

# HEPATITIS C

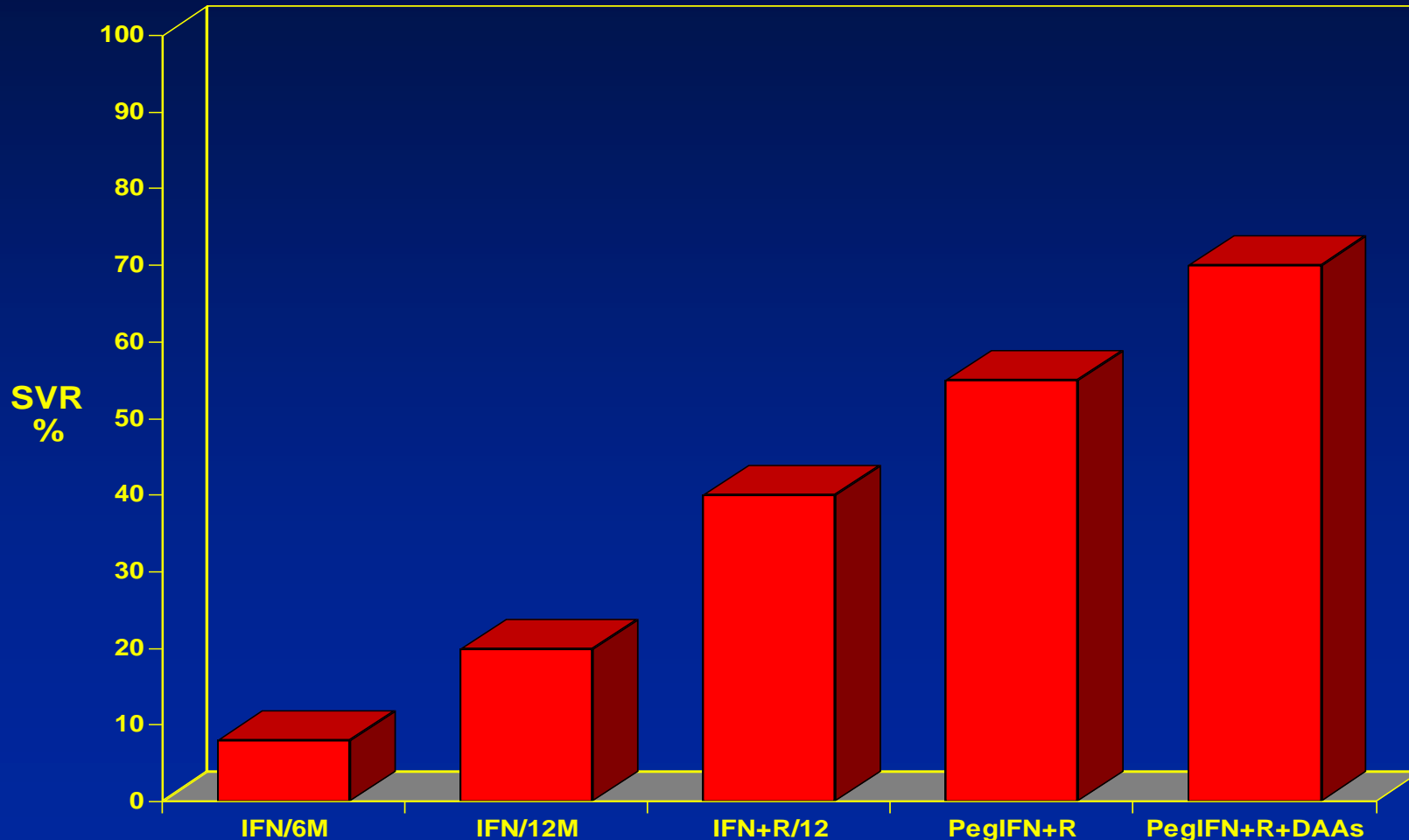
## Long-term Outcome after Treatment

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Service de Gastroentérologie

