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Case study
Therapeutic options in cirrhotic HIV/HCV patients

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Istanbul, ESCMID Course, Februray 2014

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, treated with risperidone

HIV parameters	Value
CD4 cell count	540 cell/mm^3
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 (partial responder)

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%

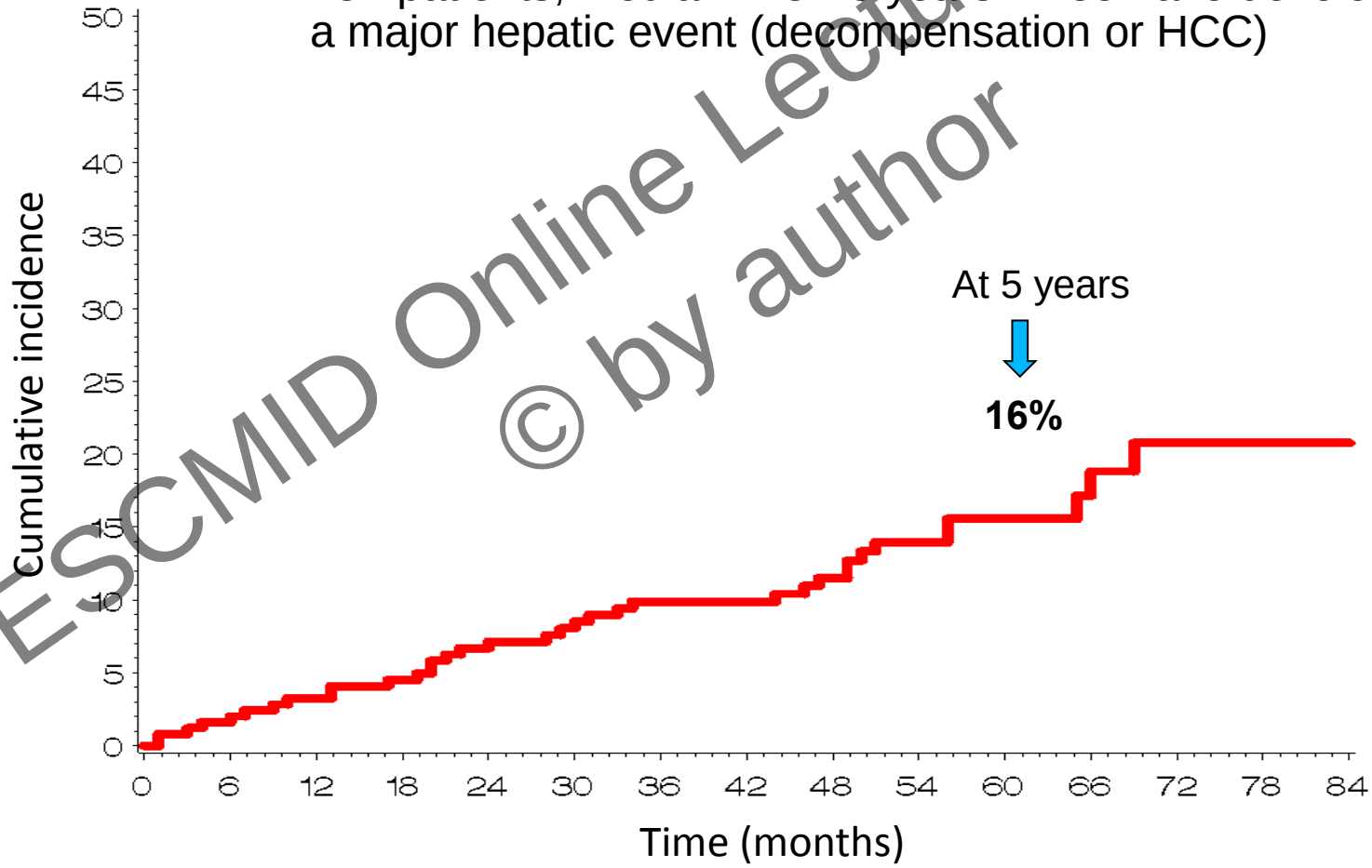
?

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

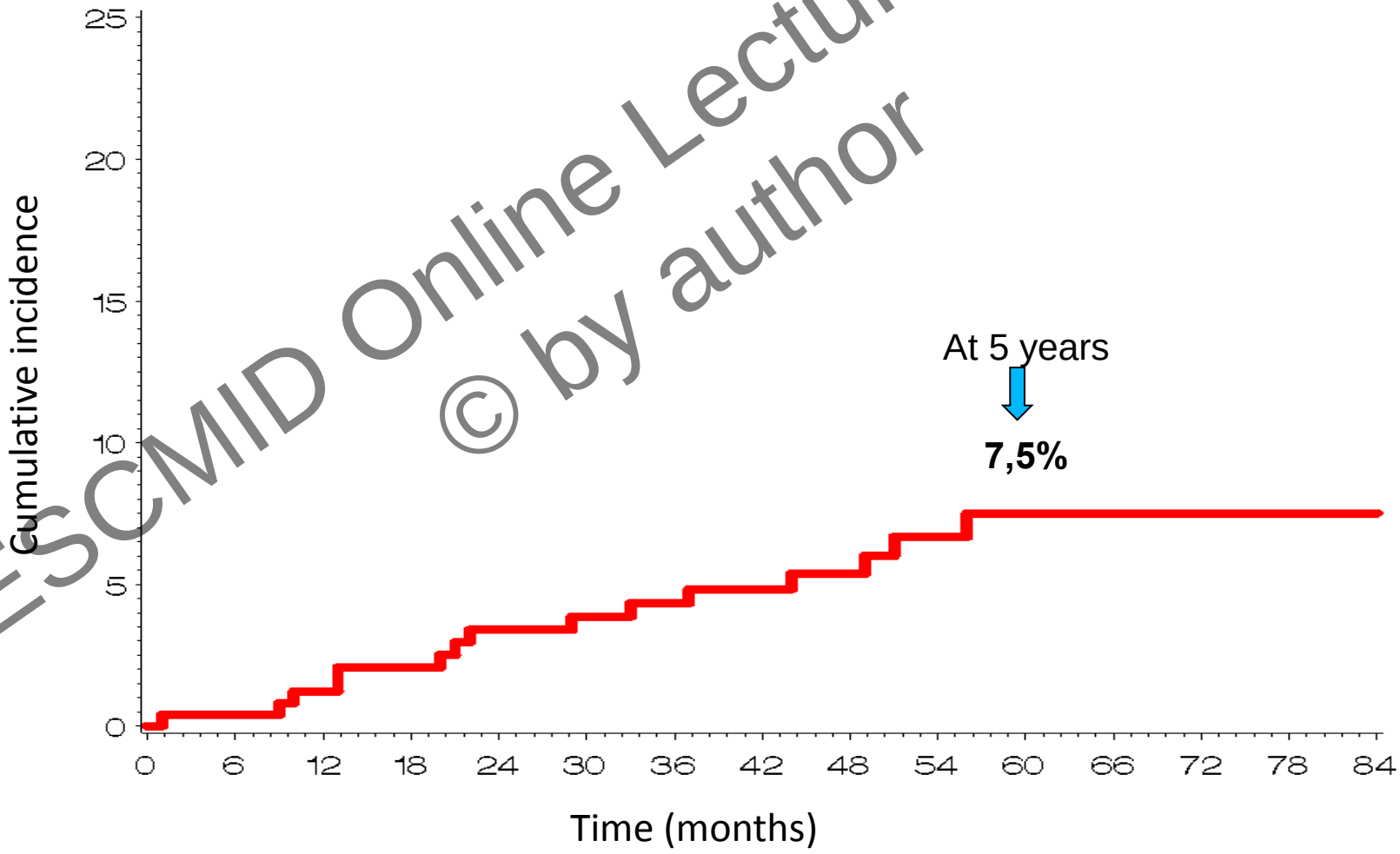
- <5 %
- 6–10 %
- 11–15 %
- 16–20 %
- >20 %

