Managing Chronic Hepatitis C in the Primary Care Setting: Best Practices From Screening to Treatment

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This activity is supported by an educational grant from Gilead Sciences, Inc.
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Identifying and Overcoming Barriers to HCV Screening and Diagnosis in Primary Care
Global Burden of HCV Infection: 150-170 Million People Infected and 500,000 Deaths Annually¹

HCV: hepatitis C virus.
Prevalence of HCV Infection in the United States¹-³

- 2.7 to 5.0 million living with chronic HCV in the United States
- 45%-60% unaware of infection
- Not included or underestimated in NHANES estimate:
  - Homeless
    (142,761-337,610)
  - Incarcerated
    (372,754-664,826)
  - Veterans
    (1,237,461-2,452,006)
  - Active military
    (6,805)
  - Healthcare workers
    (64,809-259,234)

NHANES: National Health and Nutrition Examination Survey.
Increases in HCV Infection Related to Injection Drug Use Among Persons Aged ≤30 Years¹

Changes in Who is Starting to Inject Drugs

Percent of new PWID by race suggests fewer blacks, and more whites, are starting to inject drugs.

Heroin use has increased more than 60% (114% in whites) in recent years.

1. https://www.cdc.gov/vitalsigns/hiv-drug-use/infographic.html#graphic
HCV Infection Causes More Deaths in the US Than 60 Other Infectious Pathogens, Including HIV\(^1\)

Chronic HCV Infection May Lead to Chronic Liver Disease and Liver Cancer\(^1\)\(^-\)\(^4\)

**Fibrosis**
- Chronic HCV infection can lead to the development of fibrous scar tissue within the liver

**Cirrhosis**
- Over time, fibrosis can progress, causing severe scarring of the liver, restricted blood flow, impaired liver function, and eventually liver failure

**Hepatocellular carcinoma** (with cirrhosis)
- Cancer of the liver can develop after years of chronic HCV infection

**Decompensated cirrhosis:**
- Ascites
- Bleeding gastroesophageal varices
- Hepatic encephalopathy
- Jaundice

HCC: hepatocellular carcinoma.
HCV: Underdiagnosis and Undertreatment\(^1\)

Despite its high prevalence and increasing disease burden, chronic HCV has not been diagnosed in most Americans with this disease, and few cases have been treated.

Overall: 3.2 Million of US Population Have Chronic HCV

- **Diagnosed:** 50% (1.6M)
- **Referred to Care:** 32%-38% (1.0-1.2M)
- **Treated:** 7%-11% (220,000-360,000)
- **Successfully Treated:** 5%-6% (170,000-200,000)

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Serologic Pattern of Acute HCV Infection With Progression to Chronic Infection

1. Hoofnagle JH. *Hepatology*. 1997;26:15S-20S.
## Potential Barriers to HCV Identification\(^1,2\)

<table>
<thead>
<tr>
<th>Patient Barriers</th>
<th>Patients reluctant to discuss HCV risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician Barriers</td>
<td>Healthcare professionals may be unaware of or reluctant to ask about risk factors</td>
</tr>
<tr>
<td>Systemic Barriers</td>
<td>Stigmatization of HCV infection in healthcare system and community</td>
</tr>
</tbody>
</table>

Revised HCV Screening Recommendation to Identify HCV-Infected Adults: “Birth Cohort”\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>CDC Recommendations</th>
<th>USPSTF Grade B Recommendations\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everyone born from 1945 through 1965 (one time)</td>
<td>Everyone born from 1945 through 1965 (one time)</td>
</tr>
<tr>
<td>Persons who ever injected illegal drugs</td>
<td>Past or present injection drug use</td>
</tr>
<tr>
<td>Persons who received clotting factor concentrates produced before 1987</td>
<td>Sex with an injection drug user; other high-risk sex</td>
</tr>
<tr>
<td>Recipients of chronic (long-term) hemodialysis</td>
<td>Blood transfusion prior to 1992</td>
</tr>
<tr>
<td>Persons with persistently abnormal ALT levels</td>
<td>Persons with hemophilia</td>
</tr>
<tr>
<td>Recipients of transfusions or organ transplants prior to 1992</td>
<td>Long-term hemodialysis</td>
</tr>
<tr>
<td>Persons with recognized occupational exposures</td>
<td>Born to an HCV-infected mother</td>
</tr>
<tr>
<td>Children born to HCV-positive women</td>
<td>Incarceration</td>
</tr>
<tr>
<td>HIV-positive persons</td>
<td>Intranasal drug use</td>
</tr>
<tr>
<td></td>
<td>Receiving an unregulated tattoo</td>
</tr>
<tr>
<td></td>
<td>Occupational percutaneous exposure</td>
</tr>
<tr>
<td></td>
<td>Surgery before implementation of universal precautions</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Only pertains to persons with normal liver enzymes; if elevated liver enzymes, need hepatitis B virus and HCV testing.

USPSTF: U.S. Preventive Services Task Force.
Baby Boomers (Those Born Between 1945 and 1965) Account for 76.5% of HCV Cases in the US\(^1\)

- Up to 75% of people with HCV in the United States are undiagnosed
- An estimated 35% of Baby Boomers with undiagnosed HCV currently have advanced fibrosis (F3-F4, bridging fibrosis to cirrhosis)\(^3\)

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Screening of Baby Boomers Could Prevent More Than 120,000 HCV-Related Deaths\textsuperscript{1,2}

- 1,070,840 new cases of HCV identified with birth-cohort screening
- 552,000 patients treated
- 364,000 patients cured\textsuperscript{a}
- 121,000 deaths averted\textsuperscript{b}

\textsuperscript{a} Cured with PEG-IFN and RBV plus direct-acting antiviral treatment.

\textsuperscript{b} Deaths due to decompensated cirrhosis or HCC within the 1945-1965 birth cohort; 470,000 deaths under birth-cohort screening vs 592,000 deaths under risk-based screening.

