Hepatitis C: Management update

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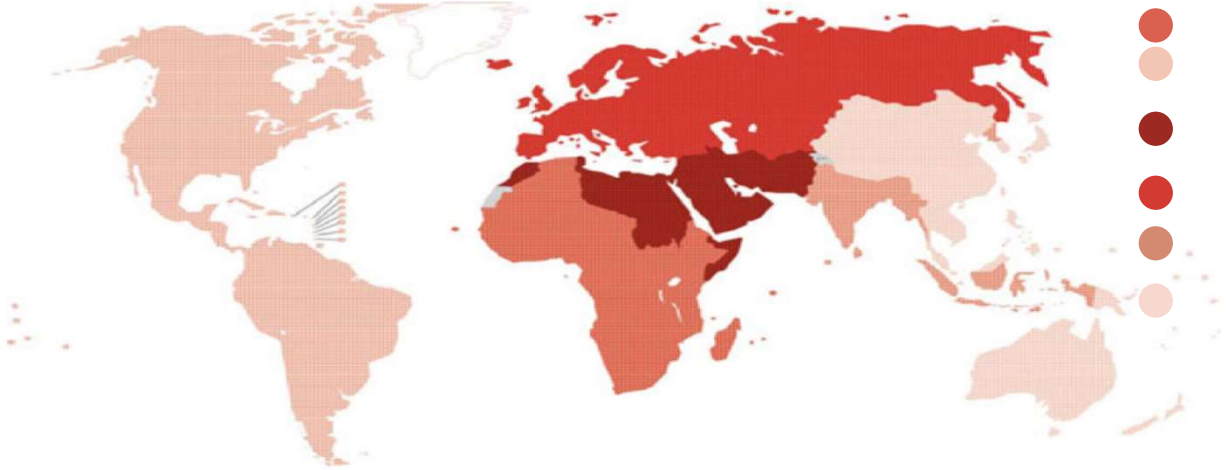
Hepatitis C

- One of the leading causes of infectious disease, approximately 71 million chronically infected worldwide (67,000 deaths/year)
- Major cause of chronic liver disease, may lead to liver cirrhosis with/or Hepatocellular Ca
- Hepatitis C is a curable disease
- Treatment is recommended for all patients with Hepatitis C

Epidemiology of HCV

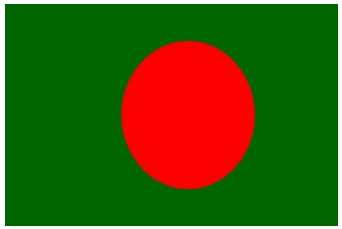
- Estimated global prevalence of HCV in 2015: 1.0% (95% uncertainty interval 0.8–1.1)[1]
- Corresponds to **71.1 million** (62.5–79.4) viraemic infections[1,2]
- ~**399,000** deaths each year, mostly from cirrhosis and HCC[2]
- GT 1 and 3 are the most common causes of infection (44% and 25%, respectively)[1]

Incidence of HCV infection and new HCV infections in the general population, by WHO region, 2015[2]



1. Polaris Observatory HCV Collaborators. Lancet Gastroenterol Hepatol 2017;2:161–76; 2. World Health Organization. Global Hepatitis Report 2017. Available at: http://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf?sequence=1;
EASL CPG HCV. J Hepatol 2018;69:461–511.

HCV: Prevalence in Bangladesh 0.8%



Total area: 1,47570sq. km

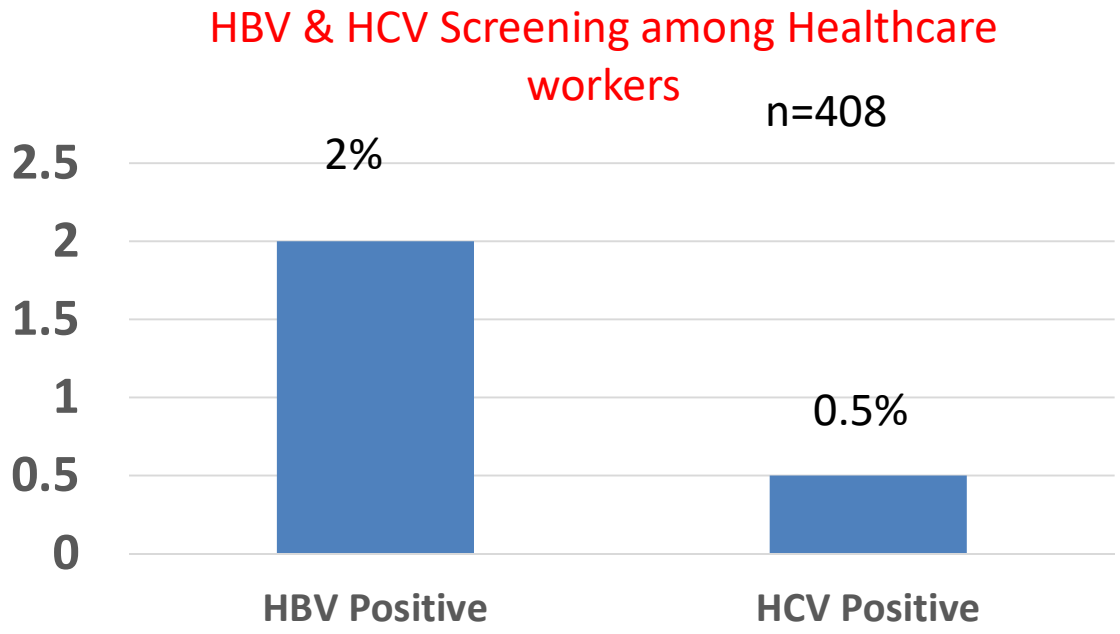
Population: 158.8 mil

Population density/sq. km: 1090

World bank, 2007

Find The Missing Millions.

Study Design: In 2017,Hepatitis C and Hepatitis B was screened among 408 healthcare workers of tertiary care hospital (DMCH)

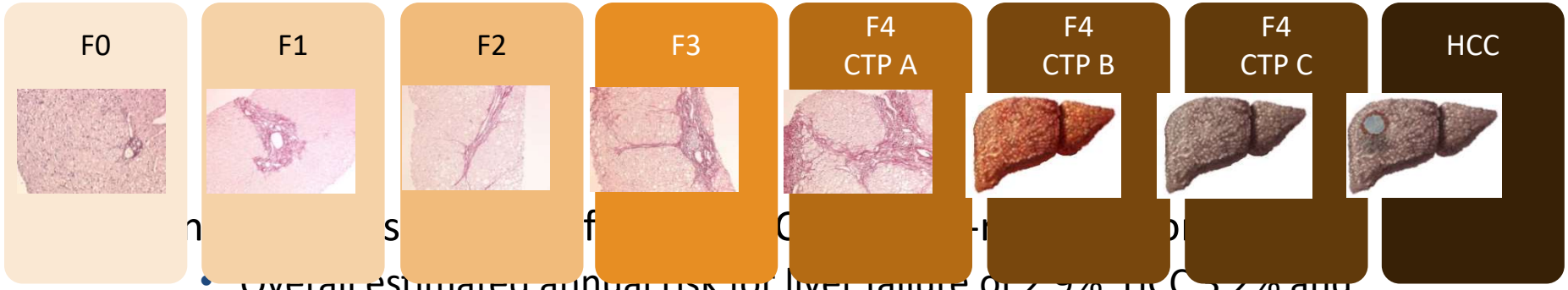


Result: Among 408 participants, 2 persons were found to be affected by Hepatitis C and 8 persons were affected by Hepatitis B