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)



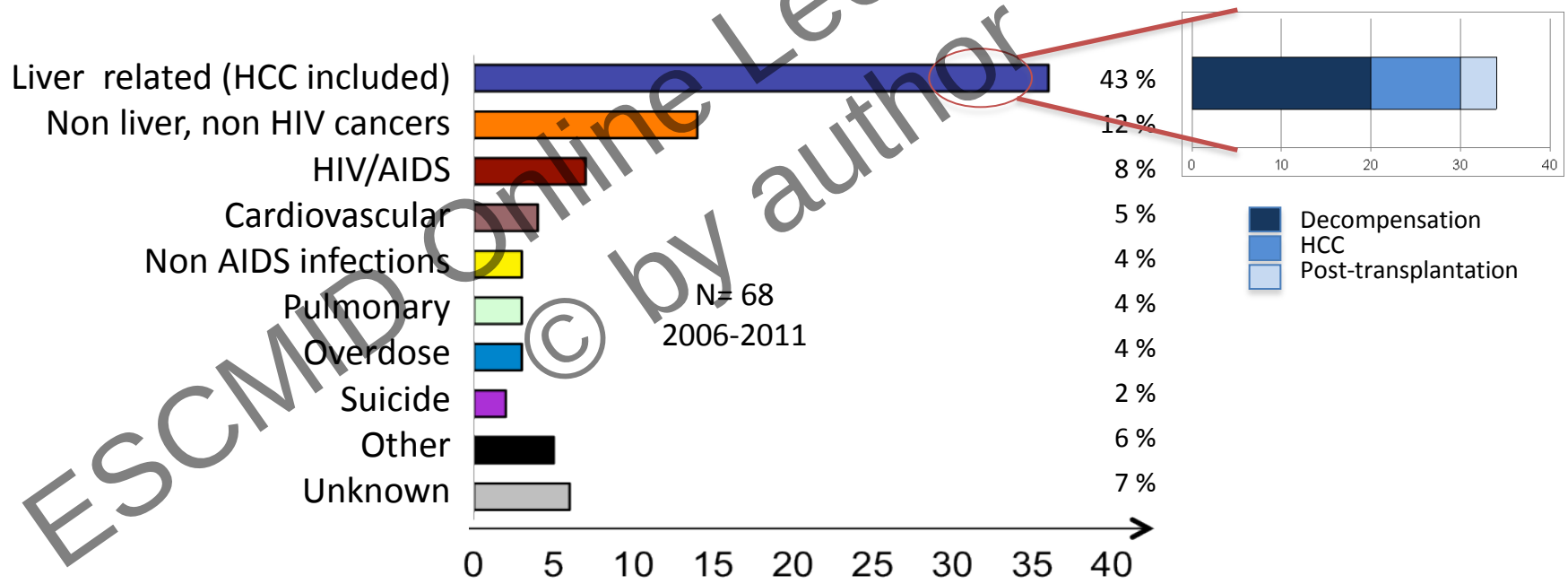
Cumulative incidence of HCC in cirrhotic patients
Hepavih ANRS CO13



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?

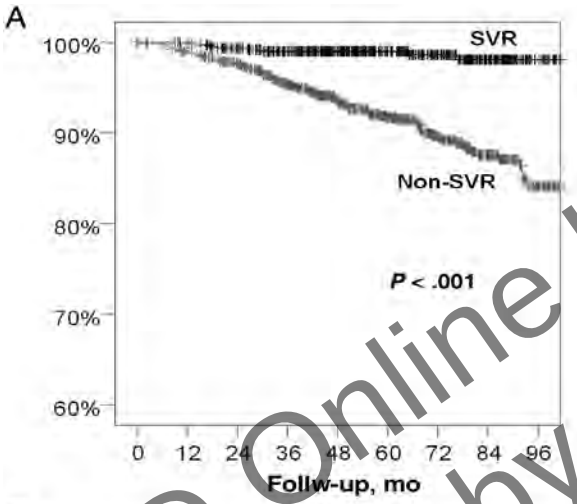
2- The incidence of non hepatic events?

