

CLINICAL IMPACT OF SVR AFTER ANTIVIRAL THERAPY FOR HCV

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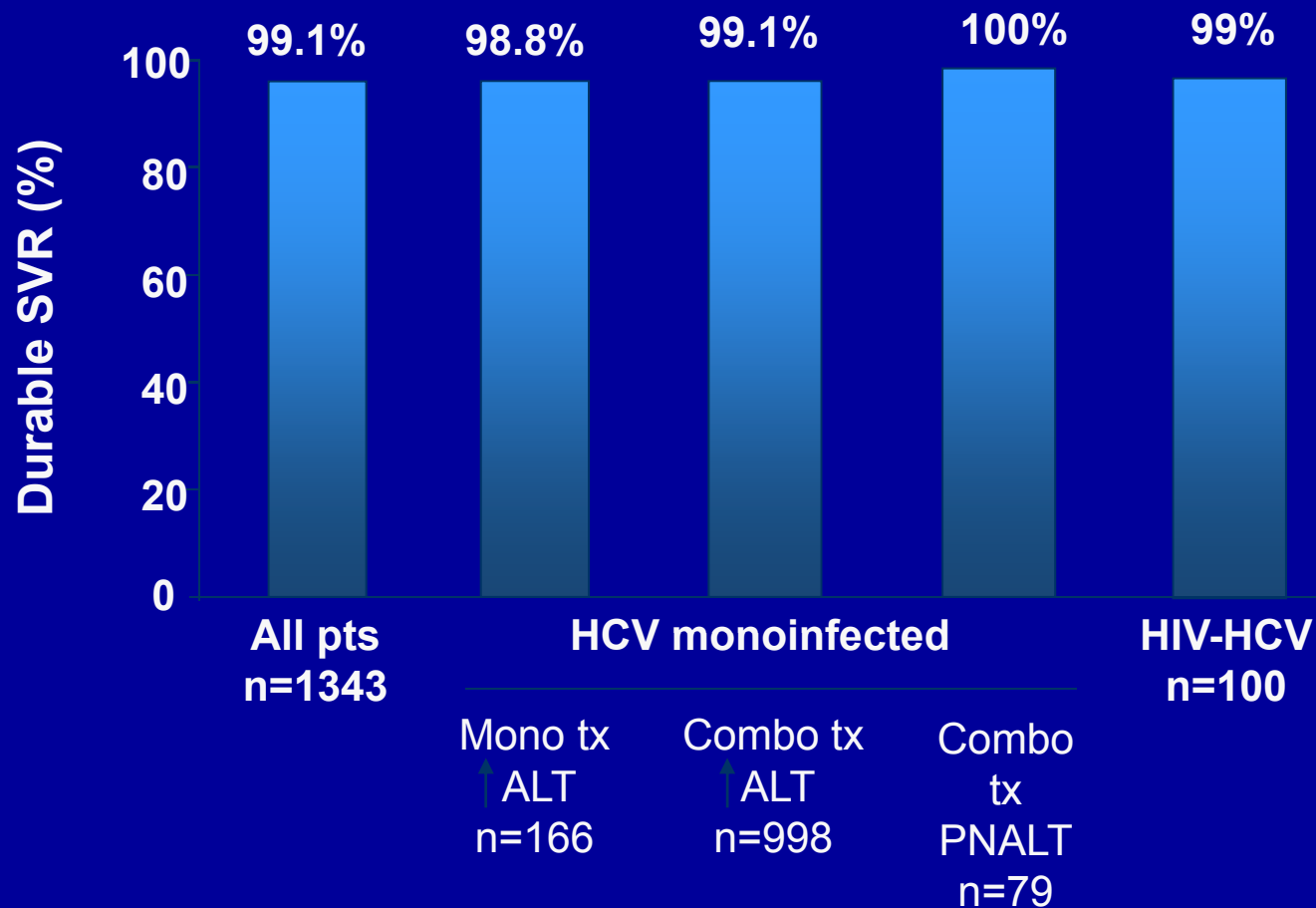
IMPACT OF SVR ON LONG-TERM OUTCOMES IN CHRONIC HCV

Key points of this presentation

- Chronic hepatitis C is curable with HCV eradication
- HCV eradication is predicted by SVR 12-24 wks after therapy
- SVR improves clinical outcomes particularly in patients with advanced fibrosis/compensated cirrhosis
- In cirrhotics, SVR doesn't guarantee completely from the risk of HCC
- The clinical benefit of SVR in mild, non-progressive disease remains unproven
- SVR associates with improvement in extrahepatic HCV related-disorders (metabolic, haematological, ...)

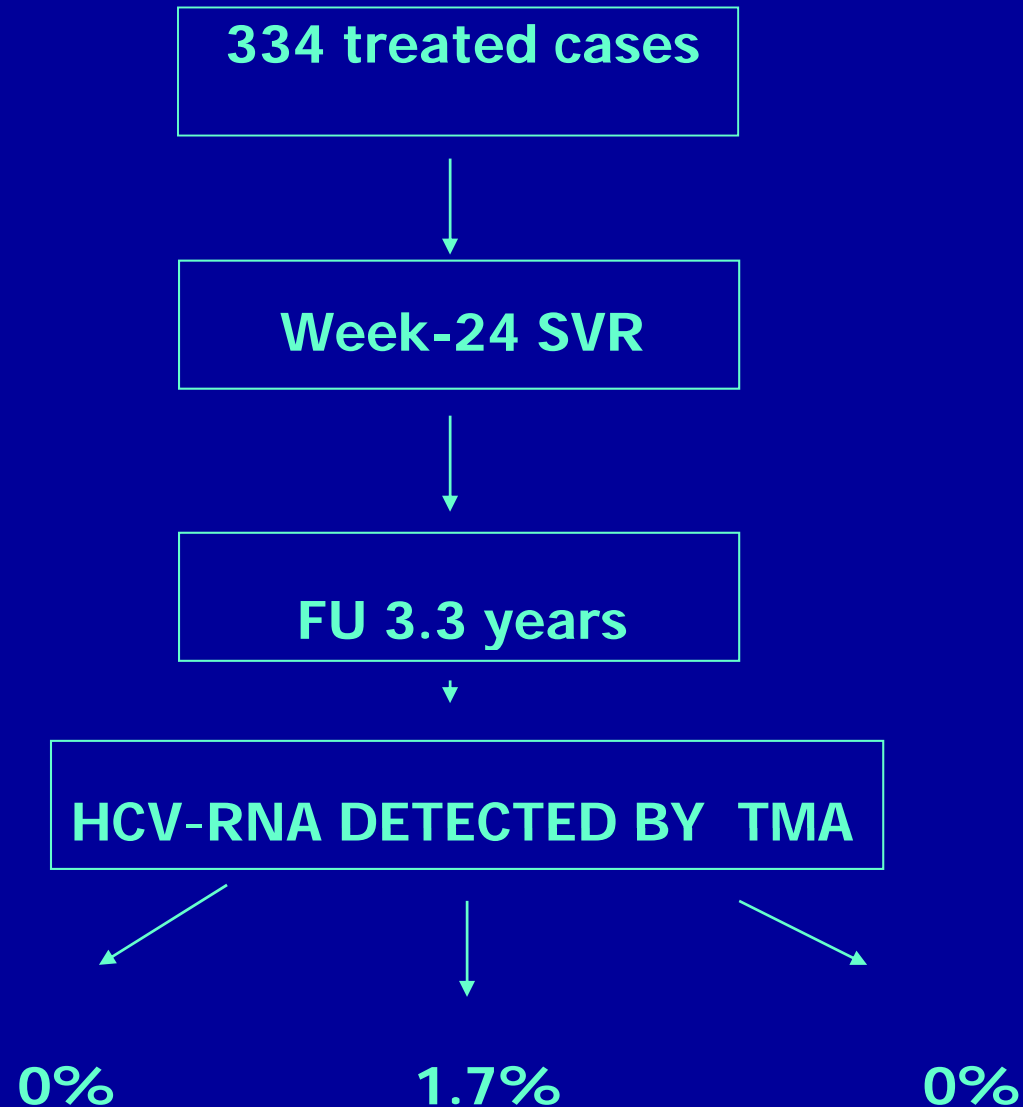
A SVR is Durable in Patients with HCV Infection Treated with PegIFNalpha2a and Ribavirin

Patients outcomes 4 years after therapy



WEEK-24 SVR AND ERADICATION OF HCV

Maylin et al Gastroenterology 2008



POST-TREATMENT TIMING FOR THE PREDICTION OF SVR

573 treated cases → TMA week 4-12-24 post-treatment → SVR-24 w 71%

HCV-RNA negative by

PPV for SVR

SVR-week 4

96% (93.1-98.1)

SVR-week 12

99.7 (99.1-100%)

