4es JOURNÉES du GREPI

1-2/12/2016 Chantilly

Atteintes pulmonaires du VIH en 2016

Jacques Cadranel

Pas de conflit d'intérêt pour le sujet traité

Hôpitaux Universitaires Paris Est

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

UPMC PARIS UNIVERSITAS

HIV and AIDS, along time

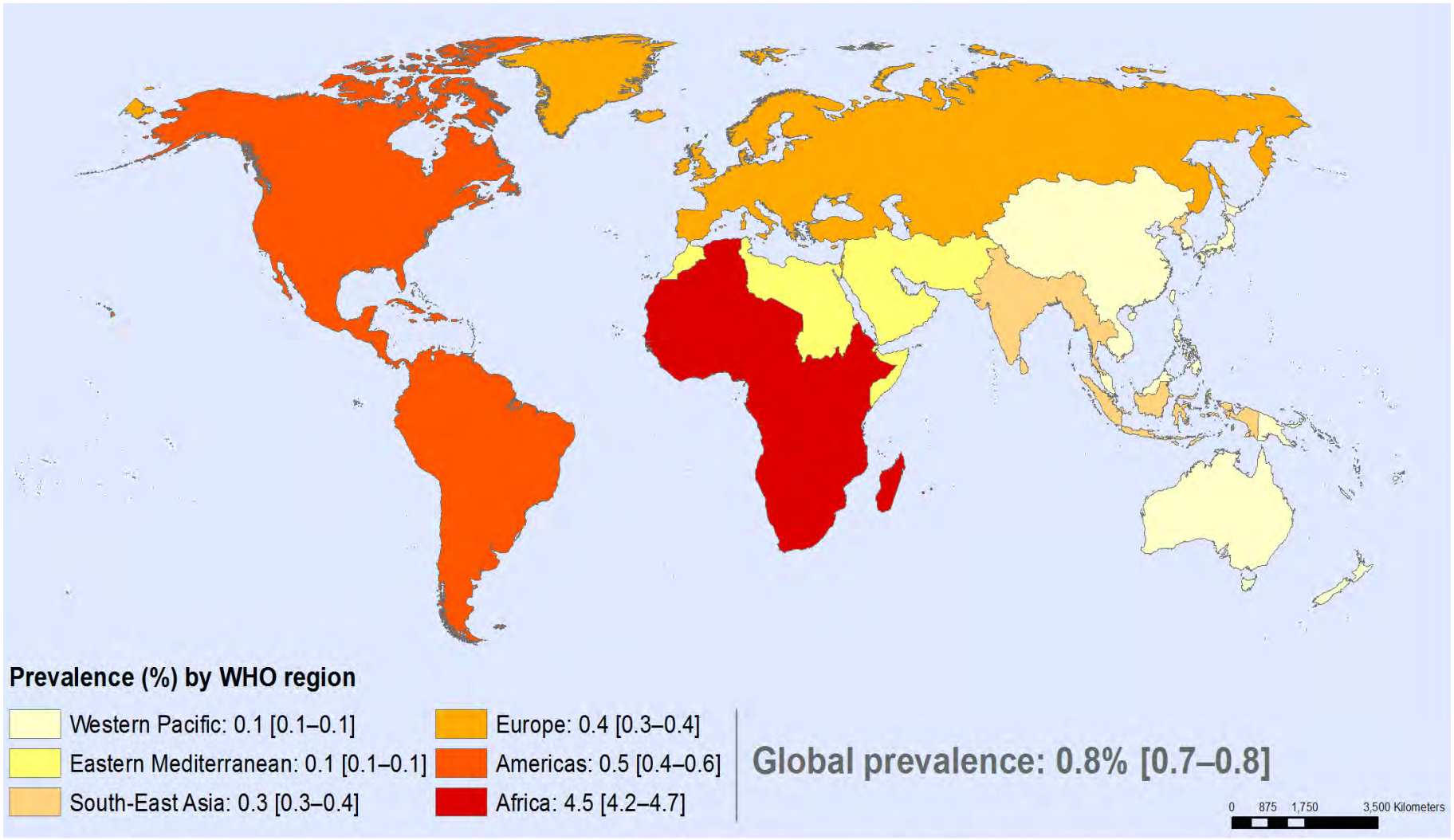
Global summary AIDS epidemic

Number of people living with HIV in 2013	**Total**	35.0 million [33.1 million – 37.2 million]
	Adults	31.8 million [30.1 million – 33.7 million]
	Women	16.0 million [15.2 million – 16.9 million]
	Children (<15 years)	3.2 million [2.9 million – 3.5 million]
People newly infected with HIV in 2013	**Total**	2.1 million [1.9 million – 2.4 million]
	Adults	1.9 million [1.7 million – 2.1 million]
	Children (<15 years)	240 000 [210 000 – 280 000]
AIDS deaths in 2013	**Total**	1.5 million [1.4 million – 1.7 million]
	Adults	1.3 million [1.2 million – 1.5 million]
	Children (<15 years)	190 000 [170 000 – 220 000]

