Simplified HCV Treatment for All HCV Genotypes

Introduction

The advent of direct-acting antiviral (DAA) therapy has revolutionized the landscape of hepatitis C virus (HCV) therapy, allowing for shorter, safer, and more effective treatment of chronic HCV. This success has led to a paradigm shift in HCV treatment, with national and international guidelines calling for the treatment of all adults with HCV, regardless of fibrosis stage or active substance use.[1,2]

Owing to the success of DAA therapy, in 2016, the World Health Organization (WHO) released strategic targets to help achieve the elimination of viral hepatitis by 2030.[3] In addition, in 2017, the National Academies of Science, Engineering, and Medicine similarly released a strategy to eliminate viral hepatitis in the United States, calling for a 90% reduction in incident cases of HCV by 2030.[4] However, achieving these ambitious targets is predicated on expanding the availability of HCV treatment, a process that can be facilitated by simplified care pathways and treatment algorithms.

This lesson will review the hepatitis C simplified treatment approach for treatment-naïve adults (without cirrhosis or with compensated cirrhosis) based on guidance from the American Association for the Study of the Liver (AASLD) and Infectious Disease Society of America (IDSA).[5,6,7] As outlined in further detail below, the simplified treatment approach generated by the AASLD-IDSA HCV Guidance applies to most patients with chronic HCV, and it can help to streamline the pretreatment evaluation, treatment choices, and monitoring during and after treatment.[5,6,7]

Eligibility for Simplified HCV Treatment: Initial Assessment

Initial Assessment for HCV Treatment

The AASLD-IDSA HCV Guidance recommends treatment for all persons with chronic HCV, except for individuals who have a short (e.g., less than 12 months) life expectancy.[1] Therefore, all persons diagnosed with chronic HCV should be considered candidates for HCV treatment. Further, all persons with chronic HCV should be evaluated as potential candidates for the simplified treatment approach. As outlined below, it is important to assess liver fibrosis as part of the initial screening process. From a clinical standpoint, we have outlined the practical general flow of evaluating a person with chronic HCV who may be a candidate for the simplified treatment algorithm: this initial assessment should include initial laboratory studies, evaluation of fibrosis status, and screening for the simplified treatment criteria. All individuals with cirrhosis should have further evaluation for evidence of hepatic decompensation. Once a person has been determined to meet the criteria for the simplified treatment approach, they can be stratified into the evaluation and treatment categories for either (1) persons without cirrhosis or (2) persons with compensated cirrhosis.

Simplified Treatment Approach

The simplified treatment guidance primarily applies to adults with chronic HCV who are treatment naïve, including persons without cirrhosis and those with compensated cirrhosis.[5,6,7] Persons with decompensated cirrhosis are not eligible for the simplified treatment approach.[7] The simplified treatment approach utilizes the pangenotypic regimens glecaprevir-pibrentasvir and sofosbuvir-velpatasvir. Prior treatment experience excludes use of the simplified treatment approach because glecaprevir-pibrentasvir and sofosbuvir-velpatasvir are not uniformly appropriate for treatment-experienced patients.[7,8] Clinicians should follow the AASLD/IDSA guidance for treatment-experienced individuals, which is subdivided by the type of prior treatment.[8] Similarly, the simplified treatment guidelines are not intended for patients with chronic hepatitis B virus (HBV) coinfection due to the potential for HBV reactivation during treatment.[7,9] Further, the simplified algorithm should not be used to guide HCV treatment in pregnant women given limited data regarding use of DAAs in pregnancy.[7] Finally, any patient with known or suspected hepatocellular carcinoma (HCC) and those with a history of liver transplantation should not be treated under the simplified algorithm.[7] Patients with HCC have lower sustained virologic response (SVR12) rates when compared with patients without HCC, and they require additional evaluation by a liver tumor specialist prior to undergoing treatment.[10] Similarly, patients with a history of liver transplantation require careful evaluation for drug interactions that may impact the pharmacokinetics of DAAs and common post-transplant immunosuppressant medications.[11]

Table 1. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment Eligibility Criteria^**

Who is Eligible for Simplified HCV Treatment Algorithm	W Simplifie
Adults with chronic HCV infection, including persons living with HIV: • Infected with any HCV genotype • Have NOT previously received HCV treatment • Without cirrhosis • With compensated cirrhosis (Child-Pugh*A) • The determination of cirrhosis can be based on the presence of any of the following: - Liver stiffness >12.5 kPa by FibroScan - FIB-4 >3.25 - Non-invasive serologic test (HCV FibroSure or enhanced liver fibrosis test)	**Adults with chronic HCV infect** • Previously received HCV tr • Hepatitis B surface antiger • Compensated cirrhosis (Ch mL/min/m^2 • Current or prior decompen • Current pregnancy • Known or suspected hepat • Prior liver transplantation

Source: - Liver biopsy
- Liver nodularity or splenomegaly on imaging
- PLT < 150,000/mm^3

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C.
- Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]
- Child-Turcotte-Pugh* score
- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]

Authors Note: The above table was generated from several resources from the AASLD-IDSA HCV Guidance.[5,6,7,12] In this table, we have clarified which criteria can be used to determine cirrhosis status and which criteria are used to distinguish compensated cirrhosis or decompensated cirrhosis. See the Fibrosis-4 (FIB-4) and Child-Turcotte-Pugh (CTP) calculators on this website.

Assessing Liver Fibrosis Status

For all persons who have been diagnosed with HCV and are considering HCV treatment, it is essential to evaluate liver fibrosis status. We recommend evaluating liver fibrosis status as soon as possible after HCV diagnosis. For treatment-naïve adults under consideration for the simplified treatment approach, determining liver fibrosis status is extremely important to perform for the following four reasons:

1. Persons identified with cirrhosis need subsequent evaluation to determine whether they have compensated or decompensated cirrhosis, since persons with decompensated cirrhosis are not eligible for the simplified treatment approach, and they need a prompt referral to a liver specialist for expert management.
2. Once cirrhosis status is determined, the treatment-naïve patient with chronic HCV can be stratified into one of the simplified treatment algorithm categories: persons without cirrhosis or persons with compensated cirrhosis. The simplified treatment approach has a slightly different algorithm for persons without cirrhosis compared to those with compensated cirrhosis.
3. All persons identified with cirrhosis will need a liver ultrasound examination performed within 6 months prior to treatment to evaluate for hepatocellular carcinoma, as persons with hepatocellular carcinoma are not eligible for the simplified treatment approach and they need a referral to a liver cancer specialist.
4. All persons identified with cirrhosis need long-term, regular screening for hepatocellular carcinoma, typically every 6-month liver ultrasound, with or without alfa-fetoprotein.

