Faut-il adapter à la coinfection les recommandations de l'AFEF ?

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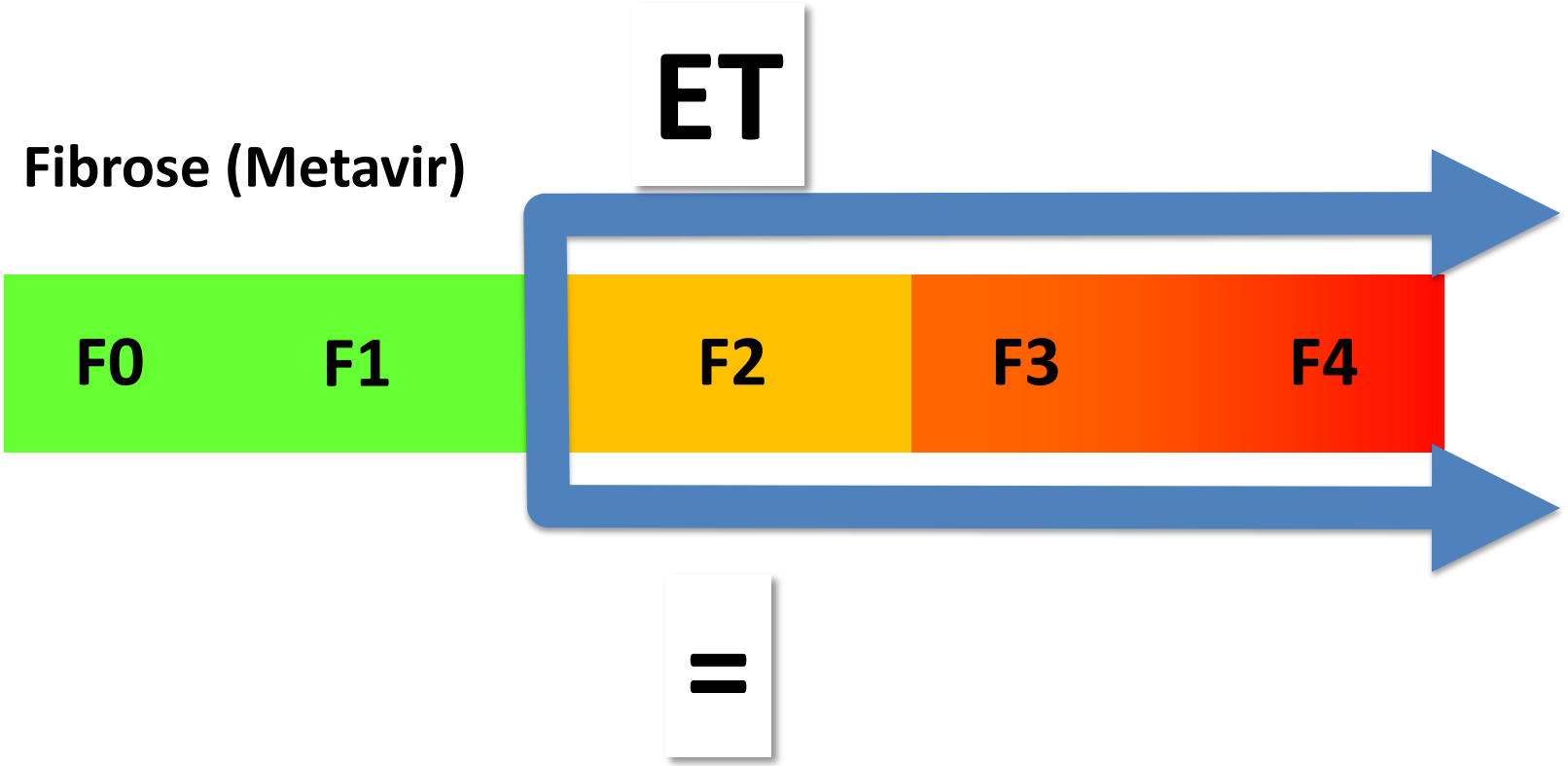
Conflits d'intérêts

- Membre de board : Abbott ; BMS ; Boerhinger Ingelheim ; Gilead ; Merck ; Tibotec/Janssen Cilag ; ViiV Healthcare
- Orateur : BMS ; Tibotec/Janssen Cilag ; Gilead ; Merck ; ViiV Healthcare

Recommandations AFEF

PCR VHC POS ± ALT > N

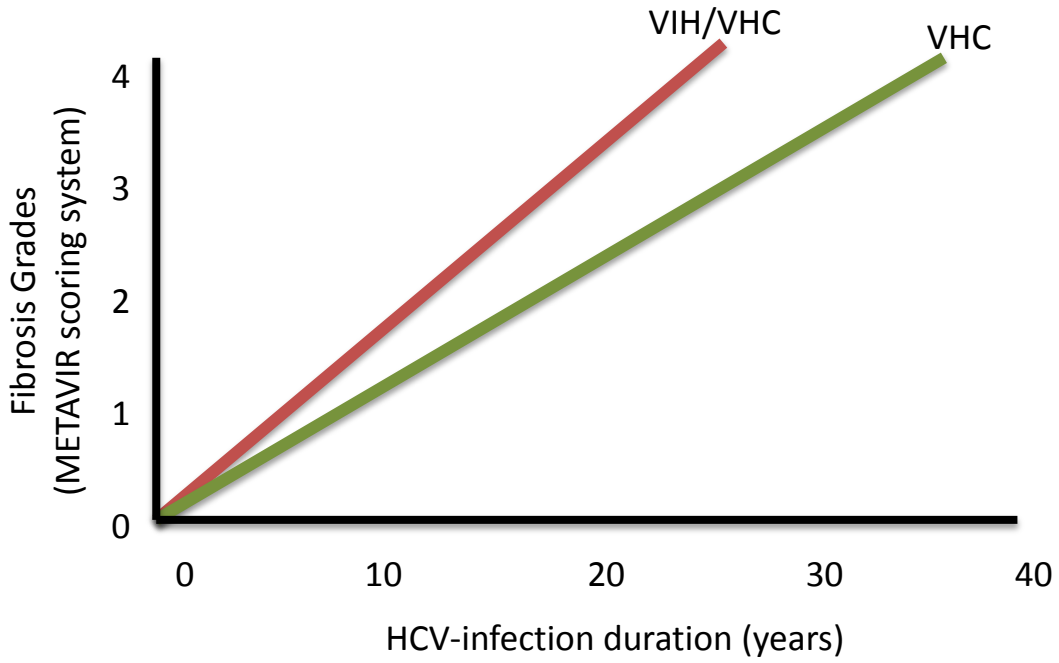


Traitement antiviral
(PR ou PR T/Boc en fonction du génotype)