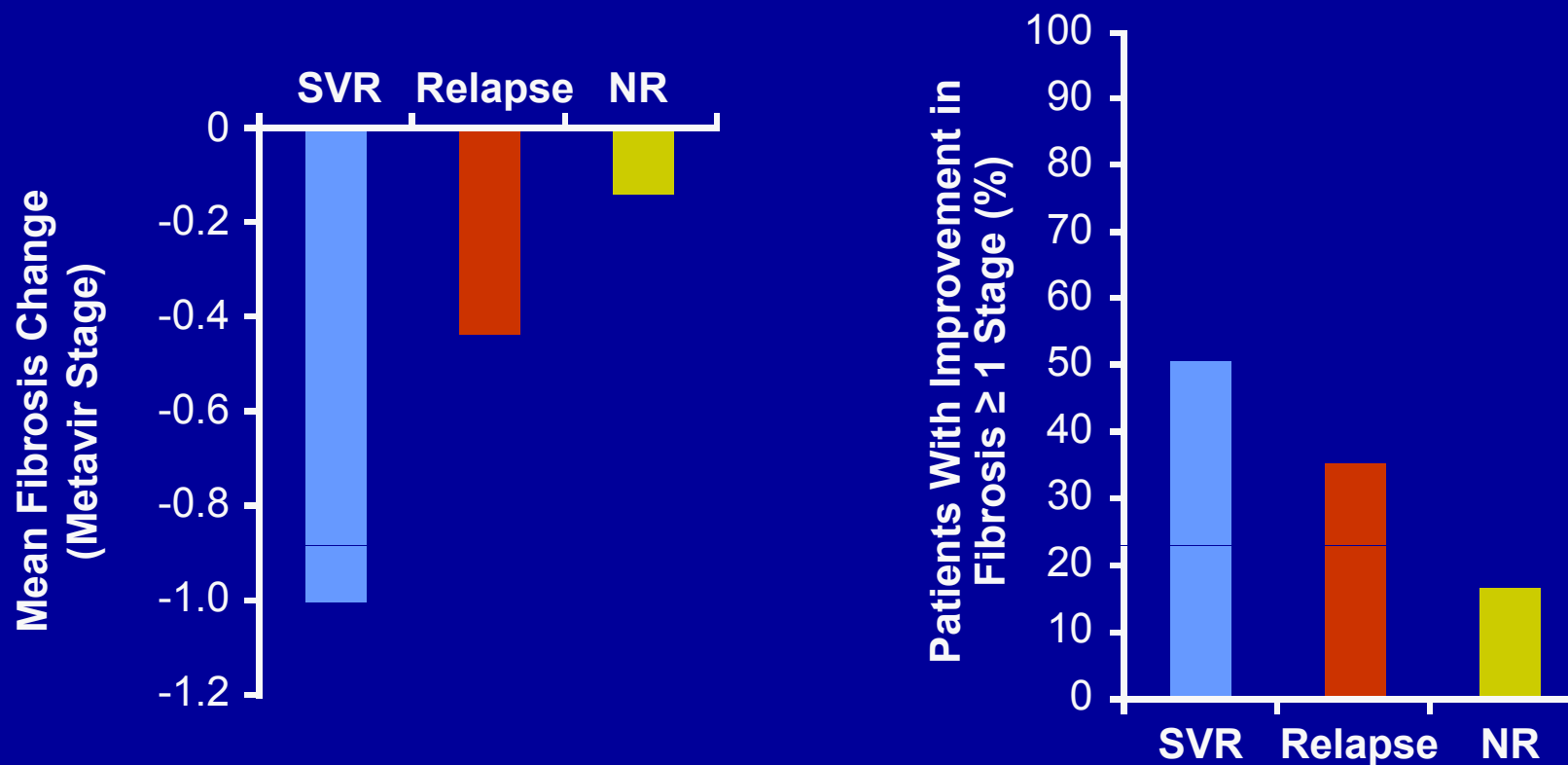
SVR-week 24

100%

Martinot-Peignaux, 2010

Improvement in Fibrosis at Week 72 Following Start of HCV Therapy

Varied With Response to Treatment



SVR Associated With Improved Histologic Outcome

- 150 patients with SVR underwent long-term follow-up
- 128 patients reached 4-year follow-up, biopsy offered to those with fibrosis \geq F2
- Of 49 patients with paired biopsies:
 - 82% experienced decrease in fibrosis score,
 - 92% decrease in activity index
 - 20% had normal to near-normal histology

LIVER STIFFNESS IN RELATION TO SVR / non-SVR

Liver biopsy
before therapy

Liver stiffness 4 years after therapy

	SVR	non-SVR	p
F0 / F1	5.3 (4.4-5.6)	6.1 (4.7-11.1)	0.56
F2 / F3	5.4 (4.3-6.8)	9.4 (8.6-10.1)	<0.001
F4	6.8 (6.0-10.1)	24.0 (17.0-36.4)	<0.001

Anderson et al., Europ J Gastro Hepatol, 2011

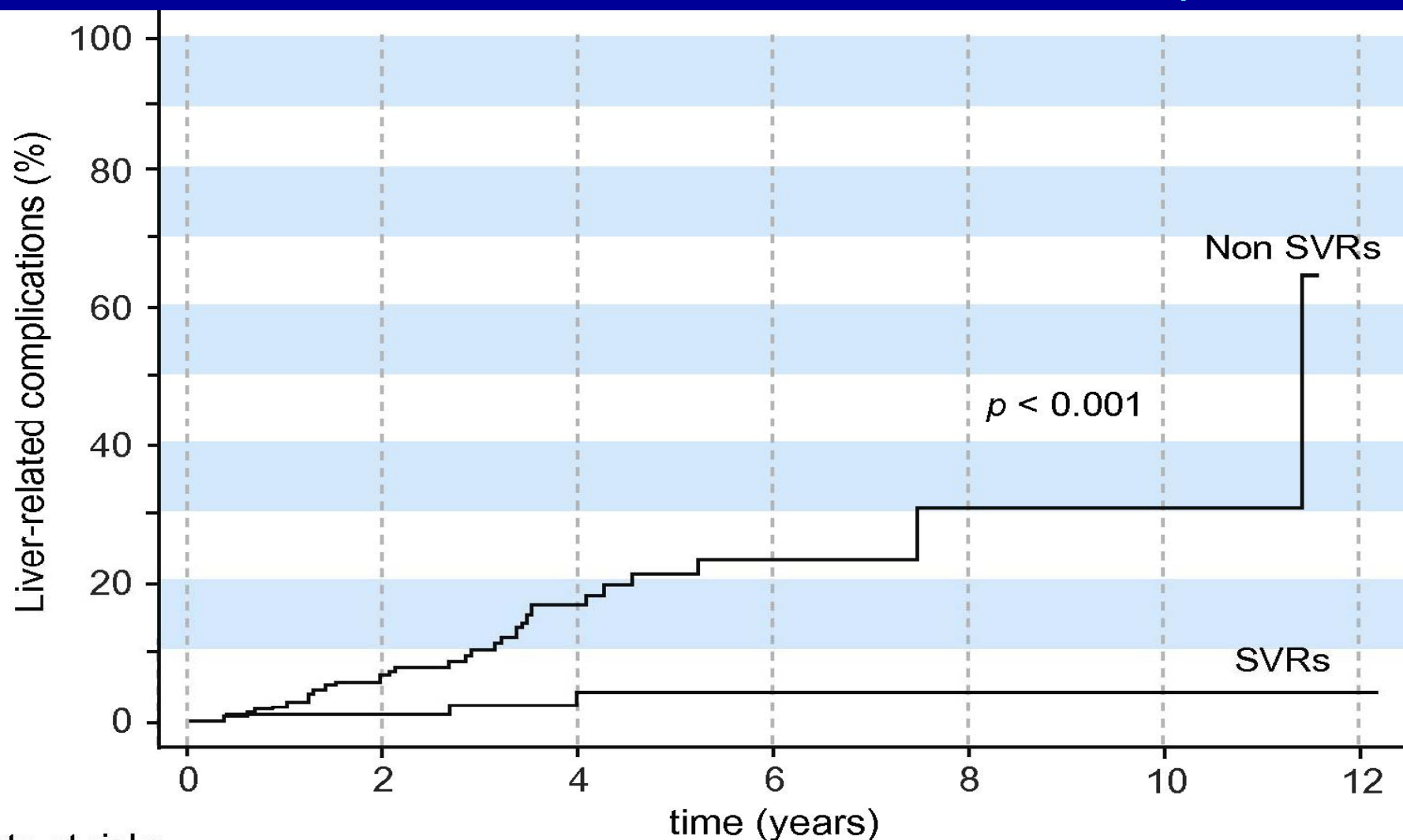
Mortality ratio of 2889 patients with chronic hepatitis C Followed for 65 months (1986-1998)

Patients	Overall deaths		Liver-related deaths		Liver-unrelated deaths	
	No.	SMR	No.	SMR	No.	SMR
Untreated	30	1.9 (1.3-28)	23	13.5 (8.6-20.3)	7	0.5 (0.2-1.0)
Interferon treated						
All	56	0.9 (0.7-1.1)	35	4.7 (3.3-6.5)	21	0.4 (0.2-0.6)
SVR	7	0.4 (0.1-0.7)	2	0.8 (0.1-3.0)	5	0.3 (0.1-0.7)
Non SVR	49	1.1 (0.8-1.5)	33	6.5 (4.5-9.1)	16	0.4 (0.2-0.7)