For the purpose of the simplified treatment algorithm, the FIB-4 can be used to identify patients with or without cirrhosis. This simple, non-invasive test utilizes the patient's age, aspartate aminotransferase (AST) level, alanine aminotransferase (ALT) level, and platelet count to calculate a score that is used to predict the degree of fibrosis. In clinical studies, a lower cutoff value of 1.45 (FIB-4 score 3.25) has been shown to be 97% specific for advanced fibrosis with a positive predictive value of 65%. Patients with a FIB-4 score of >3.25 should be considered to have cirrhosis and follow the simplified treatment algorithm outlined in this section.[13] In addition, the AASLD-IDSA HCV Guidance provides additional methods, even if they were previously performed, that can be used to establish a presumptive diagnosis of cirrhosis:[5,6,7]

- FibroScan indicates liver stiffness with a score greater than 12.5 kPa
- Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (e.g., FibroSure, Enhanced Liver Fibrosis Test)
- Evidence of cirrhosis on imaging (e.g., liver nodularity and/or splenomegaly) or a platelet count less than 150,000/mm^3, etc.)
- Prior liver biopsy showing cirrhosis

Evaluation for Decompensated Cirrhosis

All persons identified with cirrhosis should have a clinical and laboratory evaluation to determine whether the cirrhosis is compensated or decompensated. In the setting of presumptive or confirmed cirrhosis (or advanced fibrosis), clinicians should calculate a Child-Turcotte-Pugh (CTP) score. See the CTP Calculator on this website. This score, which is a proxy of overall liver function, takes into consideration both laboratory values (bilirubin, albumin, and international ionized ratio [INR]) and clinical manifestations (encephalopathy and ascites). A CTP score of 7 or greater (class B or C) is used to identify patients with decompensated cirrhosis.[6,14] Although studies indicate that most patients with decompensated cirrhosis experience improvement in clinical and laboratory markers of liver disease following treatment with DAAs, they remain at high risk for liver-related death and may progress to need transplantation regardless of HCV treatment.[15,16] Furthermore, DAA regimens containing a protease inhibitor as shown in bold (e.g., **glecaprevir**-pibrentasvir, sofosbuvir-velpatasvir-**voxilaprevir**, elbasvir-**grazoprevir**) are not recommended for use in patients with decompensated cirrhosis, because of limited data and the potential risk of causing hepatic decompensation.[17,18] As such, patients identified to have decompensated cirrhosis are not eligible for the simplified treatment approach, and they should be managed by a hepatologist (or another health professional who has expertise in liver disease), ideally at a liver transplantation center.[19]

Simplified Treatment: Pretreatment Assessment for Patients without Cirrhosis

As part of the initial assessment to determine eligibility for the simplified treatment algorithm, most pretreatment laboratory studies have already been conducted. Nevertheless, it is important to ensure all pretreatment laboratory studies and recommended education have been completed and reviewed prior to initiation of treatment. In addition, individuals who qualify for the simplified treatment algorithm should have a comprehensive medication reconciliation performed, which includes a review of over-the-counter medications.[5,12] This medication review serves to identify potential drug-drug interactions with commonly used DAA regimens. Resources to screen for drug interactions are available online, including in the Monitoring Section on the AASLD/IDSA guidance website and the University of Liverpool Hep Drug Interactions website, a resource that can also be downloaded as an app on mobile devices. The necessary pretreatment laboratory studies for persons without cirrhosis, as recommended in the AASLD-IDSA HCV Guidance, are listed in the Table below.[5]

Table 2. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Pretreatment Assessment for Treatment-Naive Adults without Cirrhosis

Before Initiating Antiviral Therapy
• Calculate a FIB-4 score[a]
• Assess for Cirrhosis[b]
• Obtain CBC
• Obtain hepatic function panel ◦ Total and direct bilirubin ◦ Albumin ◦ ALT, AST
• Determine eGFR
• Perform medication reconciliation[c]
• Assess for drug-drug interactions[d]
• Check quantitative HCV RNA (viral load)
• Obtain HIV-1/2 antigen-antibody test
• Check hepatitis B surface antigen (*see Author's Notes*)
• Obtain serum pregnancy testing and counsel about pregnancy risk and DAAs
• Educate about DAA administration and adherence, prevention of reinfection, and avoiding excess alcohol

Abbreviations: CBC = complete blood count; DAA = direct-acting antiviral; eGFR = estimated glomerular filtration rate; FIB-4 = fibrosis-4 index for liver fibrosis; HCV = hepatitis C virus; INR = international normalized ratio.

[a] FIB-4 is a noninvasive measure of hepatic fibrosis that is calculated using age (years), AST, ALT, and platelet count.
[b] A patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 or if they have any of the following from a previously performed test: transient elastography indicating cirrhosis (ie, liver stiffness >12.5 kPa), noninvasive serologic test above the proprietary cutoff indicating cirrhosis (eg, FibroSure, enhanced liver fibrosis test), clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3), or prior liver biopsy showing cirrhosis.
[c] Medication reconciliation should record currently prescribed medications, over-the-counter drugs, and herbal/dietary supplements.
[d] Drug-drug interaction assessment should be performed using the table in the Monitoring

Section of the HCV Guidance website or theUniversity of Liverpool drug interaction checker.

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]
- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [PubMed Abstract]

Authors Notes:

1. As noted in the table above, the AASLD/IDSA recommends checking hepatitis B surface antigen. In 2023, the Centers for Disease Control and Prevention (CDC) issued updated hepatitis B screening recommendations that included the recommendation that when screening, the following three tests should be ordered: hepatitis B surface antigen HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc).[20]

Recommended Simplified Treatment Regimens for Patients without Cirrhosis

Routine genotype assessment is not part of the simplified HCV treatment algorithm for patients without cirrhosis, and as such, the AASLD-IDSA HCV Guidance recommends the following two pangenotypic regimens for persons without cirrhosis who have met eligibility for the simplified treatment approach.[5,7]

Table 3. AASLD-IDSA HCV Simplified Guidance for All Genotypes: Initial Treatment
Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Regimens listed alphabetically

Recommended for Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis
Glecaprevir-Pibrentasvir **Fixed-dose combination of glecaprevir (300 mg)-pibrentasvir (120 mg): 3 tablets once daily for 8 weeks*
Note: *Take with food

Recommended for Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis
Sofosbuvir-Velpatasvir **Fixed-dose combination of sofosbuvir (400 mg)-velpatasvir (100 mg): one tablet once daily for 12 weeks*
Note: *Take with or without food

The glecaprevir-pibrentasvir and sofosbuvir-velpatasvir regimens have proven efficacy in treatment-naïve patients without cirrhosis, regardless of genotype. Below is a brief summary of the main registration trials of glecaprevir-pibrentasvir and sofosbuvir-velpatasvir in treatment-naïve patients without cirrhosis.