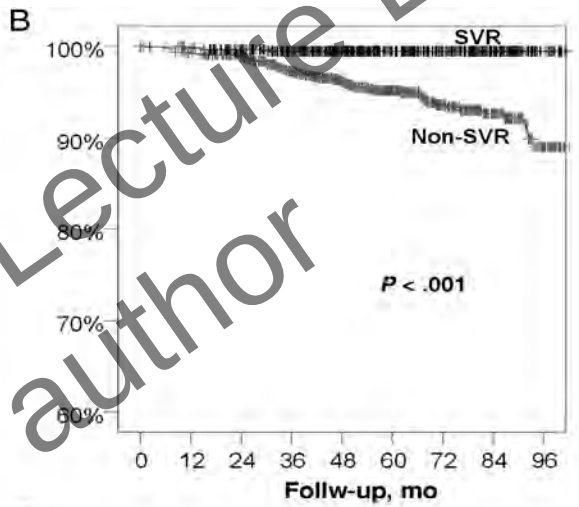
3- The fibrosis course?

Effect of SVR on the occurrence of hepatic events

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

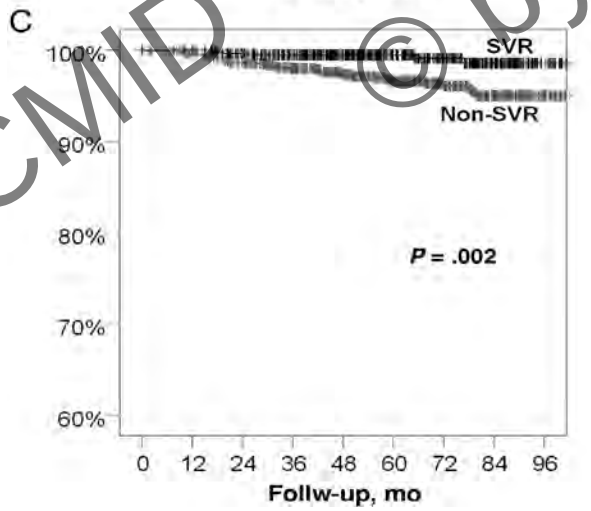
Overall deaths

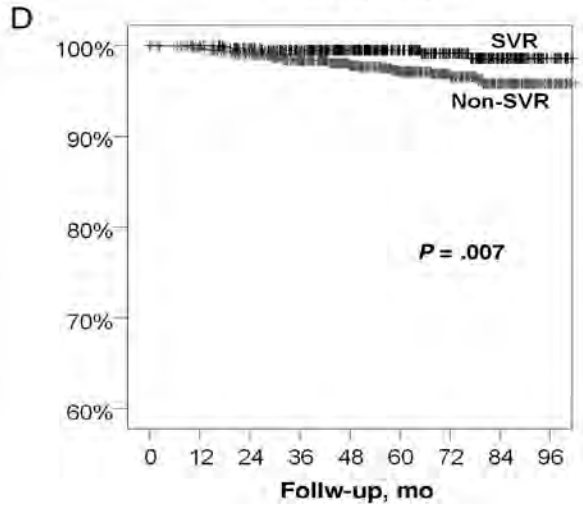




Liver-related deaths

Non liver-related deaths



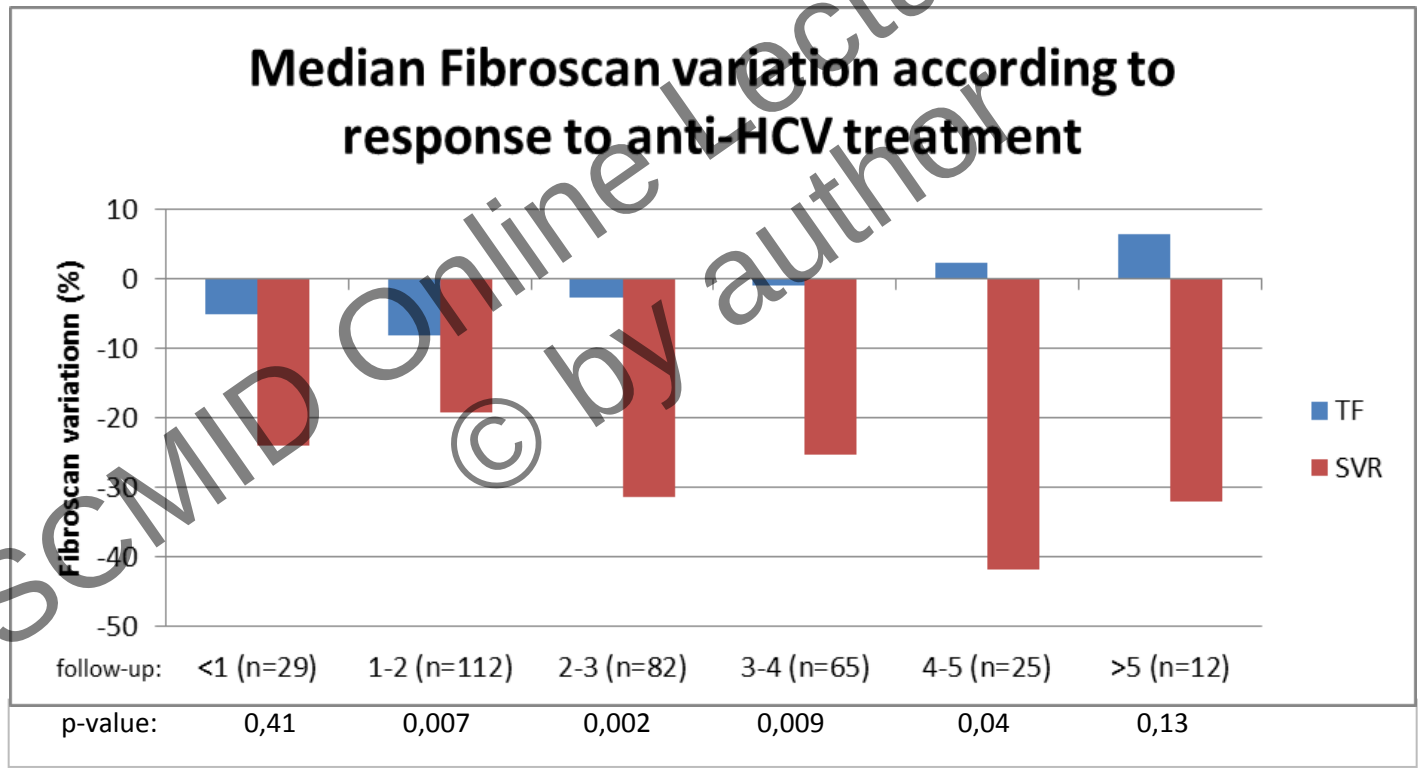


Non HIV, non liver-related deaths

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)

