FROM DIAGNOSIS TO TREATMENT:
How to Build an HCV Clinical Toolkit

Part 1 for Music City PrEP

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AETC AIDS Education & Training Center Program Southeast

Objectives

At the end of this training, the learner will be able to:

- Describe screening criteria for HCV and apply to clinical practice;
- Describe the natural history of HCV;
- Identify clinical manifestations of HCV;
- Outline the clinical evaluation of HCV, including history, laboratory studies, and liver fibrosis staging;
- Select HCV therapy using evidence-based tools.

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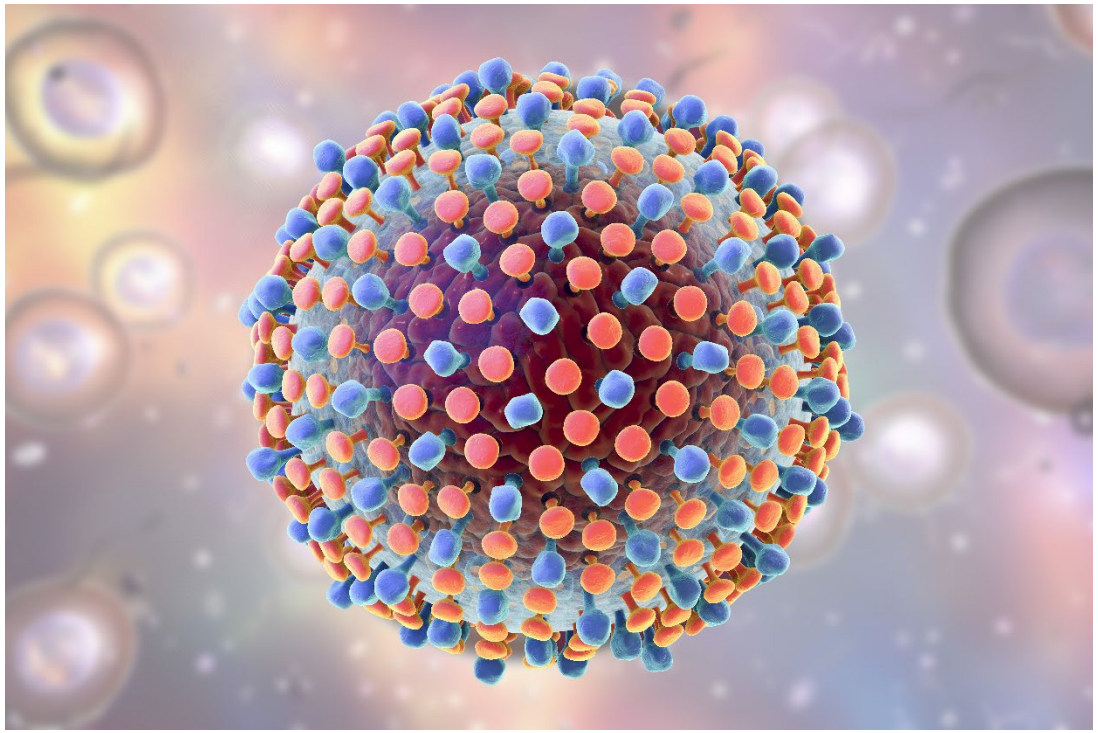
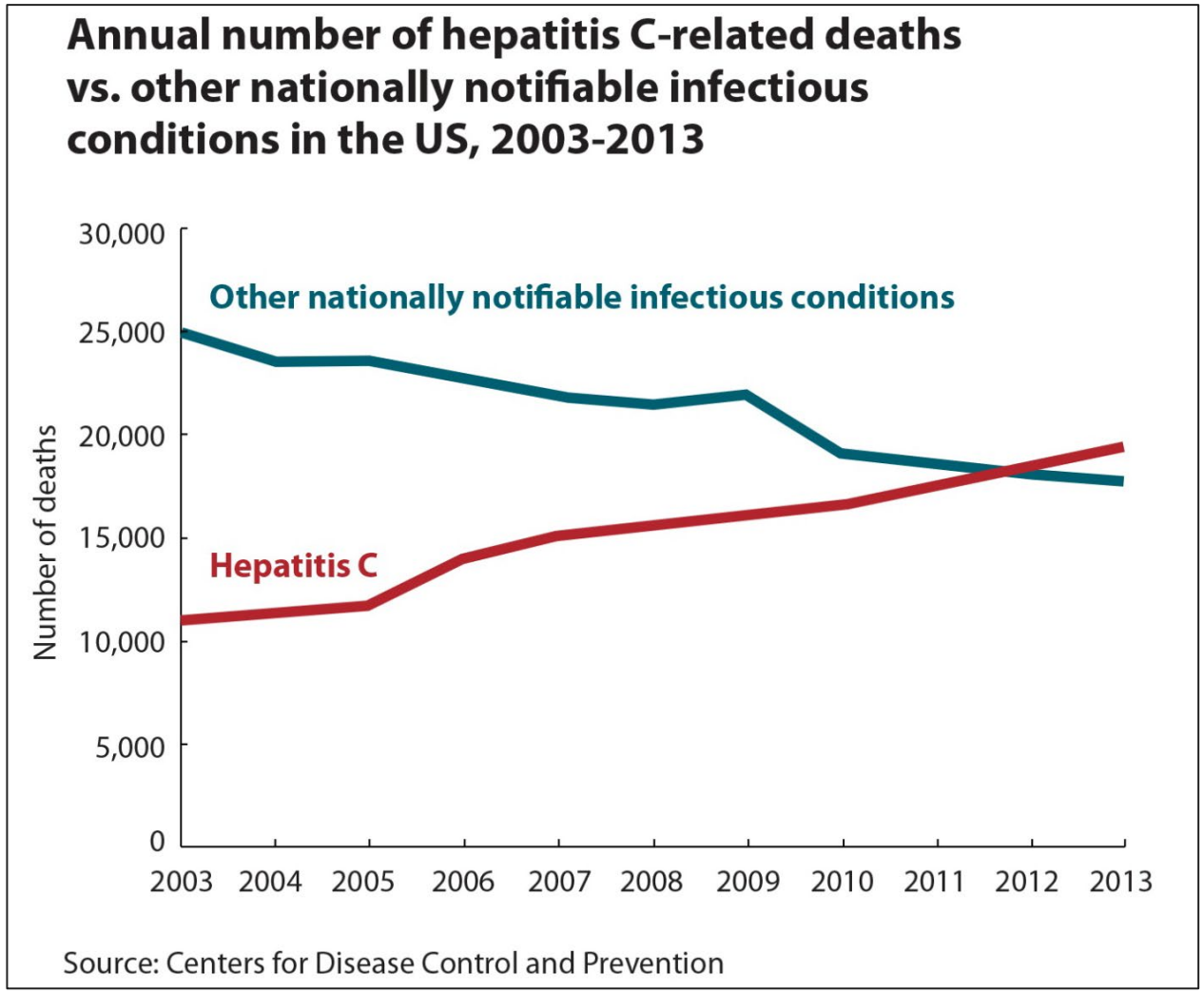
Hepatitis C Virus (HCV)