Pourquoi des recommandations différentes chez les patients VIH/VHC?

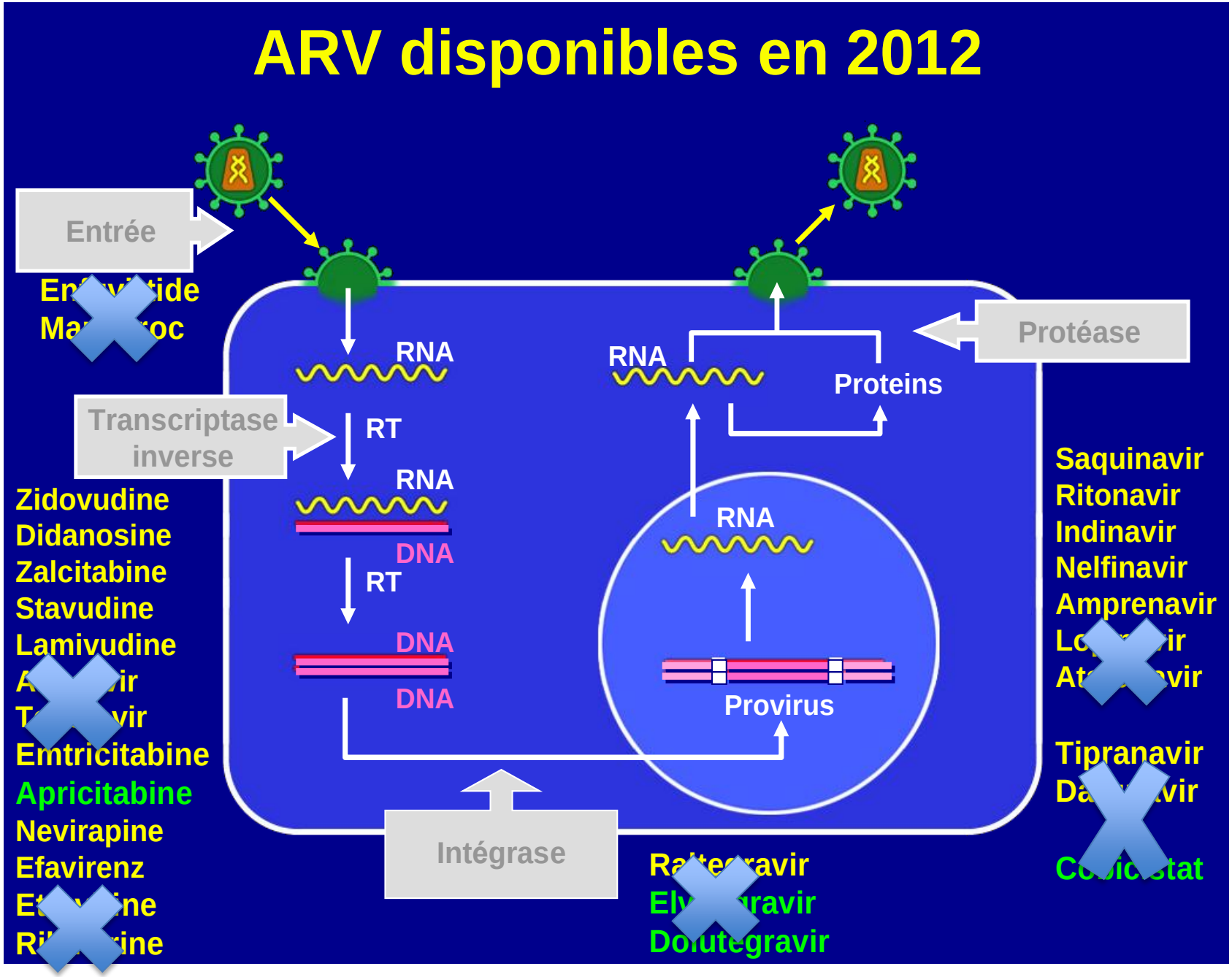
- Evolution de la fibrose plus rapide

F0-F1 un jour ≠ F0-F1 toujours



Benhamou Y et al. Hepatology 1999

ARV disponibles en 2012



Journal of Viral Hepatitis, 2011, **18**, e307–e314 doi:10.1111/j.1365-2893.2010.01417.x

