Treatment of hepatitis C virus infection

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Treatment of acute HCV infection

Optimal regimens have not yet been established.

EASL recommendation:

sofosbuvir plus a nonstructural 5A protein (NS5A) inhibitor for eight weeks

AASLD recommendation:

waiting six months to evaluate for spontaneous clearance and to treat those with persistent viremia with regimens recommended for chronic HCV infection

Uptodate authors recommendation:

Treating during acute HCV infection , even with an interferon-containing regimen, may be preferable for certain circumstances. These include:

- Individuals at risk of complications with acute HCV infection (eg, those with underlying liver disease or a severe presentation)
- Individuals at high risk of transmission (eg, people who inject drugs, HIV-infected persons)
- Individuals who desire and are committed to early treatment

Uptodate authors recommendation:

For genotypes 1 and 4 , we are more likely to suggest treatment in the acute setting with these abbreviated regimens, acknowledging that data are still preliminary.

By contrast, for genotypes 2 and 3, optimal short-course DAA regimens have not yet been defined, and we are thus more likely to wait and treat promptly once viremia has been documented at six months.

Timing of treatment initiation

If the decision is made to treat during acute infection, Uptodate authors generally wait 12 weeks from the time of suspected inoculation (or diagnosis if the time of inoculation is unknown) before starting therapy to allow time for spontaneous viral clearance to occur.

Timing of treatment initiation

However, immediate treatment is reasonable for those patients with a low chance of spontaneous clearance:

- Asymptomatic infection
- Male sex
- High peak viremia
- Patients from whom there is concern about adherence with follow-up testing

Regimen selection

For patients with genotype 1 or 4 infection, Uptodate authors suggest sofosbuvir-ledipasvir. They treat for six weeks for most patients; if the pretreatment HCV RNA level exceeded 7 log international units/mL, they extend therapy to 12 weeks.

Regimen selection

For patients with genotypes 2, 3, 5, or 6 infection, Uptodate authors generally wait to confirm persistent viremia at six months and promptly initiate genotype-appropriate DAA therapy for chronic infection at that point.

ASSESSING TREATMENT RESPONSE

Virologic response to treatment is assessed by checking the viral load at 12 weeks following the cessation of therapy.

Management of chronic hepatitis C virus infection

INDICATIONS

All patients with virologic evidence of chronic HCV infection (ie, detectable HCV viral level over a six-month period) should be considered for treatment.

The introduction of direct-acting antivirals (DAAs) has revolutionized therapy of HCV infection.

PATIENT EVALUATION

- The objectives of the evaluation of patients diagnosed with chronic hepatitis C virus (HCV) include the following:
- Assessment of the extent of liver disease. Specifically, identification of advanced fibrosis or cirrhosis informs the need for additional monitoring and management.

PATIENT EVALUATION

- Assessment of viral and host factors that inform the optimal antiviral selection. These factors include:
- viral genotype
- liver fibrosis stage (and signs of decompensated disease in those with cirrhosis)
- history of prior antiviral treatment
- renal function
- concurrent medication use

PATIENT EVALUATION

- Identifying comorbidities associated with HCV infection. These include:
- Extrahepatic manifestations of chronic HCV infection, such as cryoglobulinemia
- HCV-associated renal disease
- Porphyria cutanea tarda
- Autoimmune disorders
- Coinfection with HIV or hepatitis B virus (HBV)

Diet and behaviors

Patients should be informed about the natural history of HCV infection and counseled on potentially modifiable factors that are associated with accelerated liver disease, including alcohol use, obesity and insulin resistance, and cigarettes and marijuana use.