Reference: Unpublished Data(DMCH,Hepatology Dept)

Natural history/disease burden

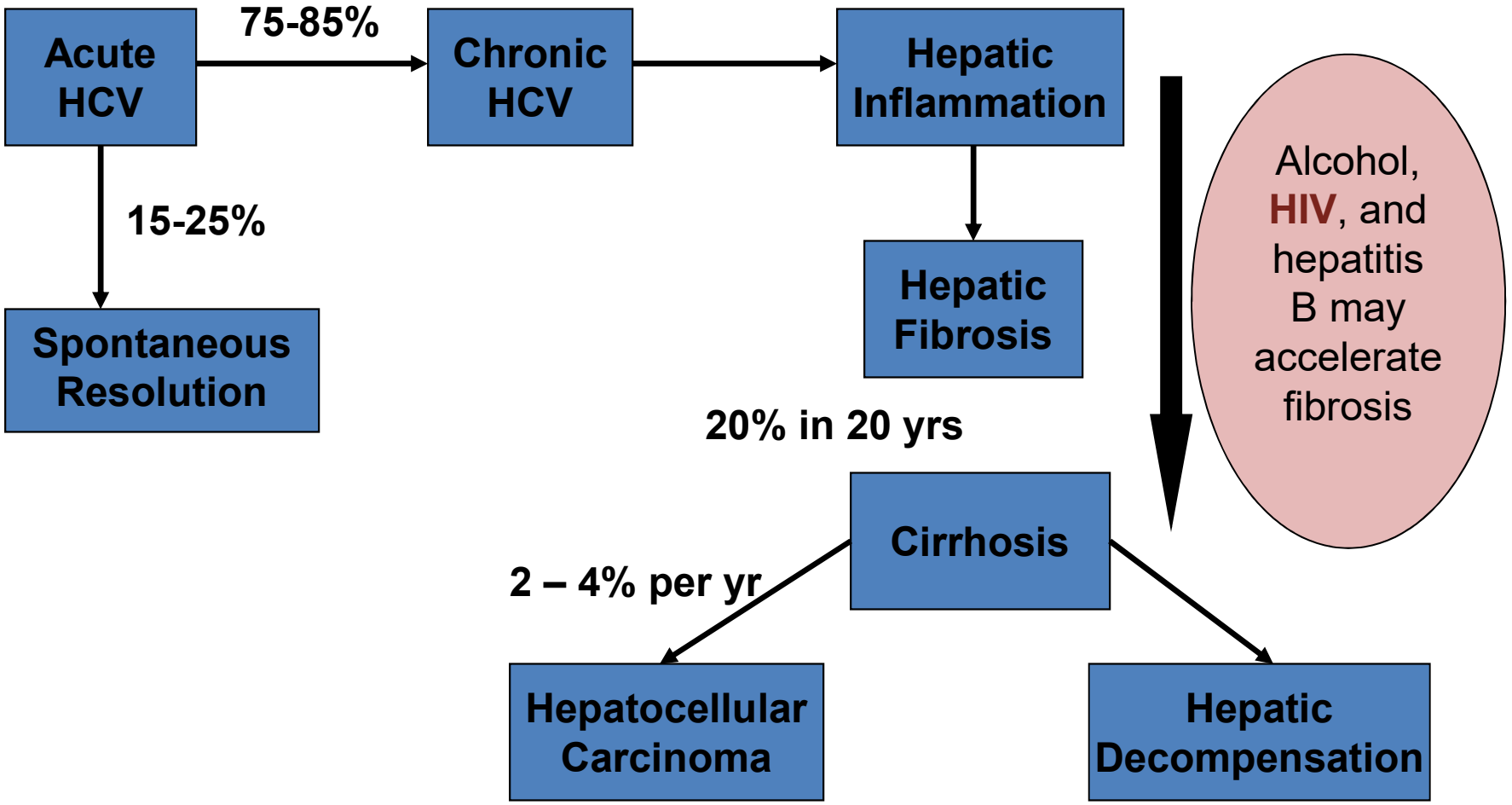
- Long-term natural history of HCV infection is highly variable
- Chronic HCV infection is accompanied by
  - Extrahepatic manifestations reported in up to 75% of patients, including:[1]
    - Mixed cryoglobulinaemia vasculitis, renal disease (elevated creatinine), type 2 diabetes, cardiovascular disease (vasculitis, arterial hypertension), porphyria cutanea tarda, lichen planus and lymphoproliferative disorders
    - Non-specific symptoms: fatigue, nausea, abdominal pain, weight loss
  - Rapid development of hepatic fibrosis and accelerated time to cirrhosis[2]



- Overall estimated annual risk for liver failure of 2.9%, HCC 3.2% and liver-related death 2.7% in patients with advanced fibrosis[1,3]

Figure adapted from Asselah T, et al. J Hepatol 2014;61:193–5

1. van der Meer AJ, et al. J Hepatol 2016;65:S95–S108; 2. Butt AA, et al. JAMA Intern Med 2015;175:178–85;
3. Singh AG, et al. Clin Gastroenterol Hepatol 2010;8:280–8;
EASL CPG HCV. J Hepatol 2018;69:461–511.



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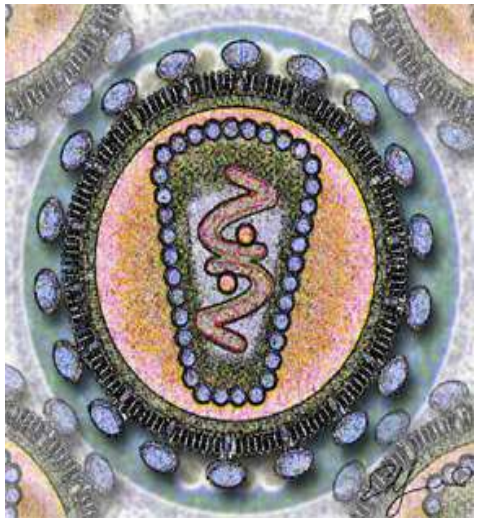
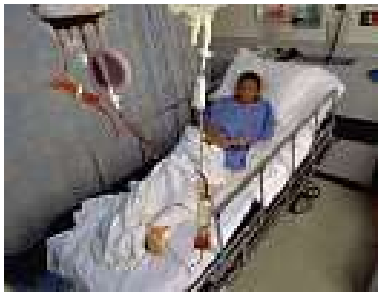
HCV



- Identified and genome cloned in 1989
- Family : Flaviviridae
- Genus : Hepacivirus
- Spherical, enveloped, single-stranded RNA virus
- Replication - > 1 trillion per day

HCV: MODE OF TRANSMISSION



Dialysis

blood products

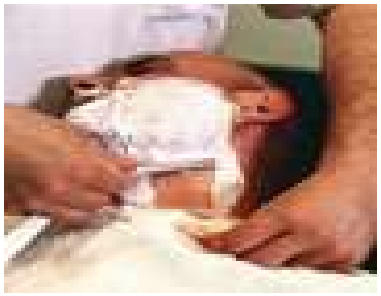
blood

mother to baby

IV drug use

sexual contact

tattooing



barber

Sharing Razors

HCV : Mode of Transmission

Contact with infectious blood, primarily through:

- Sharing needles, syringes or Inj. drug accessories
- Needle-stick or sharp instrument injuries
- Tattooing/body piercing
- Sexual contact with a person infected with hepatitis C
- Birth from a mother infected with hepatitis C
- Receipt of blood and Blood product or organs
- Long-term haemodialysis
- Occupational exposure to blood

