XVII Annual Meeting of Hepatology

Malaga 18,19 May 2018

Chronic Hepatitis C and HCC : What is new?

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Financial Disclosures

Advisory committees:	Merck, Roche, Novartis, Bayer, BMS, Gilead Science, Tibotec, Vertex, Janssen, Achillion, Lundbeck, GSK, GenSpera, AbbVie, Alfa Wasserman,Intercept.
Speaking and teaching:	Tibotec, Roche, Novartis, Bayer, BMS, Gilead Science, Vertex, Merck, Janssen, AbbVie

Where Therapy of Hepatitis C Stands Now

- **SVR in >95% of patients**

- **Difficult-to-cure populations no longer difficult**
  - HIV co-infections,renal failure
  - Cirrhosis,transplant population
  - DAA failures

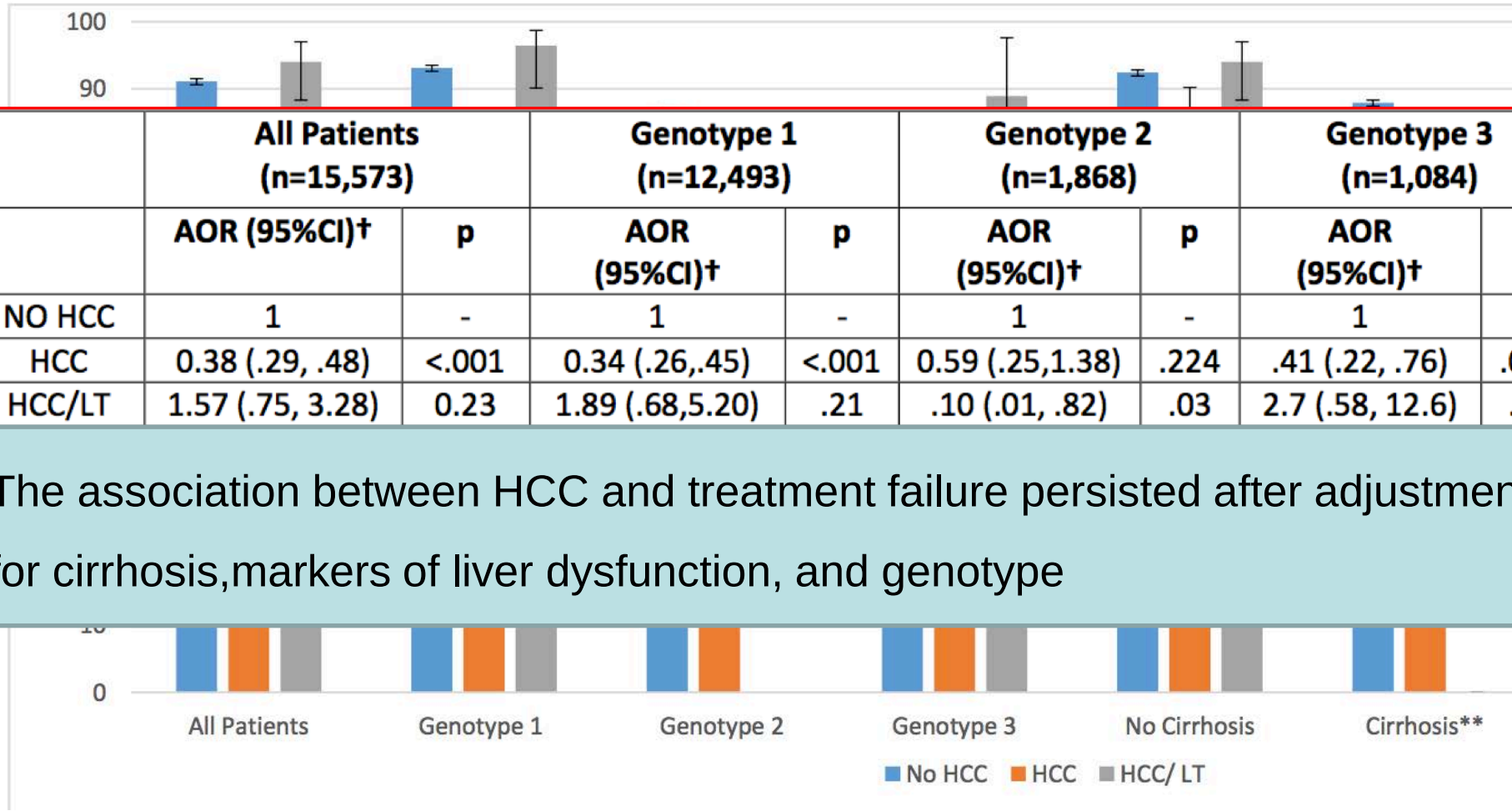
- **Current ”suboptimal” treatment outcomes**
  - Decompensated cirrhosis
  - HCV-3 cirrhosis with treatment failure

- **Areas of uncertainty**
  - HBV-HCV co-infected
  - Patients with active HCC

Chronic Hepatitis C and HCC : What is new?

1. Should HCV infection be treated prior to cancer ablation/resection?
2. Is HCC risk modified by DAA therapy of HCV?
3. Is HCC recurrence prevented by DAA therapy of HCC?
4. Is the clinical pattern of HCC modified by DAA therapy of HCV ?

Efficacy of IFN-free HCV Therapy in Patients with Active HCC. The Veterans Affairs Cohort



	All Patients (n=15,573)		Genotype 1 (n=12,493)		Genotype 2 (n=1,868)		Genotype 3 (n=1,084)	
	AOR (95%CI)†	p	AOR (95%CI)†	p	AOR (95%CI)†	p	AOR (95%CI)†	p
NO HCC	1	-	1	-	1	-	1	-
HCC	0.38 (.29, .48)	<.001	0.34 (.26,.45)	<.001	0.59 (.25,1.38)	.224	.41 (.22, .76)	.005
HCC/LT	1.57 (.75, 3.28)	0.23	1.89 (.68,5.20)	.21	.10 (.01, .82)	.03	2.7 (.58, 12.6)	.20

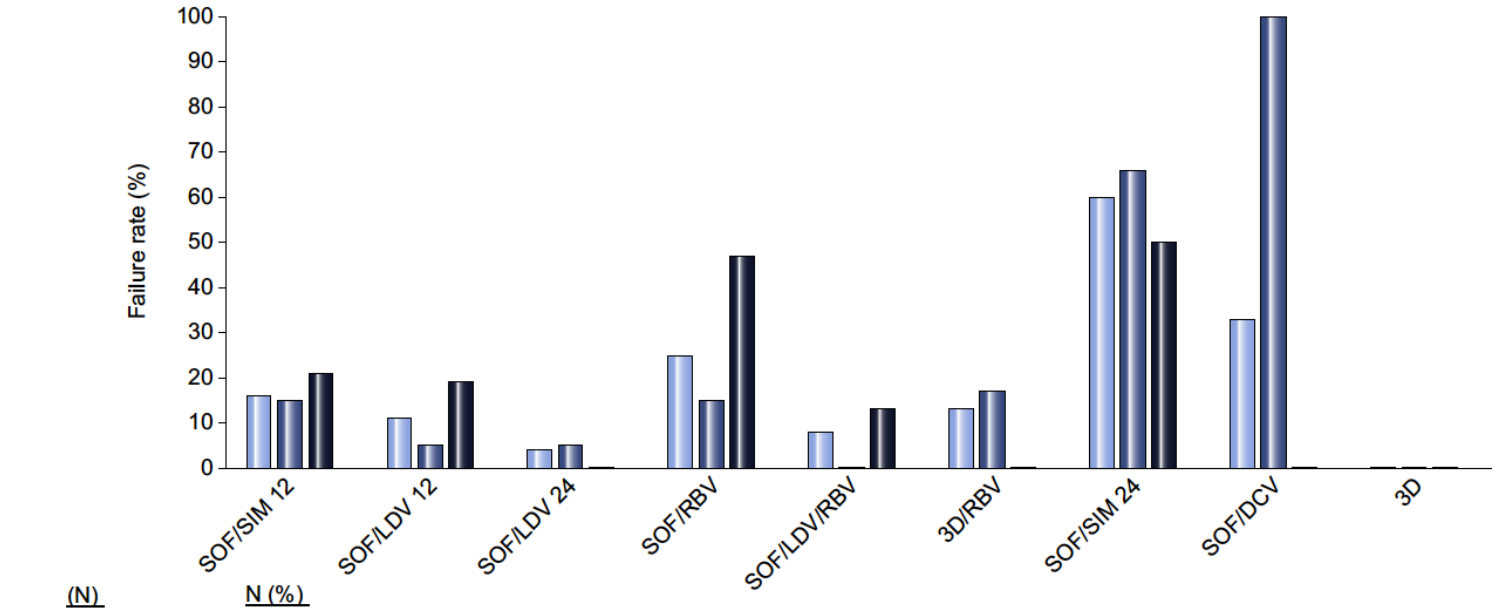
The association between HCC and treatment failure persisted after adjustment for cirrhosis,markers of liver dysfunction, and genotype

Beste L et al J Hepatol 2017

Decreased Response to DAA of Patients with HCC
NW University of Chicago

Failure Rates : 42% in HCC *vs* 3% in HCC-free

Inadequate regimen*	2.85	1.32–6.16	0.008
Active tumor	8.49	3.90–18.49	<0.001



(N)	N (%)								
All (421)	192 (46)	74 (18)	56 (13)	56 (13)	25 (6)	8 (2)	5 (1)	6 (1)	1 (0.2)
Non-HCC (284)	139 (49)	42 (15)	44 (15)	39 (14)	9 (3)	6 (2)	3 (1)	1 (0.3)	1 (0.4)
HCC (137)	53 (39)	32 (23)	12 (9)	17 (12)	16 (12)	2 (1.5)	2 (1.5)	5 (3.5)	0 (0)

Prenner S. et al J Hepatol. 2017

Antiviral Therapy of Waitlisted Patients with Compensated Cirrhosis and HCC

Potential benefits	Potential harm
▪ High SVR rates can be achieved	▪ If treatment failure, viral resistance is likely and may limit retreatment options in short-term
▪ Reduce posttransplant recurrence rate if SVR achieved before transplant	▪ If ribavirin-inclusive DAA regimen, tolerability may be reduced
▪ May reduce risk of decompensation and death on the waiting list	▪ May disadvantage patients from receiving HCV-positive grafts
▪ May increase likelihood of tolerating locoregional therapy for HCC	▪ Potential increase in HCC activity after SVR
▪ May improve QOL while on waiting list	▪ Treatment to prevent recurrence is a lower priority as effective therapies are available posttransplant

International Liver Transplantation Society

Recommendation 1.1

We suggest that waitlisted HCV-infected patients with compensated cirrhosis and HCC be treated with antiviral therapy.

