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Follow-up of patients with SVR

Lawrence Serfaty

Service d'Hépatologie, UMR_S 938

Hôpital Saint-Antoine

Université Pierre&Marie Curie

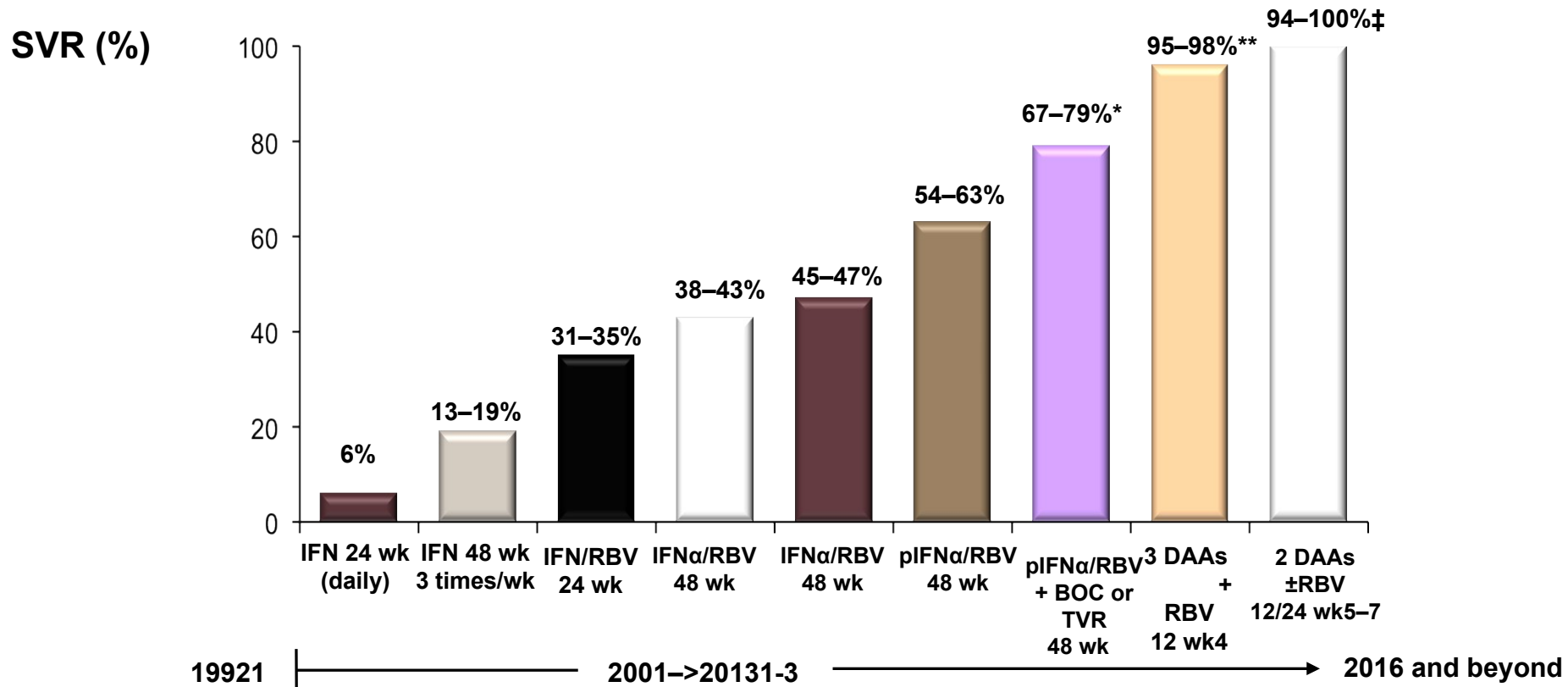
Paris, France



Disclosures

- Consulting, advisory committees or review panel
 - Abbvie, Bristol-Myers Squibb, Gilead, GlaxoSmithKline, Janssen, Merck Sharp & Dohme, Roche
- Speaking and teaching
 - Abbvie, Aptalis, Bristol-Myers Squibb, Gilead, Janssen, Merck Sharp & Dohme, Roche

New all-oral regimens are transforming the HCV treatment landscape



in patients with HCV genotype 1 only; ** In treatment-naïve patients; ‡Includes treatment-naïve and -experienced patients

BOC, boceprevir; IFN, interferon; RBV, ribavirin; SVR, sustained virologic response; TVR, telaprevir

1. Adapted from Manns MP, et al. *Gut* 2006;55:1350–9. 2. Tran TT. *Am J Manag Care* 2012;18(14 Suppl.):S340–9.

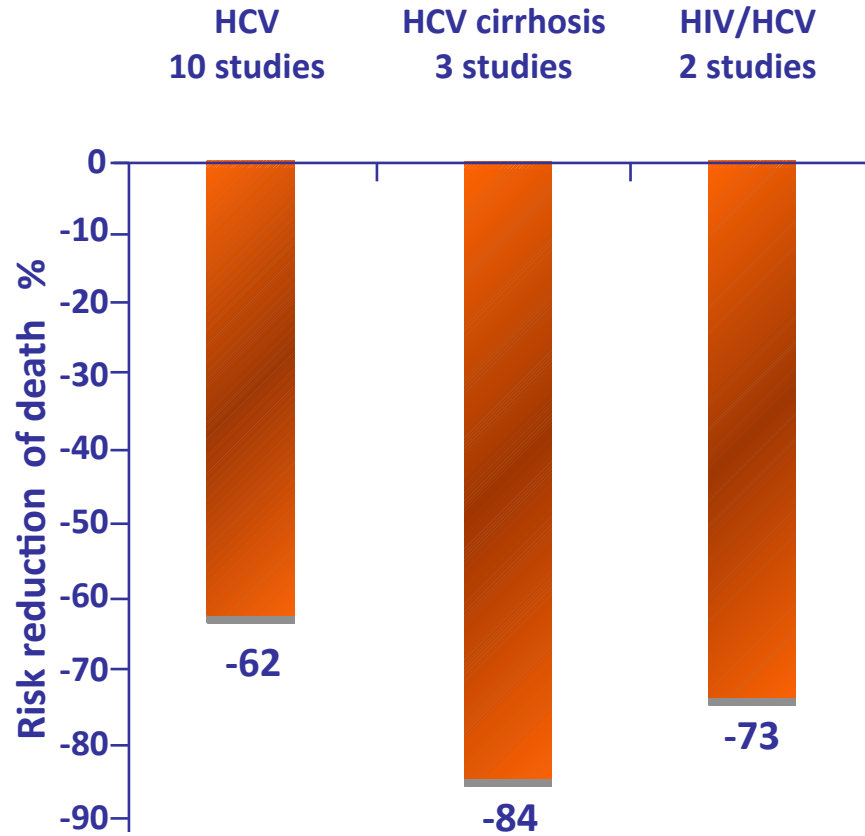
3. Goralczyk AD, et al. *BMC Gastroenterology* 2013;13:148. 4. Feld JJ, et al. *N Engl J Med*. 2014;370:1594-603.

5. Sulkowski M, et al. *N Engl J Med*. 2014;370(3):211-21. 6. Afdhal N, et al. *N Engl J Med*. 2014;370:1889–98.

7. Afdhal N, et al. *N Engl J Med*. 2014;370:1483-93.

SVR is associated with improvement of survival (meta-analysis n=34 563)

Effect of SVR on death (all cause)



Plan

The durability of SVR with DAAs regimens

Liver-related morbidity/mortality in SVR patients

Long term fibrosis outcome in SVR patients

Predictors of liver disease outcome in SVR patients: the role of comorbidities

Monitoring of SVR patients: the value of non invasive markers

Plan

The durability of SVR with DAAs regimens

Liver-related morbidity/mortality in SVR patients

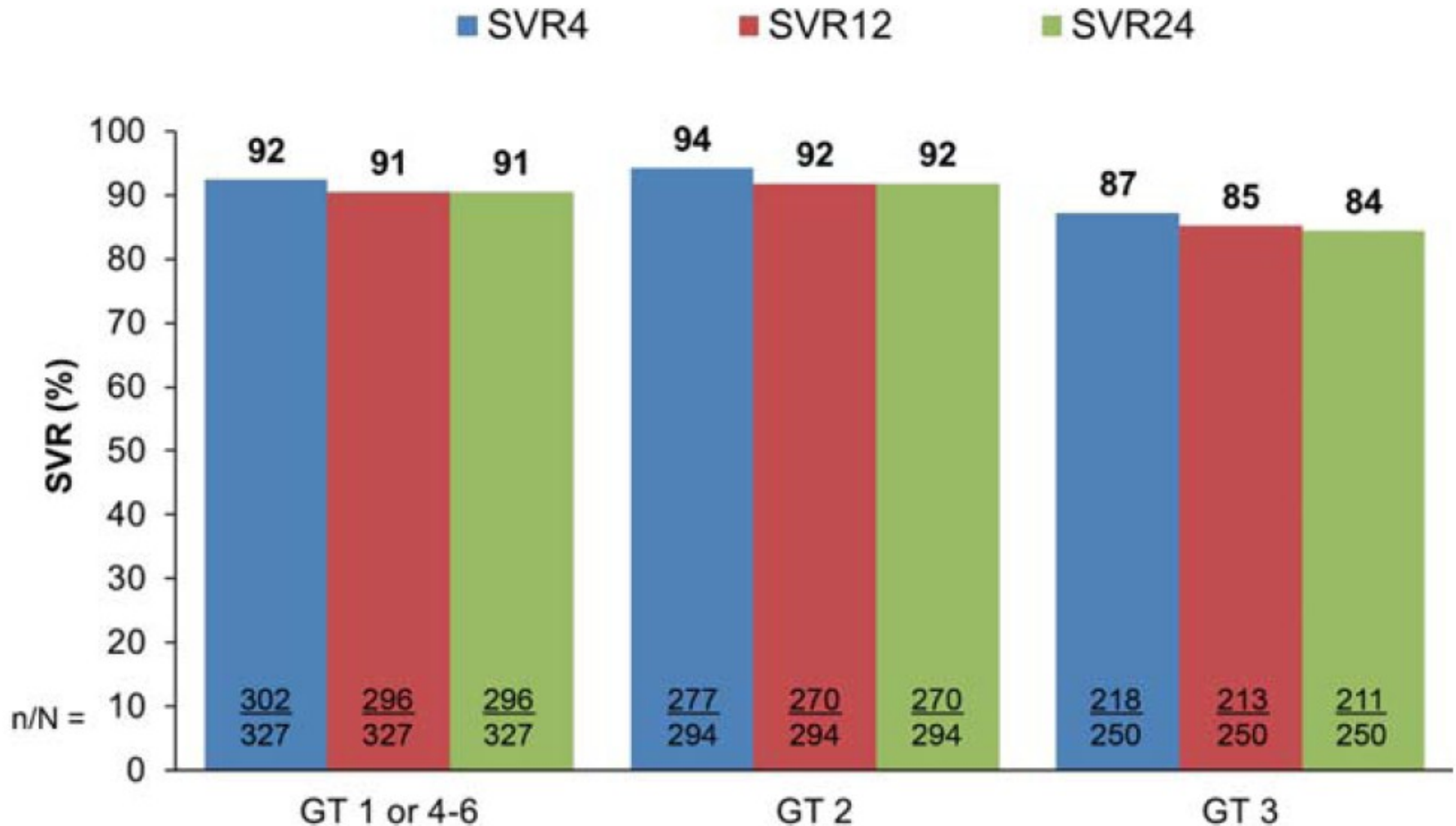
Long term fibrosis outcome in SVR patients