Grading evidence and recommendations

- Grading is adapted from the GRADE system[1]

Evidence quality	Notes	Grade
High	Further research is very unlikely to change our confidence in the estimate of effect	A
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	B
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Any change of estimate is uncertain	C
Recommendation	**Notes**	**Grade**
Strong	Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes, and cost	1
Weak	Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, higher cost or resource consumption	2

1. Andrews J, et al. J Clin Epidemiol 2013;66:719e725;
EASL CPG HCV. J Hepatol 2018;69:461–511.

HCV: WHO SHUOLD BE SCREENED

- Recipients of blood and blood products
- Parenteral drug abusers
- Those who take frequent injections or blood tests
- Persons with raised ALT
- Persons who have hepatomegaly or signs of CLD
- Patients on haemodialysis
- H/O Surgery
- Health care workers
- Pregnant women

Recommendations for Counseling Those with Current (Active) HCV Infection

RECOMMENDED	RATING
Persons with current (active) HCV infection should receive education and interventions aimed at reducing progression of liver disease and preventing transmission of HCV.	IIa, B
1. Abstinence from alcohol and, when appropriate, interventions to facilitate cessation of alcohol consumption should be advised for all persons with HCV infection.	IIa, B
2. Evaluation for other conditions that may accelerate liver fibrosis, including HBV and HIV infections, is recommended for all persons with HCV infection.	IIb, B
3. Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see When and in Whom to Initiate HCV Therapy).	I, A
4. Vaccination against hepatitis A and hepatitis B is recommended for all susceptible persons with HCV infection.	IIa, C
5. Vaccination against pneumococcal infection is recommended to all patients with cirrhosis (Marrie, 2011).	IIa, C
6. All persons with HCV infection should be provided education on how to avoid HCV transmission to others.	I, C

Primary goal and impact of HCV therapy

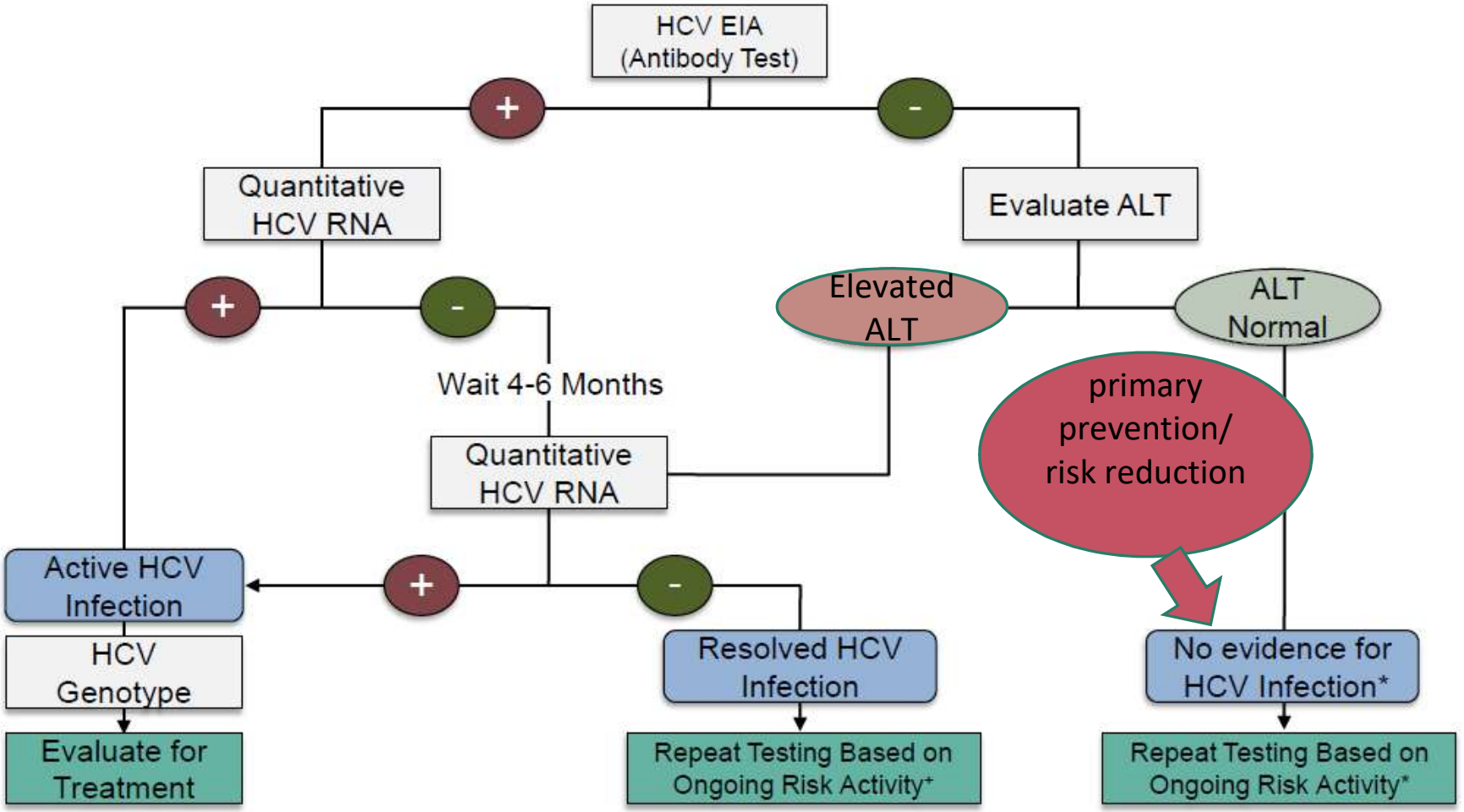
Primary goal of therapy – cure HCV infection (SVR12 or SVR24)
Sustained Virological Response(SVR) defined as undetectable HCV RNA 12 weeks after completion of treatment

- SVR corresponds to a definitive cure of HCV infection in nearly all cases and is frequently associated with
  - Improvement in extrahepatic manifestations[1]
  - Improvement/disappearance of liver necroinflammation and fibrosis[1]
  - Regression of advanced hepatic fibrosis (F3) or cirrhosis (F4)[2]
  - Reduced risk of HCC, hepatic decompensation, non-liver- and liver-related mortality, and liver transplantation[3–7]
- HCV therapy is one of the interventions necessary to reduce global burden of disease[8]

1. van der Meer AJ, et al. J Hepatol 2016;65:S95–S108; 2. D'Ambrosio R, et al. Hepatology 2012;56:532–43; 3. Nahon P, et al. Gastroenterology 2017;152:142–56; 4. van der Meer AJ, et al. JAMA 2012;308:2584–93; 5. Bruno S, et al. J Hepatol 2016;64:1217–23; 6. Lee M-H, et al. J Infect Dis 2012;206:469–77; 7. Singh AG, et al. Clin Gastroenterol Hepatol 2010;8:280–8;
8. Hefferman A, et al. Lancet 2019; doi: 10.1016/S0140-6736(18)32277-3;
EASL CPG HCV. J Hepatol 2018;69:461–511.