Quality of evidence: Low
Strength of recommendation: Conditional

Terrault N et al Transplantation 2017

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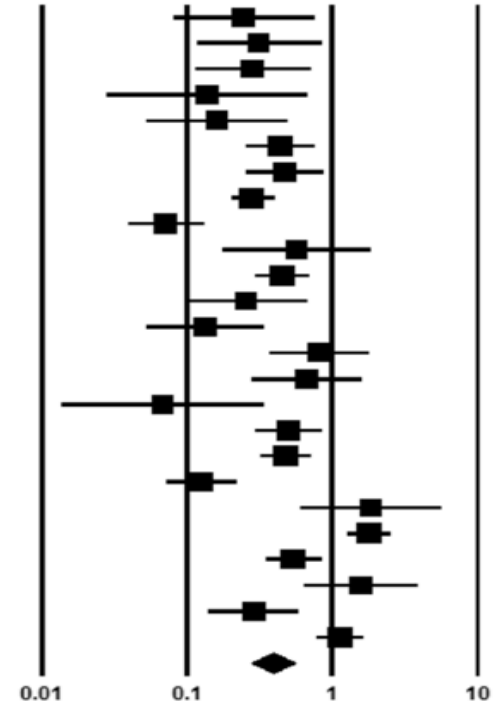
Partial Prevention of HCC by IFN Therapy
A Meta-analysis of 59 Studies

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Mazella G et al (1996)	0.245	0.080	0.754	-2.452	0.014
Bruno S et al (1997)	0.312	0.115	0.843	-2.296	0.022
Fattovich G et al (1997)	0.282	0.113	0.706	-2.703	0.007
Serfaty L et al (1998)	0.136	0.028	0.668	-2.457	0.014
Benvegnu L et al (1998)	0.161	0.052	0.496	-3.176	0.001
International Interferon-α Hepatocellular Carcinoma Study Group (1998)	0.438	0.253	0.756	-2.961	0.003
Imai Y et al (1998)	0.471	0.254	0.873	-2.393	0.017
Yoshida H et al (1999)	0.281	0.199	0.397	-7.210	0.000
Okanoue T et al (1999)	0.071	0.039	0.131	-8.534	0.000
Valla DC et al (1999)	0.569	0.176	1.838	-0.943	0.346
Ikeda K et al (2001)	0.452	0.291	0.702	-3.534	0.000
Gramenzi A et al (2001)	0.254	0.095	0.680	-2.726	0.006
Nishiguchi S et al (2001)	0.132	0.052	0.337	-4.244	0.000
Testino G et al (2002)	0.816	0.375	1.776	-0.513	0.608
Coverdale SA et al (2004)	0.664	0.277	1.594	-0.916	0.360
Azzaroli F et al (2004)	0.068	0.014	0.338	-3.283	0.001
Shiratori Y et al (2005)	0.501	0.296	0.845	-2.589	0.010
Yu ML et al (2006)	0.477	0.321	0.710	-3.653	0.000
Sinn DH et al (2008)	0.127	0.072	0.223	-7.147	0.000
Di Martino V et al (2011)	1.841	0.605	5.603	1.075	0.282
Tateyama M et al (2011)	1.799	1.264	2.561	3.260	0.001
Maruoka D et al (2012)	0.538	0.345	0.840	-2.730	0.006
Cozen ML et al (2013)	1.569	0.634	3.885	0.974	0.330
Aleman S et al (2013)	0.287	0.139	0.590	-3.390	0.001
Cozen ML et al (2016)	1.132	0.775	1.654	0.641	0.522
	0.392	0.275	0.557	-5.209	0.000



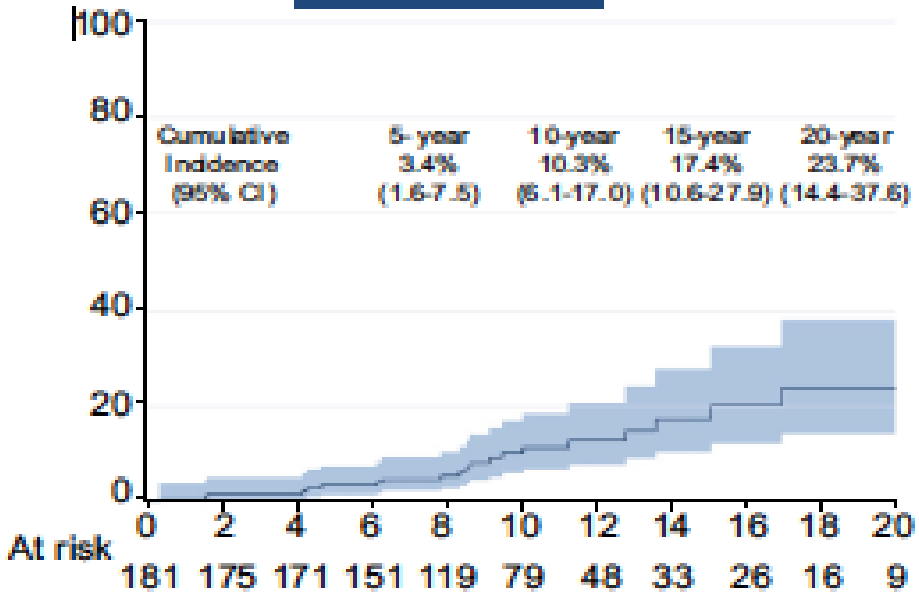
OR for SVR vs non-SVR: **HCC** **0.203 (CI 0.164-0.251)**
AC Mortality **0.255 (CI 0.199-0.326)**

Bang and Song BMC Gastroenterology 2017,17;46

Survival of HCV Cirrhotics and SVR to Peg/RBV Is Comparable to the General Population.

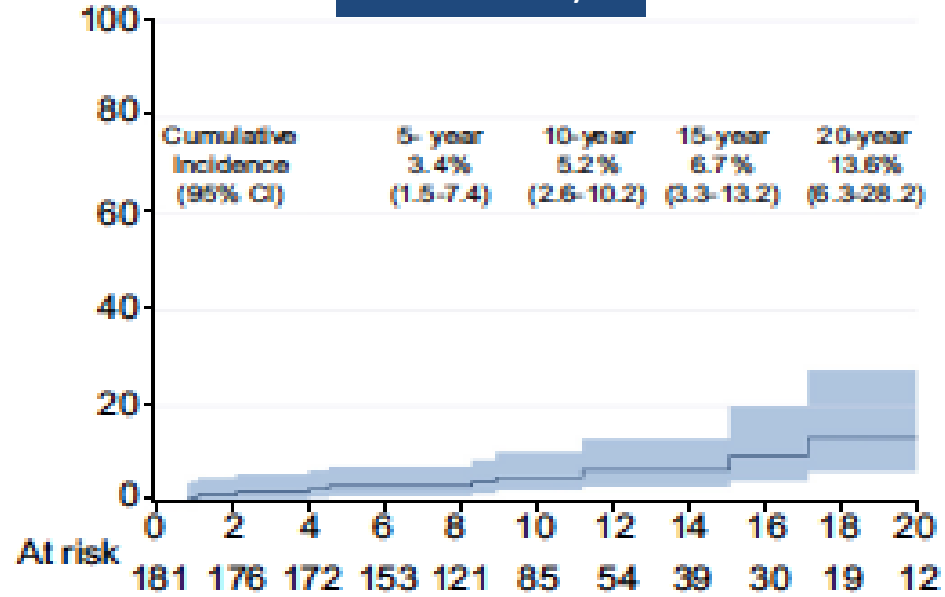
Hepatocellular Carcinoma

10.3% at 10 yrs
23.7% at 20 yrs



Liver Decompensation

5.2% at 10 yrs
13.6% at 20 yrs



Bruno et al J Hepatol 2016; 64:1217–23

Is De Novo Occurrence of HCC Modified by DAA Therapy of HCV?

