7th International Symposium on Hepatitis Care in Substance Users

Cascais, 21° September 2018

Life Beyond SVR - It is not just about SVR: The Clinical Benefits of Succesful DAA Therapy Beyond Cure

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Financial Disclosures

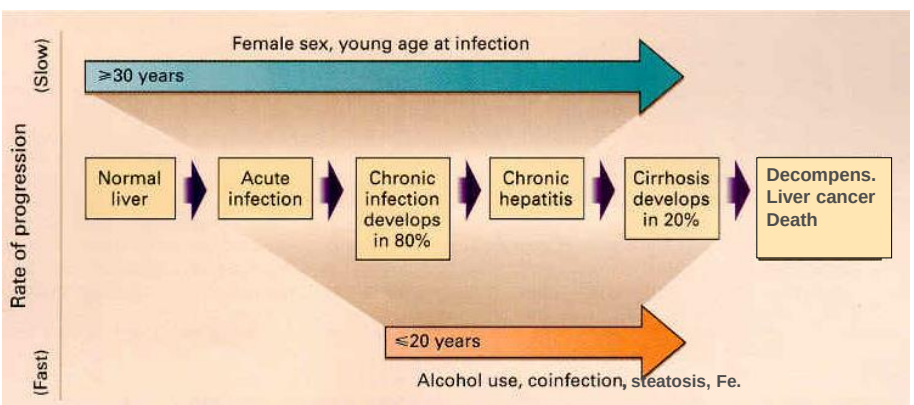
Grant and research support:	AbbVie
Advisory committees:	Merck, BMS, Gilead Sciences, Janssen, AbbVie and Alfasigma
Speaking and teaching:	Merck, BMS, Gilead Sciences, Janssen, AbbVie

The Endpoint of Treatment in HCV: SVR

- To cure HCV infection, in order to:
  - Prevent the complications of HCV-related liver and extra-hepatic diseases, including hepatic necro-inflammation, fibrosis, cirrhosis, decompensation of cirrhosis, HCC and death
  - Improve quality of life and remove stigma
  - Prevent onward transmission of HCV

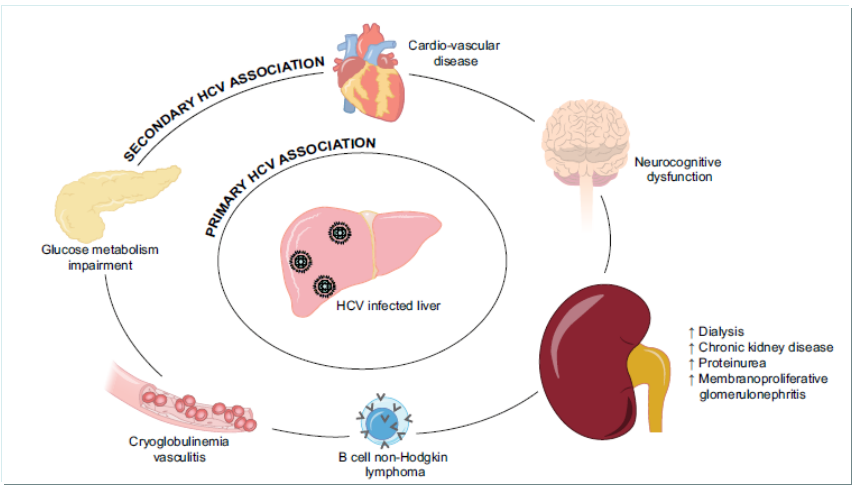
EASL Recommendations on Treatment of Hepatitis C 2018

Natural History of hepatitis C



(Modified by Lauer and Walker NEJM 2001;345:41-52)

