european hiv hepatitis co-infection

HIV/Hepatitis C in France: data from real life cohorts

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anrs France REcherche Nord & sud Sida-hiv Hépatites

The need

Burden of HIV and hepatitis C co-infection: the changing epidemiology of hepatitis C in HIV-infected patients in France

Patrice Cacoub[1,2,3,4], François Dabis[5], Dominique Costagliola[6,7], Kayigan Almeida[8,9], France Lert[8,9], Lionel Piroth[10] and Caroline Semaille[11]

Decreasing prevalence of chronic hepatitis C in French people living with HIV:

From **24%** in 2000 to **16-19%** in 2010

➔ 20,000 to 25,000 HIV-infected people with positive HCV serology currently in France

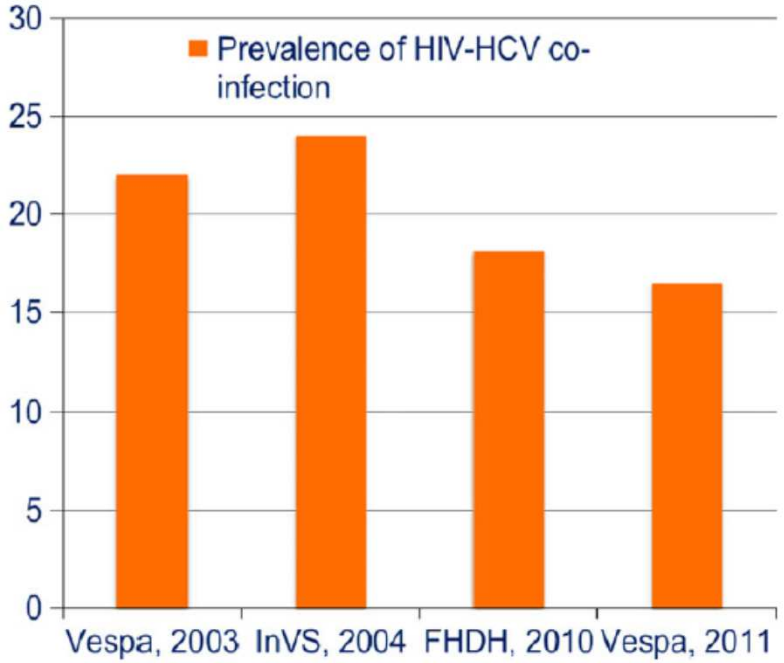
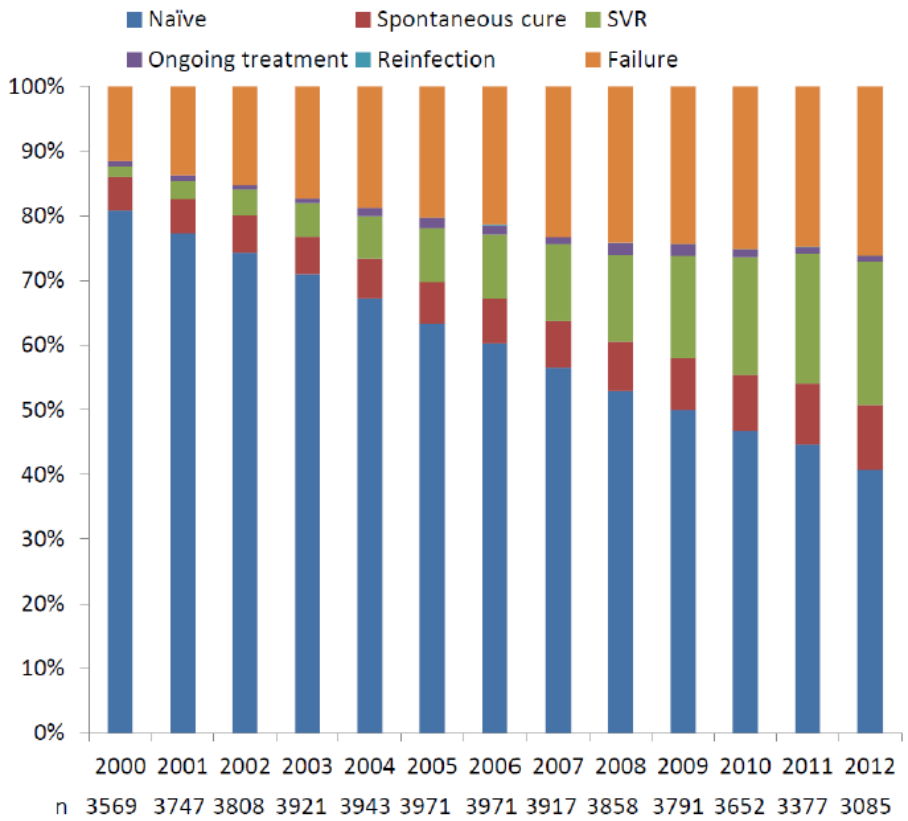