Predictors of liver disease outcome in SVR patients: the role of comorbidities

Monitoring of SVR patients: the value of non invasive markers

The durability of SVR with DAAs regimens

779 patients treated with sofosbuvir-containing regimen



The durability of SVR with DAAs regimens

Long term follow-up studies in DAAs-related SVR patients are ongoing.

Persistence of occult HCV infection ?

Radkowski M, et al. Persistence of hepatitis C virus in patients successfully treated for chronic hepatitis C. Hepatology 2005; 41: 106–14.

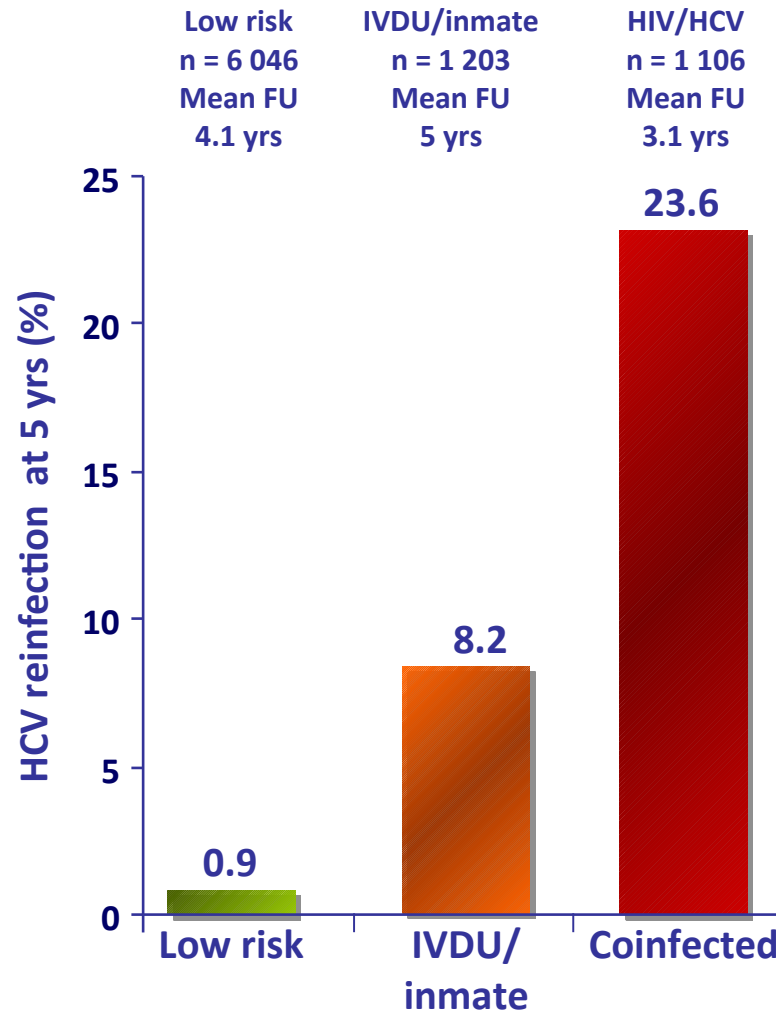
Castillo L, et al. Hepatitis C virus replicates in the liver of sustained responder patients to antiviral treatment. Clin Infect Dis 2006; 43: 1272–5.

Long term SVR and shorter duration regimen ?

Risk of reinfection following SVR

(meta-analysis n=34 563)

5 yrs risk of reinfection post SVR



EASL guidelines
Following SVR, monitoring for HCV reinfection through annual HCV RNA assessment should be undertaken in people who inject drugs or men who have sex with men with on-going risk behaviour (B2)

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The risk of liver transplantation or HCC according to SVR (*meta-analysis n=34 563*)

Liver transplantation risk at 5 yrs

HCC risk at 5 yrs

HCV
n = 108
Mean FU
4.2 yrs

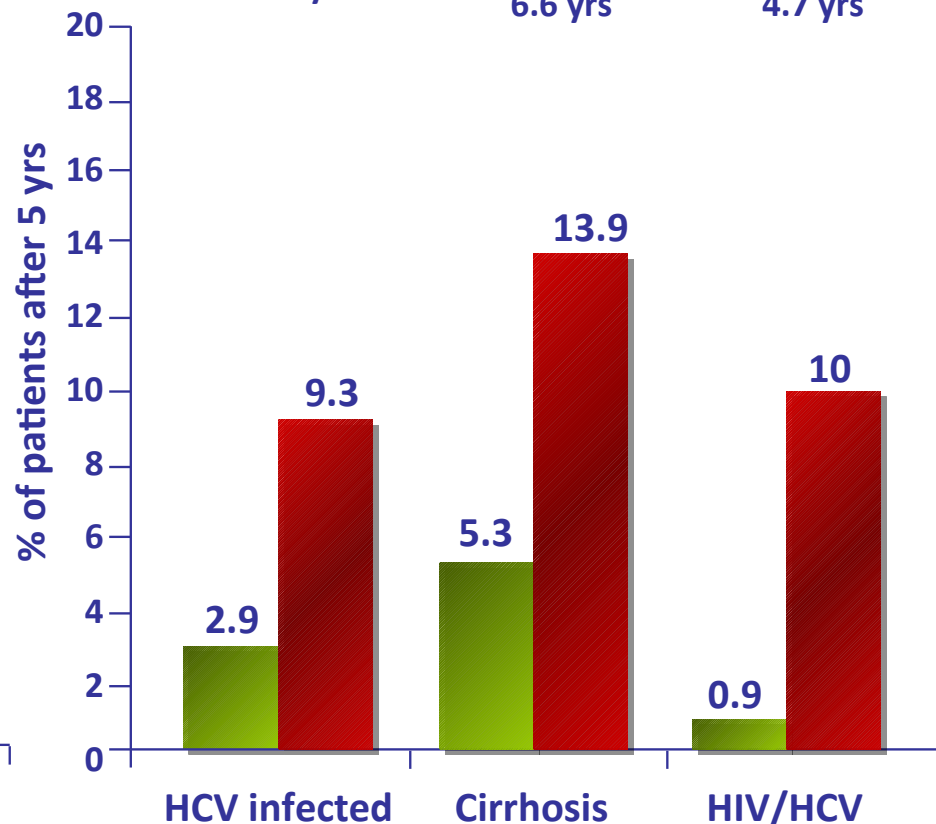
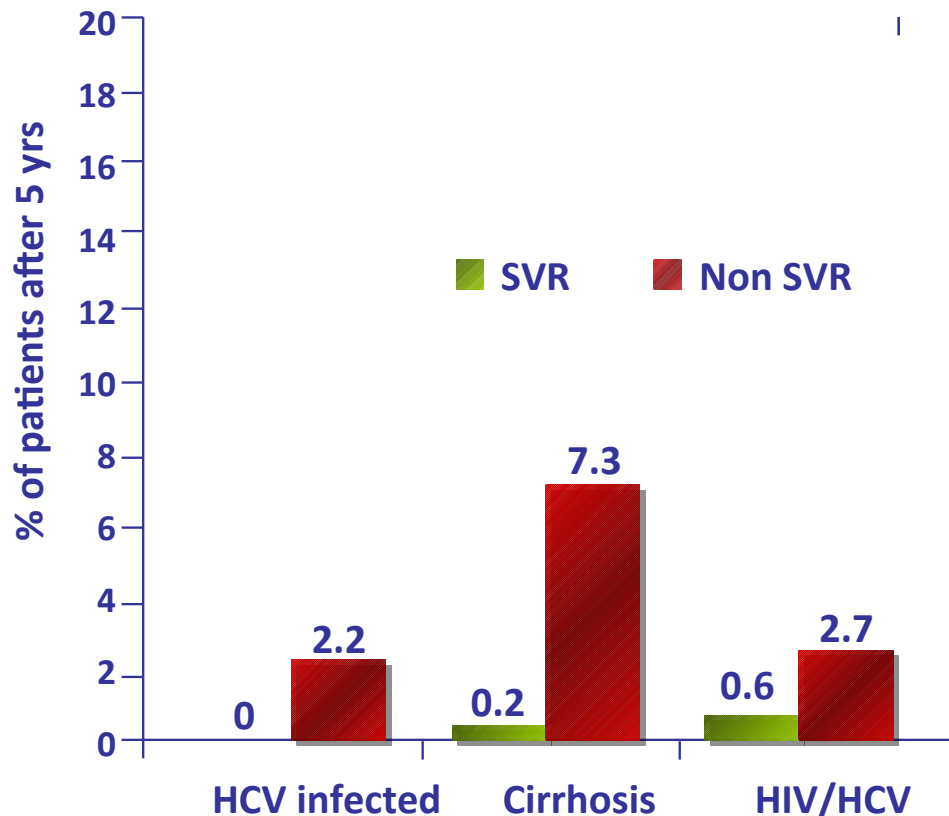
HCV cirrhosis
n = 1 046
Mean FU
7.7 yrs