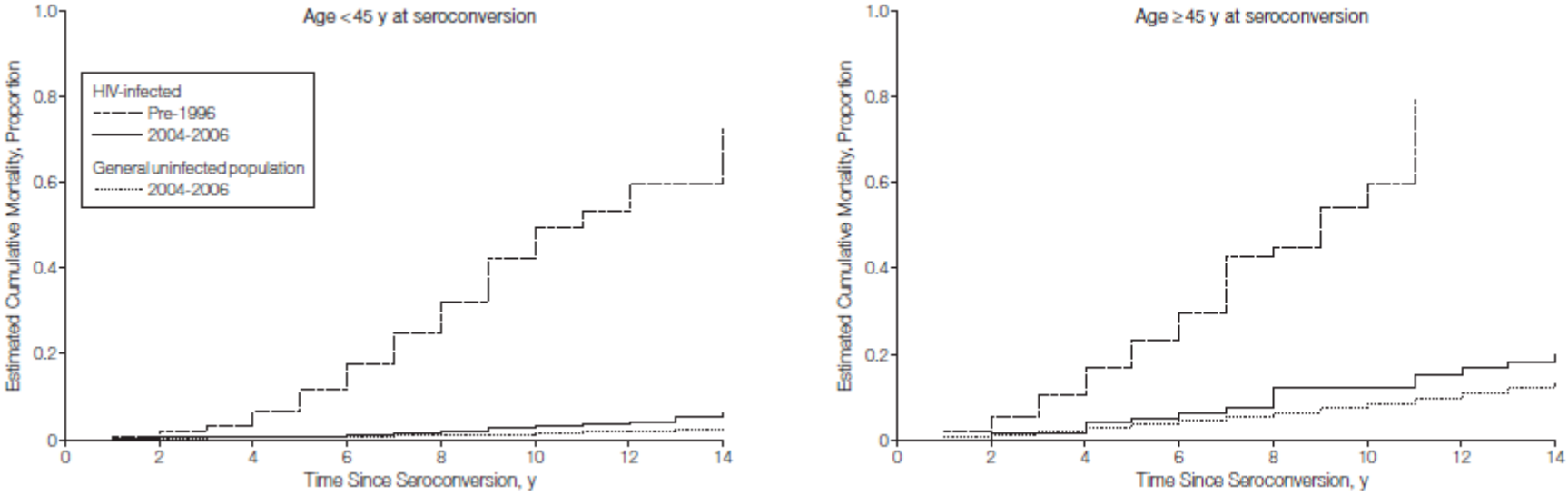
Impact of HAART exposure and associated lipodystrophy on advanced liver fibrosis in HIV/HCV-coinfected patients

M.-A. Loko,[1] F. Bani-Sadr,[1,2] M. Winnock,[1] K. Lacombe,[3] P. Carrieri,[4] D. Neau,[5] P. Morlat,[1,6] L. Serfaty,[7] F. Dabis[1] and D. Salmon[2] for the ANRS CO 13 HEPAVIH Study Group

Table 3 Factors associated with fibrosis severity. Multivariate logistic regression analysis

	Multivariate analysis	
	Odds ratio (95% CI)	*P*-value
Male sex	2.0 (1.1–3.5)	0.018
HCV infection through intravenous drug use	2.0 (1.3–3.6)	0.018
Median didanosine therapy >5 months	1.69 (1.02–2.79)	0.04
Lipodystrophy	2.0 (1.2–3.3)	0.01
HOMA value	1.12 (1.04–1.2)	0.005

Changes in the Risk of Death After HIV Seroconversion Compared With Mortality in the General Population

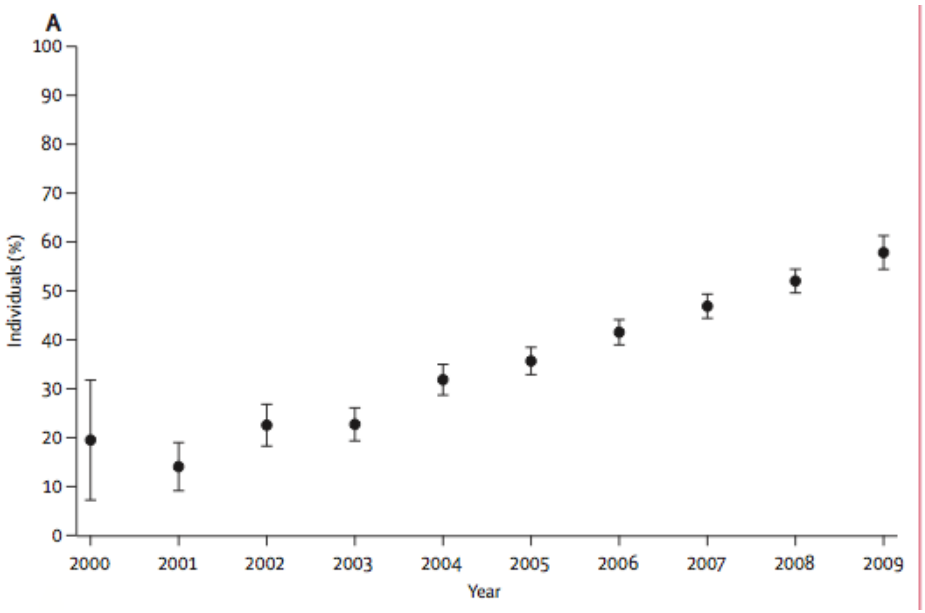


"By 2004-2006, no excess mortality was observed in the first 5 years following HIV seroconversion among those infected sexually, though a cumulative excess probability of death remained over the longer term"

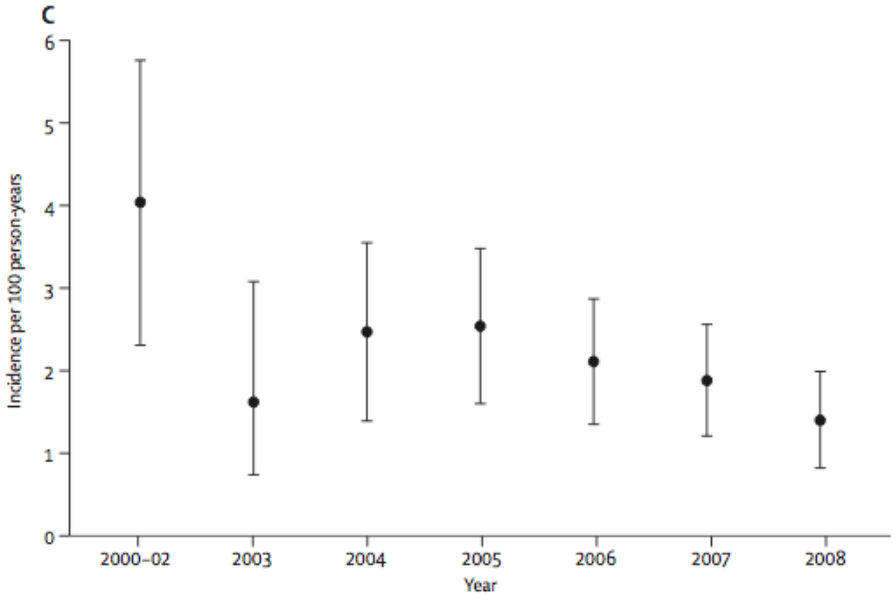
Trends in virological and clinical outcomes in individuals with HIV-1 infection and virological failure of drugs from three antiretroviral drug classes: a cohort study