Author	HCC /Cirrhosis	Follow-up (mo.)	HCC Incidence
Kozbial	16/173	12	4.8% SVR *vs* 6.0% all
Cardoso	4/54	12	7.4% (all SVR)
Conti	9/285	6	2.5% SVR *vs* 3.2% all
Cheung	38/667	6	5.4% SVR *vs* 11.1% untreated
Kobayashi	2/77	60	2.6% *vs* 2.3% IFN treated

Kozbial et al. J Hepatol 2016, Cardoso et al. J Hepatol 2016, Conti et al. J Hepatol 2016, Cheung et al. J Hepatol 2016. Kobayashi et al J Med Virol 2017

Increased Risk of HCC in HCV Cirrhotic Patients After DAA. A Multicenter Study Spain

A Multicenter Prospective Study in Italy and Spain

Cohort : 94 HCV,30 HBV and 133 NASH and/or ASH

Independent predictors of de-novo HCC

- DAA (OR 4.770, CI 1.395-16.316, p=0.013
- Large varices (OR 3.857 ,CI 1.127-13.203, p=0.032

Faillaci et al Hepatology 208

Reig M et al EASL ILC Paris 2018 LBP-024

Incidence of HCC Is Reduced After DAA Therapy 129 Veterans Affairs Hospitals

- Adjusted HR of HCC in SVR : 0.28 (0.22-0.36) p < .0001
- 44.8% HCC diagnosed during DAA treatment were classified as stage I
- Predictors of persistent HCC risk after SVR:

  Advanced age,cirrhosis,diabetes

<u>Caveats</u>

- HCC diagnosed with ICD-9 and10 codes
- 7.7% patients excluded due to lack of SVR data

Kanwal et al Gatroenterology 2017

All-causes Mortality Is Reduced by DAA in Parallel 129 Veterans Affairs Hospitals

Non advanced HCV : full report in Hepatology

- SVR to DAA	39,374 (96,8%)	*mortality = 1.18
- Non SVR to DAA	1,290 (3,2%)	mortality = 2.84
- Untreated	62,682	mortality = 3.84

*x 100 patients x yr

Buckus et al. Hepatology. 2018 Jan 29. doi: 10.1002/hep.29811

Backus LI et al AASLD Washington 2017 abs # 78;

A Prospective Observational Study with Planned Surveillance for HCC.NAVIGATOR

Second year follow-up

- **HCC rates** :
  - Metavir stage F3 = 0%
  - Child-Pugh A = 0.25%
  - Child-Pugh B = 0.69%

- **Aggressive tumor** : 29% , mostly within 6 mo.of DAA therapy
  - non SVR > SVR

Romano A et al J Hepatol 2018

Romano A.et al AASLD 2016 abs #19

HCC after DAA in HCV Compensated Cirrhosis Prospective Multicenter CIR-VIR Study

- 1270 patients
- 3 yr HCC in SVR : DAA 6.0% *vs* IFN 2.9% *vs* non SVR 30.3%, p < 0.0001
- SVR-DAA *vs* SVR-IFN = HR 2.46 ,CI 1.18-5.11, p = 0.01

HCC Predictors

Lack of surveillance pre DAA, co-morbidities & CPT stage

Groups	Number at risk (events)										
DAAs	336	(12)	263	(3)	117	(0)	13	(0)	6	(0)	4
SVR-IFN	495	(2)	474	(9)	436	(3)	391	(6)	352	(3)	260
Non-SVR	923	(17)	797	(33)	676	(42)	518	(22)	400	(18)	288

Groups	Number at risk (events)					
DAAs (IPTW weights)	956	698	384	92	53	43
SVR-IFN (IPTW weights)	1076	1043	965	849	771	532
Non-SVR (IPTW weights)	1029	892	760	613	478	357

Nahon P et al EASL ILC Paris 2018 PS-020

De-novo HCC after DAA Driven by Pre-existing Nodules.A Multicenter Prospective Study

Annual rates - 6.4% in non malignant nodules *vs* 2.7% in nodule-free.

De novo

Pretreatment Lesions on Magnetic Resonance Imaging in Patients With Hepatitis C Virus Infection Diagnosed With Hepatocellular Carcinoma After Initiating Direct-Acting Antiviral Therapy

Scott RA , Aithal GP & Francis ST Gatroenterology 2018

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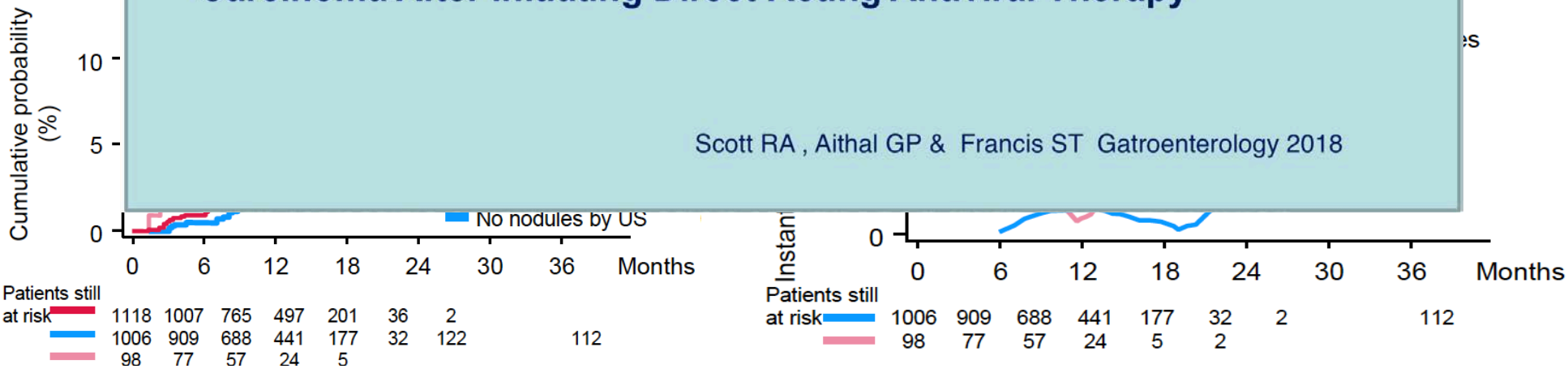

Sangiovanni A et al EASL ILC Paris 2018 PS-152

Chronic Hepatitis C and HCC : What is new?

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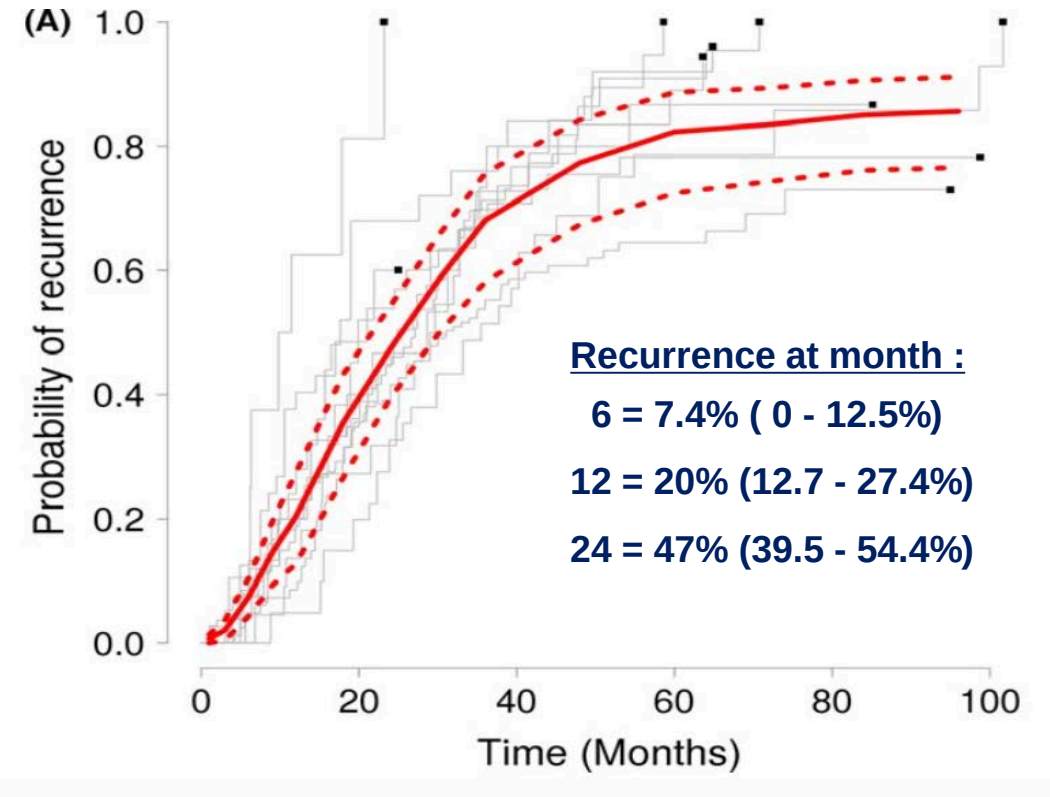
Recurrence Rates of HCC in HCV Viremic Patients After Curative Resection or Ablation

META ANALYSIS

Ikeda 2000
Suou 2001
Shiratori 2003
Hung 2005
Nishiguchi 2005
Yamanaka 2005
Mazzaferro 2006
Kudo 2007
Jeong 2007
Kanogawa 2014
Petta 2016

Total of 701 viremic patients



Recurrence at month :

6 = 7.4% (0 - 12.5%)

12 = 20% (12.7 - 27.4%)

24 = 47% (39.5 - 54.4%)

Recurrence risk : albumin, RCT and follow-up

Mortality risk : tumor size and AFP

Cabibbo G et al Liver Intern 2017;37:1157-66

HCV Decompensation Drives Mortality After a Cure of Early HCC.A Multicenter Study

