EASL Recommendations

HCV

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About these slides

- These slides give a comprehensive overview of the EASL 2018 recommendations on the management of hepatitis C virus infection
- The recommendations were first presented at the International Liver Congress 2018 and are published in the Journal of Hepatology
  - The full publication can be downloaded from the Clinical Practice Guidelines section of the EASL website
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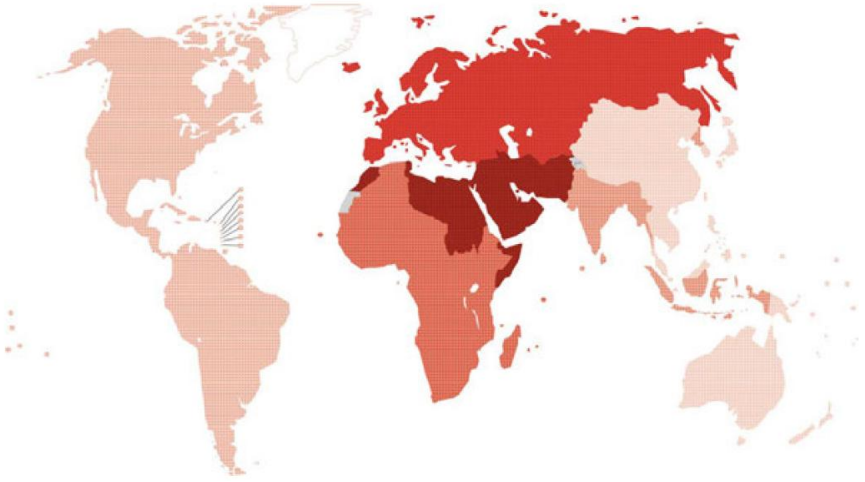
Epidemiology of HCV

- 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]



WHO region	Map key	HCV incidence rate per 100,000: Best estimate (uncertainty level)	New HCV infections (x 1,000): Best estimate (uncertainty level)
African		31.0 (22.5–54.4)	309 (222–544)
Americas		6.4 (5.9–7.0)	63 (59–69)
Eastern Mediterranean		62.5 (55.6–65.2)	409 (363–426)
European		61.8 (50.3–66.0)	565 (460–603)
South-East Asia		14.8 (12.5–26.9)	287 (243–524)
Western Pacific		6.0 (5.6–6.6)	111 (104–124)
Global		**23.7 (21.3–28.7)**	**1,751 (1,572–2,120)**

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.

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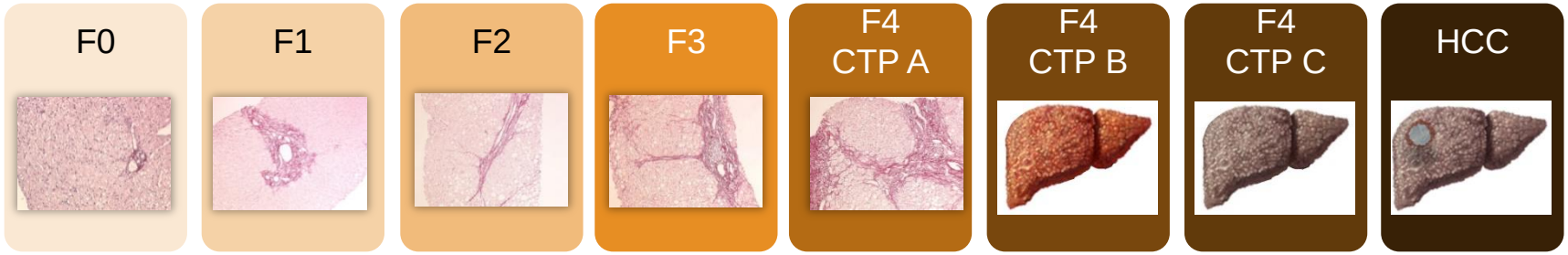
Natural history/disease burden

- 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]



  - Increased risk for liver failure, HCC and liver-related mortality
    - 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;
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Primary goal and impact of HCV therapy

Primary goal of therapy – cure HCV infection (SVR12 or SVR24)

- 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;
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Pre-therapeutic assessment

- Other causes of chronic liver disease, i.e. other blood-borne viruses, particularly HBV and HIV, should be investigated and ruled out

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

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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
• 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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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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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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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)
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Treatment recommendations for TN or TE patients with CHC without cirrhosis