Loko et al, 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 μg 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

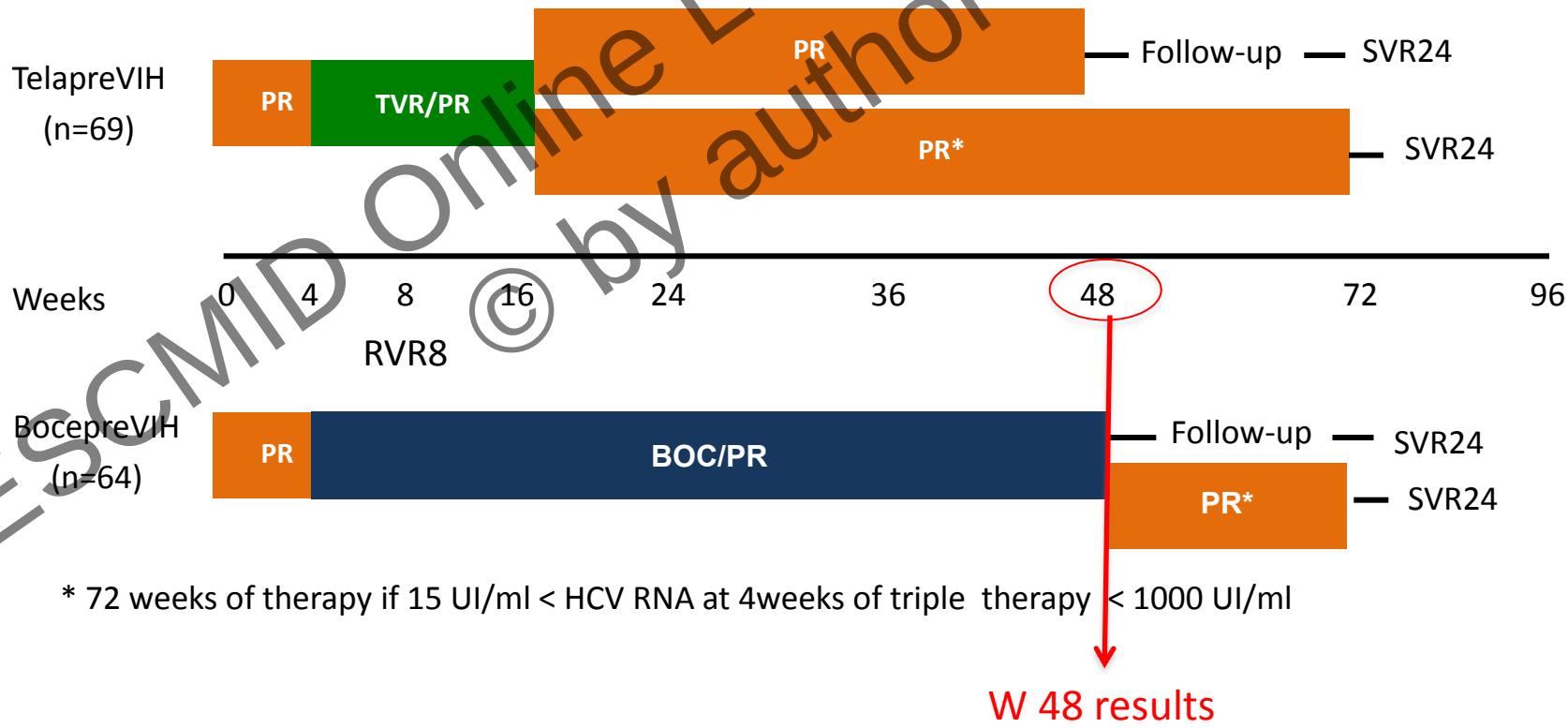
?

What do you decide ?

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

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

- Patients with failure of PegIFN/RBV
- CD4 > 200/mm^3 and HIV RNA < 50 c/ml for at least 6 mos
- No decompensated cirrhosis + nul response

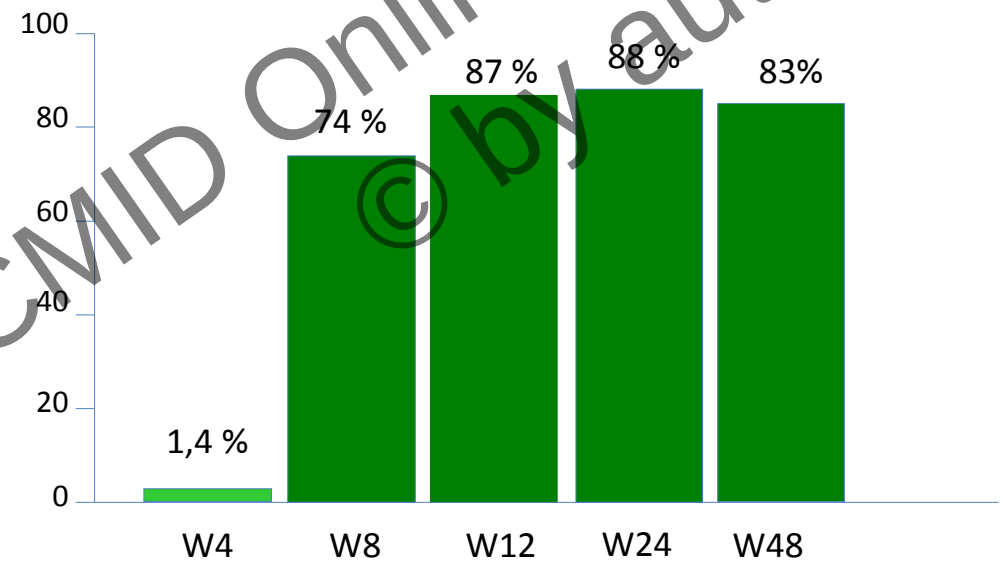


* 72 weeks of therapy if 15 UI/ml < HCV RNA at 4weeks of triple therapy < 1000 UI/ml