# Chronic Hepatitis C

## *SVR according to treatment*



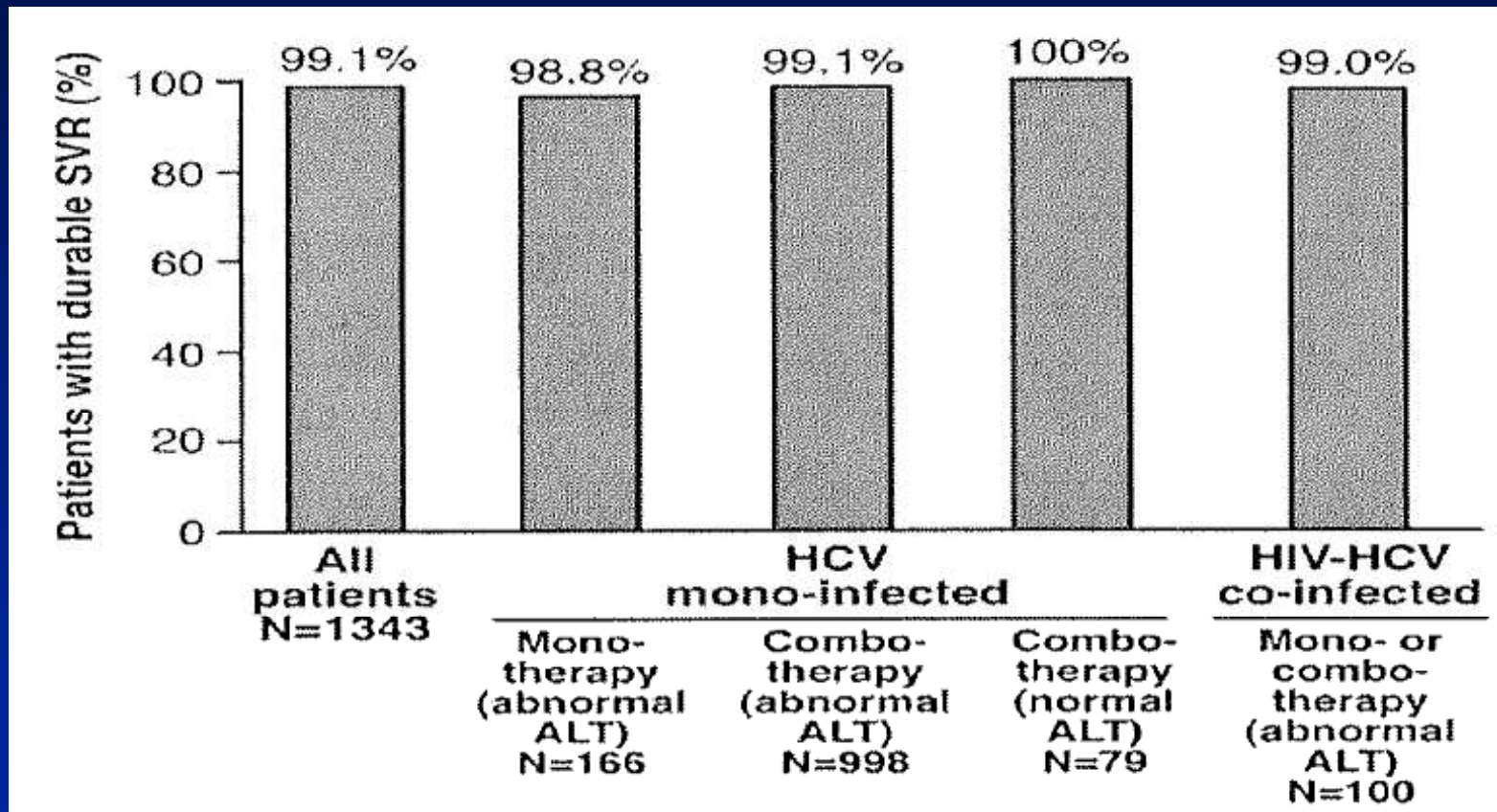
# L-T Outcome after TT for HCV

## *Prognosis and Clinical Outcomes*

- **SVR = virologic cure?**
- **Persisting side effects of treatment?**
- **Risk of cirrhosis and/or HCC depending on treatment results?**
- **Improvement of liver morbidity and mortality?**
- **Impact on quality of life and overall survival?**

# L-T Outcome after TT for HCV

## *Durability of SVR?*



Mark G. Swain et al. Gastroenterology 2010 ;139 :1593-1601

# L-T Outcome after TT for HCV

## *Durability of SVR?*

- Late recurrence of viremia < 1%
- 1,8 year after EOT (1,1 - 2,9)
- Independent of TT, HIV-coinfection, ALT levels
- Case reports in immune suppressed patients but prolonged SVR after LT
- HCV RNA + on liver histology in 2/114 patients but undetectable in serum (1300 samples / 334 pts) and PBMCs (156 specimens)

S. Maylin et al. Gastroenterology 2008 ;135 :821-829

- True recurrence >< reinfection?