Glecaprevir-Pibrentasvir

- ENDURANCE-1: This phase 3, single-arm open-label trial evaluated the safety and efficacy of 8 versus 12 weeks of glecaprevir-pibrentasvir in 703 genotype 1 patients without cirrhosis, 62% of whom were treatment naïve.[21] Among the 336 patients enrolled in the 8-week arm, 99.1% achieved an SVR12, compared with 99.7% of the 334 patients enrolled in the 12-week arm.[21]
- SURVEYOR-II (Part 4): This phase-3, single-arm, open-label trial evaluated the safety and efficacy of 8 weeks of glecaprevir-pibrentasvir in 203 adults without cirrhosis and with genotype 2, 4, 5, or 6.[22] In the intention-to-treat analysis, the overall SVR12 rate was 96% across all genotypes.[22]
- ENDURANCE-3: This phase-3, randomized trial compared the safety and efficacy of 8 or 12 weeks of glecaprevir-pibrentasvir versus 12 weeks of sofosbuvir and daclatasvir in treatment-naïve adults without cirrhosis and with HCV genotype 3.[21] In total, 157 people were assigned to 8 weeks of glecaprevir-pibrentasvir, of whom 95% achieved an SVR12.[21] Similar results were observed in the 12-week arm.[21]

Sofosbuvir-Velpatasvir

- ASTRAL-1: This phase-3 trial randomized treatment-naïve and treatment-experienced adults with hepatitis C genotypes 1, 2, 4, 5, or 6 to receive 12 weeks of sofosbuvir-velpatasvir versus placebo.[23] Among the 624 people who received sofosbuvir-velpatasvir, 99% achieved an SVR12.[23]
- ASTRAL-3: This phase-3 randomized, open-label trial compared sofosbuvir-velpatasvir for 12 weeks versus sofosbuvir plus ribavirin for 24 weeks in adults with genotype 3.[24] Among the 206 treatment-naïve participants, 97% achieved an SVR12, which was significantly better than the 87% of treatment-naïve patients who received sofosbuvir plus ribavirin.[24]
- MINMON (ACTGA5360): This international phase 4 open-label, single-arm trial used a simplified treatment approach to provide a 12-week course of sofosbuvir-velpatasvir for 399 treatment-naïve adults with chronic HCV.[25] This trial allowed persons with HIV and/or compensated cirrhosis to participate; 42% of those enrolled had HIV and 9% had compensated cirrhosis. In this trial, the key elements of the simplified approach were: cirrhosis was determined by FIB-4, no pretreatment genotyping was performed, and the full course of sofosbuvir-velpatasvir was dispensed upon study entry, no scheduled on-treatment labs or in-person visits were performed, and investigators had remote contact (e.g., phone call) with participants at week 4 and week 22, with SVR12 labs being drawn at week 24.[25] Overall, 95% of study participants were cured of HCV, including 95% with HCV monoinfection and 95% with HCV and HIV coinfection.[25] Among the participants without cirrhosis, 96% were cured.[25]

Monitoring on and after HCV Treatment in Patients without Cirrhosis

Monitoring Patients without Cirrhosis While On Treatment

Limited on-treatment monitoring is needed for treatment-naïve, noncirrhotic patients while on DAA therapy. Testing of HCV RNA level as well as hepatic enzymes/function is not necessary while on treatment as these results have not been shown to change management in patients without cirrhosis.[5] Treatment of HCV with DAAs has been shown to improve glycemic control in patients with chronic HCV, and, thus, patients undergoing treatment with DAAs who are concomitantly taking medications for diabetes should be informed about the potential for symptomatic hypoglycemia, and monitoring for hypoglycemia is recommended.[5,26] Although neither glecaprevir-pibrentasvir nor sofosbuvir-velpatasvir is likely to affect the pharmacokinetics of warfarin, close monitoring of INR is recommended for patients on warfarin therapy, given that it may change as the result of improved liver function.[27,28]

Table 4. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

On-Treatment Monitoring
• Monitor for hypoglycemia in patients taking medications for diabetes.
• Monitor for sub-therapeutic INR in patients taking warfarin.
• No laboratory monitoring is required for other patients.
• In-person or remote (telehealth/phone) visits may be scheduled, as needed, for patient support and to assess tolerance of new medications.
Abbreviations: INR – international normalized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Post-Treatment Assessment of Cure in Patients without Cirrhosis

A follow-up HCV RNA level and repeat liver function testing are recommended 12 weeks following the completion of therapy to assess for cure and ongoing evidence of liver inflammation, respectively.[5,7] If the HCV RNA level is undetectable 12 or more weeks following the completion of therapy, this is considered a sustained virologic response or cure. If transaminase levels remain elevated despite the achievement of an SVR, further investigation is warranted to assess for other causes of liver disease.[5,7]

Table 5. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Post-Treatment Monitoring: Assessment of Cure (SVR)
• Obtain quantitative HCV RNA and hepatic function panel 12 weeks or

later following completion of HCV therapy.	
• If quantitative HCV RNA is undetectable 12+ weeks following completion of HCV therapy, the patient is considered to have achieved a sustained virologic response (SVR), also known as a cure.	
• Assess for other causes of liver disease if transaminase levels remain elevated after achieving an SVR.	
Abbreviations: SVR = sustained virologic response	

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Monitoring Post-Treatment Patients who Achieve VIrologic Cure

Patients without cirrhosis who achieve a virologic cure do not require any screening or monitoring for hepatocellular carcinoma.[7,29] Patients should, however, be counseled that they are not immune to HCV following successful treatment and are susceptible to reinfection.[5,7] Patients with ongoing risk factors (e.g., people who inject drugs, men who have sex with men and engage in condomless anal intercourse) should be tested annually for reinfection using HCV RNA testing.[7,30]

Table 6. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

Post-Treatment Monitoring: Follow-up After Achieving Virologic Cure (SVR)
• No liver specific follow up is needed for patients without advanced fibrosis following SVR.