- Single-strand, positive sense RNA flavivirus
- Spread through blood and body fluids
- Predominantly infects liver cells
- No latent reservoir
  - No integration with host DNA as with HIV
  - No covalently closed DNA within host cell nuclei as with HBV
  - Can be eradicated/cured with treatment

HCV and Mortality in the USA



U.S. Preventive Services TASK FORCE

Hepatitis C Virus Infection in Adolescents and Adults: Screening

Release Date: March 2020

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B

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Risk Factors for Screening (www.hcvguidelines.org)

- Risk Behaviors
  - Injection drug use (current or ever)
  - Intranasal drug use
  - Men who have sex with men

- Risk Exposures
  - Hemodialysis
  - Percutaneous/parenteral exposures in unregulated setting
  - Healthcare occupational exposure
  - Children born to HCV-infected women
  - Prior clotting factor concentrate administration prior to 1987 or blood transfusion prior to 1992
  - Incarceration

- Other Conditions
  - HIV
  - **Sexually active person about to start PrEP**
  - Unexplained chronic liver disease
  - Solid organ donors and solid organ transplant recipients

Role of Repeat Screening (www.hcvguidelines.org)

- HCV RNA testing may be indicated if acute infection suspected (e.g., recent risk exposure with symptoms and/or elevated liver function tests)

- Repeat testing after high-risk exposure or intermittently in populations at chronic high risk may be appropriate

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	RATING ⓘ
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years or older.	I, B
One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).	I, B
Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy.	I, B
Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).	IIa, C
Annual HCV testing is recommended for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP).	IIa, C