HIV/HCV
n = 2 039
Mean FU
4.9 yrs

HCV
n = 12 496
Mean FU
6.1 yrs

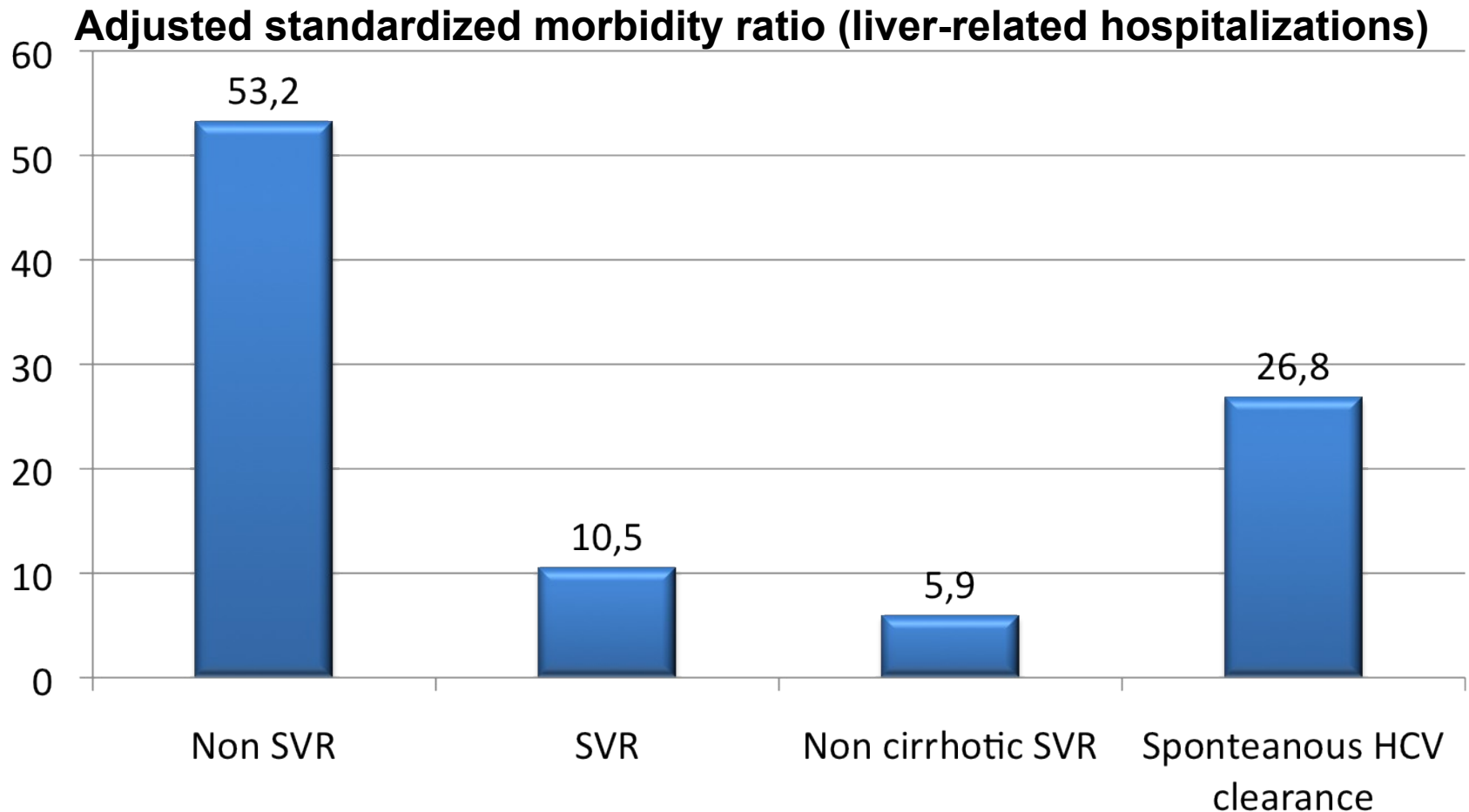
HCV cirrhosis
n = 4987
Mean FU
6.6 yrs

HIV/HCV
n = 2 085
Mean FU
4.7 yrs



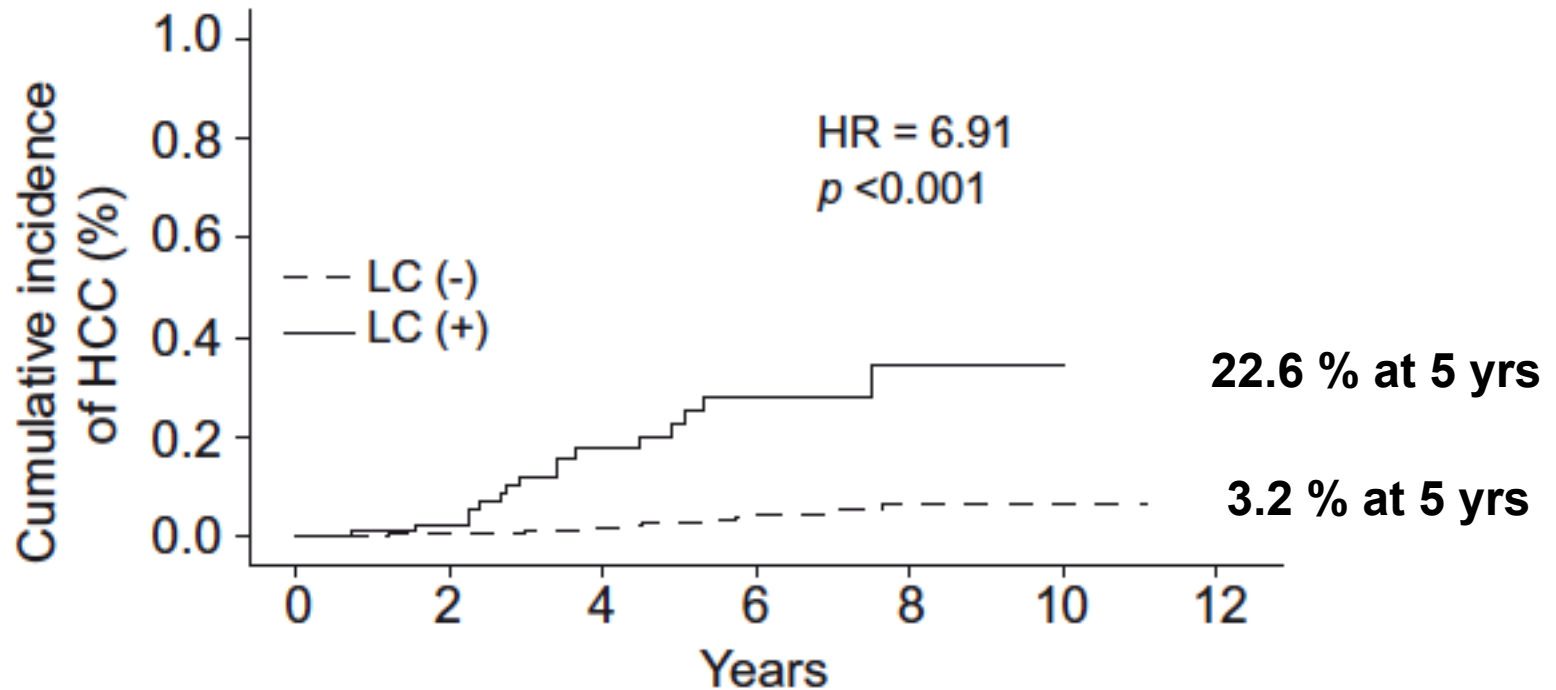
Excess liver-related morbidity following discharge of SVR patients

1215 HCV patients treated between 1996-2007, follow-up 5.3 yrs



Risk of HCC in non cirrhotic patients following HCV eradication

642 SVR patients followed 53 mo: 86 cirrhotics, 556 non-cirrhotics



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The durability of SVR with DAAs regimen