GT		SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
1a	TN	12 weeks	8 weeks	No	8–12 weeks	12 weeks (HCV RNA ≤800,00 IU/mL)	No
	TE	12 weeks	8 weeks	No	No	12 weeks (HCV RNA ≤800,00 IU/mL)	No
1b	TN	12 weeks	8 weeks	No	8–12 weeks	8 weeks (F0–F2) 12 weeks (F3)	8 weeks (F0–F2) 12 weeks (F3)
	TE	12 weeks	8 weeks	No	12 weeks	12 weeks	12 weeks
2	TN	12 weeks	8 weeks	No	No	No	No
	TE	12 weeks	8 weeks	No	No	No	No
3	TN	12 weeks	8 weeks	No	No	No	No
	TE	12 weeks	12 weeks	No	No	No	No
4	TN	12 weeks	8 weeks	No	12 weeks	12 weeks (HCV RNA ≤800,00 IU/mL)	No
	TE	12 weeks	8 weeks	No	No	No	No
5	TN	12 weeks	8 weeks	No	12 weeks	No	No
	TE	12 weeks	8 weeks	No	No	No	No
6	TN	12 weeks	8 weeks	No	12 weeks	No	No
	TE	12 weeks	8 weeks	No	No	No	No

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

GT		SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
1a	TN	12 weeks	12 weeks	No	12 weeks	12 weeks (HCV RNA ≤800,00 IU/mL)	No
	TE	12 weeks	12 weeks	No	No	12 weeks (HCV RNA ≤800,00 IU/mL)	No
1b	TN	12 weeks	12 weeks	No	12 weeks	12 weeks	12 weeks
	TE	12 weeks	12 weeks	No	12 weeks	12 weeks	12 weeks
2	TN	12 weeks	12 weeks	No	No	No	No
	TE	12 weeks	12 weeks	No	No	No	No
4	TN	12 weeks	12 weeks	No	12 weeks	12 weeks (HCV RNA ≤800,00 IU/mL)	No
	TE	12 weeks	12 weeks	No	No	No	No
5	TN	12 weeks	12 weeks	No	12 weeks	No	No
	TE	12 weeks	12 weeks	No	No	No	No
6	TN	12 weeks	12 weeks	No	12 weeks	No	No
	TE	12 weeks	12 weeks	No	No	No	No

For GT 3 recommendations, see next slide

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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;
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Contraindications to therapy

- There are few contraindications to treatment with DAAs

Recommendations	Grade of evidence	Grade of recommendation
Certain CYP/P-gp-inducing agents (e.g. carbamazepine, phenytoin) are contraindicated with all regimens; risk of significantly reduced DAA concentrations	A	1
PIs must not be used in patients with Child–Pugh B or C decompensated cirrhosis or in patients with previous episodes of decompensation	A	1
In patients with eGFR <30 mL/min/1.73 m^2, SOF should only be used if no alternative treatment approved for use in patients with severe renal impairment is available	B	1

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Simplified treatment of CHC with pangenotypic drug regimens

- Simplified anti-HCV treatment recommendations are now available due to approval of efficacious, well-tolerated pangenotypic anti-HCV regimens (**B1**)

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
Follow-up		
• Checking SVR12 after EOT is dispensable (given high expected SVR12 rates)	B	1
• Test patients with high-risk behaviour/reinfection risk for SVR12 and yearly where possible	B	1
• HCC surveillance (when treatment for HCC is available) in patients with advanced fibrosis (F3) or compensated cirrhosis (F4)	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)

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Retreatment of DAA failures

- Retreatment strategy depends on initial regimen

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
• Very difficult-to-cure patients:† SOF/VEL/VOX + RBV or SOF + GLE/PIB + RBV for 12 weeks or for 16 or 24 weeks	C	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
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Patients with severe liver disease (1)

- Due to efficacy, ease of use, safety and tolerability, IFN-free regimens are the only options in patients with decompensated (Child–Pugh B or C) 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 (2)

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
HCC with an indication for liver transplant		
• Liver transplantation must be considered the main therapeutic goal	A	1
• 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	1/2
HCC without an indication for liver transplant		
• HCV treatment should not be withheld but HCC surveillance should be carried out post-SVR	A	1
• 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
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Treatment of special groups

- HBV-HCV coinfection
- Immune-complex mediated manifestations of CHC
- Patients with renal impairment, including haemodialysis
- Non-hepatic solid organ transplant recipients
- Recipients of an HCV+ organ transplant
- PWID and patients receiving OST
- Haemoglobinopathies and bleeding disorders
- Adolescents and children

- Details on the management of these special groups can be found in **Appendix 2**

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Treatment of acute hepatitis C

- Most patients with acute hepatitis C are asymptomatic
  - Chronicity is expected in 50–90% of cases
- Patients with acute hepatitis C should be considered for antiviral therapy
  - Highly cost-effective compared with deferring treatment until chronicity
  - Ideal time point for starting therapy has not been firmly established

Recommendations	Grade of evidence	Grade of recommendation
• Treatment with the same regimens as for CHC for 8 weeks, according to HCV genotype – Can treat with: SOF/LDV (GT 1, 4, 5 and 6) or OBV/PTV/r + DSV (GT 1b) – May treat with: SOF/VEL (all genotypes), GLE/PIB (all genotypes), GZR/EBR (GT 1b and 4) pending confirmation in clinical trials	B C	1 2
• SVR12 and SVR24 should be assessed*	B	2
• No indication for antiviral therapy as post-exposure prophylaxis in the absence of documented HCV transmission	B	1