- 328 BCLC 0/A HCV viremic patients with a fully eradicated HCC
- After 5 years : 44% OS , 64% had recurrence , 44% decompensated

Predictors of 5-year OS

- Early hepatic decompensation (10%)	HR 7.52 (1.23–13.48)
- Early recurrence (21%)	HR 2.50 (1.23–5.05)
- Esophageal varices at baseline (38%)	HR 1.66 (1.02–2.70)
- Age	HR 1.04 (1.02–1.07)

Cabibbo G et al J Hepatol 2017;67:65–71

DAA and Increased Risk of HCC Recurrence
The Start of the Debate

CONFIRMATORY STUDIES

- **Conti et al, J Hepatol 2016**
- **Reig et al, Multicenter study in Spain, EASL ILC Amsterdam 2017**
- **El Kassas et al, JVH 2018 (increased severity not confirmed)**

Reig M et al J Hepatol 2016

Studies Denying Increased Recurrence of HCC After DAA Therapy of HCV

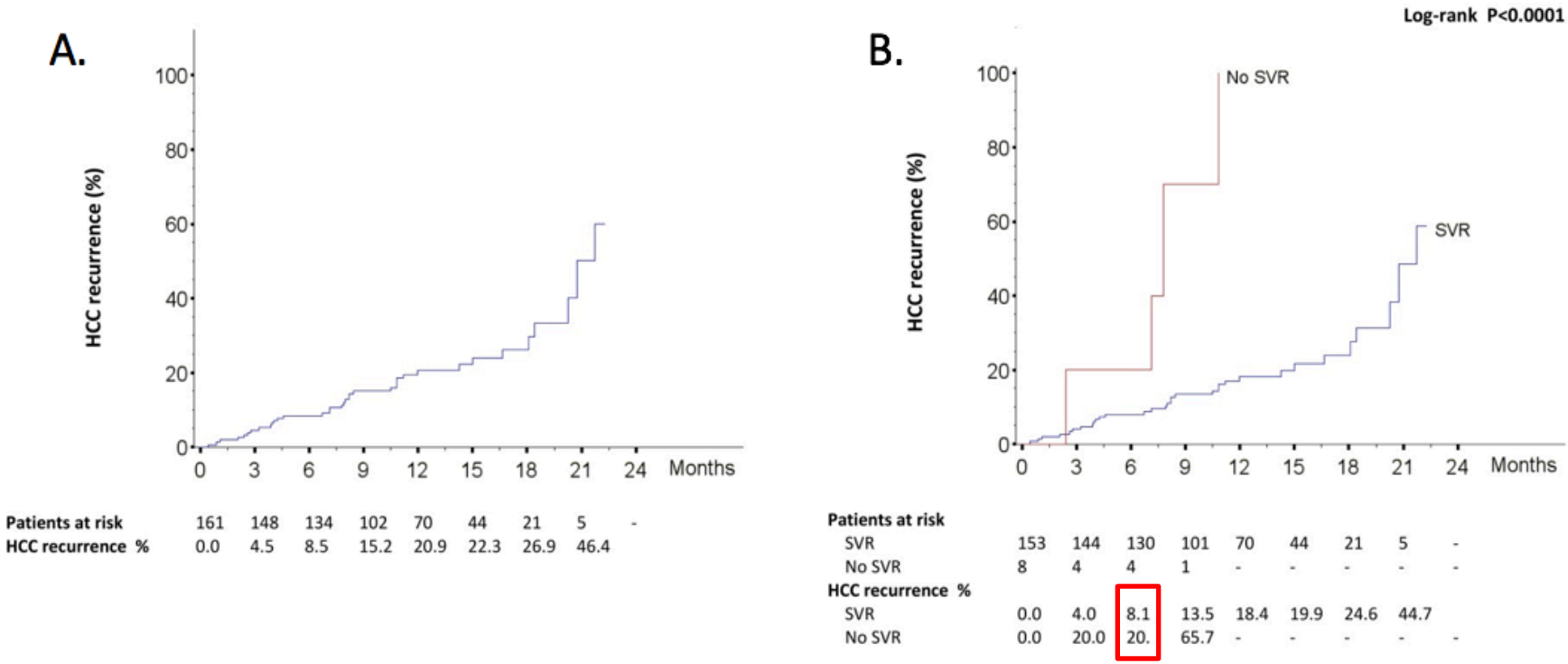
Study	Design	N (DAAs)	% cirrhosis % CPT-B	Time 0	Follow-up (months)	Recurrence
Zavaglia et al. J. Hep 2016 (Letter)	Retrospective	31	100 19	Start DAA	8	3.2%
Cheung J. Hep 2016	Prospective*	29	100 83	Start DAA	15	6.89%
HEPATHER J. Hep 2016	Prospective*	189	80 NR	NR	26	0.73 vs 0.66 /100p/mo
CIRVIR J. Hep 2016	Prospective*	13	100 NR	HCC treatment	21	1.1 vs 1.73 /100p/mo
Virlogeux Liver Int 2017	Prospective*	23	100 0	HCC treatment	15	1.7 vs 4.2 /100p/mo
Nagata J. Hep 2017	Prospective*	83	NR	HCC treatment	24	29%

*** HCC not a primary endpoint, retrospectively analysed from prospective databases**

Reviewed by Dr Lens at EASL HCC Summit, Geneva 1-3 April 2018

HCC Recurrence after DAA Therapy of HCV A Multicenter Prospective Study,Italy

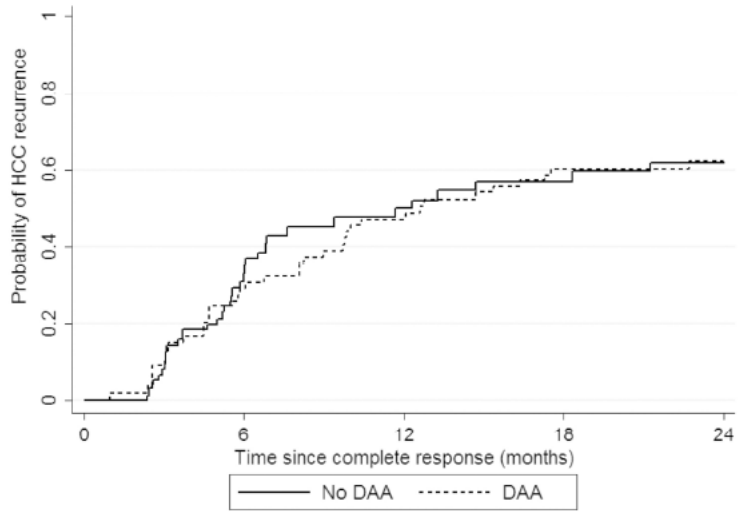
- A prospective population study from 10 referral centers in Italy
- HCC after 1-yr : 50/1766 de-novo and 38/166 recurrences



Lleo A et al EASL ILC Paris 2018 ;Gut in press

HCC Recurrence after LAT in Waitlisted Patients at UCSF Transplant Center

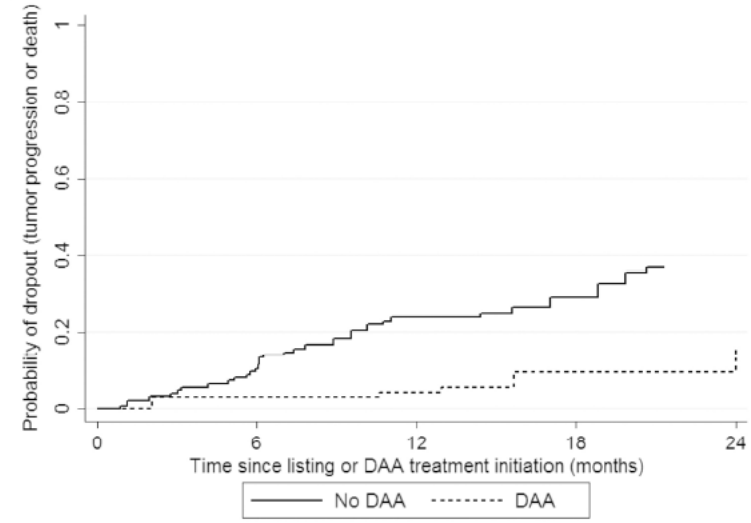
HR 0.91, 95% CI 0.58-1.42, p=0.67



Number of patients at risk

Month	0	6	12	18	24
No DAA	59	30	13	3	1
DAA	61	38	23	6	3

HR 0.30, 95% CI 0.13-0.69,p=0.005



Number of patients at risk

Month	0	6	12	18	24
No DAA	87	57	32	11	0
DAA	62	45	25	15	7

Huang et al Hepatology 2018

Post-transplant HCC Recurrence Following DAA Therapy of HCV in the Wait List

Study	Pt #	HCC at explant	Months btwn HCC diagnosis to LT	Recurrence
Yang et al	18	60% > Milan	n.a.	5 (27.8%) * 4-17 mo.post-LT 60% MVI
Donato et al	28	29% > Milan 35% complete necrosis 35% MVI	3-38	3 (10.7%)* 13-20 mo. post-LT 100% MVI
Pascual et al	15	-	-	1(6.6%) 5 mo.post-LT 10 bridged with TACE

Yang J Hepatol 2016 ; Donato J Hepatol 2017; Pascual AASLD 2018 abs1638 ** All bridged with RFA or TACE*

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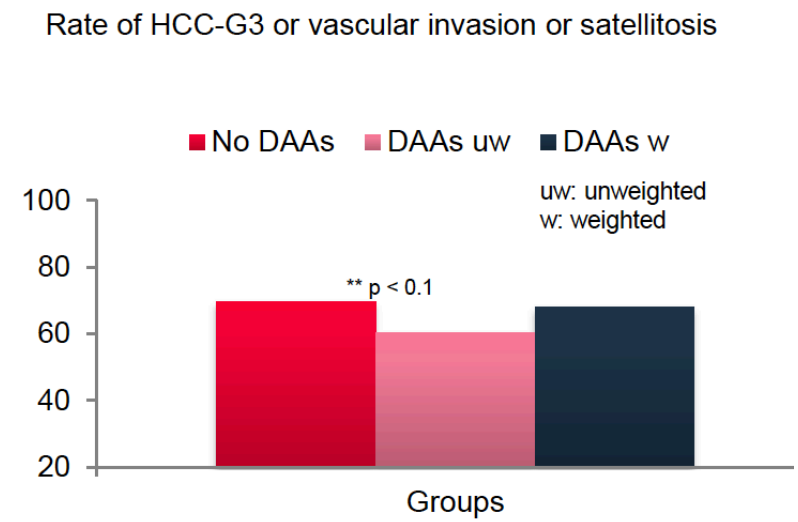
Is HCC Developing After DAA More Aggressive ?