WHO May 2015

HIV and AIDS, along time

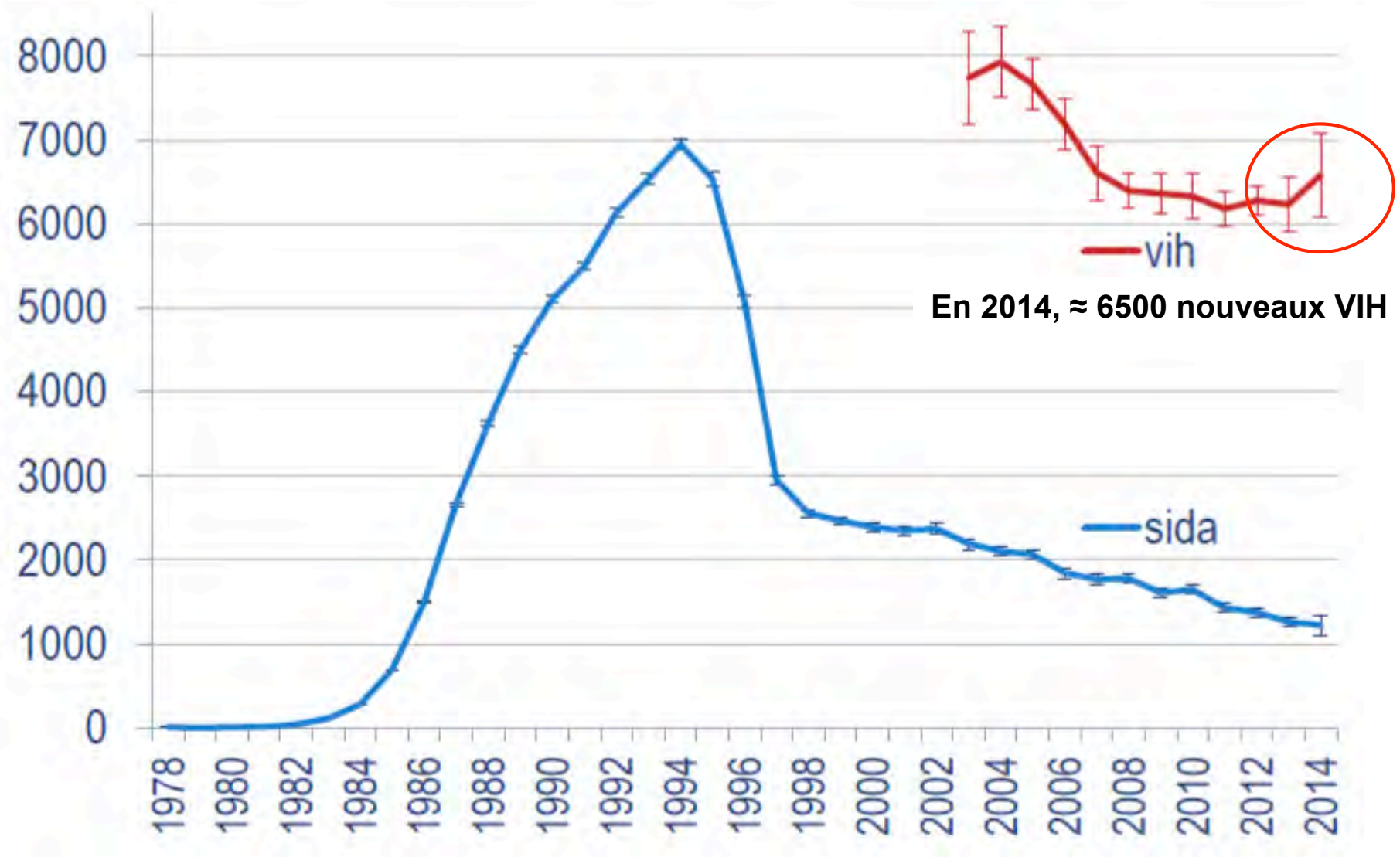
Population living with HIV, 2013



WHO May 2015

HIV and AIDS, along time

Population living with HIV, France 2014

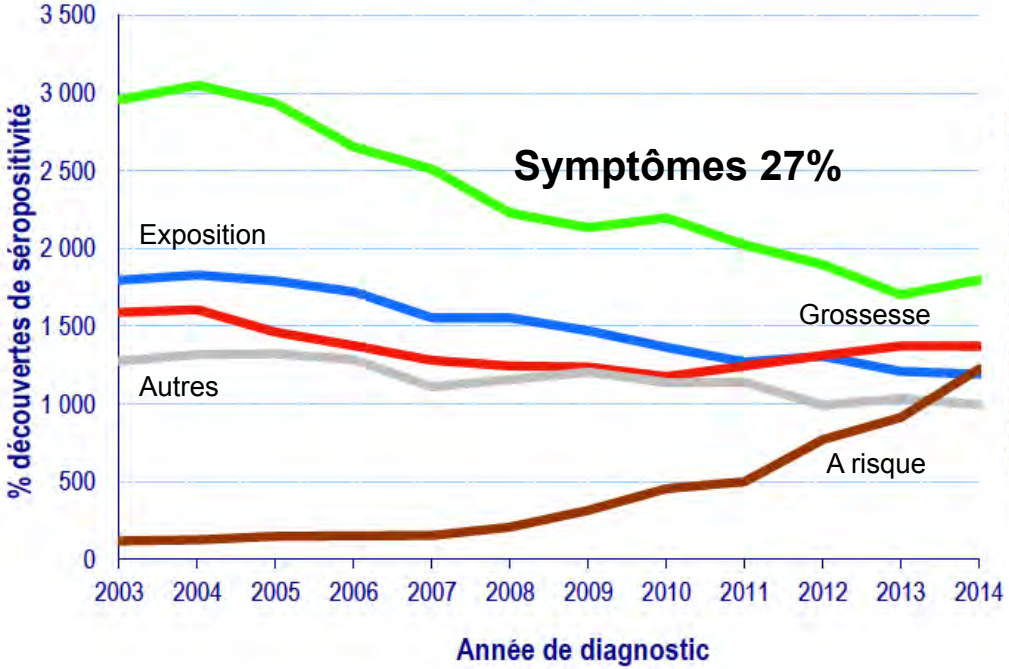


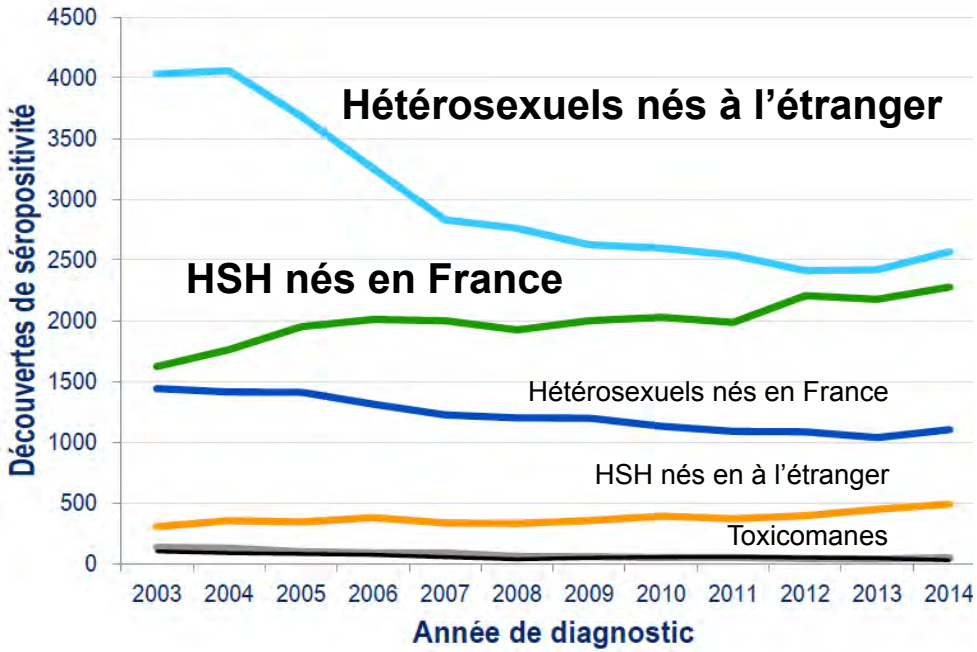
En 2014, ≈ 6500 nouveaux VIH

Données InVS 31/12/2014

HIV and AIDS, along time

Population living with HIV, France 2014

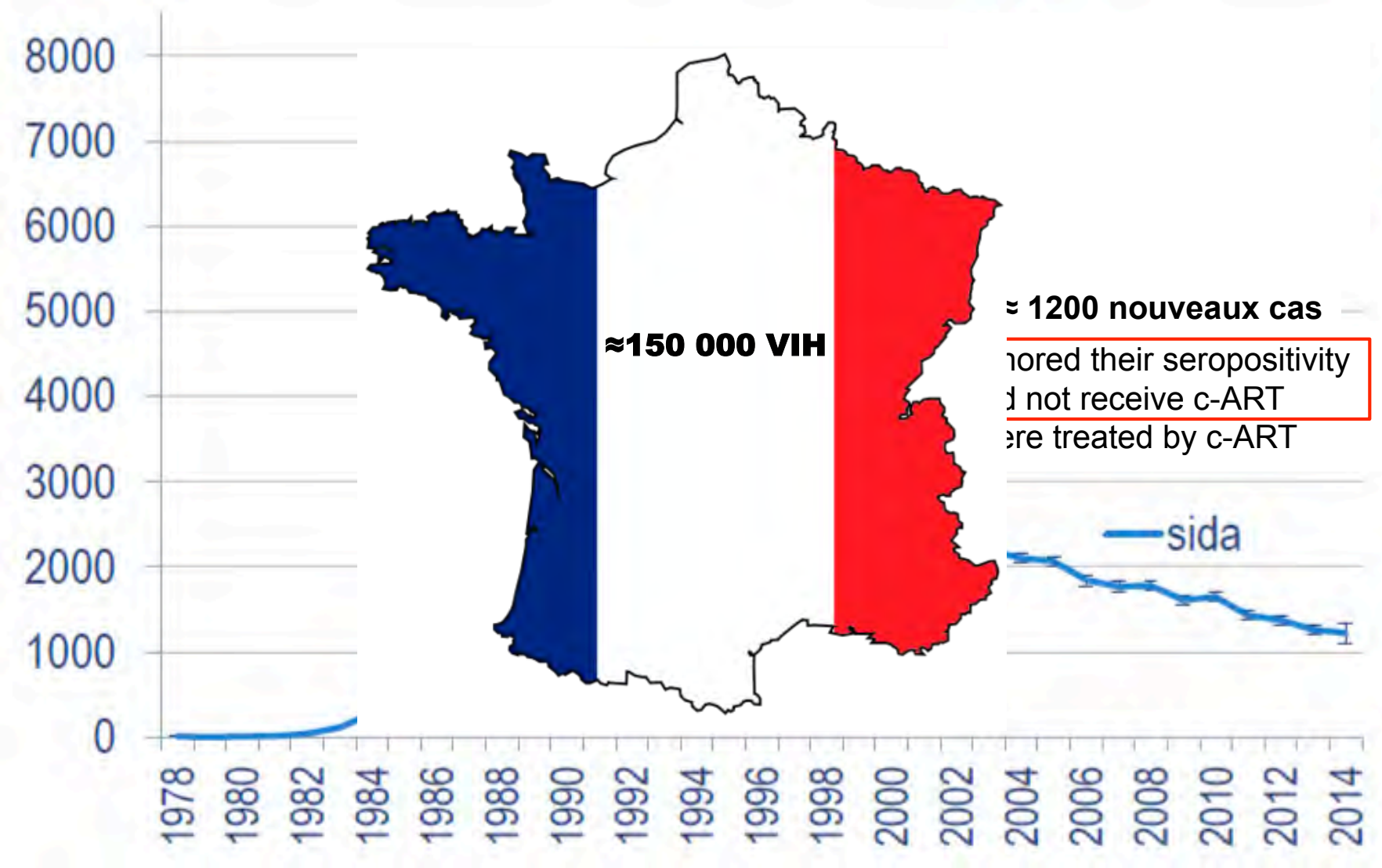




Données InVS 31/12/2014

HIV and AIDS, along time

Population living with HIV, France 2014

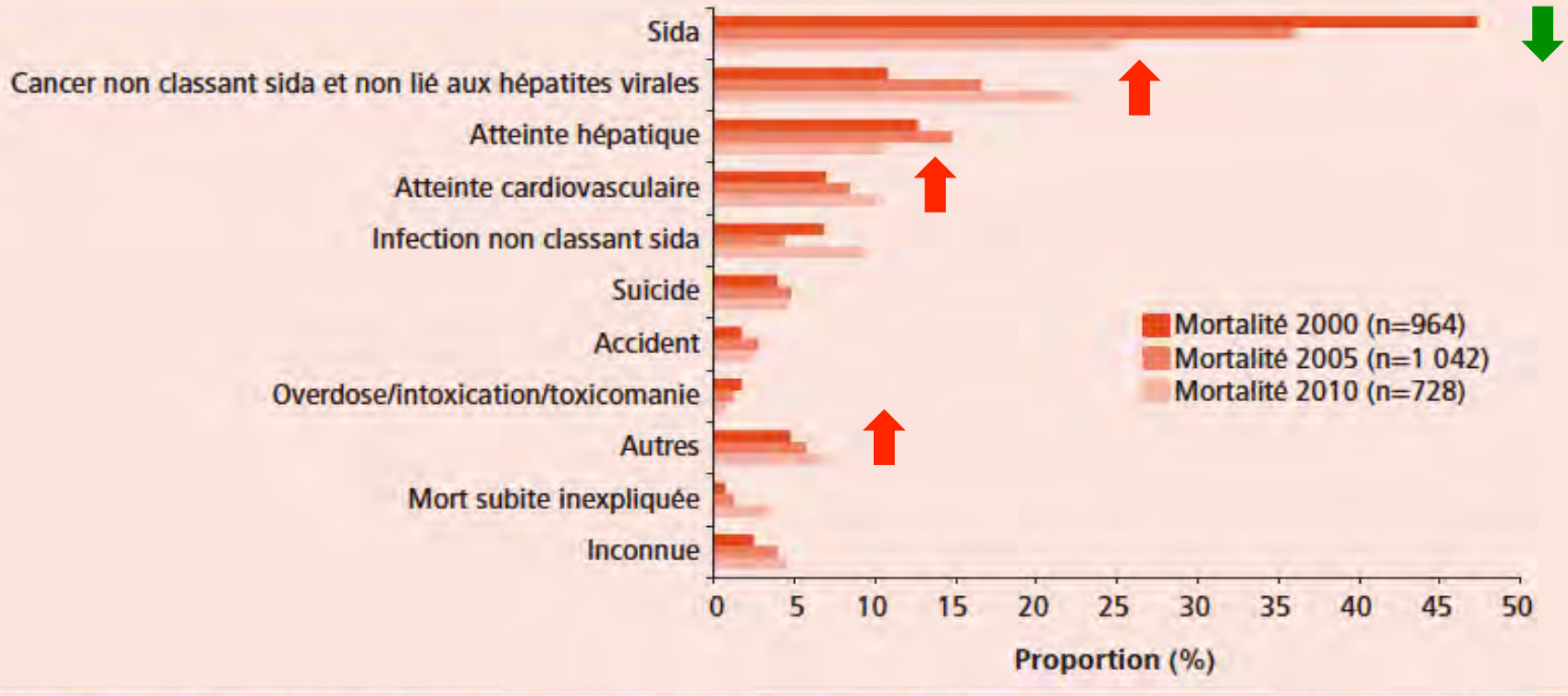


Données InVS 31/12/2014

HIV and AIDS, along time

AIDS/HIV mortality, France 2010

Figure 1 Évolution entre 2000, 2005 et 2010 de la répartition des causes initiales de décès des adultes infectés par le VIH, enquêtes Mortalité 2000, Mortalité 2005 et Mortalité 2010, France / *Figure 1 Distribution of underlying cause of death among HIV-infected adults, Mortalité 2000, Mortalité 2005 and Mortalité 2010 surveys, France*



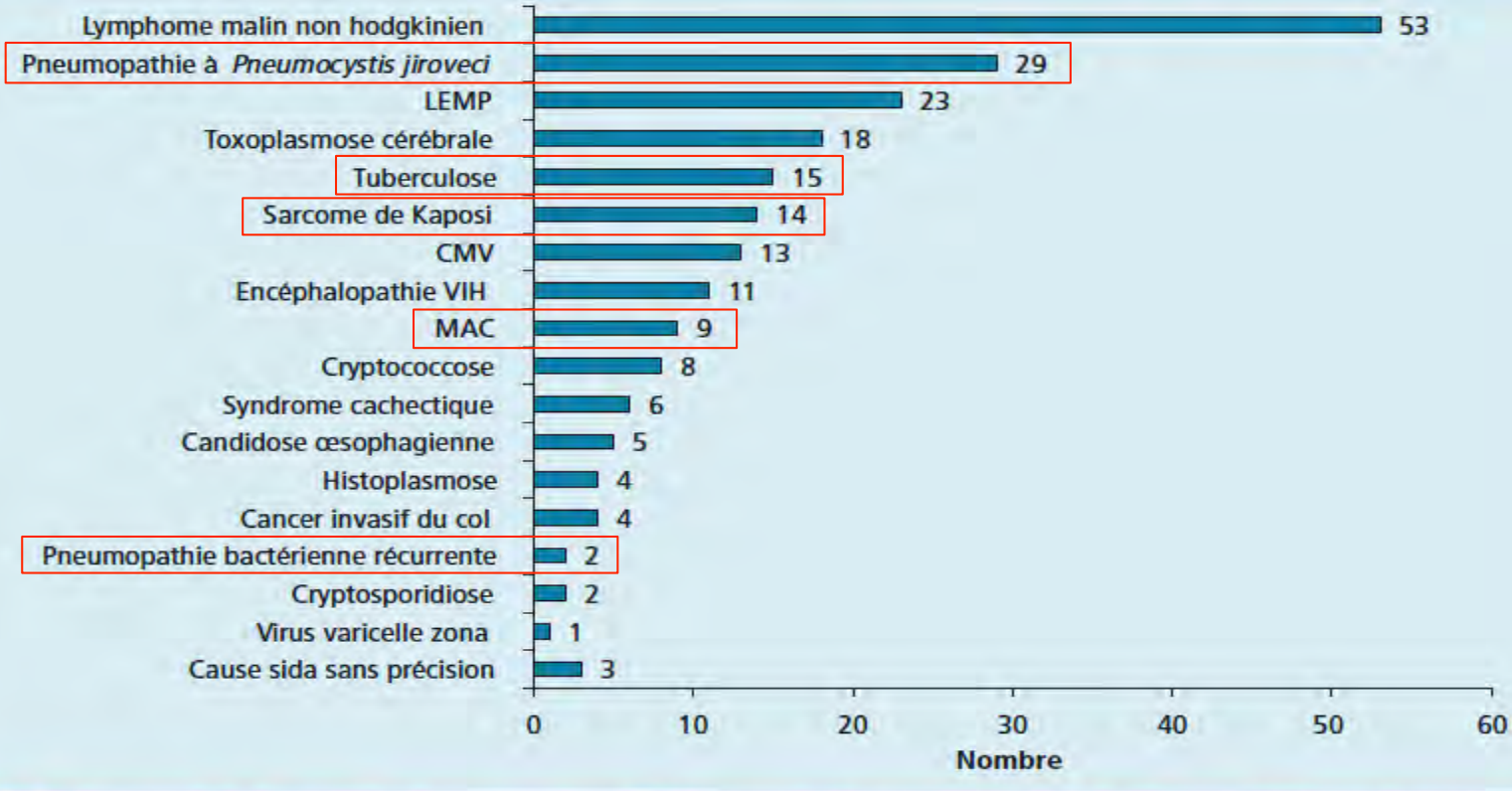
Autres : atteintes neurologiques, bronchopulmonaires, métaboliques, rénales, digestives, psychiatriques, endocriniennes, hématologiques et causes iatrogènes.

Roussillon C, BEH 46/47 1er décembre 2012

HIV and AIDS, along time

AIDS/HIV mortality, France 2010

Figure 2 **Fréquence des maladies classant sida (n=220) parmi les adultes décédés de cause sida (n=182), enquête Mortalité 2010, France / *Figure 2 Distribution of AIDS-defining diseases (n=220) among HIV-infected adults dying of an AIDS-related cause of death (n=182), Mortalité 2010 survey, France***



LEMP : leucoencéphalite multifocale progressive ; CMV : cytomégalovirus ; VIH : virus de l'immunodéficience humaine ; MAC : mycobactériose atypique.