Goals of therapy

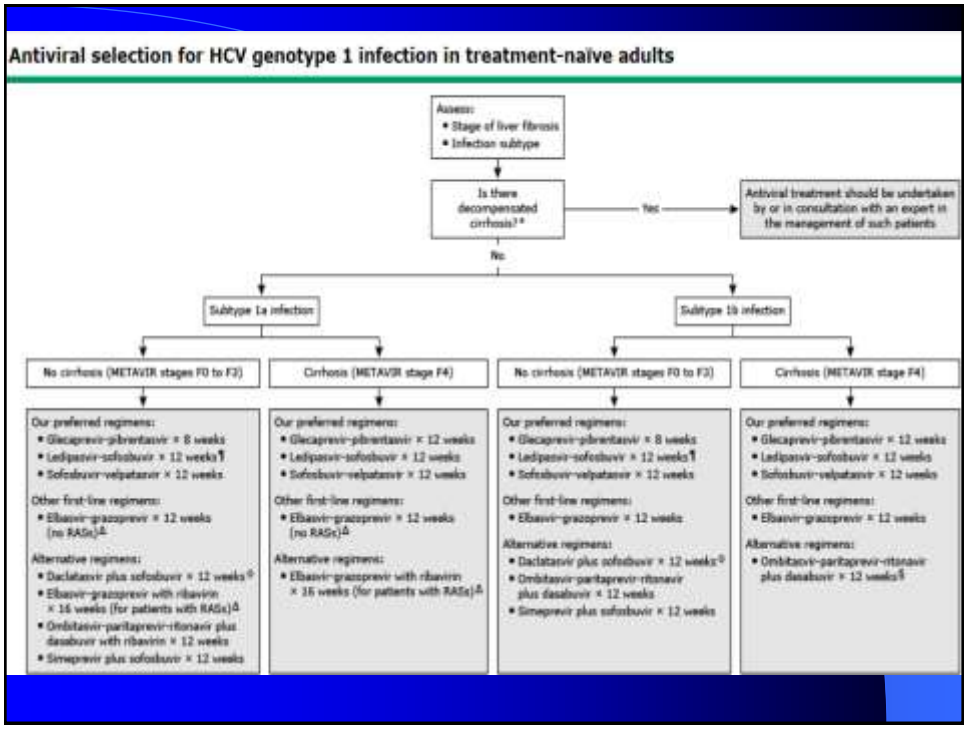
The goal of antiviral therapy in patients with chronic hepatitis C virus (HCV) is to eradicate HCV RNA, which is predicted by attainment of a sustained virologic response (SVR), defined as an undetectable RNA level 12 weeks following the completion of therapy.

An SVR is associated with a 97 to 100 percent chance of being HCV RNA negative during long-term follow-up and can therefore be considered cure of the HCV infection.

Regimen selection

Regimen selection varies by genotype and other patient factors, such as the presence of cirrhosis and treatment history.