- 420 consecutive patients with HCC/HCV cirrhosis undergoing liver resection in 18 Italian centers.
- 77 (18.3%)developed either recurrent or de novo HCC after DAA therapy.
- The study group showed significantly smaller tumors than the control group (25 mm vs. 35 mm).
- The study group showed a significantly lower incidence of severe complications (3.4% vs. 9.3%) and early postoperative mortality (2.0% vs 5.4%).

Variables	No DAAs (n=342) N° of patients evaluated Median (IQR) or n° %	DAAs pre resection (n=324) N° of patients evaluated Median (IQR) or n° %
Largest Diameter (mm)**	34 (22-55)	27 (20-43)
Multinodular	76 (22.2)	78 (24.1)
Microvascular invasion	134 (39.2)	112 (34.5)
Macrovascular invasion	27 (7.9)	33 (10.1)
Poorly differentiated	164 (48.0)	155 (47.7)
Satellitosis	59 (17.3)	49 (15.1)
Margin < 2 mm	135 (39.4)	135 (41.6)
Aggressive pathology	238 (69.6)	222 (67.9)



Vitale A et al EASL ILC Paris 2018 PS-023

Increased Recurrence/Aggressiveness After DAA
A Confirmatory Multicenter Study

Whole cohort (n=77)	
Median follow-up,months	12.4 (IQR: 8.4-18-7)
HCC progression	n= 24 (31.2%)
Death	n=5 (6.5%)

HCC recurrence (n=24)	
Median months between start DAA and 1st HCC recurrence	3.5 (IQR: 2-7.6)
2nd recurrence / progression	n=10
Median months between 1st- 2nd HCC recurrence/progression	6 (IQR:3.2-8.2)
Recurrence/progression within 6 months of 1st recurrence	6/20 (30%)
Death	n=5 (20.8%)

16.7%
BSC

37.5 %
Ablation
Resection
LT

45.8 %
TACE
Sorafenib
Regorafenib
RE
Clinical Trials

Reig M et al EASL ILC Amsterdam 2017; Abstract PS-031

Is HCC Recurrence Exacerbated by DAA Therapy? AASLD Liver Meeting 2017

Author	Abstract #	N of patients	HCC Recurrence Rates
Nakagawa	66	725	Unchanged
Degasperi	77	565	Unchanged
Sangiovanni	370	594	Reduced, >% at 30 weeks
Joko	1386	347	Unchanged*
Cimavilla	1391	1,126	>BCLC B-D
Monto	1412	164	Rapid onset
Ohki	1418	51	Reduced*
Minami	421	163	Unchanged
Yousif	459	158	Unchanged, > Aggressive
Kuftinec	1554	177	Rapid growth
Nakao	1565	843	Unchanged
Urabe	1579	119	Unchanged
Teng	1609	123	Reduced
Singal	1361	191	Not increased, shorter time to recurrence

*Compared to IFN treated patients

Hepatology oct 2017; 66(1 Suppl)

Increased Incidence *vs* Accelerated Recurrence of HCC in DAA Treated Patients?

A retrospective study of 191 patients in 10 US centers

- Jan 2013 - dec 2016	107 DAA treated
- HCC treatment	32% Res, 35% LAT, 27% TACE
- Recurrence rates	n. 87, 42% DAA *vs* 53% untreated(p=n.s)
- Days to recurrence	223 DAA *vs* 554 untreated (p<.006)
- HCC beyond Milan	27%

Singal A AASLD Washington 2017 abs 191

Increased Occurrence/Recurrence of HCC After IFN-free DAA. Facts or Artifacts?

Hypothesis : a swift removal of HCV might cause

- Impairment of NK cells-mediated tumor immuno-surveillance.
- TRAIL-related de-escalation of apoptosis.
- Impaired tumor control following reduction of non-specific inflammatory cells.

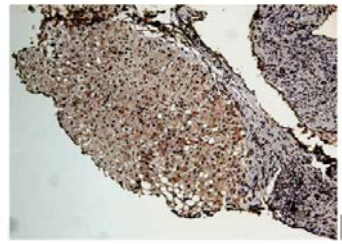
Clues : reactivation of HBV and Herpes virus in HCV co-infected patients treated with DAA. Coagulation pattern modified during DAA therapy.

Debes Lancet Gastroenterol Hepatol ;Bersoff-Matcha AIM 2017;Tripodi Liv Intern 2017

Liver Angiopoietin-2 Predicts De Novo and Recurrent HCC after DAA Therapy of HCV

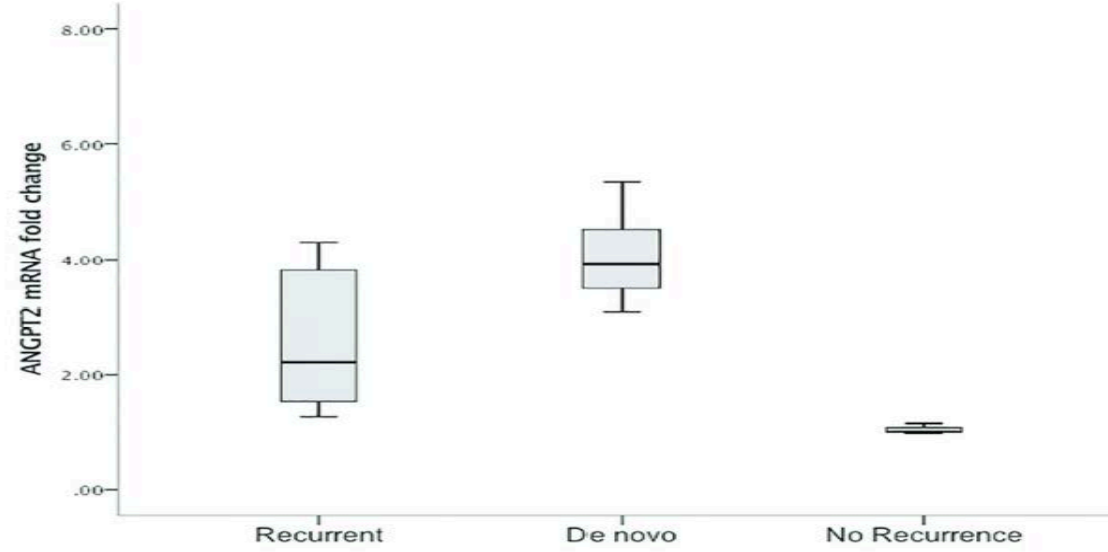
Recurrent and **de novo HCCs** had significantly higher liver fibrosis scores, portal pressure, and systemic inflammation than non-recurrent HCC or patients never developing HCC

Before DAA



Liver after DAA

De-novo HCC After DAA



Fallaci F et al Hepatology 2018

EASL Recommendations for HCV Therapy 2018

Recommendations

- HCV treatment should not be withheld in patients with cirrhosis and these patients will require post-SVR HCC surveillance, because the risk of *de novo* or incident HCC is reduced but not abolished by SVR (**A1**).
- Whether antiviral therapy leads to a long-term survival benefit by reducing the risk of recurrent HCC in patients with treated HCV-associated HCC is unknown. However, these patients frequently have advanced fibrosis or cirrhosis and should receive appropriate antiviral therapy for their liver disease, while careful HCC surveillance is required in these patients (**B1**).

Cost-effectiveness Analysis of HCC Screening in Hepatitis C Cirrhosis after SVR

Parameter	ICER ($/QALY)		HCC Incidence[1,2] %/Year
	q6m	q12m	
No cirrhosis	$339,876	$134,345	0.16–0.34
Cirrhosis	$42,823	$31,096	1.39–1.82
FIB-4 < 3.25	$103,976	$63,635	0.41
FIB-4 > 3.25	$38,928	$28,898	2.16
APRI < 2	Dominated	$841,181	0.093
APRI >2	$55,916	$38,516	0.89

Under/over willingness to pay threshold of $50,000/QALY

.