Roussillon C, BEH 46/47 1er décembre 2012

HIV in the lung, along time

Pathophysiology

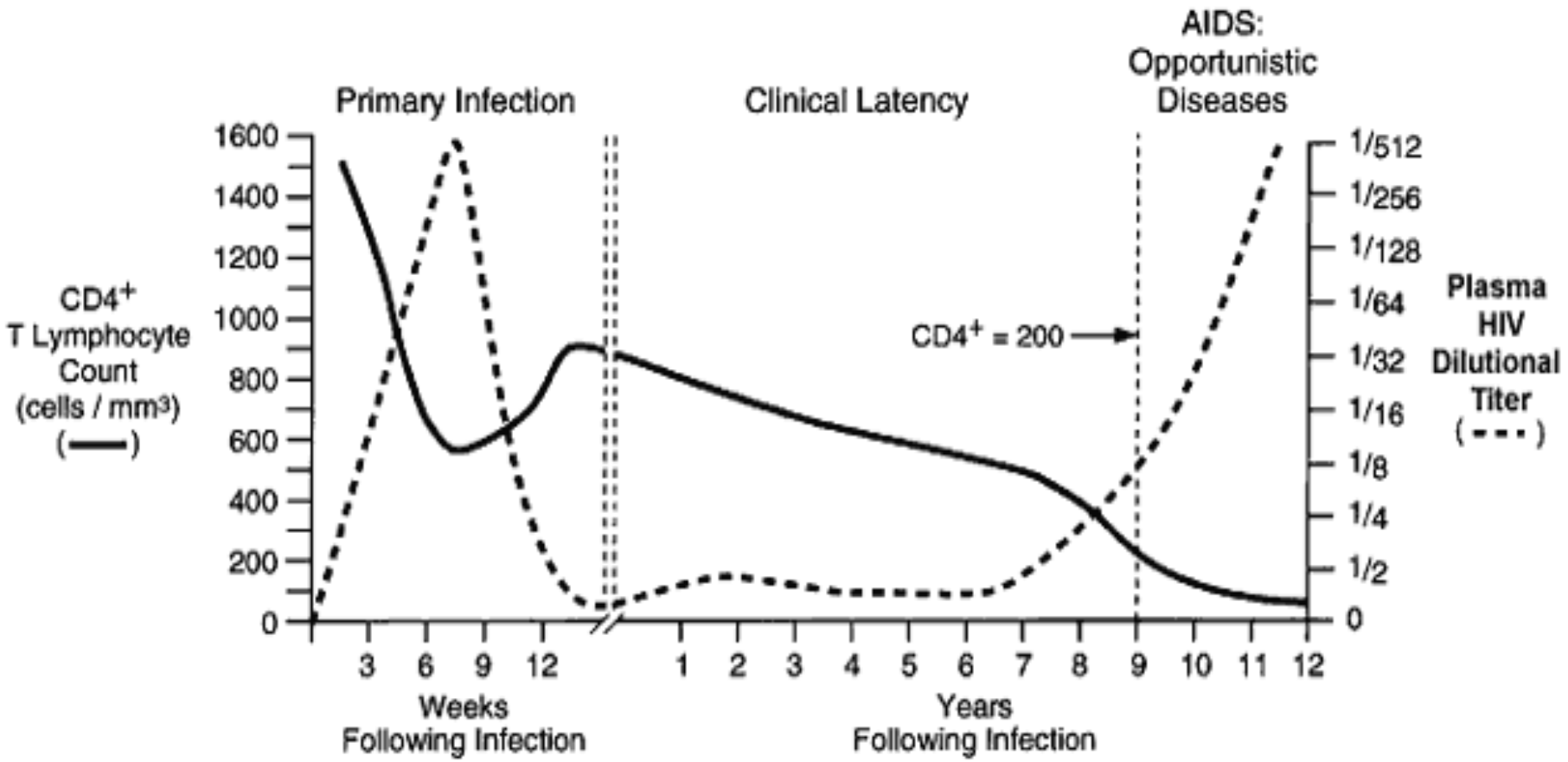
Immune deficiency

Viral infection

Immune response

HIV in the lung, along time

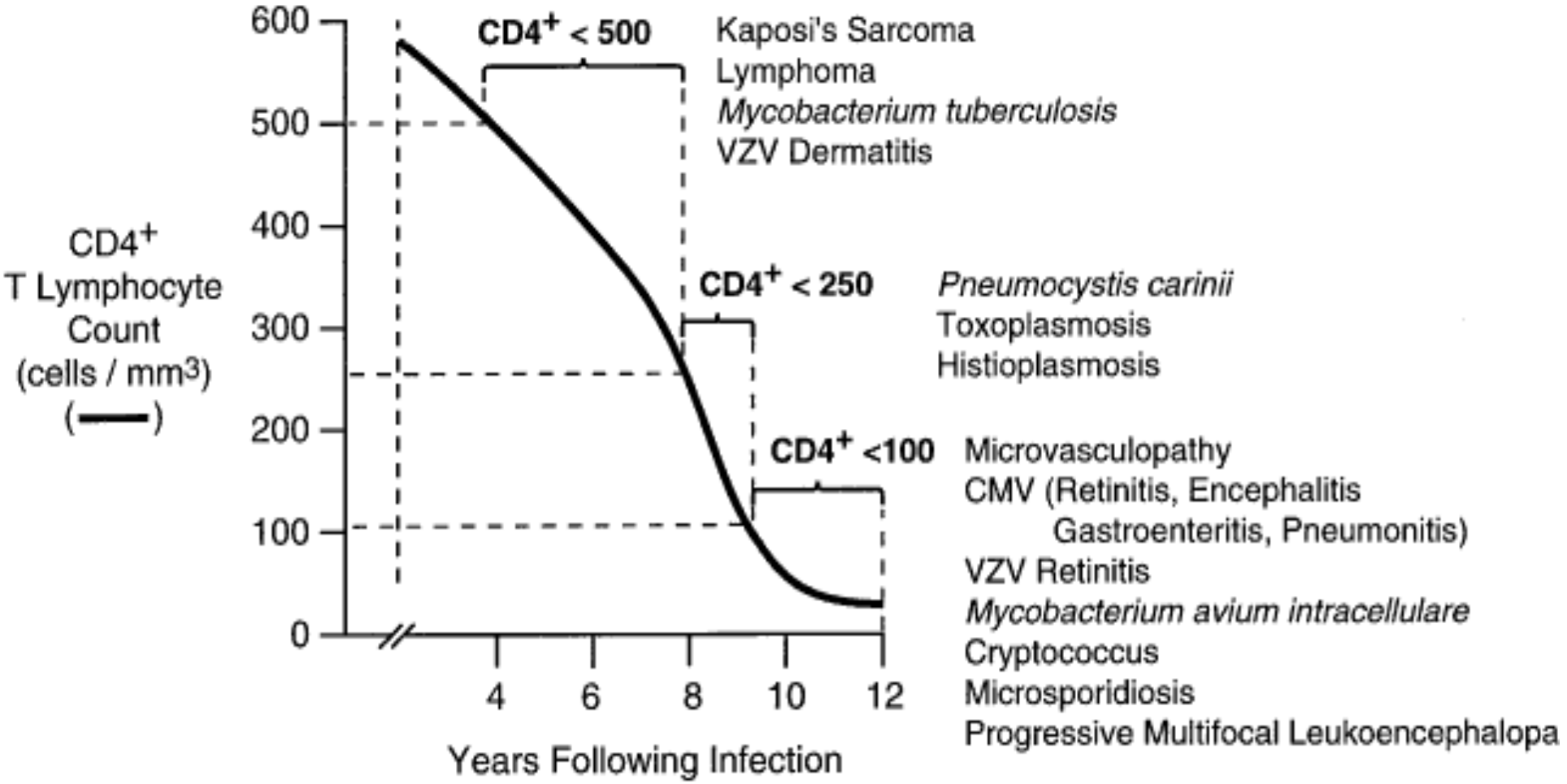
Pathophysiology



Lucas et al. J Pathol 2015, 235:229

HIV in the lung, along time

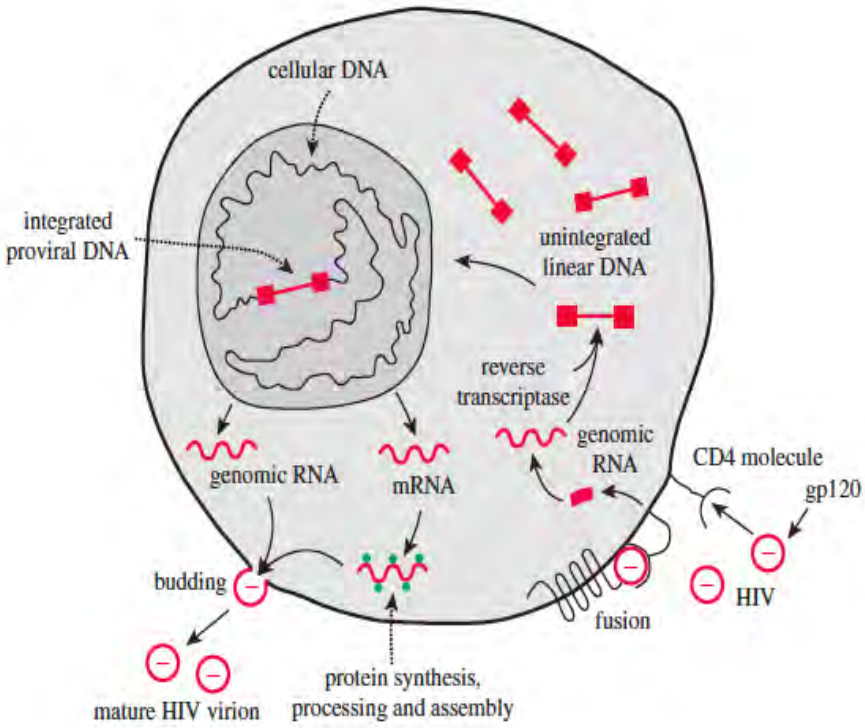
Pathophysiology



Lucas et al. J Pathol 2015, 235:229

HIV in the lung, along time

Pathophysiology

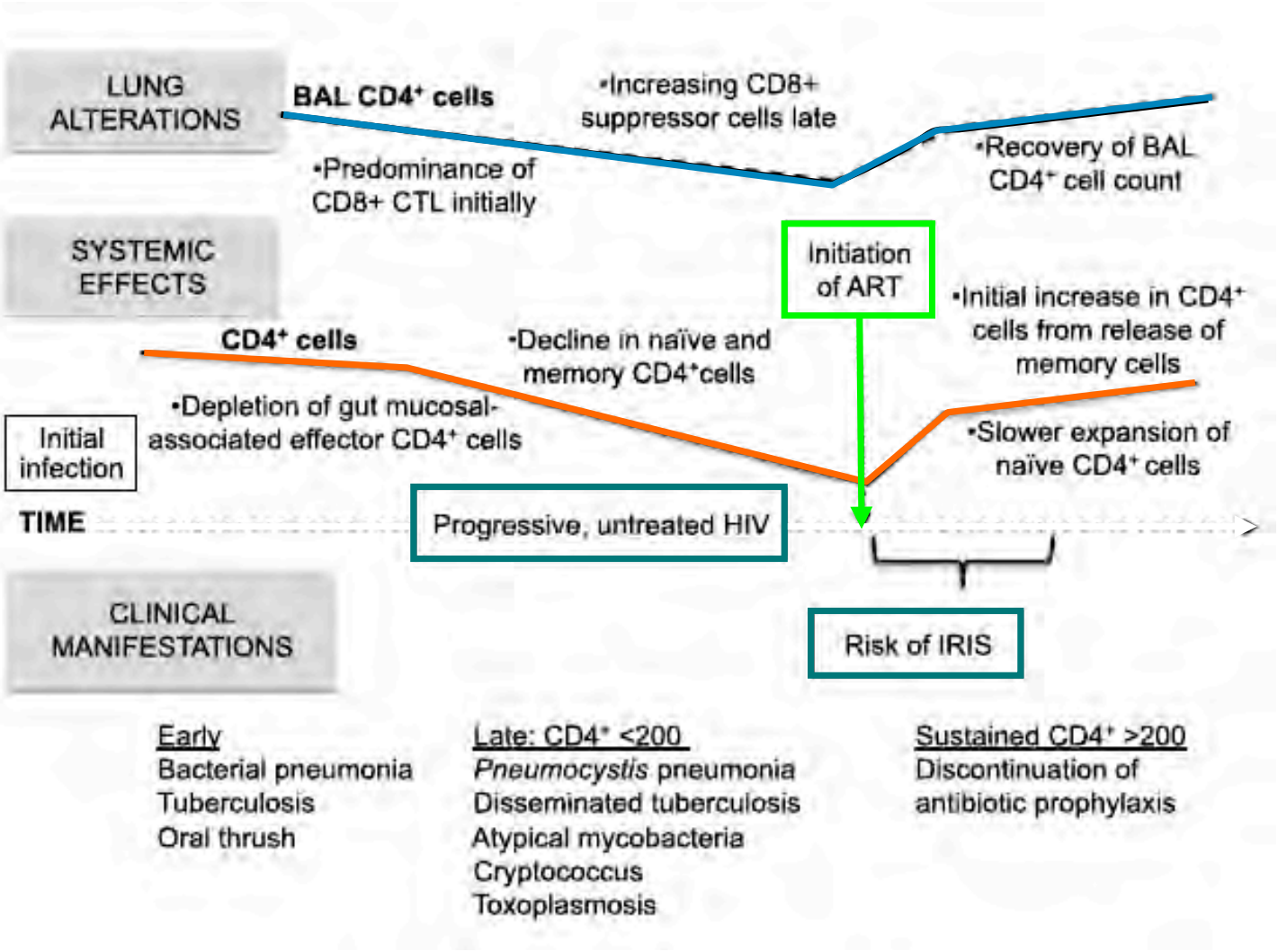


Class	Action point on HIV life cycle	Examples
Fusion inhibitors	Interfere with HIV's ability to fuse to gp120 receptors on the outer surface of the cell, and blocking entry	Enfuvirtide
Entry inhibitors	Interfere binding of HIV with chemokine receptors, blocking entry	Maraviroc
Nucleoside reverse transcriptase inhibitors (NRTI)	Inhibits reverse transcriptase activity, preventing the conversion of HIV RNA into dsDNA	Zidovudine (AZT) Lamivudine (3TC) Abacavir (ABV) Didanosine (ddI)
Nucleotide reverse transcriptase inhibitors (NtRTI)	As for NRTI	Tenofovir
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	As for NRTI	Efavirenz Nevirapine
Integrase inhibitors	Blocks HIV integrase, preventing integration of its genes into the host cell DNA	Raltegravir
Protease inhibitors (PI)	Inhibits the assembly line of new HIV viruses	Ritonavir Darunavir Atazanavir

Lucas et al. J Pathol 2015, 235:229

HIV in the lung, along time

Pathophysiology



Crothers et al. Prom Am Thorac Society 2011, 8:275

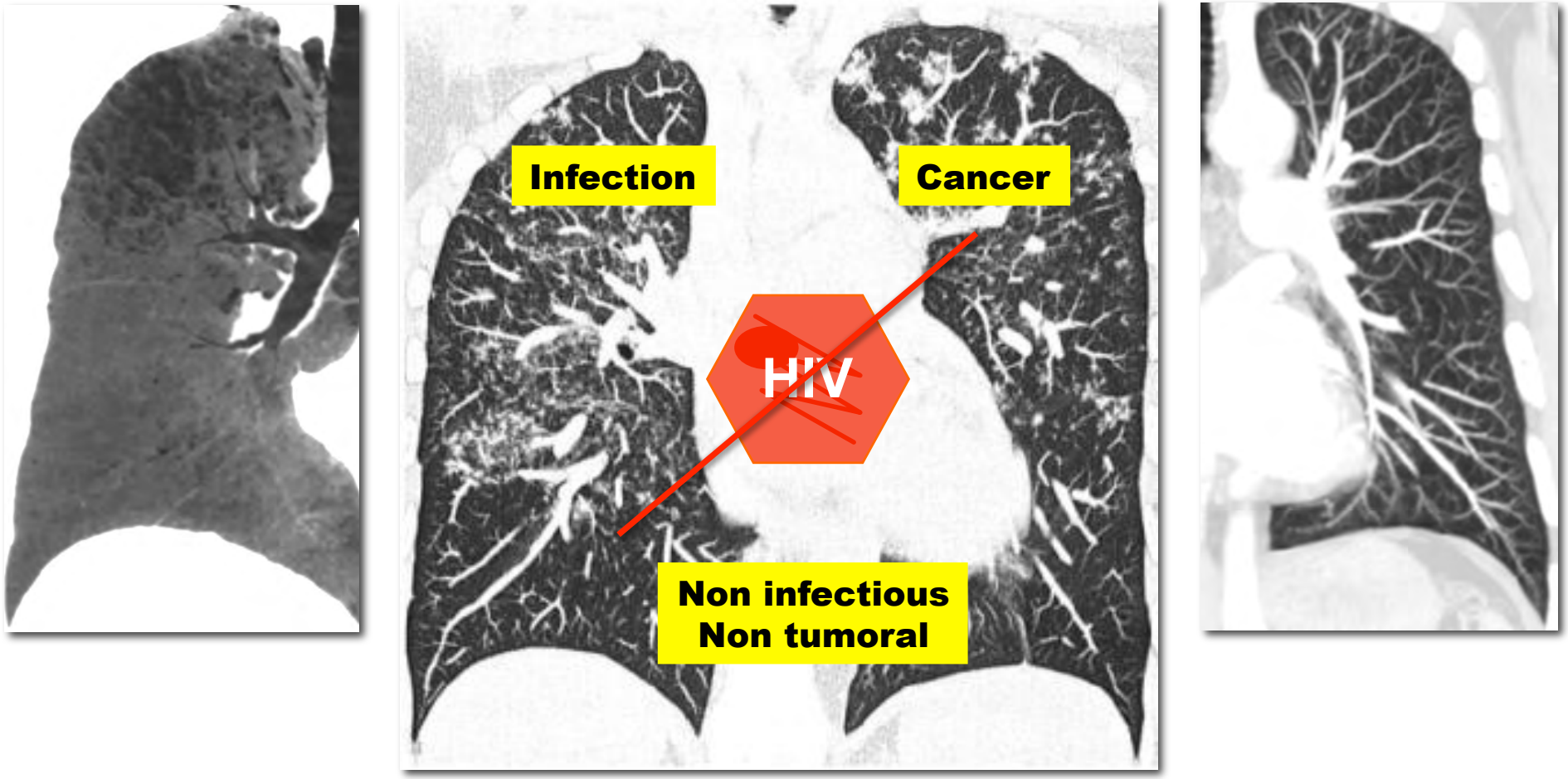
HIV in the lung, along time

What questions at the HAART era?

- Two situations
  - Naive patients or treatment failure
  - Responders to HAART
- What questions
  - What disorders involved?
  - What diagnostic procedures?
  - What treatments?

HIV in the lung, along time

What disorders involved?



HIV in the lung, before HAART?

Infectious diseases

- Number of respiratory events observed in 1130 HIV pts followed-up during 5 years (/100 pts yr)

Disorders	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
Upper airways infection	47	35	40	40	52
Bronchitis	13	14	13	14	14
Bacterial pneumonia	3.9	4.7	6.1	6.4	7.3
PJ pneumonia	2.8	4.3	5.8	5.8	9.5
Tuberculosis	0.5	0.6	0.5	0.5	1.0
Other OI	0.6	0.9	1.1	1.1	1.8

Wallace et al. Am Rev Respir Dis 1997, 155: 72

HIV in the lung, before HAART?