HCV Infection Is a Systemic Disease



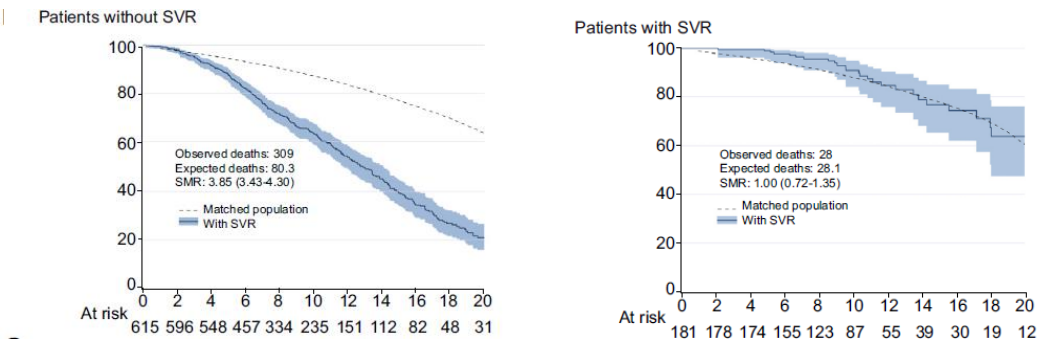
Cacoub P, et al. J Hepatol 2016; 65: S82-S94

All-cause Mortality Is Reduced by DAA Veteran Affairs HCV Cohort

- 80.5% reduction of HCC incidence
- 80.5% reduction of all-cause mortality rates
- SVR strongly associated with delayed time to death and development of first HCC (both p<.001)

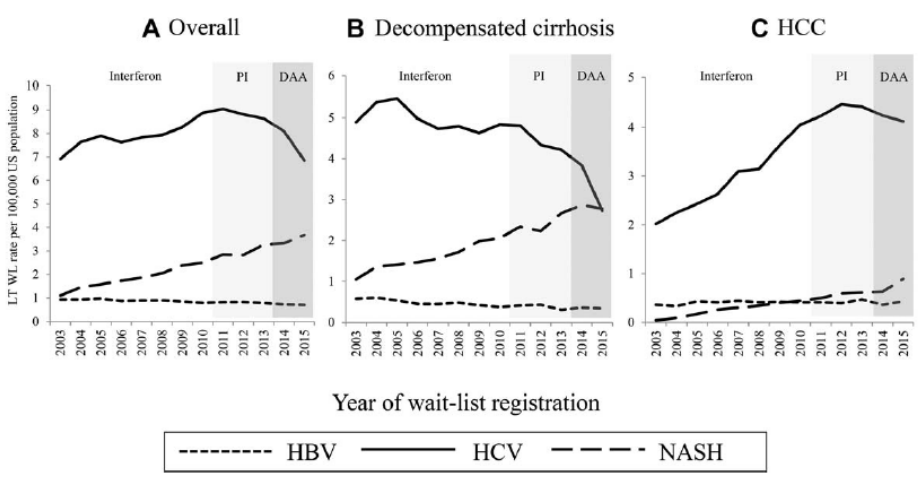
Backus LI et al Hepatology 2018 x 2 **** x 100 Patient/yr ; f-up 1.3 yrs***