Liver-related morbidity/mortality in SVR patients

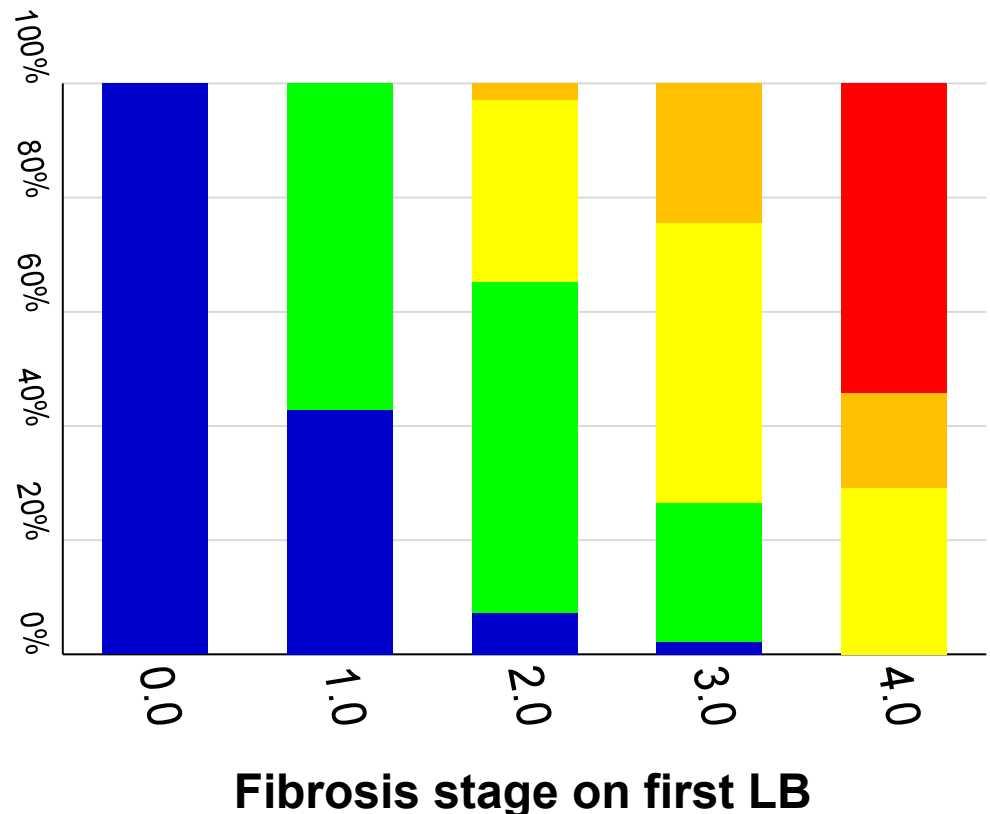
Long term fibrosis outcome in SVR patients