- Cost effectiveness sensitive to HCC incidence (~1.1%/year threshold for q6m US).
- US surveillance cost effective in cirrhosis, unlikely in non cirrhosis
- APRI and FIB-4 can identify patients for whom post-SVR surveillance is likely to be cost-effective

1.Kanwal F, et al. Gastroenterology 2017; 2. El-Serag HB, et al. Hepatology 2016; Zangneh HF, et al. ILC 2018, PS-061

DAA Therapy and HCC . Clues From the Literature

1. Should HCV be treated prior to HCC eradication?	No, maybe in listed?
2. Is the incidence of de-novo HCC increased?	No, likely to be reduced
3. Are de-novo tumors more aggressive?	No, sparse cases only
4. Is time to recurrence from a tumor cure shortened?	Yes, significantly
5. Is the pattern of recurrent HCC modified?	Unclear, prospective studies needed

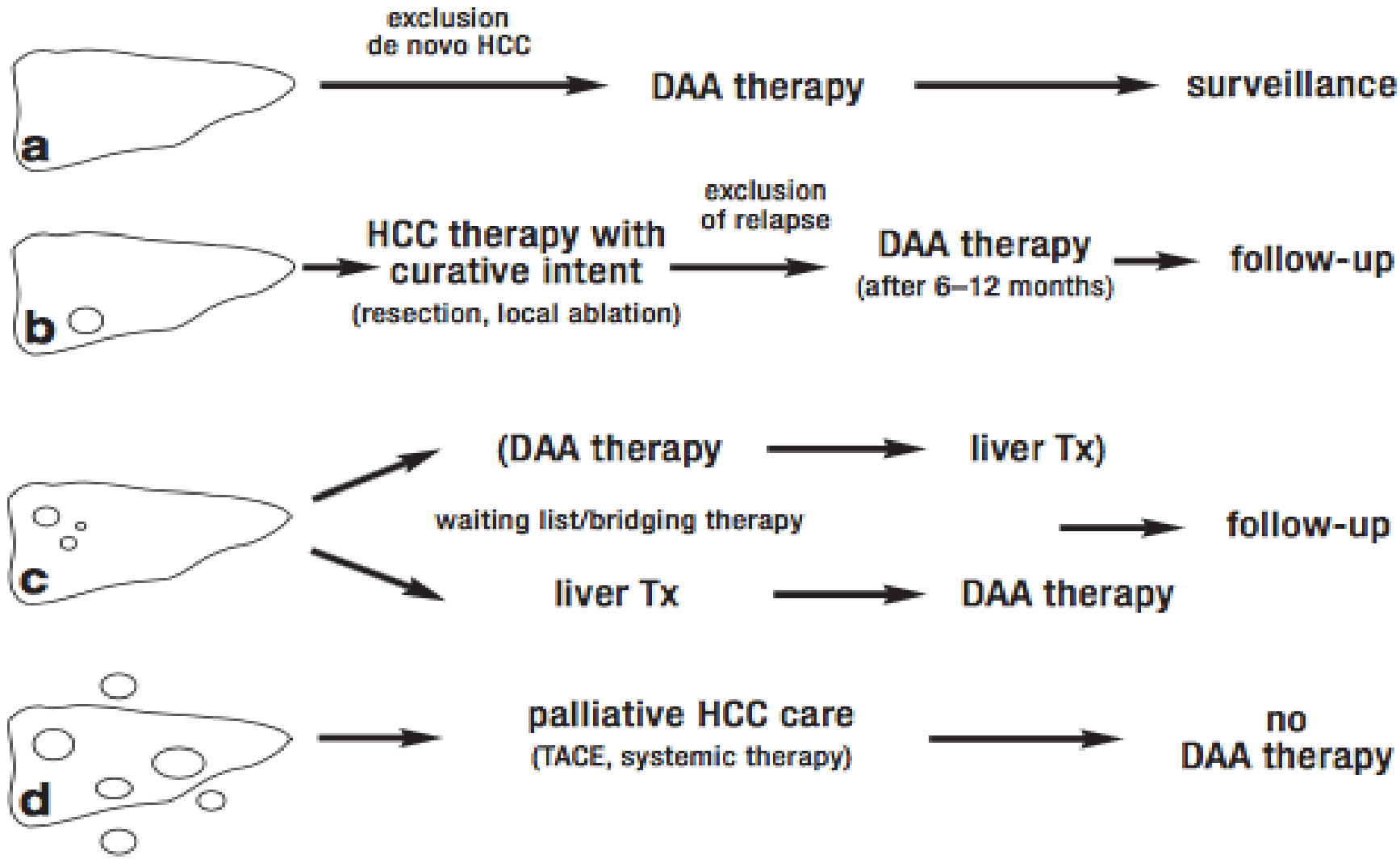
Personal communication, Dr Colombo

EASL Recommendations for Management of HCC

Recommendations	Level of evidence	Grade of recommendation
Once cirrhosis is established: • **Antiviral therapy*** is beneficial in **preventing cirrhosis progression** and decompensation • Successful **antiviral therapy reduces but does not eliminate** the risk of **HCC** development	Moderate	
For patients with HCV-associated cirrhosis and treated HCC: • **HCC recurrence rate is high** even after SVR with DAA therapy† • **Close surveillance is advised** in these patients • The benefit of viral cure must be weighed against a potentially higher recurrence risk	Low	Strong

EASL CPG J Hepatology 2018

Reccomendations of the German Alliance for Liver Cancer (GALC)



Worns MA et al Dtsch Arztebl Int 2017; 114: 597–602

EASL CPG. Post-treatment Surveillance of Patients Who Achieve an SVR

- Non-cirrhotic patients with SVR should be retested for ALT and HCV RNA at 48 weeks post-treatment, then discharged if ALT is normal and HCV RNA is negative.

- Patients with pre-existing cofactors for liver disease (notably, history of alcohol drinking and/or type 2 diabetes) should be carefully and periodically subjected to a thorough clinical assessment.

- The exact duration of HCC surveillance in patients with advanced fibrosis or cirrhosis who achieve an SVR is unknown in the current state of knowledge, but is probably indefinite .

EASL Clinical Practice Guidelines J Hepatol.2016

Propensity Score Analysis of a Prospective Database of HCC After IFN-free DAA. Japan

Cohorts	1145 treated with IFN *vs* 752 with IFN-free DAA .	
Incident HCC (3-yr)	3.3% in IFN *vs* 1.4% in IFN-free	*p* = 0.49
Recurrent HCC (5-yr)	54.2% in IFN *vs* 45.1% in IFN-free	*p* = 0.54
HCC Predictor	higher levels of post-treatment AFP or *Wisteria floribunda* agglutinin positive Mac-2 binding protein (WFA+M2BP)	

Nagagawa M et al AASLD Washington 2017 abs # 66

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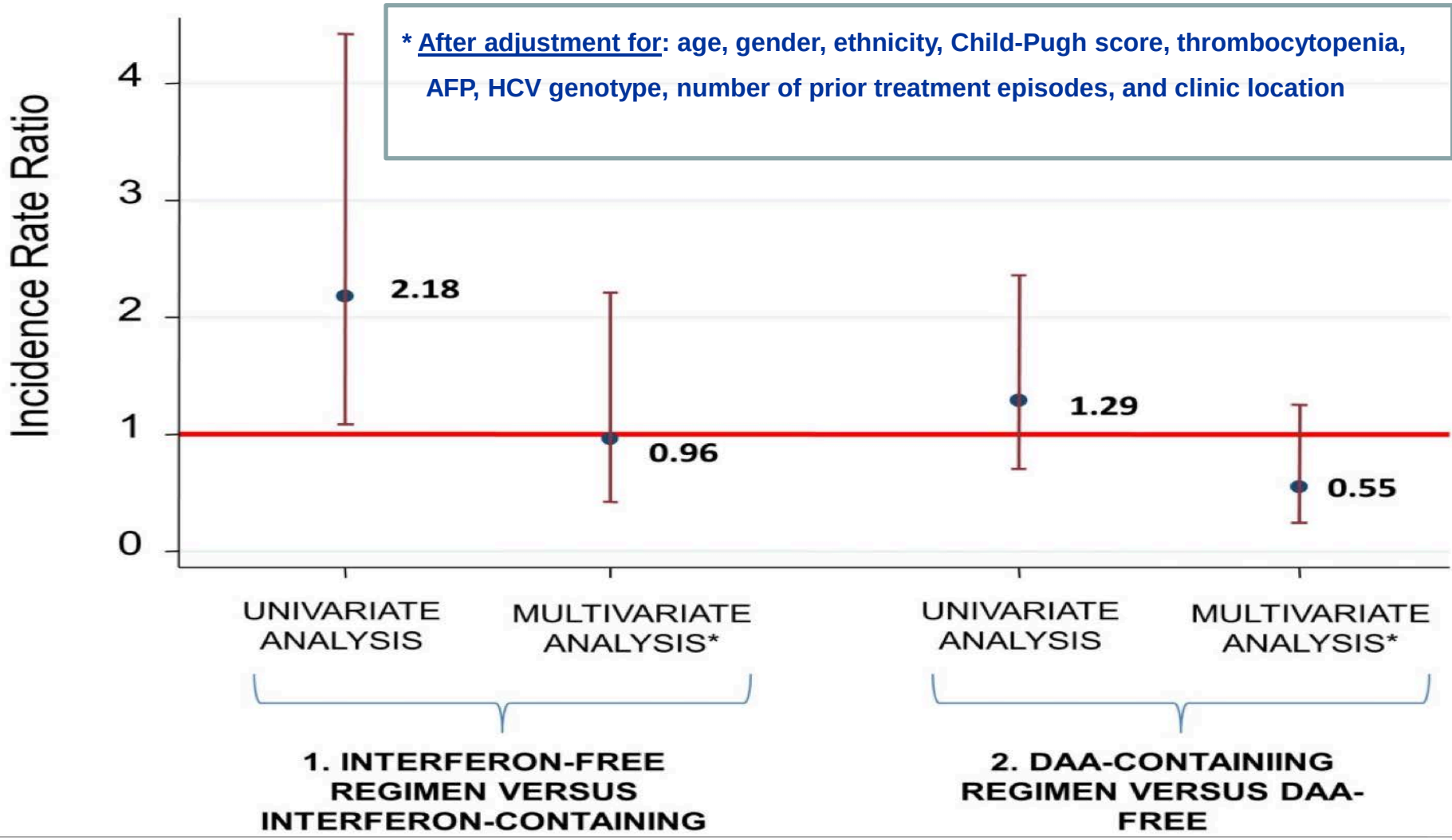
Nagagawa M et al AASLD Washington 2017 abs # 66

HCC Occurrence After IFN vs DAA Therapy



Innes et al EASL ILC Amsterdam 2017

DAA and Increased HCC risk. Facts or Artifacts?