CUMULATIVE INCIDENCE OF LIVER-RELATED COMPLICATIONS

307 cases with F3 or F4

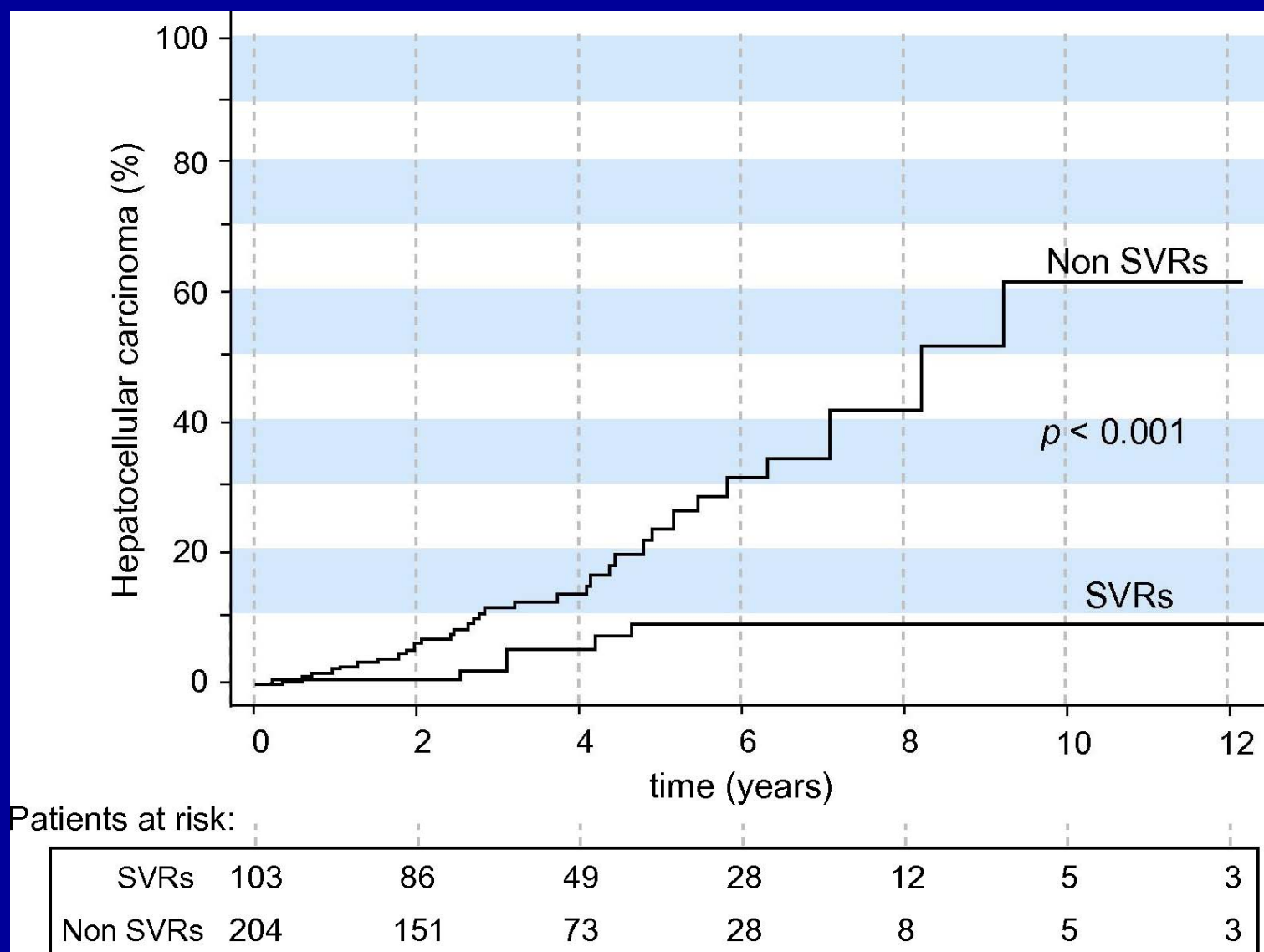
Cardoso AC et al., J Hepatol 2010



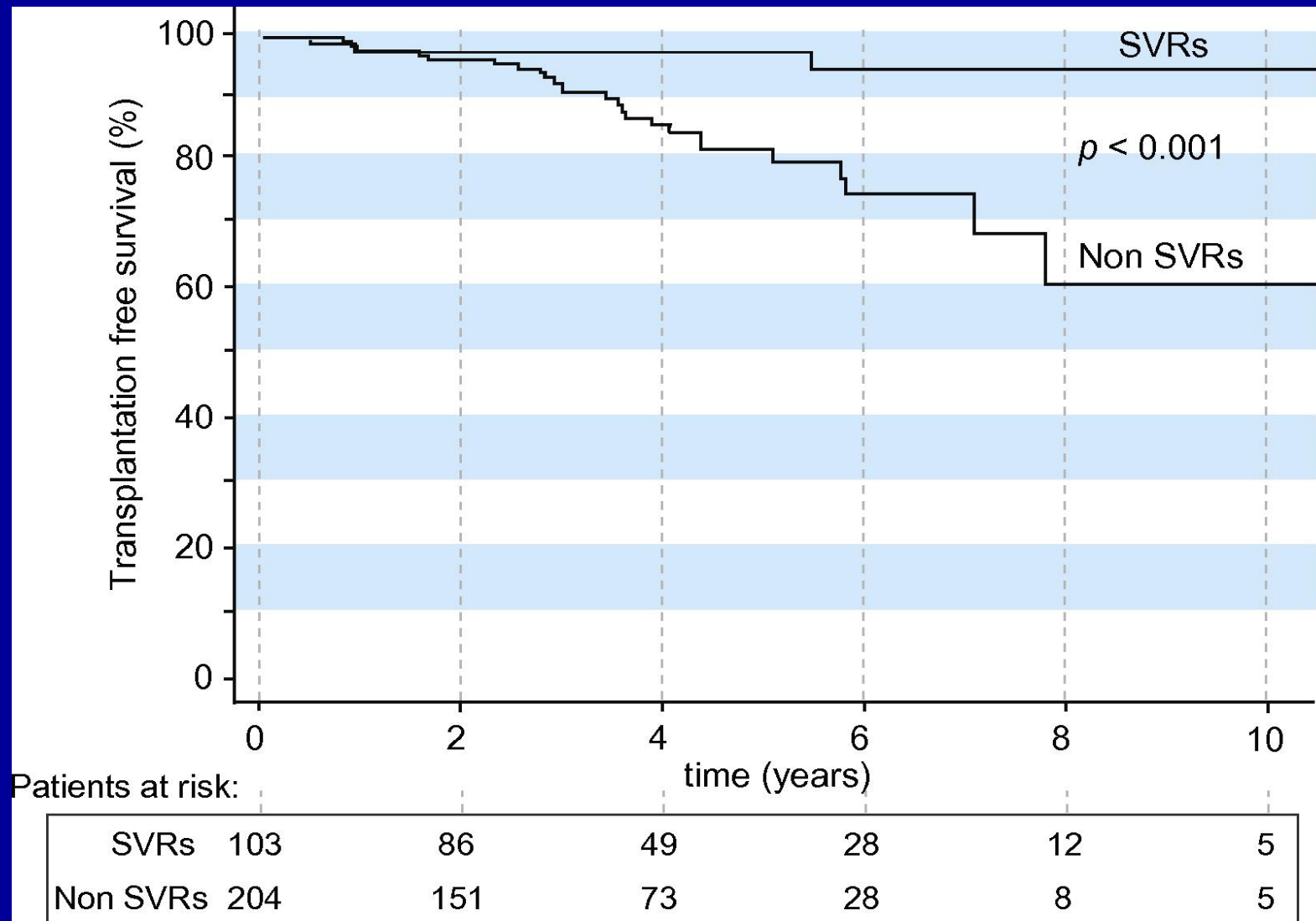
Patients at risk:

SVRs	103	86	49	28	12	5	3
Non SVRs	204	151	73	28	8	5	3

CUMULATIVE INCIDENCE OF HEPATOCELLULAR CARCINOMA

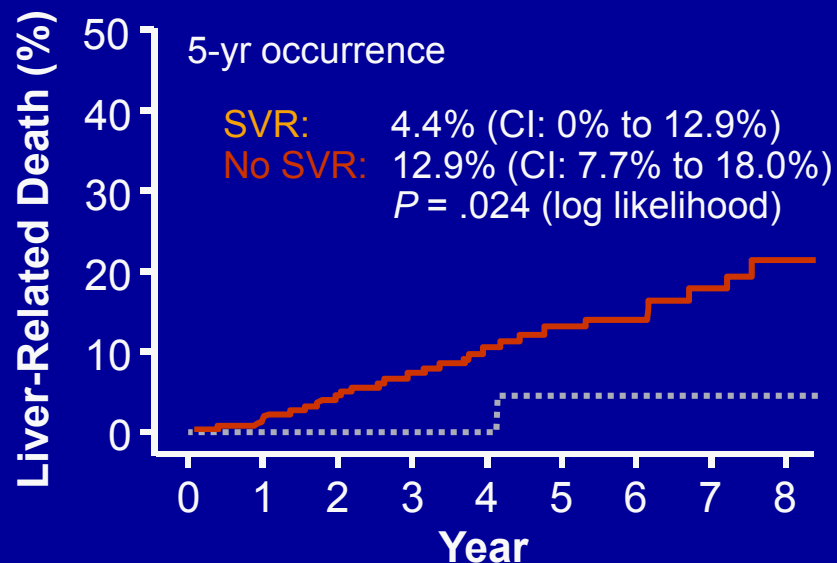


CUMULATIVE INCIDENCE OF LIVER-RELATED DEATHS



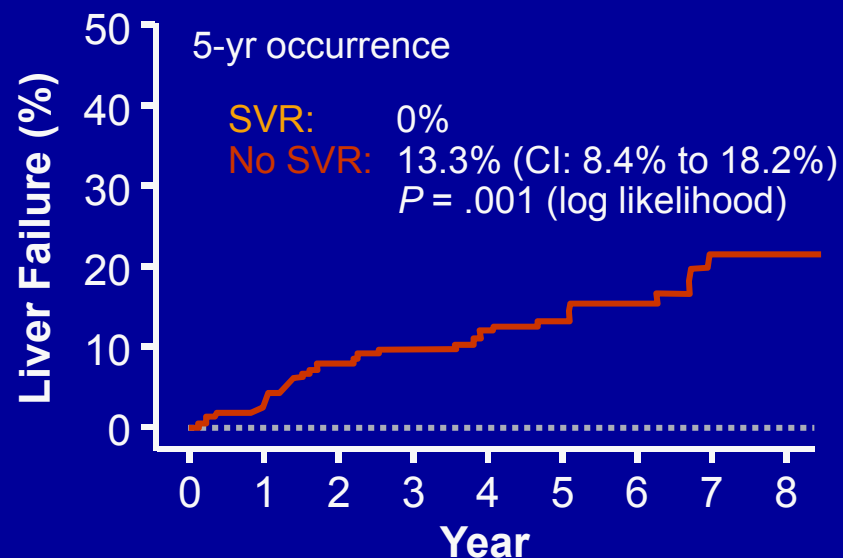
Posttreatment Outcomes in Patients With Advanced Fibrosis With/Without SVR