Fig 1. Prevalence of hepatitis C infection in the HIV-infected population in France, during the period 2004–2011.

Liver International (2014)

The need



Cotte L et al, AASLD 2015

The need

		Hepatitis C directly acting antivirals									
% patients		BOC	DCV	LED /SOF	OBV /PTVr	OBV /PTVr + DSV	SMV	SOF	TVR	Peg IFN	RBV
HIV nucleosides/nucleotides reverse transcriptase inhibitors											
ABC	23.0%										
ddI	0.9%										
FTC	59.3%										
LAM	27.0%										
TDF	64.0%										
ZDV	4.8%										
HIV non nucleosides/nucleotides reverse transcriptase inhibitors											
EFV	10.3%										
ETV	8.1%										
NVP	5.5%										
RPV	1.7%										
HIV entry/integrase inhibitors											
DLG	0.2%										
EVGc	0.0%										
MRV	3.3%										
RAL	26.9%										
HIV protease inhibitors											
ATV/ ATVr	20.1%										
DRVr	24.0%										
fAPV	4.7%										
IDVr	0.3%										
LPVr	9.6%										
SQVr	1.3%										
TPVr	0.2%										

Poizot-Martin I et al, Plos One 2015

The need

	Hepatitis C directly acting antivirals									
Proportion of patients	BOC	DCV	LED/SOF	OBV/PTVr	OBV/PTVr + DSV	SMV	SOF	TVR	Peg IFN	RBV
Contraindicated administration	0.0%	0.0%	0.2%	34.4%	34.4%	78.8%	0.2%	0.0%	4.8%	5.6%
Potential interaction	82.3%	49.4%	67.6%	52.2%	52.2%	0.0%	0%	98%	91.6%	92.4%
No clinically significant interaction	17.7%	50.6%	32.2%	13.4%	13.4%	21.2%	99.8%	2.0%	3.5%	2.0%

Poizot-Martin I et al, Plos One 2015

The need

CO-PRESCRIPTIONS

% of populations	All patients N = 21 430	HIV+/HCV- N = 18 491	HIV+/HCV+ N = 2 939	P*	INSTI experienced
Non Steroidal Anti-Inflammatory	10.3	10.3	10.1	0.7	29.5
Corticoids	3.7	3.6	3.9	0.4	38.9
Vitamin K antagonists	4.4	4.5	4.1	0.3	33.8
Tuberculosis treatment	2.1	2.1	2.1	0.8	38.3
Cardiovascular drugs	31.3	31.7	28.5	0.0005	30.5
Fibrates	7.5	7.7	6.1	0.001	32.9
Statins	25.9	26.8	19.9	$<10^{-3}$	31.1
Proton Pump Inhibitors	21.5	21.1	24.1	0.0003	33.8
Psychiatric treatments**	40.2	38.8	49.1	$<10^{-3}$	29.2
Erectile stimulants	3.9	4.1	3.6	0.3	30.3
Number of co-prescription/patient				$<10^{-3}$	
0	39.7	40.6	34.1		14.6
1	20.1	19.1	25.7		23.2
2	13.8	13.5	15.8		29.3
3	9.7	9.6	10.0		31.3
4	7.2	7.3	6.4		32.6
≥5	9.5	9.8	8.0		33.7

*: comparison between groups; **: including hypnotics

Cuzin L et al EACS 2015

	SIM	DCV	SOF	SOF/ LDV	3D
Atorvastatin	•	•	•	•	•
Bezafibrate	•	•	•	•	•
Ezetimibe	•	•	•	•	•
Fenofibrate	•	•	•	•	•
Fluvastatin	•	•	•	•	•
Gemfibrozil	•	•	•	•	•
Lovastatin	•	•	•	•	•
Pitavastatin	•	•	•	•	•
Pravastatin	•	•	•	•	•
Rosuvastatin	•	•	•	•	•
Simvastatin	•	•	•	•	•