• Patients with ongoing risk factors for HCV should be counseled regarding their risk for reinfection and undergo testing for HCV RNA annually and with any elevation in ALT, AST or bilirubin.	
• Patients should be advised to avoid excessive alcohol.	
Abbreviations: SVR = sustained virologic response	

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Monitoring Post-Treatment Patients who Do Not Achieve Virologic Cure

If initial treatment fails to achieve a virologic cure, patients should be referred to a specialist who can evaluate them for repeat treatment.[7] In the setting of prior treatment experience, patients are not eligible for the simplified treatment algorithm, and the treatment plan should follow the AASLD-IDSA HCV Guidance for repeat treatment.[8] While a patient is awaiting repeat treatment, a CBC, hepatic function panel, and INR should be obtained every 6 to 12 months.[5,7]

Table 7. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Post-Treatment Monitoring: Follow-up for Patients who Do *NOT* Achieve Virologic Cure

• When initial HCV treatment fails to achieve a cure (SVR), patients should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA HCV guidance.
• Assess disease progression with a CBC, hepatic function panel, and INR every 6 – 12 months until retreatment occurs.
• Patients should be advised to avoid excessive alcohol.
Abbreviations: SVR = sustained virologic response; CBC = complete blood count; INR = international ionized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Simplified Treatment: Pretreatment Assessment for Patients with Compensated Cirrhosis

As part of the initial assessment to determine eligibility for the simplified treatment algorithm, most pretreatment laboratory studies have already been conducted. Nevertheless, it is important to ensure all pretreatment laboratory studies and recommended education have been completed and reviewed prior to initiation of treatment. In addition, individuals who qualify for the simplified treatment algorithm should have a comprehensive medication reconciliation performed, which includes a review of over-the-counter medications.[6,12] This medication review serves to identify potential drug-drug interactions with commonly used DAA regimens. Resources to screen for drug-drug interactions are available online, including in the Monitoring Section on the AASLD/IDSA guidance website and the University of Liverpool Hep Drug Interactions website, a resource that can also be downloaded as an app on mobile devices. Note that for patients with compensated cirrhosis, a baseline HCV genotype is recommended if considering the use of sofosbuvir-velpatasvir, as resistance associated substitutions (RAS) can adversely impact SVR12 rates among genotype 3 patients with compensated cirrhosis.[24,31,32] The necessary pretreatment laboratory studies for persons with compensated cirrhosis recommended in the AASLD/IDSA HCV Guidance are listed in the table below.[5]

Table 3. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis

Pretreatment Assessment for Treatment-Naive Adults With Compensated Cirrhosis

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Abbreviations: CBC =		

complete blood count; DAA = direct-acting antiviral; eGFR = estimated glomerular filtration rate; FIB-4 = fibrosis-4 index for liver fibrosis; HCV = hepatitis C virus; INR = international normalized ratio.

[a] Child–Pugh score based on presence of ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7. P

atients with a Child–Pugh score ≥7 (ie, Child–Pugh B or C) have decompensated cirrhosis; this simplified treatment approach is not recommended for patients with decompensated cirrhosis.[b]	Obtain liver ultrasound within 6 months prior to initiating antiviral treatment to exclude hepatocellular carcinoma and subclinical ascites. This simplified treat			

ment approach is not recommended for patients with hepatocellular carcinoma and/or decompensated cirrhosis [c]				
Medication reconciliation should record currently prescribed medications, over-the-counter drugs, and herbal/dietary supplements. [d] Drug-drug interaction assessment should be performed using the table in the Monitoring Section				

of the HCV Guidance website or the University of Liverpool drug interaction checker.		

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]
- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [PubMed Abstract]

Authors Notes:

1. For patients with cirrhosis, clinicians should calculate a Child-Turcotte-Pugh (CPT) score, which is the same as a Child's Pugh score (see the CTP calculator on this website).[14] In the recommendations listed above in the table, the CTP calculation requires first obtaining several items listed later in table (total bilurubin, albumin, and INR). Although studies indicate that most patients with decompensated cirrhosis experience improvement in clinical and laboratory markers of liver disease following treatment with DAAs, they remain at high risk for liver-related death, and may progress to need transplantation regardless of HCV treatment.[15,16] Furthermore, DAA regimens containing a protease inhibitor (e.g. glecaprevir-pibrentasvir, sofosbuvir-velpatasvir-voxilaprevir, elbasvir-grazoprevir) are not recommended for use in patients with decompensated cirrhosis, owing to the potential risk of hepatic decompensation and overall limited data.[17,18] As such, patients identified to have decompensated cirrhosis should not be treated using the simplified algorithm and should be managed by a liver specialist and/or liver transplant center.[6,19]
2. As noted in the table above, the AASLD/IDSA recommended screening for hepatitis B is to check hepatitis B surface antigen. In 2023, the Centers for Disease Control and Prevention (CDC) issued updated hepatitis B screening recommendations that included the recommendation that when screening, hepatitis B testing should consist of the following three tests: hepatitis B surface antigen HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc).[20]

Recommended Simplified Treatment Regimens for Patients with Compensated Cirrhosis

The AASLD-IDSA HCV Guidance recommends the following two pangenotypic regimens for persons with compensated cirrhosis who have met eligibility for the simplified treatment approach: glecaprevir-pibrentasvir or sofosbuvir-velpatasvir.[6,7] If sofosbuvir-velpatasvir is planned for the treatment of a patient with compensated cirrhosis, an HCV genotype should be performed. If HCV genotype 3 is identified, then baseline resistance-associated substitution (RAS) testing is recommended. If the patient has compensated cirrhosis, HCV genotype 3 HCV, and a baseline Y93H mutation is present, sofosbuvir-velpatasvir should not be used, due to evidence of decreased efficacy in this specific setting.[6,24] If baseline NS5A resistance-associated substitution (RAS) testing is not sent or not available, then glecaprevir-pibrentasvir should be used.[6]

Table 9. AASLD-IDSA HCV Simplified Guidance for All Genotypes: Initial Treatment
Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis^

Regimens listed alphabetically

Recommended for Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis^
Glecaprevir-Pibrentasvir **Fixed-dose combination of glecaprevir (300 mg)-pibrentasvir (120 mg): 3 tablets once daily for 8 weeks*
For Genotypes 1-6 Note: *Take with food

Recommended for Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis^
Sofosbuvir-Velpatasvir **Fixed-dose combination of sofosbuvir (400 mg)-velpatasvir (100 mg) one tablet once daily for 12 weeks*
Patients with compensated cirrhosis and HCV genotype 3 require baseline NS5A RAS testing prior to use of sofosbuvir-velpatasvir. Only those without Y93H mutations can be treated with 12 weeks of sofosbuvir-velpatasvir. Note: *Take with or without food

^For patients with decompensated cirrhosis, refer to a liver specialist and see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Both glecaprevir-pibrentasvir and sofosbuvir-velpatasvir have proven efficacy in treatment-naïve patients with cirrhosis. The following is a brief summary of the main registration trials of glecaprevir-pibrentasvir and sofosbuvir-velpatasvir in treatment-naïve patients with compensated cirrhosis.