Liver-Related Death



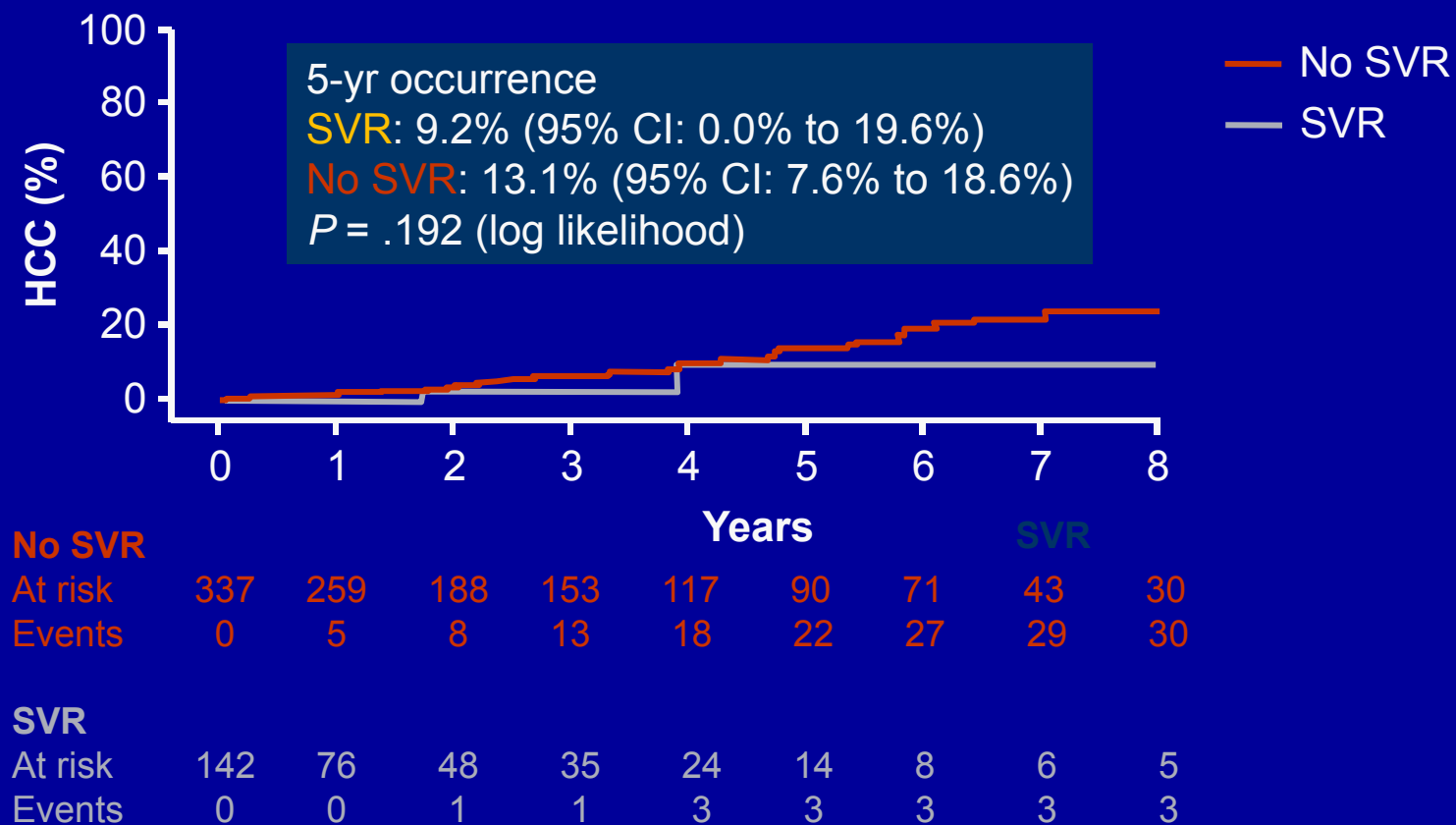
No SVR	At risk	337	261	192	160	124	95	79	49	31
	Events	0	5	11	16	20	24	25	28	30
SVR	At risk	142	76	48	35	25	14	8	6	5
	Events	0	0	0	0	0	1	1	1	1

Liver Failure

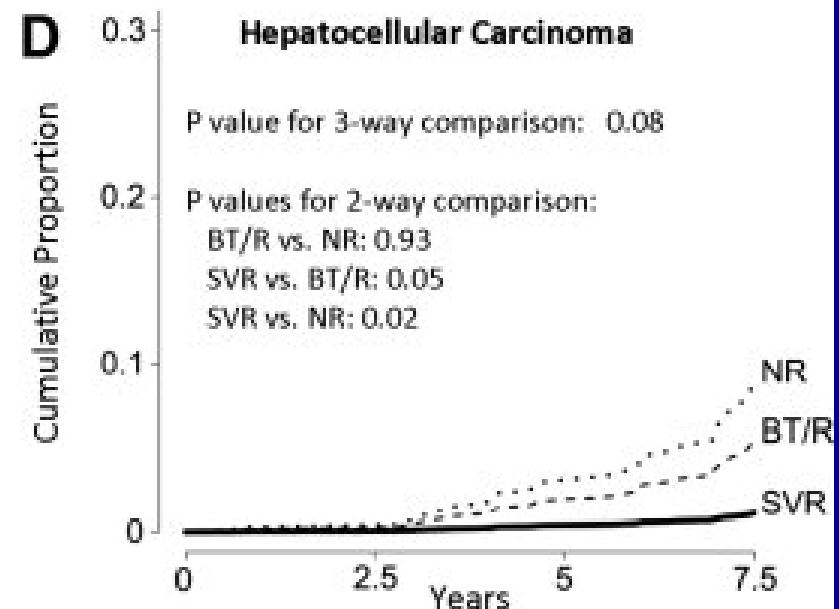
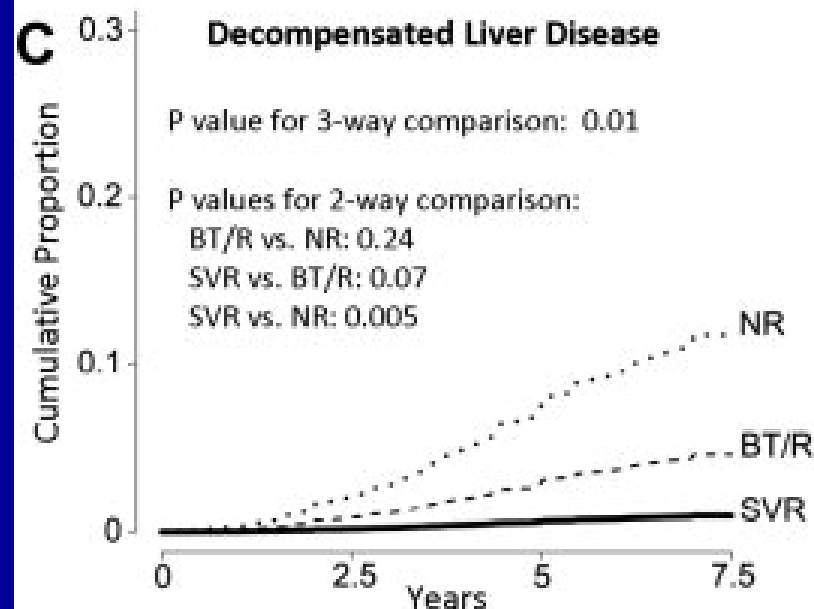
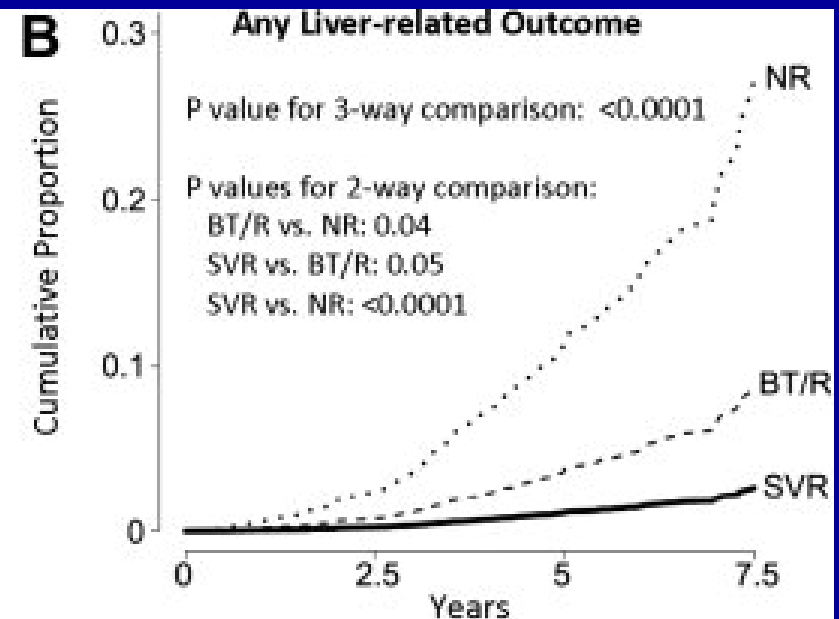
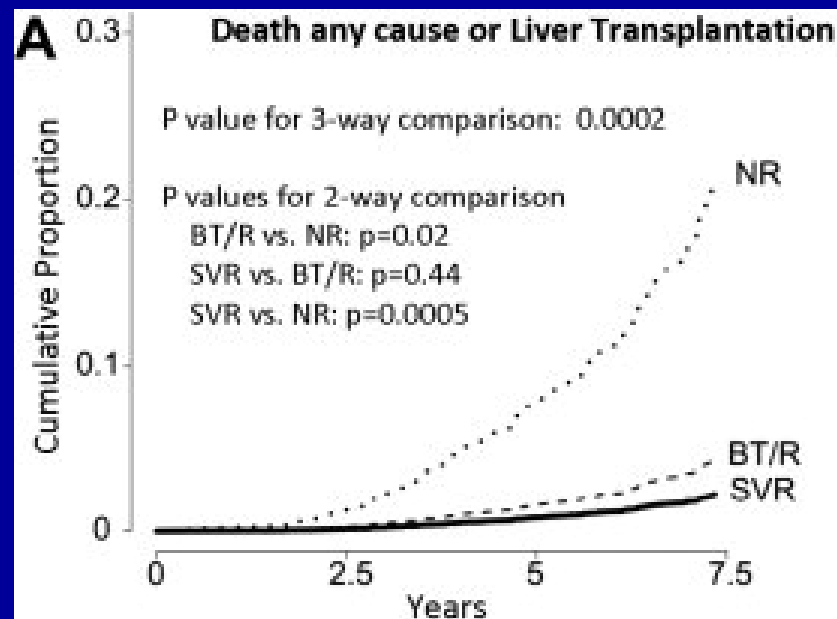


No SVR	At risk	337	256	183	155	121	92	74	44	27
	Events	0	8	21	24	27	29	31	35	35
SVR	At risk	142	76	48	35	25	14	8	6	5
	Events	0	0	0	0	0	1	1	1	1