	SIM	DCV	SOF	SOF/ LDV	3D
Amphetamine	•	•	•	•	•
Cannabis	•	•	•	•	•
Cocaine	•	•	•	•	•
Diamorphine	•	•	•	•	•
Diazepam	•	•	•	•	•
Gamma-hy-droxybutyrate	•	•	•	•	•
Ketamine	•	•	•	•	•
MDMA (ecstasy)	•	•	•	•	•
Methamphetamine	•	•	•	•	•
Phencyclidine (PCP)	•	•	•	•	•
Temazepam	•	•	•	•	•

EASL recommandations 2015

The means

2014

Sofosbuvir (Sovaldi®)
Polymerase nuc inh
All genotypes

Simeprevir (Olysio®)
Protease inh
GT 1, 4

Daclatasvir (Daklinza®)
Replication Complex inh
GT 1, 3, 4, 5, 6

Ribavirine
GT 1-6

2015

Ledipasvir (+SOF=Harvoni®)
Replication Complex inh
GT 1, 4, 5, 6

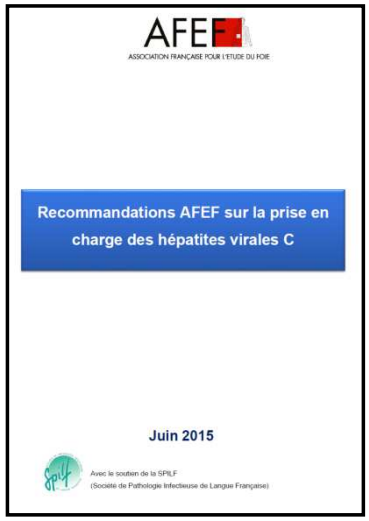
Paritaprevir (ABT-450)
Protease inh
GT 1, 4

Ombitasvir (ABT-267)
Replication compl inh
GT 1, 4, 5, 6

Dasabuvir (ABT-333)
Polymerase non nuc inh
GT 1

In 2016… ***MK 5172 (Protease Inh) + MK 8742 (Replication Complex Inh), Velpatasvir…***

The French recommendations



RECOMMANDATIONS

CHEZ LES PATIENTS COINFECTES VHC-VIH, LE TRAITEMENT DE L'HEPATITE C EST RECOMMANDE INDEPENDAMMENT DE LA FIBROSE HEPATIQUE

1. Les patients coinfectés VHC-VIH doivent être traités avec les mêmes schémas thérapeutiques (doses, durées, utilisation de la ribavirine) que les personnes mono-infectées VHC (A)

2. En 1ère intention, du fait des interactions médicamenteuses, les schémas thérapeutiques par Sofosbuvir + inhibiteur de NS5A sont à privilégier (A)

In HIV-HCV co-infected patients, HCV therapy is indicated **in all patients whatever their fibrosis stage.**

1. HIV-HCV co-infected patients have to be treated with the **same therapeutic schemes** (doses, durations) as those in HCV mono-infected patients.
2. Because of drug-drug interactions, **sofosbuvir + NS5A inhibitor combinations** have to be preferred as first intention treatments.