Glecaprevir-Pibrentasvir

- EXPEDITION-8: This was a single-arm, multicenter, phase 3b trial evaluating the efficacy of glecaprevir-pibrentasvir for 8 weeks in treatment-naïve participants with compensated cirrhosis and genotypes 1-6.[33] Among the 343 people included in this trial, 97.7% achieved an SVR12 in the per protocol analysis.[33]

Sofosbuvir-Velpatasvir

- ASTRAL-1: This was a randomized, placebo-controlled, phase 3 trial using a fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks in treatment-naïve and treatment-experienced patients with genotypes 1, 2, 4, 5, or 6.[23] Both patients without cirrhosis and those with compensated cirrhosis were included. Ninety-nine percent of patients with compensated cirrhosis achieved an SVR12, including 99% of those with baseline NS5A RASs.[23]
- ASTRAL-3: This randomized, placebo-controlled, open-label, phase 3 trial compared sofosbuvir-velpatasvir for 12 weeks to sofosbuvir plus ribavirin for 24 weeks in genotype 3 patients with and without compensated cirrhosis.[24] Ninety-three percent of treatment-naïve patients with compensated cirrhosis achieved an SVR12 in the sofosbuvir-velpatasvir arm, in comparison to 73% in the sofosbuvir plus ribavirin arm.[24] Among those who received sofosbuvir-velpatasvir and had baseline NS5A RASs, 88% achieved an SVR12, compared with 97% of those without baseline substitutions.[24]
- POLARIS-3 This open-label, randomized, phase 3 trial compared the efficacy of sofosbuvir-velpatasvir-voxilaprevir for 8 weeks versus sofosbuvir-velpatasvir for 12 weeks in patients with compensated cirrhosis and genotype 3.[34] Among treatment-naïve patients receiving sofosbuvir-velpatasvir, 99% achieved an SVR12. Four patients in the sofosbuvir-velpatasvir arm had a baseline Y93H mutation, all of whom achieved an SVR12.[34]
- Sofosbuvir-Velpatasvir in Patients with Compensated Cirrhosis and HCV Genotype 3 (Spain): This was a phase 2 trial of sofosbuvir-velpatasvir for 12 weeks versus sofosbuvir-velpatasvir plus ribavirin for 12 weeks in 204 patients with genotype 3 HCV and compensated cirrhosis.[31] Among the patients who received 12 weeks of sofosbuvir-velpatasvir, the SVR12 rate was 91%; participants who received sofosbuvir-velpatasvir and ribavirin had an SVR12 rate of 96%.[31] Among participants in the sofosbuvir-velpatasvir arm, 19 had NS5A RASs, 16 (84%) achieved an SVR12.[31]

Monitoring On and After Treatment for Patients with Compensated Cirrhosis

Monitoring Patients with Compensated Cirrhosis While On Treatment

Due to the rare but potential risk for hepatic decompensation among patients with compensated cirrhosis on DAA therapy,[35] the AASLD/IDSA guidelines recommend providers consider monitoring for liver injury during treatment.[6] Many experts recommend monitoring a hepatic function panel monthly in patients with compensated cirrhosis who are on DAA therapy, with referral to a specialist if patients develop jaundice, ascites, encephalopathy, significant liver laboratory abnormalities, or other signs and symptoms of hepatic decompensation. Treatment with DAAs has been shown to improve glycemic control in patients with chronic HCV, and patients taking any medication for diabetes should be informed about the potential for symptomatic hypoglycemia, and monitoring of blood sugars is recommended.[6,26] Although neither glecaprevir-pibrentasvir nor sofosbuvir-velpatasvir is likely to affect the pharmacokinetics of warfarin, close monitoring of INR is recommended for patients on warfarin therapy, given that it may change as the result of improved liver function.[]

Table 10. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

On-Treatment Monitoring

• Health care providers may order blood tests to monitor for liver injury or hepatic decompensation, both of which occur rarely among patients with cirrhosis undergoing antiviral treatment for HCV
• Patients should see a liver specialist if they develop jaundice, ascites, encephalopathy, other new liver-related symptoms, or worsening liver blood tests (e.g., AST, ALT, bilirubin) during treatment.
• Monitor for hypoglycemia in patients taking medications for diabetes.
• Monitor for subtherapeutic INR in patients taking warfarin.
• No laboratory monitoring is required for other patients.
• In-person or remote (telehealth/phone) visits may be scheduled, as needed, for patient support and to assess tolerance of new medications.
Abbreviations: AST = aspartate aminotransferase; ALT = alanine aminotransferase; INR – international normalized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Post-Treatment Assessment of Cure in Patients with Compensated Cirrhosis

A follow-up HCV RNA level and liver function testing are recommended 12 weeks following the completion of therapy to assess for cure and ongoing evidence of liver inflammation, respectively. If the HCV RNA level is undetectable 12 or more weeks following the completion of therapy, this is considered a sustained virologic response or cure. If transaminase levels remain elevated despite the achievement of an SVR, further investigation is warranted to assess for other causes of liver disease.[6]

Table 11. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

Post-Treatment Monitoring: Assessment of Cure (SVR)

• Obtain quantitative HCV RNA and hepatic function panel 12 weeks or later following completion of HCV therapy.
• If quantitative HCV RNA is undetectable at least 12 weeks following completion of HCV therapy, the patient is considered to have achieved a sustained virologic response (SVR), also known as a cure.
• Assess for other causes of liver disease if transaminase levels remain elevated after achieving an SVR.
Abbreviations: SVR = sustained virologic response

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Monitoring After Achieving Virologic Cure (SVR)

Patients with cirrhosis require ongoing monitoring for hepatocellular carcinoma, even after achieving an SVR12.[29] This is done via a hepatic ultrasound every 6 months, with or without an alpha-fetoprotein level, in accordance with AASLD guidelines on screening for hepatocellular carcinoma.[29] Patients should also be counseled that they are not immune to HCV following successful treatment and are susceptible to reinfection. Individuals with ongoing risk factors (e.g., people who inject drugs, men who have sex with men and engage in condomless anal intercourse) should be screened annually for reinfection using HCV RNA.[30]