PEG-IFN: pegylated interferon; RBV: ribavirin.

### Other At-Risk Groups Who Should Be Screened

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>Past or present injection drug users</td>
</tr>
<tr>
<td>✓</td>
<td>Those who have had sex with an injection drug user or who engaged in other high-risk sexual behaviors</td>
</tr>
<tr>
<td>✓</td>
<td>Recipients of blood transfusion or organ transplant prior to 1992</td>
</tr>
<tr>
<td>✓</td>
<td>Those with hemophilia</td>
</tr>
<tr>
<td>✓</td>
<td>Recipients of long-term hemodialysis</td>
</tr>
<tr>
<td>✓</td>
<td>Those with HIV infection</td>
</tr>
<tr>
<td>✓</td>
<td>Those born to an HCV-infected mother</td>
</tr>
<tr>
<td>✓</td>
<td>Persons who have been or who are incarcerated</td>
</tr>
</tbody>
</table>

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Other At-Risk Groups Who Should Be Screened (Cont’d)\(^ 1-3\)

<table>
<thead>
<tr>
<th>✔️</th>
<th>Those with history of intranasal drug use</th>
</tr>
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<tbody>
<tr>
<td>✔️</td>
<td>Long-term daily alcohol users</td>
</tr>
<tr>
<td>✔️</td>
<td>Those who have received an unregulated tattoo</td>
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<tr>
<td>✔️</td>
<td>Those with history of occupational percutaneous exposure</td>
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<td>✔️</td>
<td>Those who underwent surgery before implementation of universal precautions</td>
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<tr>
<td>✔️</td>
<td>Those with persistently elevated ALT levels</td>
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## Talking to Patients About Hepatitis C Testing

<table>
<thead>
<tr>
<th>Aim</th>
<th>Sample Conversation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide rationale for testing</td>
<td>“It’s common.”</td>
</tr>
<tr>
<td>Provide reassurance about testing</td>
<td>“It’s curable”</td>
</tr>
<tr>
<td>Obtain consent</td>
<td>“If it is alright with you, I would like to test you for hepatitis C today.”</td>
</tr>
</tbody>
</table>

## Screening Tests for HCV\(^1-4\)

<table>
<thead>
<tr>
<th>ELISA Screening Tests</th>
<th>HCV RNA Assays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serologic assays to detect circulating HCV antibodies</td>
<td>Use sensitive quantitative assay</td>
</tr>
<tr>
<td>Sensitivity (97%-100%)</td>
<td>When to test?</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td></td>
</tr>
</tbody>
</table>
  - If anti-HCV Ab test result is positive |
|   - 95% with risk factors + elevated ALT |  
  - If antiviral treatment is being considered |
|   - 50% without risk factors + normal ALT |  
  - If unexplained liver disease and anti-HCV Ab test result is negative and person is immunocompromised |
| False-positive results |  
  - If acute HCV infection is suspected |
|   - More likely in patients with low risk of HCV infection | |
| False-negative results | |
|   - More likely in severely immunocompromised patients | |

Ab: antibody; ELISA: enzyme-linked immunosorbent assay.
Recommended Testing Sequence for Identifying Current HCV Infection

Newly Diagnosed Patients with HCV:
Next Steps for the Primary Care Clinician

• Educate regarding HCV transmission
  – Screen sexual partners, but CDC does not recommend barrier methods for monogamous heterosexual partners
  – Higher risk of sexual transmission among MSM, particularly those with HIV infection
  – Children born to HCV-positive mothers should be screened (<3% risk)

• Screen for immunity to hepatitis A Ab total and hepatitis B (HBsAb) and vaccinate if non-immune

MSM: men who have sex with men.
Newly Diagnosed Patients with HCV: Next Steps for the Primary Care Clinician (Cont’d)

• Assess alcohol use in all patients with HCV (CDC guidelines)
  – There is no “safe” amount of alcohol consumption for patients with HCV
  – Refer patients with risky use for alcohol treatment
    ➢ Men: >2 drinks/day (>14/week) or more than 4 in one day
    ➢ Women: >1 drink/day (>7/week) or more than 3 in one day

• Advise on a liver-healthy diet, which equates to a normal body mass index

HBsAb: hepatitis B surface antibody test.
All persons with current active HCV infection should be linked to a practitioner who is prepared to provide comprehensive management.

CURE IS POSSIBLE!

A Closer Look at Current Recommendations and Options for the Treatment of HCV
Guidance for the Treatment of HCV Infection

The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America Present

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

Last Updated: April 12, 2017
www.hcvguidelines.org
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 (SVR).

Rating: Class I, Level A.
HCV: hepatitis C virus.
When and in Whom to Initiate HCV Therapy

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

Rating: Class I, Level A.
HCV: hepatitis C virus.
Assessing Readiness for HCV Treatment: PREP-C

Motivation
Information
Medication adherence
Self-efficacy
Social support and stability
Alcohol and substance use
Psychiatric stability
Energy level
Cognitive functioning

Psychosocial Readiness
HCV Treatment Adherence

www.prepc.org
Patient Case

Male patient

- 62 years old
- Hypertension, diabetes, prior percutaneous exposure to HCV-positive blood, newly diagnosed with hepatitis C infection
  - BP controlled; HbA1c 7.6%
  - Meds: simvastatin, insulin, lisinopril

Work-up to date

- HCV antibody +
- ALT 35 U/L; AST 21 U/L; Cr 1.1 mg/dL
- Platelet count 155,000/mm³; Hb 13.6 g/dL

Cr: creatinine; HbA1c: hemoglobin A1c.
Recommended Assessments Prior to Starting Antiviral Therapy

- Staging of hepatic fibrosis is essential prior to HCV treatment.