Diagnosis of acute and chronic HCV infection

Recommendations	Grade of evidence	Grade of recommendation
All patients with suspected HCV infection should be tested for anti-HCV Ab in serum or plasma as first-line diagnostic test	A	1
In cases of suspected acute hepatitis C, in immunocompromised patients and patients on haemodialysis, serum or plasma HCV RNA testing should be part of the initial evaluation	A	1
If anti-HCV Ab detected, HCV RNA should be determined by a sensitive molecular method (LLOD: ≤15 IU/mL)	A	1
Anti-HCV Ab+, HCV RNA– individuals should be retested for HCV RNA 12 and 24 weeks later to confirm definitive clearance	A	1
In low- and middle-income countries, and specific high-income country settings, a qualitative HCV RNA assay (LLOD: ≤1000 IU/mL) can be used to provide broad affordable access to HCV diagnosis and care	B	2
Serum or plasma HCV core antigen (a marker of HCV replication) can be used instead of HCV RNA to diagnose acute or chronic HCV infection when HCV RNA assays are not available and/or not affordable	A	1



Sulkowski M. 2011. HRSA http://hab.hrsa.gov

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Additional Laboratory Testing

The following laboratory tests are recommended within 12 weeks prior to starting antiviral therapy:

- Complete blood count (CBC); international normalized ratio (INR)
- Hepatic function panel (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase levels)
- Calculated glomerular filtration rate (GFR)

The following laboratory testing is recommended at any time prior to starting antiviral therapy:

- Quantitative HCV RNA (HCV viral load)
- HCV genotype and subtype

Pre-therapeutic assessment

Recommendations	Grade of evidence	Grade of recommendation
Evaluate contribution of comorbidities to progression of liver disease and implement corrective measures	A	1
Liver disease severity must be assessed prior to therapy	A	1
Identify patients with cirrhosis (F4): adjust treatment accordingly; mandatory post-treatment surveillance for HCC	A	1
Post-treatment surveillance for HCC must also be performed in patients with advanced fibrosis (METAVIR score F3)	B	1
Initially, assess fibrosis stage by non-invasive methods; reserve liver biopsy for when there is uncertainty or potential additional aetiologies	A	1
Renal function (creatinine/eGFR) should be ascertained	A	1
Identify extrahepatic manifestations of HCV infection in case of symptoms*	A	1
HBV and HAV vaccination should be proposed to patients who are not protected	A	1

*Alcoholism, cardiac disease, renal impairment, autoimmunity, genetic or metabolic liver diseases (e.g. genetic haemochromatosis, diabetes mellitus or obesity) and the possibility of drug-induced hepatotoxicity

EASL CPG HCV. J Hepatol 2018;69:461–511.

Staging Liver Fibrosis due to HCV

Important part of chronic HCV work-up

- Identify cirrhosis:
  - ↑ hepatocellular ca risk: need to screen
  - Monitor for hepatic decompensation
  - Consider liver transplant evaluation
- Determine cirrhosis by:
  - Liver biopsy
  - Non-invasive tests

Non-invasive assessment of liver disease severity

Test	Stage of fibrosis	Number of patients	Cut-off(s)	AUROC	Sensitivity	Specificity	PPV	NPV
FibroScan®	F3	560 HCV+	10 kPa*	0.83	72%	80%	62%	89%
	F4	1,855 HCV+	13 kPa*	0.90–0.93	72–77%	85–90%	42–56%	95–98%
ARFI (VTQ®)	F3	2,691 (1,428 HCV+)	1.60–2.17 m/sec	0.94 (0.91–0.95)‡	84% (80–88%)‡	90% (86–92%)‡	NA	NA
	F4	2,691 (1,428 HCV+)	2.19–2.67 m/sec	0.91 (0.89–0.94)‡	86% (80–91%)‡	84% (80–88%)‡	NA	NA
Aixplorer®	F3	379 HCV+	9 kPa*	0.91	90% (72–100%)‡	77% (78–92%)‡	NA	NA
	F4	379 HCV+	13 kPa*	0.93	86% (74–95%)‡	88% (72–98%)‡	NA	NA
FibroTest®	F4	1,579 (1,295 HCV+)	0.74	0.82–0.87	63–71%	81–84%	39–40	93–94
FIB-4	F4	2,297 HCV+	1–45† 3.25†	0.87§ (0.83–0.92)	90% 55%	58% 92%	NA	NA
APRI	F4	16,694 HCV+	1.0† 2.0†	0.84§ (0.54–0.97)	77% 48%	75% 94%	NA	NA

*Scales for liver stiffness cut-offs (in kPa) are different between FibroScan® and Aixplorer®;
†Two cut-offs are provided for FIB-4 and for APRI, respectively, with their own sensitivities and specificities;
‡95%CI; §Median (range)
EASL CPG HCV. J Hepatol 2018;69:461–511.

Indications for treatment: who should be treated?

Recommendations	Grade of evidence	Grade of recommendation
All patients with HCV infection must be considered for therapy, including treatment-naïve and treatment-experienced* patients	A	1
Patients who should be treated without delay • Significant fibrosis or cirrhosis (METAVIR score ≥F2): including compensated (Child–Pugh A) and decompensated (Child–Pugh B or C) cirrhosis • Clinically significant extra-hepatic manifestations† • HCV recurrence after liver transplantation • Patients at risk of rapid evolution of liver disease due to concurrent comorbidities‡ • Individuals at risk of transmitting HCV – PWID – MSM with high-risk sexual practices – Women of child-bearing age who wish to get pregnant – Haemodialysis patients – Incarcerated individuals	A	1

*[illegible] HCV immune complex-related nephropathy and non-Hodgkin B-cell lymphoma; ‡Non-liver solid organ or stem cell transplant recipients, HBV coinfection, diabetes

EASL CPG HCV. J Hepatol 2018;69:461–511.

Indications for treatment: who should be treated? –cont..

Recommendations	Grade of evidence	Grade of recommendation
• In patients with decompensated cirrhosis and an indication for liver transplantation (MELD score ≥18–20), transplant first and treat after transplantation	B	1
• For waiting time >6 months, treat before transplant (clinical benefit not well established)	B	2
• Treatment is generally not recommended in patients with limited life expectancy due to non-liver-related comorbidities	B	2

*Individuals who failed to achieve SVR after prior treatment; †Symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B-cell lymphoma; ‡Non-liver solid organ or stem cell transplant recipients, HBV coinfection, diabetes

