Case study:
Therapeutic options in cirrhotic HIV/HCV patients

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Case study (1)

- Lisa, 50, lives in Paris
- Short period of IVDU when she was 18-20
- Long period of HIV/HCV seropositivity
- Suffers of a mild psychotic disorder

HIV parameters	Value
CD4 cell count	540 cell/mm3
HIV RNA	< 40 cop/mL

HIV treatment
Abacavir/lamivudine
Efavirenz

Case study (2)

- HCV disease
  - Cirrhosis, proven on a liver biopsy in 2004, never decompensated
  - Failure of a previous pegIFN/RBV treatment

Parameter	Value
HCV RNA	850.000 UI/mL
HCV genotype	1a
HBS Ag	Negatif
HBC Ab	+
Elastometry	21 Kpa

Hepatic tests	Value
AST	70 UI/L
ALT	89 UI/L
Platelets	145.000/mm3
Albumin	33 g/l
PT	85%

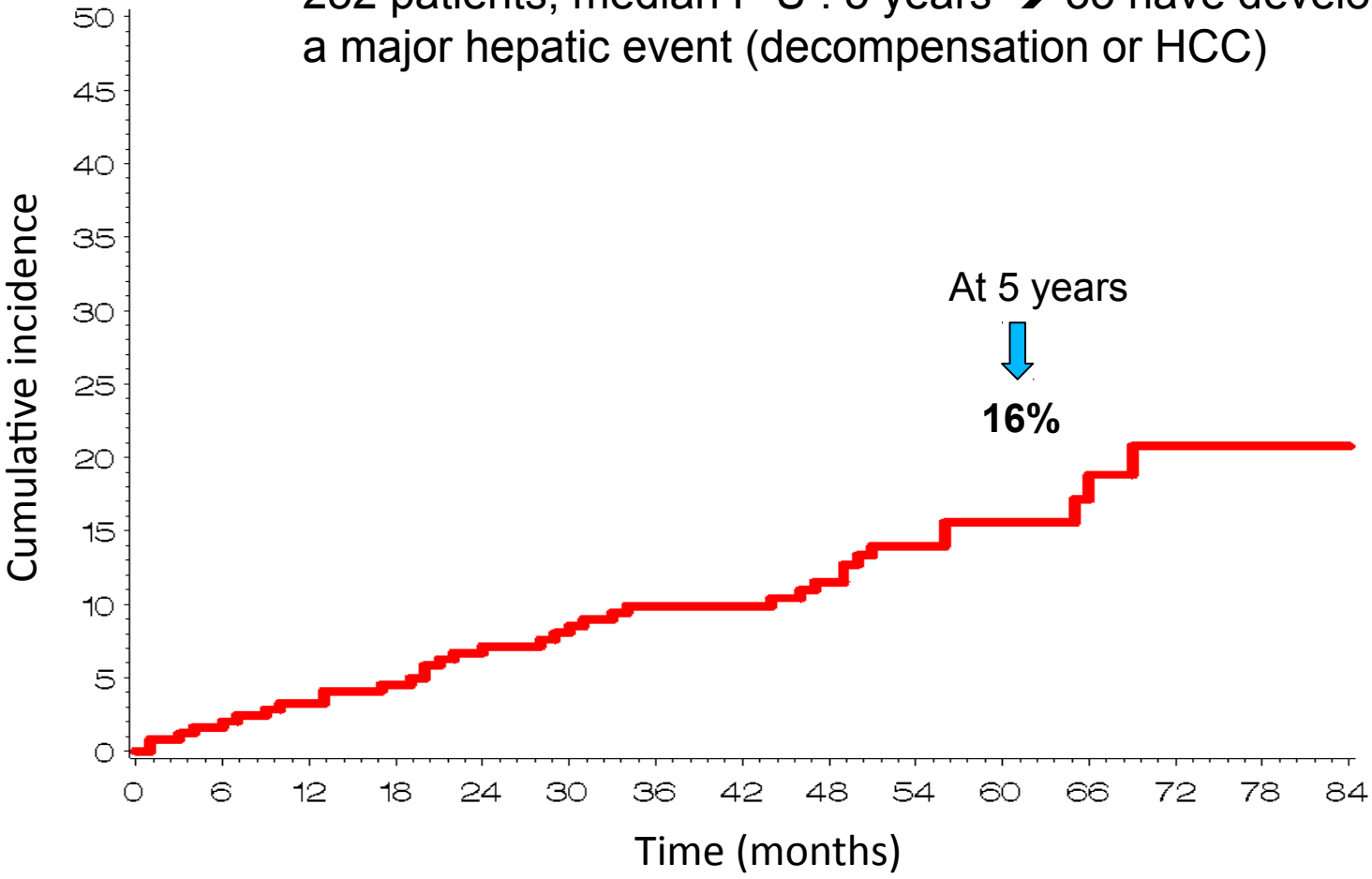
?

What is the risk of decompensation at 5 years in this patient ?