Incidence of HCC in Patients With Advanced Fibrosis With/Without SVR

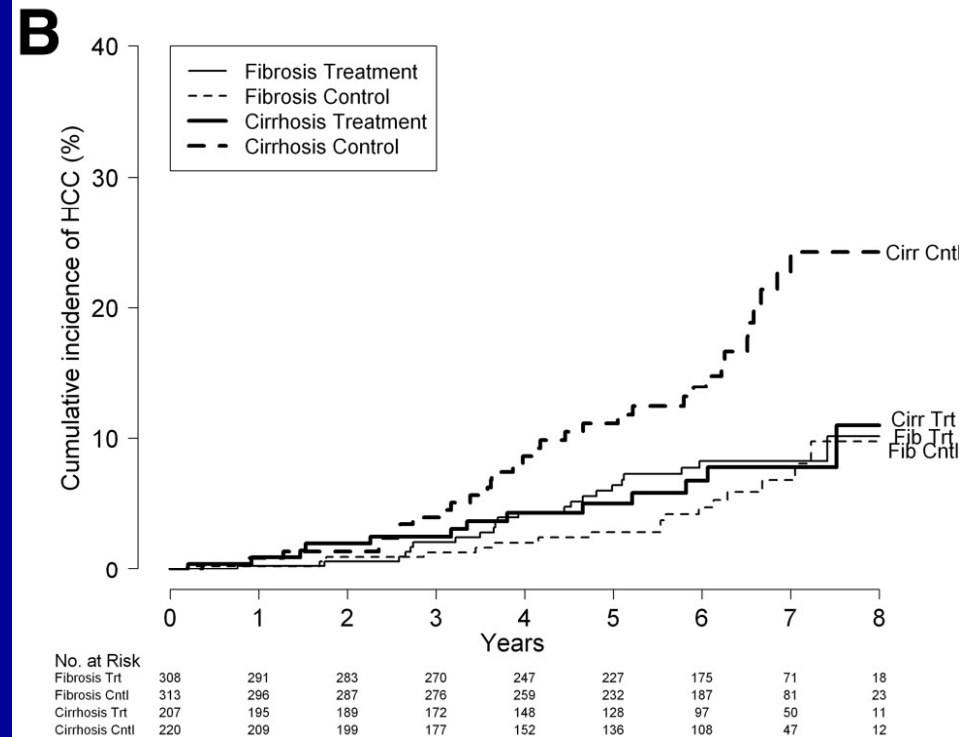
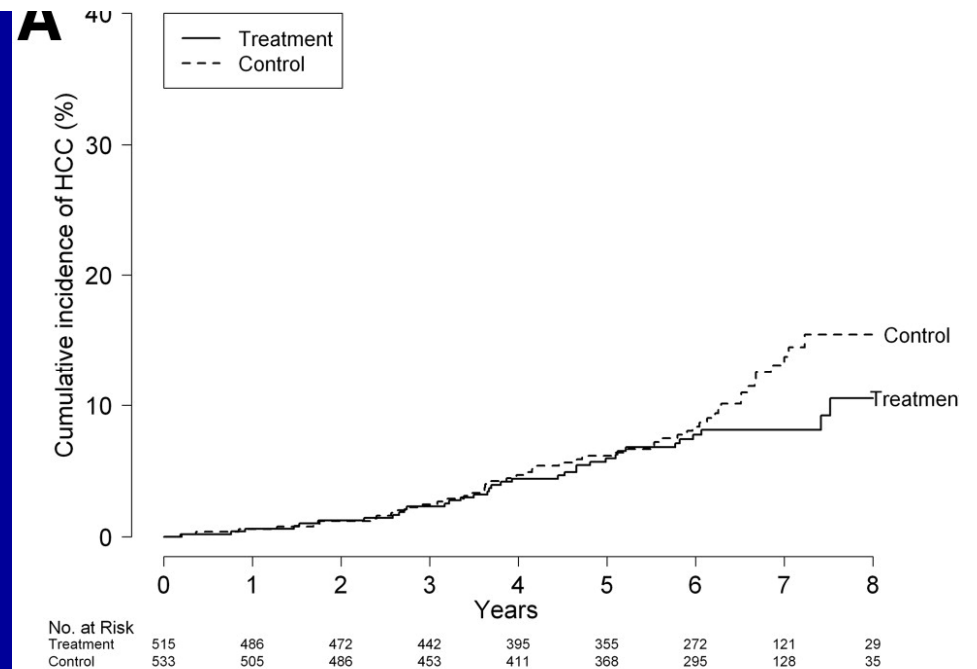


CLINICAL OUTCOMES IN HCV PATIENTS TREATED IN HALT-C WITH ADVANCED LIVER FIBROSIS *Morgan et al 2010*



THE LONG-TERM EFFECT OF 3.5 YRS PEG-IFN MAINTENANCE THERAPY IN NON-RESPONDERS IN THE HALT-C TRIAL

Lok et al Gastroenterology 2011



IMPACT OF SVR ON ALL-CAUSE MORTALITY BY HCV GENOTYPE

- 16.864 patients (75% HCV-1, 15% HCV-2, 10% HCV-3)
- Hypertension (52%) , Diabetes (20%) COPD (15%) CVD (12%) Depression (36%) Alcohol (24%) IDU (12%)
- SVR : 44% (HCV-1: 35% , HCV-2 : 72% , HCV-3 : 62%)

IMPACT OF SVR ON MORTALITY (HR)

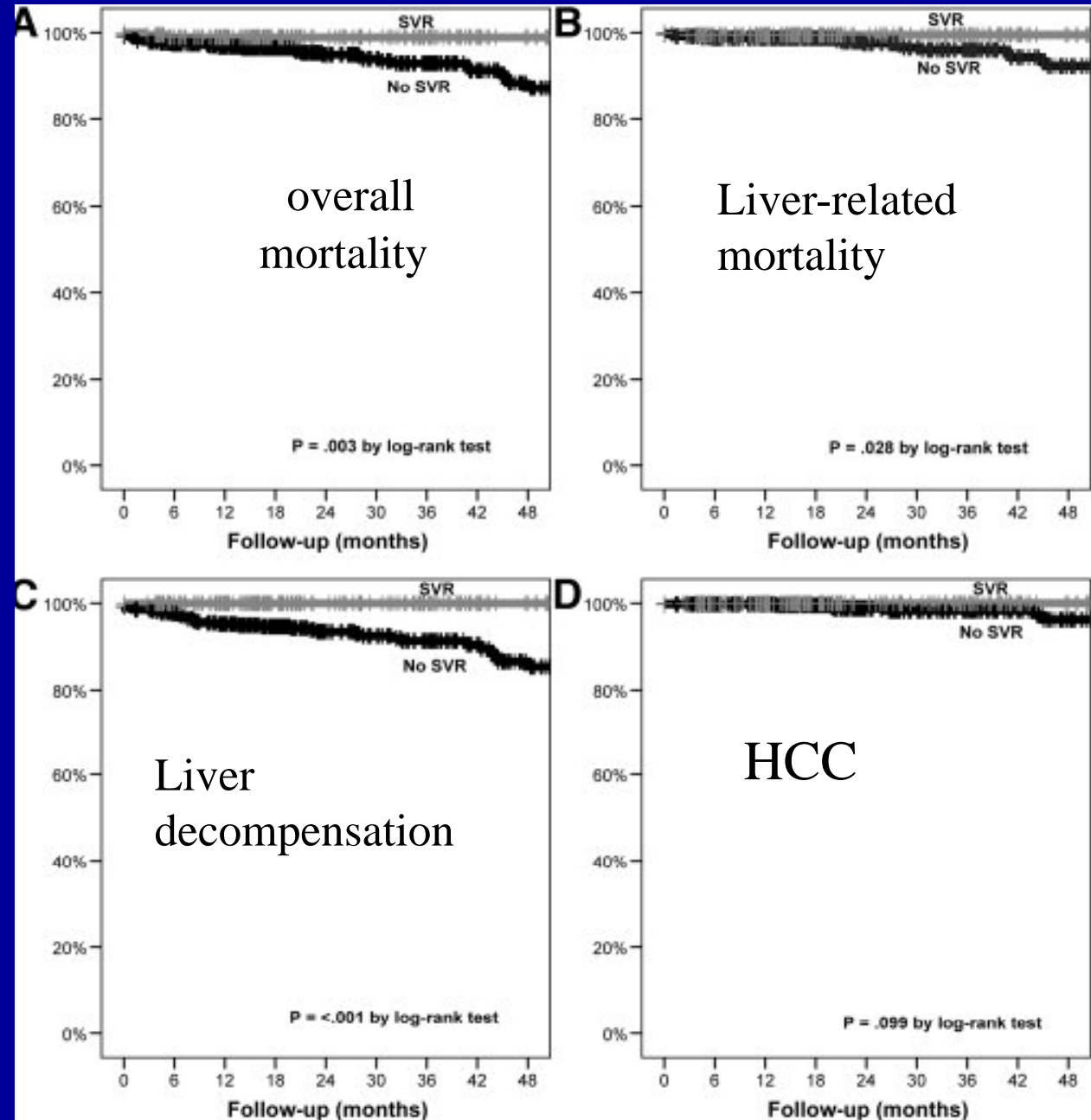
	HCV-1	HCV-2	HCV-3
Unadjusted	0.45	0.50	0.30
Adjusted	0.67	0.63	0.45