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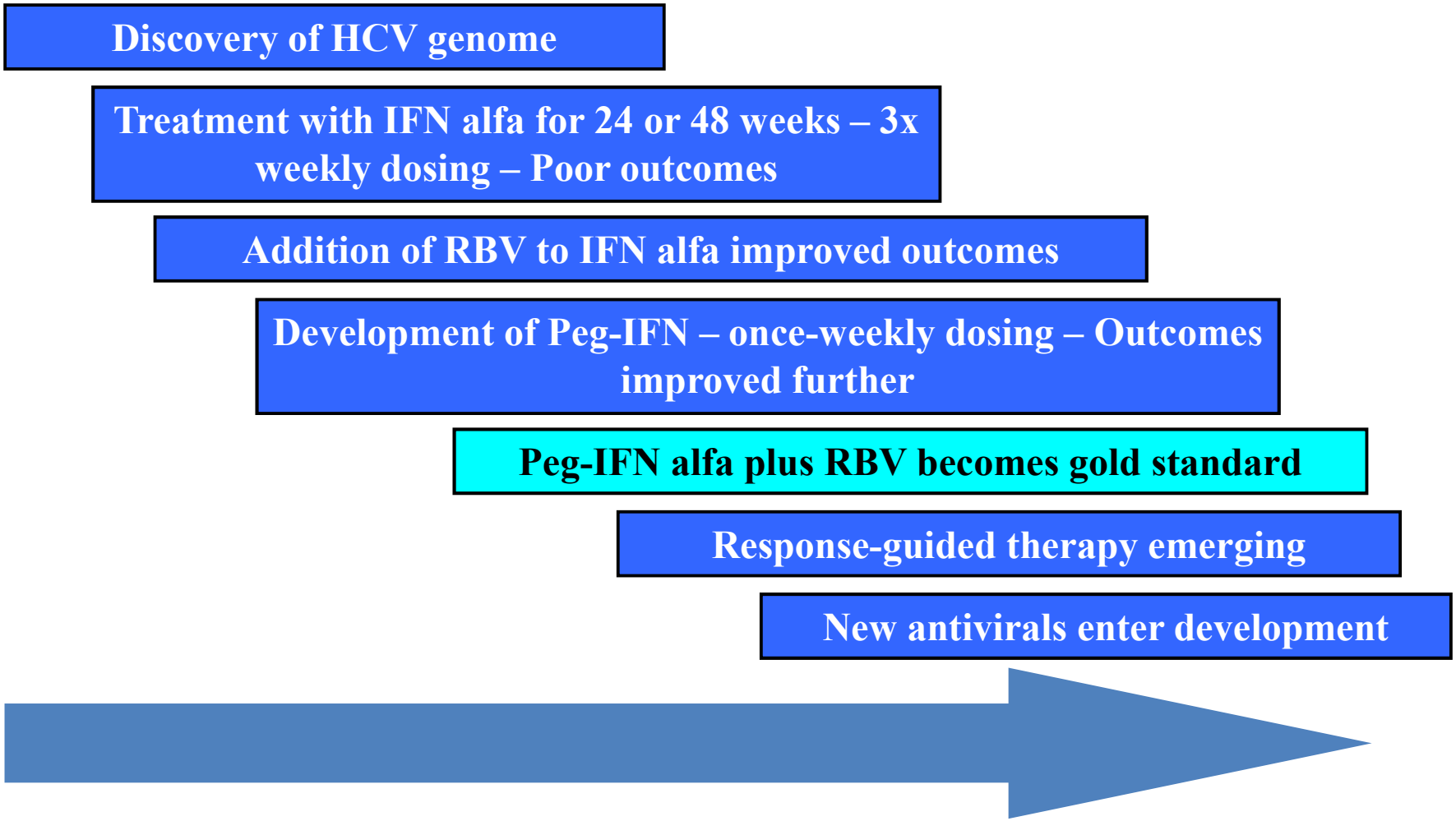
EVOLUTION OF HCV TREATMENT



HCV DAAs approved in Europe in 2018 and recommended in this document

Product	Presentation	Posology
Pangenotypic drugs or drug combinations		
Sofosbuvir	Tablets containing: 400 mg SOF	1 tablet QD
Sofosbuvir/velpatasvir	Tablets containing: 400 mg SOF, 100 mg VEL	1 tablet QD
Sofosbuvir/velpatasvir/ voxilaprevir	Tablets containing: 400 mg SOF, 100 mg VEL, 100 mg VOX	1 tablet QD
Glecaprevir/pibrentasvir	Tablets containing: 100 mg GLE, 40 mg PIB	3 tablets QD
Genotype-specific drugs or drug combinations		
Sofosbuvir/ledipasvir	Tablets containing: 400 mg SOF, 90 mg LDV	1 tablet QD
Ombitasvir/ paritaprevir/ritonavir	Tablets containing: 75 mg PTV, 12.5 mg OBV, 50 mg RTV	2 tablets QD
Dasabuvir	Tablets containing: 250 mg DSV	1 tablet BID (am & pm)
Grazoprevir/elbasvir	Tablets containing 100 mg GZR, 50 mg EBR	1 tablet QD

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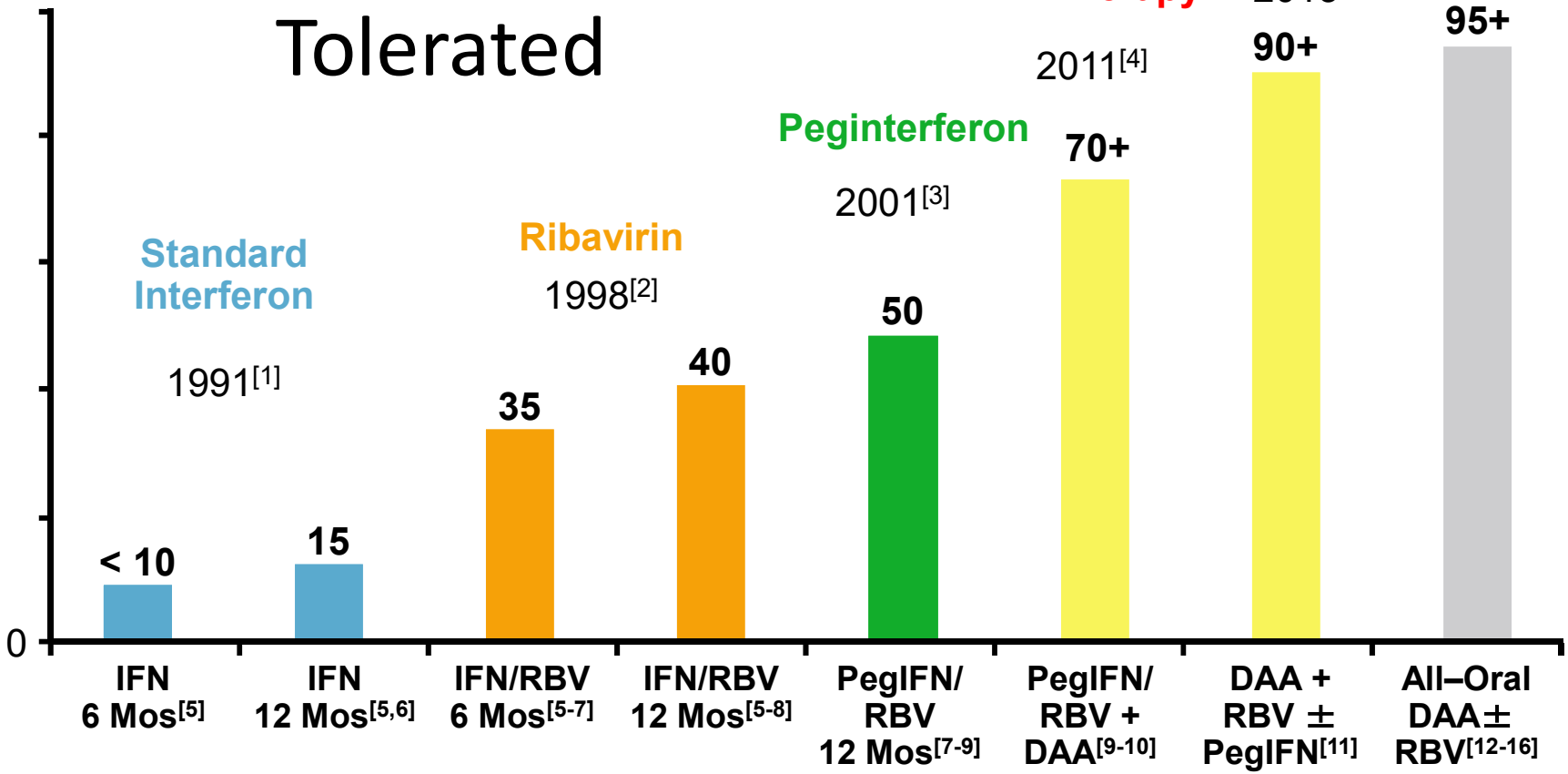
Current All-Oral Therapies Highly Effective, Simple, Well Tolerated