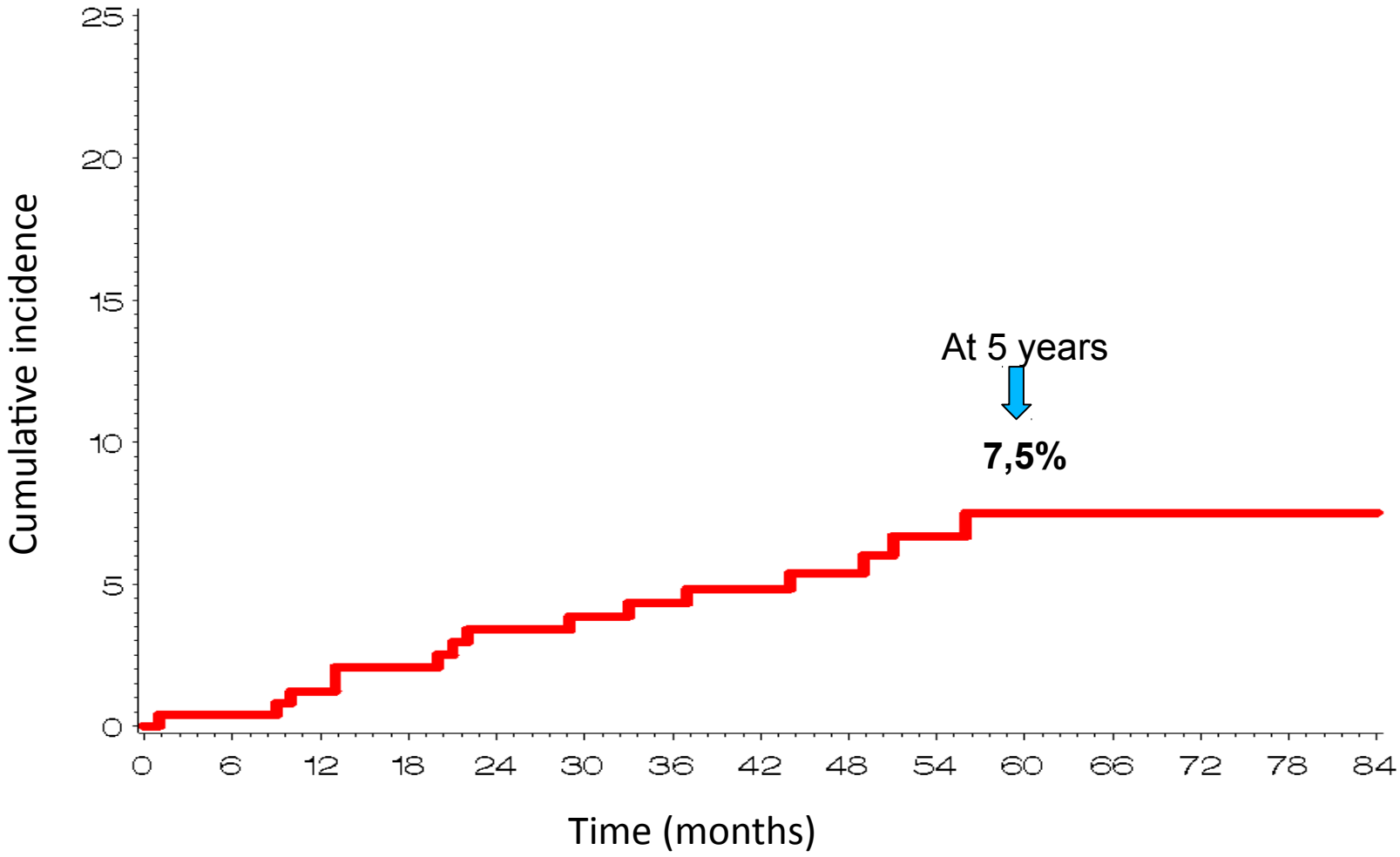
- . <5 %
- . 6–10 %
- . 11–15 %
- . 16–20 %
- . >20 %

Cumulative incidence of 1st hepatic event in cirrhotic patients - Hepavih ANRS CO13

252 patients, median F-U : 5 years ➔ 35 have developed a major hepatic event (decompensation or HCC)



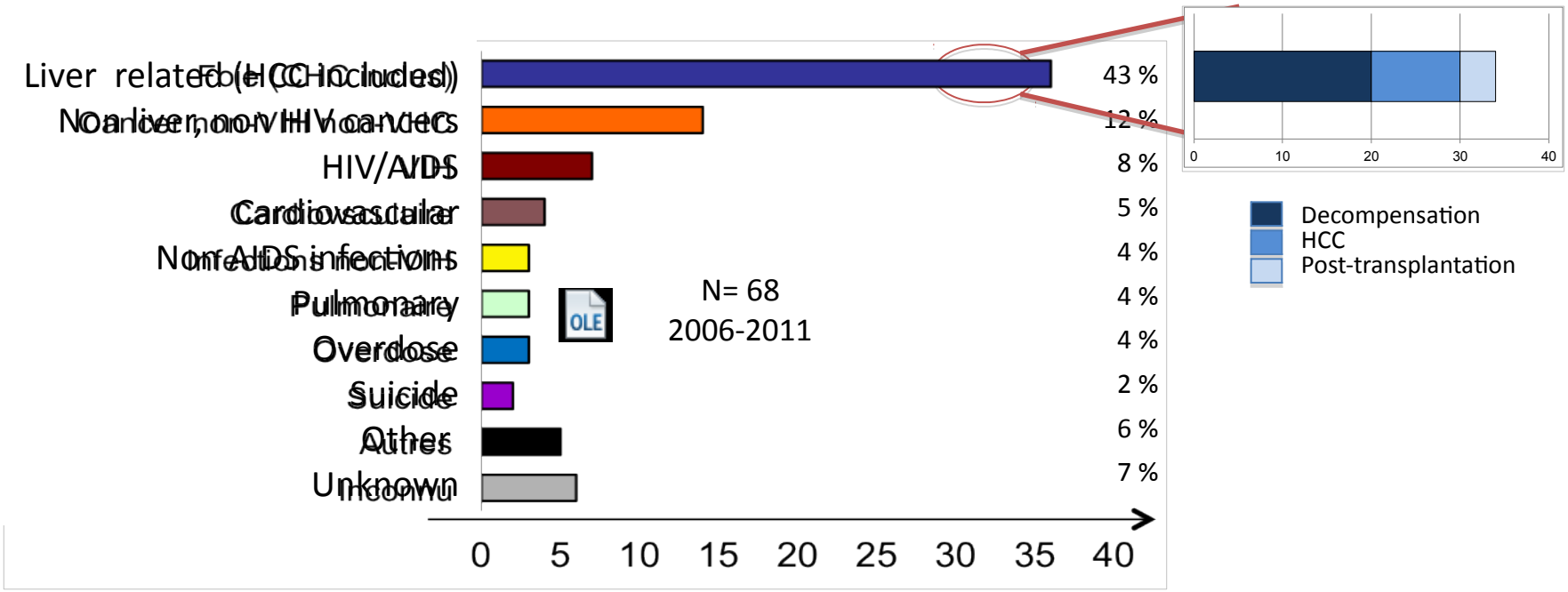
Cumulative incidence of HCC in cirrhotic patients Hepavih ANRS CO13



Liver related mortality remains the 1st cause of death

- HIV population : 3rd cause of death
- HIV/HCV population : 1st cause

Causes of death in HIV/HCV patients in France



Cirrhotic s : > 50% deaths HCV related
Non cirrhotics : 60% deaths non related to HCV or HIV

Etude Mortavic 2010 / Cohorte HepaVIH 2012

?

Does the effect of SVR impact on:

1- The incidence of hepatic events?