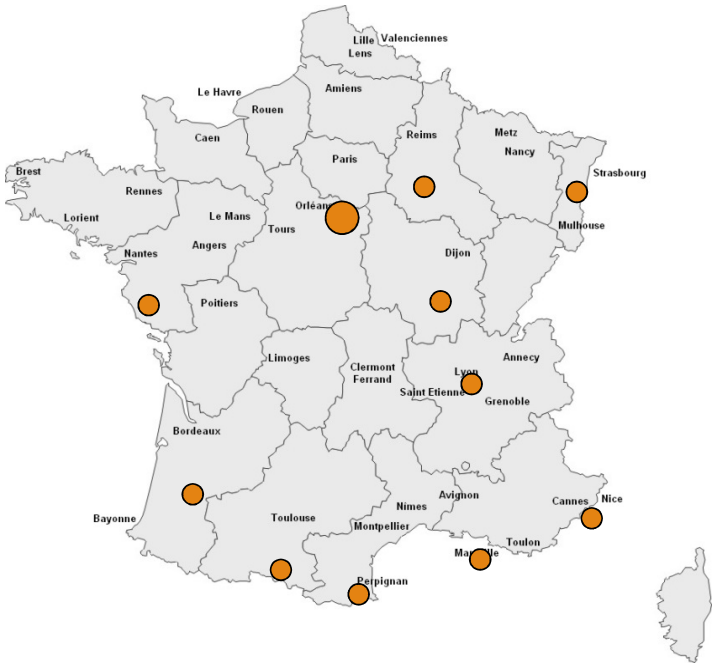
The data from real life

- **ANRS CO13 HEPAVIH Cohort** (PIs: D Salmon/F Dabis)

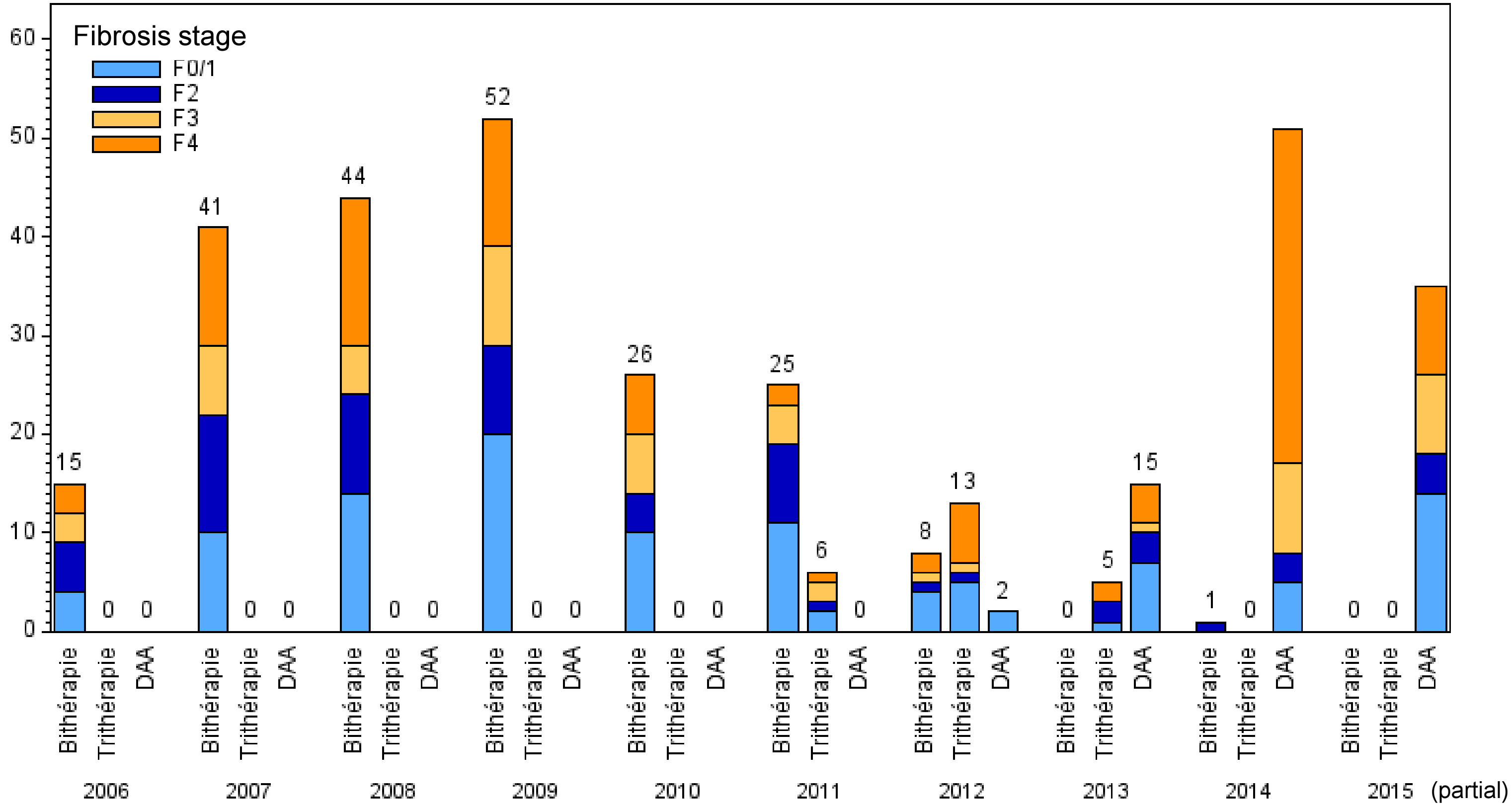
- Created in 2005 with the general objective to better define the natural history of HIV/HCV co-infection in terms of morbidity and mortality.