Table 12. **AASLD-IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

Post-Treatment Monitoring: Follow-up After Achieving Virologic Cure (SVR)

• The AASLD recommends ultrasound surveillance for HCC

(with or without alpha-fetoprotein testing) every 6 months in patients with cirrhosis.		
• An upper endoscopy should be performed for surveillance of esophageal varices in certain patients, in accordance with the AASLD guidelines on portal hypertensive bleeding in cir		

rhosis.			
• Patients with ongoing risk factors for HCV should be counseled regarding their risk for reinfection and undergo testing for HCV RNA annually and with any elevation in ALT, AST or bilirubin.			
• Patients should be advised to avoid excessive alcoho			

l.
Abbreviations: HCC = hepatocellular carcinoma; SVR = sustained virologic response

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Monitoring Post-Treatment Patients who Do Not Achieve VIrologic Cure

If initial treatment fails to achieve a virologic cure, patients should be evaluated for repeat treatment. In the setting of prior treatment experience, patients with compensated cirrhosis are not eligible for the simplified treatment algorithm, and patients should be evaluated by a specialist in accordance with AASLD/IDSA guidance.[6] Similarly, as mentioned above, patients with cirrhosis should undergo ultrasound surveillance for hepatocellular carcinoma every six months, with or without the addition of an alpha-fetoprotein level.[29] This surveillance is done in all patients with advanced fibrosis, regardless of SVR12. While a patient is awaiting repeat treatment, CBC, hepatic function panel, and INR should be obtained every 6 to 12 months.

Table 13. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis

Post-Treatment Monitoring: Follow-up for Patients who Do *NOT* Achieve Virologic Cure

• When initial HCV treatment fails to achieve a

cure (SVR), patients should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA HCV guidance

.

- The AASLD recommends ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months

in patients with cirrhosis.			
• Assess disease progression with a CBC, hepatic function panel, and INR every 6–12 months un			

til re tr ea t m en t o cc ur s.
• Pa tie nt s sh ou ld be ad vi se d to av oi d ex ce ssi ve al co ho l.
Abbreviations: SVR = sustained virologic response; HCC = hepatocellular cancer; CBC = complete blood count; INR = international ionized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Treatment Interruptions

Incomplete adherence to DAAs is relatively common among persons receiving treatment for HCV and has the potential to impact SVR12 rates.[37,38] Although short periods of nonadherence (e.g., 1-2 days) are very unlikely to affect treatment responses, longer periods of nonadherence can lead to virologic failure.[39,40]

AASLD/IDSA Recommendations for Management of Treatment Interruptions

Based on a review of the literature and expert consensus, the AASLD-IDSA HCV Guidance has addressed this important issue and developed recommendations for the management of nonadherence events, which considers the duration and timing of nonadherence.[7] This guidance is specific to whether the interruption occurred before the person received 28 days of DAA therapy or whether it occurred after they had received at least 28 days of DAA therapy.[7] In addition, this guidance is only applicable to DAA treatment-naïve individuals and is intended to reflect recommendations for management of nonadherence events in patients who qualify for the AASLD/IDSA simplified treatment algorithms (e.g., simplified HCV treatment for treatment-naïve individuals without cirrhosis and with compensated cirrhosis) who are receiving glecaprevir-pibrentasvir or sofosbuvir-velpatasvir.[7] Management of incomplete adherence in patients who fall outside of this guidance should be done in consultation with an HCV specialist. The following table summarizes the 2023 AASLD HCC Guidance for the management of treatment interruptions in persons while receiving glecaprevir-pibrentasvir or sofosbuvir-velpatasvir in the simplified treatment approach.[7]

Table 14. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients without Cirrhosis or with Compensated Cirrhosis Receiving Glecaprevir-Pibrentasvir or Sofosbuvir-Velpatasvir

Interruptions Before Receiving 28 Days of DAA Therapy
Missed ≤7 Days • **Restart** DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).
Missed ≥8 Days • **Restart** DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level. • **Obtain** HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy. ◦ If HCV RNA is negative (undetectable),

complete originally planned DAA treatment course (8 or 12 weeks; total planned dosage[a]). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 infection and/or compensated cirrhosis.
    - If HCV RNA is positive (>25 IU/L) or not obtained, extend DAA treatment for an additional 4 weeks.

Interruptions After Receiving ≥28 Days of DAA Therapy

Missed ≤7 Days

- **Restart** DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).

Missed 8-20 Consecutive Days

- **Restart** DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.
- **Obtain** HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy.
    - If HCV RNA is negative (undetectable), complete originally

planned DAA treatment course (8 or 12 weeks; total planned dosage[a]). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 infection and/or compensated cirrhosis.
- If HCV RNA is positive (>25 IU/L) or not obtained, **stop** DAA treatment and retreat according to recommendations in the Retreatment Section in the AASLD-IDSA Guidance.

Missed ≥21 Consecutive Days

- **Stop** DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to recommendations in the Retreatment Section.

Abbreviations: DAA = direct-acting antiviral; HCV = hepatitis C virus; SVR = sustained virologic response
[a]Extend duration of therapy such that the patient receives the total planned dosage (ie, the total number of daily pills). For example, if a patient missed 10 days of a planned 8-week course of therapy, treatment would be extended to 8 weeks plus 10 days.

Source:

- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [PubMed Abstract]

Summary Points

- The AASLD/IDSA simplified HCV treatment algorithm can help streamline treatment initiation and on-treatment monitoring in select populations of treatment-naïve individuals.
- For the purposes of the simplified treatment assessment, a patient is presumed to have cirrhosis if their FIB-4 score is greater than 3.25.
- An HCV genotype is not necessary to obtain in noncirrhotic treatment-naïve patients eligible for the simplified HCV treatment algorithm.
- The use of 8 weeks of glecaprevir-pibrentasvir or 12 weeks of sofosbuvir-velpatasvir is recommended for treatment-naïve patients without cirrhosis as part of the AASLD/IDSA simplified HCV treatment algorithm.
- On-treatment monitoring of hepatic function tests is not necessary for treatment-naïve patients without cirrhosis who are eligible for the simplified treatment algorithm.
- Genotype 1, 2, 4, 5, or 6 cirrhotic patients on the simplified treatment algorithm can be treated with either 8 weeks of glecaprevir-pibrentasvir or 12 weeks of sofosbuvir-velpatasvir.
- For patients with genotype 3 HCV and compensated cirrhosis, sofosbuvir-velpatasvir should not be used if a baseline Y93H mutation is present. If baseline RAS testing is not sent, 8 weeks of glecaprevir-pibrentasvir should be used.
- Providers may elect to check on-treatment hepatic function tests for patients with compensated cirrhosis on the simplified treatment regimen, given that hepatic decompensation and liver injury rarely occur in cirrhotic patients during antiviral therapy.
- Patients with cirrhosis should undergo ongoing surveillance for HCC with liver ultrasound with or without the addition of a serum alpha-fetoprotein level every 6 months, regardless of HCV cure.