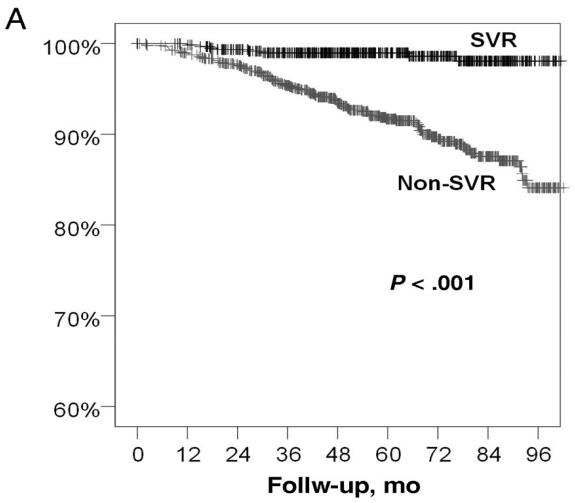
2- The incidence of non hepatic events?

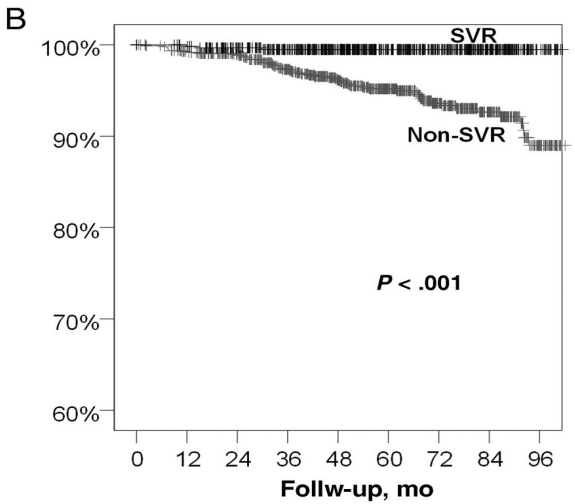
3- The fibrosis course?