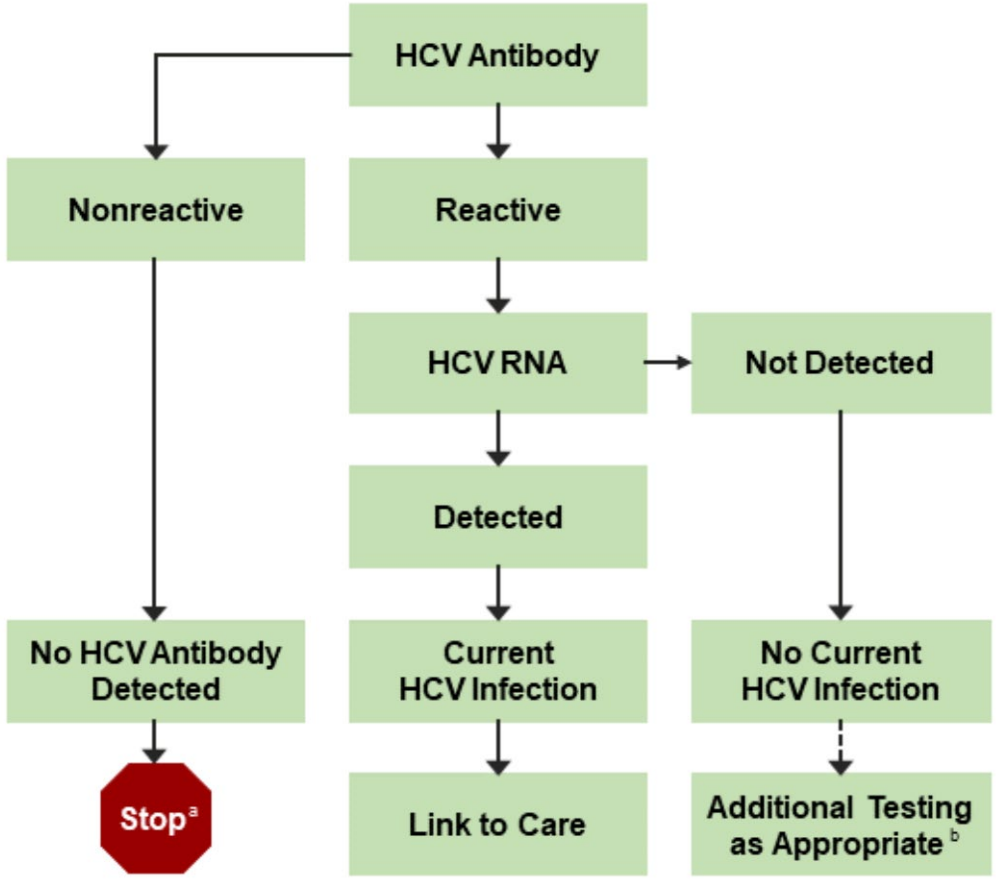
Diagnostics Review

- HCV Antibody
  - Tests for ***exposure***
  - Near 100% sensitivity once >6 months after infection

- HCV RNA
  - Tests for ***active infection***
  - 20% or more patients spontaneously clear HCV

- HCV Genotype
  - Defines genetic subtype for prognostic information and treatment guidance

Figure 1. CDC-Recommended Testing Sequence for Identifying Current HCV Infection



www.hcvguidelines.org

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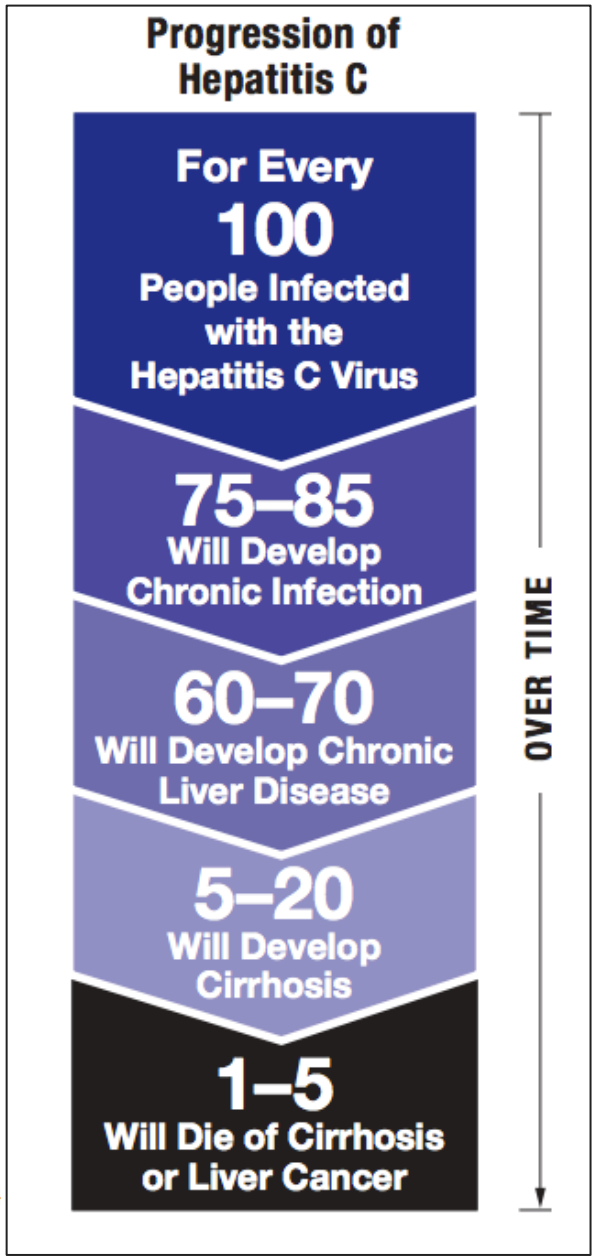

HCV Natural History

- Minority develop advanced liver disease
- Cirrhosis usually takes years to develop in the absence of comorbidities
- Timeline may be accelerated by comorbidities, including alcohol use, HBV, HIV, insulin resistance, and/or obesity

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Manifestations of HCV

Acute HCV (~20%)

- Fever
- Fatigue and anorexia
- Nausea and vomiting
- Abdominal pain
- Jaundice, dark urine, and clay-colored stools
- Arthralgias

Chronic HCV

Often asymptomatic

May cause fatigue, insomnia, depression, and mental status changes

May cause extrahepatic manifestations including vasculitis and renal disease

Long-term outcomes include cirrhosis, liver failure, and hepatocellular carcinoma

History of HCV

- Timing and context of diagnosis
- Prior symptoms of acute hepatitis
- Prior staging
- Prior treatment