Non infectious disorders

• Number of respiratory events observed in 1130 HIV pts followed-up during 5 years (/100 pts yr)

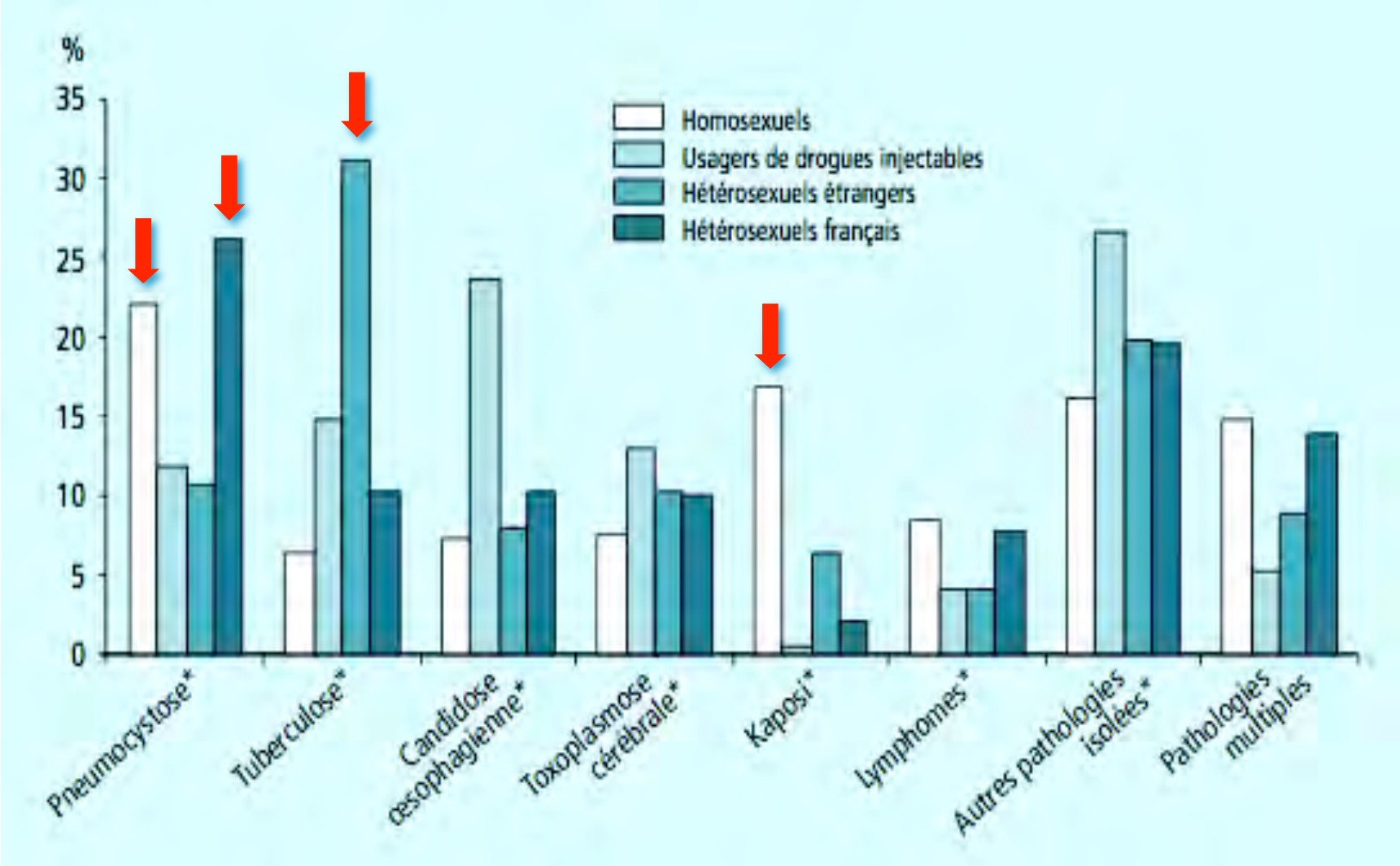
Disorders	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
Cardiovascular*	0.1	0.4	1.0	1.5	0.8
Cancer**	0.3	0.5	0.6	0.5	0.6
ILD***	0.9	0.5	0.2	0.4	0.2

* : 17 cardiac failure, 12 pulmoray embolism et 1 PAH
** : 12 Kaposi's sarcoma et 8 cancer
*** : 20 NSIP et 1 LIP

Wallace et al. Am Rev Respir Dis 1997, 155: 72

HIV in the lung, before HAART?

Mode of HIV transmission



BEH thématique, 27 novembre 2007

HIV in the lung, before HAART?

Diagnostic strategy

What features to consider?

- Mode of HIV transmission
- Prior history of infection with possible reactivation
- **Severity of the immune deficiency**
- Use of specific prophylaxies
- Type of thoracic involvement
- Presence or not of extra-pulmonary symptoms
- Onset and severity of the pulmonary disorder

Mayaud C, Cadranel J, Manifestations cliniques de l'infection VIH et du SIDA, In SIDA 2011, Doin éditeurs

HIV in the lung, before HAART?

Severity of the immune deficiency

- Blood CD4 count observed in 80 % of patients with a specific respiratory disorder

[399-300]

Bacterial pneumonia (8.4)*

Tuberculosis (0.8)

LIP (0.1)

[299-200]

Non TB mycobacteria (2.6)

Recurrent pneumonia (2.1)

[199-100]

Pneumocystosis (7.3)

Disseminated TB (0.9)

< 100/µl

Pulmonary candidiasis (0.2)

*% observed in 7824 pts between 01/90 and 08/93

Hanson et al. Arch Intern Med 1995, 155: 1537

HIV in the lung, before HAART?

Severity of the immune deficiency

- Blood CD4 count observed in 80 % of patients with a specific respiratory disorder

> 500/µl
Sinusitis, mastoiditis, otitis (14.2)*
Bronchitis (12.2)
Pharyngitis (9.5)
Respiratory viral infection (2.2)
Lung cancer (0.1)

*% observed in 7824 pts between 01/90 and 08/93

Hanson et al. Arch Intern Med 1995, 155: 1537

HIV in the lung, before HAART?

Severity of the immune deficiency

Infection	**CD4/µl median [range] ; reference**
Nocardiosis	109 [12-266] ; *Uttamchandani et al. CID 1994*
M. kansasii	66 [0-198] ; *Levine et al. Ann Intern Med 1991*
Toxoplasmosis	40 [1-250] ; *Rabaud et al. CID 1996*
Aspergillosis	27 [1-152] ; *Lortholary et al. Am J Med 1993*
Cryptococcosis	24 [2-200] ; *Meyohas et al. CID 1995*
Cryptosporidiosis	21 [3-70] ; *Stern et al. Rev Mal Respir 1997*
Rhodococcus equi	20 [5-80] ; *Harvey et al. Rev Infect Dis 1991*
Histoplasmosis	20 [7-40] ; *Wheat et al. Medicine 1990*

HIV in the lung, before HAART?

Severity of the immune deficiency

- For a CD4 count ≥ 250/µl, benign infections (BI) represent 90% of respiratory events
- For a CD4 count <250/µl, BI still represent 70% of respiratory events; severe infections account for the remaining cases
- For a CD4 count <250/µl, bacterial pneumonia, pneumocystosis and tuberculosis account for 90% of severe infections

HIV in the lung, before HAART?

Severity of the immune deficiency

- For a CD4 count <100/µl, bacterial pneumonia, pneumocystosis and tuberculosis are still the most frequent infections involved even if all the other IO can also be discussed
- Whatever the CD4 count nonspecific lesions (heart disease, LIP, NSIP, PAH) and neoplasms (SK, NHL, LC) are rare

HIV in the lung, before HAART?

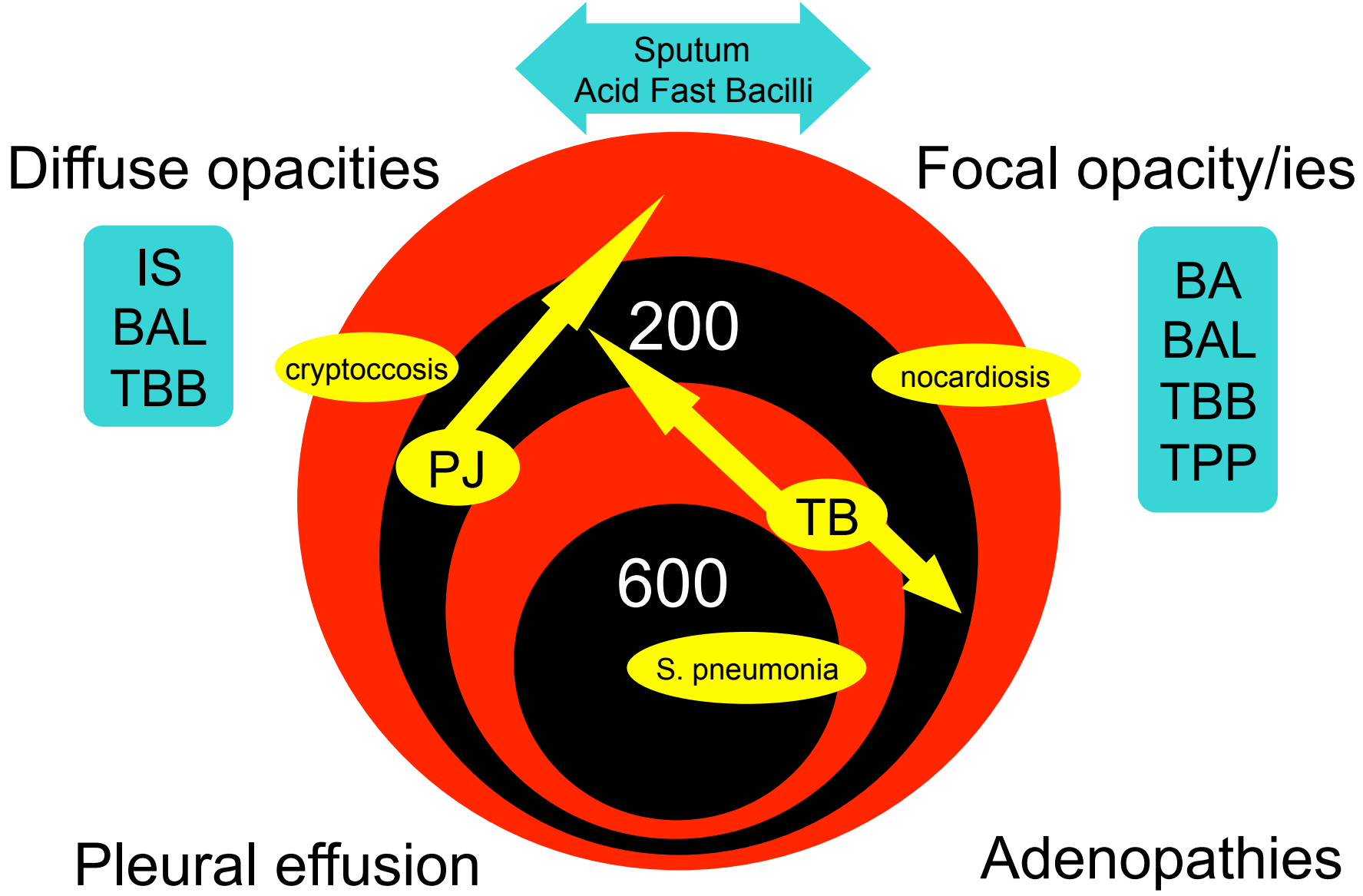
Types of pulmonary opacities

Diffuse intertitial pneumonitis	Alveolar opacities/macronodules
Frequent Pneumocystosis Kaposi's sarcoma Tuberculosis	Frequent Bacterial pneumonia Tuberculosis
Possible Other opportunistic infections (toxoplasmosis, cryptococcosis, aspergillosis, NT mycobacteria) Bacterial pneumonia	Possible Mycosis (aspergillosis, cryptococcosis) NT mycobacteria Other opportunistic bacterial pneumonia Pneumocystosis
Rare Lymphoid interstitial pneumonia	Rare Lymphoma Toxoplasmosis
Differential diagnosis Pulmonay oedema Drug induced pneumonia	Differential diagnosis Lung cancer Pulmonary infarctus

Mayaud C, Cadranel J, Manifestations cliniques de l'infection VIH et du SIDA, In SIDA 2011, Doin éditeurs

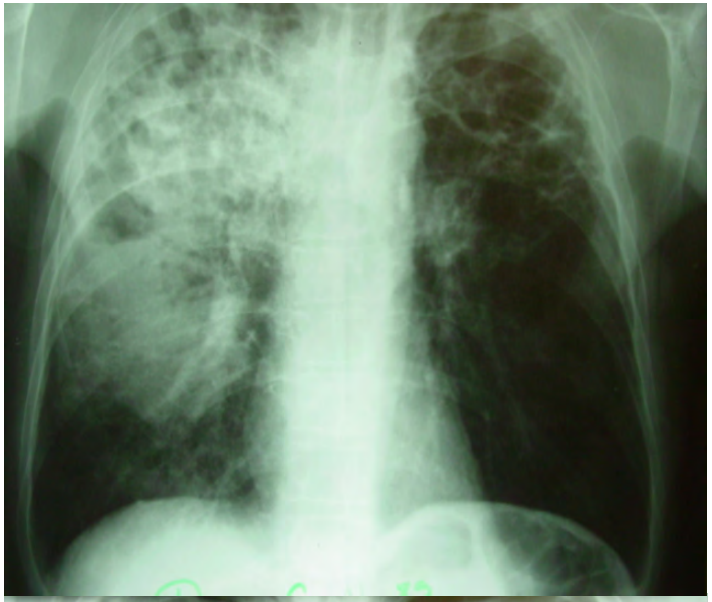
HIV in the lung, before HAART?

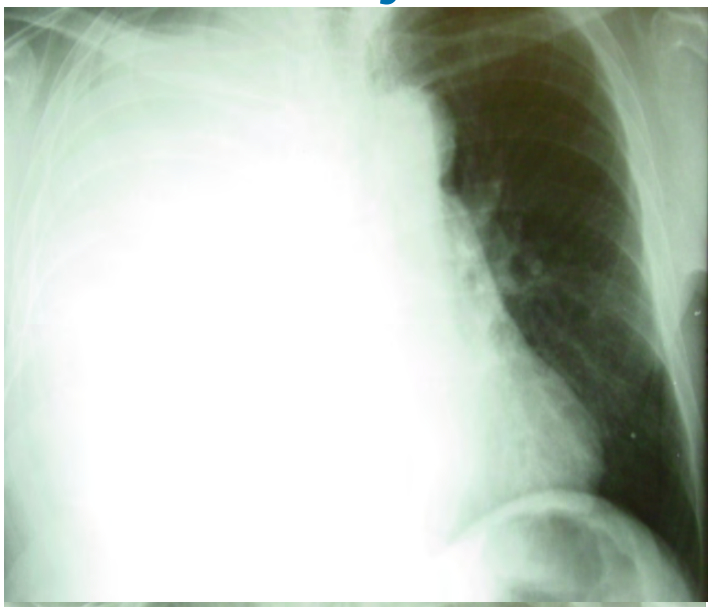
Diagnostic strategy

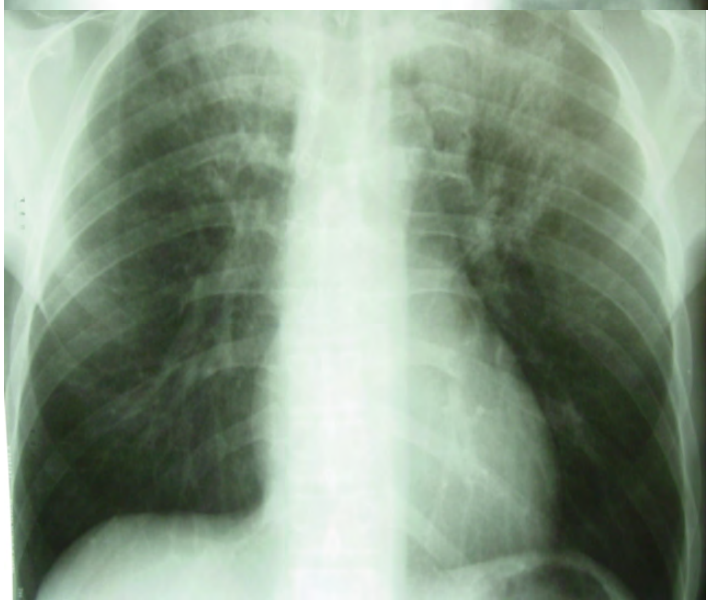


HIV in the lung, before HAART?