Predictors of liver disease outcome in SVR patients: the role of comorbidities

Monitoring of SVR patients: the value of non invasive markers

Regression of fibrosis in SVR patients is slow

183 HCV patients with SVR
2nd liver biopsy at 3.7 yrs



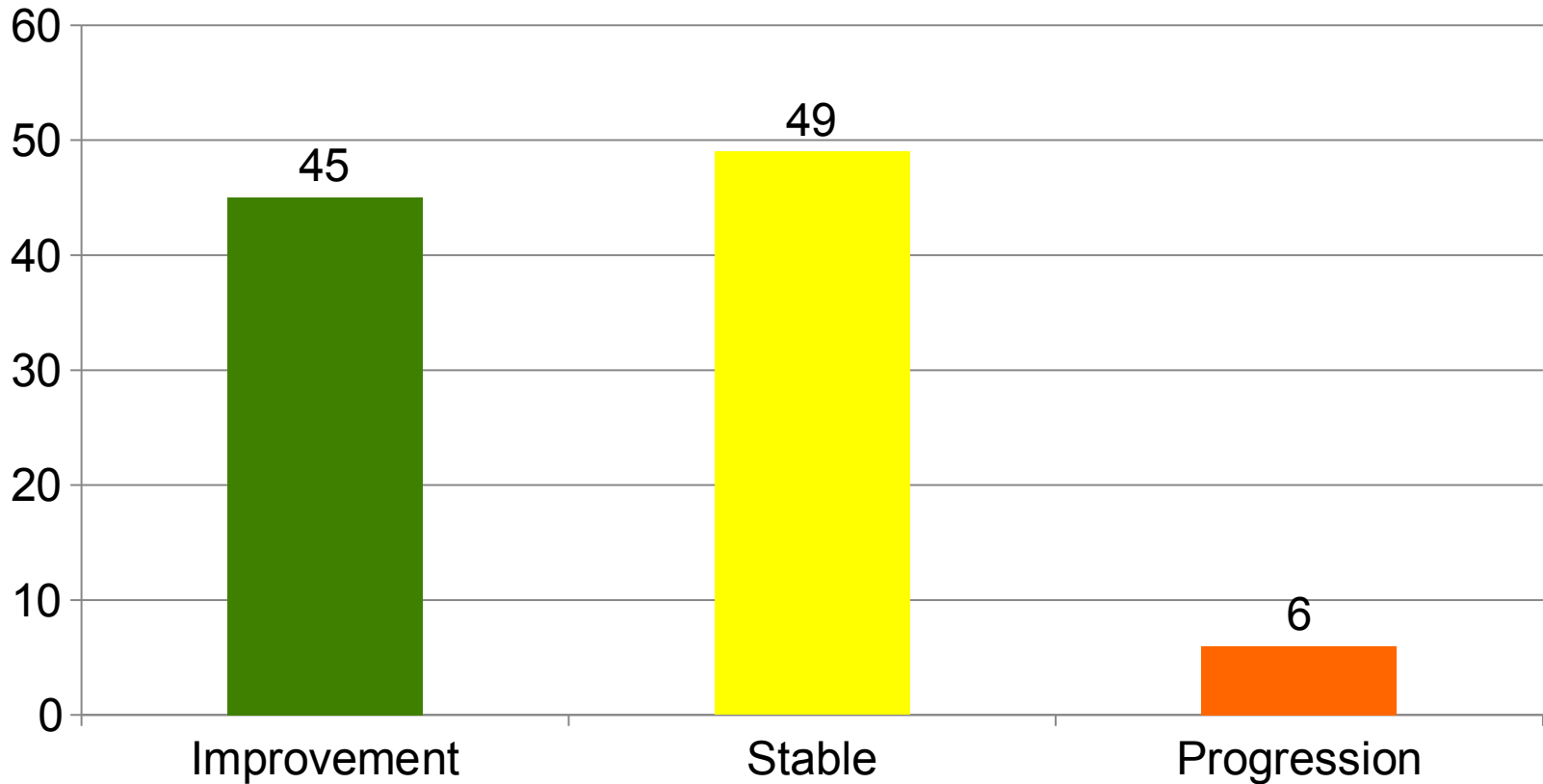
Fibrosis stage on second LB

- 4
- 3
- 2
- 1
- 0

Mean rate of fibrosis regression:
 0.28 ± 0.03 unit/yr

Regression of fibrosis in SVR patients is slow

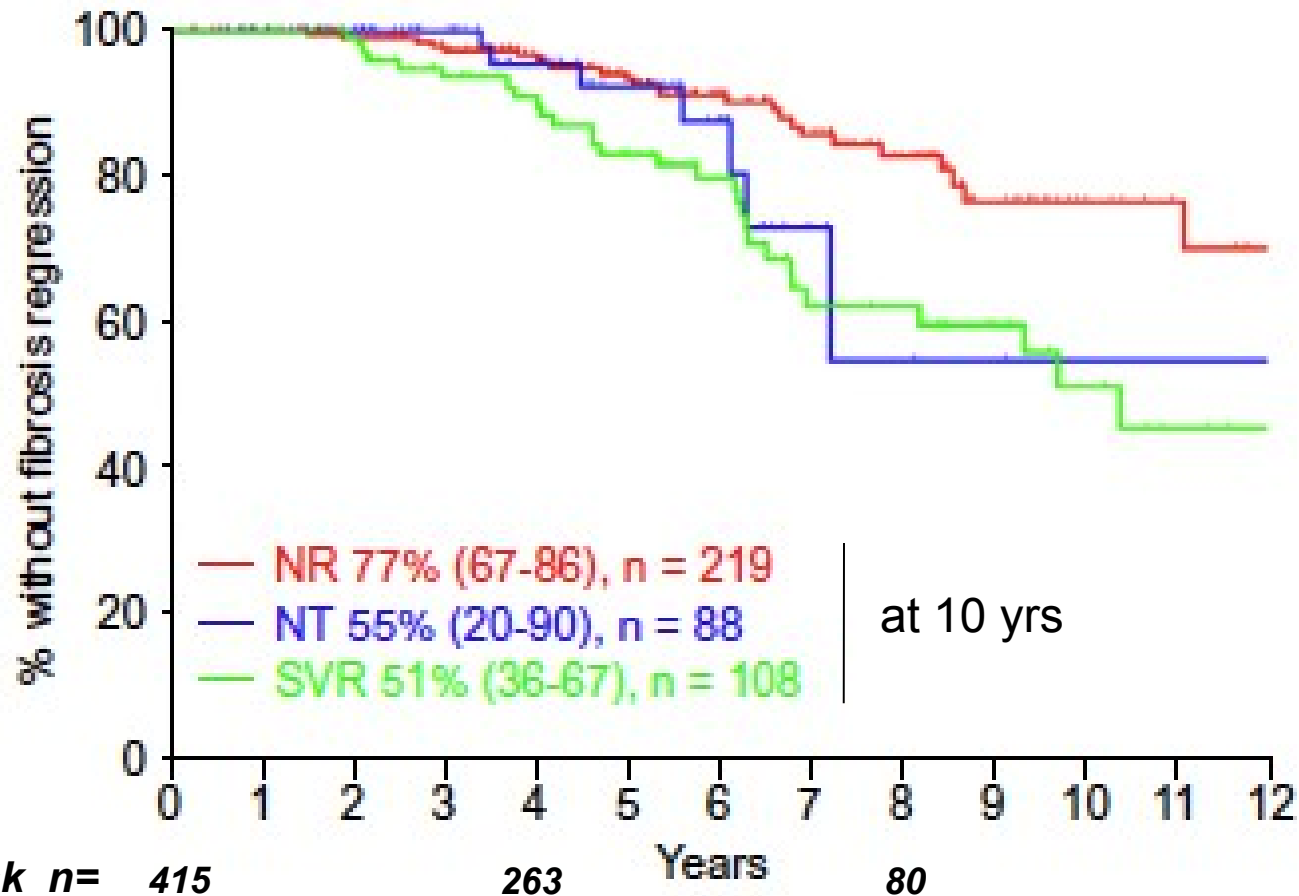
97 SVR patients with paired LB, 5.8 yrs



Long term fibrosis outcomes in SVR patients according to non invasive markers

933 HCV patients with paired Fibrotest™, median FU 5.3 yrs

415 patients with advanced fibrosis



Patients at risk n= 415

Plan

The durability of SVR with DAAs regimens

Liver-related morbidity/mortality in SVR patients

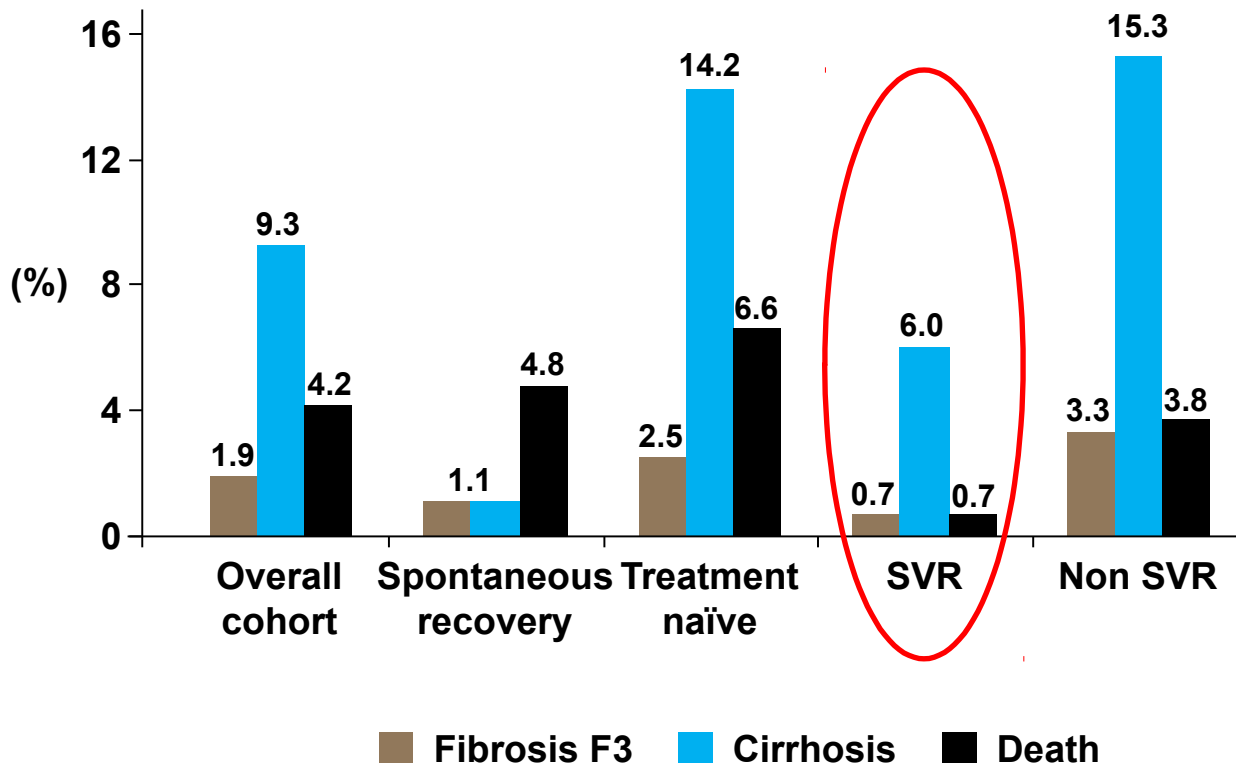
Long term fibrosis outcome in SVR patients

Predictors of liver disease outcome in SVR patients: the role of comorbidities

Monitoring of SVR patients: the value of non invasive markers

Overweight is a risk factor of cirrhosis occurrence in SVR patients

German HCV (1b)-contaminated anti-D cohort:
Clinical outcome after 35 yrs follow-up



Overall survival was significantly enhanced after SVR, compared to treatment-naïve patients or non-SVR ($p=0.027$)

Independent factors associated with cirrhosis

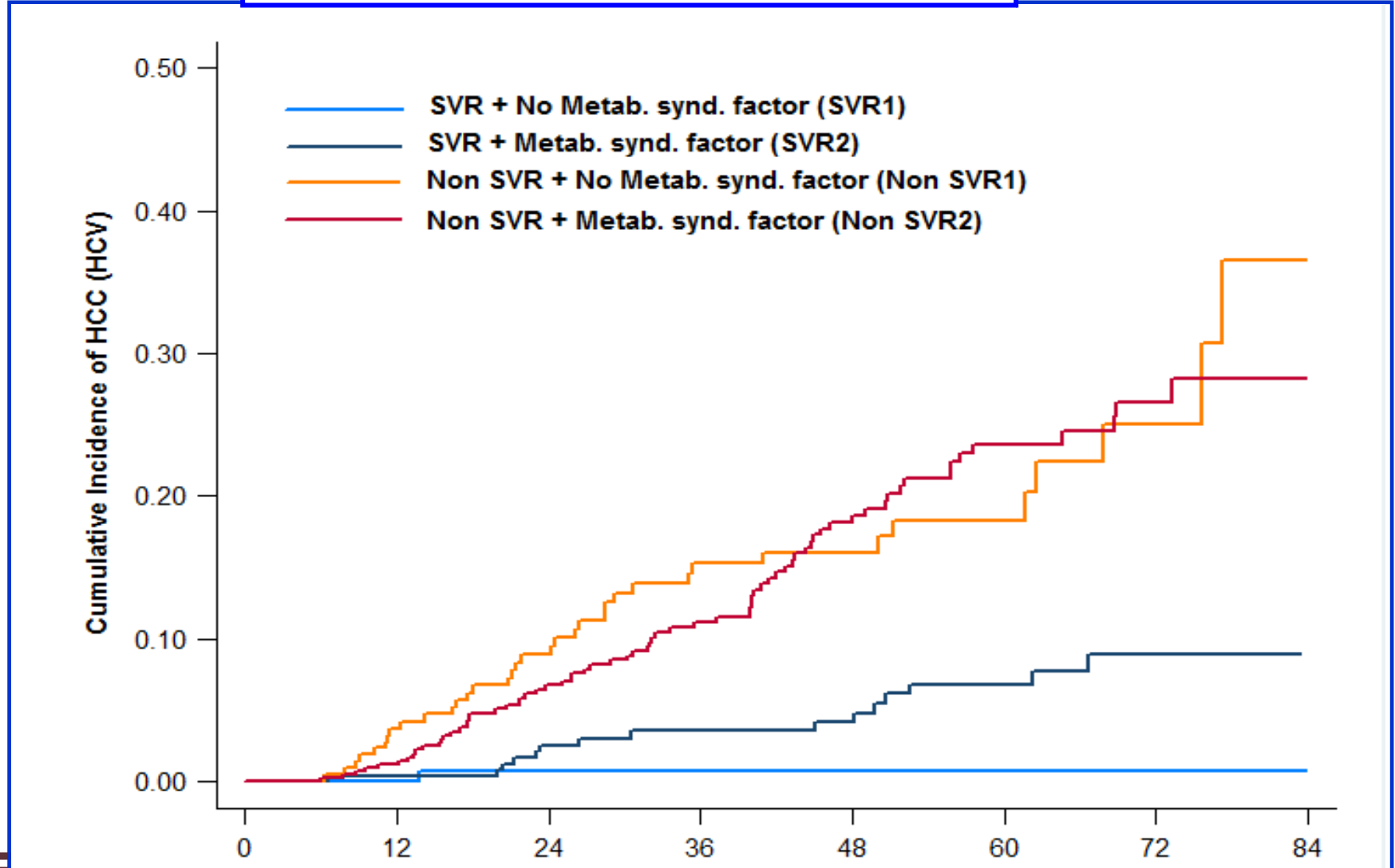
- No response to treatment
- No spontaneous recovery
- **BMI >25 kg/m² (RR: 1.125)**

Risk factors of HCC following SVR

	SVR patients	Follow-up (yrs)	Risk factors
Chang 2012	871	3.4	-Age -Fibrosis -Post SVR AFP
Arase 2013	1751	8.1	-Age -Male -Alcohol -Diabetes
Oze 2014	1425	3.3	-Age -Post SVR AFP
Yamashita 2014	562	4.8	-Age -Fibrosis -Alcohol -Post SVR AFP
Huang 2014	642	4.4	-Age -Fibrosis -Diabetes
Chang 2015	801	5.0	-Age -Fibrosis -Post SVR AFP