Slide credit: clinicaloptions.com

Mnemonic to Remember DAAs

Look at end of the drug's name

PREvir = **PR**ot**E**ase inhibitor

- Tela**pre**vir, boce**pre**vir, sime**pre**vir, grazo**pre**vir , gleca**pre**vir, voxila**pre**vir

Uvir = n**U**cleotide or non-n**U**cleotide polymerase inhibitor

- Sofosb**uvir**, dasab**uvir**

Asvir = NS5**A** inhibitor

- Ledip**asvir**, ombit**asvir**, daclat**asvir,** velpat**asvir,** elb**asvir,** pibrent**asvir**

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Factors Associate with Treatment and Cure

HCV Genotype

- 1, 2, 3, 4, 5, 6
- Subtype: 1a, 1b

Stage of liver fibrosis

- Cirrhosis versus no cirrhosis
- Metavir score F0-F4

HCV treatment status

- Naïve versus treatment experienced

Special populations

- Transplant, chronic kidney dis, children

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Treatment of patients without cirrhosis or with compensated cirrhosis: general considerations

- Because of their virological efficacy, ease of use, safety and tolerability, **IFN-free, ribavirin-free, DAA-based regimens** must be used in
  HCV-infected patients without cirrhosis or with compensated (Child–Pugh A) cirrhosis, including:
  - **Treatment-naïve (TN) patients**: never been treated for their HCV infection
  - **Treatment-experienced (TE) patients**: previously treated with PEG-IFNα + RBV; PEG-IFNα + RBV + SOF; or SOF + RBV
- The same IFN-free treatment regimens should be used in HIV-coinfected patients as in patients without HIV infection

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IFN-free, RBV-free combination regimens recommended for each genotype

Genotype	Pangenotypic regimens			Genotype-specific regimens		
	SOF/VEL	GLE/PIB	SOF/VEL/ VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
1a	Yes	Yes	No*	Yes†	Yes‡	No
1b	Yes	Yes	No*	Yes	Yes	Yes
2	Yes	Yes	No*	No	No	No
3	Yes§	Yes	Yes‖	No	No	No
4	Yes	Yes	No*	Yes†	Yes¶	No
5	Yes	Yes	No*	Yes†	No	No
6	Yes	Yes	No*	Yes†	No	No

*Triple combination therapy efficacious but not useful due to the efficacy of double combination regimens;
†TN patients without cirrhosis or with compensated (Child–Pugh A) cirrhosis;
‡TN and TE patients without cirrhosis or with compensated (Child-Pugh A) cirrhosis with HCV RNA ≤800,000 IU/mL (5.9 Log_{10} IU/mL);
§TN and TE patients without cirrhosis;
‖TN and TE patients with compensated (Child–Pugh A) cirrhosis;
¶TN patients without cirrhosis or with compensated (Child–Pugh A) cirrhosis with HCV RNA ≤800,000 IU/mL (5.9 Log_{10} IU/mL)
EASL CPG HCV. J Hepatol 2018;69:461–511.

AASLD/IDSA Recommendations for First-line HCV Treatment

HCV GT	Regimen	Duration, Wks	
		No Cirrhosis	Compensated Cirrhosis
1	GLE/PIB	8	12
	GZR/EBR	12	12
	*	8 or 12†	12
	SOF/LDV	12	12
	SOF/VEL		
2 or 3	GLE/PIB	8	12
	SOF/VEL	12	12‡
4	GLE/PIB	8	12
	SOF/VEL	12	12
	GZR/EBR	12	12
	SOF/LDV	12	12
5 or 6	GLE/PIB	8	12
	SOF/LDV	12	12
	SOF/VEL	12	12

*If GT1a, use only if no baseline NS5A elbasvir RASs detected.

†If nonblack, no HIV, and HCV RNA < 6 million IU/mL, 8-wk duration recommended.

‡For GT3, if Y93H RAS detected, add RBV or consider SOF/VEL/ VOX

Slide credit: clinicaloptions.com

AASLD/IDSA. HCV guidelines. September 2017.

Treatment recommendations for TN or TE patients with CHC with HCV genotype 3 and compensated (Child–Pugh A) cirrhosis

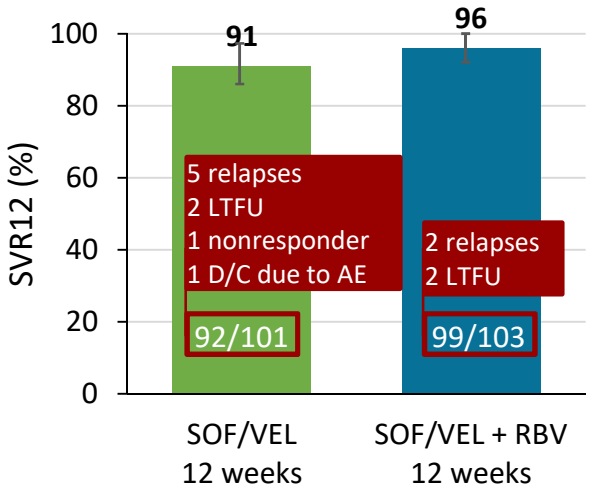
Patients infected with HCV genotype 3 with compensated cirrhosis				
Availability/ performance of HCV NS5A resistance testing	**Results of HCV NS5A resistance testing***	**SOF/VEL-based regimen**		**GLE/PIB-based regimen**
		SOF/VEL/VOX available and affordable	**SOF/VEL/VOX not available or affordable**	**GLE/PIB available**
Not available/ not performed	-	SOF/VEL/VOX for 12 weeks	SOF/VEL + RBV for 12 weeks	GLE/PIB for 12 weeks in TN or 16 weeks in TE patients†
Available and performed	Presence of Y93H RAS at baseline	SOF/VEL/VOX for 12 weeks	SOF/VEL + RBV for 12 weeks	GLE/PIB for 12 weeks in TN or 16 weeks in TE patients†
	No Y93H RAS at baseline	SOF/VEL for 12 weeks	SOF/VEL for 12 weeks	GLE/PIB for 12 weeks in TN or 16 weeks in TE patients†

*The presence of the NS5A RAS Y93H at baseline is by population sequencing or >15% by deep sequencing;
†Data with 12 weeks of treatment with GLE/PIB in TE patients with cirrhosis are needed
EASL. J Hepatol 2018; doi: 10.1016/j.jhep.2018.11.004;
EASL CPG HCV. J Hepatol 2018;69:461–511.

