

Making a Decision on When to Initiate HCV Therapy

This is a PDF version of the following document:

Module 4: [Evaluation and Preparation for Hepatitis C Treatment](#)

Lesson 2: [Making a Decision on When to Initiate HCV Therapy](#)

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<http://www.hepatitisc.uw.edu/go/evaluation-treatment/treatment-initiation-decision/core-concept/all>

Indications for Treatment

Background

Multiple studies have shown that successful antiviral therapy of chronic hepatitis C infection dramatically reduces both liver-related morbidity and mortality (including rates of end-stage liver disease and hepatocellular carcinoma), as well as all-cause mortality. Direct-acting antiviral treatment for hepatitis C has proven much safer, better tolerated, and more effective than treatments used in the interferon era, rendering the decision of when to initiate therapy much easier in some respects. The cooperative guidance issued from the American Association for the Study of Liver Disease (AASLD) and Infectious Diseases Society of America (IDSA) notes that evidence clearly supports treatment of nearly all persons infected with HCV.[1] Decisions regarding initiating therapy will naturally be influenced by the patient's willingness to undertake treatment and the ability to have the medication regimen paid for.

Generally Accepted Indicators for Treatment

The AASLD/IDSA guidance has previously provided a priority ranking for treatment based on both clinical and public health factors, with the highest priority for treatment conferred to those at increased risk of liver-related complications and severe extrahepatic HCV-related complications, high priority status to those with moderate fibrosis or other concomitant complications, and a priority status given to those persons with elevated risk of HCV transmission to others. In 2016, the AASLD/IDSA removed priority tables from the guidance—the AASLD/IDSA guidance emphasizes that all patients with chronic hepatitis C should, except for those individuals with short life expectancies, be considered for treatment given the preponderance of data demonstrating benefit on clinical outcomes as well as patient-reported improvements in quality of life and other factors.[1,2] The AASLD/IDSA guidance does, however, highlight specific subgroups of patients who should not be singled out for treatment as much as appreciated for their particular characteristics that make treatment all the more compelling, either because of the significant benefit conferred by treatment to their natural history (e.g. patients with cirrhosis or HIV or hepatitis B coinfection) or to the public health (e.g. healthcare workers, persons who inject drugs) (Figure 1).[1] For further discussion regarding liver disease staging, please refer to Module 2 (Evaluation, Staging, and Monitoring of Chronic Hepatitis C), Lessons 4 ([Evaluation and Staging of Liver Fibrosis](#)) and 5 ([Evaluation and Prognosis of Patients with Cirrhosis](#)).

Contraindications for Treatment

Absolute Contraindications

Many fewer contraindications exist in the modern hepatitis C treatment era, as therapy has evolved to predominantly interferon-free regimens. Even patients with decompensated cirrhosis or renal failure can undergo treatment if managed by a provider expert in the management of hepatitis C. The AASLD/IDSA hepatitis C treatment guidance recommends against treating persons with short life expectancies. Available data from animal studies indicate that ribavirin has significant teratogenic and embryocidal adverse effects.[3] Accordingly, use of ribavirin is contraindicated in women who are pregnant, women who may become pregnant, or men whose female partners are pregnant.[4,5] Patients with chronic hepatitis C who are of reproductive age and are to receive a regimen that includes ribavirin should be advised to use two forms of contraception during treatment and for at least 6 months following the end of treatment.

Relative Contraindications

In addition to some absolute contraindications, there are several situations in which the clinician should exert careful consideration before starting hepatitis C treatment: active severe substance abuse, psychiatric issues not optimally controlled, and social issues that may negatively impact a patient's ability to adhere with therapy, to make visits to monitor treatment safety, or to show up for scheduled office visits.[6,7]

Patient Readiness

Assessing Readiness

A patient's readiness to start therapy can be difficult to assess, but a checklist can be used as a general guide ([Figure 2](#)). Note that many current regimens no longer use ribavirin or peginterferon and checklist items related to these medications pertain only to those patients who will receive them. It is important to have a frank discussion with each patient about the chance of cure, the potential side effects of therapy, the cost of treatment, and, if using interferon or ribavirin-based therapy, the impact of treatment on their quality of life.