- National multicenter cohort study (28 clinical centres) with prospective data collection and constitution of a biobank.

- Aims: to study the response and tolerance to new anti-HCV drugs in patients co-infected with HIV/HCV managed in routine care settings.

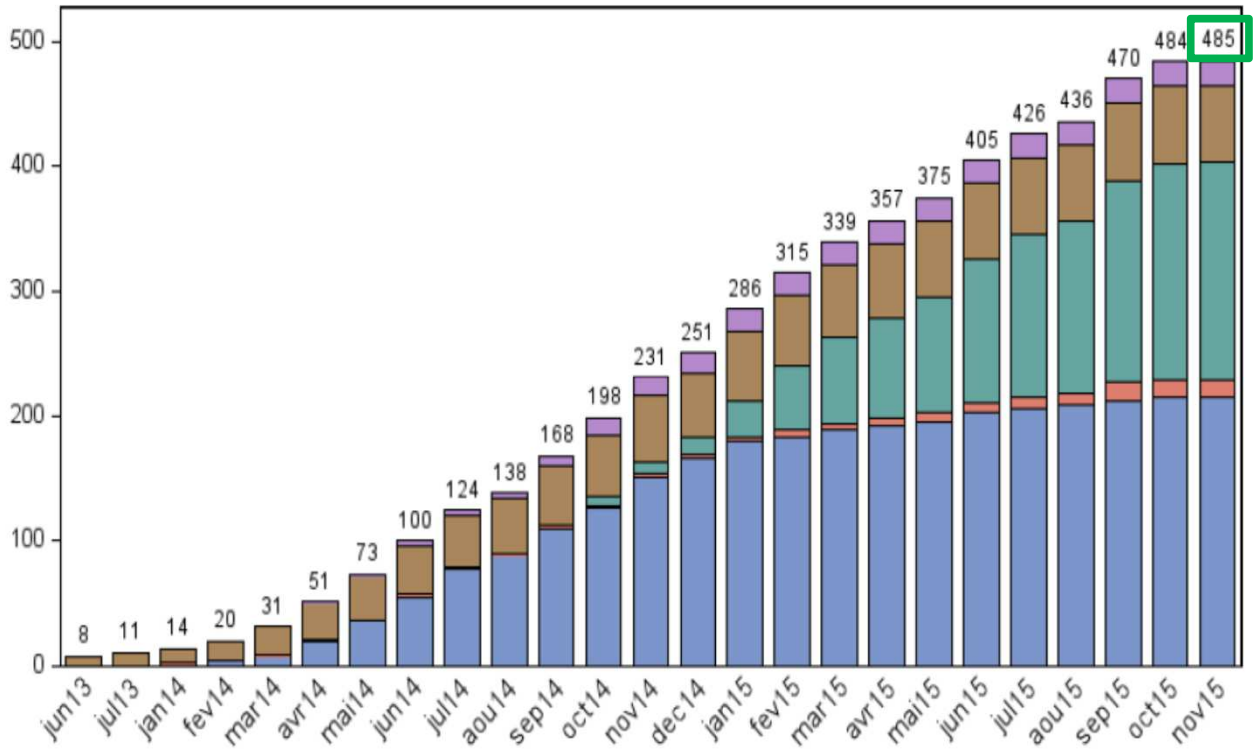


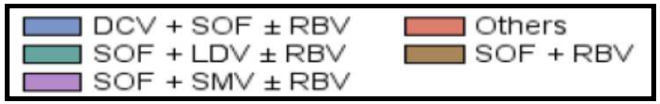
The data from real life – HEPAVIH cohort