Risk Factors

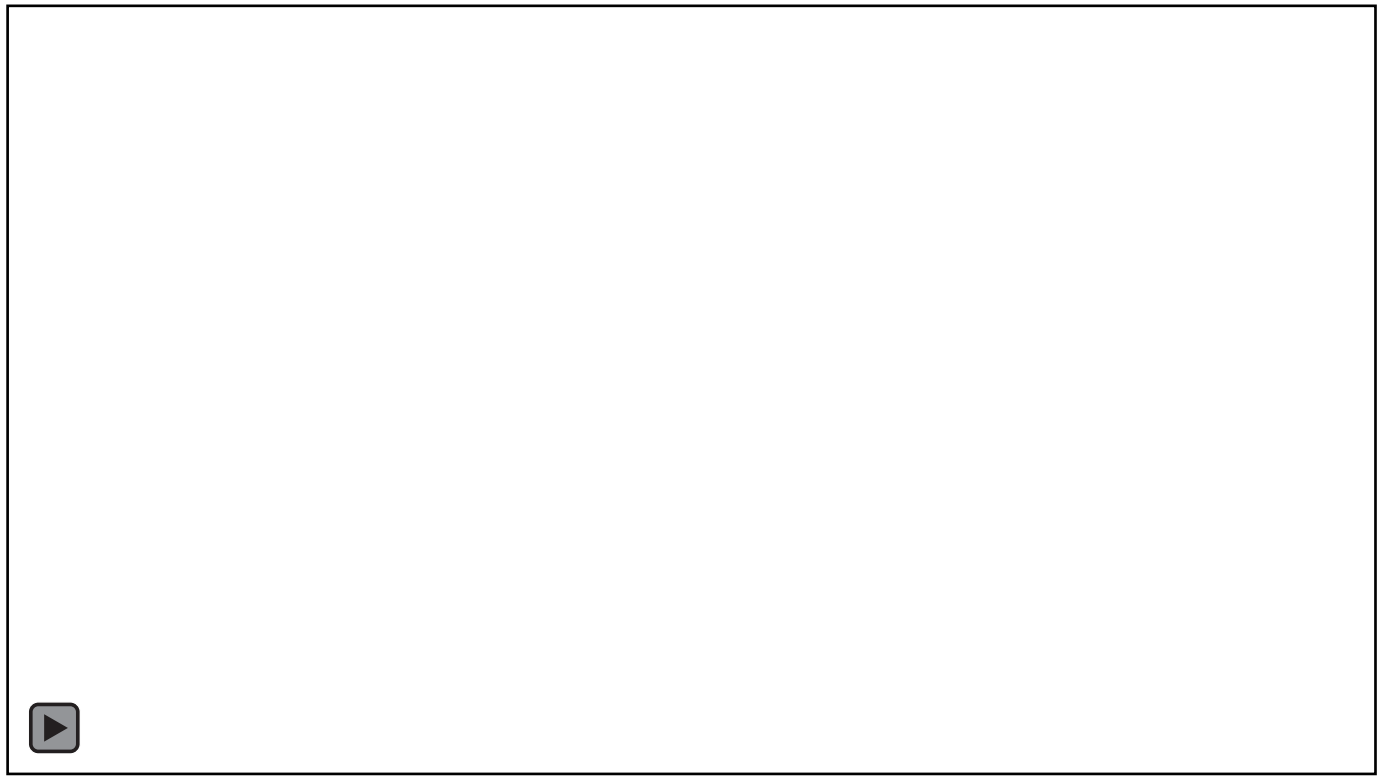
- Blood products
- Prior surgeries in distant past
- Tattoos
- Piercing
- Injection and inhaled drug use
- Unprotected sex
- Age (i.e., baby boomer cohort)

Brau N. *Clin Infect Dis* 2013.

Symptoms of Chronic HCV Infection

- Fatigue
- Arthralgias
- Chronic abdominal pain
- Insomnia
- *Many patients are asymptomatic*

Symptoms of Advanced Liver Disease



- Upper GI bleeding
- Ascites
- Hepatic encephalopathy
- Liver failure

Related History

- Other medical diagnoses
- Family history
- Alcohol use
- Non-prescription drugs
- Prescription medication review
- Over-the-counter medication, herb, and supplement review

Additional Social History

- Current living situation
- Occupational/work history
- Transportation
- Support system

Physical Exam

May be normal without evidence of disease!

Focus on signs of chronic liver disease and/or injection drug use:

- Palmar erythema
- Spider nevi
- Gynecomastia
- Jaundice
- Ascites
- Encephalopathy
- Track marks
- Thrombophlebitis

Suggested Laboratory Testing Prior to Treatment

- Within 6 months
  - Complete blood count (CBC)
  - Calculated glomerular filtration rate (eGFR)
  - Hepatic function panel
  - International normalized ratio (INR)
    - ***If concerned for advanced fibrosis***
- Anytime Prior
  - Quantitative HCV RNA
  - HCV genotype
    - ***Not clinically required***
  - HIV antigen/antibody
  - Hepatitis B surface antigen
    - ***Additional HBV testing may assist in determining vaccination status and/or eligibility***
- Before Starting
  - Pregnancy testing

Staging Liver Fibrosis/METAVIR

Importance of Staging

- Identify patients with greatest need for therapy
- Identify patients for cirrhosis-specific care
- Triage resources

Types of Staging

- Liver biopsy
- Biomarkers
- Elastography

METAVIR Scoring

Score	Pathologic Description
0	No fibrosis
1	Periportal fibrosis
2	Periportal septae
3	Bridging fibrosis (portal-central septae)
4	Cirrhosis