# L-T Outcome after TT for HCV

## *Persistent Adverse Effects of IFN?*

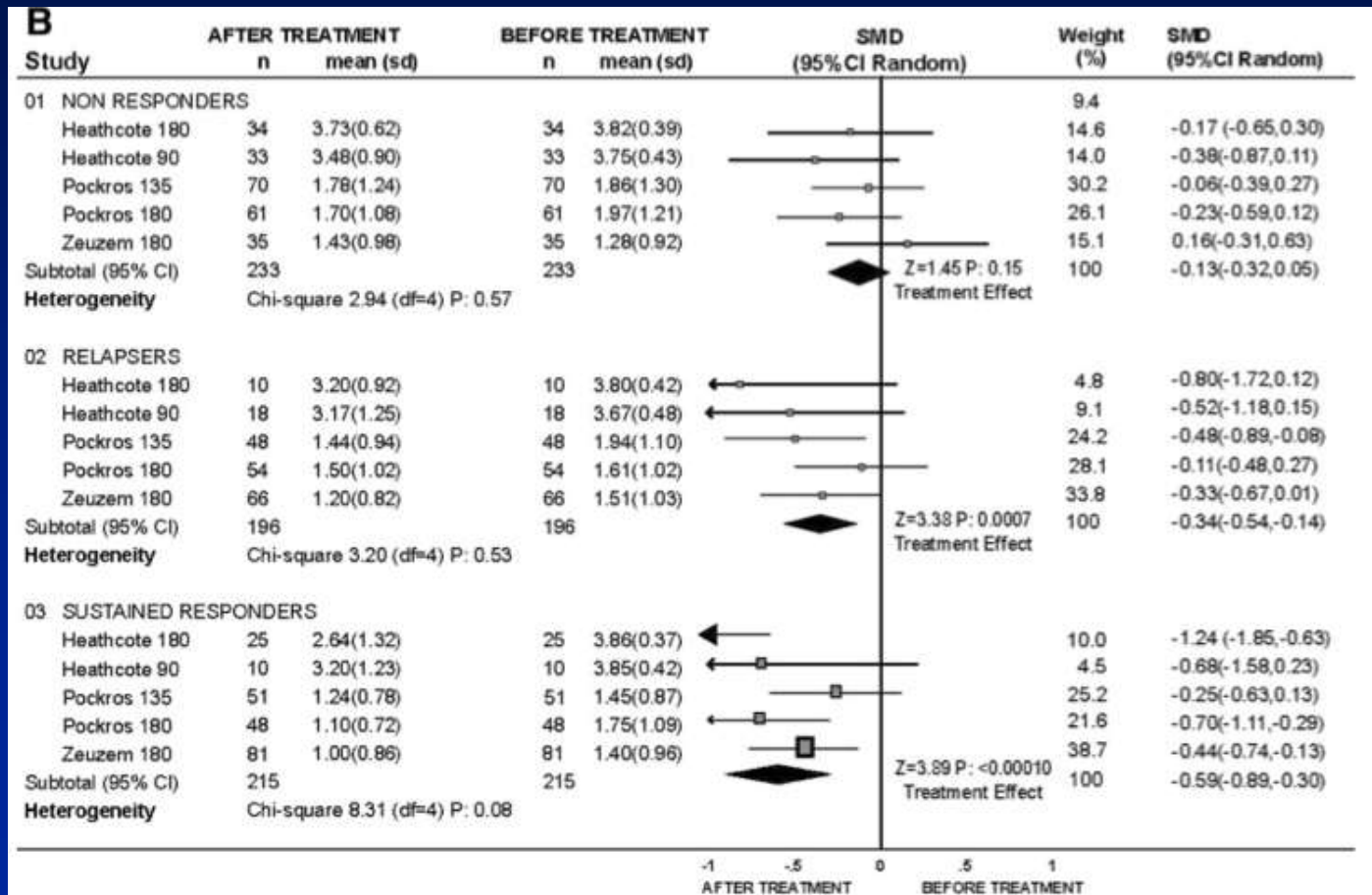
- **Autoimmune diseases**
  - Hypothyroidism: 3 - 4%
  - Hyperthyroidism
  - Type 1 diabetes: 0,1-0,7%
  - Rheumatoid arthritis or SLE
- **Sarcoidosis, interstitial pneumonitis, PHT**
- **Myocardial ischemia and cardiomyopathy**
- **Various ocular disorders up to blindness**

# L-T Outcome after TT for HCV

## *Impact on Fibrosis Progression*

- **Improvement in necrosis and inflammation in 39% to 73 % in 3010 patients (4 studies)**
- **Reduced fibrosis correlated with SVR and treatment with PegINF+R**
- **Benefits in non-responders and relapsers?**
- **Reversibility of cirrhosis in up to 49% patients (F4 => F3)?**