The Pursuing Later Treatment Option II (PLATO II) project team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Group**

- **2476 participants**



Virological succes



Deaths

Lancet Infect Dis 2012; 12: 119–27

Antiretroviral therapy and sustained virological response to HCV therapy are associated with slower liver fibrosis progression in HIV–HCV-coinfected patients: study from the ANRS CO 13 HEPAVIH cohort

Marc-Arthur Loko[1,2], Firouze Bani-Sadr[3], Marc-Antoine Valantin[4,5], Caroline Lascoux-Combe[6], Hélène Fontaine[7], Philippe Bonnard[8], Anne Gervais[9], Olivier Bouchaud[10], Daniel Garipuy[11], Yann Quertainmont[12], Daniel Vittecoq[13], Michka Shoai Tehrani[14], Maria Winnock[1,2], François Dabis[1,2], Dominique Salmon[3], the ANRS CO 13 HEPAVIH Study Group†*

Antiviral Therapy 2012; 17:1335–1343

French nation-wide prospective hospital-based cohort of HIV–HCV-coinfected adults initiated in 2005

Undetectable plasma HIV RNA = 72%

ART>114.5 months associated with no increase (OR = 0.5)

Relationship of Liver Disease Stage and Antiviral Therapy With Liver-Related Events and Death in Adults Coinfected With HIV/HCV

Berkeley N. Limketkai, MD
Shruti H. Mehta, PhD
Catherine G. Sutcliffe, PhD
Yvonne M. Higgins, MAS, MS/ITS
Michael S. Torbenson, MD
Sherilyn C. Brinkley, MSN, CRNP
Richard D. Moore, MD
David L. Thomas, MD, MPH
Mark S. Sulkowski, MD

Context Human immunodeficiency virus (HIV) accelerates hepatitis C virus (HCV) disease progression; however, the effect of liver disease stage and antiviral therapy on the risk of clinical outcomes is incompletely understood.

Objective To determine the incidence of end-stage liver disease (ESLD), hepatocellular carcinoma (HCC), or death according to baseline hepatic fibrosis and antiviral treatment for HIV/HCV coinfected individuals.

Design, Setting, and Participants Prospective cohort of 638 coinfected adults (80% black, 66% men) receiving care at the Johns Hopkins HIV clinic and receiving a liver biopsy and who were prospectively monitored for clinical events between July 1993 and August 2011 (median follow-up, 5.82 years; interquartile range, 3.42-8.85 years). Histological specimens were scored for hepatic fibrosis stage according to the METAVIR scoring system.

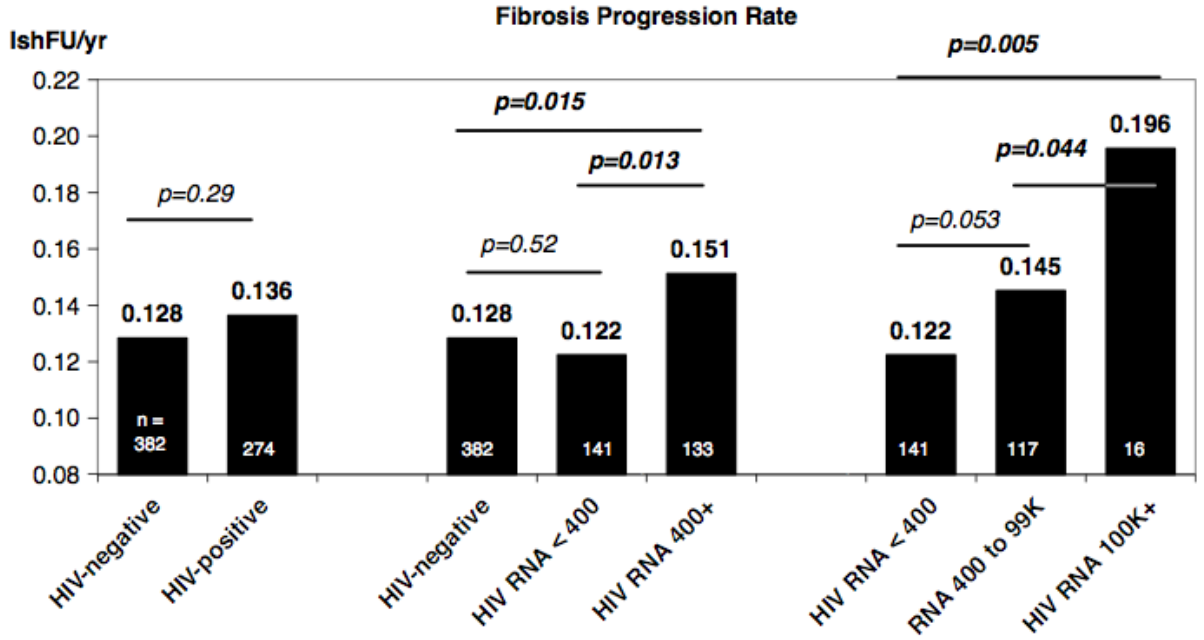
638 adults coinfected with HIV/HCV who received medical care at the Johns Hopkins University HIV and HIV/HCV Coinfection Clinics and who had a liver biopsy between July 1993 and August 2011.