- Assessment of potential drug-drug interactions with concomitant medications is recommended prior to starting antiviral therapy.
  - Patients should also be educated on the proper administration of medications (e.g., dose, frequency of medicines, food effect, missed doses, adverse effects, etc), the crucial importance of adherence, and the necessity for close supervision and blood tests during and after treatment.

\(^a\)Rating: Class I, Level C.
Liver Disease Staging Is Important but Does NOT Require Liver Biopsy

- Blood tests
  - FIB-4, APRI, or FibroTest
- Liver elastography to measure liver stiffness
  - FibroScan®

**Fibrosis-4 (FIB-4) Calculator**

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

\[
FIB-4 = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10^9/L)} \times \sqrt{\text{ALT (U/L)}}}
\]

**Interpretation:**

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis ( Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

APRI: AST to platelet ratio index; FIB-4: fibrosis-4.
Patient Case: Liver Disease Stage

Fibrosis-4 (FIB-4) Calculator

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

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\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (}10^9/L\text{)}} \times \sqrt{\text{ALT (U/L)}}
\]

\[
\begin{align*}
\text{Age (years)} & \quad 62 \\
\text{AST Level (U/L)} & \quad 21 \\
\text{Platelet Count (}10^9/L\text{)} & \quad 155 \\
\text{ALT (U/L)} & \quad 35
\end{align*}
\]

\[
\text{FIB-4} = \frac{62 \times 21}{155} \times \sqrt{35} = 1.42
\]

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Sources

• Staging of hepatic fibrosis is essential prior to HCV treatment.

• **Assessment of potential drug-drug interactions with concomitant medications is recommended prior to starting antiviral therapy.**
  - Patients should also be educated on the proper administration of medications (eg, dose, frequency of medicines, food effect, missed doses, adverse effects, etc), the crucial importance of adherence, and the necessity for close supervision and blood tests during and after treatment.
Evaluating Potential Drug-Drug Interactions with Selected Antiviral Medications

http://www.hep-druginteractions.org
Recommended Laboratory Testing¹,a

<table>
<thead>
<tr>
<th>Within 12 weeks prior to starting antiviral therapy</th>
<th>At any time prior to starting antiviral therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ CBC, INR</td>
<td>✓ HCV genotype and subtype</td>
</tr>
<tr>
<td>✓ Hepatic function panel (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase levels)</td>
<td>✓ Quantitative HCV RNA (HCV viral load)</td>
</tr>
<tr>
<td>✓ TSH if IFN is used</td>
<td></td>
</tr>
<tr>
<td>✓ Calculated GFR</td>
<td></td>
</tr>
</tbody>
</table>

INR: international normalized ratio.

¹Rating: Class I, Level C.

HCV genotypes 1, 2, and 3 are the most prevalent genotypes in the US, representing >98% of all infections.

Patient Case: HCV Work-Up

Male patient

62 years old
Hypertension, diabetes, prior percutaneous exposure to HCV-positive blood, newly diagnosed with hepatitis C infection
- BP controlled; HbA1c 7.6%
- Meds: simvastatin, insulin, lisinopril

HCV antibody +

ALT 35 U/L; AST 21 U/L; Cr 1.1 mg/dL
Platelet count 155,000/mm³; Hb 13.6 g/dL

HCV work-up

HCV genotype 1a
HCV RNA level = 3.4 million U/mL
HAV antibody total +
HBsAb non-reactive; HBcAb non-reactive; HBsAg non-reactive

HBcAb: hepatitis B core antibody; HBsAb: hepatitis B surface antibody test; HBsAg: hepatitis B surface antigen.
## 62-year-old man

- HCV genotype/subtype? **1a**
- HCV RNA level? **3.4 million U/mL**
- Liver disease stage? **Cirrhosis**
- Prior treatment experience? **None**
- Concern with ribavirin use (eg, anemia or renal dysfunction)? **No**
Interferon-Based Treatments Were a Major Barrier to HCV Treatment Before October 2014

Patient genetics (IL28B SNP) determine likelihood of response to interferon

SVR: sustained virologic response.
HCV Life Cycle Presents Multiple Targets for Direct Acting Antiviral Drugs

FDA Approved Direct-Acting Antiviral Agents From Multiple Classes

Ribavirin

NS3 Protease Inhibitors
- Boceprevir (BOC)
- Telaprevir (TVR)
- Simeprevir (SMV)
- Paritaprevir (PTV)
- Grazoprevir (GZR)

NS5A Inhibitors
- Daclatasvir (DCV)
- Ledipasvir (LDV)

NS5B NUC Inhibitors
- Ombitasvir (OMV)
- Elbasvir (EBR)
- Velpatasvir (VEL)

NS5B Non-NUC Inhibitors
- Sofosbuvir (SOF)
- Dasabuvir (DSV)

NS5B: nonstructural protein 5B; NUC: nucleotide.
Treatment-Naïve Genotype 1
## Genotype 1a Without Cirrhosis: Recommended Regimens

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg); for patients in whom no baseline NS5A RASs for elbasvir are detected</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg); for patients who are non-black, HIV-uninfected, and whose HCV RNA level is &lt;6 million IU/mL</td>
<td>8 weeks</td>
<td>I, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg), with weight-based ribavirin</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily simeprevir (150 mg) plus sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, B</td>
</tr>
</tbody>
</table>

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RASs: resistance-associated substitutions.
### Genotype 1a With Compensated Cirrhosis: Recommended Regimens

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
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</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg); for patients in whom no baseline NS5A RASs§ for elbasvir are detected</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

§ Includes G1a substitutions at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.