Liver Biopsy To Stage Liver Fibrosis

Historical gold standard

May be helpful in evaluating other causes of liver disease

Results may be impacted by quality of specimen (i.e., length of biopsy)

Limited by invasive nature of test, cost, and access to proceduralist

Risks/complications can be significant

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Indirect Markers of Liver Fibrosis

APRI (AST-To-Platelet Ratio Index)

- Includes AST and Platelet Count
- Sens 76% and Spec 72% at cutoff of 1.0 for predicting cirrhosis
- Sens 46% and Spec 91% at cutoff of 2.0 for predicting cirrhosis

FIB-4 Index

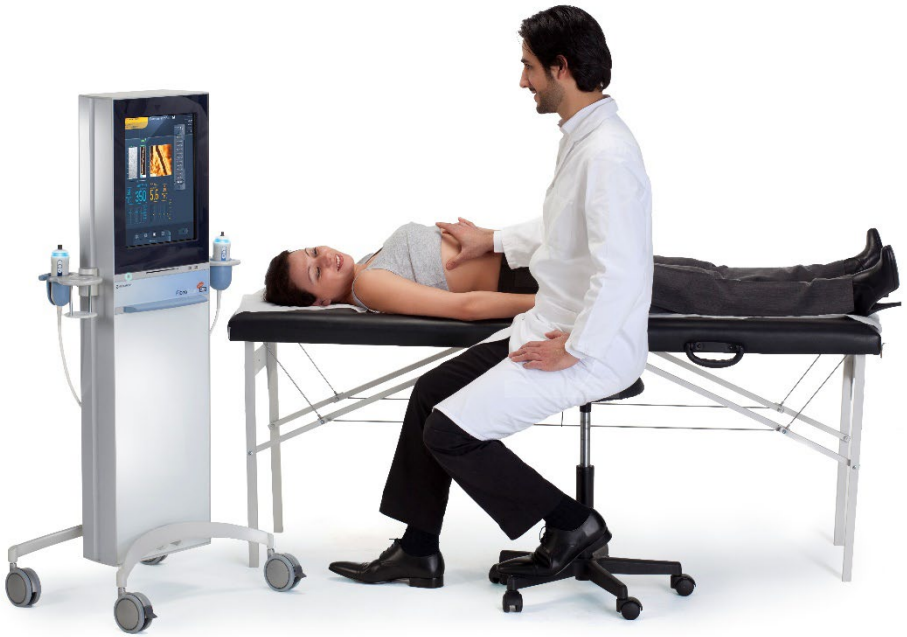
- Includes Age, ALT, AST, and Platelet Count
- Negative predictive value 90% for advanced fibrosis if <1.45
- Positive predictive value 65% and specificity 97% for advanced fibrosis if >3.25
- Indeterminate when >1.45 but <3.25

FibroSURE®

- Multiple known inputs and proprietary equation
- Recognized by many payers

Elastography

- Measures mechanical shear wave velocity, which is proportional to liver stiffness
- Multiple methods (transient, magnetic resonance, acoustic radiation force impulse)
- May be a reasonable alternative to biopsy



Notes About Anatomic Imaging

- Anatomic imaging (i.e., ultrasound, CT, MRI) NOT adequate for staging
  - Insensitive for underlying fibrosis
  - If seen, advanced fibrotic changes likely correlate with pathology

- Appropriate for hepatocellular carcinoma monitoring

Immunizations

- Hepatitis A
- Hepatitis B
- Influenza
- COVID-19
- Pneumococcal immunization (for those with cirrhosis)

Interventions to Reduce Progression of Liver Disease

- Immunizations as noted
- Alcohol abstinence
- Appropriate acetaminophen use
- Limited non-steroidal anti-inflammatory drug use, particularly in setting of advanced fibrosis