	No. of Events[b]	Person-Years[b]	ESLD, HCC, or All-Cause Mortality, Incidence RR (95% CI)	
			Crude	Adjusted[c]
ART exposure[e]				
No	74	929	1 [Reference]	1 [Reference]
Yes	76	2856	0.27 (0.19-0.39)	0.27 (0.19-0.38)
CD4 cell count/μL[e]				
<200	67	594	1 [Reference]	1 [Reference]
200-350	28	824	0.29 (0.18-0.46)	0.27 (0.16-0.44)
>350	55	2364	0.22 (0.15-0.32)	0.21 (0.14-0.31)
HIV-1 RNA measures <400 copies/mL, %[e,f]				
≥75	45	1891	1 [Reference]	
26-75	43	981	1.87 (1.20-2.90)	
0-25	62	908	3.00 (1.98-4.54)	

Norbert Bräu[1,*], Mirella Salvatore[1], Carlos F. Ríos-Bedoya[2], Alberto Fernández-Carbia[3], Fiorenzo Paronetto[1], José F. Rodríguez-Orengo[4], Maribel Rodríguez-Torres[2,5], for the Puerto Rico-New York Hepatitis Study Group

[1]*Bronx Veterans Affairs Medical Center and Mount Sinai School of Medicine, New York, NY, USA*
[2]*Ponce School of Medicine, Ponce, PR, USA*
[3]*University Pathologists, San Juan, PR, USA*
[4]*University of Puerto Rico School of Medicine, San Juan, PR, USA*
[5]*Fundación de Investigación de Diego, San Juan, PR, USA*

Journal of Hepatology 44 (2006) 47–55



. Fibrosis progression rate by HIV status and HIV viral load patients with chronic hepatitis C. IshFu/yr, Ishak fibrosis units per year; HIV
n copies per mL; K = 1,000.

Clin Gastroenterol Hepatol. 2010 December ; 8(12): 1070–1076. doi:10.1016/j.cgh.2010.08.004.

Similar Progression of Fibrosis between HIV/HCV- and HCV-Infected Patients: Analysis of Paired Liver Biopsy Samples

Richard K. Sterling[1,2], Jacob A Wegelin[3], Paula G. Smith[1], R. Todd Stravitz[1], Velimir A Luketic[1], Michael Fuchs[1], Puneet Puri[1], Mitchell L. Shiffman[1], Melissa A. Contos[4], A. Scott Mills[4], and Arun J. Sanyal[1]

Knodell fibrosis stages at initial and final biopsy

First Biopsy					Total
0					14
1					29
3					16
Total					59

"Because a significant proportion did not progress, similar to those with HCV alone, decisions on whether or not to begin HCV therapy depend on……. and not on concerns about rapid disease progression.

Mono-infected patients
5.8 années entre 2 biopsies

co-infected patients
4.7 years entre 2 biopsies

Relationship of Liver Disease Stage and Antiviral Therapy With Liver-Related Events and Death in Adults Coinfected With HIV/HCV

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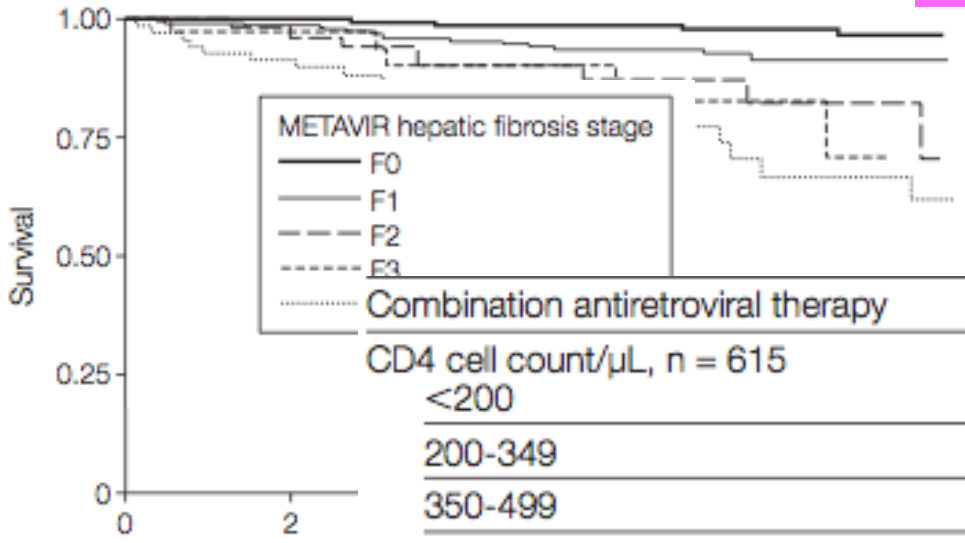
"Our finding that patients with no fibrosis had a relatively low incidence of liver-related events over approximately 6 years provides support for the expert recommendation for the deferral in such persons of current HCV therapies"

B Time to liver-related death, end-stage liver disease, or hepatocellular carcinoma