Metabolic syndrome and risk of HCC in SVR cirrhotic patients

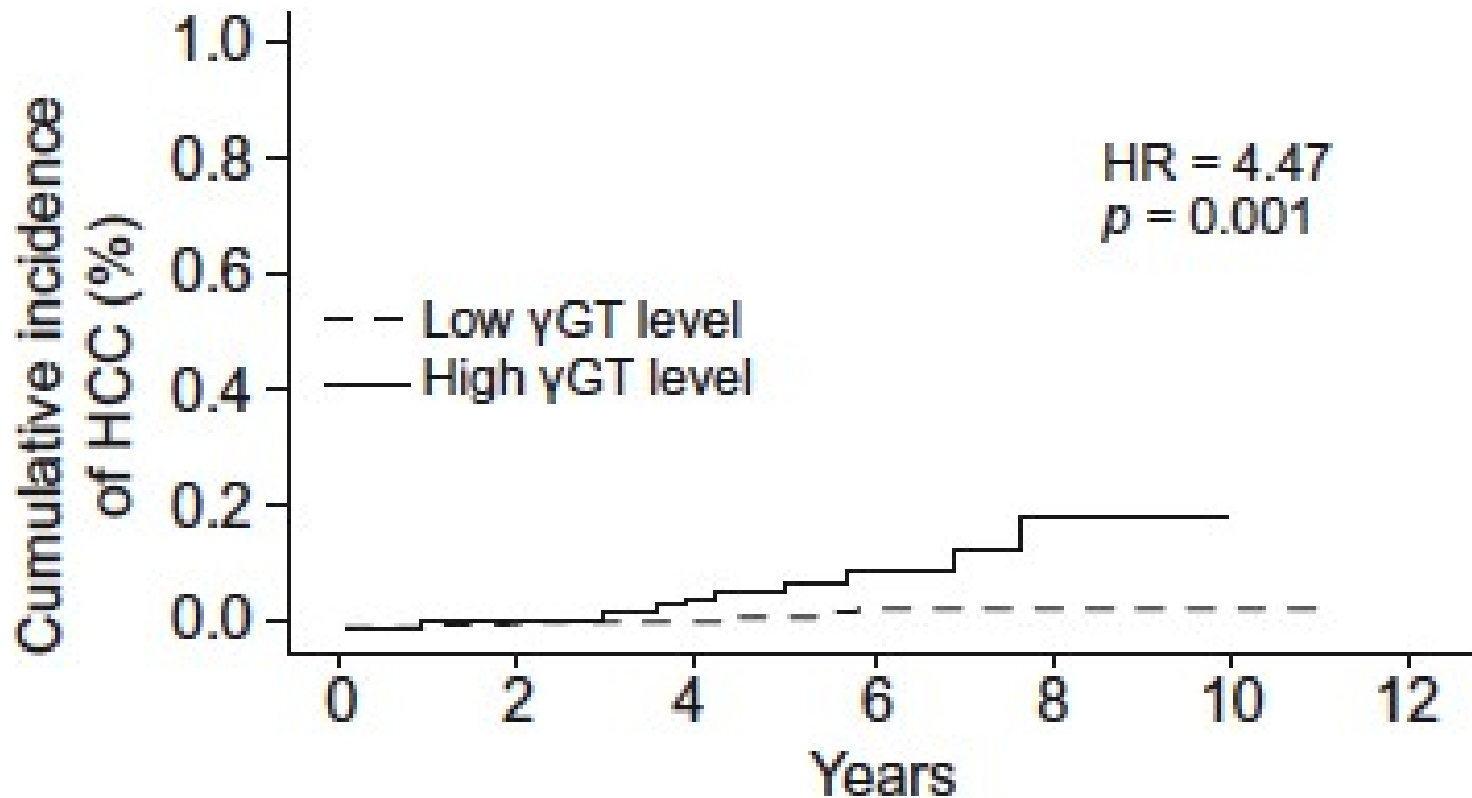
Risk of HCC according to SVR and Met S



Risk factors of HCC following SVR in non cirrhotic patients

556 non-cirrhotic patients with SVR

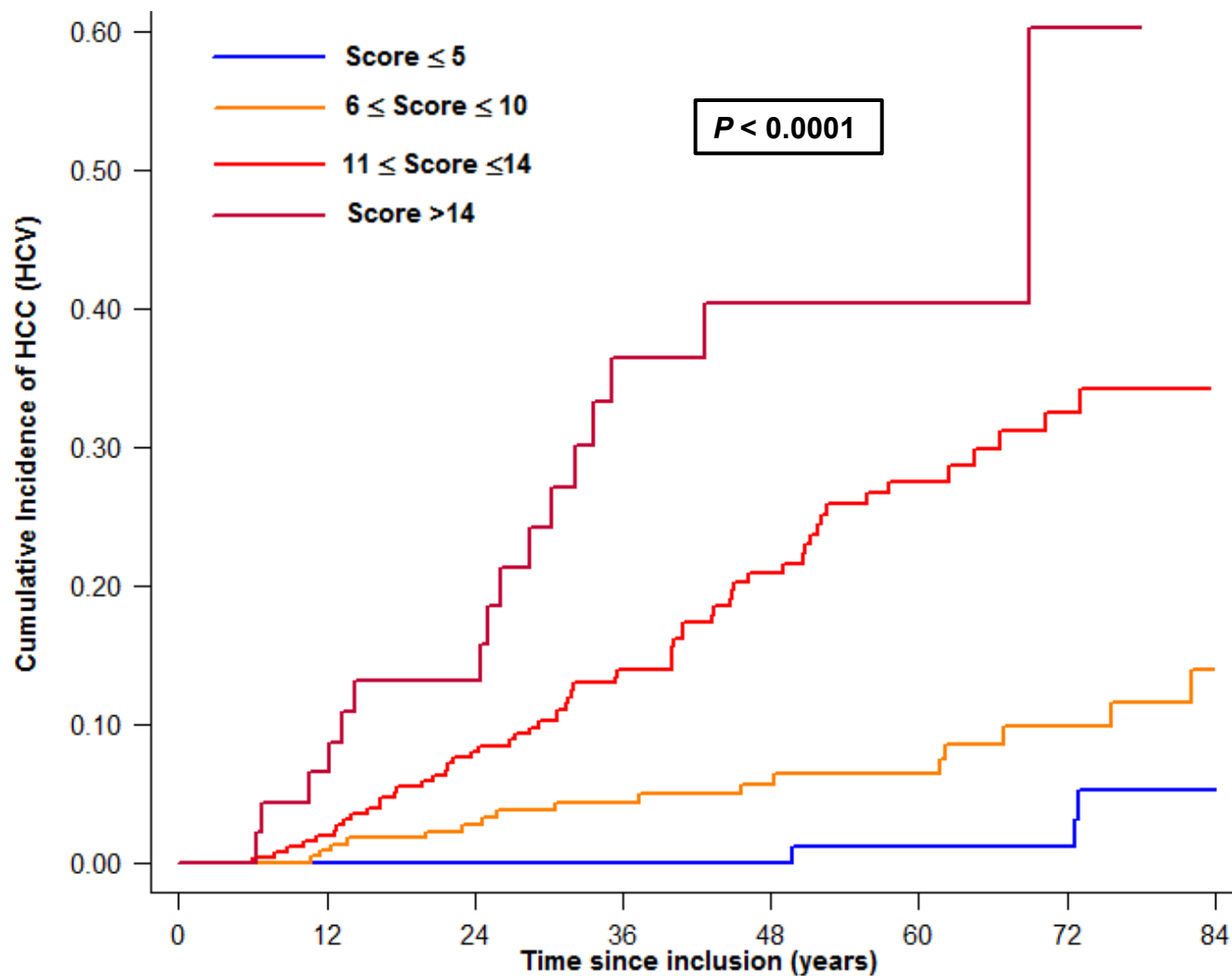
Predictive factors of HCC : age, GGT, type 2 diabetes and APRI



Predictive score of HCC occurrence in cirrhotic patients

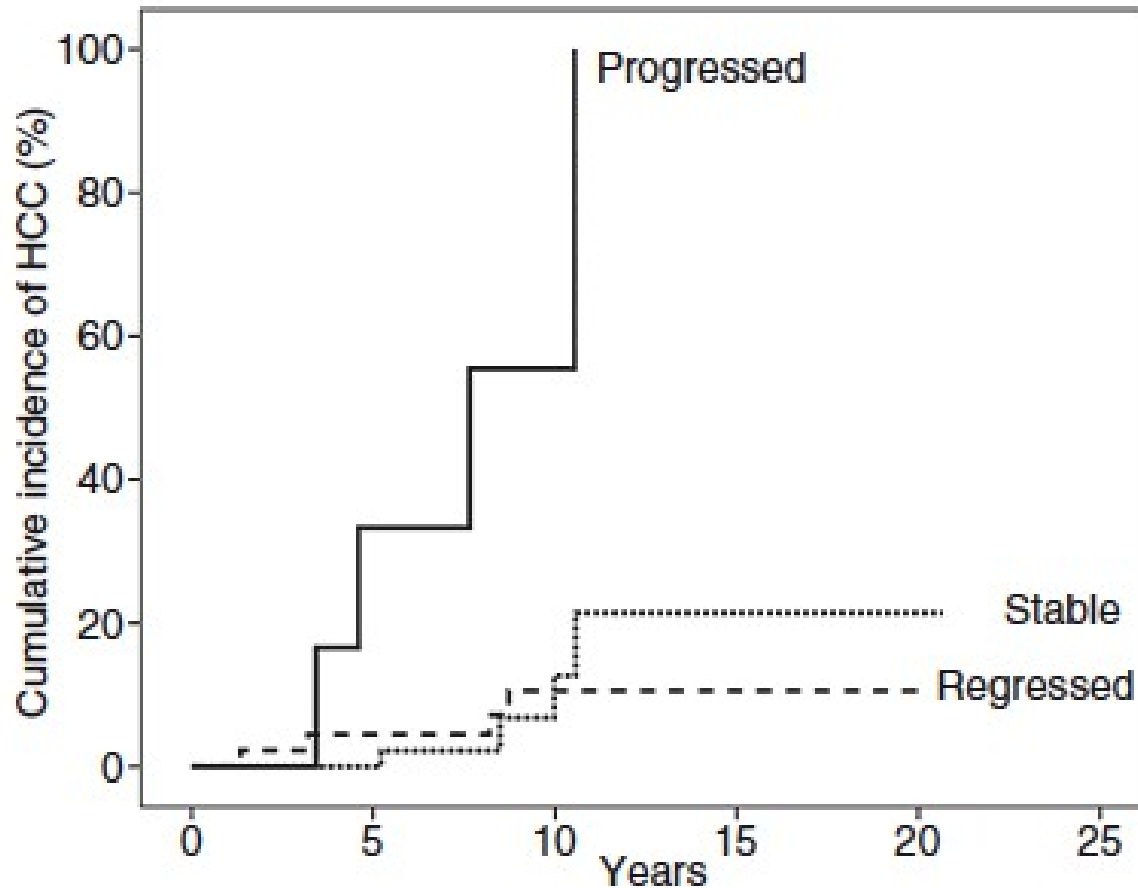
Independent predictors: Age>50yrs, Alcohol, GGT>N, platelets, SVR