Antiviral selection for HCV genotype 1 infection


Antiviral selection for HCV genotype 1 infection in treatment-naïve adults
Assess:
• Stage of liver fibrosis
• Infection subtype
Is there decompensated cirrhosis?*
Yes
Antiviral treatment should be undertaken by or in consultation with an expert in the management of such patients
No
Subtype 1a infection
Subtype 1b infection
No cirrhosis (METAVIR stages F0 to F3)
Cirrhosis (METAVIR stage F4)
No cirrhosis (METAVIR stages F0 to F3)
Cirrhosis (METAVIR stage F4)
Our preferred regimens:
• Glecaprevir-pibrentasvir × 8 weeks
• Ledipasvir-sofosbuvir × 12 weeks¶
• Sofosbuvir-velpatasvir × 12 weeks
Other first-line regimens:
• Elbasvir-grazoprevir × 12 weeks (no RASs)Δ
Alternative regimens:
• Daclatasvir plus sofosbuvir × 12 weeks◊
• Elbasvir-grazoprevir with ribavirin × 16 weeks (for patients with RASs)Δ
• Ombitasvir-paritaprevir-ritonavir plus dasabuvir with ribavirin × 12 weeks
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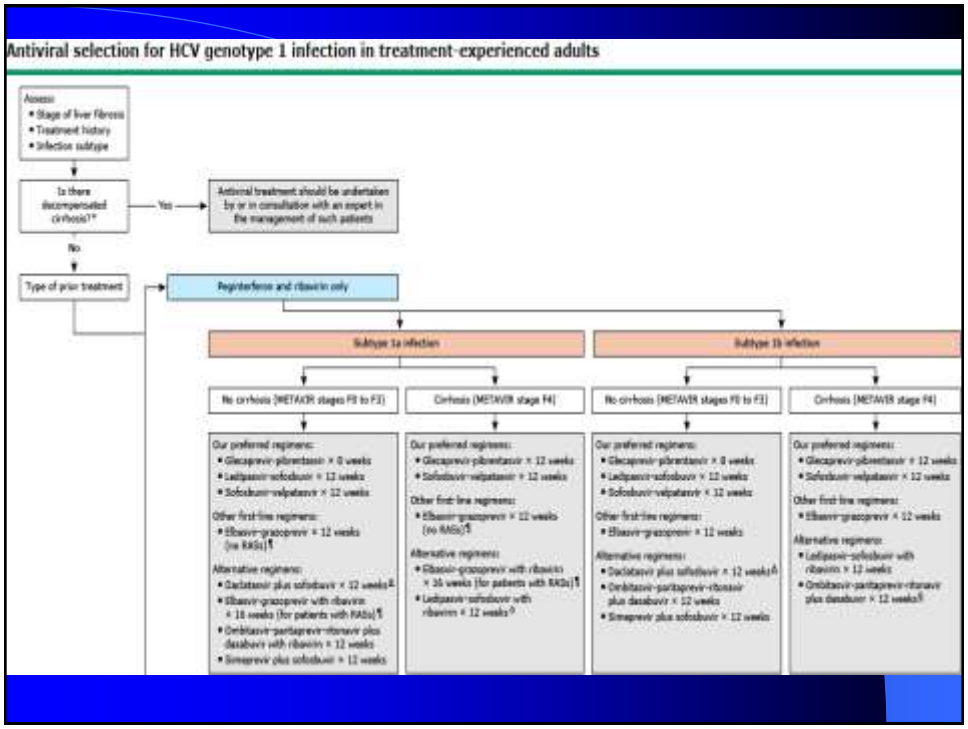
Antiviral selection for HCV genotype 1 infection in treatment-experienced adults
Assess:
• Stage of liver fibrosis
• Treatment history
• Infection subtype
Is there decompensated cirrhosis?*
Yes
Antiviral treatment should be undertaken by or in consultation with an expert in the management of such patients
No
Type of prior treatment
Peginterferon and ribavirin only
Subtype 1a infection
Subtype 1b infection
No cirrhosis (METAVIR stages F0 to F3)
Cirrhosis (METAVIR stage F4)
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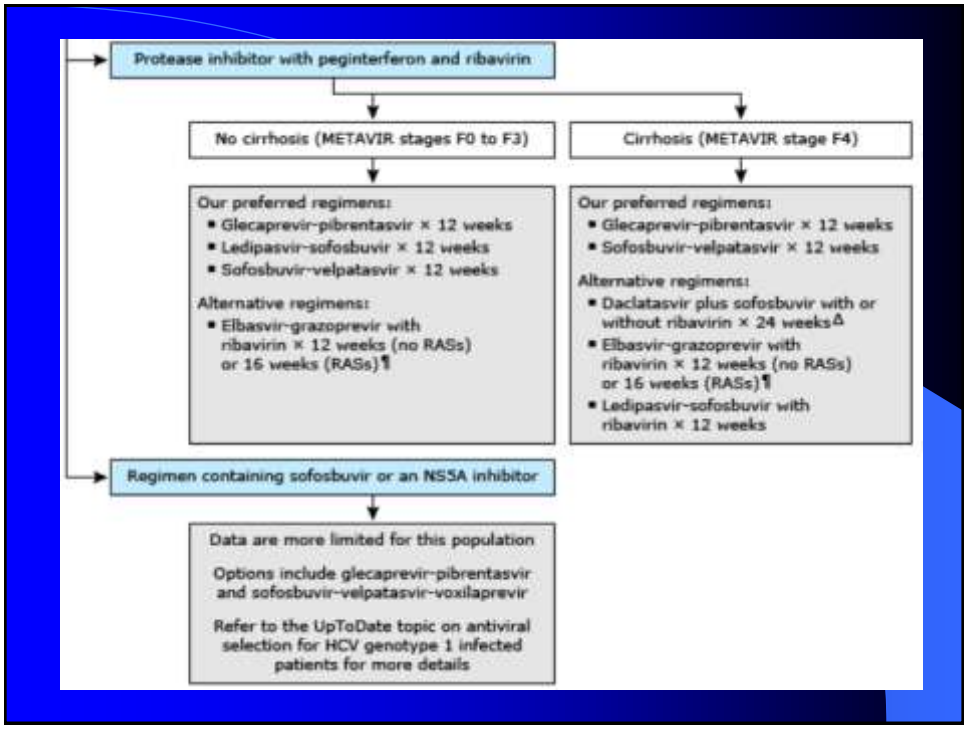
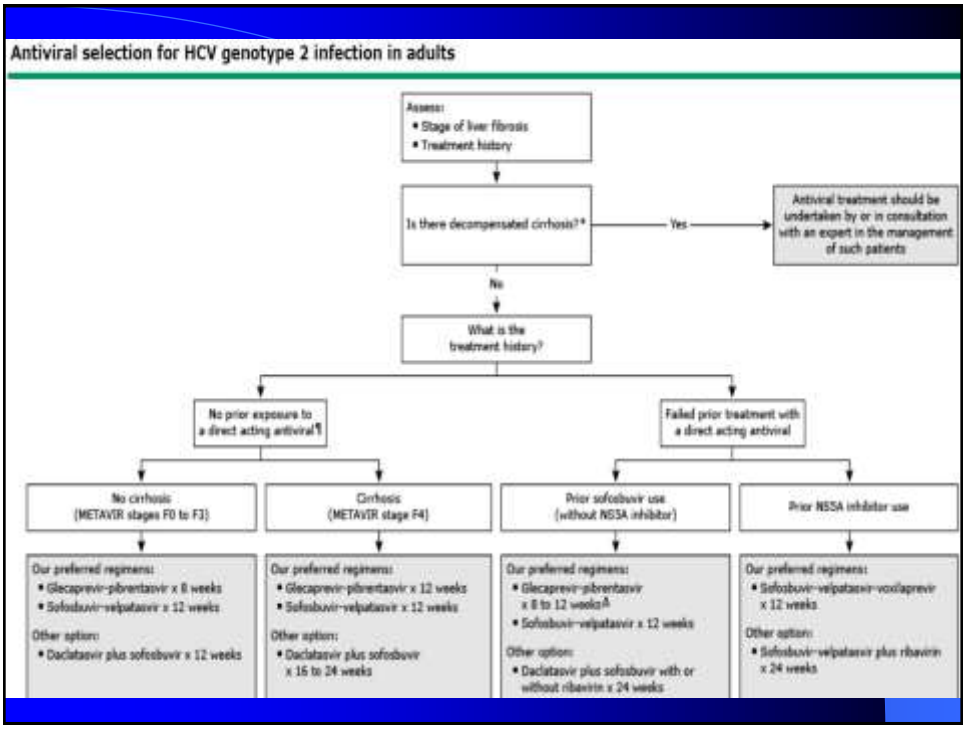
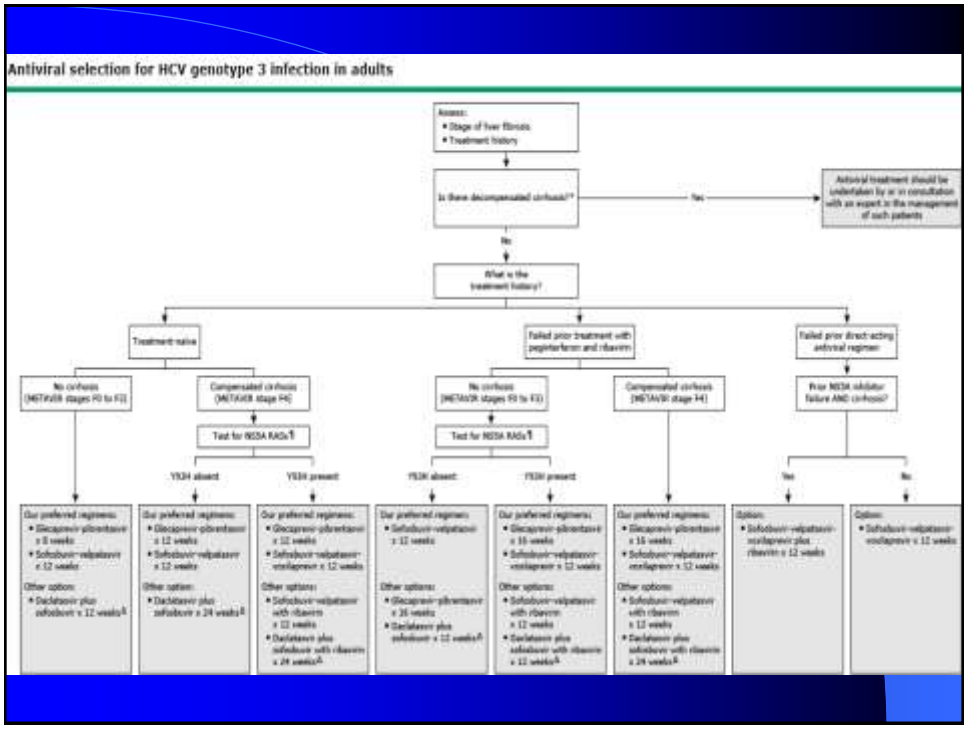


