AASLD 2016 Recommendations for Testing, Managing, and Treating Hepatitis C

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GOAL OF TREATMENT

The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.
Rating: Class I, Level A

RECOMMENDATIONS FOR WHEN AND IN WHOM TO INITIATE TREATMENT

Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.
Rating: Class I, Level A

RECOMMENDATIONS FOR PRETREATMENT ASSESSMENT

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.
Rating: Class I, Level A

<u>INITIAL TREATMENT OF HCV INFECTION</u>

Genotype 4

Genotype 4 Treatment-naïve Patients without Cirrhosis - Recommended

- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25mg) and weight-based RBV for 12 weeks .Rating: Class I, Level A
- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks.
- Rating: Class IIa, Level B
- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks. Rating: Class IIa, Level B

Genotype 4 Treatment-naïve Patients with Compensated Cirrhosis Recommended

- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100mg)/ombitasvir (25 mg) and weight-based RBV for 12 weeks. Rating: Class I, Level B
- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks. Rating: Class IIa, Level B
- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks. Rating: Class IIa, Level B

Genotype 4 Treatment-naïve Patients with or without Cirrhosis - Alternative

Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an Alternative regimen for treatment-naïve patients with HCV genotype 4 infection who are IFN eligible, regardless of cirrhosis status.
Rating: Class II, Level

RETREATMENT OF PERSONS IN WHOM PRIOR THERAPY HAS FAILED

Genotype 4 PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis

- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25mg) (PrO) and weight-based RBV for 12 weeks.
  Rating: Class I, Level A
- Daily fixed-dose combinatoin of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a recommended regimen for patients who have HCV genotype 4 infection, who do not have cirrhosis, who experienced virologic relapse after prior PEG-IFN/RBV therapy. Genotype 4 patients with prior on-treatment virologic failure (failure to suppress or breakthrough) while on PEG-IFN/RBV should be treated with 16 weeks and have weight-based RBV added to the treatment regimen.
  Rating: Class IIa, Level B
- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks.
  Rating: Class IIa, Level B

Genotype 4 PEG-IFN/RBV Treatment-experienced Patients with Compensated cirrhosis – Recommended

- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100mg)/ombitasvir (25 mg) (PrO) and weight-based RBV for 12 weeks.
  Rating: Class I, Level A
- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a recommended regimen for patients who have HCV genotype 4 infection, who have compensated cirrhosis, and who experienced virologic relapse after prior PEG-IFN/RBV therapy. Genotype 4 patients with prior on-treatment virologic failure (failure to suppress or breakthrough) while on PEG-IFN/RBV should be treated with 16 weeks and have weightbased RBV added to the treatment regimen.
  Rating: Class IIa, Level B
- Daily ledipasvir (90 mg)/sofosbuvir (400 mg) and weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 4 infection, in whom prior treatment with PEG-IFN/RBV has failed, and who are eligible for RBV.
  Rating: Class IIa, Level B

- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 24 weeks.
  Rating: Class IIa, Level B

Genotype 4 Treatment-experienced Patients with or without cirrhosis –Alternative

- Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an Alternative regimen for patients with HCV genotype 4 infection, who do not have cirrhosis, in whom prior treatment has failed, and who are eligible for PEG-IFN.
  Rating: Class IIa, Level B
- Daily sofosbuvir (400 mg) and weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 4 infection, in whom prior treatment has failed, and who IFN ineligible are.
  Rating: Class IIa, Level B

PATIENTS WITH DECOMPENSATED CIRRHOSIS

Recommended Regimens for Patients with Genotype 4 HCV Infection with Decompensated Cirrhosis (Moderate or Severe Hepatic Impairment; CTP Class B or C Who May or May Not be Candidates for Liver Transplantation, Including Those with Hepatocellular Carcinoma

- Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of RBV (600 mg, increased as tolerated) for 12 weeks.
- Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with low initial dose of RBV (600 mg, increased as tolerated) for 12 weeks.