CD4 count and TB chest X-ray



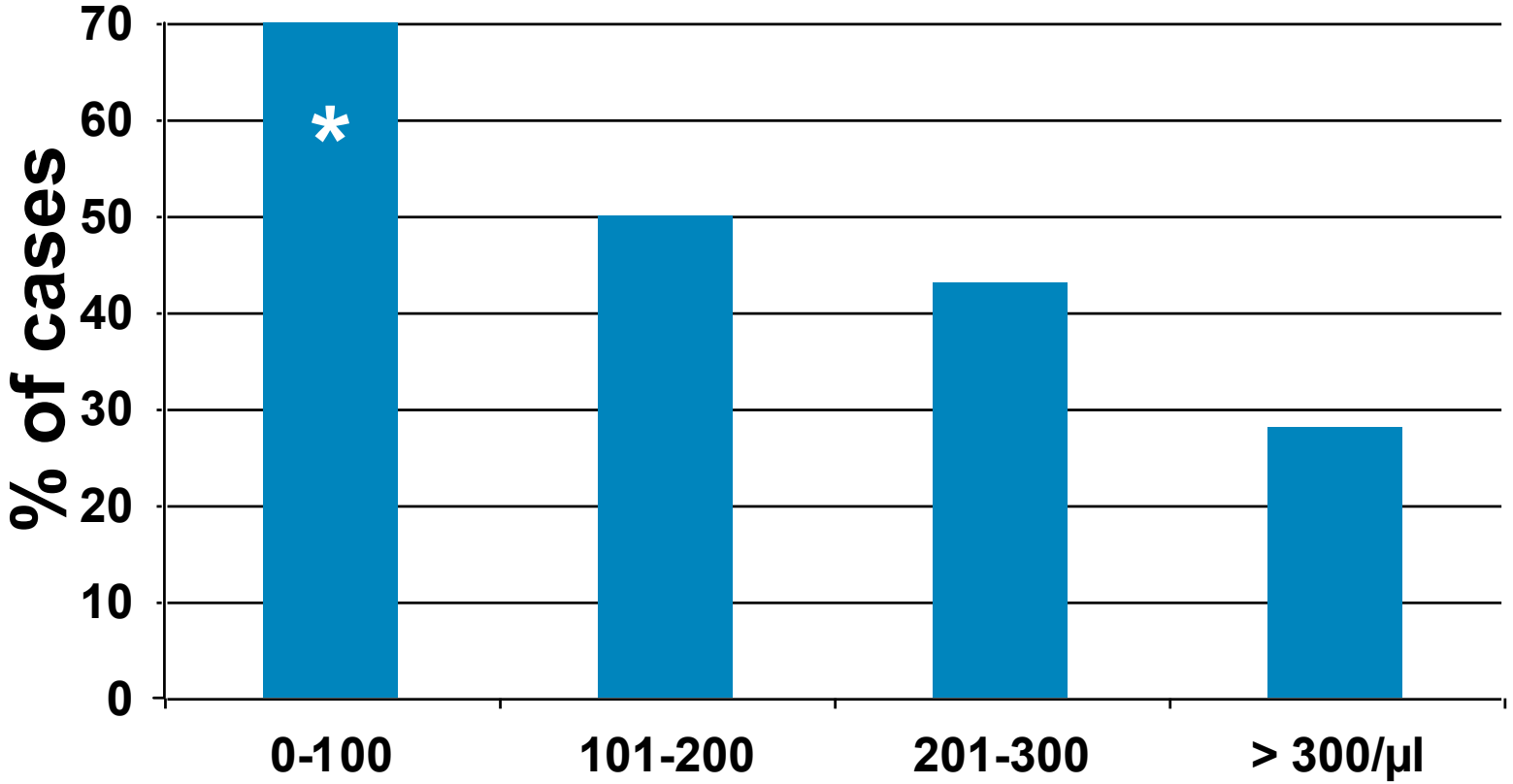




HIV in the lung, before HAART?

CD4 count and TB chest X-ray

- % of extra-thoracic tuberculosis observed in 97 pts according to the CD4 count



Jones et al. Am Rev Respir Dis 1993, 148: 1292

HIV in the lung, during HAART?

Impact of HAART

- Only concerns treated and controlled patients
- Reduction in morbidity and mortality
- Variable according to the different pathologies
- Improvement of as yet incurable diseases
- Discontinuation of primary and secondary prophylaxis
- HAART lung toxicity
- Immune reconstitution and inflammatory syndrome “IRIS“
- Emergence of new diseases

Mayaud C, Cadranel J, Thorax 1999, 54:567

HIV in the lung, during HAART?

HAART lung toxicity

Class	Action point on HIV life cycle	Examples	Specific toxicities
Fusion inhibitors	Interfere with HIV's ability to fuse to gp120 receptors on the outer surface of the cell, and blocking entry	Enfuvirtide	Uncommon
Entry inhibitors	Interfere binding of HIV with chemokine receptors, blocking entry	Maraviroc	Uncommon
Nucleoside reverse transcriptase inhibitors (NRTI)	Inhibits reverse transcriptase activity, preventing the conversion of HIV RNA into dsDNA	Zidovudine (AZT) Lamivudine (3TC) Abacavir (ABV) Didanosine (ddI)	Generic: mitochondrial toxicity. Muscle and nerve damage Lactic acidosis, liver steatosis, hepatitis Hypersensitivity reaction (ABV)
Nucleotide reverse transcriptase inhibitors (NtRTI)	As for NRTI	Tenofovir	Kidney tubular damage
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	As for NRTI	Efavirenz Nevirapine	Liver necrosis Stevens–Johnson syndrome; toxic epidermal necrolysis
Integrase inhibitors	Blocks HIV integrase, preventing integration of its genes into the host cell DNA	Raltegravir	Uncommon
Protease inhibitors (PI)	Inhibits the assembly line of new HIV viruses	Ritonavir Darunavir Atazanavir	Generic: dyslipidaemias Lipodystrophy Liver damage

Lucas et al. J Pathol 2015, 235:229

HIV in the lung, during HAART?

HAART lung toxicity

- Interaction between protease inhibitors and corticosteroids
- Risk of adrenal insufficiency and hypercorticism
- Regardless of the administration route (oral, inhaled)
- All inhaled steroids, except beclomethasone

Collet-Gaudillat et al. Ann Endocrinol 2009, 70:252; Ramanathan et al. Clin Infect Dis 2008, 47:e97; Yombi et al. Clin Rheumatol 2008, 27:S79; Busse et al. J Acquir Immune Defic Syndr 2008, 48:561

HIV in the lung, during HAART

"IRIS" criteria

Shelburne et al (2002):[9] any cases

Criteria for diagnosis

- HIV-infected patient
- Receipt of effective ART as shown by a decrease in HIV RNA concentration from baseline or an increase in CD4 cell count from baseline
- Clinical symptoms consistent with inflammatory process
- Clinical course not consistent with expected course of previously or newly diagnosed opportunistic infection, or with toxic effects of drug treatment

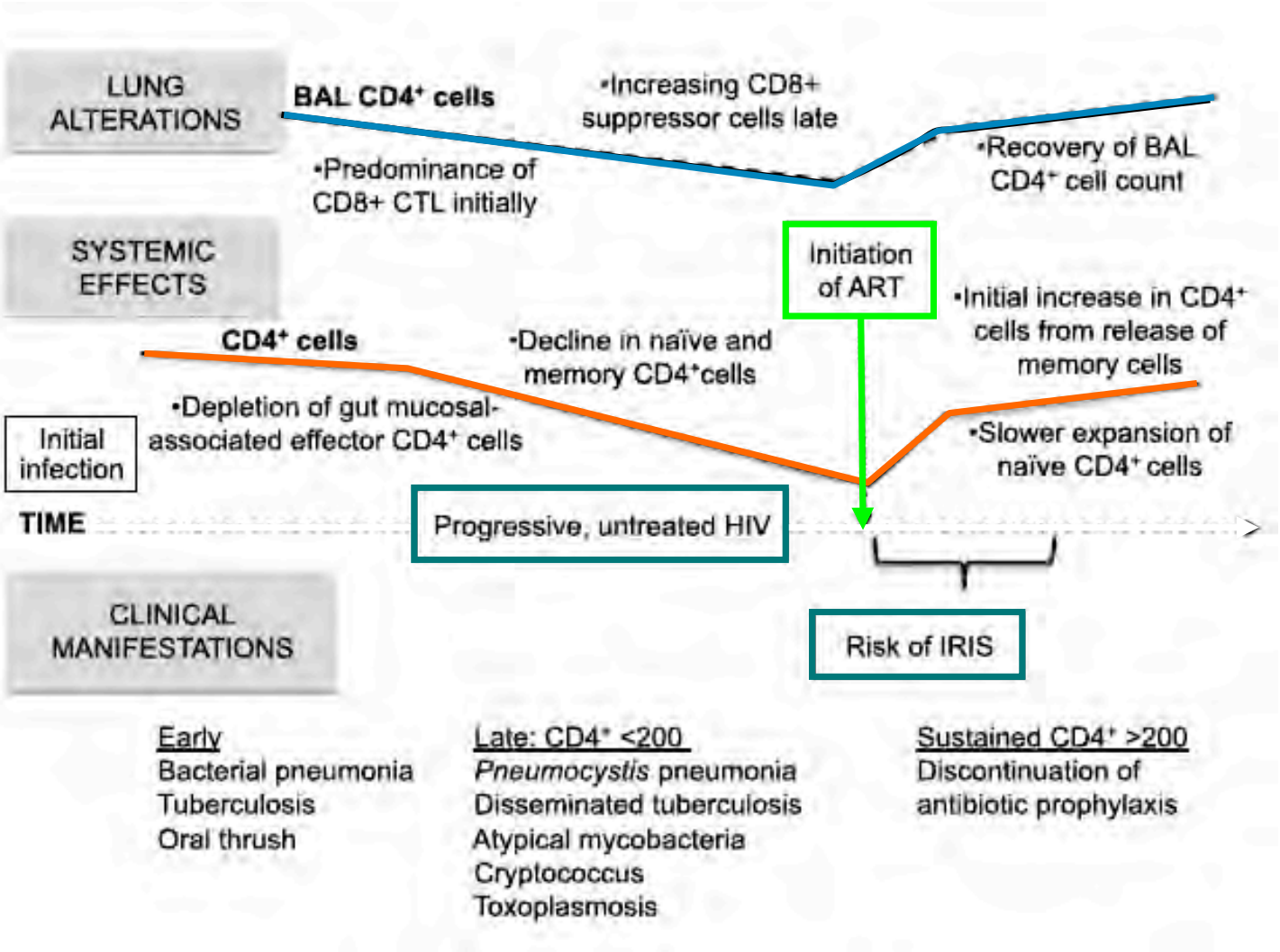
Additional criteria for cryptococcal meningitis

- Decrease in CSF antigen concentration
- Negative CSF fungal cultures
- Inflammatory reaction in CSF (increased white blood cell count)

Shelburne et al. Medicine 2002, 81:213

HIV in the lung, along time

Pathophysiology of "IRIS"



Crothers et al. Prom Am Thorac Society 2011, 8:275

HIV in the lung, during HAART

"IRIS", infectious diseases involved

Infections	n	Extra-thoracic	Thoracic
MAIC	32	LN, skin, bone, GI tract	LN, lung
M. tuberculosis	37	CNS, LN, eyes	lung, LN, pleura
B. hensellae	1	LN	
C. neoformans	12	meninges, LN, skin	lung
P. carinii	1		lung
Cytomegalovirus	22	eyes, parotide	lung
Zoster/Herpes virus	42	skin/eyes	
HCV/HBV	11	liver	
JC virus	5	brain	

Shelburne et al. Medicine 2002, 81:213

HIV in the lung, during HAART

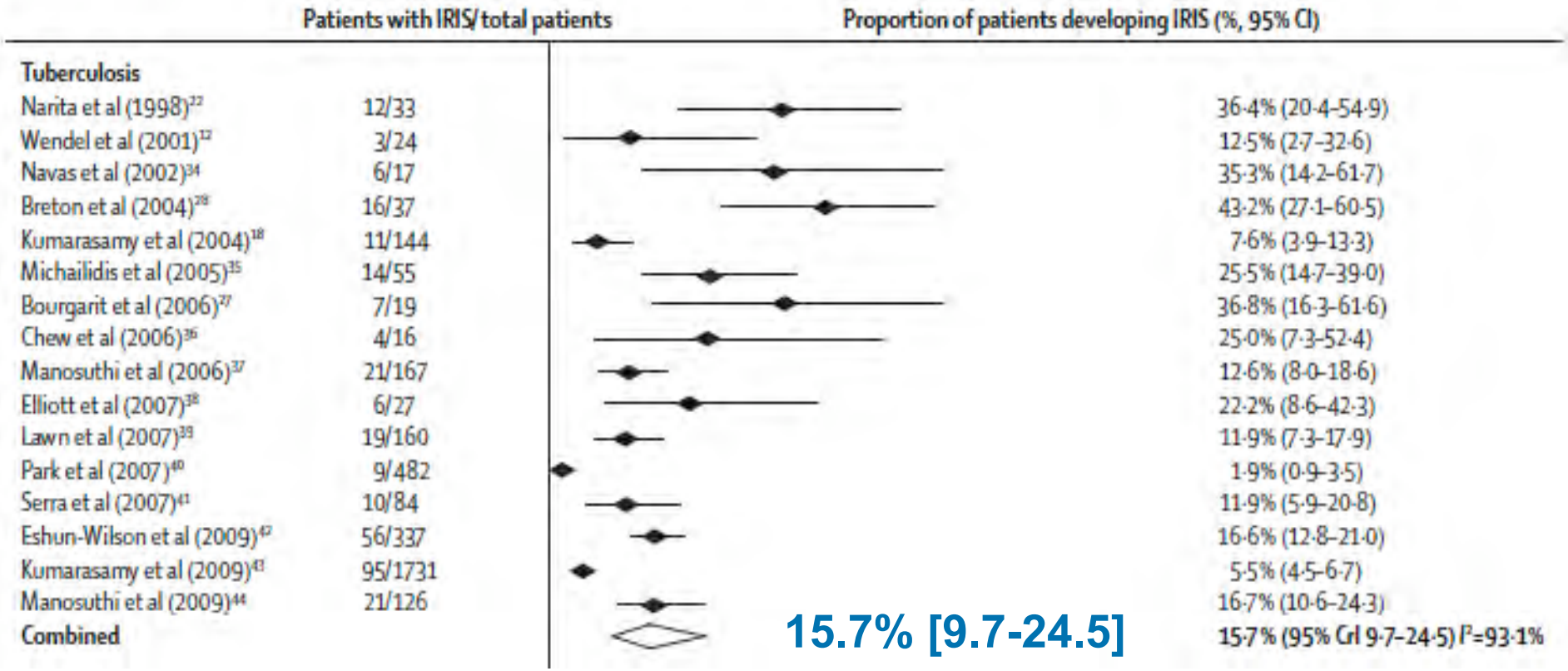
"IRIS", non infectious diseases involved

Disorders	n	Extra-thoracic	Thoracic
Kaposi's sarcoma	3	skin, LN, NTE	lung
Sarcoidosis	10	Löfgren, LN, skin, fever	lung, LN
Thyroiditis	9	hyperthyroidism	