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

Patients with failure of HCV therapy : TélapreVIH ANRS trial

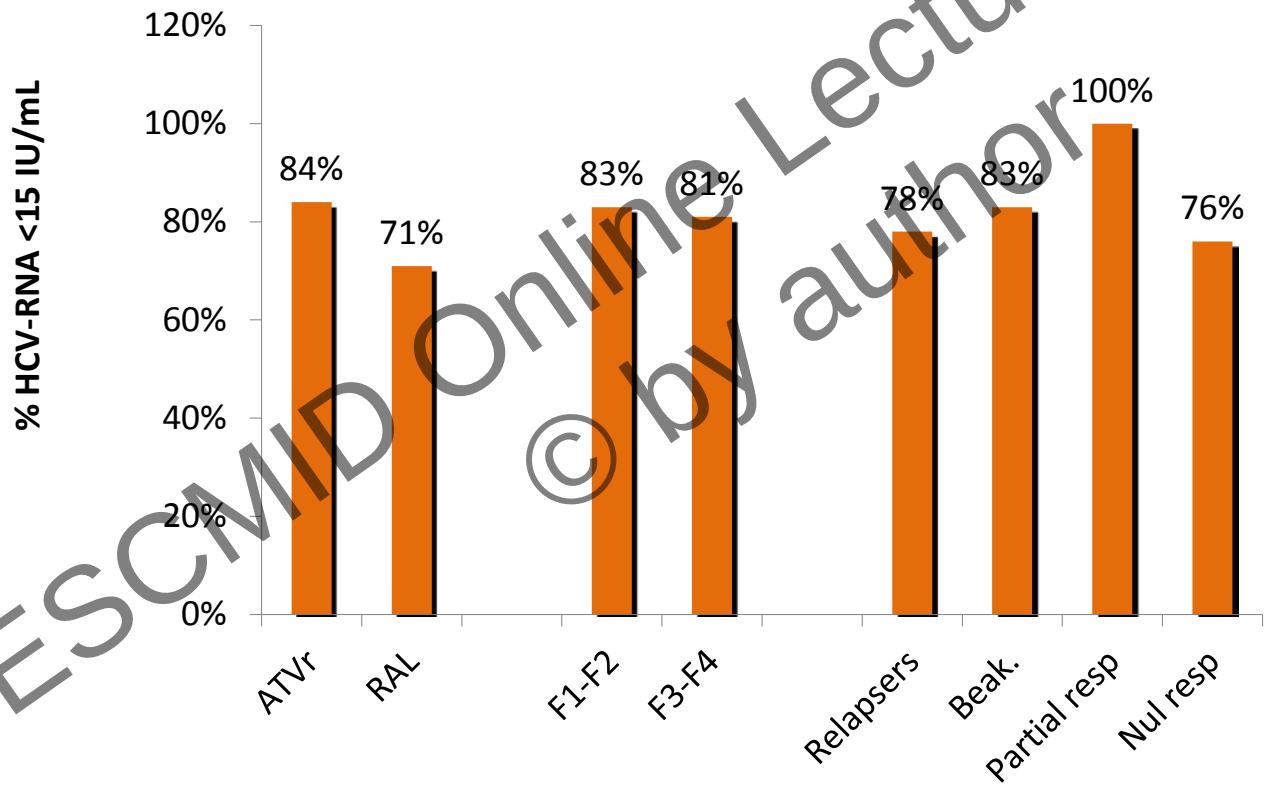
N=69 patients
70% genotype 1a
39% F3-F4
30% nul responders



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

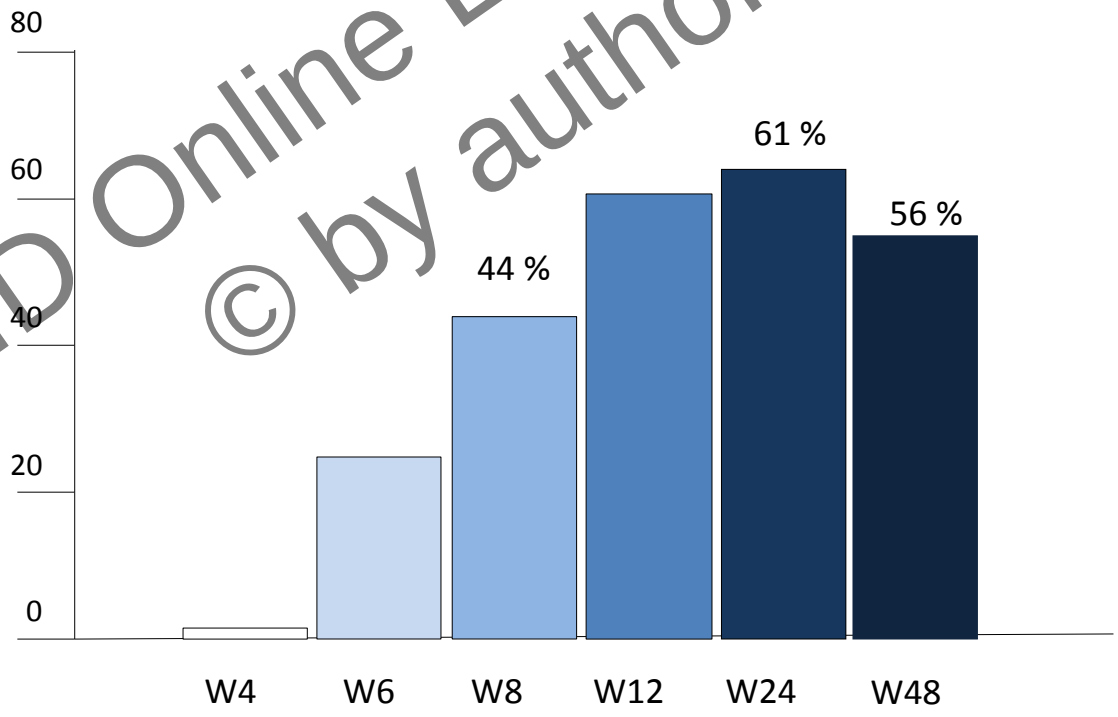
More frequent adverse events : grade 4 anemia (<7g/dl): 16%
No HIV rebound