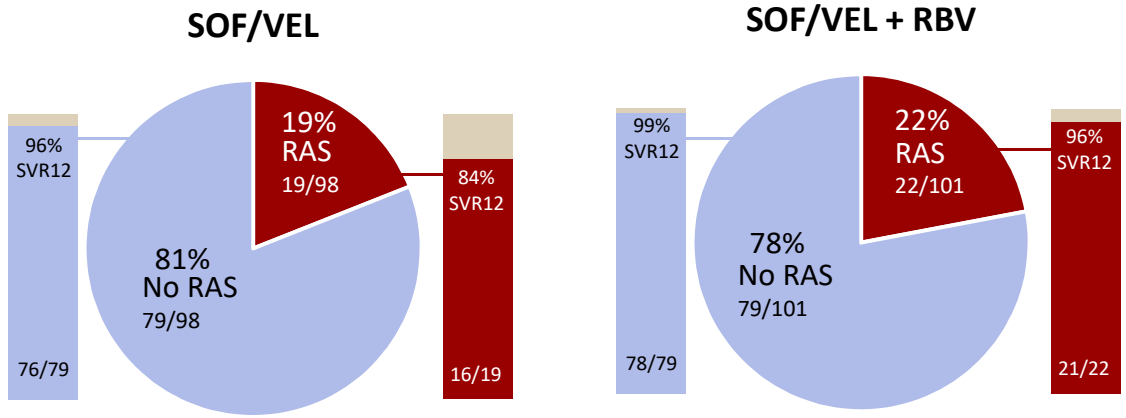
Sofosbuvir/velpatasvir with and without ribavirin in GT 3 HCV-infected patients with cirrhosis

- 204 patients were randomised to receive SOF/VEL or SOF/VEL + RBV for 12 weeks in an open-label study in GT 3 patients with compensated cirrhosis (TN and TE)

Overall SVR rates



SVR rates and presence of NS5A RAS



- SVR12 in patients with Y93H
  - SOF/VEL: 50% (2/4)
  - SOF/VEL + RBV: 89% (8/9)

This study was not powered to assess noninferiority of the two treatment arms, and the numeric difference in relapse rate between the two treatment arms does not suggest a clinically meaningful difference in outcome

Esteban R, et al. Gastroenterology 2018;155:1120–7.e4.

Simplified treatment of CHC with pangenotypic drug regimens

Recommendations	Grade of evidence	Grade of recommendation
Pre-treatment assessment		
• Proof of HCV replication (presence of HCV RNA or of HCV core antigen)	B	1
• Assessment of cirrhosis by simple non-invasive markers (e.g. FIB-4 or APRI)*		
Treatment		
• TN and TE patients† (without cirrhosis/with compensated cirrhosis)		
– Fixed-dose SOF/VEL for 12 weeks	B	1
– Fixed-dose GLE/PIB (8 weeks without cirrhosis;‡ 12 weeks with cirrhosis)	B	1
– Generic drugs can be used, provided quality controls met and guaranteed	A	1
– Check possible DDIs and implement dose modifications when necessary	A	1

*Determines whether the patient needs post-treatment follow-up; †Without testing genotype; ‡If cirrhosis can be reliably excluded by means of a non-invasive marker in TN patients, fixed-dose combination GLE/PIB can be administered for 8 weeks only (A1)

EASL CPG HCV. J Hepatol 2018;69:461–511.

Retreatment of DAA failures

Recommendations	Grade of evidence	Grade of recommendation
After failure of PEG-IFNα + RBV, SOF + PEG-IFNα/RBV or SOF + RBV • Retreat according to recommendations for TE patients, by HCV genotype	A	1
HCV resistance testing after failure of any DAA-based regimen (excluding regimens with SOF as the only DAA) is a useful guide to retreatment	B	2
After failure of DAA (PI and/or NS5A inhibitor)-containing regimen		
• First-line retreatment – SOF/VEL/VOX for 12 weeks (without cirrhosis/with compensated cirrhosis)	A	1
– SOF/VEL + RBV* for 24 weeks (decompensated cirrhosis)	B	2
• Patients with predictors of poor response, SOF + GLE/PIB for 12 weeks: – Advanced liver disease – Multiple courses of DAA-based treatment – Complex NS5A RAS profile	B	2

*Daily weight-based RBV (1,000 mg or 1,200 mg in patients <75 kg or ≥75 kg, respectively); start RBV at a dose of 600 mg daily and adjust dose depending on tolerance;

†Patients with NS5A RASs who failed twice to achieve SVR after a combination regimen including a PI and/or an NS5A inhibitor

EASL CPG HCV. J Hepatol 2018;69:461–511.

Patients with severe liver disease

- **IFN-free regimens are the only options in patients with decompensated cirrhosis without HCC awaiting liver transplantation (A1)**

Recommendations	Grade of evidence	Grade of recommendation
Indications for treatment		
• MELD score <18–20: treat prior to liver transplantation	A	1
• MELD score ≥18–20:		
– Transplant first without antiviral treatment and treat HCV infection after transplantation	B	1
– Treat before transplant if waiting time exceeds 6 months (depending on the local situation)	B	2
Treatment (MELD score <18–20)		
• SOF/LDV (GT 1, 4, 5 and 6) or SOF/VEL (all genotypes) + RBV* for 12 weeks	A	1
• PI-containing regimens are contraindicated	A	1
• Contraindications/poor tolerance to RBV: SOF/LDV (GT 1, 4, 5, 6) or SOF/VEL (all genotypes) for 24 weeks	A	1

*Daily weight-based RBV (1,000 mg or 1,200 mg in patients <75 kg or ≥75 kg, respectively); start RBV at a dose of 600 mg daily and adjust dose depending on tolerance

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Patients with severe liver disease cont..

Recommendations	Grade of evidence	Grade of recommendation
Post-liver transplant recurrence		
• All patients with post-transplant recurrence should be considered for therapy	A	1
• Treatment should be initiated early after transplantation (≥3 months)	A	1
• Treatments include:		
– SOF/VEL for 12 weeks (all genotypes)	A	1
– SOF/LDV for 12 weeks (GT 1, 4, 5, 6)	A	1
– GLE/PIB for 12 weeks (eGFR ≤30 mL/min/1.73 m^2; all genotypes)*	B	1
– SOF/LDV or SOF/LDV + RBV for 24 weeks (decompensated cirrhosis)†	B	1

*Monitor immunosuppressant drug levels and dose adjust;

†Daily weight-based RBV (1,000 mg or 1,200 mg in patients <75 kg or ≥75 kg, respectively); start RBV at a dose of 600 mg daily and adjust dose depending on tolerance

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Patients with severe liver disease cont..

Recommendations	Grade of evidence	Grade of recommendation
Patients with severe liver disease (2)		
HCC with an indication for liver transplant	A	1
• Liver transplantation must be considered the main therapeutic goal		
• Make treatment decisions on a case by case basis through MDT discussion	A	1
• HCV treatment can be initiated before or delayed until after transplantation, depending on circumstances	A	2
HCC without an indication for liver transplant	A	1
• HCV treatment should not be withheld but HCC surveillance should be carried out post-SVR		
• Use the same DAA regimens as for patients with decompensated cirrhosis without HCC awaiting liver transplantation		

*Monitor immunosuppressant drug levels and dose adjust;
†Daily weight-based RBV (1,000 mg or 1,200 mg in patients <75 kg or ≥75 kg, respectively); start RBV at a dose of 600 mg daily and adjust dose depending on tolerance
EASL CPG HCV. J Hepatol 2018;69:461–511.

HBV-HCV coinfection

Recommendations	Grade of evidence	Grade of recommendation
Treat with the same anti-HCV regimens, following the same rules as HCV monoinfected patients	B	1
Patients fulfilling the standard criteria for HBV treatment should receive NA treatment according to EASL 2017 CPG on the management of HBV infection	A	1
Patients who are HBsAg+ should receive NA prophylaxis at least until Week 12 post anti-HCV therapy and be monitored monthly if HBV treatment is stopped	B	1
In patients who are HBsAg–, anti-HBc Ab+ on anti-HCV therapy • Monitor serum ALT levels monthly • Test HBsAg and HBV DNA if ALT levels do not normalise or rise • Initiate NA therapy if HBsAg and/or HBV DNA are present	B	1

EASL CPG HCV. J Hepatol 2018;69:461–511.