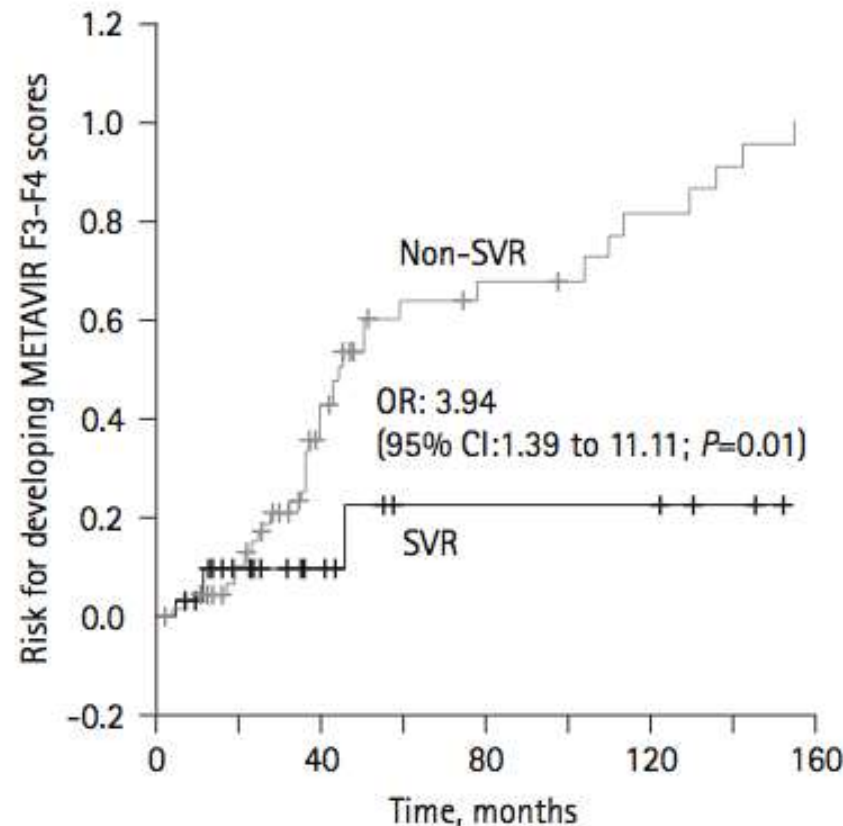
# L-T Outcome after TT for HCV Impact on Fibrosis Progression



# L-T Outcome after TT for HCV

## *Impact on Fibrosis Progression in HIV-Coinfection*

Figure 1. Risk for advanced liver fibrosis stages (Metavir F3-F4) according to virological response after HCV therapy (Kaplan-Meier and Cox regression analyses)



# L-T Outcome after TT for HCV

## *Impact on the Risk of HCC*

- **419 patients treated with IFN/6 months (Osaka HCC Prevention Study Group)**
- **Relative Risk for HCC**
  - SVR: 0,06 ( $p < ,007$ )
  - Relapsers: 0,51 ( $p = ,15$ )
  - Nonresponders: 0,95 ( $p > ,2$ )

