

ANRS VIRAL HEPATITIS RESEARCH

Colloque : *Vers un contrôle mondial des hépatites virales*
19 mai 2015, Institut Pasteur, Paris

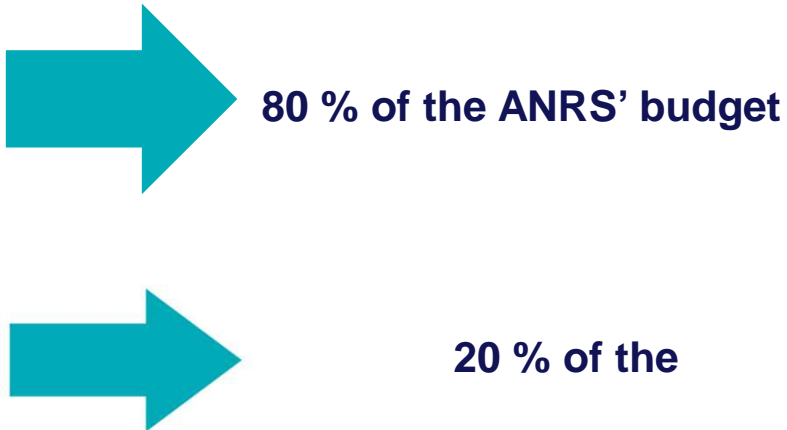
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Organisation of biomedical research in France

- ✚ Research organisations: Inserm, CNRS, Institut Pasteur, CEA, IRD, ... (infrastructure, staff)

- ✚ Project Funding for biomedical research:
 - > ANR (National Research Agency) 250 M euros
 - > PHRC (hospital programme for clinical research) 60 M euros
 - > INCa (Cancer Institute) 80 M euros
 - > ANRS 48 M Euros
 - > Private foundations (Genethon, ARC, FRM, Axa, Total...)

Focus on ANRS

- **Public Agency aimed at funding and coordinating research in all areas relevant to HIV/AIDS and viral hepatitis**
 - **Before 1st January 2012, an autonomous agency then integrated within Inserm**
 - **Annual budget of research: 48 Millions euros**
 - **Supported by :**
 - > **Ministry of Research (39M€)**
 - > **Ministry of Health**
 - > **Ministry of Foreign Affairs**
 - > **Public institutions**
 - > **Private pharmaceutical companies**
- 
- The diagram consists of two teal arrows pointing to the right. The top arrow originates from the list of government supporters (Ministry of Research, Ministry of Health, Ministry of Foreign Affairs, and Public institutions) and points to the text '80 % of the ANRS' budget'. The bottom arrow originates from the 'Private pharmaceutical companies' entry and points to the text '20 % of the ANRS' budget'.

% Distribution of funds according to research area 2014 (46,3 M €)

↘ Basic Science HIV	16 %
↘ Vaccine HIV-HCV	1.1%
↘ Clinical trials and cohorts HIV	31 %
↘ Epidemiology/socio-behavioral science	6 %
↘ Resources limited countries (HIV-Hepatitis)	18 %
↘ Hepatitis B and C	21 %
↘ GLOBAL HEPATITIS 30 % : 11 M €	
↘ GLOBAL HIV : 70 % : 17 M €	

ANRS «Scientific performance »

- **550 publications/year**
- **Approximately 50% of publications have IF > 5.**
- **1% of ANRS publications are in the 10 top international journals**
- **6.2% of ANRS publications (HIV/AIDS and hepatitis) are in the 1% group of excellence (number of citations), higher than the national average in the field of biology/health**
- **France is ranked 2nd or 3rd international position in the field of HIV and 2nd in the field of hepatitis**

ANRS Funding Mechanisms

- ✚ **> 93 % of ANRS' budget dedicated to research**
- ✚ **2 main calls for proposals/year**
- ✚ **Top-down vaccine research program**
- ✚ **Clinical Trials: committees for approval and funding**
- ✚ **ANRS: essentially only funder for HIV and viral hepatitis research in France**

Organisation of ANRS

↘ **9 offices :**

- > Clinical and therapeutic research on HIV/AIDS
- > Basic research on HIV/AIDS
- > Basic, clinical and therapeutic research on viral hepatitis
- > Research in public health and the human and social sciences
- > Clinical research safety
- > Research in resource-limited settings
- > Scientific information and communication
- > International affairs and scientific relations
- > Quality assurance
- > Financial and general affairs