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

Patients with failure of HCV therapy: BocepreVIH ANRS trial

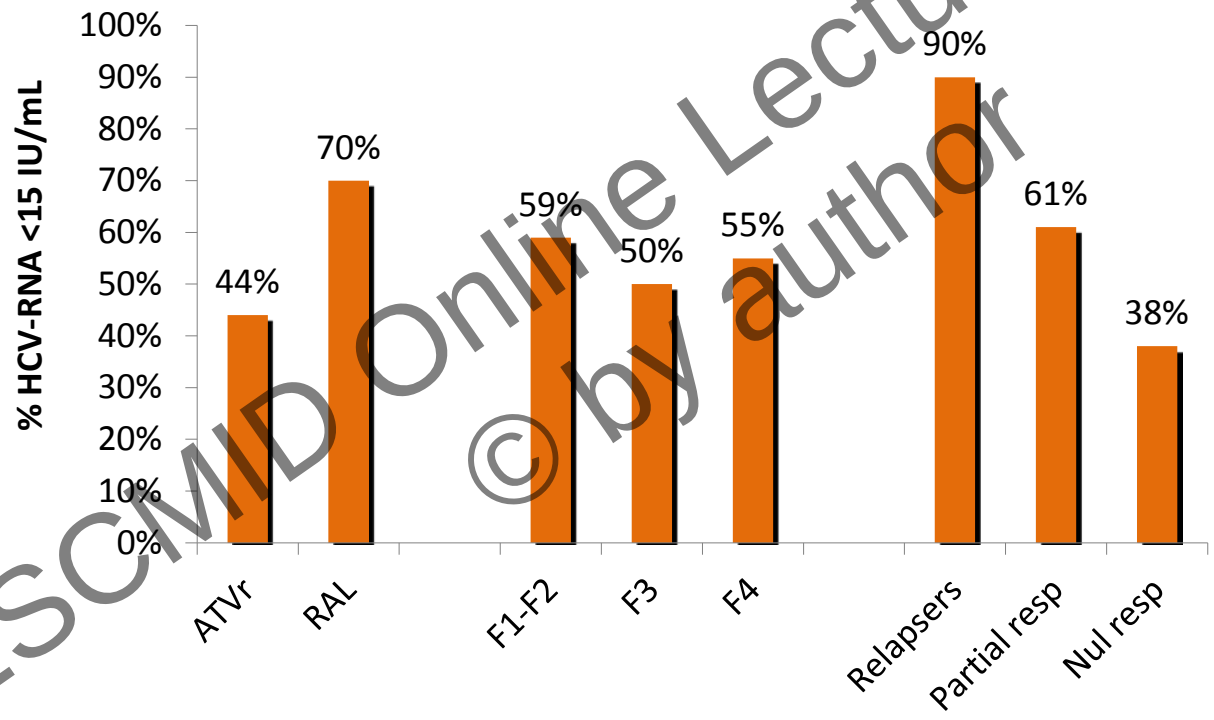
N=64 patients
78% genotype 1a
39% F3-F4
33% nul responders

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

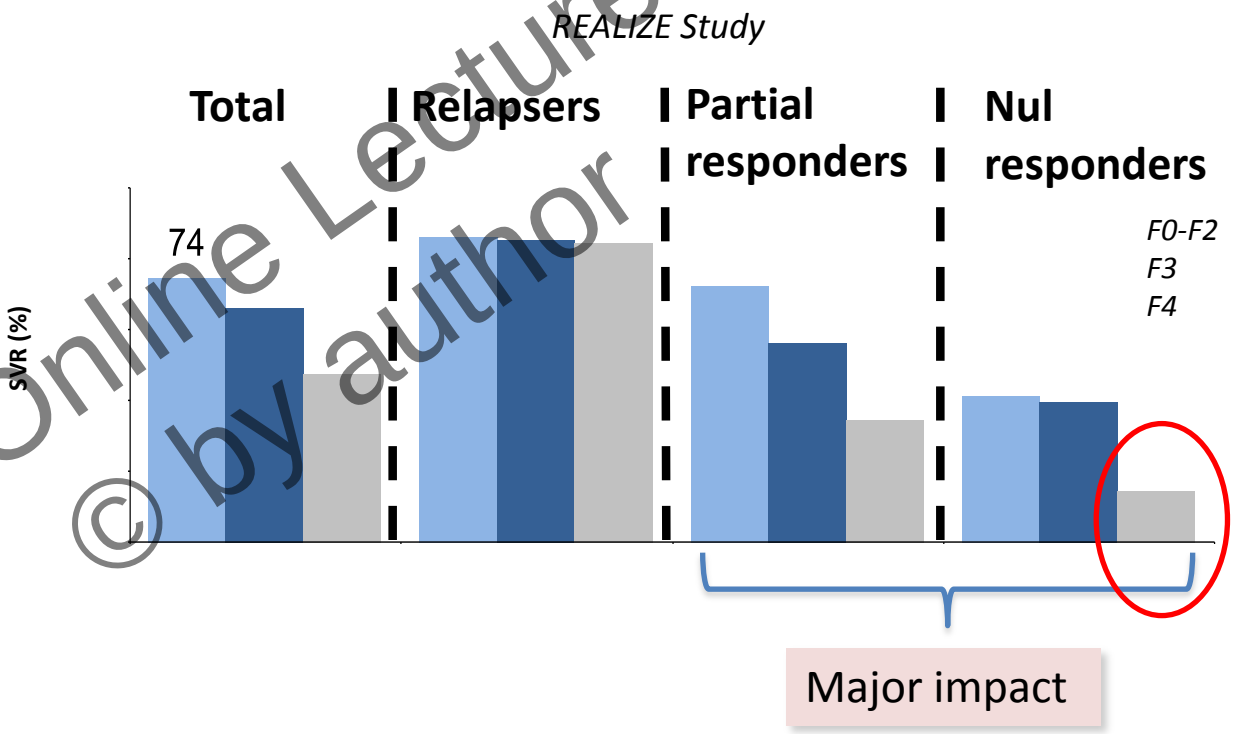
More frequent adverse events : grade 4 anemia in 3 patients (4.7%)
HIV rebound in 6 patients (9.4%)