Score ≤ 5 : low risk; 6 -10 : moderate risk; 11-14: high risk; > 14: very high risk

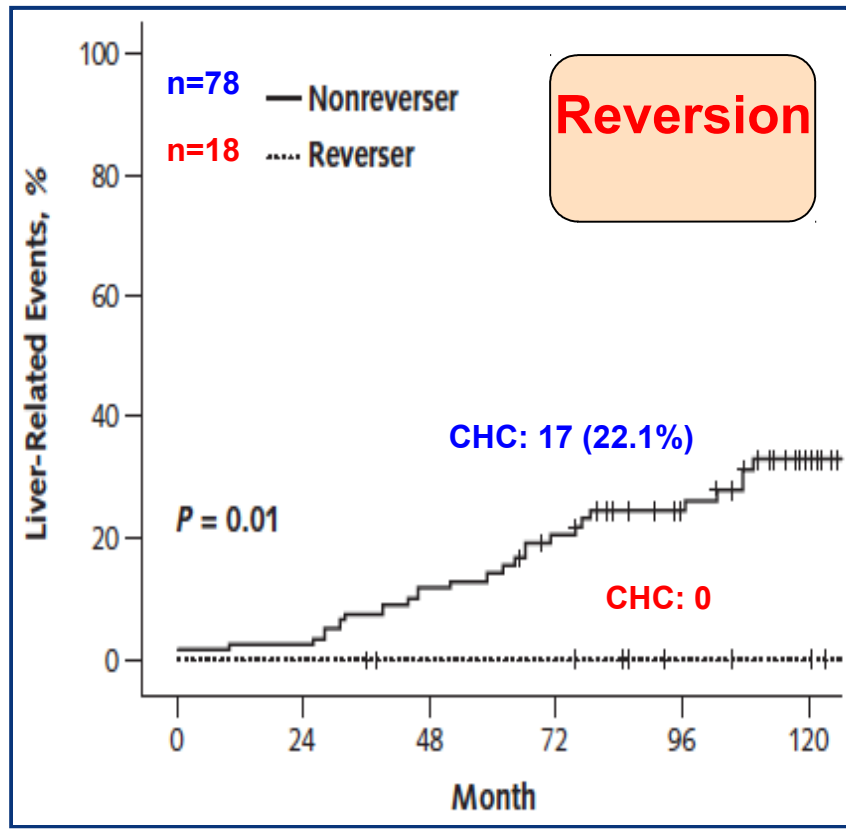
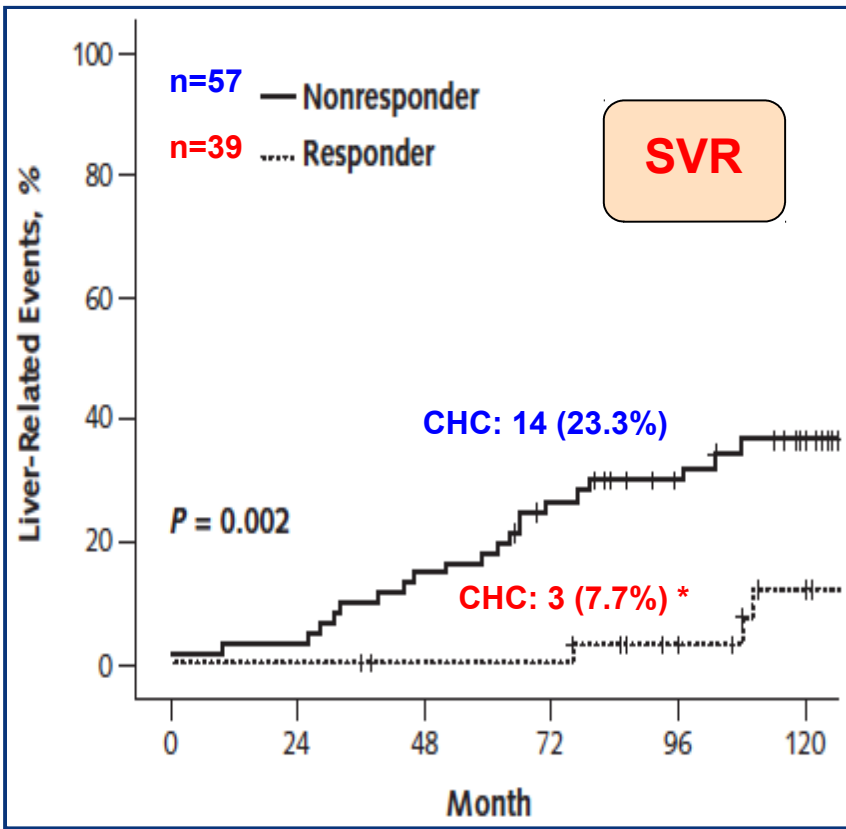


Progression of fibrosis is associated with HCC occurrence in SVR patients

97 SVR patients with paired LB, 5.8 yrs



Reversion of cirrhosis and clinical outcome



Plan

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Liver-related morbidity/mortality in SVR patients

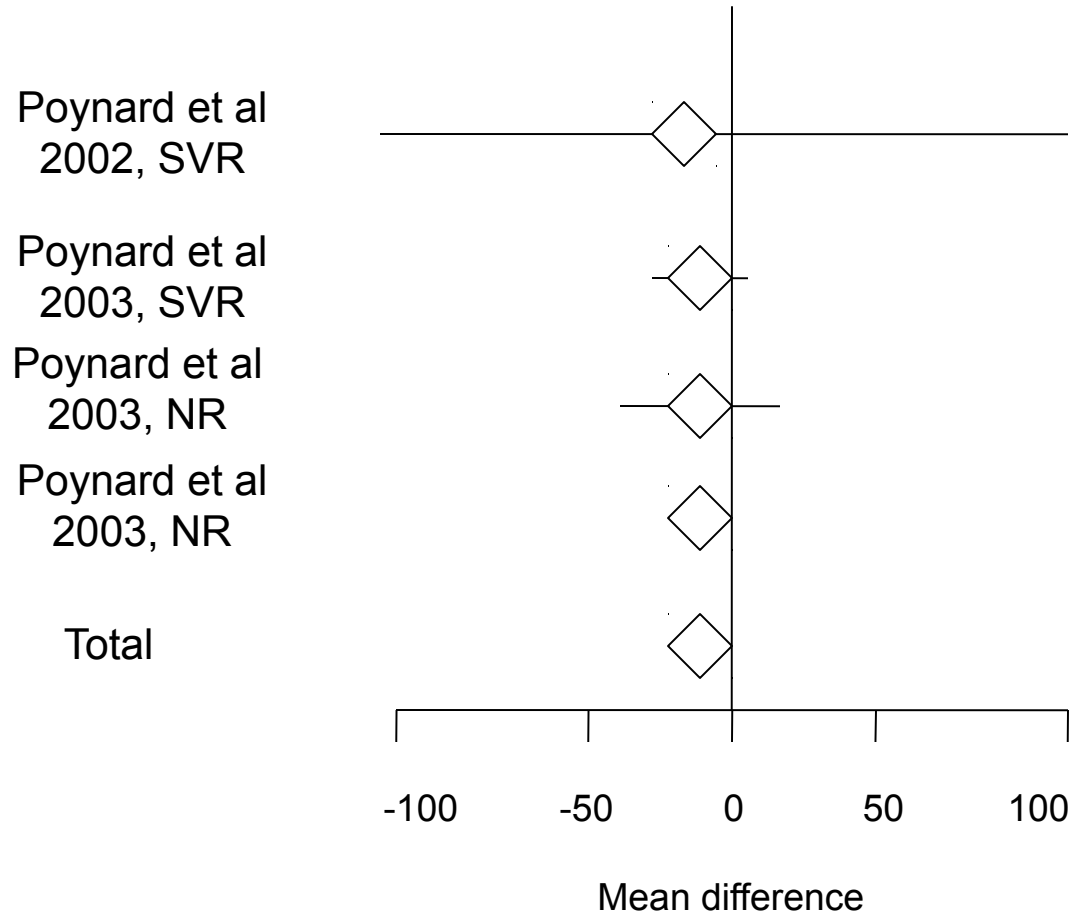
Long term fibrosis outcome in SVR patients

Predictors of liver disease outcome in SVR patients: the role of comorbidities

Monitoring of SVR patients: the value of non invasive markers

Difference between biopsy and FibroTest® estimates of fibrosis progression in treated patients