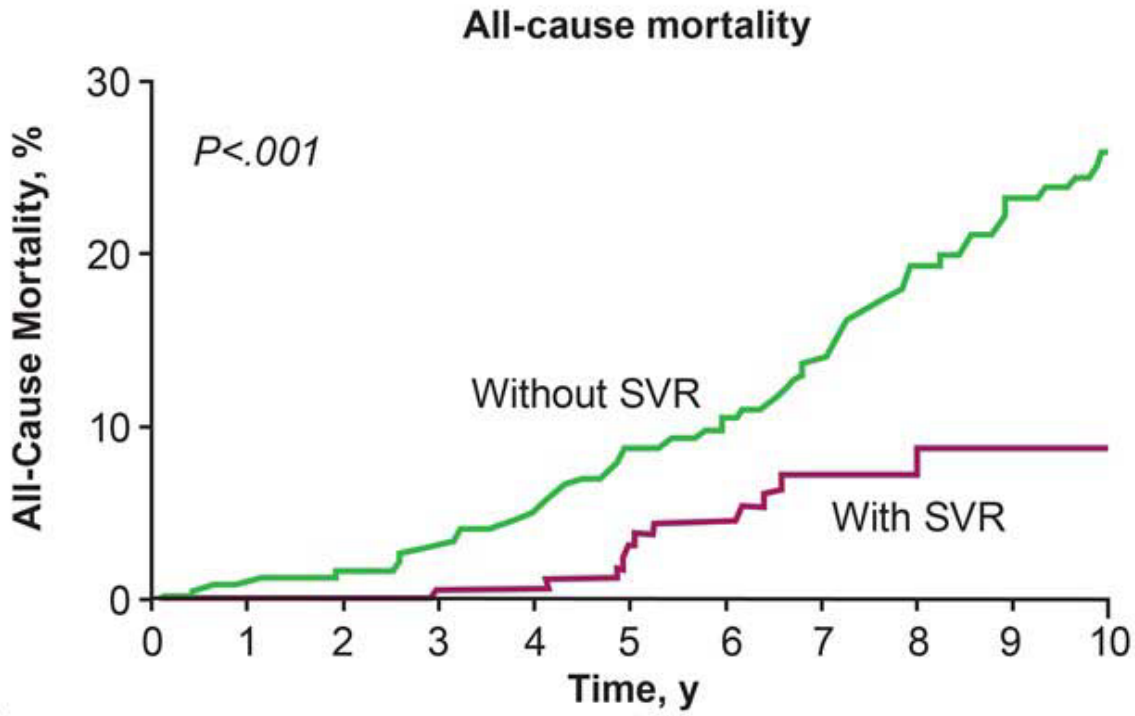
Educate Clients/Patients

- Assess current understanding
- Explain principles of infection and impact on liver disease
- Introduction to treatment and prognosis

Counseling to Reduce Transmission of HCV

- Keep wounds covered
- Clean up blood or body fluid spills with alcohol and/or bleach
- Shared personal devices such as razors, toothbrushes, or nail clippers
- Barrier protection for intimate contact
- Safer approaches to injection drug use

Effective Treatment Will Significantly Reduce Mortality from HCV Infection[14]



No. at risk

Without SVR	405	393	392	363	344	317	295	250	207	164	135
With SVR	192	181	168	162	155	144	125	88	56	40	28

van der Meer AJ et al. JAMA. 2012

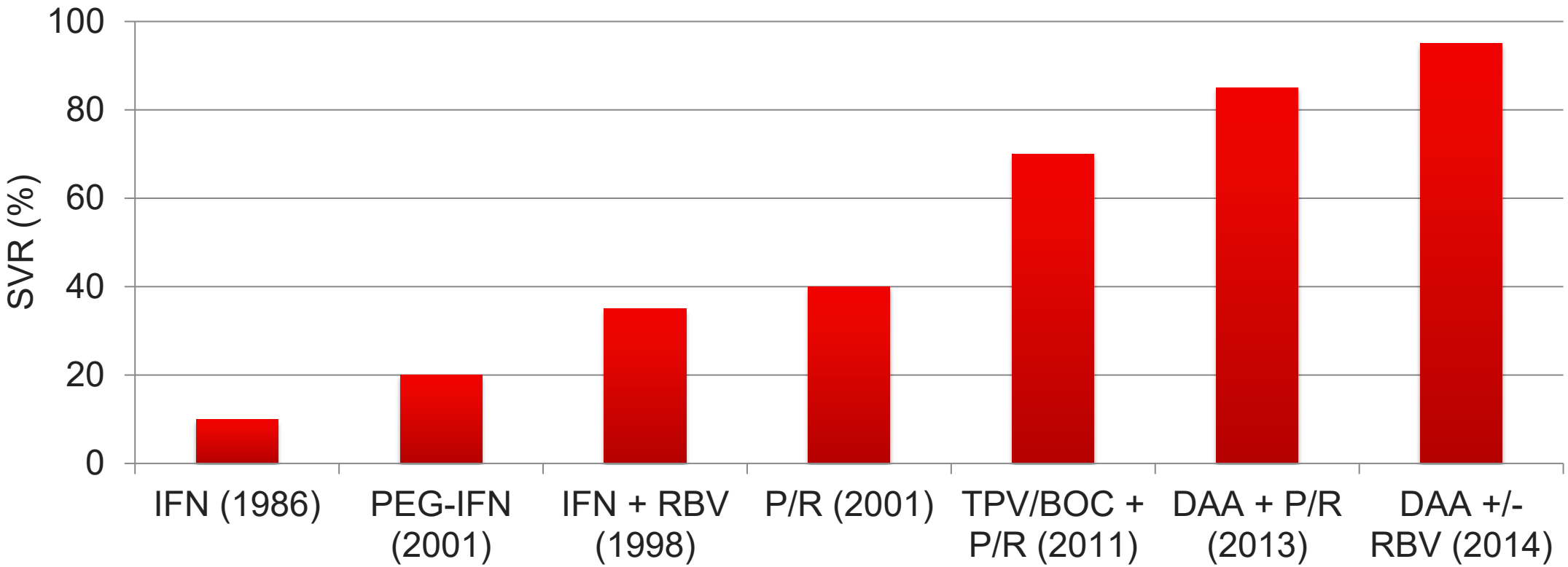
Goal of Treatment	
RECOMMENDED	RATING
The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic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

www.hcvguidelines.org

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

Recommendation for Linkage to Care	
RECOMMENDED	RATING
All persons with active HCV infection should be linked to a healthcare provider who is prepared to provide comprehensive management.	IIa, C

Treatment Response in Direct Acting Antiviral (DAA) Era



Slide adapted courtesy of Dr. Susanna Naggie

HCV Approved Agents

FDA Approved Therapies Through 2010

Interferon (1986)

Ribavirin (1998)