Shelburne et al. Medicine 2002, 81:213

HIV in the lung, during HAART

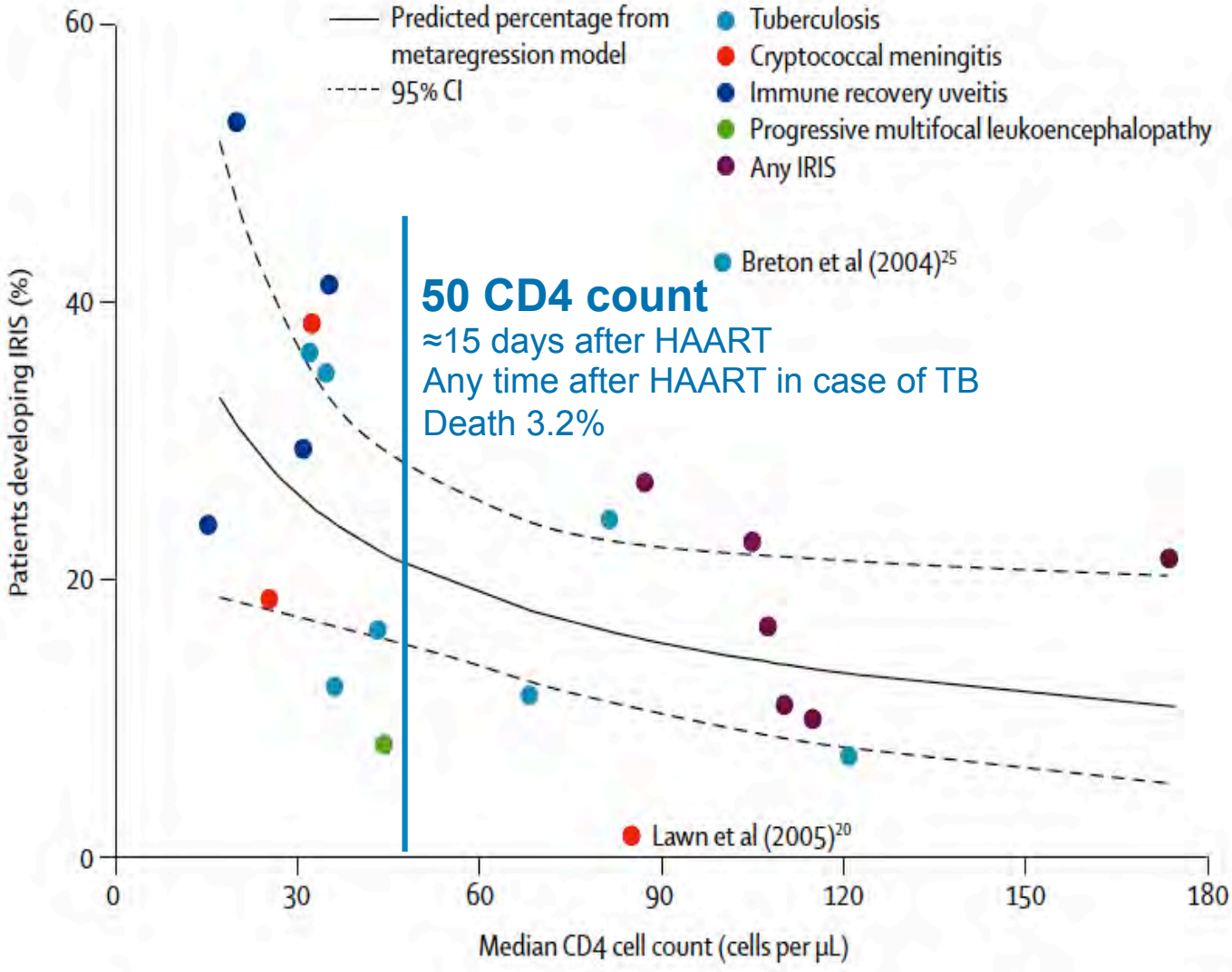
"IRIS" frequency during tuberculosis



Muller et al. Lancet Infect Dis 2010, 10:251

HIV in the lung, during HAART

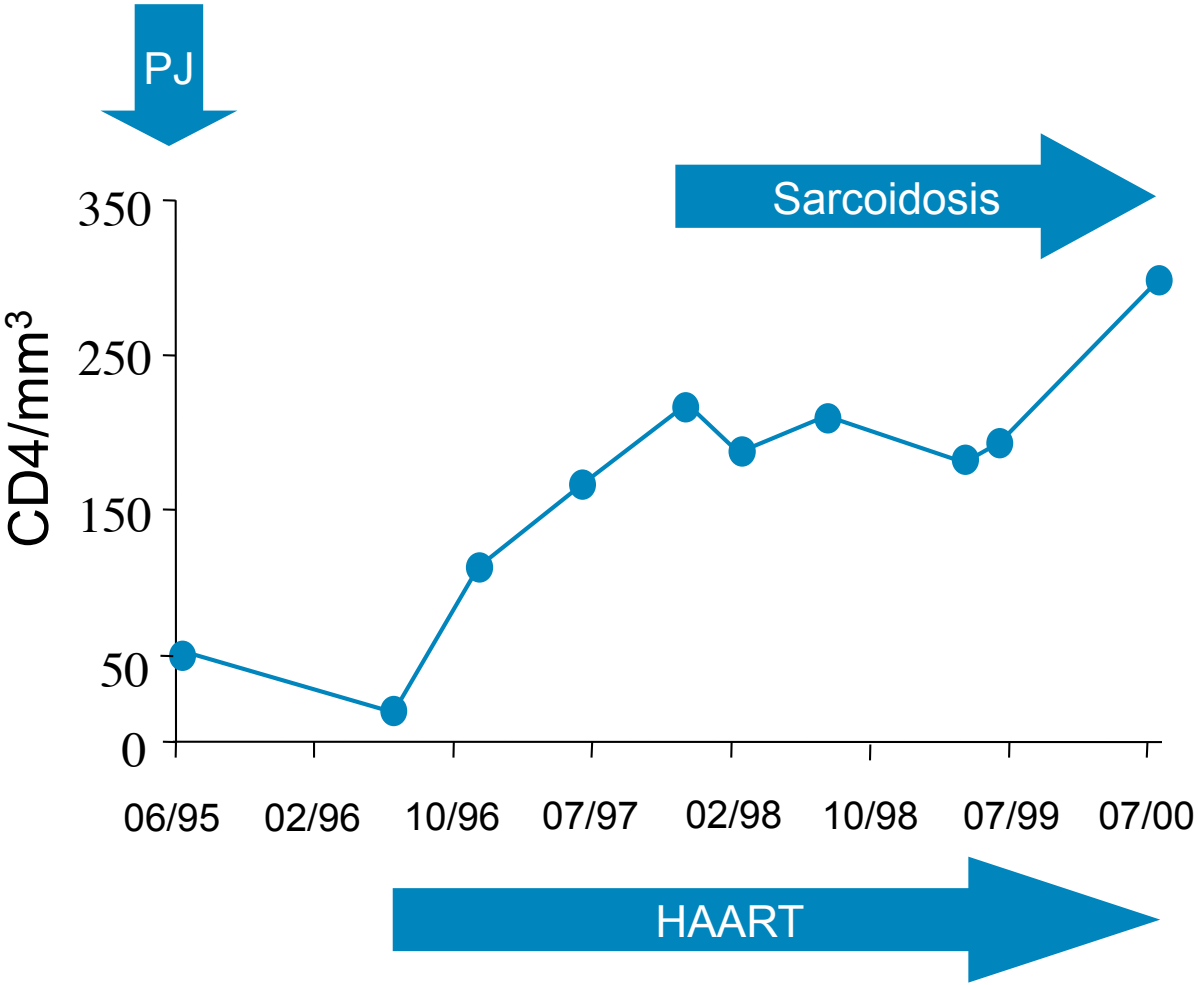
"IRIS", risk factors and kinetic

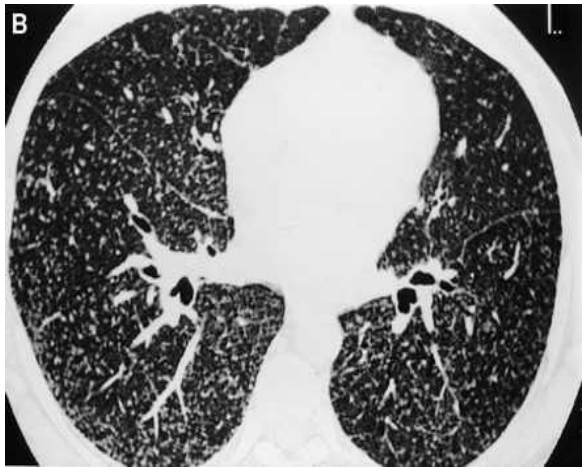


Muller et al. Lancet Infect Dis 2010, 10:251

HIV in the lung, during HAART

"IRIS", sarcoidosis occurrence





Naccache et al. AJRCCM 1998, 159:2009

HIV in the lung, during HAART

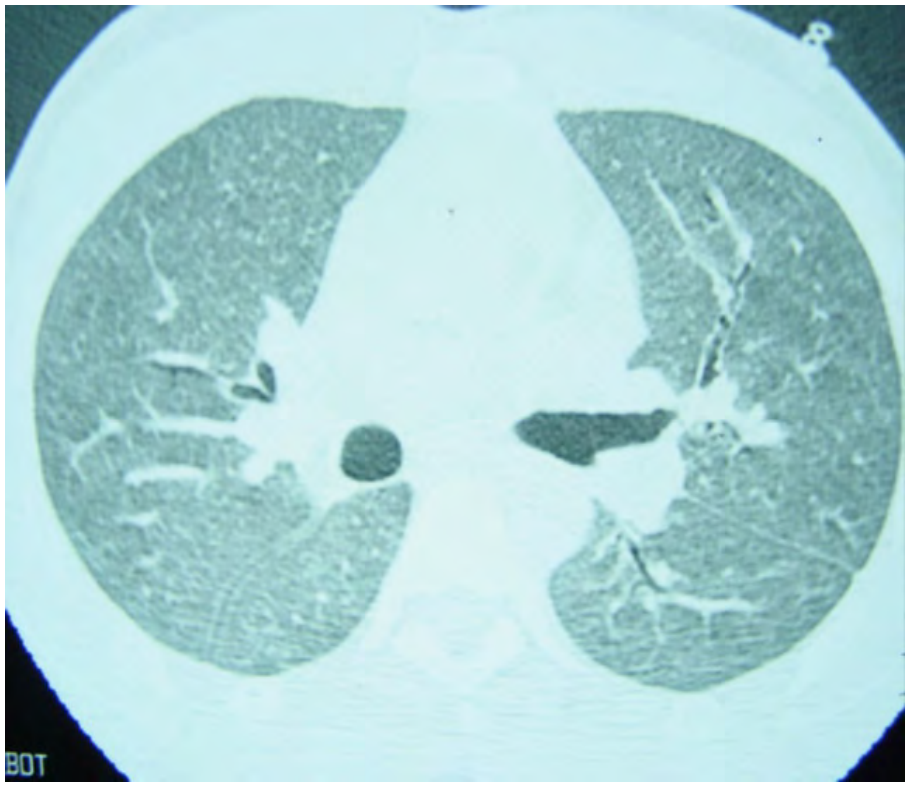
"IRIS", sarcoidosis occurrence

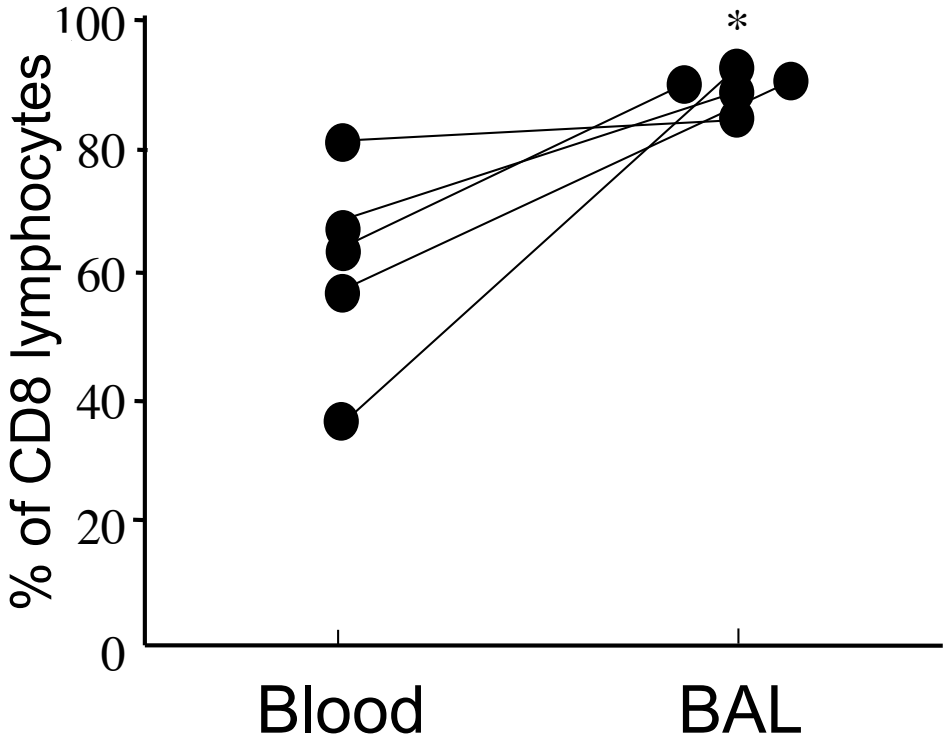
- Dozens of cases reported, mostly on HAART
- Clinical and radiological characteristics similar to conventional sarcoidosis
- Sarcoid granuloma and CD4 cell lymphocytic alveolitis
- Late onset after starting HAART (3-43 months)
- Promoting role of IL-2 or interferon treatement (?)
- Similar evolution to conventional sarcoidosis

Naccache et al. AJRCCM 1998, 159:2009; Shelburne et al. Medicine 2002, 81:213; Foullon et al. Clin Infect Dis 2004, 418:25

HIV in the lung, during HAART

LIP improvement by HAART





Dufour et al. Clin Infect Dis 2003, 36:127

HIV in the lung, during HAART

LIP improvement by HAART

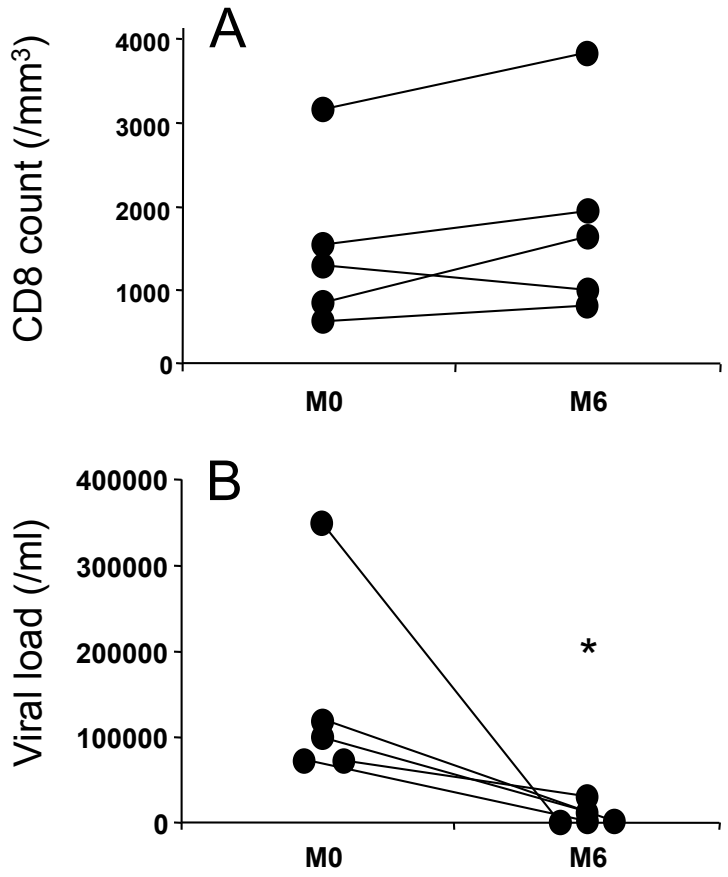
Table 1. Main characteristics of HIV-infected patients with lymphoid interstitial pneumonia at the time of admission to the hospital and during follow-up.