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Table 1. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment Eligibility Criteria^**

Who is Eligible for Simplified HCV Treatment Algorithm	W Simplifie
Adults with chronic HCV infection, including persons living with HIV: • Infected with any HCV genotype • Have NOT previously received HCV treatment • Without cirrhosis • With compensated cirrhosis (Child-Pugh*A) • The determination of cirrhosis can be based on the presence of any of the following: - Liver stiffness >12.5 kPa by FibroScan - FIB-4 >3.25 - Non-invasive serologic test (HCV FibroSure or enhanced liver fibrosis test) - Liver biopsy - Liver nodularity or splenomegaly on imaging - Platelet count <150,000/mm^3 • The determination of compensated versus uncomplicated cirrhosis is based on Child-Pugh* score	**Adults with chronic HCV infect** • Previously received HCV tr • Hepatitis B surface antiger • Compensated cirrhosis (Ch mL/min/m^2 • Current or prior decompen • Current pregnancy • Known or suspected hepat • Prior liver transplantation

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]
- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]

Table 2. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

Pretreatment Assessment for Treatment-Naive Adults without Cirrhosis

Before Initiating Antiviral Therapy
• Calculate a FIB-4 score[a]
• Assess for Cirrhosis[b]
• Obtain CBC
• Obtain hepatic function panel ◦ Total and direct bilirubin ◦ Albumin ◦ ALT, AST
• Determine eGFR
• Perform medication reconciliation[c]
• Assess for drug-drug interactions[d]
• Check quantitative HCV RNA (viral load)
• Obtain HIV-1/2 antigen-antibody test
• Check hepatitis B surface antigen (*see Author's Notes*)
• Obtain serum pregnancy testing and counsel about pregnancy risk and DAAs
• Educate about DAA administration and adherence, prevention of reinfection, and avoiding excess alcohol

Abbreviations: CBC = complete blood count; DAA = direct-acting antiviral; eGFR = estimated glomerular filtration rate; FIB-4 = fibrosis-4 index for liver fibrosis; HCV = hepatitis C virus; INR = international normalized ratio.

[a] FIB-4 is a noninvasive measure of hepatic fibrosis that is calculated using age (years), AST, ALT, and platelet count.
[b] A patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 or if they have any of the following from a previously performed test: transient elastography indicating cirrhosis (ie, liver stiffness >12.5 kPa), noninvasive serologic test above the proprietary cutoff indicating cirrhosis (eg, FibroSure, enhanced liver fibrosis test), clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3), or prior liver biopsy showing cirrhosis.
[c] Medication reconciliation should record currently prescribed medications, over-the-counter drugs, and herbal/dietary supplements.
[d] Drug-drug interaction assessment should be performed using the table in the Monitoring Section of the HCV Guidance website or theUniversity of Liverpool drug interaction checker.

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]
- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [PubMed Abstract]

Table 3. AASLD-IDSA HCV Simplified Guidance for All Genotypes: Initial Treatment
Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Regimens listed alphabetically

Recommended for Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis
Glecaprevir-Pibrentasvir **Fixed-dose combination of glecaprevir (300 mg)-pibrentasvir (120 mg): 3 tablets once daily for 8 weeks*
Note: *Take with food

Recommended for Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis
Sofosbuvir-Velpatasvir **Fixed-dose combination of sofosbuvir (400 mg)-velpatasvir (100 mg): one tablet once daily for 12 weeks*
Note: *Take with or without food

Table 4. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

On-Treatment Monitoring

• Monitor for hypoglycemia in patients taking medications for diabetes.
• Monitor for sub-therapeutic INR in patients taking warfarin.
• No laboratory monitoring is required for other patients.
• In-person or remote (telehealth/phone) visits may be scheduled, as needed, for patient support and to assess tolerance of new medications.
Abbreviations: INR – international normalized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Table 5. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

Post-Treatment Monitoring: Assessment of Cure (SVR)

• Obtain quantitative HCV RNA and hepatic function panel 12 weeks or later following completion of HCV therapy.
• If quantitative HCV RNA is undetectable 12+ weeks following completion of HCV therapy, the patient is considered to have achieved a sustained virologic response (SVR), also known as a cure.
• Assess for other causes of liver disease if transaminase levels remain elevated after achieving an SVR.
Abbreviations: SVR = sustained virologic response

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Table 6. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

Post-Treatment Monitoring: Follow-up After Achieving Virologic Cure (SVR)

• No liver specific follow up is needed for patients without advanced fibrosis following SVR.
• Patients with ongoing risk factors for HCV should be counseled regarding their risk for reinfection and undergo testing for HCV RNA annually and with any elevation in ALT, AST or bilirubin.
• Patients should be advised to avoid excessive alcohol.
Abbreviations: SVR = sustained virologic response

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Table 7. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

Post-Treatment Monitoring: Follow-up for Patients who Do *NOT* Achieve Virologic Cure

• When initial HCV treatment fails to achieve a cure (SVR), patients should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA HCV guidance.
• Assess disease progression with a CBC, hepatic function panel, and INR every 6 – 12 months until retreatment occurs.
• Patients should be advised to avoid excessive alcohol.
Abbreviations: SVR = sustained virologic response; CBC = complete blood count; INR = international ionized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance]]

Table 8. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis**

Pretreatment Assessment for Treatment-Naive Adults With Compensated Cirrhosis

Before Initiating Antiviral Therapy
• Calculate a Child-Pugh Score[a] (*see Author's Notes*)
• Perform liver ultrasound[b]
• Obtain complete blood count (CBC)
• Check international ionized ratio (INR)
• Obtain hepatic function panel ◦ Total and direct bilirubin ◦ Albumin ◦ ALT, AST
• Determine eGFR
• Perform medication reconciliation[c]
• Assess for drug-drug interactions[d]
• Check quantitative HCV RNA
• Obtain HIV-1/2 antigen-antibody test
• Check hepatitis B surface antigen (*see Author's Notes*)
• Check HCV genotype (if treating with sofosbuvir-velpatasvir)
• Obtain serum pregnancy testing and counsel about pregnancy risk and DAAs
• Educate about DAA administration and adherence, prevention of reinfection, and avoiding excess alcohol

Abbreviations: CBC = complete blood count; DAA = direct-acting antiviral; eGFR = estimated glomerular filtration rate; FIB-4 = fibrosis-4 index for liver fibrosis; HCV = hepatitis C virus; INR = international normalized ratio.