LEADING : the ANRS Coordinated Action (AC) in the field of viral hepatitis



Basic Research

- ↘ AC 29: Entry and assembly mechanisms of hepatitis viruses in their target cells (**J Dubuisson**)
- ↘ AC 33: Resistance to antiretrovirals of Hepatitis B and C viruses (**JM Pawlotsky and F Zoulim**)

Clinical Research

- ↘ AC 7: Cohorts
- ↘ AC 24: Clinical trials in viral hepatitis infection (**M Bourliere**)
- ↘ AC 5/24: Clinical trials in HIV-Hepatitis co-infection (**M Bourliere and JM Molina**)

The AC common to hepatitis and to HIV field



AC 12: Resource-limited countries (F Dabis)

**AC 23: Dynamics of the HIV, HCV and HBV epidemics
(D Costagliola)**

**AC 25: Research in public health, human and social
sciences in the field of viral hepatitis (Pr JC Desenclos)**

FUNDING : Two calls each year, with peer review

Specific scientific committees (CSS) in the hepatitis field

CSS with Hepatitis area of expertise

CSS 4: Basic Research (JM Pawlotsky)

CSS 7: Clinical Research (F Zoulim)

CSS assessing both hepatitis and HIV researchs

CSS5: Research in public health and in human and social sciences
(pending appointment)

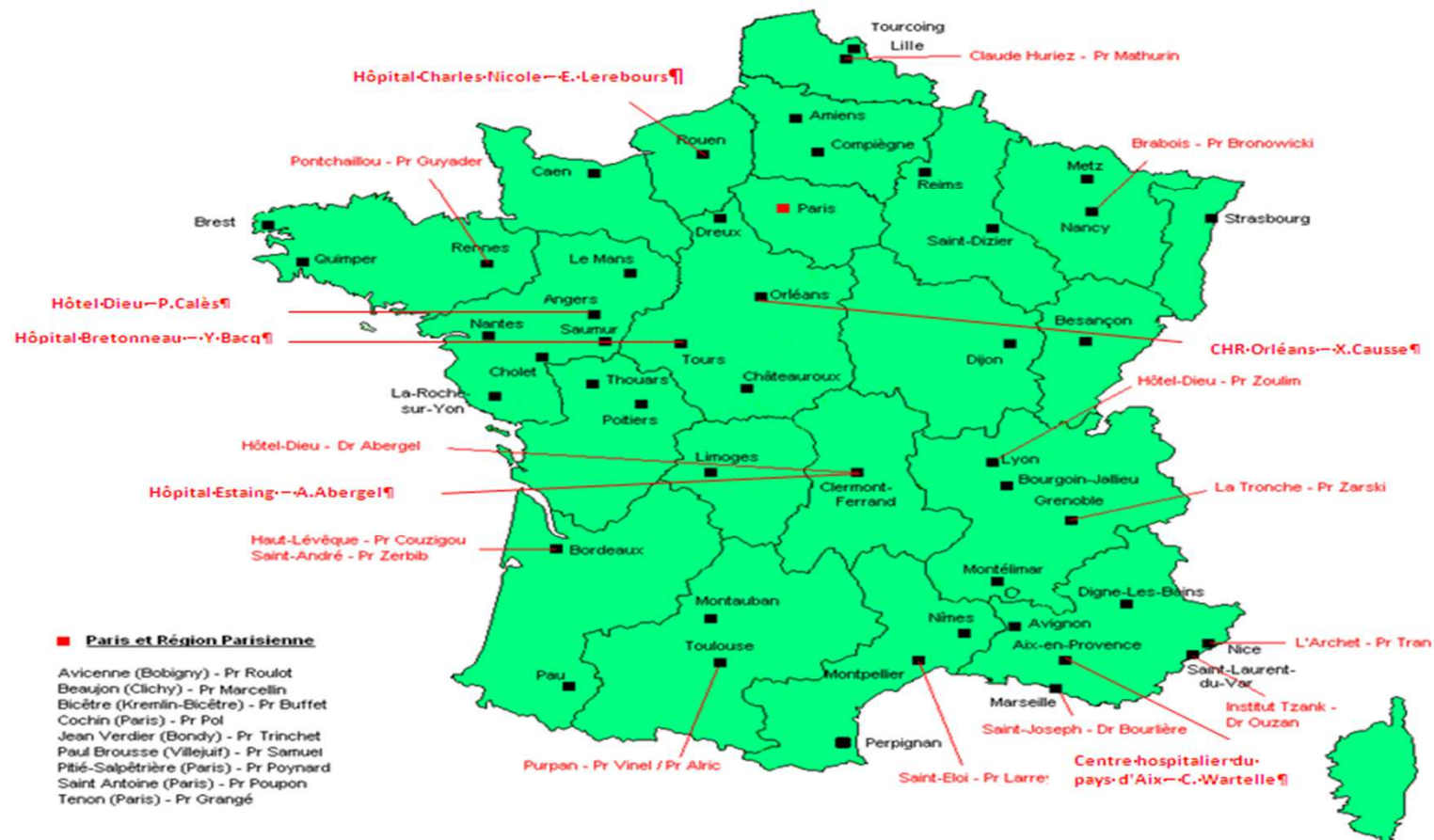
CSS6: Research in low and middle-income countries (A Calmy)