Survival of HCV Cirrhotics with an SVR Is Comparable to the General Population



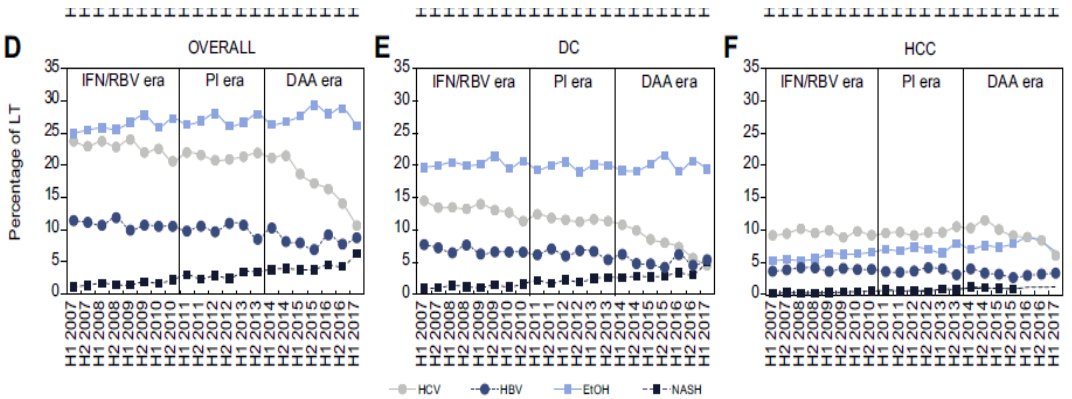
Bruno S et al J Hepatol 2017

The Impact of DAAs on LT Wait-Listing: US



Flemming J et al, Hepatology 2018

The Impact of DAAs on LT Wait-Listing: EU



Belli L et al, Journal of Hepatology in press

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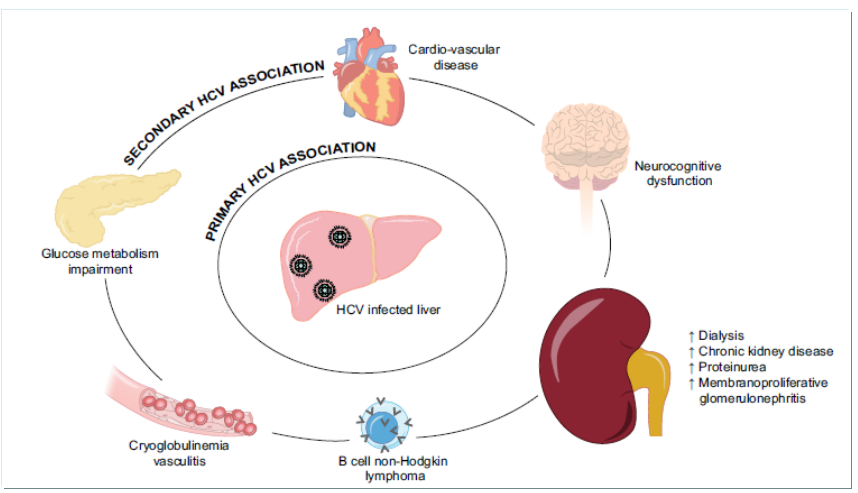
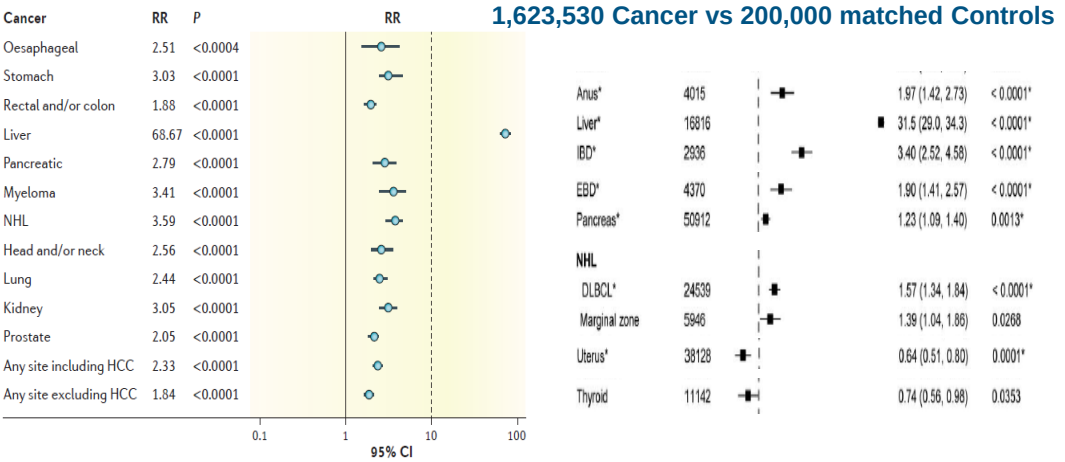