Pre-Treatment Counseling

In addition, the pre-treatment discussion should cover counseling on adherence, drug-drug interactions, potential side effects, contact numbers for after-hour questions or issues, and specific information on follow-up visits. Given the high cost of direct-acting antiviral agents (DAAs) and the potential for drug resistance, it is very important that patients fully understand the importance of remaining 100% adherent with the treatment regimen.

Timing of Initiation of Treatment

The availability of DAAs has provided tremendous opportunities for highly effective, convenient, well-tolerated therapy. The high cost of these medications has created difficulty in payment and reimbursement in many regions—see Module 4 (Evaluation and Preparation for Hepatitis C Treatment), Lesson 3 ([Cost and Access to Direct-Acting Antiviral Agents](#)). In general, nearly all patients with chronic hepatitis C have an indication to receive HCV therapy, but cost issues have forced an approach whereby those likely to receive the most immediate benefit, such as those with advanced fibrosis, are prioritized to receive therapy first. There is, however, accumulating data that deferral of treatment until advanced stages of liver disease is a suboptimal and short-sighted approach to care.[\[8,9\]](#)

Advanced Age and Comorbid Conditions

Many North American patients with hepatitis C are older than age 50. With the availability of new highly effective, safe, well-tolerated regimens, it is likely that more interest and experience will accumulate in treating patients with advanced age. Notably, some clinical trials with newer direct acting antivirals have enrolled patients older than 70, but overall relatively little experience exists with treatment of HCV in patients older than 70. In some circumstances, patients may have advanced age and minimal HCV-related fibrosis and thus HCV may not be expected to play a major role in shortening their lifespan. In addition, some patients may have limited life expectancy due to other co-morbid conditions, and as such, hepatitis C treatment would not be expected to alter their quality of life or life expectancy. Thus, in some situations involving patients with advanced age or significant medical comorbidities associated with expected short lifespan (less than 12 months), it may be sensible to withhold therapy.

Obtaining Authorization and Payment for Medications

If a patient has been deemed to be an appropriate candidate for antiviral therapy and is in need of therapy, the medical provider should begin investigating payment for the treatment. Because these antiviral agents are quite costly, they typically need to be pre-approved. The authorization process may last several months, with the exact time dependent on the insurance coverage and state of residence.

Monitoring and Follow-Up if Not Treated

General Recommendations for Monitoring and Follow-Up

There may be a variety of reasons that treatment of HCV is deferred, including patient-specific barriers such as active psychosocial instability or insurance denial. At least annual follow-up is recommended for these patients. During these visits, patients should have counseling regarding behaviors that will optimize liver health. This includes avoiding a diet high in saturated fat, achieving an optimal body weight, limiting intake of hepatotoxic medications and abstaining from or limiting alcohol intake. Medical providers should have awareness of indicators associated with accelerated hepatic fibrosis progression, such as older age at the time of HCV infection, male sex, alcohol consumption, non-alcoholic steatohepatitis (NASH), genotype 3 HCV, and coinfection with hepatitis B or HIV ([Figure 3](#)). Patients should receive information and education on the warning signs and symptoms of liver dysfunction, including jaundice, melena, clay-colored stools, confusion, abdominal distention and lower extremity edema.

Reassessing Hepatic Fibrosis

For patients with mild to moderate fibrosis (F0 to F2), fibrosis progression can occur, so it is recommended that at least a liver function panel that includes an aspartate aminotransferase (AST) and complete blood cell count with platelet count be performed annually; from these basic laboratory tests, an AST to Platelet Ratio Index (APRI) can be calculated. In addition, subsequent noninvasive testing to re-evaluate hepatic fibrosis (with a Fibrosure or Fibrotest) is recommended, although the optimal interval for retesting remains to be determined and may be dependent on clinical factors and patient's initial stage of disease. The AASLD guidelines recommend an annual update of lab markers of hepatic function and re-evaluation interval of no greater than 6 months for patients with cirrhosis for liver cancer screening.