**ANRS CLINICAL RESEARCH
IN VIRAL HEPATITIS**

ANRS Staff support in hepatitis clinical sites



ANRS hepatitis network # 150 centers
 More than 65 000 patients
 28 Clinical Centers with ANRS funded staff

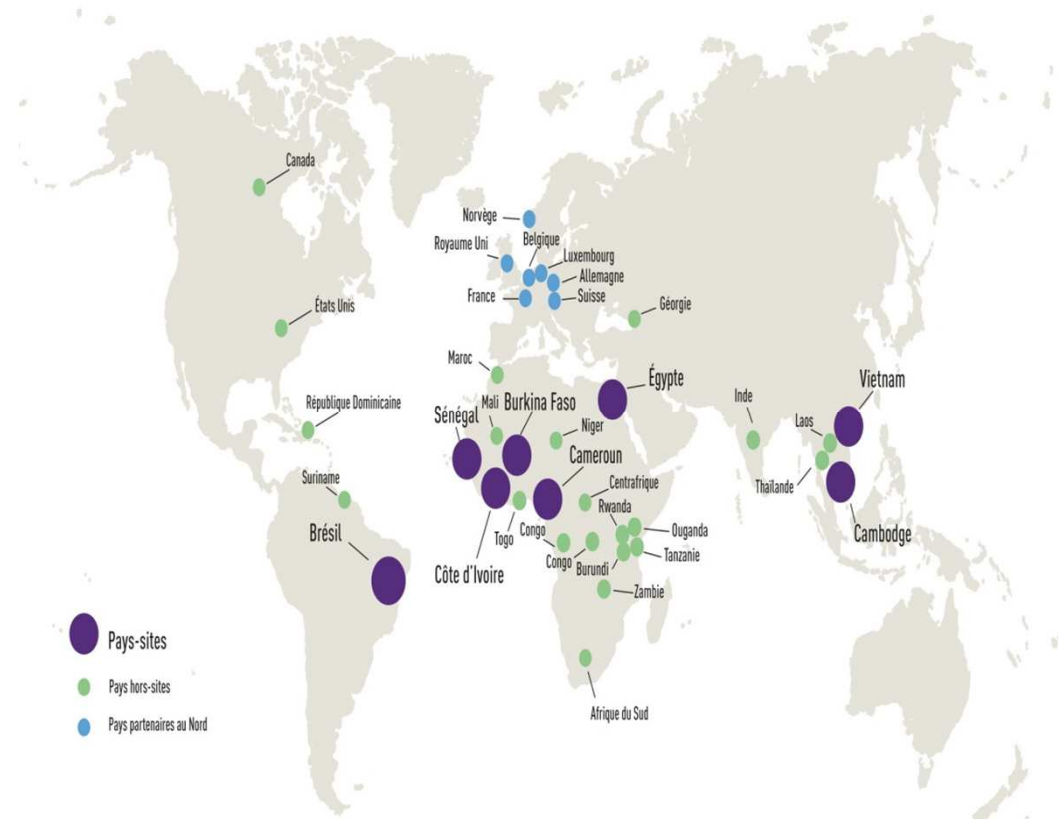


ANRS Involvement In Resource-Limited Countries

- 20% of the total budget (12M€, salaries not included)
- About 30 new projects per year (2 calls for proposals / year)
Fellowships, Contrat initiation, projects
- Research Fields
 - Clinical Research Social sciences Prevention
 - Epidemiology Basic Science
- Networking
 - Supporting and organizing working groups meeting
 - Organization of seminars
- Evaluation-call for proposals
 - Scientific Specific Committee (CSS6)
 - Multidisciplinary, community representatives