Cacoub P, et al. J Hepatol 2016; 65: S82-S94

HCV infection and Risk of Non Hepatic Cancer



Pol S et al, Nat Rev Gastro and Hep 2018
Mahale P et al, Cancer 2017

Competing Risks of Death in Compensated Cirrhosis A Multicenter Study in France

35 Centers : follow-up 34 months from 2006 to 2012

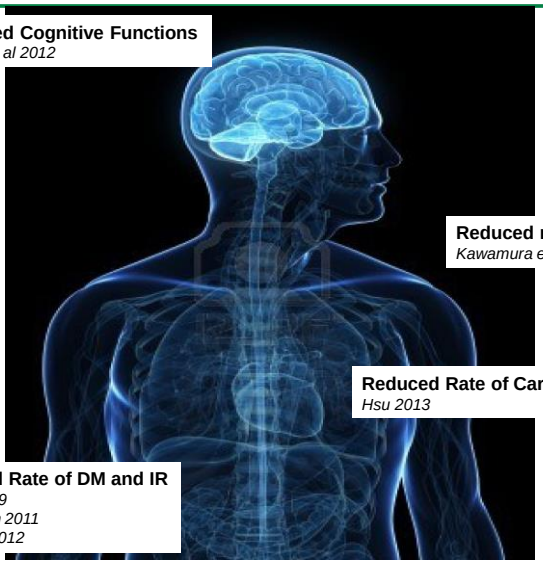
	HCV (n=1308)	HBV (n=315)	HCV and HBV (n=31)	Whole cohort (n=1654)
Death	**93 (7.1%)**	**6 (1.9%)**	**3 (10%)**	**102 (6.2%)**
HCC-related	17 (19.5%)	1 (16.6%)	0	18 (18.7%)
Non-HCC liver-related	27 (30.7%)	2 (33.3%)	1 (50%)	30 (31.2%)
Bacterial infection	13 (14.7%)	0	0	13 (13.5%)
Extrahepatic cancer	7 (7.9%)	3 (50%)	0	10 (10.4%)
Cardiovascular disease	5 (5.7%)	0	0	5 (5.2%)
Other extrahepatic dis.	19 (21.5%)	0	1 (50%)	20 (20.8%)
Missing data	*5 (5.4%)*	*0*	*1 (33.3%)*	*6 (5.8%)*

49.8%

Trinchet et al, Hepatology. 2015;62:737-50

Courtesy of Massimo Colombo

Extra-Hepatic Manifestations of HCV: The Benefit of an SVR



Improved Cognitive Functions
Byrnes et al 2012

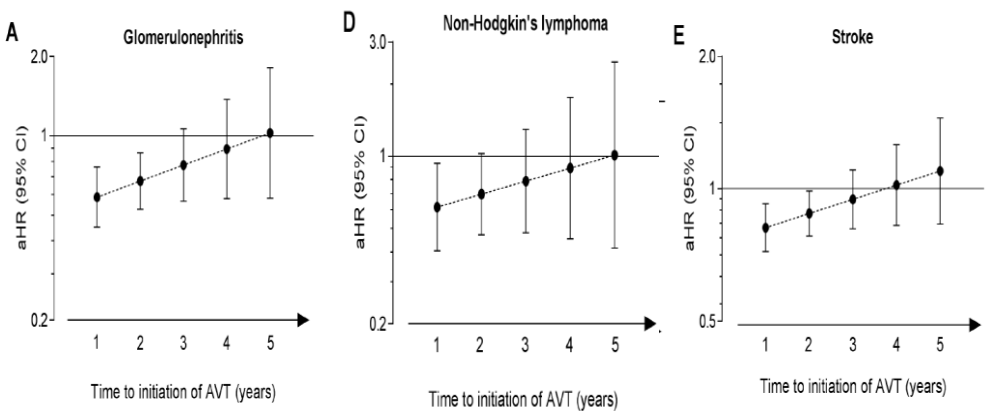
Reduced rate of NHL
Kawamura et al 2007

Reduced Rate of Cardiovascular Complications
Hsu 2013

Reduced Rate of DM and IR
Arase 2009
Thompson 2011
Aghemo 2012

Aghemo A, Lampertico P, Colombo M. J Hepatol 2012 57(6):1326-35

Extra-Hepatic Manifestations of HCV: The Benefit of an SVR



Mahale P, et al. Gut 2018;67:553–561

Extra-Hepatic Manifestations of HCV: The Benefit of an SVR

Received: 14 August 2017 | Accepted: 19 September 2017
DOI: 10.1002/jmv.24954

RESEARCH ARTICLE

WILEY JOURNAL OF MEDICAL VIROLOGY

Significant improvement of glycemic control in diabetic patients with HCV infection responding to direct-acting antiviral agents