Backus et al AASLD 2010

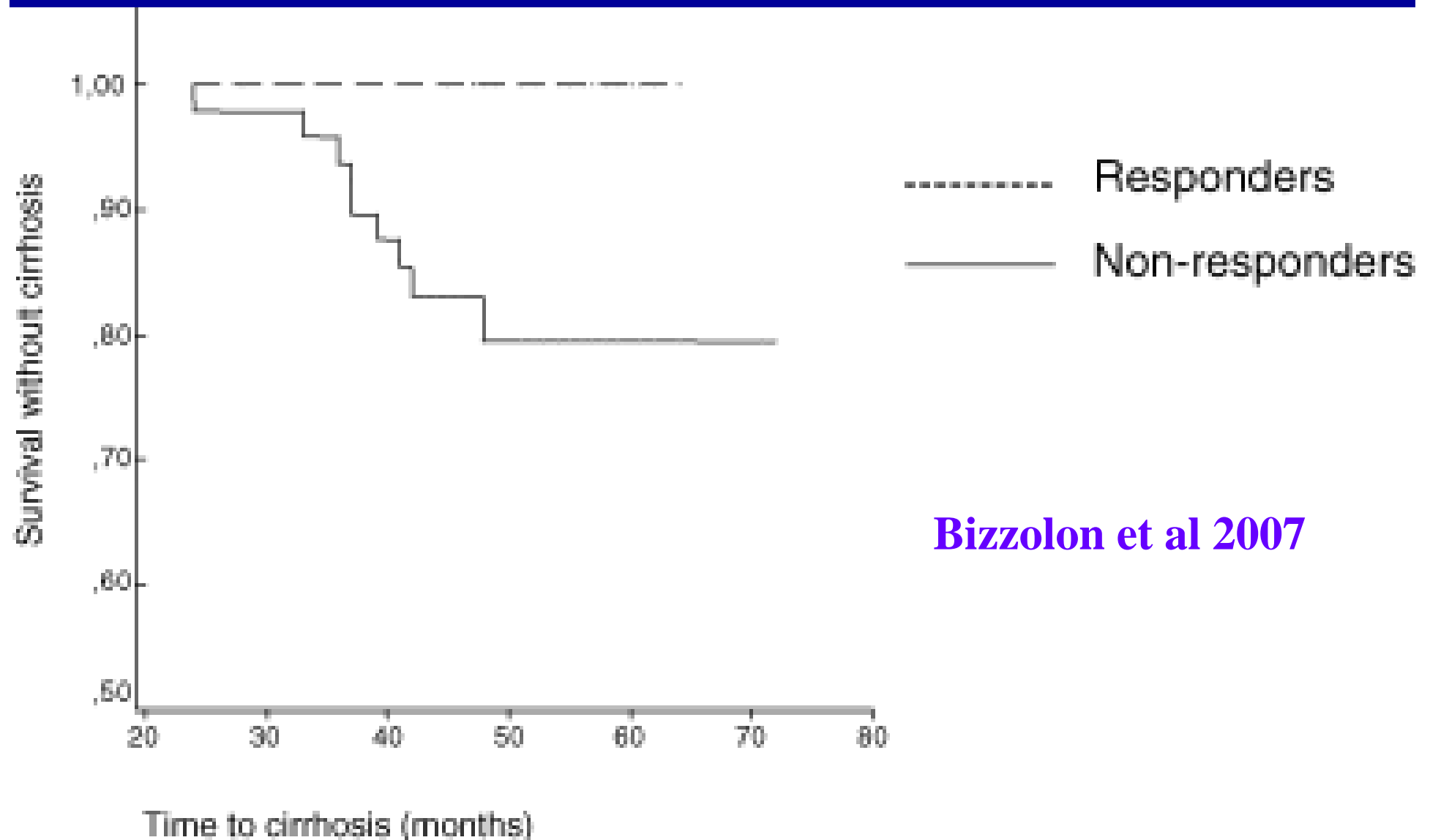
THE IMPACT OF SVR IN HIV/HCV COINFECTED PATIENTS

711 PATIENTS

SVR : 31%



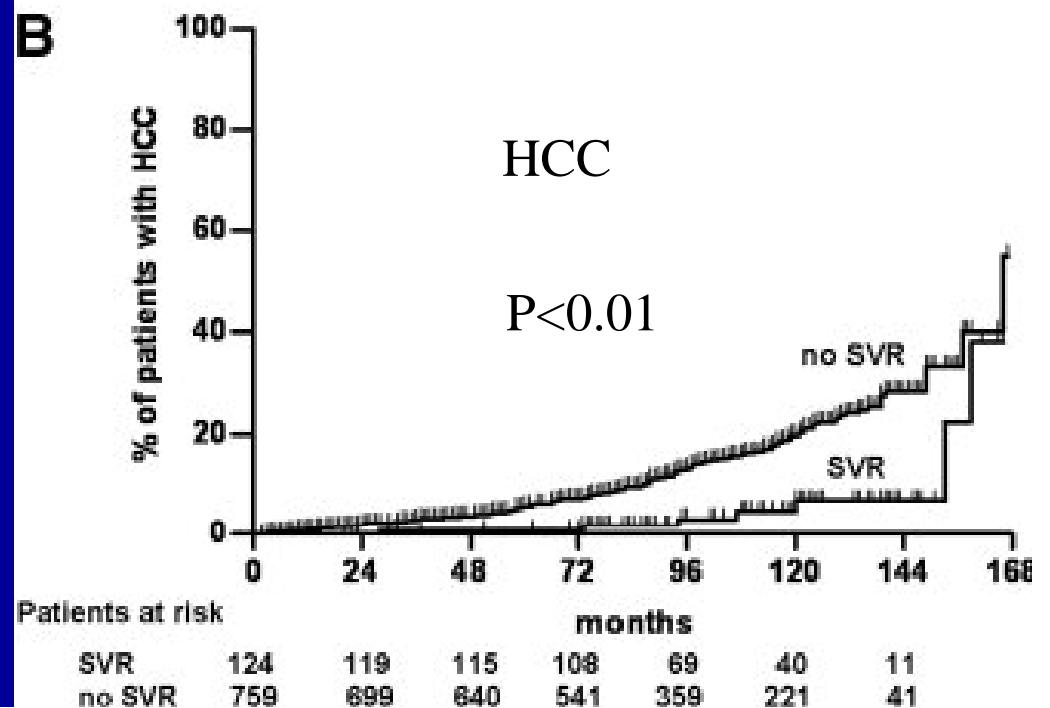
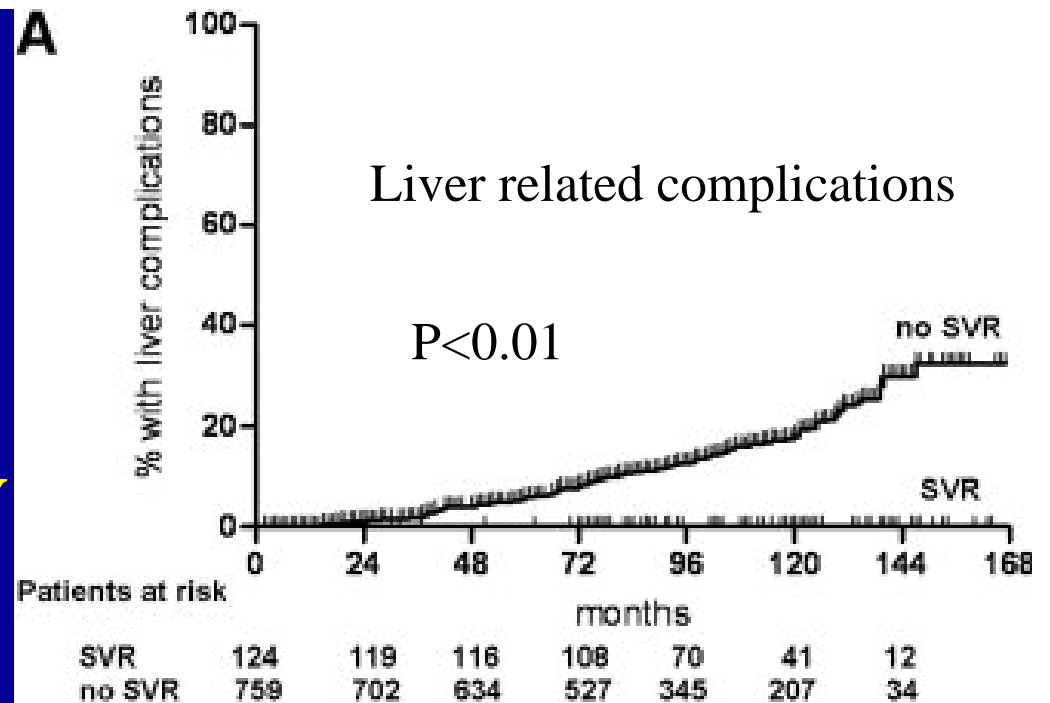
DEVELOPMENT OF CIRRHOSIS IN LIVER TRANSPLANT PATIENTS WITH HCV RECURRENCE IN RELATION TO RESPONSE TO ANTIVIRAL THERAPY