Recommended Regimens for Patients with Genotype 4 HCV Infection with Decompensated Cirrhosis Who are RBV Ineligible.

- Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 24 weeks.
- Daily fixed dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 24 weeks is a recommended regimen for patients with decompensated cirrhosis [4] who are RBV ineligible.

Recommended Regimens for Patients with Genotype 1 or 4 HCV Infection with decompensated Cirrhosis in Whom Prior Sofosbuvir-based Treatment has failed

- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of RBV (600 mg, increased as tolerated) for 24 weeks.

PATIENTS WITH RENAL IMPAIRMENT

- For patients with mild to moderate renal impairment (CrCl 30 mL/min-80 mL/min), no dosage adjustment is required when using daclatasvir, fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg), or fixed-dose combination of paritaprevir (150mg)/ritonavir (100 mg)/ombitasvir (25 mg) with (or without for HCV genotype 4 infection) twice-daily dosed dasabuvir (250 mg), simeprevir, or sofosbuvir to treat or retreat HCV infection in patients with appropriate genotypes.
  Rating: Class I, Level A
- For patients with genotype 4 infection and CrCl below 30 mL/min for whom the urgency to treat is high and kidney transplant is not an immediate option, daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100mg) for 12 weeks is a recommended regimen.
  Rating: Class IIb, Level B

Recommended Assessments Prior to Starting Antiviral Therapy

- Assessment of potential drug-drug interactions with concomitant medications is recommended 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)
- Thyroid-stimulating hormone (TSH) if IFN is used
- HCV genotype and subtype
- Quantitative HCV RNA (HCV viral load)
- Patients scheduled to receive an HCV NS3 protease inhibitor (paritaprevir, simeprevir, grazoprevir) should be assessed for a history of decompensated liver disease and for severity of liver disease using CTP score. Patients with current or prior history of decompensated liver disease or with a current CTP (Child Turcotte Pugh) score of 7 or greater should not receive treatment with regimens that contain NS3 protease inhibitors due to increased exposures and/or lack of safety data.

Recommended Monitoring During Antiviral Therapy

- Complete blood count (CBC), creatinine level, calculated glomerular filtration rate (GFR), and hepatic function panel are recommended after 4 weeks of treatment and as clinically indicated. Thyroid-stimulating hormone (TSH) is recommended every 12 weeks for patients receiving IFN. More frequent assessment for drug-related toxic effects (eg, CBC for patients receiving RBV) is recommended as clinically indicated. Patients receiving EBR/GZR should be monitored with hepatic function panel at 8 weeks (and again at 12 weeks if receiving 16 weeks of treatment).
- A 10-fold increase in alanine aminotransferase (ALT) activity at week 4 should prompt discontinuation of therapy. Any increase in ALT of less than 10-fold at week 4 and accompanied by any weakness, nausea, vomiting, jaundice, or significantly increased bilirubin, alkaline phosphatase, or international normalized ratio should also prompt discontinuation of therapy. Asymptomatic increases in ALT of less than 10-fold elevated at week 4 should be closely monitored and repeated at week 6 and week 8. If levels remain persistently elevated, consideration should be given to discontinuation of therapy.
- Quantitative HCV viral load testing is recommended after 4 weeks of therapy and at 12 weeks following completion of therapy. Antiviral drug therapy should NOT be interrupted or discontinued if HCV RNA levels are not performed or available during treatment.
- Quantitative HCV viral load testing can be considered at the end of treatment and 24 weeks or longer following the completion of therapy.
- Patients with compensated cirrhosis‡ who are receiving paritaprevir /ritonavir-based regimens should be assessed for clinical signs of decompensated liver disease (e.g. ascites, encephalopathy) and for biochemical evidence of liver injury with a hepatic function panel at week 2 and week 4 of treatment, and as needed during the remainder of treatment. Paritaprevir/ritonavir-based regimens should be discontinued if patients develop ascites or encephalopathy or a significant increase in direct bilirubin or ALT or AST.