Partnerships : 8 research sites

- **Brazil**
Hep/HIV – Viro-Immuno/Economic
- **Burkina Faso**
Hep/HIV – Viro/PMTCT/ART adults
- **Cambodia**
Hep/HIV±TB – Adults&ped treat.
- **Cameroun**
Hep/HIV – Viro/Adults&ped treat.
- **Côte d'Ivoire**
HIV – Viro/Adults&ped treat
- **Egypte**
Hep C – Viro/Adults treat.
- **Sénégal**
HIV – Viro/Adults ped treat/IDU
- **Vietnam**
Hep C/HIV – Viro/Adults treat/IDU

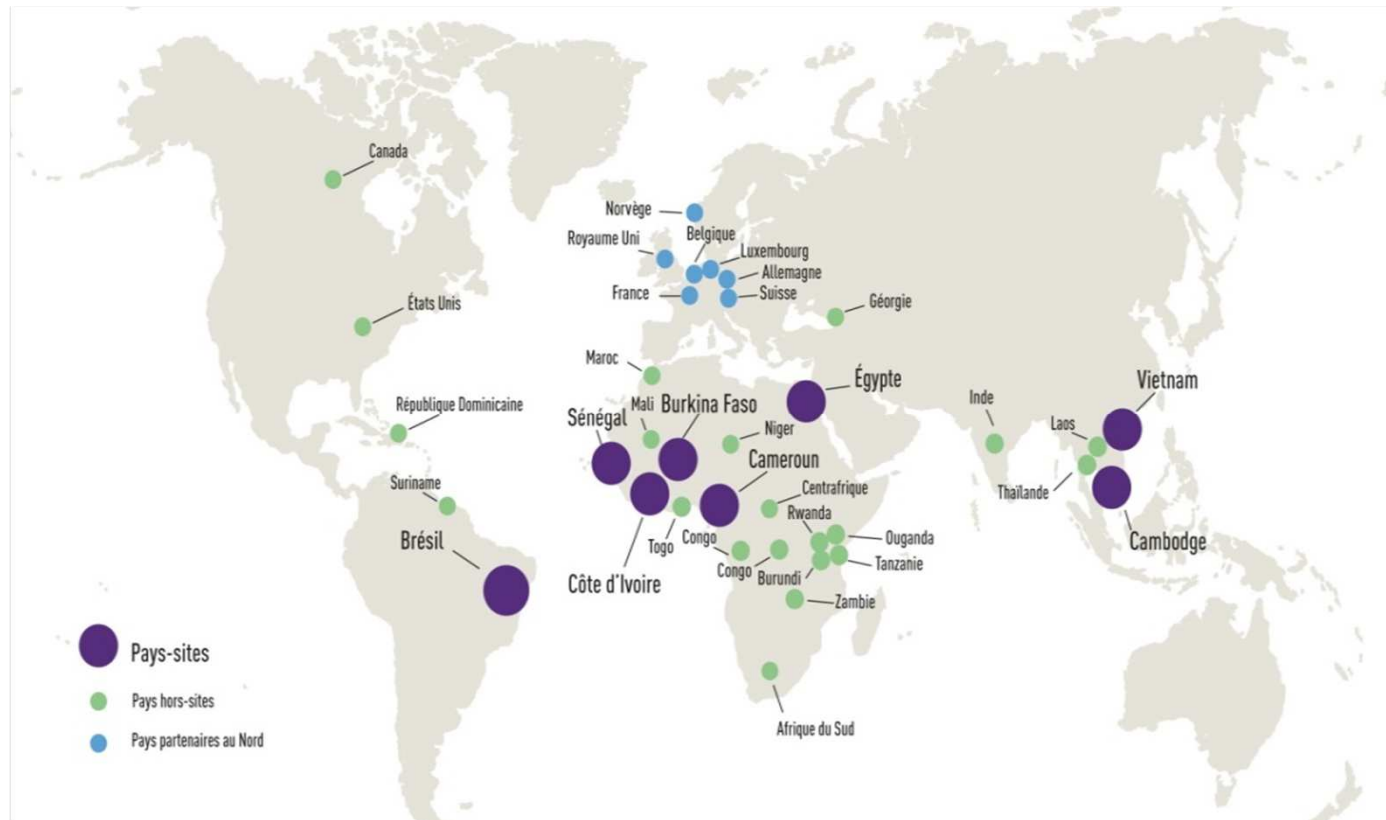


➤ 24 countries

- 17 Sub-saharian Africa
- 5 Asia
- 2 South America

➤ 100 ongoing projects