# L-T Outcome after TT for HCV

## *Impact on the Risk of HCC*

**Table 2.** Cause of Death

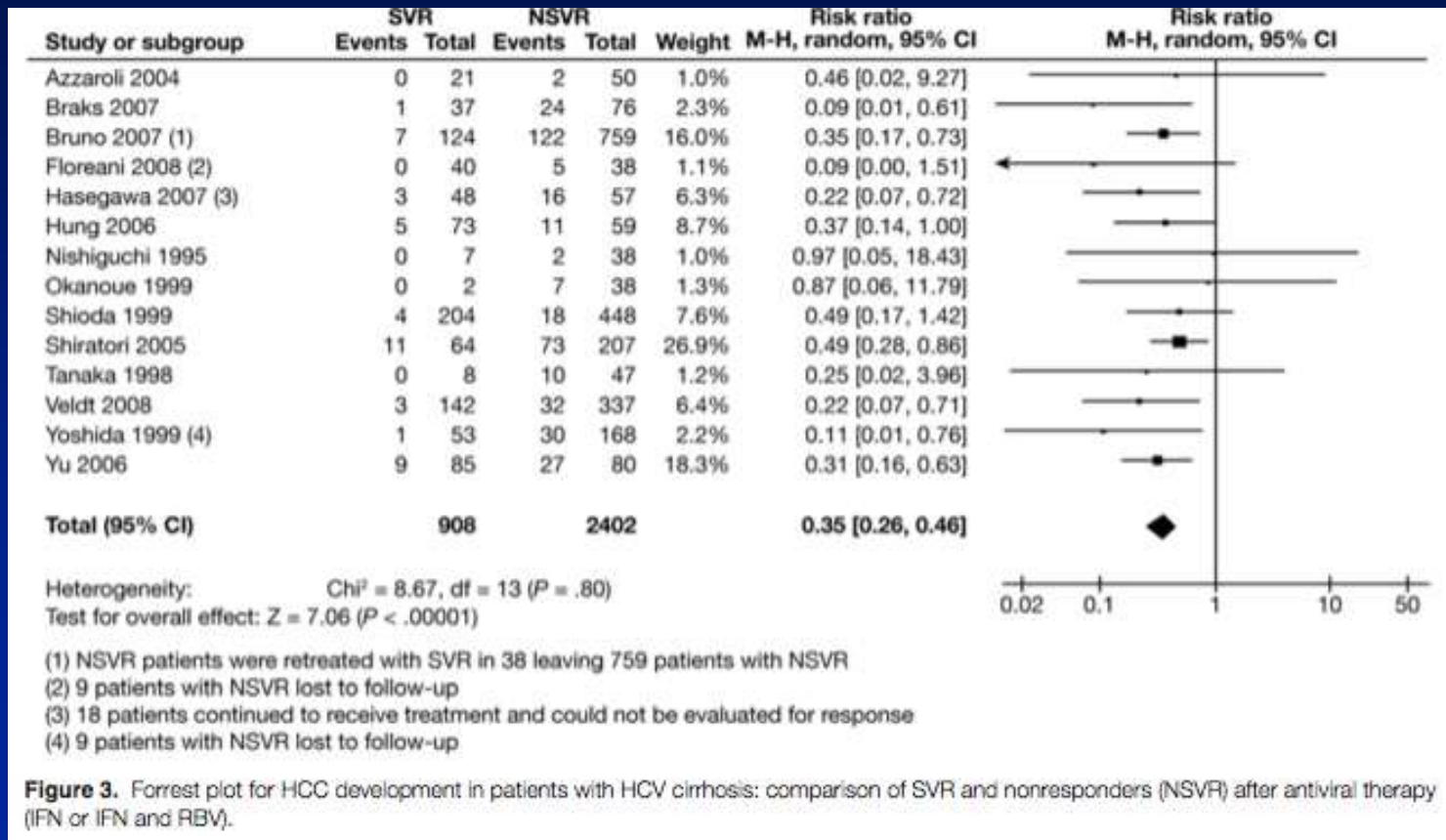
	Untreated (n = 459)	Interferon-treated		
		All (n = 2430)	Sustained response (n = 817)	Nonsustained response (n = 1613)
Deaths, n	30	56	7	49
Liver related, n	23 (77%)	35 (63%)	2 (29%)	33 (67%)
Hepatocellular carcinoma	14	25	1	24
Liver failure	8	4	0	4
GI bleeding	1	6	1	5
Liver unrelated, n	7 (23%)	21 (37%)	5 (71%)	16 (33%)
Malignancies <sup>a</sup>	2	11	4	7
Heart diseases	2	5	0	5
Cerebrovascular diseases	1	3	1	2
Pulmonary disease	1	1	0	1
Injury	0	1	0	1
Unknown	1 <sup>b</sup>	0	0	0

<sup>a</sup>Excluding hepatocellular carcinoma.

<sup>b</sup>Disseminated intravascular coagulation with unknown etiology.