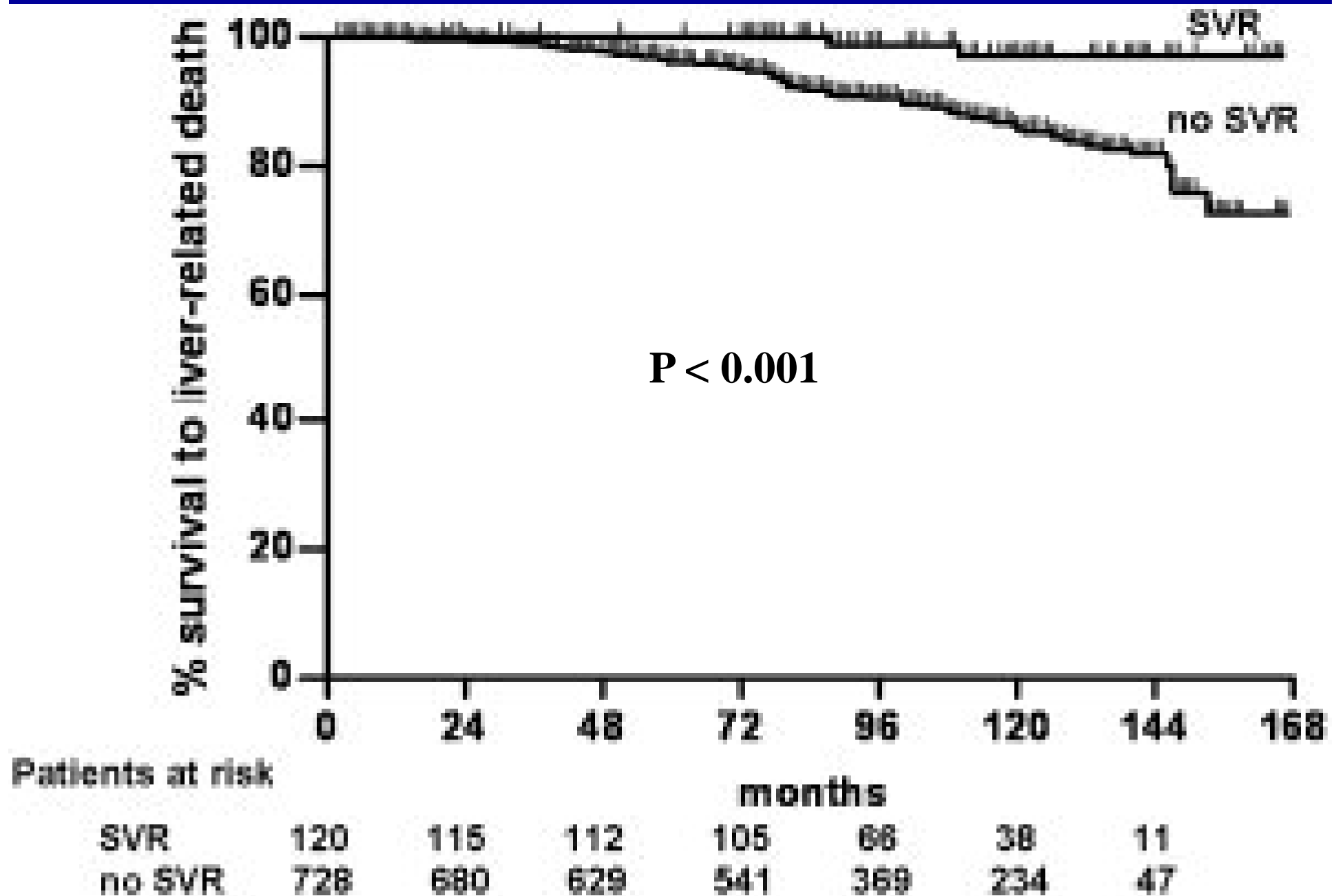
THE EFFECT OF SVR AFTER IFN MONOTHERAPY IN 920 PATIENTS WITH CIRRHOSIS

SVR : 13.5%

Bruno et al Hepatology 2007



LIVER RELATED DEATH IN 920 PATIENTS WITH HCV CIRRHOSIS



SVR AND PORTAL HYPERTENSION IN PATIENTS WITH COMPENSATED CIRRHOSIS

218 EV free cirrhotics → SVR 22.8% → Endoscopy every 3 ys → FU 11.4 ys

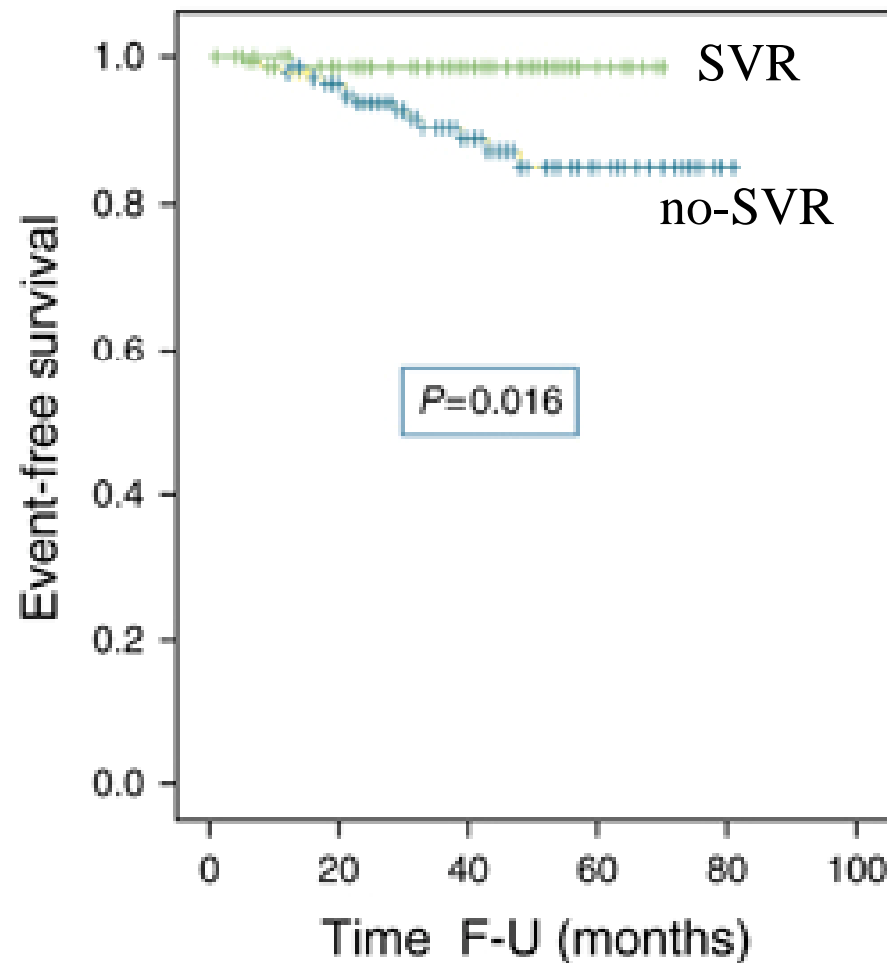
	% developing esophageal varices
SVR	0%
No SVR	39.1%
Untreated	31.8%

Bruno et al., Hepatology 2010

LIVER EVENT-FREE SURVIVAL ACCORDING TO STAGE OF CIRRHOSIS AT THE TIME OF ANTIVIRAL THERAPY

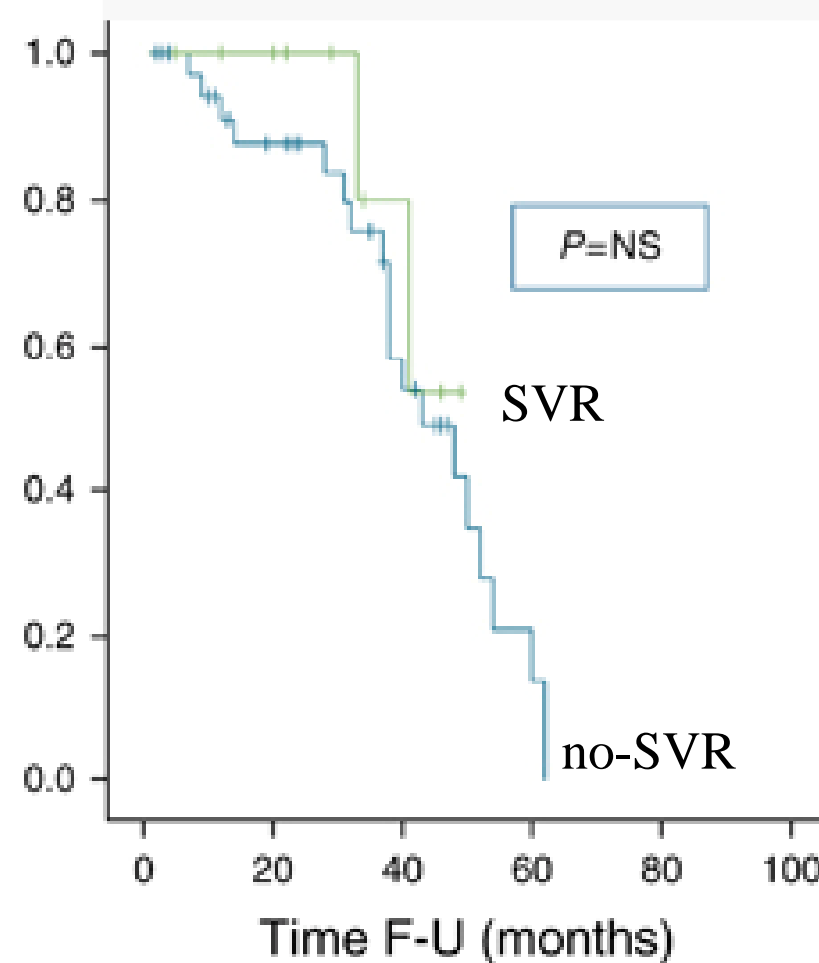
Fernandez-Rodriguez 2010

a ALBUMIN>3.9g/no varices



Subjects at risk

b ALBUMIN<3.9/varices



MODELLING THE LONG TERM BENEFIT OF ANTIVIRAL THERAPY IN INITIALLY MILD CHC

	Mean cost (£)/QALY	Cost-effective?
Overall	9,535	Yes
Genotype I	25,188	Yes
Genotype non-I	4,535	Yes
Genotype I		
Age 20 years	28,515	Yes
Age 65 years	53,017	No
Genotype non-I		
Age 20 years	5,182	Yes
Age 65 years	8,668	Yes
No gain in HRQoL		
Genotype I	98,227	No
Genotype non-I	10,569	Yes
30-year perspective		
Genotype I	34,392	No
Genotype non-I	5,742	Yes
Up to 24 weeks if viral load drops sufficiently, 12 weeks if it does not		
Genotype I	17,051	Yes
Genotype non-I	1,425	Yes
The intervention was judged 'cost-effective' if the mean cost per QALY gained was below £30,000 per QALY.		

Wright M et al 2006

RETROSPECTIVE ANALYSIS OF DISEASE OUTCOME IN INITIALLY MILD CHC

effect of host genetics and of SVR

HOST GENETICS	HISTOLOGIC OUTCOME (7yrs) WITH PROGRESSION TO F3/F4		
	SVR	no-SVR	untreated
“Celera” CRS Signature > 0.7	0%	33%	41%
< 0.7	0%	6%	5%