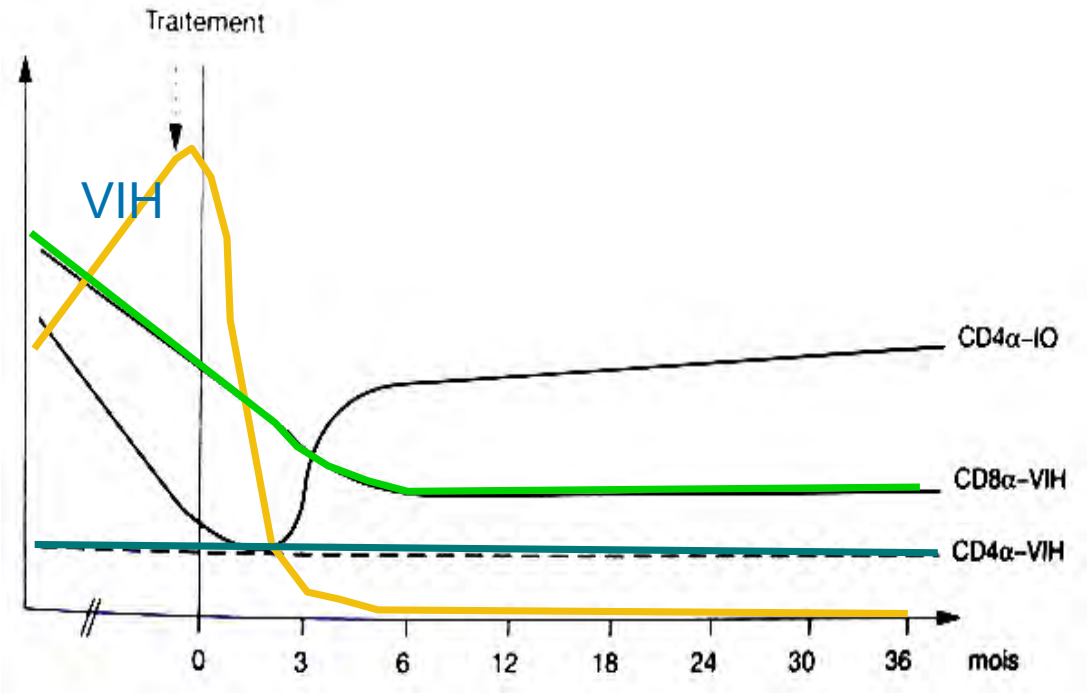
			Characteristics at hospital admission				Characteristics at 6 months of follow-up			
Patient	Sex, age in years	Race	Symptoms	CT scan finding(s)	PaO_2,[a] mm Hg	DLCO,[b] %	Outcome	CT scan finding	PaO_2[a] mm Hg	DLCO,[b] %
1	M, 53	White	Cough, dyspnea, fever, sicca syndrome	ggo	70	50	Improved	Normalization	82	65
2	F, 34	Black	Cough, dyspnea, fever	ggo, mn	85	65	Cured	Improvement	85	80
3	M, 64	White	Cough, dyspnea, weight loss, sicca syndrome	ggo	69	44	Cured	Normalization	79	102
4	F, 24	Black	Cough, dyspnea	ggo, mn, ao, ln	50	NA	Cured	Normalization	66	NA
5	M, 32	Black	Cough, dyspnea, weight loss, thoracic pain	ggo	68	28	Improved	Normalization	86	65

Dufour et al. Clin Infect Dis 2003, 36:127

HIV in the lung, during HAART

LIP improvement by HAART



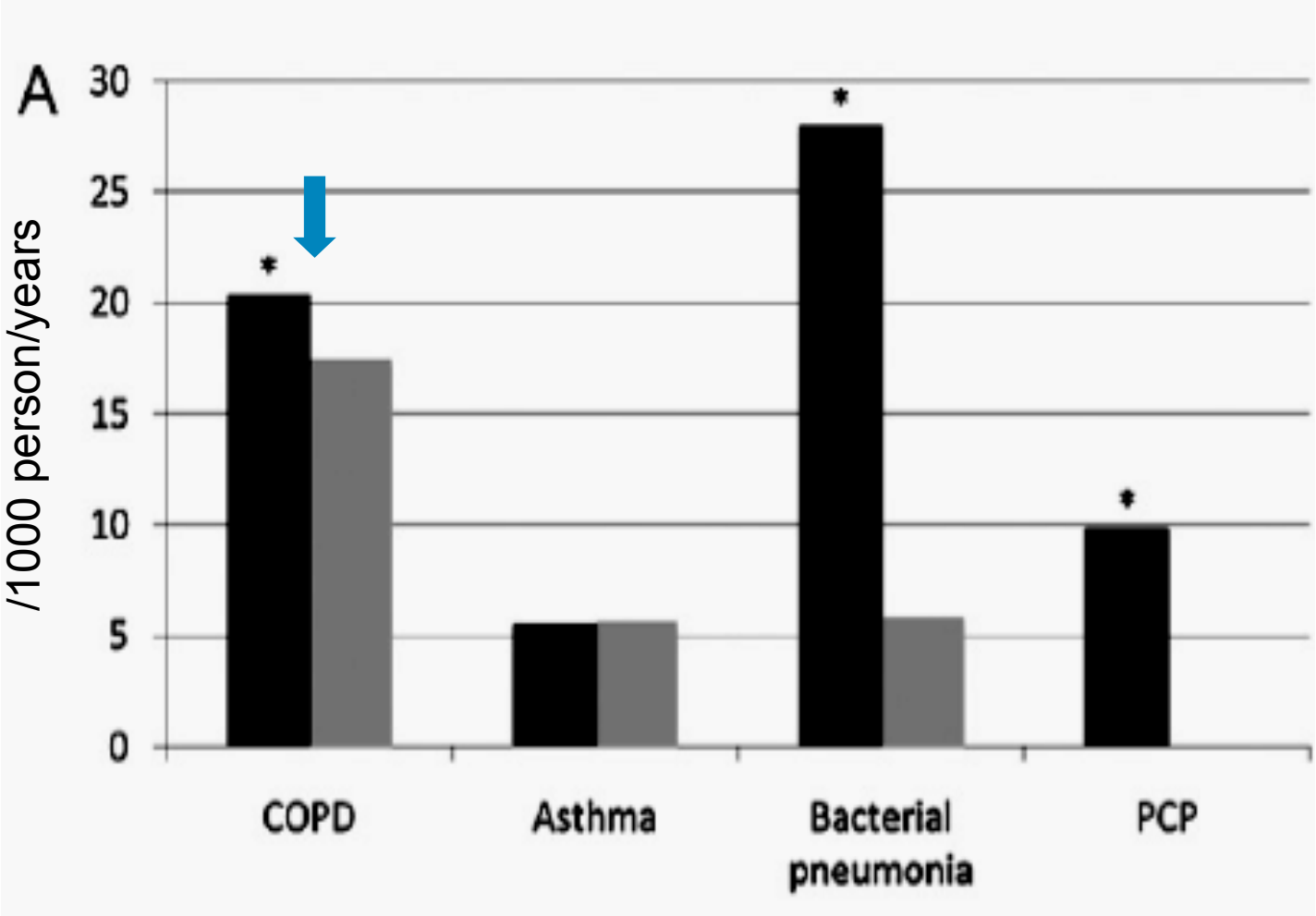


- Rapid reduction of HIV infected target cells
- Slow decrease of anti-HIV specific CD8 cells
- Absence of anti-VIH CD4 specific CD4 cell

Dufour et al. Clin Infect Dis 2003, 36:127

HIV in the lung, after HAART

Emergence of new disorders

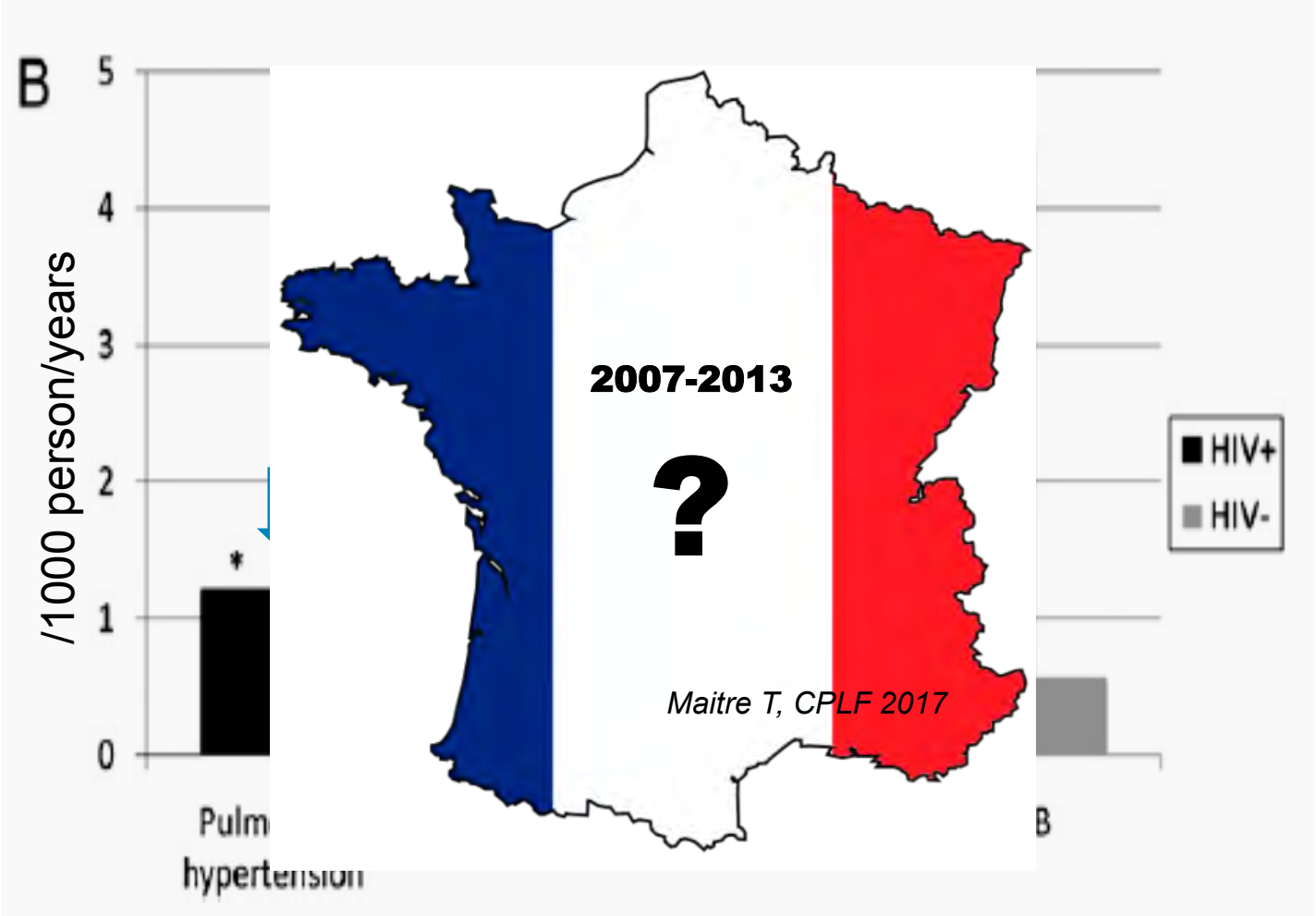


Veterans cohort 33 420 HIV+ vs 66 840 HIV- (1999-2007)

Crothers et al. Am J Respiratory and Crit Care Med 2011, 183:388

HIV in the lung, after HAART

Emergence of new disorders



Veterans cohort 33 420 HIV+ vs 66 840 HIV- (1999-2007)

Crothers et al. Am J Respiratory and Crit Care Med 2011, 183:388

HIV in the lung, after HAART

Emergence of new disorders, COPD

Epidemiology

Asthma?
Emphysema/COPD, yes
Bronchiectasy, yes
Pediatric HIV population

TVO

Clinic

Non specific
VEMS normal/lower DLCO
VEMS decreased with HAART
Bronchiectasy
MAIC and aspergillosis

Pathogenesis

Recurrent infection
Smoking
HIV viral load rather than CD4 count
Chronic inflammation
Oxydative stress and telomeropathy
Increase of IgE, eosinophils and IL8
COPD and HIV myopathy
Bronchiectasy and LIP

Treatment

Stop smoking
Rehabilitation
Danger of inhaled steroids

Crothers et al. Am J Respir Crit Care Med 2011, 183:388; Staitieh et al. Am J Med Sci 2014, 348: 502; Drummond et al. Lancet Respir Med 2014, 2:583; Raynaud C et al. Resp Res 2011, 12:17

HIV in the lung, after HAART

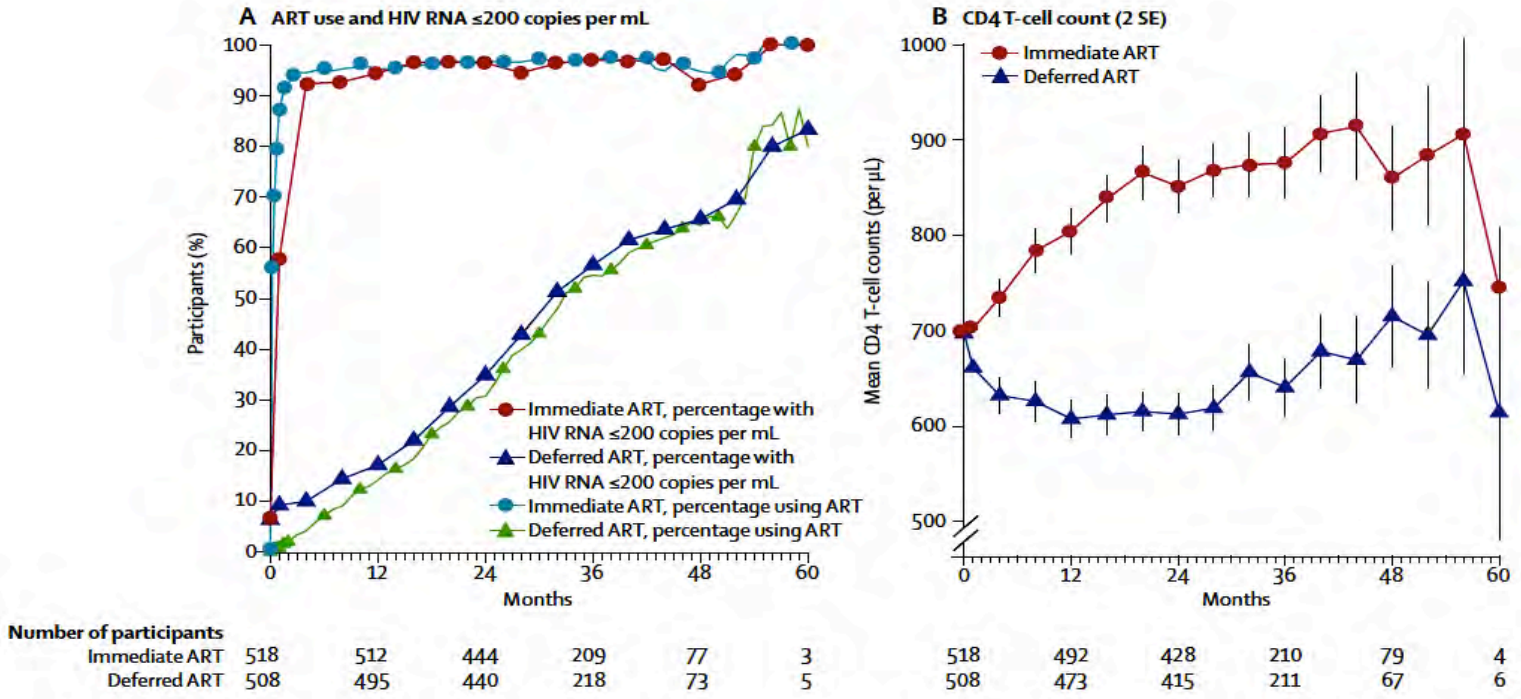
Emergence of new disorders, COPD

Pulmonary effects of immediate versus deferred antiretroviral therapy in HIV-positive individuals: a nested substudy within the multicentre, international, randomised, controlled Strategic Timing of Antiretroviral Treatment (START) trial