Effect of SVR on the occurrence of hepatic events

- 1599 patients treated with Peg/RBV, followed for 5 years. SVR in 39%

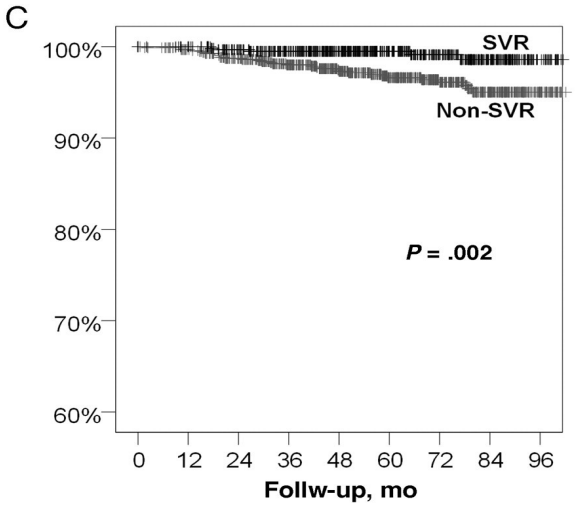
Overall deaths

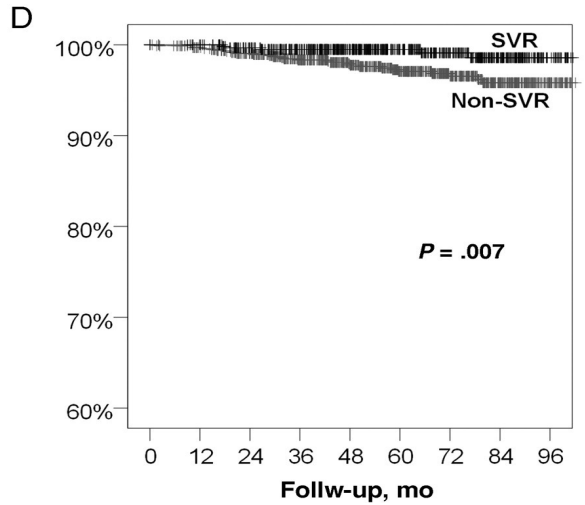




Liver-related deaths

Non liver-related deaths



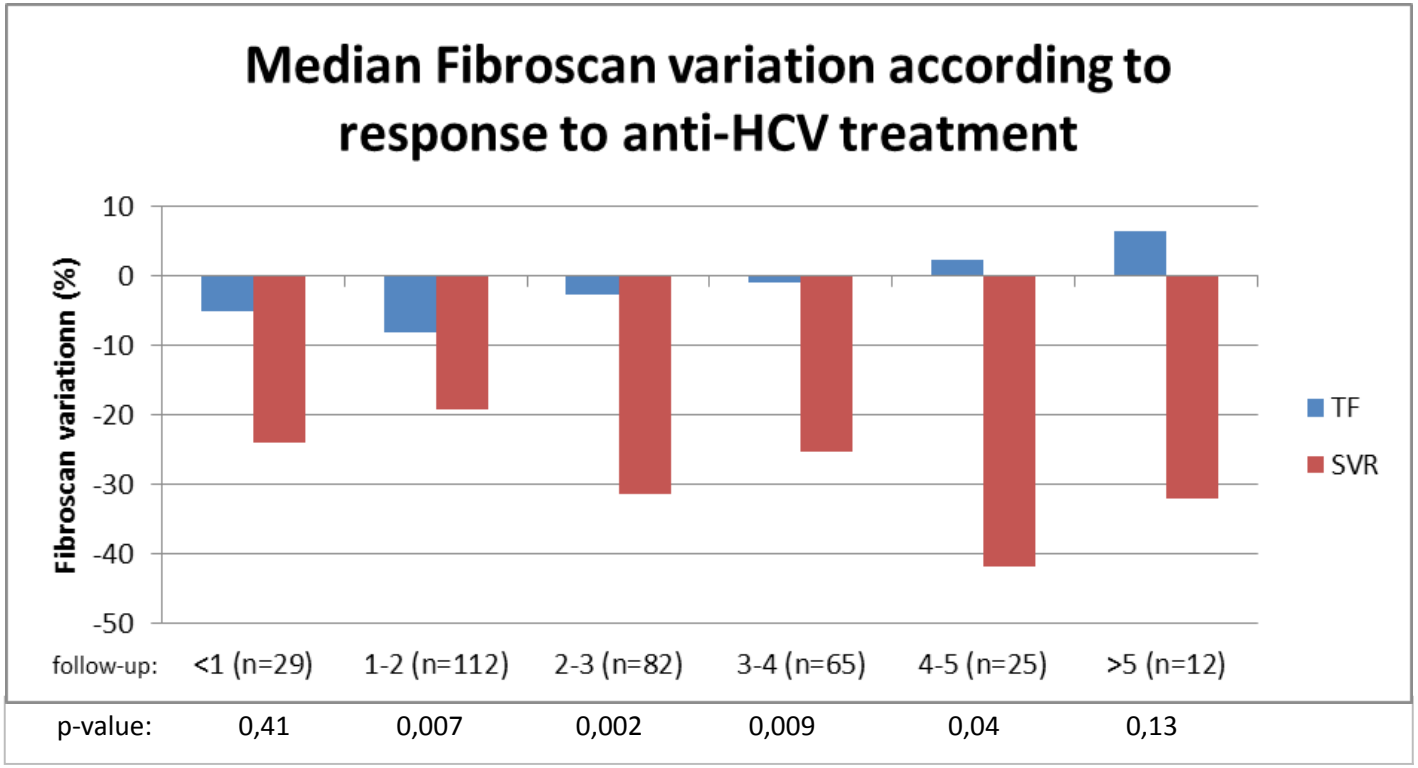


Non HIV, non liver-related deaths

Berenguer J, CID, 2012;55

Regression of elasticity values in patients with SVR in Hepavih Cohort

160 patients , at least 1 fibroscan before and 1 after the end of anti HCV therapy



Only SVR was associated in a Cox model with fibrosis regresison (adjusted RR: 2.79)

Salmon et al.. JNI 2013, Croi 2014

Case study (3)

In June 2012, Lisa was ready to begin a new treatment

?

What do you decide ?

Case study (4)

Lisa began a triple therapy with:

- Telaprevir 3 caps BID
- Peg-IFN alfa-2a 180 mg weekly
- RBV 1000 mg QD

At W4:

-HCV RNA decreased from 850.000 UI/mL to 1540 UI/mL

-Hb from 14 to 9.9 g/dl

Case study (5)

At W4:

-HCV RNA decreased from 850.000 UI/mL to 1540 UI/mL

-Hb from 14 to 9.9 g/dl

?

What do you decide ?

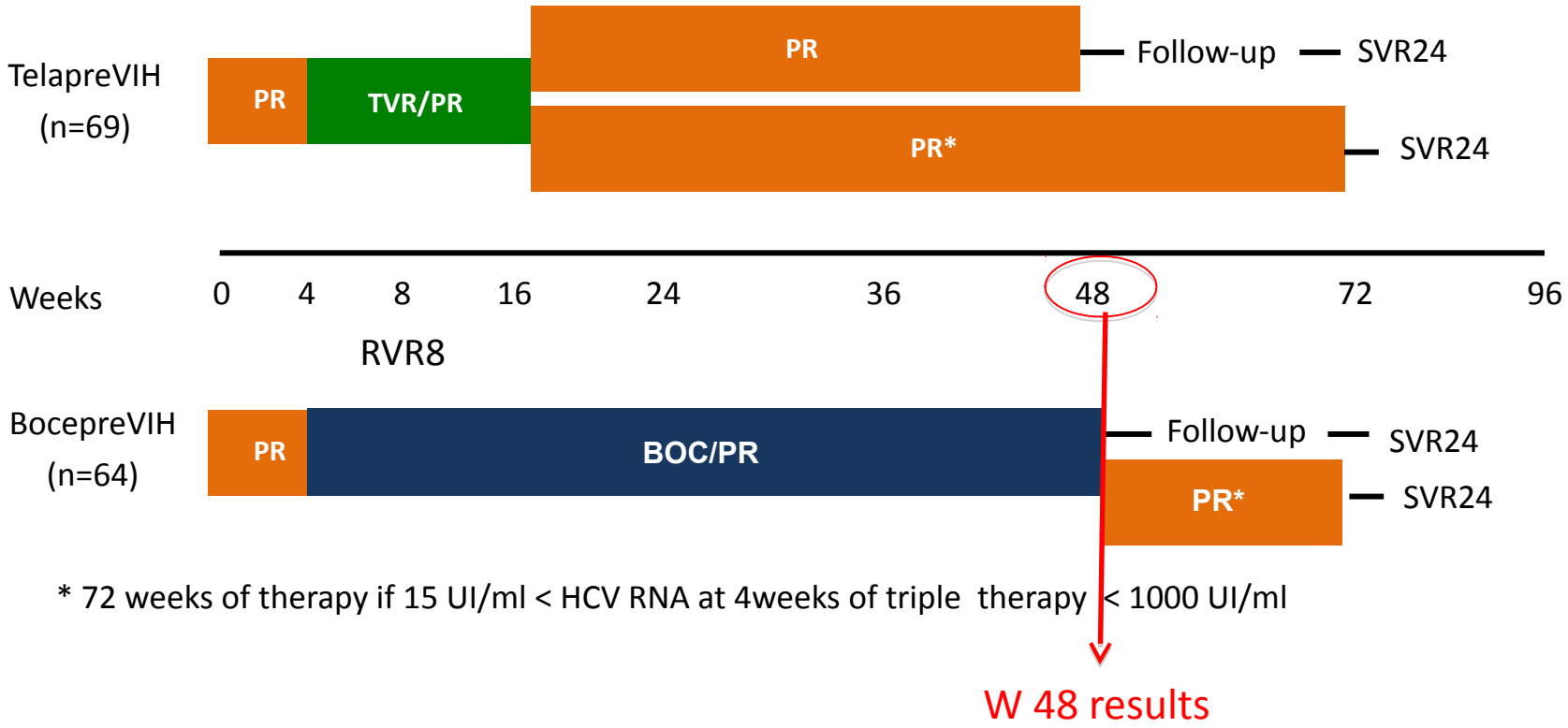
- Stop all the treatments
- Decrease telaprevir dosage
- Decrease ribavirin dosage
- Introduce EPO

Approved therapeutic options with 1st generation PI in G1, pretreated HIV/HCV coinfected patients