# L-T Outcome after TT for HCV

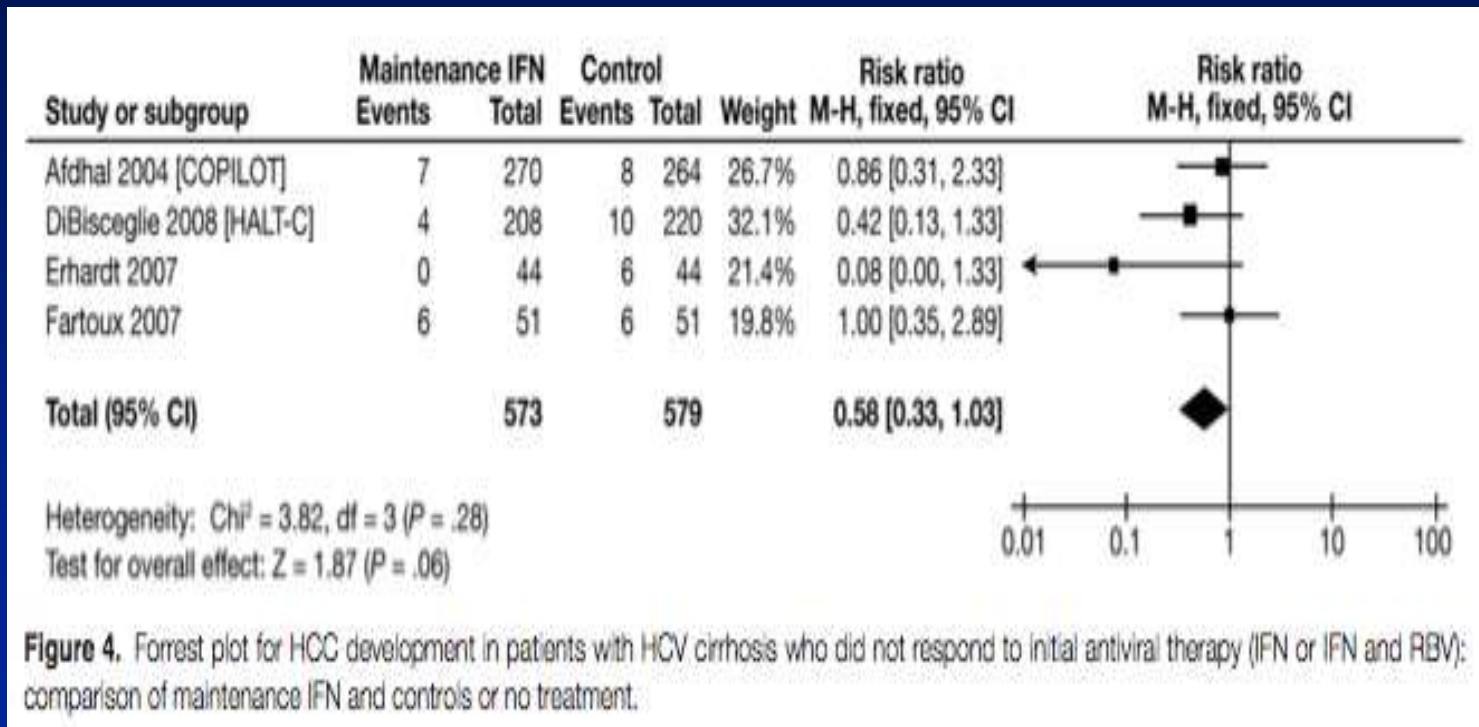
## Impact on the Risk of HCC depending on SVR



**Figure 3.** Forrest plot for HCC development in patients with HCV cirrhosis: comparison of SVR and nonresponders (NSVR) after antiviral therapy (IFN or IFN and RBV).

# L-T Outcome after TT for HCV

## *Impact of Maintenance Therapy in Non-responders with Advanced Fibrosis on the Risk of HCC*



# L-T Outcome after TT for HCV

## *Progression to Decompensated Liver Disease*

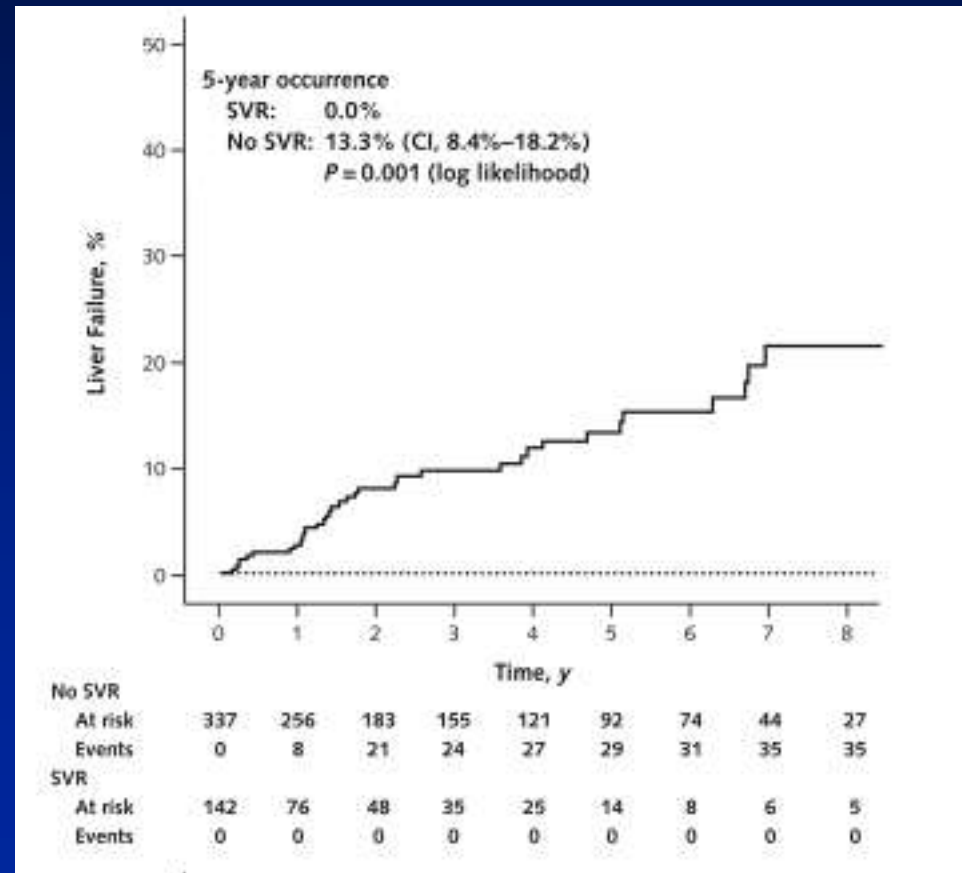
**Table 3** Association between host/viral factors and progression towards liver complications