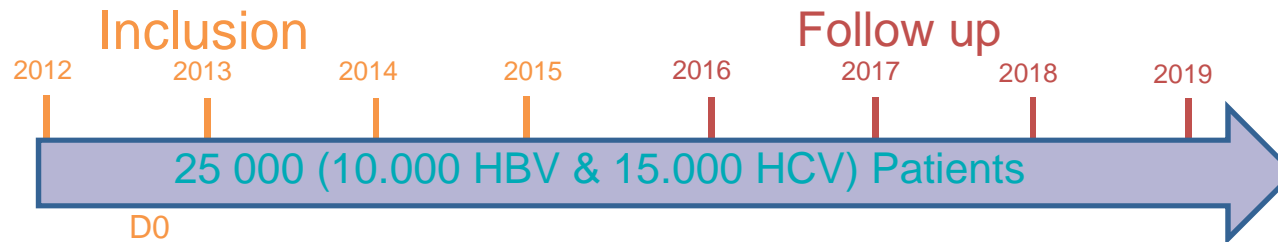
- 80% in 8 countries
- ANRS Research Sites



ANRS' global research priorities

- **New tools for prevention / key populations**
- **HBV Cure**
- **Strategic evaluation of new molecules anti HCV**
- **Study reservoirs with the objective of eradication or functional cure**
- **Test and treat / treatment as prevention**
- **Develop new vaccine strategies**

Cohort ANRS CO22 HEPATHER



Clinical follow-up by interval:

1 to 2 yearly visits according to the status

« A la carte » clinical follow-up :