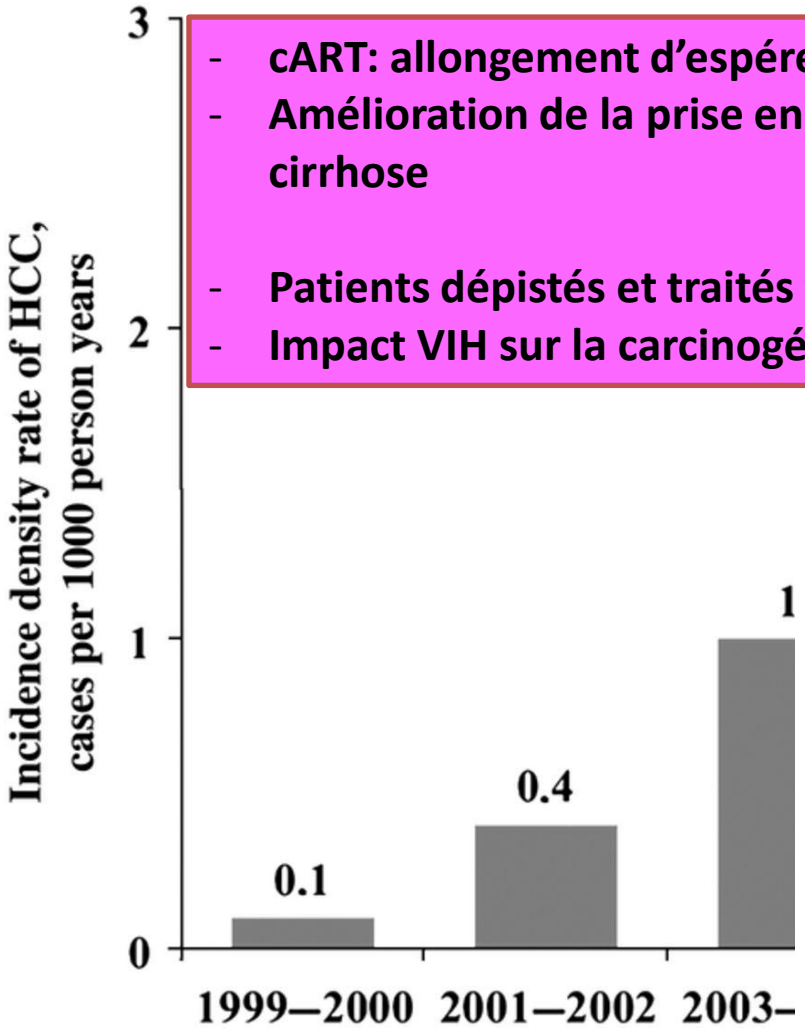
Combination antiretroviral therapy	440 (69)
CD4 cell count/μL, n = 615	
<200	111 (18)
200-349	152 (25)
350-499	148 (24)
≥500	202 (33)
HIV RNA, copies/mL, n = 601	
<400	338 (56)
400-10 000	102 (17)
>10 000	161 (27)

- La co-infection reste mortelle
- Les complications des co-infections élévées

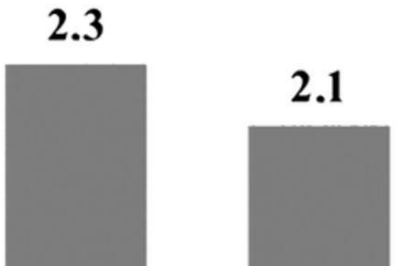
Evolution of the incidence density rate of hepatocellular carcinoma in patients coinfected with human immunodeficiency virus and hepatitis C virus during the study period (n = 76).

- cART: allongement d'espérence de vie
- Amélioration de la prise en charge de la cirrhose

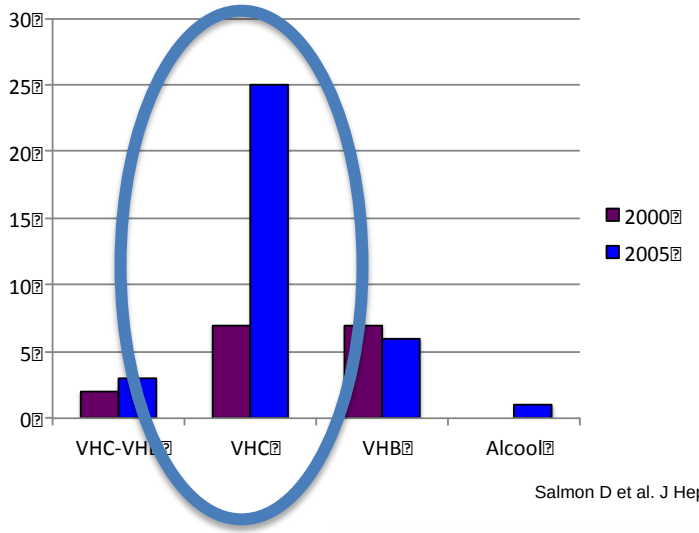
- Patients dépistés et traités tard pour le VIH
- Impact VIH sur la carcinogénèse