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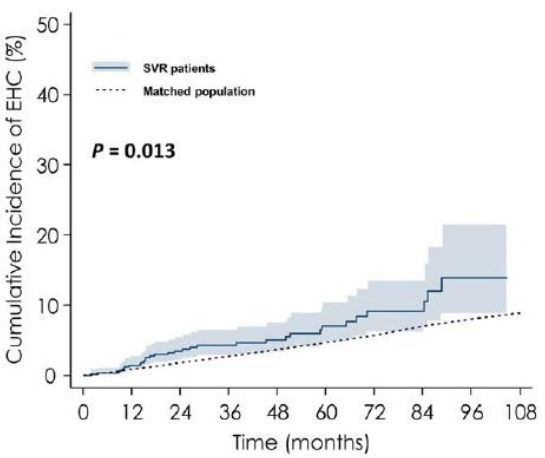
Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

Hepatitis C virus eradication by direct-acting antiviral agents improves carotid atherosclerosis in patients with severe liver fibrosis

Salvatore Petta[1,*], Luigi Elio Adinolfi[2], Anna Ludovica Fracanzani[3], Francesca Rini[1],

Extra-Hepatic Manifestations of HCV: SVR and Extrahepatic Cancer



	Number at risk (events)
SVR	663 (8) 483 (9) 374 (3) 287 (2) 216 (4) 165 (3) 115 (0) 69 (3) 25 (0) 3

Nahon P et al, Gastroenterology 2017 & Allaire M et al, Hepatology in press

Who Should be Followed After an SVR?

- Patients with no to moderate fibrosis (METAVIR score F0-F2), with SVR and no ongoing risk behaviour should be discharged, provided that they have no other comorbidities (A1).

- Patients with advanced fibrosis (F3) or cirrhosis (F4) with SVR should undergo surveillance for HCC every 6 months by means of ultrasound (A1).

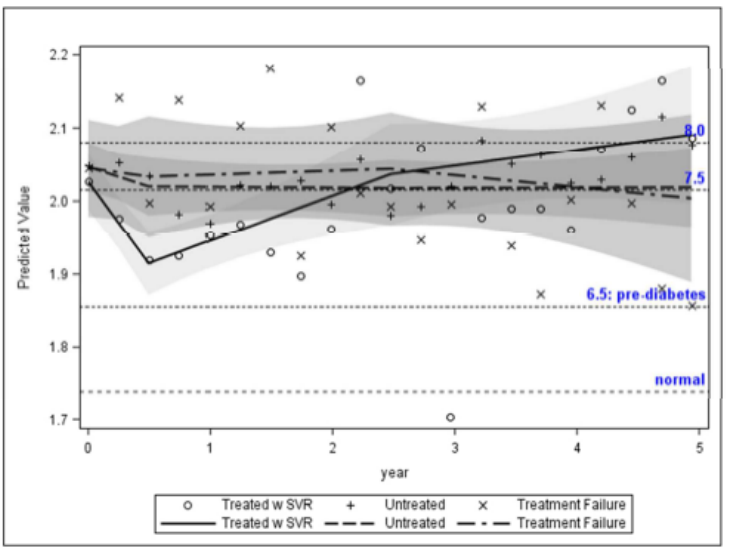
EASL Recommendations on Treatment of Hepatitis C 2018