- Populations with incremental higher risk of HCC than IFN candidates

- Imbalance of pro- and anti-tumour function of the immune system:

  - altered NK function

  - altered expression of IFN response

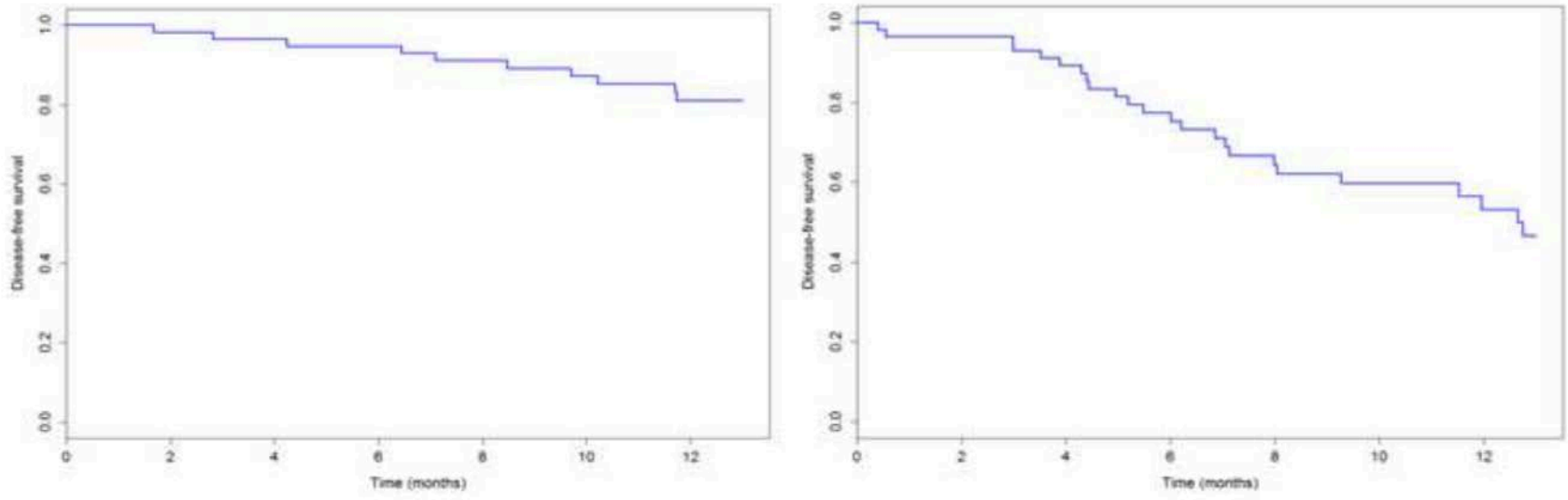
  - altered immuno surveillance

A Multicenter Study of HCC Recurrence Following IFN-free Therapy of Hepatitis C

Fifty six patients treated with Resection(39%),Ablation(39%) or TA(C)E(21%)

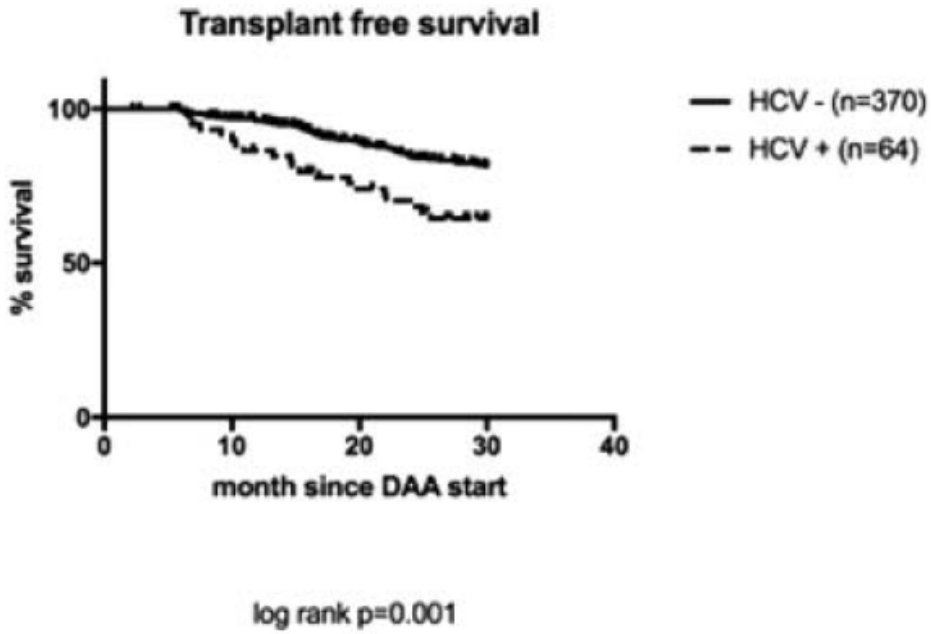
HCC diagnosis : 21 months from HCC Tx and 9.3 months from DAA Tx

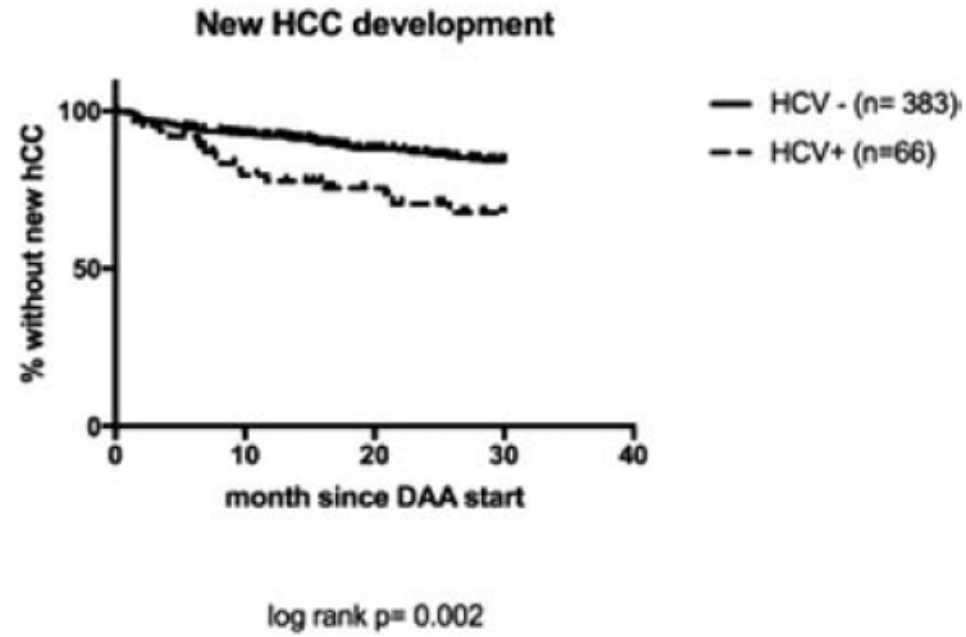
DFS = 75% at month 6 after DAA therapy and 56% at month 24 cumulatively.



Kolby et al J Hepatol 2017

U.K. Expanded Access Program to DAA of Patients with Decompensated HCV





Cheung M et al EASL ILC Paris 2018 LBP-009

Similar Rates of De-novo HCC in Patients With SVR to IFN and DAA. A Meta-analysis

Weaknesses of the meta-analysis by Waziry

Heterogeneity : country of origin,design,sample size, inclusion criteria,baseline demography,schedules of treatment and surveillance, assessment of radiological response, tumour diagnosis and treatment.