Monitoring and Assistance with Unstable Psychosocial Situation

For patients with an unstable psychosocial situation, that issue should be addressed and patients referred to the necessary resource, such as a mental health professional, substance abuse counseling. Ongoing alcohol abuse is perhaps the most worrisome behavior, because it can accelerate fibrosis and patients should be counseled strongly to abstain completely. Special effort should be made to address psychosocial issues in patients with advanced fibrosis (F3 or F4). These patients with advanced fibrosis will also need hepatocellular carcinoma surveillance with a hepatic ultrasound every 6 months.

Summary Points

- Availability of highly effective, convenient, safe, well-tolerated therapy has changed the landscape for the treatment of hepatitis C.
- Nearly all patients with hepatitis C may benefit from therapy. Those patients with a severely limited lifespan (less than 12 months) are the exception.
- The decision and timing for starting HCV therapy needs to be individualized.
- In situations when treatment is deferred (for whatever reason), the patient should periodically undergo reevaluation for disease progression and reconsideration of treatment, with the frequency of reevaluation individualized based on the patient's current fibrosis stage, likely fibrosis progression rate, and other factors that may influence treatment readiness.

Citations

1. AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. When and in whom to initiate HCV therapy. [[AASLD/IDSA Hepatitis C Guidance](#)] -
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Figures

Figure 1 Benefit of HCV Treatment to Reduce HCV Transmission

Source: American Association for the Study of Liver Disease, the Infectious Diseases Society of America. When and in whom to initiate HCV therapy. Recommendations for testing, management, and treating hepatitis C.

AASLD/IDSA: HCV Guidance
Benefit of HCV Treatment to Reduce HCV Transmission
▪ HIV-Infected men who have sex with men (MSM) with high-risk sexual practices
▪ Persons who inject drugs
▪ Incarcerated persons
▪ Persons on hemodialysis
▪ Treatment of a woman with HCV before she becomes pregnant
▪ HCV-infected health care workers who perform exposure-prone procedures
Rating: Class IIa, Level C

Figure 2 Patient Checklist Prior to Initiating Hepatitis C Therapy

Checklist Before Starting Hepatitis C Therapy
General Checklist for All Patients
<input type="checkbox"/> Good evidence of adherence and willing to comply with follow-up
<input type="checkbox"/> Adequate psychosocial support
<input type="checkbox"/> Psychiatrically stable
<input type="checkbox"/> Drug and/or alcohol use evaluated and addressed so as not to interfere with therapy
<input type="checkbox"/> Potential drug-drug interactions addressed and plan in place to monitor
IF Treatment with Ribavirin
<input type="checkbox"/> Not pregnant or planning to become pregnant during therapy and for 6 months afterwards
<input type="checkbox"/> If patient or partner of child-bearing potential, willing to use ≥ 2 reliable birth control methods
<input type="checkbox"/> No significant cardiac or respiratory issues

Figure 3 Factors Associated with Accelerated Fibrosis

Source: American Association for the Study of Liver Disease, the Infectious Diseases Society of America. When and in whom to initiate HCV therapy. Recommendations for testing, management, and treating hepatitis C.

AASLD/IDSA: HCV Guidance	
Factors Associated with Accelerated Fibrosis Progression	
Host	Viral
<ul style="list-style-type: none"> ▪ Non Modifiable Fibrosis stage Inflammation grade Older age at time of infection Male sex Organ transplant 	<ul style="list-style-type: none"> Genotype 3 Coinfection with HBV or HIV
<ul style="list-style-type: none"> ▪ Modifiable Alcohol consumption Nonalcoholic fatty liver disease Obesity Insulin resistance 	