RASs: resistance-associated substitutions.
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<td>8 weeks</td>
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</tr>
<tr>
<td>for patients who are non-black, HIV-uninfected, and whose HCV RNA level is</td>
<td></td>
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</tr>
<tr>
<td>&lt;6 million IU/mL</td>
<td></td>
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<td>I, A</td>
</tr>
<tr>
<td>/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>release regimen or plus twice-daily dosed dasabuvir (250 mg)</td>
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<tr>
<td>Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg)</td>
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</tr>
</tbody>
</table>

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

RASs: resistance-associated substitutions.
### Genotype 1b With Compensated Cirrhosis: Recommended Regimens

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</table>

† Please see statement on FDA warning regarding the use of PrOD or PrO in patients with cirrhosis.

RASs: resistance-associated substitutions.
Multiple Highly Effective HCV Treatment Regimens Are Available\(^1\)

### Oral Direct-Acting Agent Therapy for Hepatitis C Virus Infection

A Systematic Review

Oluwaseun Falade-Nwulia, MBBS, MPH*; Catalina Suarez-Cuervo, MD*; David R. Nelson, MD; Michael W. Fried, MD; Jodi B. Segal, MD, MPH; and Mark S. Sulkowski, MD

HCV Cure Can Be Achieved in >95% of Patients With HCV GT1a Infection Treated With FDA-Approved DAA Regimens

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Regimen</th>
<th>Patients, n</th>
<th>Treatment Duration, wk</th>
<th>Cirrhosis Status</th>
<th>Treatment History</th>
<th>SVR12 Rate (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV-1a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-EDGE, 2015</td>
<td>GZP-EBV</td>
<td>157</td>
<td>12</td>
<td>With/without</td>
<td>Naive</td>
<td>92 (86-86)</td>
</tr>
<tr>
<td>PEARL-IV, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>100</td>
<td>12</td>
<td>Without</td>
<td>Experienced</td>
<td>97 (94-100)</td>
</tr>
<tr>
<td></td>
<td>PTV-r + OBV + DAV + PLAC</td>
<td>205</td>
<td>12</td>
<td>Without</td>
<td>Experienced</td>
<td>90 (87-94)</td>
</tr>
<tr>
<td>SAPPHIRE-I, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>322</td>
<td>12</td>
<td>Without</td>
<td>Naive</td>
<td>95 (93-98)</td>
</tr>
<tr>
<td>SAPPHIRE-II, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>173</td>
<td>12</td>
<td>Without</td>
<td>Experienced</td>
<td>96 (93-99)</td>
</tr>
<tr>
<td>OPTIMIST-I, 2016</td>
<td>SOF + SIM</td>
<td>116</td>
<td>8</td>
<td>Without</td>
<td>Both</td>
<td>79 (72-87)</td>
</tr>
<tr>
<td></td>
<td>SOF + SIM</td>
<td>116</td>
<td>12</td>
<td>Without</td>
<td>Both</td>
<td>97 (93-100)</td>
</tr>
<tr>
<td>OPTIMIST-II, 2016</td>
<td>SOF + SIM</td>
<td>72</td>
<td>12</td>
<td>With</td>
<td>Both</td>
<td>83 (74-93)</td>
</tr>
<tr>
<td>ION-1, 2014</td>
<td>LDV-SOF</td>
<td>142</td>
<td>12</td>
<td>With/without</td>
<td>Naive</td>
<td>99 (96-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>143</td>
<td>12</td>
<td>With/without</td>
<td>Naive</td>
<td>100 (97-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF</td>
<td>143</td>
<td>24</td>
<td>With/without</td>
<td>Naive</td>
<td>100 (97-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>141</td>
<td>24</td>
<td>With/without</td>
<td>Naive</td>
<td>100 (97-100)</td>
</tr>
<tr>
<td>ION-2, 2014</td>
<td>LDV-SOF</td>
<td>86</td>
<td>12</td>
<td>With/without</td>
<td>Experienced</td>
<td>95 (88-99)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>88</td>
<td>12</td>
<td>With/without</td>
<td>Experienced</td>
<td>95 (89-99)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF</td>
<td>85</td>
<td>24</td>
<td>With/without</td>
<td>Experienced</td>
<td>99 (94-100)</td>
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<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>88</td>
<td>24</td>
<td>With/without</td>
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<td>99 (94-100)</td>
</tr>
<tr>
<td>ION-3, 2014</td>
<td>LDV-SOF</td>
<td>171</td>
<td>8</td>
<td>Without</td>
<td>Naive</td>
<td>93 (89-97)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>172</td>
<td>8</td>
<td>Without</td>
<td>Naive</td>
<td>92 (87-96)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF</td>
<td>172</td>
<td>12</td>
<td>Without</td>
<td>Naive</td>
<td>95 (90-98)</td>
</tr>
<tr>
<td>ASTRAL-I, 2015</td>
<td>VEL-SOF</td>
<td>49</td>
<td>12</td>
<td>With</td>
<td>Both</td>
<td>100 (93-100)</td>
</tr>
<tr>
<td></td>
<td>VEL-SOF</td>
<td>161</td>
<td>12</td>
<td>Without</td>
<td>Both</td>
<td>97 (94-99)</td>
</tr>
</tbody>
</table>

DAA: direct-acting antiviral agents; EBR: elbasvir; GZR: grazoprevir; LDV: ledipasvir; RVB: ribavirin; SOF: sofosbuvir; VEL: velpatasvir.
HCV Cure Can Be Achieved in >95% of Patients With HCV GT1b Infection Treated With FDA-Approved DAA Regimens