Subgroup of patients with BL elastometry

The data from real life – HEPAVIH cohort



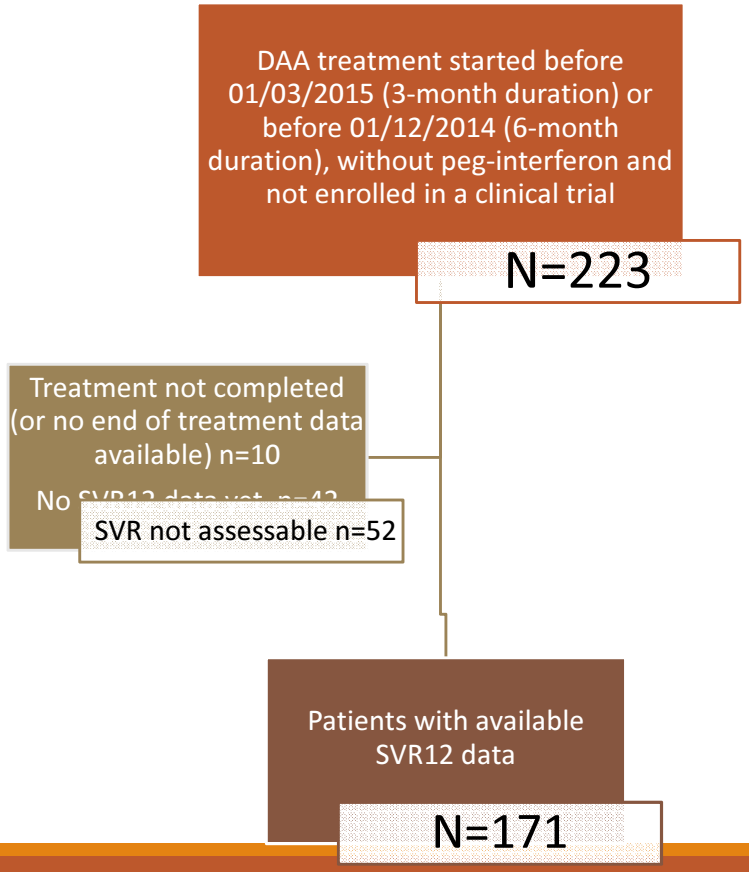


SOF+DCV +/- RBV =	44%
SOF+LDV +/- RBV =	36%
SOF+RBV =	13%
SOF+SMV +/- RBV =	4%
Others =	4%

The data from real life – HEPAVIH cohort

Response to DAA

(01/09/2015)



Salmon D et al, IAS 2015

Patients characteristics at DAA initiation

Response to DAA

Characteristic (n=171)		Statistics
Age in years, median (IQR)		53 (50-56)
Male gender, n (%)		133 (78)
Cirrhosis, n (%)		125 (73.5)
HIV RNA indetectable, n (%)		147 (86)
CD4 cells/mm^3, median (IQR)		492 (266-738)
HCV Genotype 1 - 2 - 3 - 4		106 (62.0) - 4 (2.3) - 23 (13.5) - 38 (22.2)
cART , n (%)	II-based	66 (39)
	PI-based	34 (20)
	NNRTI-based	21 (12)
DAA regimen, n (%)	SFV+DCV+/-RBV	117 (68)
	SFV+LDV+/-RBV	15 (9)
	SFV+RBV	26 (15)
	SFV+SMV+/-RBV	13 (8)