Renal impairment, including haemodialysis

Recommendations	Grade of evidence	Grade of recommendation
Mild to moderate renal impairment (eGFR ≥30 mL/min/1.73 m²)		
• Treat according to the general recommendations	A	1
• No dose adjustments are needed		
• Patients should be carefully monitored		
Severe renal impairment (eGFR <30 mL/min/1.73 m² or ESRD*)		
• Treat in expert centres with close monitoring by a MDT	B	1
• GLE/PIB for 8 or 12 weeks (all GT)	A	1
• GZR/EBR for 12 weeks (GT 1a, 1b and 4)†	A	1
• OBV/PTV/r + DSV for 12 weeks (GT 1b)	A	1
• Use SOF with caution, only if an alternative treatment is not available	B	1

*ESRD on haemodialysis (CKD stage 4/5) without an indication for liver transplant; †With HCV RNA level ≤800,000 IU/mL (GT 1a/4)

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Patients with renal impairment, including haemodialysis

Recommendations	Grade of evidence	Grade of recommendation
Mild to moderate renal impairment (eGFR ≥30 mL/min/1.73 m^2)		
• Treat according to the general recommendations • No dose adjustments are needed • Patients should be carefully monitored	A	1
Severe renal impairment (eGFR <30 mL/min/1.73 m^2 or ESRD*)		
• Treat in expert centres with close monitoring by a MDT	B	1
• GLE/PIB for 8 or 12 weeks (all GT)	A	1
• GZR/EBR for 12 weeks (GT 1a, 1b and 4)†	A	1
• OBV/PTV/r + DSV for 12 weeks (GT 1b)	A	1
• Use SOF with caution, only if an alternative treatment is not available	B	1
• Risk/benefit of treating patients with ESRD and an indication for kidney transplant before or after renal transplantation require individual assessment	B	1

*ESRD on haemodialysis (CKD stage 4/5) without an indication for liver transplant; †With HCV RNA level ≤800,000 IU/mL (GT 1a/4)

EASL CPG HCV. J Hepatol 2018;69:461–511.

Haemoglobinopathies and bleeding disorders

Recommendations	Grade of evidence	Grade of recommendation
Indications for HCV therapy are the same in patients with and without haemoglobinopathies or bleeding disorders	A	1
The same IFN-free, RBV-free anti-HCV DAA regimens can be used in patients with and without haemoglobinopathies or bleeding disorders	B	1

EASL CPG HCV. J Hepatol 2018;69:461–511.

Adolescents and children

Recommendations	Grade of evidence	Grade of recommendation
Adolescents aged ≥12 years • TN or TE, without cirrhosis or with compensated cirrhosis	B	1
• GT 1, 4, 5 or 6: fixed-dose SOF/LDV for 12 weeks	C	2
• GT 2 or 3: other regimens approved for adults, with caution pending more safety data in this population		
Children <12 years Defer treatment until DAAs, including pangenotypic regimens, are approved for this age group	B	1

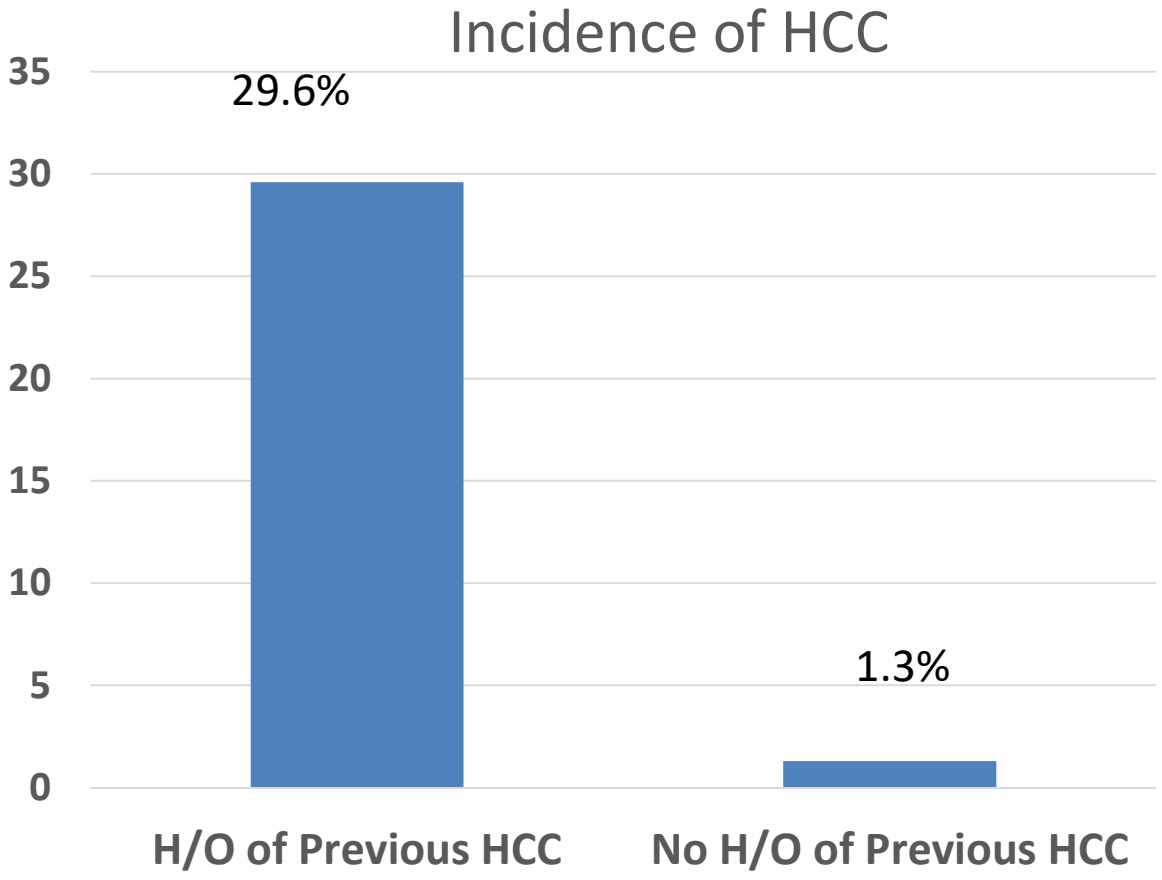
EASL CPG HCV. J Hepatol 2018;69:461–511.

HCC risk in treated patients

- Recent data suggest that in patients with cirrhosis who clear HCV (especially in the presence of cofactors of liver morbidity, such as the metabolic syndrome ,harmful alcohol consumption and/or concurrent hepatitis B virus (HBV) infection) :-

  the risk of HCC and liver-related mortality is significantly reduced, but not eliminated.

Study Design: Incidence of HCC in HCV Positive Patient who completed DAA (Direct Acting Antiviral)



Mean follow-up 15.4 Months

Mean follow-up 18.2 Months

Reference: Hepatology International 2019

Monitoring HCC occurance after DAA

- APASL recommend the following:
- In patients with previous HCC history, surveillance at 4-month intervals for HCC by ultrasonography (US) and tumor markers should be performed,
- In patients without previous HCC history, surveillance at 6- to 12-month intervals for HCC including US is recommended until the long-term DAA treatment effects, especially for the resolution of liver fibrosis, are confirmed.

Reference: Hepatology International 2019

CONCLUSION

- In last two decades, the treatment of HCV infection has dramatically improved .
- Peoples are now using Interferon free regime in all Genotypes .
- The oral DAA are now being used even in decompensated stage of the liver disease .
- With the newer regime HCV infection is now claimed to be eradicated from the planet.