Merchante N et al. Clin Infect Dis. 2012;cid.cis777



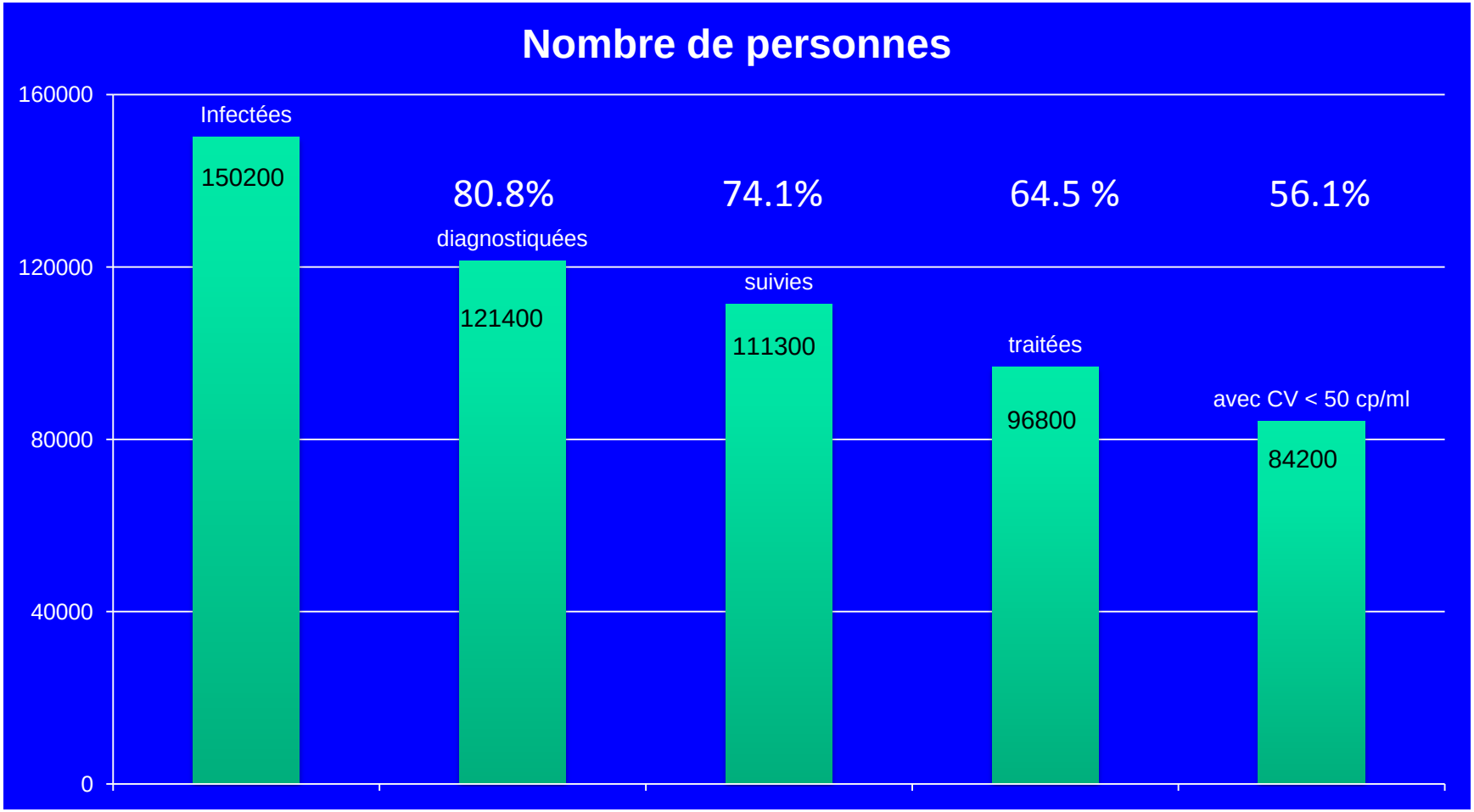
Nombre de décès rapportés au CHC (cohorte Hepavih)



Salmon D et al. J Hepatol 2009

Clinical Infectious Diseases

Estimation de la taille de l'épidémie en France



Costagliola FHDH 2012

Activation immune, activation des marqueurs des cellules endothéliales

– Parmi les facteurs impliqués: les infections virales chroniques liées au cytomégalovirus et ***au virus de l'hépatite virale C?***

Niveau de Preuve ?

JOURNAL OF VIROLOGY, Nov. 2009, p. 11407–11411 Vol. 83, No. 21
0022-538X/09/$12.00 doi:10.1128/JVI.01211-09

High Levels of Chronic Immune Activation in the T-Cell Compartments of Patients Coinfected with Hepatitis C Virus and Human Immunodeficiency Virus Type 1 and on Highly Active Antiretroviral Therapy Are Reverted by Alpha Interferon and Ribavirin Treatment[▽]

Veronica D. Gonzalez,[1] Karolin Falconer,[2] Kim G. Blom,[1] Olle Reichard,[2] Birgitte Mørn,[3] Alex Lund Laursen,[4] Nina Weis,[5,6] Annette Alaeus,[2] and Johan K. Sandberg[1]*

Center for Infectious Medicine, Department of Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, 14186 Stockholm, Sweden[1]; Unit of Infectious Diseases, Department of Medicine, Karolinska Institutet, Karolinska University Hospital Solna, 17176 Stockholm, Sweden[2]; Department of Infectious Diseases, Aalborg University Hospital, Aalborg, Denmark[3]; Department of Infectious Diseases, Aarhus University Hospital, Aarhus, Denmark[4]; Department of Infectious Diseases, Hvidovre University Hospital, Copenhagen, Denmark[5]; and Department of Infectious Diseases, Rieshospitalet. Copenhagen. Denmark[6]

HCV/HIV n =14

Shen *et al. Virology Journal* 2010, **7**:310
http://www.virologyj.com/content/7/1/310

VIROLOGY JOURNAL

RESEARCH Open Access

PD-1 expression on peripheral CD8+ TEM/TEMRA subsets closely correlated with HCV viral load in chronic hepatitis C patients

Tao Shen[1†], Jiajia Zheng[1†], Chunhui Xu[1], Jia Liu[1], Weidong Zhang[2], Fengmin Lu[1*], Hui Zhuang[1*]

HCV n =37

Original article

Changes in T-cell subsets in HIV–HCV-coinfected patients during pegylated interferon-α2a plus ribavirin treatment

*Marta Massanella[1], Cristina Tural[2], Laura Papagno[3], Elisabet Garcia[1], Antoni Jou[2], Margarita Bofill[1,4], Brigitte Autran[3], Bonaventura Clotet[1,2], Julià Blanco[1]**

HCV/HIV n =22

Activation immune, activation des marqueurs des cellules endothéliales

– Parmi les facteurs impliqués: les infections virales chroniques liées au cytomégalovirus et ***au virus de l'hépatite virale C?***

Niveau de Preuve !!

Pour le VIH : **BHIVA guidelines recommend cART <350 cells/mm^3**

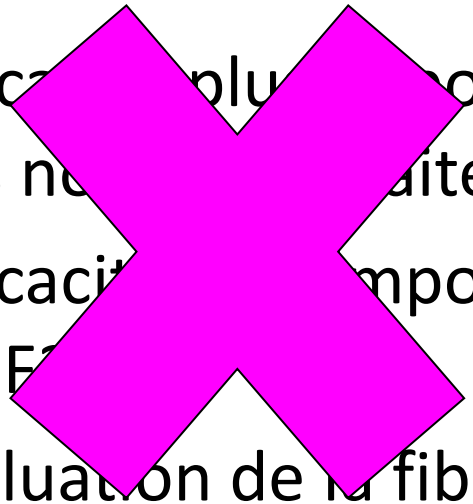
Guidelines: "A number of observational studies have failed to take lead-time into account; this may introduce serious bias into treatment comparisons"

BHIVA Guidelines 2012 Available at: www.bhiva.org/documents/Guidelines/Treatment%20Guidelines/2012/formatted__ART_guidelines_04022012_v3_IW.pdf. Accessed April 2012

Un traitement plus précoce?