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



Boceprévir

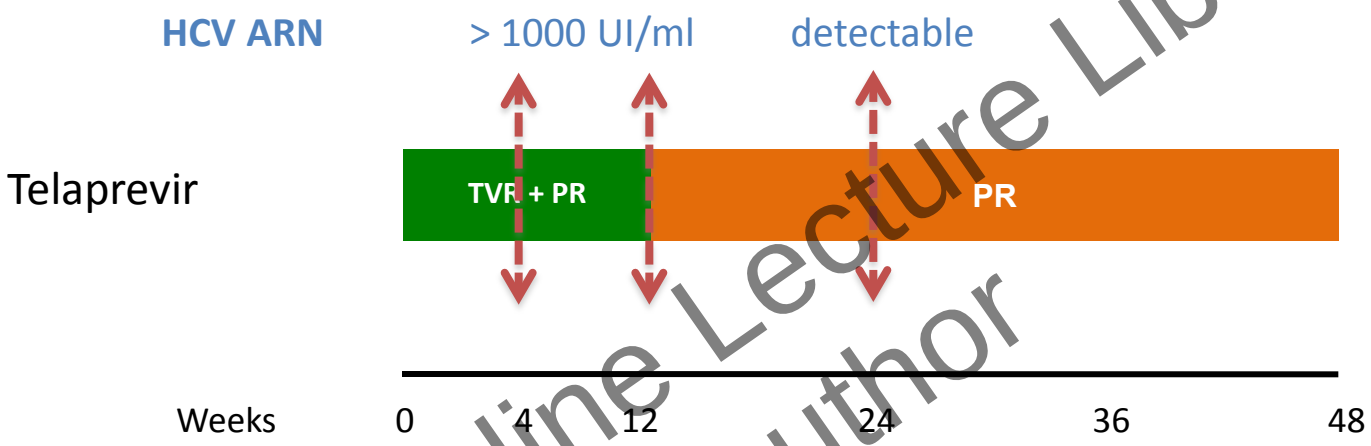
F0-F2 : 66-68% RVS → F3-F4 : 44-68% RVS

RESPOND 2 Study

- **Other predictive factors**

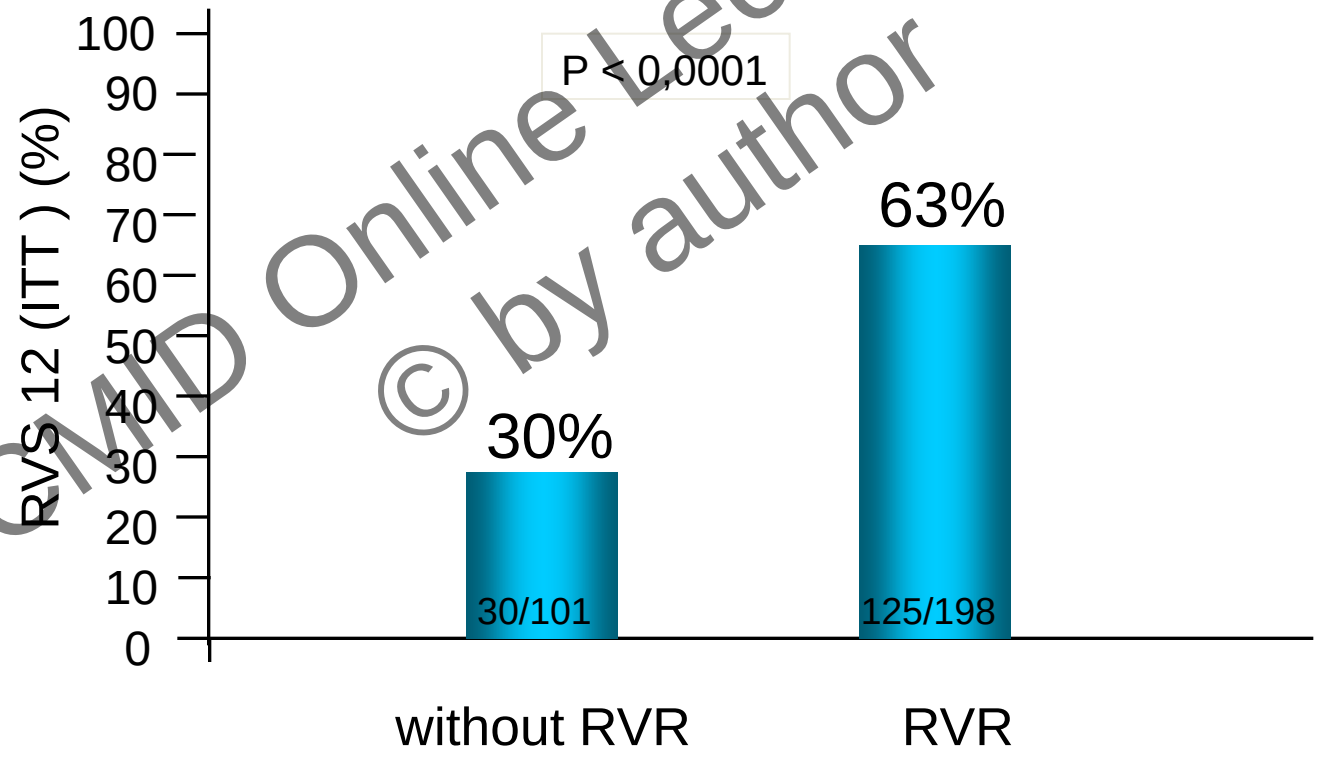
High Cholesterol LDL, genotype 1b, lox HCV RNA , low ALT