- Bocéprévir+ PR
- Télaprévir +PR

Patients with failure of HCV therapy: TélapreVIH and BocépreVIH ANRS trials

- Patients with failure of PegIFN/RBV
- CD4 > 200/mm3 and HIV RNA < 50 c/ml for at least 6 mos
- No decompensated cirrhosis + nul response

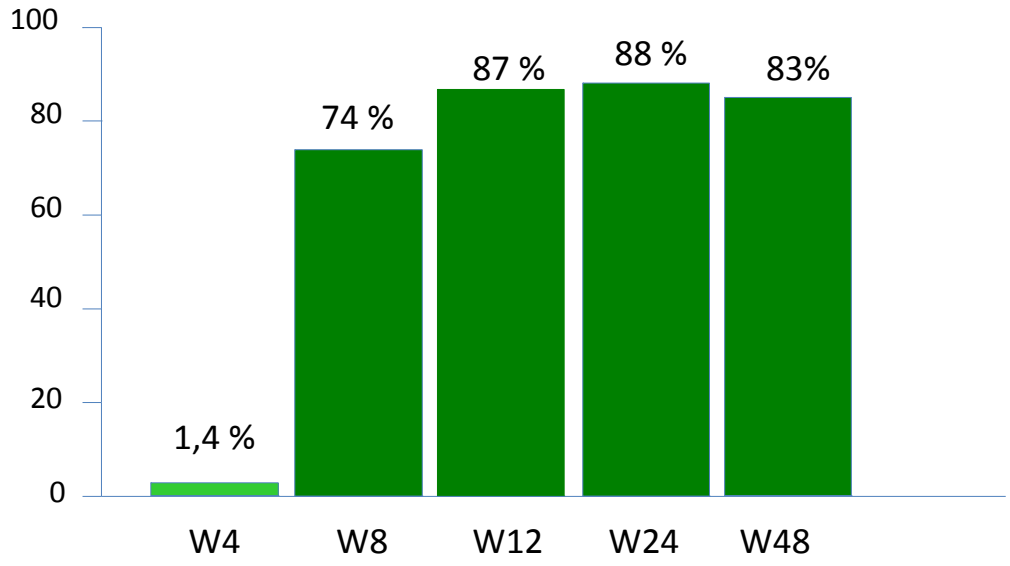


* 72 weeks of therapy if 15 UI/ml < HCV RNA at 4weeks of triple therapy < 1000 UI/ml

Cotte et al; Poizot-Martin et al. CROI 2013, Journées Foie et VIH, Nov 2013

Patients with failure of HCV therapy : TélapreVIH ANRS trial

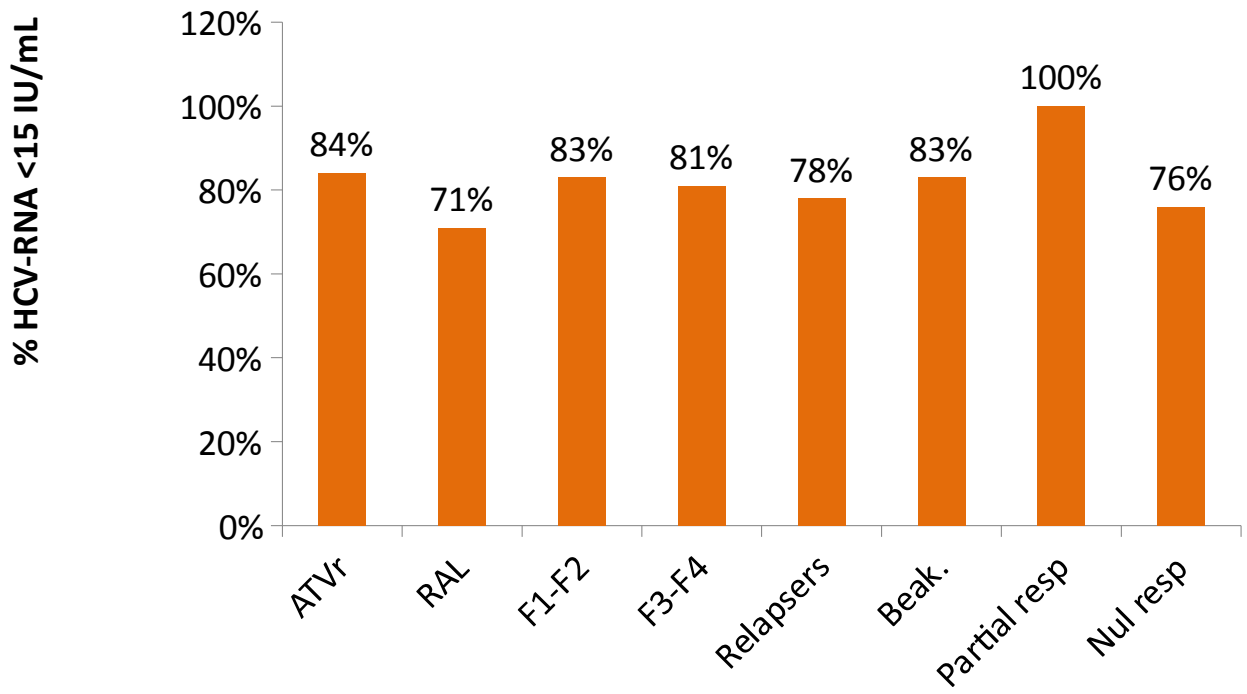
N=69 patients
70% genotype 1a
39% F3-F4
30% nul responders