	Decompensated cirrhosis	HCC	Liver transplantation/death
Age at infection (quartiles)	<0.001	<0.001	<0.001
Gender (males vs females)	0.01	0.06	0.02
Genotype (1 vs non-1)	0.36	0.06	0.05
BMI	0.41	0.74	0.16
Non-response to previous therapy	0.006	0.73	0.096
Fibrosis score at initial biopsy	<0.001	0.001	<0.001

HENCORE cohort: P. Pradat et al. J Viral Hepat. 2007 ;14 :556-563  
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# L-T Outcome after TT for HCV

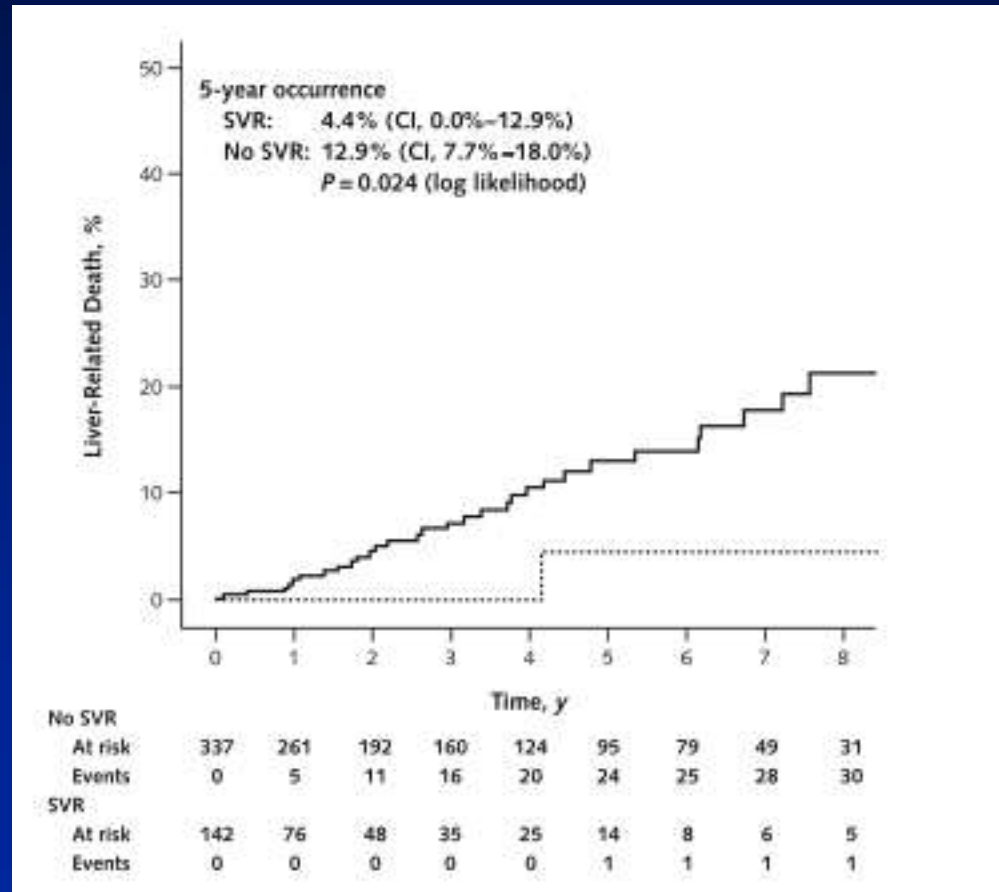
## *Progression to Decompensated Liver Disease*