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Regimen</th>
<th>Patients, n</th>
<th>Treatment Duration, wk</th>
<th>Cirrhosis Status</th>
<th>Treatment History</th>
<th>SVR12 Rate (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV-1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-EDGE, 2015</td>
<td>GZP-EBV</td>
<td>131</td>
<td>12</td>
<td>With/without</td>
<td>Naive</td>
<td>99 (95-100)</td>
</tr>
<tr>
<td>PEARL-I, 2015</td>
<td>PTV-r + OBV + RBV</td>
<td>47</td>
<td>24</td>
<td>With</td>
<td>Naive</td>
<td>98 (89-100)</td>
</tr>
<tr>
<td></td>
<td>PTV-r + OBV + RBV</td>
<td>52</td>
<td>24</td>
<td>With</td>
<td>Experienced</td>
<td>96 (87-99)</td>
</tr>
<tr>
<td></td>
<td>PTV-r + OBV + RBV</td>
<td>42</td>
<td>24</td>
<td>Without</td>
<td>Naive</td>
<td>95 (84-99)</td>
</tr>
<tr>
<td></td>
<td>PTV-r + OBV + RBV</td>
<td>40</td>
<td>24</td>
<td>Without</td>
<td>Experienced</td>
<td>90 (76-97)</td>
</tr>
<tr>
<td>PEARL-II, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>88</td>
<td>12</td>
<td>Without</td>
<td>Experienced</td>
<td>97 (93-100)</td>
</tr>
<tr>
<td></td>
<td>PTV-r + OBV + DAV + PLAC</td>
<td>91</td>
<td>12</td>
<td>Without</td>
<td>Experienced</td>
<td>100 (96-100)</td>
</tr>
<tr>
<td>PEARL-III, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>210</td>
<td>12</td>
<td>Without</td>
<td>Naive</td>
<td>99 (99-100)</td>
</tr>
<tr>
<td></td>
<td>PTV-r + OBV + DAV + PLAC</td>
<td>209</td>
<td>12</td>
<td>Without</td>
<td>Naive</td>
<td>99 (99-100)</td>
</tr>
<tr>
<td>SAPPHIRE-I, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>151</td>
<td>12</td>
<td>Without</td>
<td>Naive</td>
<td>98 (96-100)</td>
</tr>
<tr>
<td>SAPPHIRE-II, 2014</td>
<td>PTV-r + OBV + DAV + RBV</td>
<td>123</td>
<td>12</td>
<td>Without</td>
<td>Experienced</td>
<td>97 (94-100)</td>
</tr>
<tr>
<td>OPTIMIST-I, 2016</td>
<td>SIM + SOF</td>
<td>39</td>
<td>8</td>
<td>Without</td>
<td>Both</td>
<td>92 (79-98)</td>
</tr>
<tr>
<td></td>
<td>SIM + SOF</td>
<td>39</td>
<td>12</td>
<td>Without</td>
<td>Both</td>
<td>97 (87-100)</td>
</tr>
<tr>
<td>OPTIMIST-II, 2016</td>
<td>SIM-SOF</td>
<td>31</td>
<td>12</td>
<td>With</td>
<td>Both</td>
<td>84 (69-98)</td>
</tr>
<tr>
<td>ION-1, 2014</td>
<td>LDV-SOF</td>
<td>66</td>
<td>12</td>
<td>With/without</td>
<td>Naive</td>
<td>100 (94-100)</td>
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<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>67</td>
<td>12</td>
<td>With/without</td>
<td>Naive</td>
<td>100 (94-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF</td>
<td>68</td>
<td>24</td>
<td>With/without</td>
<td>Naive</td>
<td>97 (90-97)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>71</td>
<td>24</td>
<td>With/without</td>
<td>Naive</td>
<td>100 (95-100)</td>
</tr>
<tr>
<td>ION-2, 2014</td>
<td>LDV-SOF</td>
<td>23</td>
<td>12</td>
<td>With/without</td>
<td>Experienced</td>
<td>87 (66-97)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>23</td>
<td>12</td>
<td>With/without</td>
<td>Experienced</td>
<td>100 (86-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF</td>
<td>24</td>
<td>24</td>
<td>With/without</td>
<td>Experienced</td>
<td>100 (85-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>23</td>
<td>24</td>
<td>With/without</td>
<td>Experienced</td>
<td>100 (85-100)</td>
</tr>
<tr>
<td>ION-3, 2014</td>
<td>LDV-SOF</td>
<td>43</td>
<td>8</td>
<td>Without</td>
<td>Naive</td>
<td>98 (88-100)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF + RBV</td>
<td>44</td>
<td>8</td>
<td>Without</td>
<td>Naive</td>
<td>95 (84-99)</td>
</tr>
<tr>
<td></td>
<td>LDV-SOF</td>
<td>44</td>
<td>12</td>
<td>Without</td>
<td>Naive</td>
<td>98 (88-100)</td>
</tr>
<tr>
<td>ASTRAL-I, 2015</td>
<td>VEL-SOF</td>
<td>24</td>
<td>12</td>
<td>With</td>
<td>Both</td>
<td>96 (79-100)</td>
</tr>
<tr>
<td></td>
<td>VEL-SOF</td>
<td>94</td>
<td>12</td>
<td>Without</td>
<td>Both</td>
<td>100 (96-100)</td>
</tr>
</tbody>
</table>

HCV Eradication With the Fixed-Dose Combination of Ledipasvir/Sofosbuvir: ION-1 and ION-3\textsuperscript{1,2}

Persons With No Prior HCV Treatment

- **8 weeks**
  - 20 patients with relapse, 4.6%
  - HCV RNA <6 million U/mL, 2%

- **12 weeks**
  - 4 patients with relapse, 0.6%

- **24 weeks**
  - 1 patient with relapse, 0.2%

Variants in patients with virologic failure:
- NS5A, L31V/M/I, Y93H, Q30R
- NS5B, None.