Treatment initiation

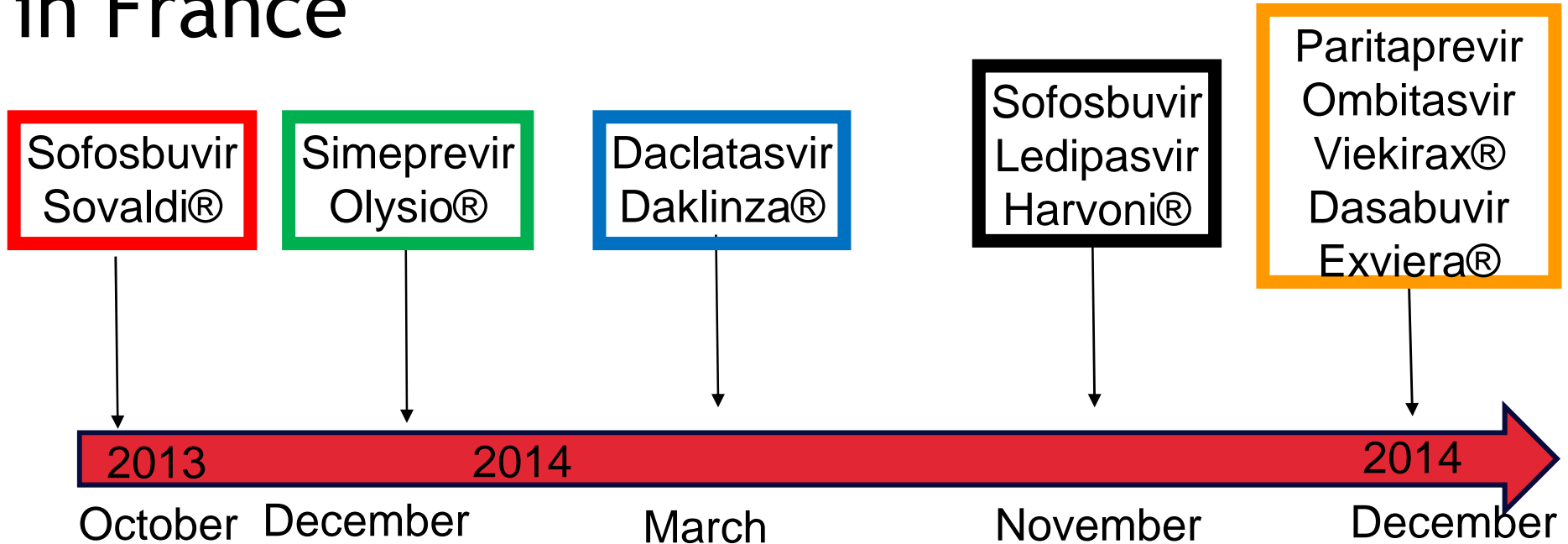
Clinical event

Follow-up by individual matching on medico-administrative database:

SNIIRAM

CEPI-DC

Flow of ATU (early access program) in France



**Restricted to
« priority » patients**

- ❑ F3F4
- ❑ Symptomatic cryoglobulinemic vasculitis
- ❑ Waiting for liver or renal transplantation
- ❑ After liver transplantation

Cohort ANRS CO22 HEPATHER

SVR results in Genotype 1-infected patients

	SOF/DCV		SOF/DCV/RBV	
	(n= 317)		(n = 92)	
	<u>12 w.</u>	<u>24 w.</u>	<u>12 w.</u>	<u>24 w.</u>
% SVR4	85.2	95.1	100.0	98.8
% SVR12	84.9	93.4	100.0	98.4
% SVR4 cirrhotic	76.5	94.0	100.0	98.3
% SVR4 non cirrhotic	100.0	100.0	100.0	100.0
% SVR4 naïve	87.1	88.7	100.0	100.0
% SVR4 experienced	82.6	96.7	100.0	98.5

SOF+DCV or SIM+/-RBV in Genotype 4

	SOF/DCV (n = 33)		SOF/DCV/RBV (n = 15)		SOF/SIM (n = 27)		SOF/SIM /RBV (n = 7)	
	12 w.	24 w.	12 w.	24 w.	12 w.	24 w.	12 w.	24 w.
Tx duration (weeks)	12 w.	24 w.	12 w.	24 w.	12 w.	24 w.	12 w.	24 w.
% SVR4	88.9	95.2	100.0	100.0	78.3	100.0	100.0	100.0
% SVR12	100.0	90.9	100.0	100.0	88.9	100.0	100.0	100.0
% SVR4 cirrhotic	85.7	93.3	100.0	100.0	69.2	100.0	100.0	100.0
%SVR4 non-cirrhotic	100.0	100.0	-	100.0	100.0	-	-	-
%SVR4 naïve	100.0	100.0	-	100.0	66.7	100.0	100.0	-
%SVR4 experienced	87.5	94.4	100.0	100.0	84.6	100.0	100.0	100.0

Conclusion: The 12 week combination of sofosbuvir-daclatasvir or sofosbuvir-simeprevir is associated with a high rate of SVR4 in genotype 4-infected patients. The addition of ribavirin increases the SVR rate in cirrhotic or experienced patients at 12 weeks without additive effect of the treatment extension to 24 weeks

REAL WORLD DATA ALL-ORAL DAA REGIMENS IN HIV–HCV COINFECTED CIRRHOTIC PATIENTS FROM THE PROSPECTIVE ANRS CO13 – HEPAVIH COHORT