Increased Body Weight in Patients with an SVR

	Group 1 (101 patients)			Group 2 (21 patients)		
	Baseline	End of study	*P*	Baseline	End of study	*P*
AST (IU/mL)[a]	42.3 ± 37.6	28.2 ± 11.0	0.02	40.3 ± 38.4	42.2 ± 39.8	0.85
ALT (IU/mL)[a]	81.2 ± 77.2	36.0 ± 12.0	<0.001	78.7 ± 67.3	82.2 ± 71.6	0.74
GGT (IU/mL)[a]	87.8 ± 81.0	62.5 ± 73.2	0.02	65.2 ± 64.0	67.0 ± 68.1	0.43
Bilirubin (mg/dL)[b]	1.0 (0.6-1.8)	0.8 (0.7-1.1)	0.12	0.9 (0.6-1.3)	1.0 (0.7-1.4)	0.52
Albumin (g/L)[b]	42 (31-48)	44 (33-49)	0.09	43 (34-47)	42 (33-48)	0.78
INR[b]	1.3 (1.0-1.8)	1.0 (1.0-1.5)	0.08	1.2 (1.0-1.7)	1.3 (1.0-2.1)	0.33
Leukocytes (x10^3/μL cells)[b]	4.2 (2.2-7.8)	5.4 (3.3-8.2)	0.07	4.4(2.8-6.2)	4.1 (2.3-7.3)	0.64
Platelets (x10^3/μL cells)[b]	155 (62-287)	173 (52-274)	0.08	164 (73-245)	162 (68-274)	0.35
Glucose (mg/dL)[a]	152.4 ± 56.4	134.3 ± 41.3	0.002	145.3 ± 30.2	140.0 ± 47.9	0.71
HbA1c (mmoL/moL)[a]	52.2 ± 15.4	46.5 ± 16.2	<0.001	53.4 ± 9.5	55.3 ± 20.6	0.78
HOMA-IR[a]	5.2 ± 2.5	3.1 ± 1.6	<0.001	4.9 ± 2.6	4.6 ± 2.3	0.29
Body weight (kg)[a]	75.3 ± 13.7	77.9 ± 19.8	0.02	76.6 ± 19.3	76.9 ± 20.7	0.56

Ciancio A et al, J Med Virol 2017

SVR Does Not Improve Long Term Glycemic Control in HCV Patients



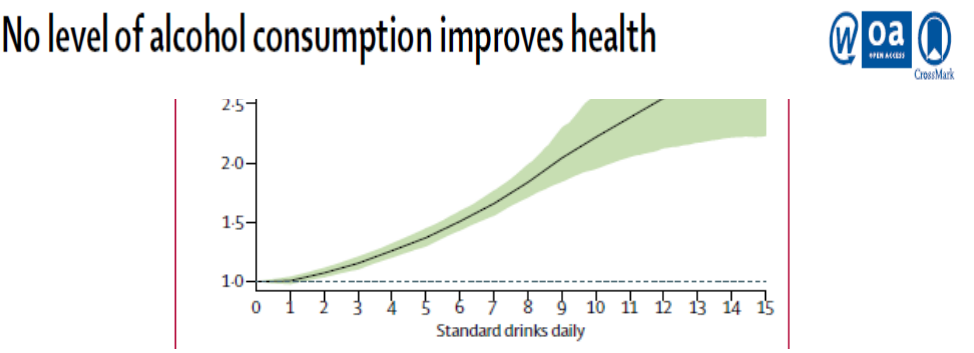
Lia Ji et al, Liver International in press

Causes of ALT Elevations Post SVR

(%)	PALT population N = 130	HCV-monoinfected N = 45	HIV-coinfected N = 85	P (HIV– vs HIV+)
Alcohol	30 (23.1)	6 (13.3)	24 (28.2)	.079
Drugs	19 (14.6)	3 (6.7)	16 (18.8)	.072
Idiopathic	11 (8.5)	4 (8.9)	7 (8.2)	1.000
NAFLD	47 (36.2)	24 (53.3)	23 (27.1)	.004
Other[a]	10 (7.7)	3 (6.7)	7 (8.2)	1.000
NAFLD + alcohol	4 (3)	1 (2.2)	3 (3.5)	1.000
NAFLD + drugs	6 (4.6)	1 (2.2)	5 (5.9)	.664
Autoimmune hepatitis	3 (2.3)	3 (6.7)	0	.040

Olveira A et al, J Viral Hepatitis in press

What is the Role of Alcohol Consumption Post-SVR?



GBD 2016 Alcohol Collaborators. Lancet. 2018 Aug 23. pii: S0140-6736(18)31310-2.

Conclusions

- SVR is associated with Clinical Benefits in all HCV Patients
- Patients with advanced fibrosis or cirrhosis with SVR need to remain under lifelong surveillance for HCC
- The best model of care for patients with mild fibrosis who achieved an SVR needs to be determined