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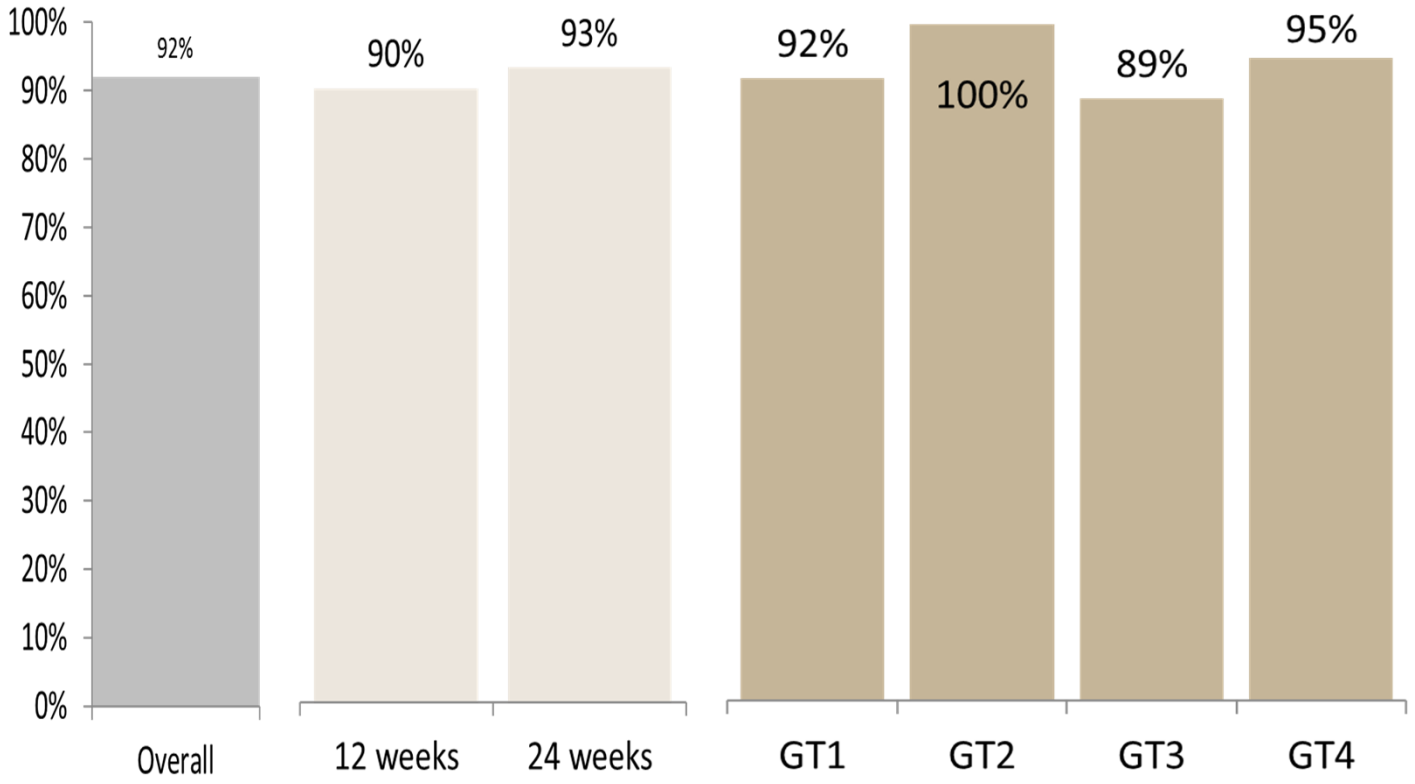
Salmon D et al, IAS 2015