B.J. Veldt et al. *Annals of Internal Medicine* 2007 ;147 :677-684  
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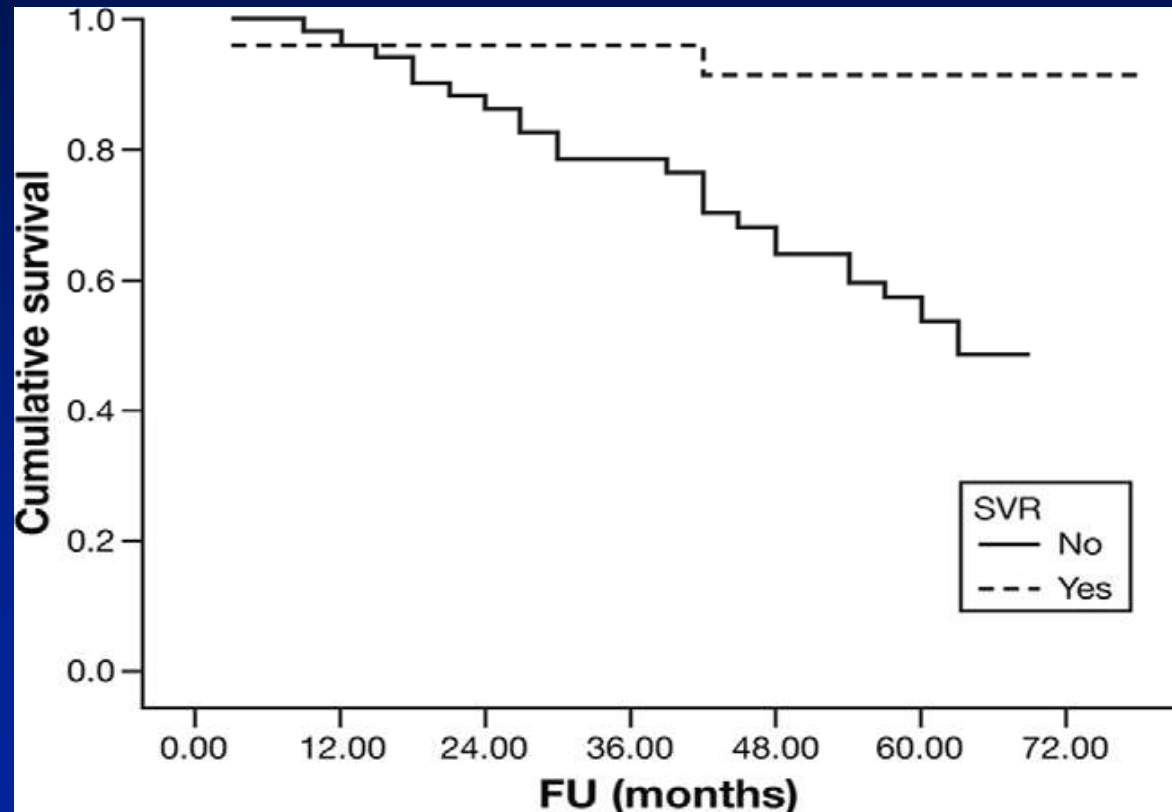
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# L-T Outcome after TT for HCV

## *Progression to Decompensated Liver Disease*



Survival according to SVR in decompensated cirrhosis  
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A. Iacobellis et al. Clinical Gastroenterology and hepatology 2011 ;9 :249-25  
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# L-T Outcome after TT for HCV

## *Impact on Extrahepatic Manifestations*

- **Mixed cryoglobulinemia:**
  - SVR associated with decrease in cryocrit and improvement of clinical manifestations
  - One report of fatal exacerbation and several case reports of new occurrences after SVR
- **Glomerulonephritis:**
  - Case reports of biochemical and clinical improvement
- **Porphyria Cutanea Tarda:**
  - Resolution but also emergence of symptoms on treatment
- **Glucose Intolerance:**
  - 50% reduction of risk of glucose abnormalities in responders (11,4%) compared to non-responders (24,3%)

# L-T Outcome after TT for HCV

*Impact on quality of life an overall survival*

- **SVR seems related to improvement of quality of life assessed by HRQOL questionnaires**
- **Prolonged life expectancy suggested in treated patients particularly those achieving SVR.**

# L-T Outcome after TT for HCV

## *Take Home Messages*

- SVR is durable, probably as close to a virologic cure as it can be.
- Most important long term adverse event of IFN is hypothyroidism.
- SVR slows down fibrosis progression and lowers risk of hepatocarcinoma
- SVR reduces liver morbidity and mortality but risk persists if advanced fibrosis
- SVR improves quality of life and probably overall survival of HCV patients