*Late relapses have been reported

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Post-treatment follow-up

Recommendations	Grade of evidence	Grade of recommendation
In patients who achieve SVR		
• Discharge patients with no/moderate fibrosis (F0–F2) and no ongoing risk behaviour or other comorbidities	A	1
• Monitor for HCC (by US every 6 months) in patients with advanced fibrosis (F3) or cirrhosis (F4)	A	1
– In patients with cirrhosis, perform surveillance for oesophageal varices by endoscopy if varices were present at pre-treatment endoscopy (A1)*		
• Explain risk of reinfection to positively modify risk behaviour	B	1
• Bi-annual/annual monitoring in PWID, MSM with ongoing risk behaviour	A	1
• Make retreatment available if reinfection is identified during post-SVR follow-up	A	1
Untreated patients or patients with treatment failure		
• Follow untreated patients and those who failed prior treatment at regular intervals	A	1
• Carry out non-invasive methods for staging fibrosis at intervals of 1 to 2 years	A	1
• Continue HCC surveillance every 6 months indefinitely in patients with advanced fibrosis and cirrhosis	A	1

*Index variceal bleed seldom seen in low-risk patients after SVR (unless additional causes for ongoing liver damage are present and persist)

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Appendix 2

Treatment of special groups

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

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Immune-complex mediated manifestations of CHC

Recommendations	Grade of evidence	Grade of recommendation
Mixed cryoglobulinaemia and renal disease associated with CHC must be treated with IFN-free, RBV-free DAA-based anti-HCV combinations, according to the above recommendations	B	1
Careful monitoring for adverse events is mandatory	B	1
The indication for RTX in HCV-related renal disease must be discussed by a MDT	B	1
HCV-associated lymphoma should be treated with IFN-free, RBV-free DAA regimens according to the above recommendations, in combination with specific chemotherapy, taking into account possible DDIs	B	1

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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)

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Non-hepatic solid organ transplant recipients*

Recommendations	Grade of evidence	Grade of recommendation
Treat HCV infection before or after transplantation, provided that life expectancy exceeds 1 year	A	1
Before transplantation, while on waiting list, patients can receive HCV treatment according to general recommendations for GT, liver disease severity and prior anti-HCV treatment	A	1
After transplantation, • Treat with fixed-dose SOF/LDV (GT 1, 4, 5 and 6) or SOF/VEL (all GT) according to the general recommendations† • Treat patients with an eGFR <30 mL/min/1.73 m^2 with GLE/PIB for 12 weeks‡	A B	1 1

*Including kidney, heart, lung, pancreas or small bowel recipients;
†Without the need for immunosuppressant drug dose adjustments;
‡Immunosuppressant drug levels need to be monitored and adjusted as needed during and after EOT

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Recipients of an HCV+ organ transplant

Recommendations	Grade of evidence	Grade of recommendation
Organs from anti-HCV Ab+, HCV RNA+ donors can be transplanted to HCV RNA+ recipients	B	1
Use of anti-HCV Ab+, HCV RNA+ organs for HCV RNA– recipients is possible, provided that: • It is allowed by local regulations • Rigorous informed consent is obtained • Rapid post-transplant DAA therapy is guaranteed	C	2
Use of liver grafts with moderate (F2) or advanced (F3) fibrosis is not recommended	B	2

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PWID and patients receiving OST

Recommendations	Grade of evidence	Grade of recommendation
Test routinely and voluntarily for anti-HCV Abs and HCV RNA; test HCV RNA annually and following any high-risk injecting episode	A	1
Provide appropriate access to OST and clean drug injecting equipment as part of widespread comprehensive harm reduction programs, including in prisons	A	1
All HCV-infected PWIDs have an indication for antiviral therapy; DAA-based therapies are safe and effective in HCV-infected patients receiving OST, those with a history of IDU and those who recently injected drugs	A	1
HCV treatment should be offered to HCV-infected patients in prison	B	1
Pre-therapeutic education: include discussions of HCV transmission, risk factors for fibrosis progression, treatment, reinfection risk, and harm reduction strategies	B	1
In patients on OST, DAA-based anti-HCV therapy does not require methadone or buprenorphine dose adjustment	A	1
Provide harm reduction, education and counselling to prevent HCV reinfection following successful treatment	B	1
Monitor after SVR in PWID with an ongoing risk behaviour*	A	1
Retreat if reinfection identified during post-SVR follow-up	A	1

*Ideally bi-annual or at least annual HCV RNA assessment

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

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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 • GT 1, 4, 5 or 6: fixed-dose SOF/LDV for 12 weeks	B	1
• GT 2 or 3: other regimens approved for adults, with caution pending more safety data in this population	C	2
Children <12 years Defer treatment until DAAs, including pangenotypic regimens, are approved for this age group	B	1

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