W48: 83%

Cotte et al. CROI 2013, Journées Foie et VIH, Nov 2013

Patients with failure of HCV therapy: TelapreVIH ANRS trial



No influence
- ARV
- fibrosis
- previous response

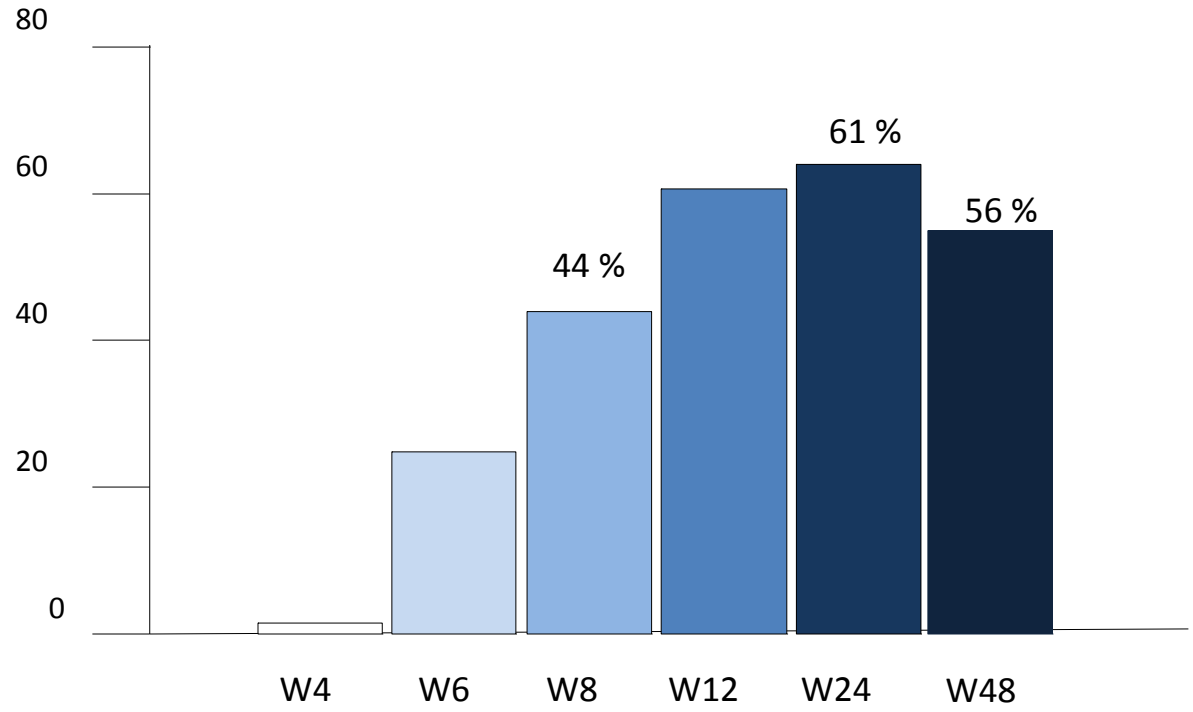
More frequent adverse events : grade 4 anemia (<7g/dl): 16%
No HIV rebound

Cotte et al. CROI 2013, Journées Foie et VIH, Nov 2013

Patients with failure of HCV therapy: BocepreVIH ANRS trial

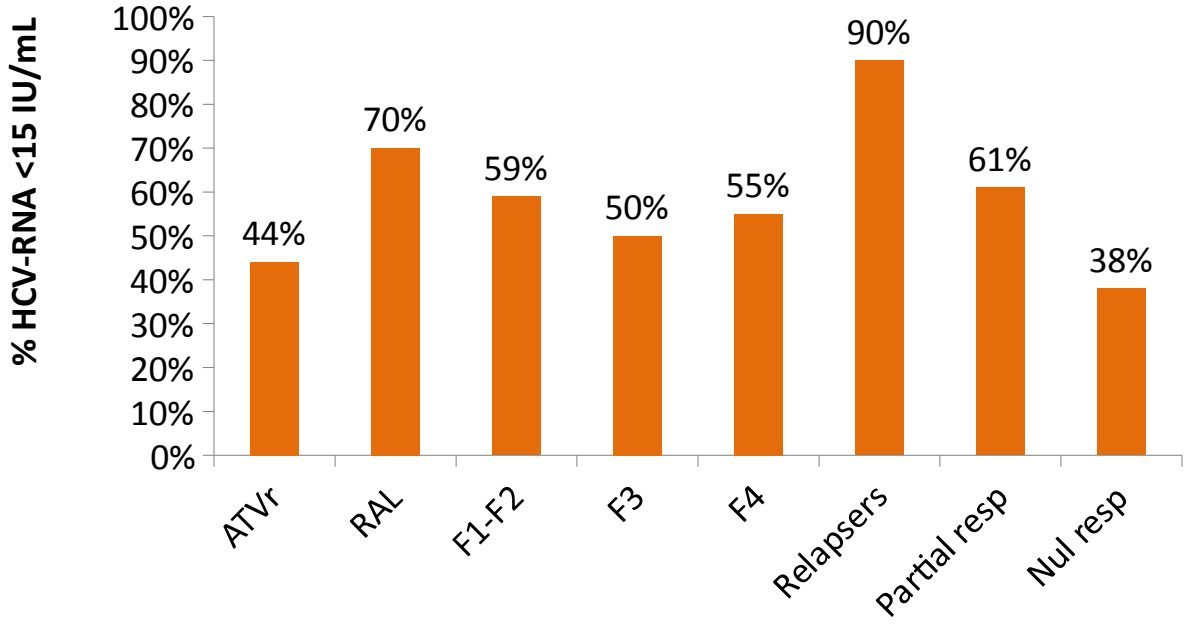
N=64 patients
78% genotype 1a
39% F3-F4
33% nul responders

W48 response: 56%



Poizot-Martin et al. CROI 2013; Journées Foie et VIH novembre 2013

Patients with failure of HCV therapy: BocepreVIH ANRS trial



No influence
- fibrosis

Influence
- previous response
- ARV

More frequent adverse events : grade 4 anemia in 3 patients (4.7%)
HIV rebound in 6 patients (9.4%)