- The choice between these combination regimens depends primarily on the potential for drug interactions and drug toxicity.
- If cost or insurance coverage is not an issue, uptodate authors suggest:
- ledipasvir-sofosbuvir
- sofosbuvir-velpatasvir
- glecaprevir-pibrentasvir

- For patients with genotype 2 and 3 infection who have not previously been treated with a DAA regimen, uptodate authors suggest
- sofosbuvir-velpatasvir (for 12 weeks) or
- glecaprevir-pibrentasvir (for 8 weeks for patients without cirrhosis and 12 weeks for patients with cirrhosis)





If glecaprevir-pibrentasvir is definitely to be used, NS5A RAS testing is not necessary.

If NS5A RAS testing is not available and a sofosbuvir-velpatasvir or daclatasvir plus sofosbuvir regimen is chosen, we favor adding ribavirin (or selecting sofosbuvir-velpatasvir-voxilaprevir or glecaprevir-pibrentasvir).

Effective interferon-free regimens for genotype 4 infection include:

ledipasvir-sofosbuvir (for 12 weeks)

sofosbuvir-velpatasvir (for 12 weeks)

glecaprevir-pibrentasvir for 8 weeks (for patients without cirrhosis) or for 12 weeks (for patients with cirrhosis)

Elbasvir-grazoprevir for 12 weeks (for treatment-naïve) or for 16 weeks with ribavirin

(for treatment-experienced)

Ombitasvir-paritaprevir-ritonavir

plus weight-based ribavirin for 12 weeks

Sofosbuvir plus weight-based ribavirin for 24 weeks.

The choice between them depends primarily on potential for drug interactions, availability, and cost.

If these are not issues, uptodate authors suggest ledipasvir-sofosbuvir, sofosbuvir-velpatasvir, or glecaprevir-pibrentasvir

Viral monitoring

Check HCV RNA quantitative testing at week 4 in clinical practice.

AASLD & IDSA additionally recommend rechecking HCV RNA quantitative testing at week 6 if the week 4 level is detectable and discontinuing therapy if the level has increased by >1 log.

- The clinical value of a week 12 (or end of treatment) viral level is uncertain, and most providers do not routinely check it.
- Virologic response to treatment should be assessed by checking the viral load at 12 weeks following the cessation of therapy.

FOLLOW-UP AFTER ANTIVIRAL THERAPY

Virologic response to treatment should be assessed by checking the viral load at 12 weeks following the cessation of therapy.

Sustained virologic response (SVR) is defined by an undetectable viral level at this time point.

A very small proportion of patients (less than 1 percent in studies of direct-acting antivirals) experience virologic relapse between weeks 12 and 24, and some of those cases may be reinfection rather than true relapse.

Thus, some practitioners also check the viral load at 24 weeks to ensure maintenance of SVR.

Patients who achieve an SVR and do not have bridging fibrosis or cirrhosis do not require any specific follow-up for their HCV infection, though some will check an HCV viral load one year after the completion of treatment to confirm that the viral load remains undetectable.

- Patients who fail to achieve an SVR should continue to be followed for signs of progression of liver disease and assessed for retreatment of HCV infection.
- Patients with advanced fibrosis or cirrhosis, regardless of whether they attain an SVR, require ongoing monitoring.