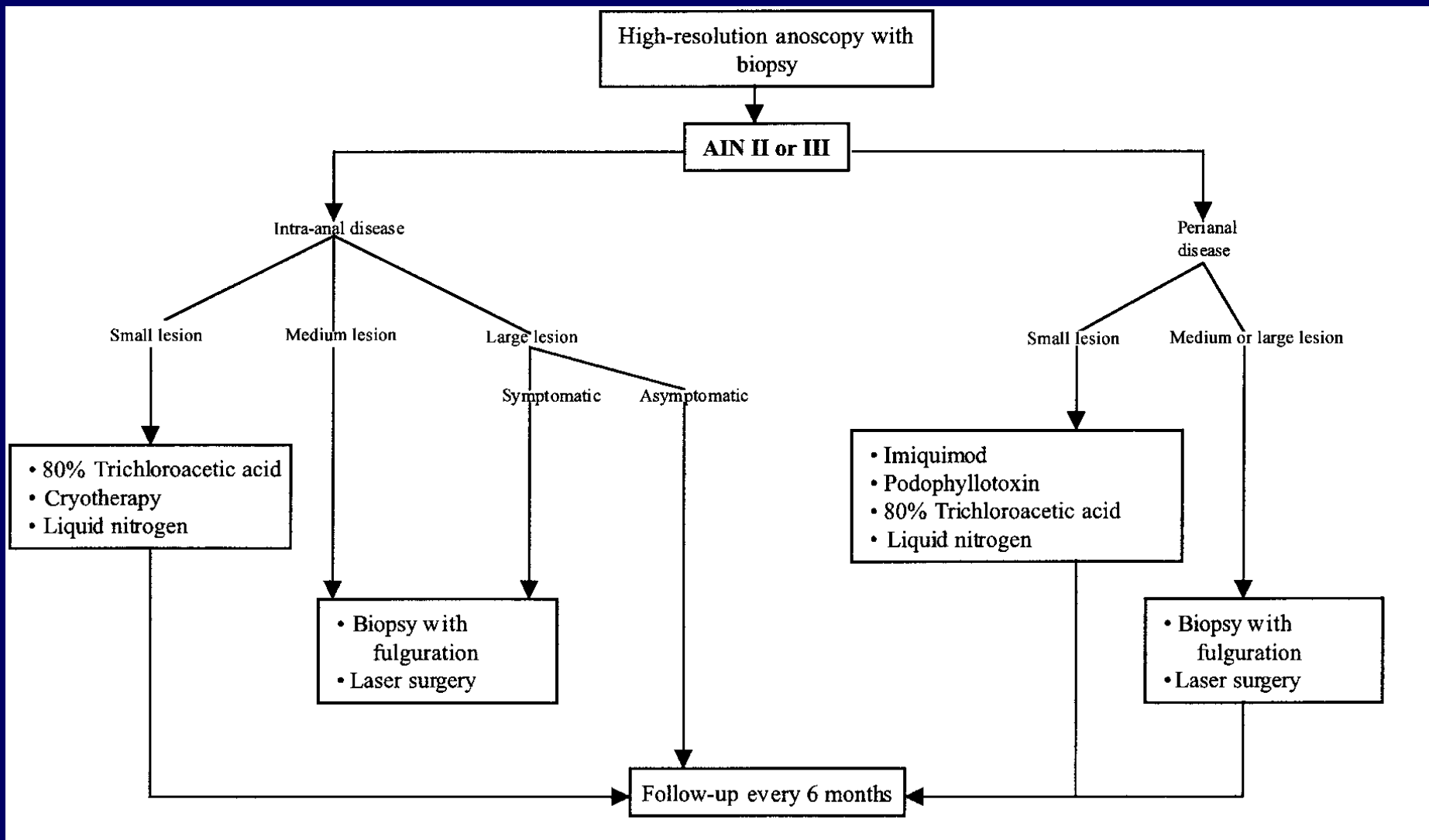
# Dépistage



# Conduite à tenir (AIN 1)



# Conduite à tenir (AIN 2-3)



# Traitements possibles

**TABLE 4. Treatment of anal intraepithelial neoplasia (AIN)\***

Lesion size	Lesion location			
	AIN-1 (anal condylomata)		AIN-2 or AIN-3	
	Perianal	Intra-anal	Perianal	Intra-anal
Discrete, <1 cm <sup>2</sup> at base	A,B,C,D,E	A,B,E,F,G,H	A,B,E,F	A,B,E,F,G
Discrete lesion >1 cm <sup>2</sup> at base, not circumferential	A,B,C,D,E,F,G,H	E,F,G,H	E,F,G	E,F,G
Diffuse or circumferential lesions	C,D,E,F,G,H	H	E,F,G,H	H

**Key:**

- A 85% trichloroacetic acid
- B Liquid nitrogen
- C Imiquimod
- D Podophyllotoxin
- E Electrocautery
- F Laser
- G Surgical cold scalpel excision
- H Observation only

\* Recommendations based on clinical experience (CIII) and not randomized clinical trials.

**Treating Opportunistic Infections Among HIV-Infected Adults and Adolescents Recommendations from CDC, the NIH, and the HIV Medicine Association/Infectious Diseases Society of America**

**MMWR décembre 2004**