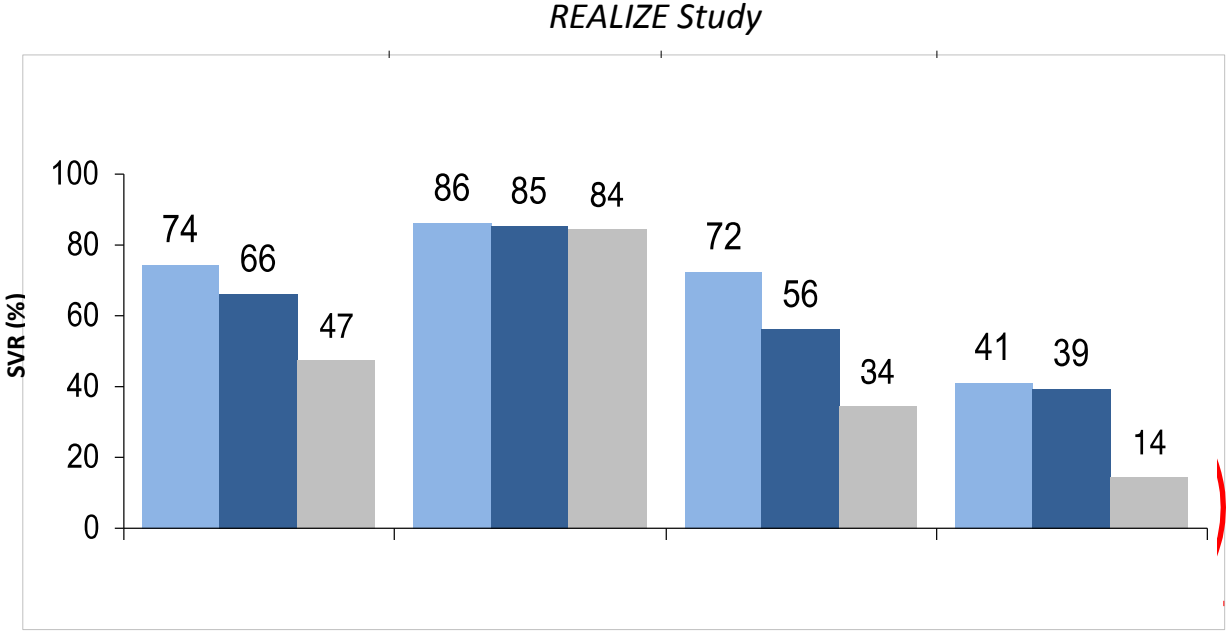
Poizot-Martin et al. CROI 2013 Journées Foie et VIH novembre 2013

Predictive factors of SVR in mono-infected patients with failure of HCV therapy

- **Fibrosis stage**

Telaprevir

REALIZE Study



Major impact

Boceprévir

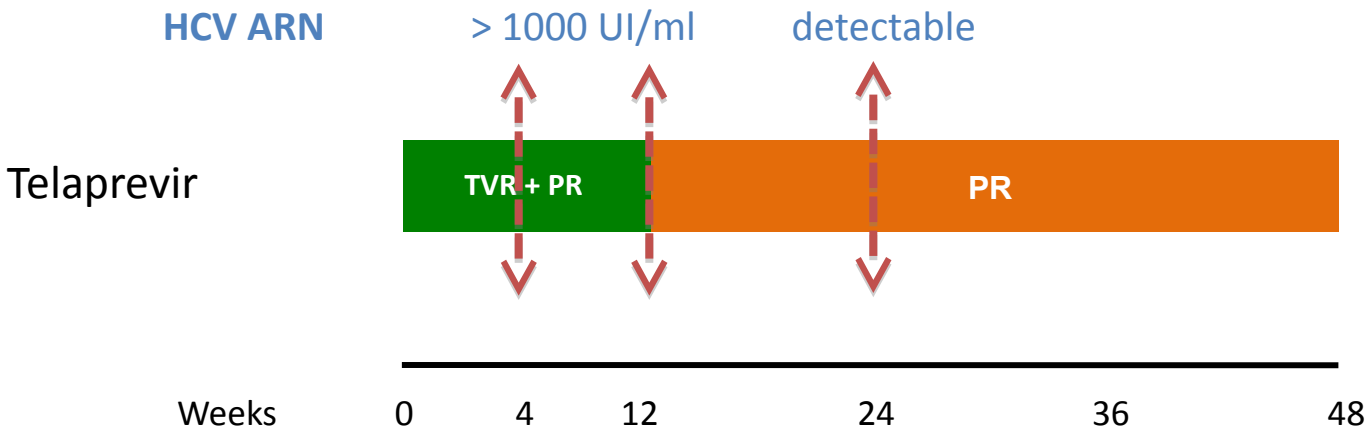
F0-F2 : 66-68% RVS → F3-F4 : 44-68% RVS

RESPOND 2 Study

- **Other predictive factors**

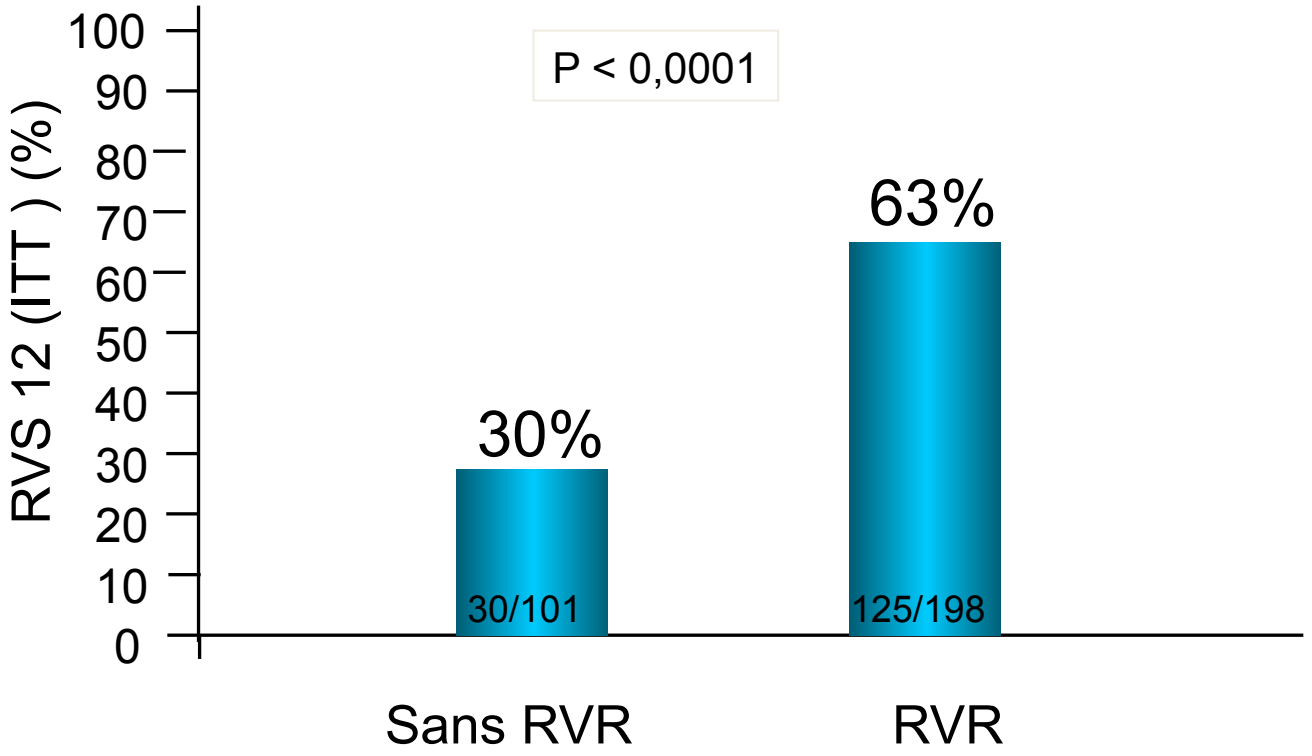
High Cholesterol LDL, genotype 1b, lox HCV RNA , low ALT