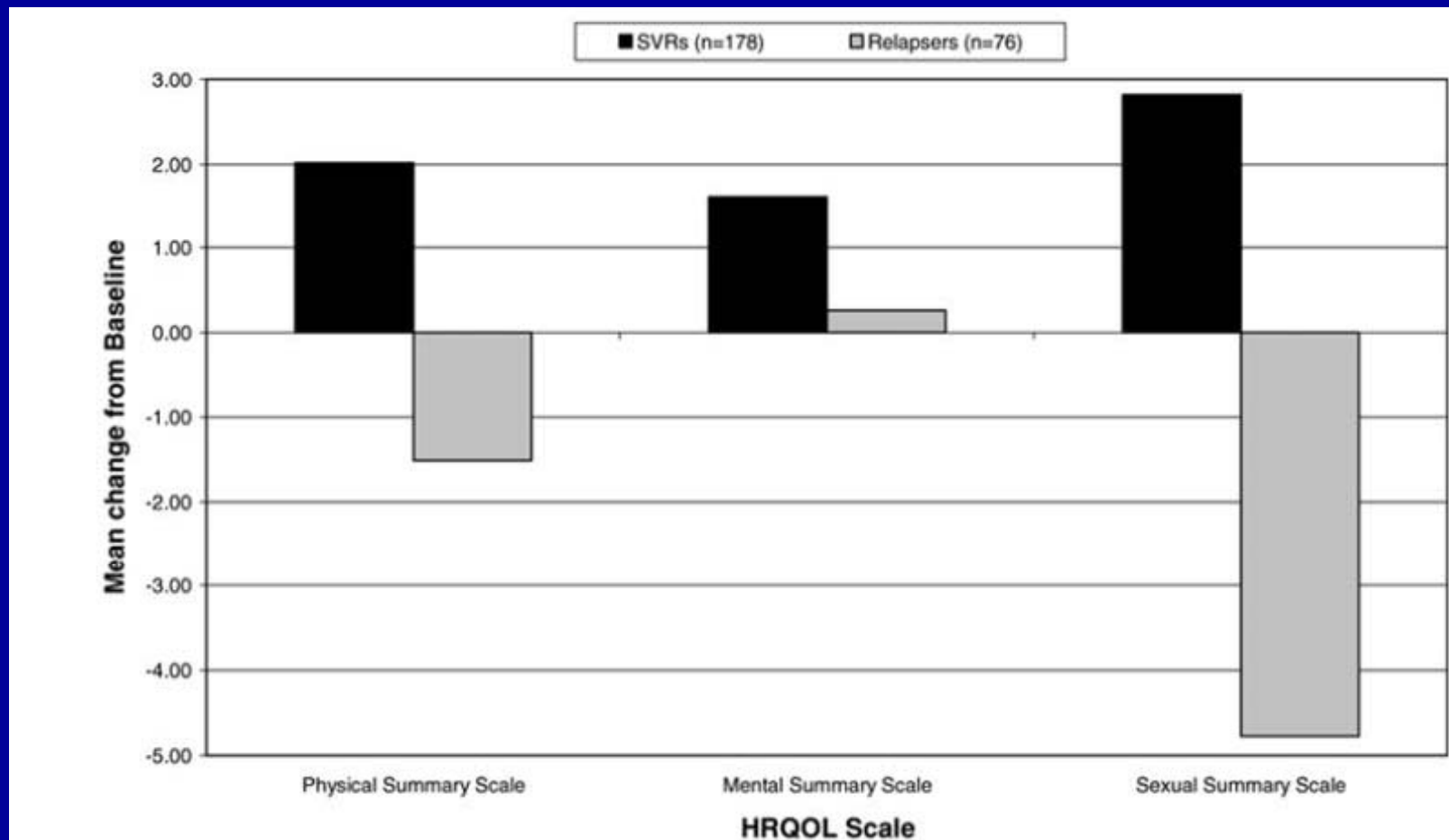
Marcolongo et al 2011

IMPACT OF SVR ON EXTRAHEPATIC MANIFESTATIONS OF HCV

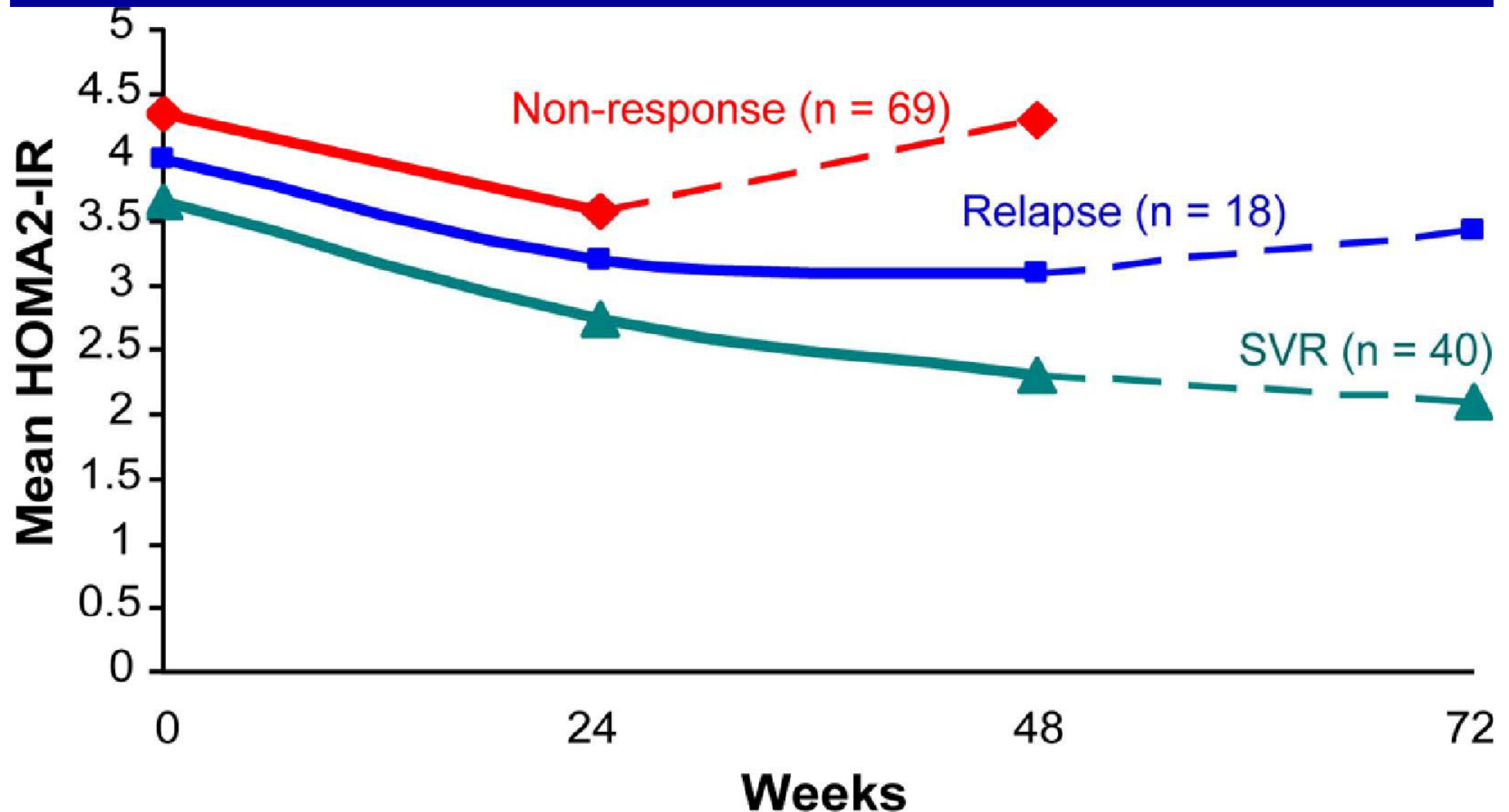
- Quality of Life
- Metabolic abnormalities
- Haematological disorders

EFFECT OF SVR ON QoL AND SEXUAL HEALTH IN PATIENTS WITH ADVANCED FIBROSIS/CIRRHOSIS

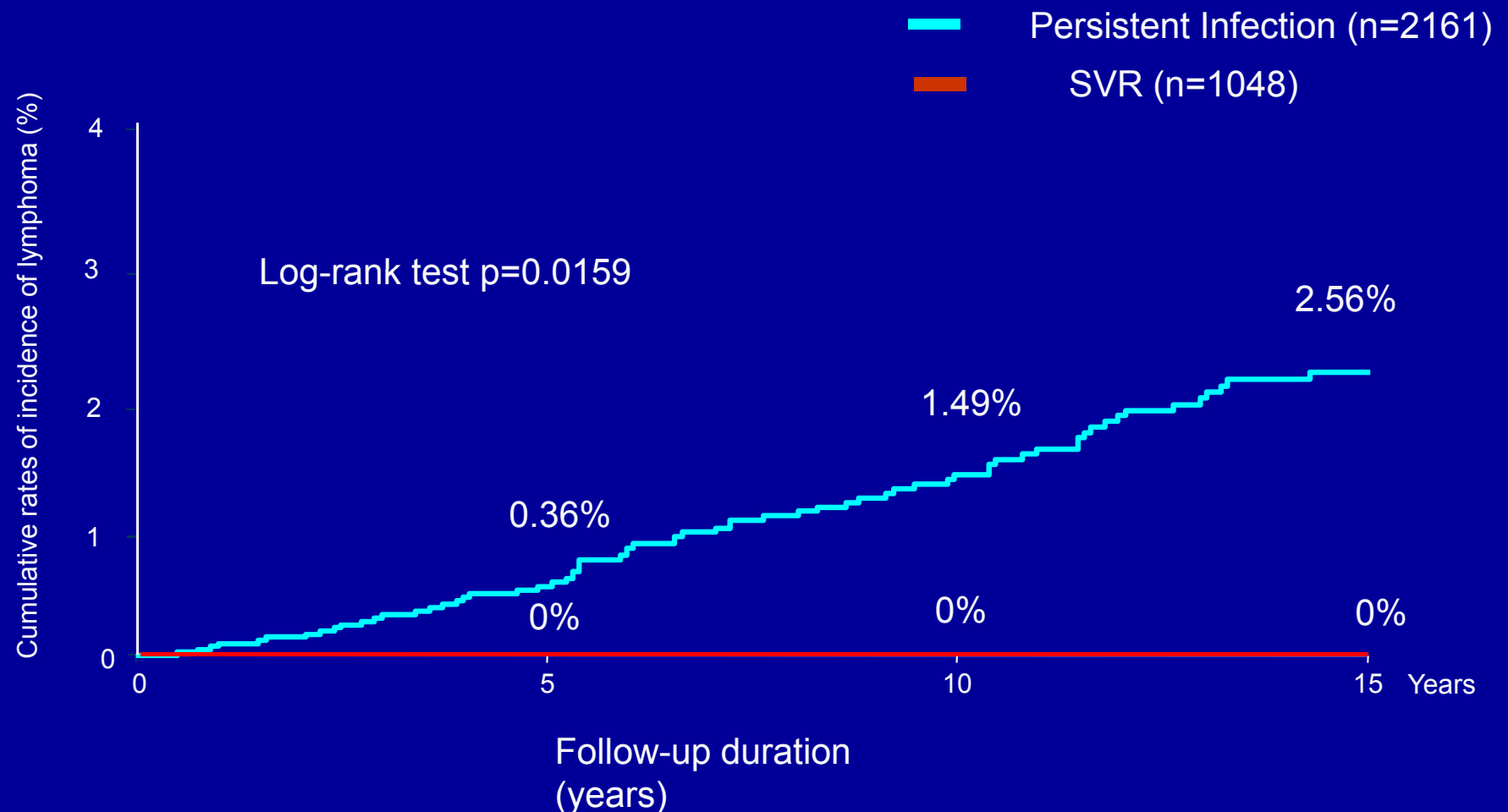
Bonkovsky et al J Hepatol 2007



CHANGES IN INSULIN RESISTANCE IN RELATION TO THE PATTERN OF RESPONSE TO THERAPY_



HCV Elimination Reduces The Incidence of Malignant Lymphoma



Kawamura Y, et al. Am J Med 2007;120:1034-1041

Kawamura Y, et al. Am J Med 2007;120:1034-1041

A SIMPLE TAKE HOME MESSAGE

Sustained Virological Response is associated with HCV eradication and has a major clinical impact in patients with chronic HCV infection particularly when antiviral therapy is initiated :

NOT TOO EARLY

NOT TOO LATE