The data from real life – HEPAVIH cohort

SVR12

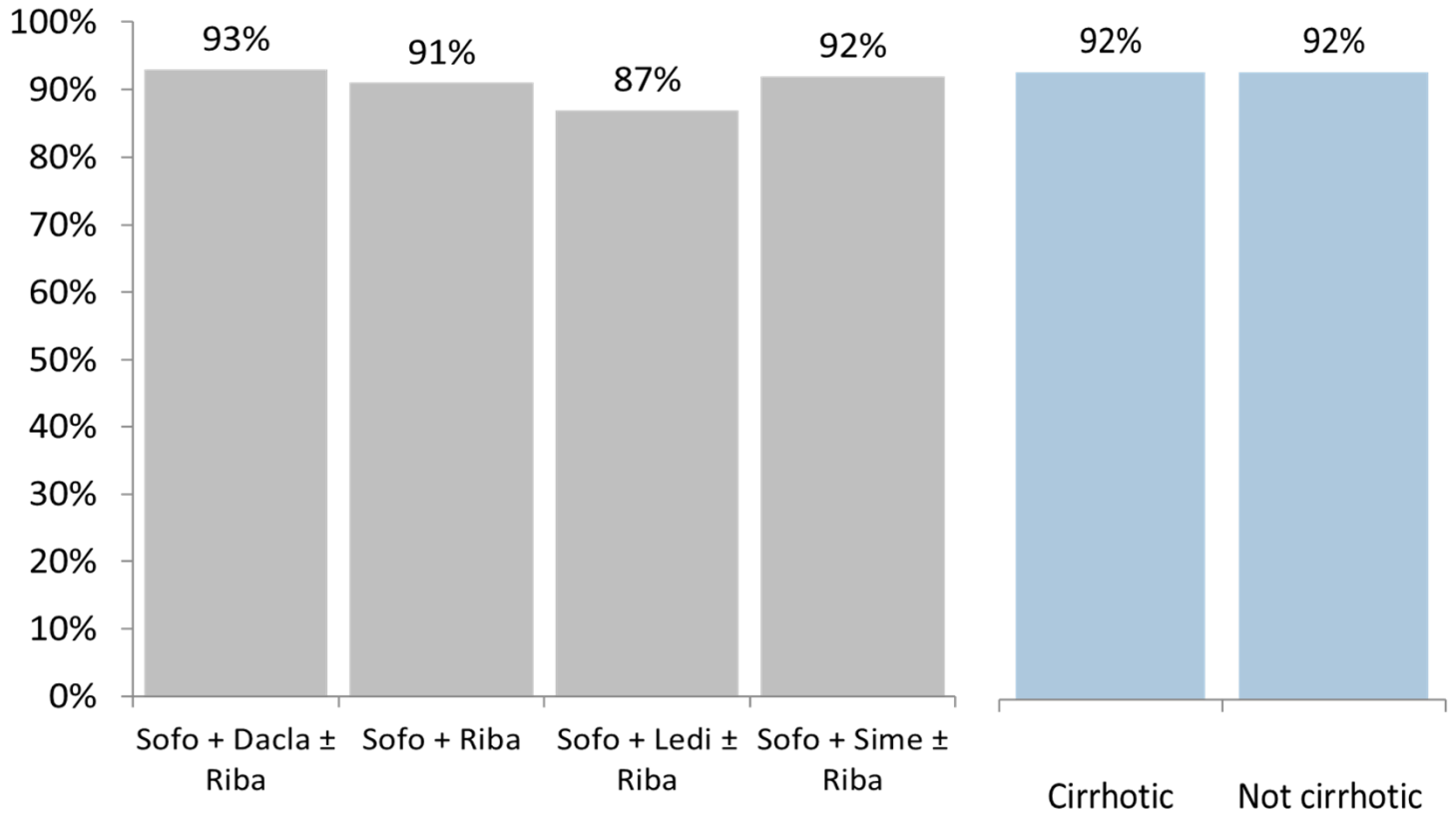
Response to DAA



The data from real life – HEPAVIH cohort

SVR12

Response to DAA



The data from real life – HEPAVIH cohort

- 14 patients (**8.2%**) experienced treatment failure:
  - 1 premature treatment interruption with detectable HCV RNA
  - 1 death before SVR12 (neg at SVR4)
  - 12 relapses (EOT HCV RNA undetectable)

	Statistics
Age years, median	55
Male gender, %	86
Cirrhosis, % Child Pugh n (%) A B Missing Data	71 7 (78%) 2(22%) 5
Genotype n (%) 1 1a 3 4	 1 (7.2) 8 (57.1) 3 (21.4) 2 (14.3)

The data from real life – HEPAVIH cohort

Treatment failures

Combinations	+ RBV	- RBV	Total
DCV+SOF (n,%)	2 (14%)	6 (43%)	8 (57%)
SOF+RBV (n,%)	3 (22%)	-	3 (22%)
SOF+LDV (n,%)	1 (7%)	1 (7%)	2 (14%)
SOF+SIM (n,%)	0	1 (7%)	1 (7%)

RBV during treatment (n,%)	6/14 (43%)
Duration of treatment (planned) 12W 24W	 6 (43%) 8 (57%)
Duration of treatment (mean+/-SD)	19+/- 8
DCV (at the beginning of the regimen) (n,%)	
30 mg	6 (75%)
60 mg	2 (25%)
Without DCV	6

Conclusions

- **Since 2015, in France, it is possible to treat all HIV-HCV co-infected patients, whatever their fibrosis stage**
- **The percentage of patients treated or on treatment is increasing**
- **The use of pegylated interferon is vanishing – the impact of ribavirin was not established**
- **Sofosbuvir plus daclatasvir was the most frequently used combination, but sofosbuvir plus ledipasvir was more often used in 2015**
- **The rate of virological failure was close to 8%**
- **No data yet on the best way to manage these patients**

Thank you for your attention