Sofosbuvir/Velpatasvir for 12 Weeks for Genotype 1 Infection: ASTRAL-1 \(^1\)

![Image of bar chart]

- **SVR12, %**
  - **1a**: 98%
    - 1 relapse
    - 2 lost to follow-up
    - 1 withdrew consent
    - 206/210
  - **1b**: 99%
    - 1 relapse
    - 117/118

Velpatasvir formally GS-5816.
Present evidence of baseline RAVs did not impact SVR12.
Paritaprevir/r-Ombitasvir + Dasabuvir (PrOD) ± Ribavirin for HCV Genotype 1 Infection

**PEARL-IV**

- **HCV Genotype 1a**
  - 97/100 (97.0%)
  - 185/205 (90.2%)

**PEARL-III**

- **HCV Genotype 1b**
  - 99.5% (209/210)
  - 99.0% (207/209)

**Genotype 1a - no ribavirin**
- 16 patients with virologic failure (6 breakthrough and 10 relapse)

**Genotype 1a + ribavirin**
- 2 patients with virologic failure (1 breakthrough and 1 relapse)

- Variants in patients with virologic failure:
  - NS3, D168V
  - NS5A, M28T and Q30R
  - NS5B, S556G

PrOD: paritaprevir/r-ombitasvir + dasabuvir
Grazoprevir/Elbasvir for 12 Weeks in Persons With HCV Genotype 1 Infection

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT4</th>
<th>GT6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SVR12 (95% CI), n/N%</strong></td>
<td>299/316</td>
<td>144/157</td>
<td>129/131</td>
<td>18/18</td>
<td>8/10</td>
</tr>
<tr>
<td>Range</td>
<td>95% (92%-97%)</td>
<td>92% (86%-96%)</td>
<td>99% (95%-100%)</td>
<td>100% (82%-100%)</td>
<td>80% (44%-98%)</td>
</tr>
<tr>
<td>Lost to follow-up or discontinued early due to reasons other than virologic failure</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Virologic breakthrough</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Virologic relapse</td>
<td>12</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

GT1a: genotype 1a; GT1b: genotype 1b; GT3: genotype 3; GT4: genotype 4; GT6: genotype 6.
Impact of NS5A RAVs on Grazoprevir/Elbasvir Efficacy in Noncirrhotic and Cirrhotic Patients With HCV GT1

RAV: resistance-associated variant.
Treatment Options for HCV Genotype 1: Summary of Practical Considerations

**Genotype 1b**
- No ribavirin; 12 weeks of treatment for most patients

**Genotype 1a**
- Guidelines increasingly favor 12 weeks or less and no ribavirin
  - Sofosbuvir-backbone
    - LDV/SOF—no RAS testing; 8 or 12 weeks for most patients and no ribavirin except for patient with TE and cirrhosis
    - SOF/VEL—no RAS testing; 12 weeks for all and no ribavirin except CTP B
  - Protease-backbone
    - PrOD—no RAS testing; 12 weeks for most with 24 weeks for cirrhosis; RBV for all
    - GZV/EBR—Resistance testing; if WT, 12 weeks; if NS5A RAS, 16 weeks + RBV

CTB B: Child-Turcotte-Pugh class B; TE: treatment experience; WT: wild type.
Treatment-Naïve Genotype 2
## Recommended Regimens

### Genotype 2, Treatment-naive Patients, Without Cirrhosis

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

### Genotype 2, Treatment-naive Patients, with Compensated Cirrhosis

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

---

Sofosbuvir/Velpatasvir vs Sofosbuvir + Ribavirin for 12 Weeks: ASTRAL-2

- All patients with baseline NS3 and NS5A RAVs achieved SVR12. No virologic relapse in the sofosbuvir/velpatasvir arm.


**Graph:**
- Overall (134/132):
  - Sofosbuvir/velpatasvir: 99% (94/96)
  - Sofosbuvir + ribavirin: 100% (100/100)

- No cirrhosis (100/96):
  - Relapse (n = 6) - Sofosbuvir/velpatasvir: 96%
  - Relapse (n = 2) - Sofosbuvir + ribavirin: 94%

- Cirrhosis (15/15):
  - Relapse (n = 6) - Sofosbuvir/velpatasvir: 99%
  - Relapse (n = 3) - Sofosbuvir + ribavirin: 100%

- No cirrhosis (15/16):
  - Relapse (n = 6) - Sofosbuvir/velpatasvir: 100%
  - Relapse (n = 3) - Sofosbuvir + ribavirin: 81%

- Cirrhosis (4/4):
  - Relapse (n = 3) - Sofosbuvir/velpatasvir: 100%
  - Relapse (n = 4) - Sofosbuvir + ribavirin: 100%

**Notes:**
- Met non-inferiority and superiority criteria.
- All patients with baseline NS3 and NS5A RAVs achieved SVR12. No virologic relapse in the sofosbuvir/velpatasvir arm.
Treatment-Naïve Genotype 3
## Recommended Regimens

### Genotype 3, Treatment-naive Patients, Without Cirrhosis

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

### Genotype 3, Treatment-naive Patients, with Compensated Cirrhosis

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with or without weight-based ribavirin</td>
<td>24 weeks</td>
<td>IIa, B</td>
</tr>
</tbody>
</table>

‡ For decompensated cirrhosis, please refer to the appropriate section.

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

† RAS testing for Y93H is recommended for cirrhotic patients and ribavirin should be included in regimen if present.

---

Daclatasvir + Sofosbuvir for HCV Genotype 3 Infection\textsuperscript{1-4}

### ALLY-3+: 12 vs 16 Weeks + Ribavirin

<table>
<thead>
<tr>
<th></th>
<th>SVR4, %</th>
<th></th>
<th>SVR12, %</th>
</tr>
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<tbody>
<tr>
<td>12 Weeks</td>
<td>88</td>
<td>21/24</td>
<td>25/26</td>
</tr>
<tr>
<td>16 Weeks</td>
<td>96</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ALLY-3: 12 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Cirrhosis absent</th>
<th>Cirrhosis present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-naïve</td>
<td>97</td>
<td>58</td>
</tr>
<tr>
<td>Treatment experienced</td>
<td>94</td>
<td>69</td>
</tr>
</tbody>
</table>

Sofosbuvir/Velpatasvir in GT3: SVR12 by Cirrhosis and Treatment History in ASTRAL-3