134 patients treated with IFN and 352 treated with IFN+RBV

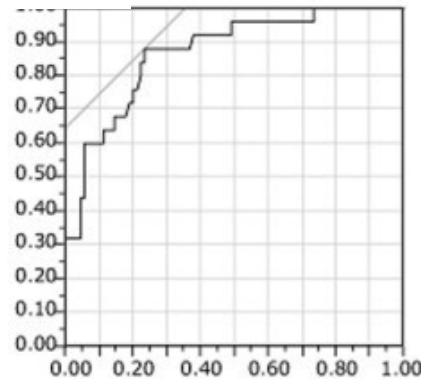


Accuracy of APRI, FIB-4 and Forns index at post-SVR for predicting fibrosis in the second liver biopsy

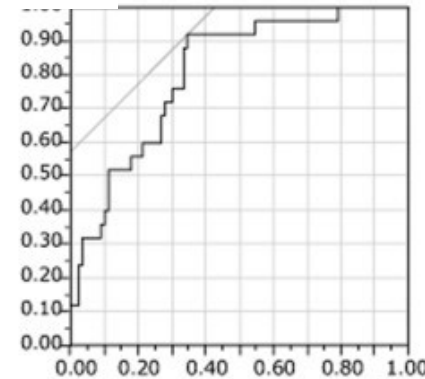
115 SVR patients with control liver biopsy at 5 yrs

Differentiation of moderate to advanced fibrosis (F2-4) from mild fibrosis (F0-1)

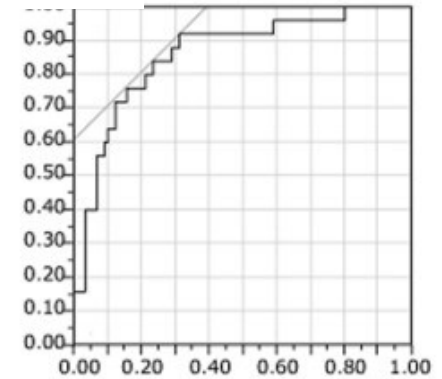
A) APRI



FIB-4



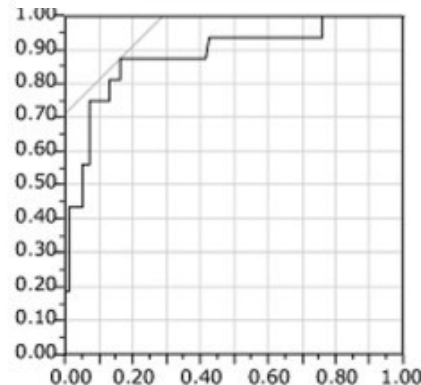
Forns



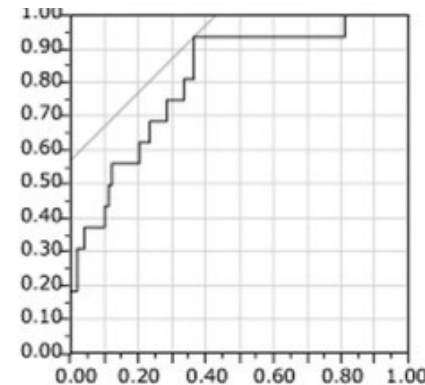
ROC > 0.8
Accuracy > 70%

Differentiation of advanced fibrosis (F3-4) from mild to moderate fibrosis (F0-2)

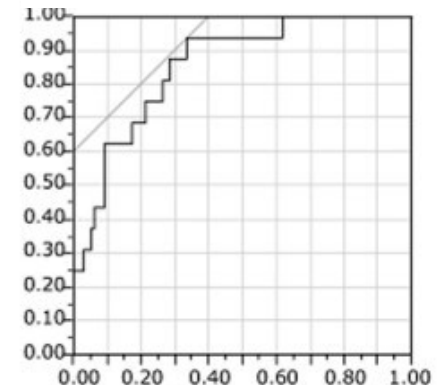
A) APRI



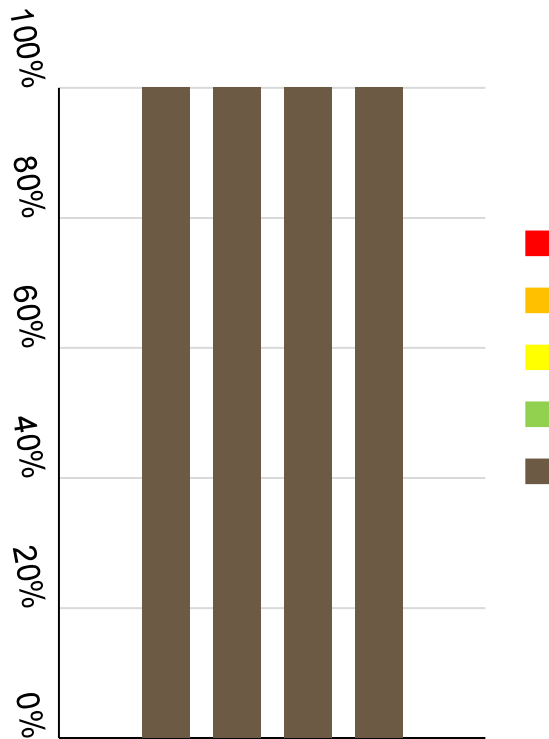
FIB-4



Forns



Accuracy of fibroscan following SVR

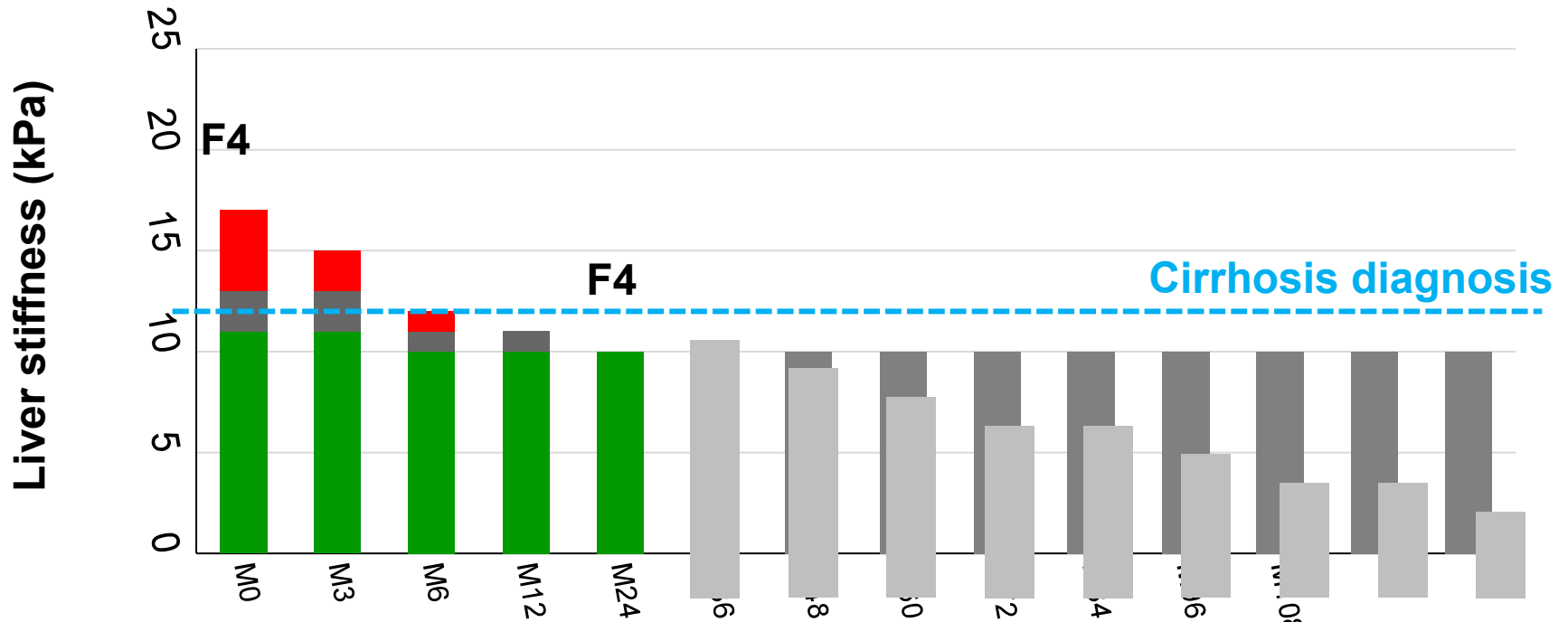


33 biopsy-proven cirrhotic CHC patients with SVR
Liver biopsy + LSM 61 (48-104) months after SVR

	F0-3	F4
TE <12 kPa	19	5
TE ≥12 kPa	1	8

Liver stiffness and antiviral treatment: lower cut-off for cirrhosis diagnosis?

■ Fibrosis ■ Steatosis ■ Inflammation



Take-Home Message

- After the cure of HCV infection, regression of fibrosis varies and the risk of liver-related complications remains, even in the absence of cirrhosis.
- Comorbidities such as diabetes, obesity or alcohol consumption can play a major role in the outcome of liver disease in SVR patients and should be managed.
- Although not currently recommended in guidelines, non-invasive tests could be useful for assessing the outcome of fibrosis in SVR patients without cirrhosis.
- Screening for HCC after HCV cure is recommended in patients with extensive fibrosis.

Baseline

F0/F1

F2/F3

Cirrhosis

Antiviral tt

SVR12

SVR12

SVR12

W48FU

**PCR
NIT=F0/F1**

**PCR
NIT=F2/F3**

PCR

Persistent risk factors

IVDU, MMS

**Age > 60, GGT
Alcohol, obesity, diabetes**

-

NIT/yr

+

**Lifestyle change
Control of diabetes
LB if abnormal LFT**

US/6mo

1 PCR/yr