Criteria for therapy interuption with telaprevir



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

Global SVR12 rate : 52 %



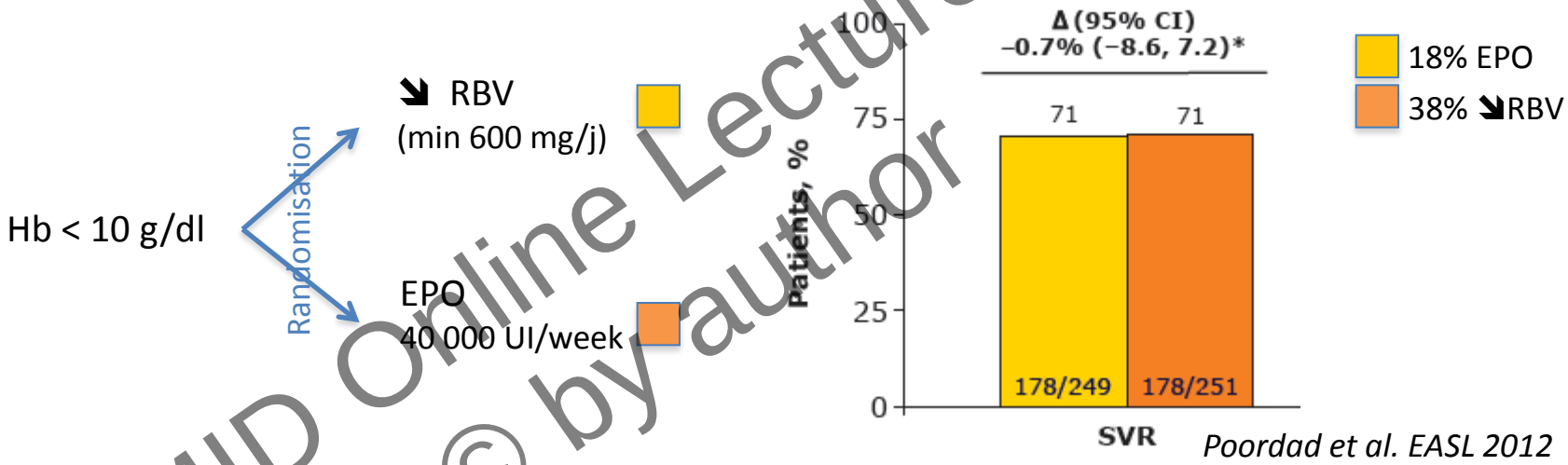
C. Hezode, EAH. Fontaine , AASLD 2013

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

C. Hezode, EAH. Fontaine , AASLD 2013

Case study (7)

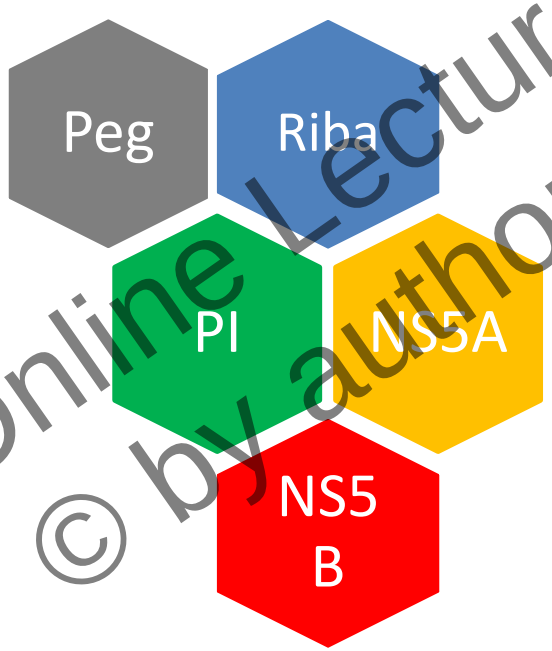
We are in February 2014

Fibroscan is 20.5 Kpa, Alb is 33 g/dl, PT is 85%

? **What are the chances of RVS with the new options?**

? **Do you decide to retreat now for hepatitis C ?**

In January 2014, already or soon available:



Different combinations

Different durations

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

Possible drug combinations	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

Antiretroviral drugs and anti HCV 1st generation PI

Antirétroviraux	Trithérapie avec télaprévir	Trithérapie avec bocéprévir
Inhibiteurs Nucléos(t)idiques de la Transcriptase inverse du HIV (iNTI)		
Zidovudine	a	a
Stavudine	b	b
Didanosine	b	b
Lamivudine		
Emtricitabine		
Abacavir	c	c
Tenofovir		
Inhibiteurs Non Nucléos(t)idiques de la Transcriptase Inverse du HIV (iNNTI)		
Nevirapine	?	?
Efavirenz	d	? e
Etravirine	?	?
Inhibiteurs de Protéase HIV boosté (IP/r)		
Lopinavir		? f
Fosamprenavir		? f
Atazanavir		? f
Darunavir		? f
Inhibiteurs d'Intégrase du HIV (II)		
Raltegravir		
Inhibiteurs d'Entrée du HIV (IE)		
Maraviroc	?	?

Association possible

Association possible sous réserve

Association déconseillée ou contre-indiquée

a Augmentation du risque d'anémie

b Augmentation du risque d'acidose lactique en association avec la ribavirine

c Interaction possible avec la ribavirine, bien que débattue – ne contre-indique pas utilisation si nécessaire

d Nécessite d'augmenter la dose de télaprévir à 1125 mg x 3 /j

e Faible diminution de l'ASC et de la Cmax du bocéprévir, mais augmentation de la Cmin de 44%, retentissement clinique inconnues - éviter

f Pas d'interactions attendues – à confirmer