Criteria for therapy interuption with telaprevir



Cupic study : Telaprevir in 299 cirrhotic patients
RVS12 depending on RVR (W4)

Global SVR12 rate : 52 %

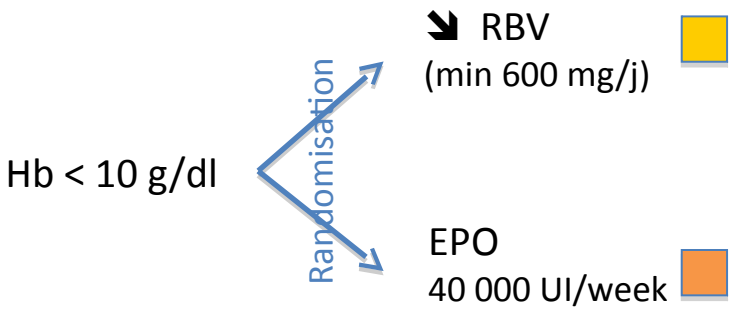


C. Hezode, EAH. Fontaine , AASLD 2013

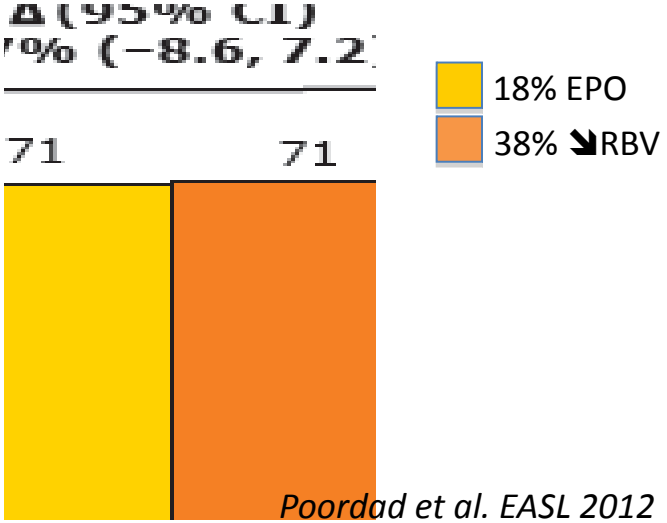
Management of anemia

↗ risk ≈ 20% / bitherapy
Hb < 10 g/dl ≈ 50% BOC
≈ 40% TVR

- Decrease of ribavirin dosage



In boceprevir HCV mono-infected



Poordad et al. EASL 2012

Hb < 10 g/dl or decrease > 2 g/dl within 2 weeks

1/ Decrease of ribavirin dosage by 200 mg down to 600 mg daily
2/ EPO introduction
Cirrhosis : EPO directly

Case study (6) : course of HCV RNA

Date	Telaprevir	Ribavirin	HCV RNA	HB	
J0	2250	1000	150.230	14.0	
S2	2250	1000	2250	12.6	
S4	2250	1000	1540	9.9	
S8	2250	↘ 800	<12	8.9	*
S12	2250 Arrêt	800	<12	9.7	EPO x1 than x2/week
S16	-	800	<12	10.5	
S24	-	800	<12	10.8	*Pneumo* bacteriemia with severe sepsis

750 neutrophils, 90.000 platelets

Treatment had to be stopped at W24

Benefice-risk ratio depending on platelets and albumin baseline level

	Platelets > 100.000/mm3	**Platelets ≤ 100.000/mm3**
Albumin ≥ 35 g/l Patients, n (%) Severe complications, n (%) RVS12, n (%)	306 (68,3 %) **19 (6,2 %)** 168 (54,9 %)	74 (16,5 %) 9 (12,2 %) 27 (36,5 %)
Albumin < 35 g/l Patients, n (%) Severe complications, n (%) RVS12, n (%)	31 (6,9 %) 5 (16,1 %) 8 (29,0 %)	37 (8,3 %) **19 (51,4 %)** 10 (27 %)

C. Hezode, EAH. Fontaine , AASLD 2013

Case study (7)

We are in January 2014

Fibroscan is 20.5 Kpa, Alb is 35 g/dl, PT is 85%

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What are the chances of RVS with the new options?

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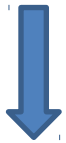
Do you decide to retreat now for hepatitis C ?

In January 2014, already or soon available:



Different combinations

Different durations

New therapeutic options for G1 cirrhotic HCV monoinfected patients that will be available in 2014

Posible drug combination	Duration	SVR rate
SOFOSBUVIR+PegIFN+RBV*	12	80%
SIMEPREVIR+PegIFN+RBV**	24	74%
SOFOSBUVIR+RBV***	24	≤ 76%
SOFOSBUVIR + DACLATASVIR	24	> 95%
SOFOSBUVIR + SIMEPREVIR +/- RBV**** *(only if genotype 1 et 4, absence of Tt with 1st generation PI and absence of* - *baseline Q80K polymorphism mutation if G1a* - *or acquired msisiance to 1st generation PI*	24	> 95%
SOFOSBUVIR+LEDISPAVIR	Not before 2015	

*Neutrino, Lawitz, NEJMed, 2013; **Pillar;***post Tx, Charlton, AASLD 2013****Cosmos

Interactions between anti HIV drugs (PI, efavirenz) and siméprévir or daclatasvir

Conclusion : Patients with failure of HCV therapy

Treat now ? Or wait to treat better ?

	Genotype 1 **Relapser**	**Genotype 1** **partial responder**	**Genotype 1** **Nul responder**
F0-F1	Wait	wait	Wait
F2	Indication No emergency	Indication No emergency	Wait
F3	Treat	Treat	Wait
F4	Treat	Treat	Treat