Pegylated Interferon (2001)

FDA Approved Therapies 2011-2014

Telaprevir (2011)

Boceprevir (2011)

Simeprevir (2013)

Sofosbuvir (2013)

Ledipasvir (2014)

Paritaprevir (2014)

Ombitasvir (2014)

Dasabuvir (2014)

Since Then

Elbasvir (2016)

Grazoprevir (2016)

Velpatasvir (2016)

Voxilaprevir (2017)

Glecaprevir (2017)

Pibrentasvir (2017)

Primary Factors when Selecting HCV Treatment

- **Genotype**
- **Degree of fibrosis**
  - I.e., Non-cirrhotic vs. cirrhotic
- **Treatment history**
  - I.e., Treatment naïve vs. treatment experienced
  - Recommendations may differ depending on what therapies were used previously (e.g., PEG-IFN vs. DAA-based therapy)

Secondary Factors when Selecting HCV Treatment

- *Side effect profile*
- *Drug-drug interactions*
- *Pharmacodynamics*
- *Access*

Do Genotypes Matter Any More?

- Historically have been important for predicting prognosis of infection and response to treatment
- More recently have allowed appropriate DAA selection
- Not required for treatment with simplified guidance
- Roles?
  - Selection of cost-effective therapies
  - Prognosis prediction (i.e., worse for GT 3)
  - Tool for determining relapse vs. reinfection (in some cases)
  - Needed for when selecting certain HCV therapy in setting of cirrhosis

HCV Simplified Guidance (www.hcvguidelines.org)

HCV GUIDANCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C

Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients with chronic hepatitis C who do not have cirrhosis and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis
- Prior liver transplant
- HIV or HBsAg positive
- End-stage renal disease (ie, eGFR <30 mL/min/m²)
- Currently pregnant

PRETREATMENT ASSESSMENT*

- **Cirrhosis assessment**
  Liver biopsy is not required. The cutoffs of the following tests suggest cirrhosis. If any test suggests cirrhosis, treat the patient as having cirrhosis.
  - FIB-4 >3.25
  - APRI >2.0
  - Platelet count <150,000/mm³
  - Fibroscan™ stiffness >12.5 kPa
- **Medication reconciliation**
  Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment**
  Drug-drug interactions can be assessed using the AASLD/IDSA guidance (https://www.hcvguidelines.org) or the University of Liverpool drug interaction checker. (https://www.hep-druginteractions.org/checker).
- **Education**
  Educate the patient about proper administration of medications, adherence, avoidance of alcohol, and prevention of reinfection.
- **Pretreatment laboratory testing**

Within 6 months of initiating treatment

- Complete blood count (CBC)
- Hepatic function panel (ie, albumin, total protein, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
- Calculated glomerular filtration rate (eGFR)

Anytime prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen (HBsAg)

Before initiating antiviral therapy

- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
to be taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Monitoring patients taking diabetes medication for hypoglycemia is recommended.
- Monitoring INR for patients taking warfarin is recommended.
- Assessment of quantitative HCV RNA and hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and international normalized ratio (INR) is recommended.
- Patients in whom initial HCV treatment fails to achieve cure (SVR) can be retreated, often successfully. Consult the AASLD/IDSA guidance for recommendations regarding the evaluation of patients for retreatment and selection of an appropriate HCV antiviral regimen. (https://www.hcvguidelines.org)

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at https://www.hcvguidelines.org. Updated: November 6, 2019

Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- **Current or prior** episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m²) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation**: Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing** (see next column)

Within 3 months of initiating treatment

- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Before initiating antiviral therapy

- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Genotype 1-6:
Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Genotype 1, 2, 4, 5, or 6:
Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.

ON-TREATMENT MONITORING

- Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.
- Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis
- Patients with ongoing risk for HCV infection (eg, IV drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Patients should abstain from alcohol to avoid progression of liver disease.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Patients should abstain from alcohol to avoid progression of liver disease.

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment can be found at www.hcvguidelines.org. Updated: December 10, 2019

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AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV GUIDANCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C

Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis

IDSA
Infectious Diseases Society of America

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients with chronic hepatitis C
who do not have cirrhosis and
have not previously received
hepatitis C treatment

WHO IS *NOT* ELIGIBLE

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis
- Prior liver transplant
- [illegible] or HBsAg positive
- End-stage renal disease (ie, eGFR <30 mL/min/m^2)
- Currently pregnant

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Simplified HCV Treatment:

Treatment Naïve Adults without Cirrhosis

- **Who Is Not Eligible**
  - Prior HCV treatment
  - Cirrhosis
  - Prior liver transplant
  - [redacted] or HBsAg positive
  - End Stage Renal disease (eGFR<30)
  - Currently pregnant

- **Pretreatment Assessment**
  - Cirrhosis assessment
  - CBC, hepatic function panel, eGFR
  - Quantitative HCV RNA (viral load)
  - HIV status, HBsAg
  - Pregnancy testing (as appropriate)
  - Med reconciliation/drug interaction assessment
  - Patient education

- **Recommended HCV Regimens**
  - Glecaprevir/pibrentasvir x 8 weeks
  - Sofosbuvir/velpatasvir x 12 weeks

- **Monitoring**
  - Laboratory studies obtained 12 weeks after completion to assess for SVR:
    - Hepatic function panel
    - Quantitative HCV RNA