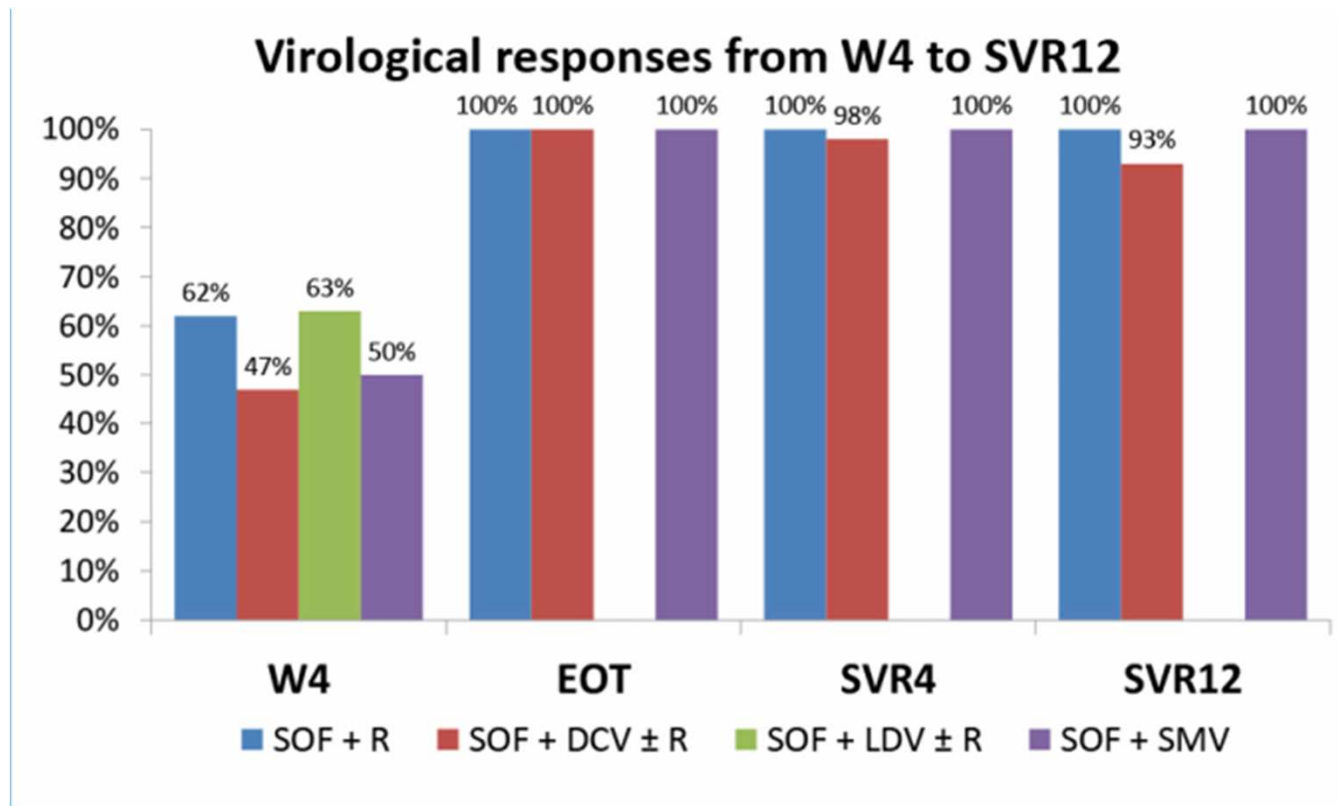
Among >1500 patients included in the ANRS HEPAVIH cohort until March 2015, 142 cirrhotic HIV-HCV coinfecting patients were analyzed

- 29% treatment naive
- 58% PR failures
- 9% First generation protease inhibitor/PR failures
- 4% failures with other treatment

Patients included:	N=142
Median age (years), med [IQR]	51 [51-56]
Male sex, n (%)	112 (79)
Genotype, n (%)	
1a	53 (37)
1b	18 (13)
1 others	11 (8)
2	4 (3)
3	29 (20)
4	27 (19)
CDC stage, n (%)	
A	43 (31)
B	50 (37)
C	44 (32)
Child Pugh, n (%)	
A	101 (89)
B	9 (8)
C	3 (3)
HIV RNA <50 copies/mL, n (%)	122 (87)
Median CD4 (/mm ³), med [IQR]	529 (336-691)

139 were on continuous antiretroviral treatment (cART)

REAL WORLD DATA ALL-ORAL DAA REGIMENS IN HIV–HCV COINFECTED CIRRHOTIC PATIENTS FROM THE PROSPECTIVE ANRS CO13 – HEPAVIH COHORT



Treatments were prematurely stopped in 3 patients: 1 for intolerance and 2 for other causes

Treatments were dose-adjusted in 13 patients (adjustment of daclatasvir dose in 8 and ribavirin dose in 5)