---

**Sofosbuvir/Velpatasvir in GT3: SVR12 by Cirrhosis and Treatment History in ASTRAL-3**

<table>
<thead>
<tr>
<th>Cirrhosis</th>
<th>Treatment-naïve</th>
<th>Treatment experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>98</td>
<td>93</td>
</tr>
<tr>
<td>Yes</td>
<td>160/163</td>
<td>40/43</td>
</tr>
<tr>
<td></td>
<td>1 relapse, 2 others</td>
<td>3 relapses</td>
</tr>
<tr>
<td>No</td>
<td>91</td>
<td>31/34</td>
</tr>
<tr>
<td>Yes</td>
<td>3 relapses(^a)</td>
<td>33/37</td>
</tr>
<tr>
<td></td>
<td>4 relapses</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>95</td>
<td>264/277</td>
</tr>
</tbody>
</table>

\(^a\) Includes patient with evidence of G1 reinfection.
Treatment-Naïve Genotype 4
## Recommended Regimens

### Genotype 4, Treatment-naive Patients, Without Cirrhosis

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and weight-based ribavirin</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</td>
<td>12 weeks</td>
<td>IIa, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>IIa, B</td>
</tr>
</tbody>
</table>

### Genotype 4, Treatment-naive Patients, with Compensated Cirrhosis

<table>
<thead>
<tr>
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</tr>
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<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</td>
<td>12 weeks</td>
<td>IIa, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>IIa, B</td>
</tr>
</tbody>
</table>

† Please see statement on FDA warning regarding the use of PrOD or PrO in patients with cirrhosis.

‡ For decompensated cirrhosis, please refer to the appropriate section.
Treatment-Naïve Genotypes 5 or 6
## Recommended Regimens

### Genotype 5 or 6, Treatment-naive Patients, with and Without Cirrhosis

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
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<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
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<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>IIa, B</td>
</tr>
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</table>

## Summary of Recommended Regimens for Treatment-Naïve Patients Without Cirrhosis

<table>
<thead>
<tr>
<th>GT</th>
<th>Elbasvir/grazoprevir +/- ribavirin</th>
<th>Ledipasvir/sofosbuvir</th>
<th>Paritaprevir/ritonavir/ombitasvir/dasabuvir +/- ribavirin</th>
<th>Simeprevir + sofosbuvir</th>
<th>Sofosbuvir/velpatasvir</th>
<th>Daclatasvir + sofosbuvir</th>
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<tbody>
<tr>
<td>1a</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
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<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Considerations for Treating HCV in the Primary Care Setting

• Decide which patients you are comfortable treating
  ➢ Genotypes?
  ➢ Degree of fibrosis?
  ➢ Co-infected?
  ➢ Renal impairment?

• Refer to a specialist for remainder of patients

cGFR: calculated glomerular filtration rate.
Potential Requirements to Acquire HCV Treatment Medications for Patients\textsuperscript{1,a}

- Provider experience
  - General medical providers may need documentation of consultation support by experts, such as through the ECHO programs

- Proof of fibrosis staging

- Baseline laboratory studies
  - eg. HCV genotype; HCV RNA; CBC; hepatic function panel

- Clinic note documentation
  - eg. Alcohol sobriety for at least 6 months; CAGE or AUDIT-C alcohol use survey if the patient is not 100% abstinent to alcohol; no injection drug use for at least 6 months; drug or alcohol screening tests; evaluation of psychosocial readiness for treatment; justification of choice of regimen and duration of treatment

\textsuperscript{a}Potential requirements vary by insurance and state.

# Hepatitis C Co-Pay and Patient Assistance Programs

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
<th>Phone Number</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daklinza™ (daclatasvir)</td>
<td>Bristol-Myers Squibb</td>
<td>(844) 44CONNECT (844) 442-6663</td>
<td>daklinza.bmscustomerconnect.com/patient-support</td>
</tr>
<tr>
<td>Epclusa® (sofosbuvir/velpatasvir)</td>
<td>Gilead Sciences</td>
<td>(855) 7MYPATH (855) 769-7284</td>
<td>mysupportpath.com</td>
</tr>
<tr>
<td>Harvoni® (ledipasvir/sofosbuvir)</td>
<td>Gilead Sciences</td>
<td>(855) 7MYPATH (855) 769-7284</td>
<td>mysupportpath.com</td>
</tr>
<tr>
<td>Moderiba™ (ribavirin)</td>
<td>AbbVie</td>
<td>(844) MODERIBA (844) 663-3742</td>
<td>moderiba.com/patient-support/financial</td>
</tr>
<tr>
<td>Olysio® (simeprevir)</td>
<td>Janssen Therapeutics</td>
<td>(855) 5OLYSIO (855) 565-9746</td>
<td>olysio.com/support</td>
</tr>
<tr>
<td>Ribasphere® (ribavirin)</td>
<td>Kadmon</td>
<td>(888) 668-3393</td>
<td>ribapak.com/hcp/resources.html</td>
</tr>
<tr>
<td>Sovaldi® (sofosbuvir)</td>
<td>Gilead Sciences</td>
<td>(855) 7MYPATH (855) 769-7284</td>
<td>mysupportpath.com</td>
</tr>
<tr>
<td>Technivie™ (ombitasvir/paritaprevir/ritonavir)</td>
<td>AbbVie</td>
<td>(844) 2PROCEED (844) 277-6233</td>
<td>viekira.com/proceed-support</td>
</tr>
<tr>
<td>Viekira Pak (dasabuvir/ombitasvir/paritaprevir/ritonavir)</td>
<td>AbbVie</td>
<td>(844) 2PROCEED (844) 277-6233</td>
<td>viekira.com/proceed-support</td>
</tr>
</tbody>
</table>
### 8 week course
- **Week 4:**
  - Laboratory test
  - Viral load
  - Complete blood count (CBC), creatinine, estimated glomerular filtration rate (eGFR), liver function test (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase)
- **Week 12 after end of treatment:**
  - Laboratory test
  - Viral load
- **Week 14-20 after end of treatment:**
  - Visit to discuss results of sustained virological response (SVR) testing and future recommendations