[a] Child–Pugh score based on presence of ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7. Patients with a Child–Pugh score ≥7 (ie, Child–Pugh B or C) have decompensated cirrhosis; this simplified treatment approach is not recommended for patients with decompensated cirrhosis.
[b] Obtain liver ultrasound within 6 months prior to initiating antiviral treatment to exclude hepatocellular carcinoma and subclinical ascites. This simplified treatment approach is not recommended for patients with hepatocellular carcinoma and/or decompensated cirrhosis
[c] Medication reconciliation should record currently prescribed medications, over-the-counter drugs, and herbal/dietary supplements.
[d] Drug-drug interaction assessment should be performed using the table in the Monitoring Section of the HCV Guidance website or the University of Liverpool drug interaction checker.

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]
- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [PubMed Abstract]

Table 9. AASLD-IDSA HCV Simplified Guidance for All Genotypes: Initial Treatment
Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis^

Regimens listed alphabetically

Recommended for Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis^
Glecaprevir-Pibrentasvir **Fixed-dose combination of glecaprevir (300 mg)-pibrentasvir (120 mg): 3 tablets once daily for 8 weeks*
For Genotypes 1-6 Note: *Take with food

Recommended for Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis^
Sofosbuvir-Velpatasvir **Fixed-dose combination of sofosbuvir (400 mg)-velpatasvir (100 mg) one tablet once daily for 12 weeks*
Patients with compensated cirrhosis and HCV genotype 3 require baseline NS5A RAS testing prior to use of sofosbuvir-velpatasvir. Only those without Y93H mutations can be treated with 12 weeks of sofosbuvir-velpatasvir. Note: *Take with or without food

^For patients with decompensated cirrhosis, refer to a liver specialist and see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Table 10. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

On-Treatment Monitoring

• Health care providers may order blood tests to monitor for liver injury or hepatic decompensation, both of which occur rarely among patients with cirrhosis undergoing antiviral treatment for HCV
• Patients should see a liver specialist if they develop jaundice, ascites, encephalopathy, other new liver-related symptoms, or worsening liver blood tests (e.g., AST, ALT, bilirubin) during treatment.
• Monitor for hypoglycemia in patients taking medications for diabetes.
• Monitor for subtherapeutic INR in patients taking warfarin.
• No laboratory monitoring is required for other patients.
• In-person or remote (telehealth/phone) visits may be scheduled, as needed, for patient support and to assess tolerance of new medications.
Abbreviations: AST = aspartate aminotransferase; ALT = alanine aminotransferase; INR – international normalized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Table 11. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

Post-Treatment Monitoring: Assessment of Cure (SVR)

• Obtain quantitative HCV RNA and hepatic function panel 12 weeks or later following completion of HCV therapy.
• If quantitative HCV RNA is undetectable at least 12 weeks following completion of HCV therapy, the patient is considered to have achieved a sustained virologic response (SVR), also known as a cure.
• Assess for other causes of liver disease if transaminase levels remain elevated after achieving an SVR.
Abbreviations: SVR = sustained virologic response

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Table 12. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

Post-Treatment Monitoring: Follow-up After Achieving Virologic Cure (SVR)

• The AASLD recommends ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months in patients with cirrhosis.
• An upper endoscopy should be performed for surveillance of esophageal varices in certain patients, in accordance with the AASLD guidelines on portal hypertensive bleeding in cirrhosis.
• Patients with ongoing risk factors for HCV should be counseled regarding their risk for reinfection and undergo testing for HCV RNA annually and with any elevation in ALT, AST or bilirubin.
• Patients should be advised to avoid excessive alcohol.
Abbreviations: HCC = hepatocellular carcinoma; SVR = sustained virologic response

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Table 13. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults WITH Compensated Cirrhosis**

Post-Treatment Monitoring: Follow-up for Patients who Do *NOT* Achieve Virologic Cure

• When initial HCV treatment fails to achieve a cure (SVR), patients should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA HCV guidance.
• The AASLD recommends ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months in patients with cirrhosis.
• Assess disease progression with a CBC, hepatic function panel, and INR every 6 – 12 months until retreatment occurs.
• Patients should be advised to avoid excessive alcohol.
Abbreviations: SVR = sustained virologic response; HCC = hepatocellular cancer; CBC = complete blood count; INR = international ionized ratio

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

Table 14. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis**

Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients without Cirrhosis or with Compensated Cirrhosis Receiving Glecaprevir-Pibrentasvir or Sofosbuvir-Velpatasvir

Interruptions Before Receiving 28 Days of DAA Therapy
Missed ≤7 Days • **Restart** DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).
Missed ≥8 Days • **Restart** DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level. • **Obtain** HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy. ◦ If HCV RNA is negative (undetectable), complete originally planned DAA treatment course (8 or 12 weeks; total planned dosage[a]). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 infection and/or compensated cirrhosis. ◦ If HCV RNA is positive (>25 IU/L) or not obtained, extend DAA treatment for an additional 4 weeks.
Interruptions After Receiving ≥28 Days of DAA Therapy
Missed ≤7 Days • **Restart** DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).
Missed 8-20 Consecutive Days • **Restart** DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level. • **Obtain** HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy. ◦ If HCV RNA is negative (undetectable), complete originally planned DAA treatment course (8 or 12 weeks; total planned dosage[a]). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 infection and/or compensated cirrhosis. ◦ If HCV RNA is positive (>25 IU/L) or not obtained, **stop** DAA treatment and retreat according to recommendations in the Retreatment Section in the AASLD-IDSA Guidance.
Missed ≥21 Consecutive Days • **Stop** DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to recommendations in the Retreatment Section.
Abbreviations: DAA = direct-acting antiviral; HCV = hepatitis C virus; SVR = sustained virologic response [a]Extend duration of therapy such that the patient receives the total planned dosage (ie, the total number of daily pills). For example, if a patient missed 10 days of a planned 8-week course of therapy, treatment would be extended to 8 weeks plus 10 days.

Source:

- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [PubMed Abstract]