Pour

- Effica[illegible]plu[illegible]portant des n[illegible]aitements
- Efficaci[illegible]mportant si F < F[illegible]
- Evaluation de la fibrose n'est pas parfait



Contre

- **<u>L'arrivée des traitements plus efficace et mieux tolérés (2015, 2017)</u>**
- Survenue de variants viraux résistants en cas de non réponse
- Coût

Antiviral Therapy 2012; 17:1223–1225 (doi: 10.3851/IMP2432)

Commentary

How important is HIV therapy for preventing liver fibrosis progression in HIV–HCV-coinfected individuals?

Jürgen Kurt Rockstroh[1]*

- "In view of the rapidly evolving HCV treatment armamentarium, and the potential for much better tolerated and more easily taken HCV therapies in the near future, the prevention of fibrosis progression through HIV therapy gains even more importance as it potentially **allows patients to wait for the development of more successful interferon-free HCV treatment strategies."**

IMMEDIATE OR DELAYED TREATMENT INITIATION WITH "PREVIR" CONTAINING REGIMENS IN HCV-INFECTED NAIVE GENOTYPE 1 (G1) PATIENTS WITHOUT SEVERE FIBROSIS? A COST-EFFECTIVENESS ANALYSIS (ANRS N°12188)

Sylvie Deuffic-Burban[1,2], Michaël Schwarzinger[2], Vincent Mallet[3,4], Stanislas Pol[3,4], Georges-Philippe Pageaux[5], Valérie Canva-Delcambre[6], Pierre Deltenre[6,7], Françoise Roudot-Thoraval[8], Dominique Larrey[5], Daniel Dhumeaux[9], Philippe Mathurin[1,6], Yazdan Yazdanpanah[2,10]

Stratégies

- Bithérapie = Référence
- Trithérapie RGT pour tous
- Trithérapie RGT si F≥2
- Trithérapie RGT
  - Si F ≥ 2 aujourd'hui
  - Pour tous dans 3 ans avec nouvelles thérapies plus efficaces
- Trithérapie RGT si F ≥ 3
- Trithérapie RGT
  - Si F ≥ 3 aujourd'hui
  - Pour tous dans 3 ans avec nouvelles thérapies plus efficaces

Deuffic-Burban S et al. Soumis

Strategies	Cost* (€)	QALY* (years)	ICER (€/QALY)
F0 at diagnosis, mean age=47:			
Treat when ≥F2 (previr<2015; new DAAs≥2015)	35600	19.9	
Treat when ≥F3 (previr<2015; new DAAs≥2015)	38300	19.4	Dominated†
<2015 treat when ≥F3 (previr), ≥2015 treat regardless to fibrosis stage (new DAAs)	***39600***	***20.1***	20000‡
<2015 treat when ≥F2 (previr), ≥2015 treat regardless to fibrosis stage (new DAAs)	39700	20.1	Dominated†
Treat immediately	***48000***	***19.8***	Dominated†
F1 at diagnosis, mean age=51:			
Treat when ≥F2 (previr<2015; new DAAs≥2015)	39800	18.6	
<2015 treat when ≥F3 (previr), ≥2015 treat regardless to fibrosis stage (new DAAs)	***40600***	***18.8***	***4000‡***
<2015 treat when ≥F2 (previr), ≥2015 treat regardless to fibrosis stage (new DAAs)	41800	18.7	Dominated†
Treat when ≥F3 (previr<2015; new DAAs≥2015)	42000	18.1	Dominated†
Treat immediately	***48800***	***18.4***	Dominated†
F2 at diagnosis, mean age=54:			
<2015 treat when ≥F3 (previr), ≥2015 treat regardless to fibrosis stage (new DAAs)	***46300***	***16.9***	
Treat when ≥F3 (previr<2015; new DAAs≥2015)	50400	16.3	Dominated†
Treat immediately	***50500***	***16.8***	***Dominated†***

SVR was considered to be 90% with new DAAs vs. 80% for “previr” containing regimens in F0/F1/F2 patients, with a 20%-reduction in F3/F4 patients.

Une modélisation mathématique

Deuffic-Burban S et al. Soumis

Conclusion (1)

Chez les patients asymptomatiques ayant un nombre de lymphocytes CD4 supérieur à 500/mm3, les données sont insuffisantes pour recommander l'instauration systématique d'un traitement antirétroviral (C). Il est toutefois possible de l'envisager dans les circonstances suivantes (BII) :

- Charge virale plasmatique > 100 000 copies/mL
- Baisse rapide des lymphocytes CD4
- **Co-infection par le VHC ou par le VHB**
- Age > 50 ans
- Facteurs de risque cardio-vasculaires
- Objectif de réduction de la transmission sexuelle du VIH

Rapport 2010
sous la direction
du Pr Patrick Yeni

Conclusion (2)

- Chez les patients VIH/VHC avec des fibroses F0, F1 attendre les nouveaux Trts
- Poids des comorbidités à prendre en compte
  - Alcool
  - Nadir CD4

Journal of Viral Hepatitis, 2010, **17**, 400–409 doi:10.1111/j.1365-2893.2

HIV–HCV co-infected patients with low CD4+ cell nadirs risk for faster fibrosis progression and portal hypertensic

T. Reiberger,[1] A. Ferlitsch,[1] W. Sieghart,[1] A. Kreil,[2] F. Breitenecker,[3] A. Rieger,[3] B. S A. Gangl[1] and M. Peck-Radosavljevic[1] [1]*Department of Gastroenterology & Hepatology, Medical University of V*