Simplified HCV Treatment:
Treatment-Naïve Patients Without Cirrhosis

- **Cirrhosis assessment**
  Liver biopsy is not required. The cutoffs of the following tests suggest cirrhosis. If any test suggests cirrhosis, treat the patient as having cirrhosis.
  - FIB-4 >3.25
  - APRI >2.0
  - Platelet count <150,000/mm^3
  - Fibroscan™ stiffness >12.5 kPa

Simplified HCV Treatment:

Treatment Naïve Adults with Compensated Cirrhosis

- **Who is not Eligible**
  - **Current or prior decompensated cirrhosis**
  - **Known or suspected hepatocellular carcinoma**
  - Prior HCV treatment
  - Prior liver transplant
  - [redacted] or HBsAg positive
  - End Stage Renal disease (eGFR<30)
  - Currently pregnant

- **Pretreatment Assessment**
  - **FIB-4, CTP score < 6**
  - **Liver ultrasound to exclude HCC and ascites**
  - CBC, hepatic function panel, eGFR, **INR**
  - Quantitative HCV RNA (viral load)
  - **HCV Genotype *if using sofosbuvir/velpatasvir**
  - HIV status, HBsAg
  - Pregnancy testing (as appropriate)
  - Med reconciliation/drug interaction assessment
  - Patient education

- **Recommended HCV Regimens**
  - Glecaprevir/pibrentasvir x 8 weeks
  - Sofosbuvir/velpatasvir x 12 weeks **(excluding GT 3)**

- **Monitoring**
  - **On treatment monitoring for hepatitis decompensation**
  - Laboratory studies obtained 12 weeks after completion to assess for SVR
    - Hepatic function panel
    - Quantitative HCV RNA
  - **Ultrasound ever 6 months for HCC monitoring**
  - **Upper endoscopy surveillance for esophageal varices per AASLD guidance**

Without Cirrhosis

RECOMMENDED REGIMENS*	
Glecaprevir (300 mg) / pibrentasvir (120 mg) taken with food for a duration of 8 weeks	**Sofosbuvir (400 mg) / velpatasvir (100 mg)** for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

Compensated Cirrhosis

RECOMMENDED REGIMENS*	ON-TREATMENT MONITORING
Genotype 1-6: **Glecaprevir (300 mg)/pibrentasvir (120 mg)** taken with food for a duration of 8 weeks *Genotype 1, 2, 4, 5, or 6:* **Sofosbuvir (400 mg)/velpatasvir (100 mg)** for a duration of 12 weeks NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.	• Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment. • Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms. • Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended. • Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended. • An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

HCV Simplified Guidance (www.hcvguidelines.org)

HCV GUIDANCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C

Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients with chronic hepatitis C who do not have cirrhosis and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis
- Prior liver transplant
- HIV or HBsAg positive
- End-stage renal disease (ie, eGFR <30 mL/min/m²)
- Currently pregnant

PRETREATMENT ASSESSMENT*

- **Cirrhosis assessment**
  Liver biopsy is not required. The cutoffs of the following tests suggest cirrhosis. If any test suggests cirrhosis, treat the patient as having cirrhosis.
  - FIB-4 >3.25
  - Platelet count <150,000/mm³
  - APRI >2.0
  - Fibroscan™ stiffness >12.5 kPa
- **Medication reconciliation**
  Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment**
  Drug-drug interactions can be assessed using the AASLD/IDSA guidance (https://www.hcvguidelines.org) or the University of Liverpool drug interaction checker. (https://www.hep-druginteractions.org/checker).
- **Education**
  Educate the patient about proper administration of medications, adherence, avoidance of alcohol, and prevention of reinfection.
- **Pretreatment laboratory testing**

Within 6 months of initiating treatment

- Complete blood count (CBC)
- Hepatic function panel (ie, albumin, total protein, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
- Calculated glomerular filtration rate (eGFR)

Anytime prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen (HBsAg)

Before initiating antiviral therapy

- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
to be taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Monitoring patients taking diabetes medication for hypoglycemia is recommended.
- Monitoring INR for patients taking warfarin is recommended.
- Assessment of quantitative HCV RNA and hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and international normalized ratio (INR) is recommended.
- Patients in whom initial HCV treatment fails to achieve cure (SVR) can be retreated, often successfully. Consult the AASLD/IDSA guidance for recommendations regarding the evaluation of patients for retreatment and selection of an appropriate HCV antiviral regimen. (https://www.hcvguidelines.org)

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at https://www.hcvguidelines.org. Updated: November 6, 2019

Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- **Current or prior** episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m²) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation**: Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing** (see next column)

Within 3 months of initiating treatment

- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Before initiating antiviral therapy

- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Genotype 1-6:
Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Genotype 1, 2, 4, 5, or 6:
Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.

ON-TREATMENT MONITORING

- Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.
- Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis
- Patients with ongoing risk for HCV infection (eg, IV drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Patients should abstain from alcohol to avoid progression of liver disease.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Patients should abstain from alcohol to avoid progression of liver disease.

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment can be found at www.hcvguidelines.org.
Updated: December 10, 2019

Thank You for Being an HCV Champion!

Questions?

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AETC AIDS Education & Training Center Program Southeast