*Ken M Kunisaki, Dennis E Niewoehner, Gary Collins, Bitten Aagaard, Nafisah B Atako, Elzbieta Bakowska, Amanda Clarke, Giulio Maria Corbelli, Ernest Ekong, Sean Emery, Elizabeth B Finley, Eric Florence, Rosa M Infante, Cissy M Kityo, Juan Sierra Madero, Daniel E Nixon, Ellen Tedaldi, Jørgen Vestbo, Robin Wood, John E Connett, for the INSIGHT START Pulmonary Substudy Group**

INSIGHT START phase III trial

started c-ART early (within 2 months) vs late (CD4<200/AIDS)



Number of participants						
Immediate ART	518	512	444	209	77	3
Deferred ART	508	495	440	218	73	5

Immediate ART	518	492	428	210	79	4
Deferred ART	508	473	415	211	67	6

Kunisaki K, Lancet Respir Med 2016, Epub 20/10/2016

HIV in the lung, after HAART

Emergence of new disorders, COPD

INSIGHT START phase III trial

started c-ART early (within 2 months) vs late (CD4<200/AIDS)

	FEV_1 slope (95% CI), mL/year	p value
Baseline smokers		
Immediate ART (n=135)	−32·9 (−58·5 to −7·4)	..
Deferred ART (n=155)	−29·7 (−54·3 to −5·0)	..
Difference	−3·3 (−38·8 to 32·2)	0·86
Baseline non-smokers		
Immediate ART (n=383)	−27·8 (−44·2 to −11·4)	..
Deferred ART (n=353)	−22·2 (−39·6 to −4·9)	..
Difference	−5·6 (−29·4 to 18·3)	0·65
Pooled analysis adjusted for baseline smoking status		
Immediate ART (n=518)	−29·1 (−42·9 to −15·4)	..
Deferred ART (n=508)	−24·5 (−38·6 to −10·3)	..
Difference	−4·7 (−24·4 to 15·1)	0·64
Pooled analysis adjusted for smoking status at each study visit		
Immediate ART (n=518)	−28·8 (−42·6 to −14·9)	..
Deferred ART (n=508)	−23·6 (−37·8 to −9·3)	..
Difference	−5·2 (−25·1 to 14·6)	0·61

	Immediate ART		Deferred ART		p value*
	n	Number (%) who had a bronchitis event	n	Number (%) who had a bronchitis event	
Smokers					
Baseline	135	49 (36%)	155	54 (35%)	
Year 1	117	34 (29%)	126	37 (29%)	1·00
Year 2	96	27 (28%)	110	24 (22%)	0·33
Year 3	58	11 (19%)	65	10 (15%)	0·64
Year 4	24	8 (33%)	22	2 (9%)	0·07
Non-smokers					
Baseline	383	96 (25%)	353	76 (22%)	
Year 1	339	62 (18%)	302	55 (18%)	1·00
Year 2	295	45 (15%)	265	37 (14%)	0·72
Year 3	130	20 (15%)	120	17 (14%)	0·86
Year 4	42	11 (26%)	29	4 (14%)	0·25

Kunisaki K, Lancet Respir Med 2016, Epub 20/10/2016

HIV in the lung, after HAART

Emergence of new disorders

Epidemiology

Include in group 1 PH
1986, first description
0.5% of HIV persons
x 1000 general population
W/M ratio: 1.4

Clinic

Possible in HIV asymptomatic persons, 25% inaugural
Non specific
dyspnea, thoracic pain
TTE then RHC

Pathogenesis

IVDU
gp120 induced endothelin 1 secretion
Tat/gp120 induced MIP1a secretion
Tat suppressed BMPR-2 expression
Endothelial cells Nef infection
Chronic inflammation

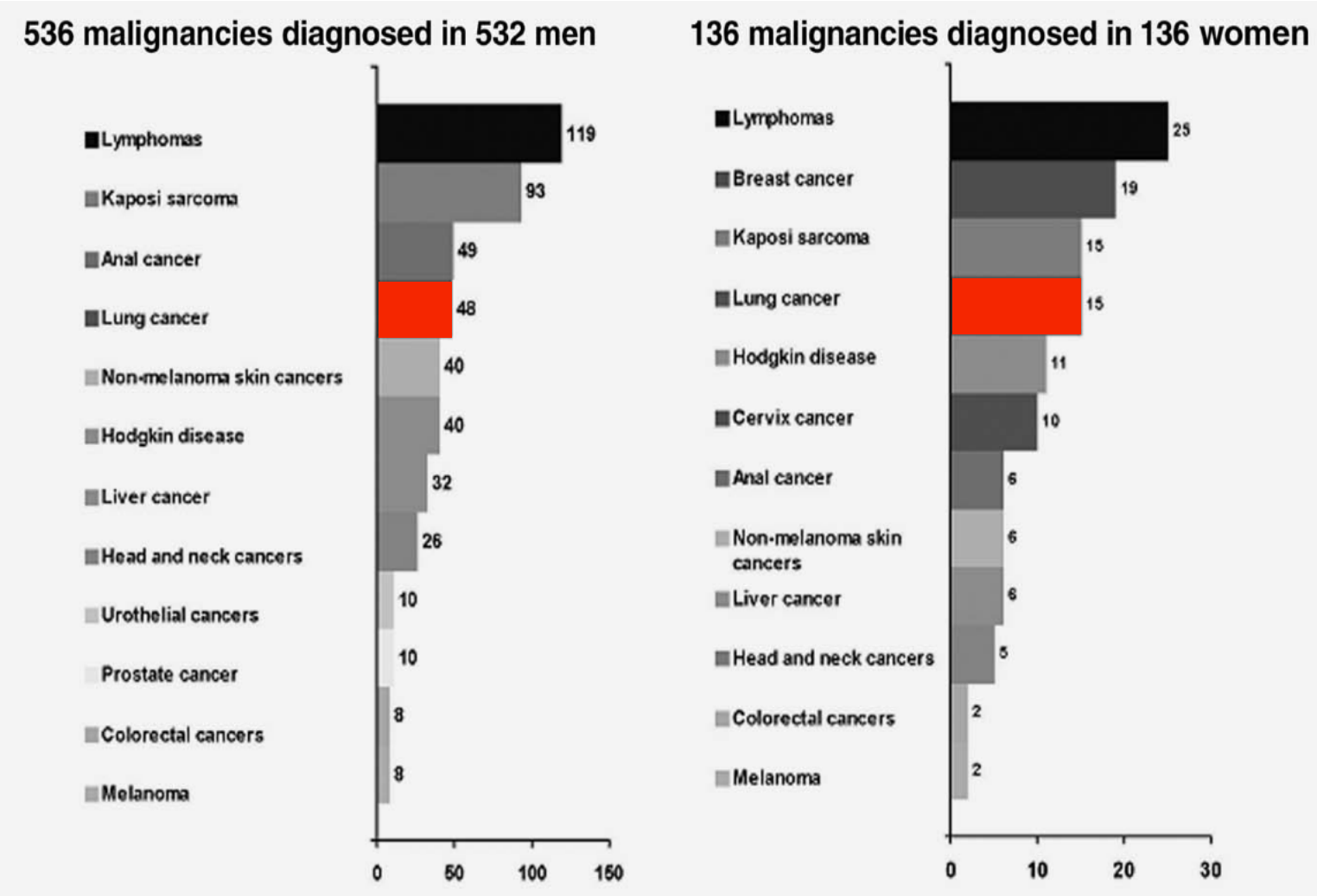
Treatment

72% survival at 3 years
cardiad function, CD4 count
HAART improves mortality
Risk of HAART specific PAH treatment interactions
sildenafil
Bosantan, prostacycline
Interest of high dose steroids?

Crothers et al. Am J Respiratory and Crit Care Med 2011, 183:388; Sitbon et al. Am J Respir Crit Care Med 2008, 177:108; Degano et al. AIDS 2010, 24:67; Degano et al. Eur Resp J 2009, 33:92

HIV in the lung, after HAART

Lung cancer and malignancies

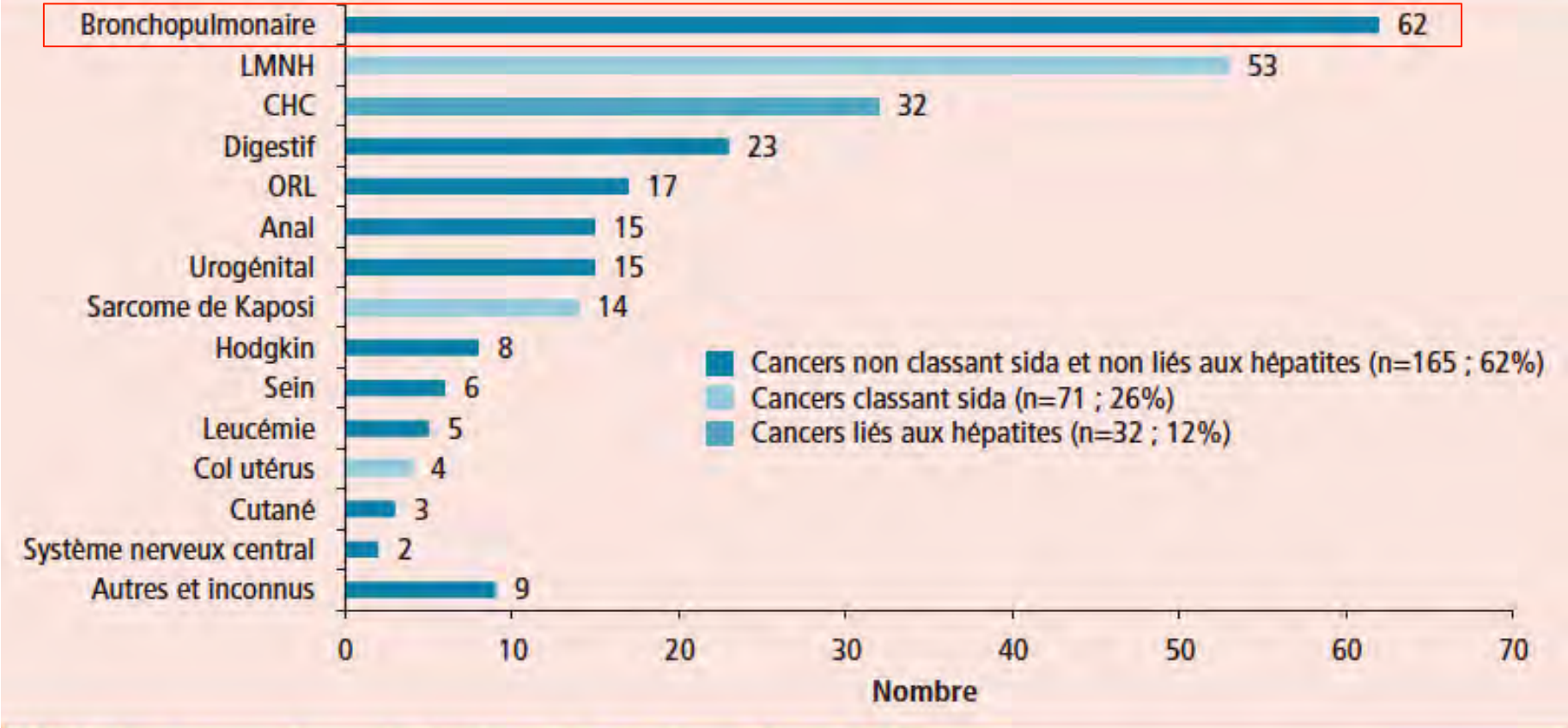


Lanoy et al. Int J Cancer 2011, 129:467

HIV in the lung, after HAART

Lung cancer and malignancies

Figure 3 Localisation des cancers (n=268) parmi les adultes décédés d'un cancer (n=250), enquête Mortalité 2010, France / *Figure 3 Cancer sites (n=268) among adults who died from cancer (n=250), Mortalité 2010 survey, France*



LMNH : lymphome malin non hodgkinien ; CHC : carcinome hépatocellulaire.

Roussillon C, BEH 46/47 1er décembre 2012

HIV in the lung, after HAART

Lung cancer and malignancies

Non-AIDS-related malignancies: expert consensus review and practical applications from the multidisciplinary CANCERVIH Working Group

J.-P. Spano[1,2,3*,†], I. Poizot-Martin[4,5,†], D. Costagliola[2,3], F. Boué[6,7], O. Rosmorduc[8,9], A. Lavolé[10], S. Choquet[2,3,11], P.-E. Heudel[12], V. Leblond[8,11,13], J. Gabarre[11], M.-A. Valantin[2,3,14], C. Solas[15], A. Guihot[8,16], G. Carcelain[8,13], B. Autran[8,13], C. Katlama[2,3,14] & L. Quéro[17,18]

- Risque de CB x2; plus jeune; plus étendu
- Première cause de mortalité par cancer chez le VIH; population exclue des essais thérapeutiques; >90% fumeurs
- Cddp/pem-pem, standard de 1ére ligne dans les CBNPC non épi; essai IFCT CHIVA (cddp/pem-pem): PFS=3,5 (2,7-4,4); OS=7,6 (5,7-13,2)
- Toxicité cumulative et/ou interactions avec c-ART pour vinorelbine, docetaxel, paclitaxel et erlotinib
- Nivolumab cohorte CANCERVIH; essai IFCT CHIVA2

Spano JP, Ann Oncol 2016, 27:397; Lavole A, ASCO 2016; Guihot A, Rev Mal Respir 2016, 33:419

HIV in the lung, after HAART

Lung cancer and malignancies

Potential benefits	Pote
• Reverse deleterious PD1 expression on anti-HIV CD8 lymphocytes (restaure HIV immune response) • Attenuate chronic inflammation (promoting chronic HIV replication and increasing cancer risk) • Effective *in vitro* and in macaque model	• HIV • HBV • HIV brain. • Imm uncon

Tableau 1 Surveillance biologique des personnes vivant avec le VIH (PVVIH) traitées par anti-PD-1/PD-L1.

Au prélèvement initial (avant anti-PD-1/PD-L1) seulement
Charge virale EBV, charge virale CMV, charge virale HHV-8 si sérologie positive ; ces analyses seront surveillées ultérieurement en cas de positivité Quantiféron®

Au prélèvement initial et à chaque cycle (avant l'injection, tous les 15 jours pour le nivolumab, toutes les 3 semaines pour le pembrolizumab)
NFS plaquettes, formule leucocytaire, ionogramme sanguin, urée, créatinine, calcium, magnésium, phosphatémie, ASAT, ALAT, bilirubine, PAL, gamma GT, glycémie, lipase, albumine, LDH, bandelette urinaire
Numération CD4/CD8, charge virale VIH

Au prélèvement initial et tous les 3 cycles
TSH (T3, T4 libre si TSH anormale), anticorps anti-nucléaires (AAN) avec anti-ADN natif et anti-ENA si AAN positifs, anti-TPO, anti-thyroglobuline
Antigène HBS, charge virale VHB/VHC si co-infection VHB ou VHC
Bêta-hCG si femme en âge de procréer

- RCP CANCERVIH par webconf/
  - Déclaration des cas
  - Suivi standardisé
  - Screening futur pour CHIVA2

Spano JP, Ann Oncol 2016, 27:397; Lavole A, ASCO 2016; Guihot A, Rev Mal Respir 2016, 33:419

HIV in the lung, after HAART

Diagnostic strategy