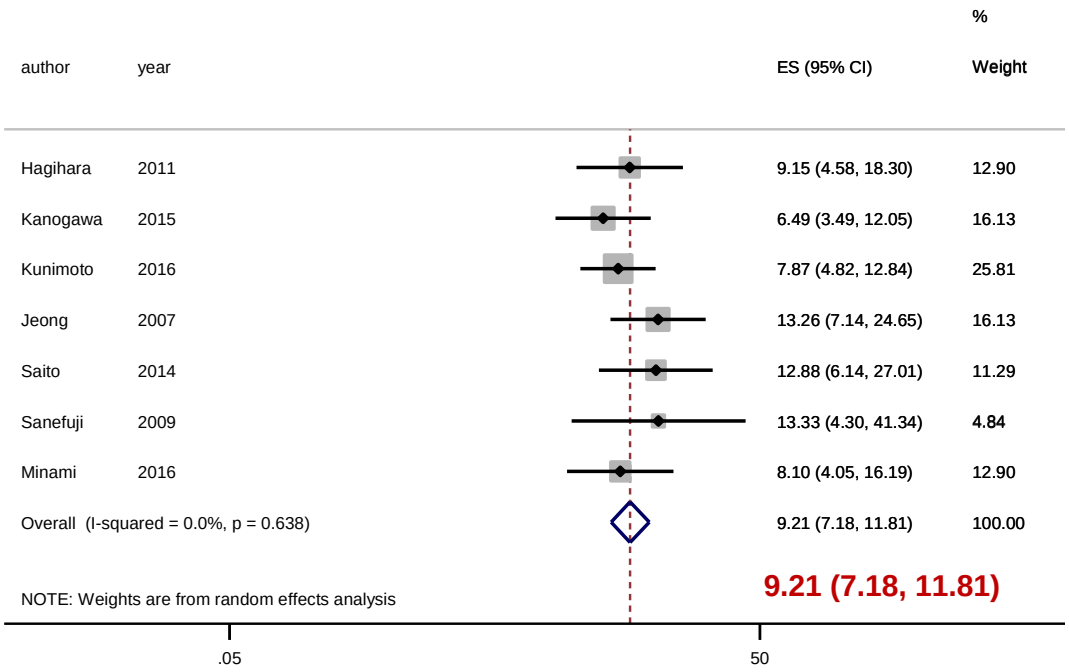
Meta-analysis of individual data needed to overcome all referral biases

Camma C. et al J Hepatology 2018; 68 : 614–615

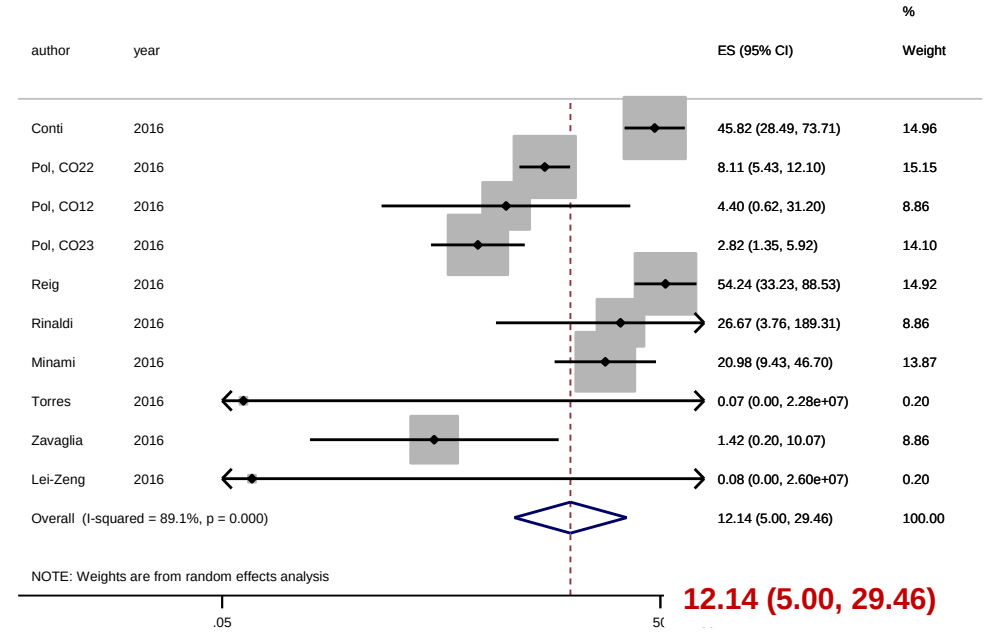
Waziry R et al J Hepatol 2017;67:1204- 1212.

Similar Rates of Recurrence in Patients With an SVR to IFN and DAA. A Meta-analysis

IFN



DAA



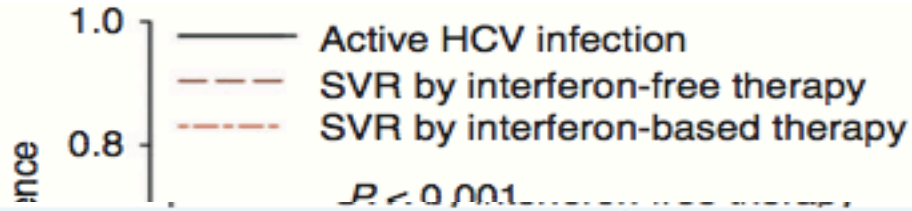
Meta regression of HCC recurrence

	RR non adjusted	RR adjusted	IC 95 %	P value
Average follow-up	0,86	0,79	0,55-1,15	0,19
Average Age	1,11	1,11	0,96-1,27	0,14
Treatment	1,36	0,62	0,11-3,45	0,56

Waziry et al J Hepatol 2017;67:1204- 1212.

HCC Recurrence in Patients with Curative Resection or Ablation.ITALICA Cohort

BCLC A/O patients with a HCC
62 yr IFN vs 66 yr DAA



	Groups		
	Active HCV infection (*N* = 328)	SVR by IFN-free therapies (*N* = 58)	SVR by IFN-based Therapies* (*N* = 57)
Recurrence during follow-up, *n* (%)	142 (43.3)	16 (27.6)	22 (38.6)
Follow-up length, median (range)	17 (1–95)	18 (3–90)	34 (0–138)
Recurence rates			
6-month	9.5%	5.2%	3.7%
1-year	21.0%	12.9%	5.6%
2-year	40.6%	26.3%	15.2%
3-year	54.5%	33.5%	29.3%
4-year	60.7%	39.1%	41.1%
5-year	64.5%	39.1%	41.1%
Median time to recurrence, mo. (95% CI)	31 (26–38)	72.0 (40.8–N.A.)	82.3 (39.8–N.A.)

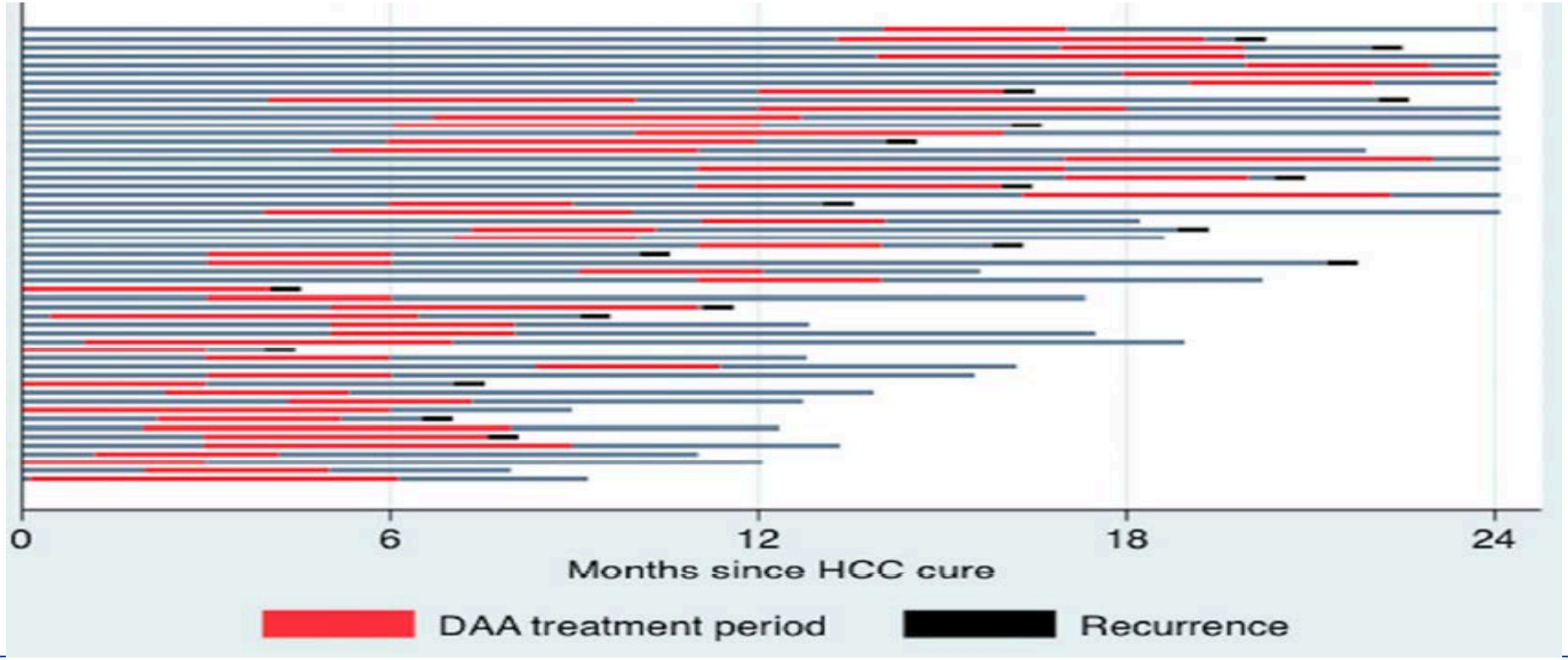
——	328	202	115	61	32	20	8	2	0
– –	58	42	22	13	8	4	4	1	0
-·-·-	57	50	41	26	19	16	14	10	6

Petta S. et al APT 2016

Increased Recurrence of HCC After DAA Therapy
A Cohort Study in Egypt

- 53 patients , 8 mo. btwn HCC therapy and DAA , 37.7% recurrence after 16 mo.

- Adjusted rate ratio *vs* untreated : 3.8 (2.0 – 7.3) p < 0.001



El Kassas et al J Viral Hepat. 2017 Dec 23. doi: 10.1111/jvh.12854.