### 12 week course
- **Week 4:**
  - Laboratory test
  - Viral load
  - CBC, creatinine, eGFR, liver function test (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase)
- **Week 12:**
  - Laboratory test
  - Viral load
- **Week 14:**
  - End of treatment visit
- **Week 12 after end of treatment:**
  - Laboratory test
  - Viral load
- **Week 14-20 after end of treatment:**
  - Visit to discuss results of SVR testing and future recommendations

### 16 week course
- **Week 4:**
  - Laboratory test
  - Viral load
  - CBC, creatinine, eGFR, liver function test (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase)
- **Week 16:**
  - Laboratory test
  - Viral load
- **Week 16-18:**
  - End of treatment visit
- **Week 12 after end of treatment:**
  - Laboratory test
  - Viral load
- **Week 14-20 after end of treatment:**
  - Visit to discuss results of SVR testing and future recommendations

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Adherence to HCV Therapy

Adherence to HCV therapy is one of the most important predictors of successful HCV treatment.

While there are well-defined and established guidelines for some disease states such as HIV, hypertension, and others, it is less clear when it comes to adherence for HCV therapy.

### Barriers to Adherence With Hepatitis C Therapy

**Factor** | **Examples**
---|---
**Patient-related** | Age; drug use; alcohol use; presence of comorbidities; literacy; physical impairment (eg, vision problems, impaired dexterity); cognitive impairment; availability of social support.

**Treatment-related** | Dosing complexity; side effects; number of medications in a treatment regimen; food requirements

**Patient–healthcare provider relationship** | Closeness of relationship; provider–patient communication skills

**System-related** | Access to healthcare; continuity of care; medication costs

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### Addressing Adherence Problems Prior to HCV Treatment

#### Potential Strategies to Maximize Adherence During Chronic Hepatitis C Treatment

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Potential Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence education</td>
<td>Encourages patients to learn about medications</td>
</tr>
<tr>
<td>Directly observed therapy</td>
<td>Might encourage adherence&lt;br&gt;Helps reporting of treatment-related AEs</td>
</tr>
<tr>
<td>Discuss adherence barriers</td>
<td>Encourages identification of barriers to adherence and consider potential solutions to overcome them</td>
</tr>
<tr>
<td>Encourage pill sorting</td>
<td>Helps establish routine</td>
</tr>
<tr>
<td>Medication diary</td>
<td>Helps establish routine&lt;br&gt;Allows identification of patterns of missed doses</td>
</tr>
<tr>
<td>Reminder alarms</td>
<td>Helps establish routine</td>
</tr>
<tr>
<td>Support group</td>
<td>Provides social support to take medications as prescribed, report treatment-related adverse effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>No advanced fibrosis (METAVIR stage F0-F2)</td>
<td>• No hepatitis C follow-up</td>
</tr>
<tr>
<td>Advanced fibrosis (METAVIR stage F3 or F4)</td>
<td>• Twice-yearly ultrasound surveillance for hepatocellular carcinoma</td>
</tr>
<tr>
<td></td>
<td>– If compensated cirrhosis (F4) also test for varices using baseline endoscopy</td>
</tr>
<tr>
<td>Ongoing hepatitis C risk or unexplained hepatic dysfunction</td>
<td>• Test for recurrence or <strong>reinfection</strong> with quantitative hepatitis C RNA assay</td>
</tr>
<tr>
<td>Persistently abnormal liver tests</td>
<td>• Test for other causes of liver disease</td>
</tr>
<tr>
<td>No virologic cure</td>
<td>• Test for disease progression every 6-12 mo with hepatic function panel, CBC, and INR</td>
</tr>
<tr>
<td></td>
<td>• Consider retreatment options</td>
</tr>
</tbody>
</table>

HCV Elimination in the US

March 28, 2017

FOR IMMEDIATE RELEASE

U.S. Could Be Rid of Hepatitis B and C as Public Health Problems, Preventing Nearly 90,000 Deaths by 2030, With Better Attention to Prevention, Screening, Treatment, and Creative Financing for Medicines

WASHINGTON – Hepatitis B and C kill more than 20,000 people every year in the United States. A new report from the National Academies of Sciences, Engineering, and Medicine presents a strategy to eliminate these diseases as serious public health problems and prevent nearly 90,000 deaths by 2030.

“Viral hepatitis is simply not a sufficient priority in the United States,” said Brian Strom, chair of the committee that carried out the study and chancellor and university professor, Rutgers Biomedical and Sciences, Rutgers University, Newark, N.J. “Despite being the seventh leading cause of death in the world – and killing more people every year than HIV, road traffic accidents, or diabetes – viral hepatitis accounts for less than 1 percent of the National Institutes of Health research budget.”

ELISA: enzyme-linked immunosorbent assay.
Conclusions

- Hepatitis C is common in the United States and is a leading cause of morbidity and mortality
  - New infection among young adults due to injection narcotic use
  - Prevalent infection among older adults due to exposure prior to HCV discovery

- Screening is recommended
  - At-risk populations should be screened initially and periodically as behavior indicates
  - All Baby Boomers born between 1945-1965 should receive a one-time HCV screen

- Patients who test positive on ELISA antibody test should receive second confirmation test (HCV RNA assay)

ELISA: enzyme-linked immunosorbent assay.
Conclusions (Cont’d)

• All persons with active HCV infection should be counseled
  – Prevention of liver disease
    ➢ Alcohol abstinence
    ➢ Immunization against HAV and HBV as needed
  – Prevention of transmission

• All persons with active HCV infection should be considered for curative HCV treatment
  – Refer to specialist when deemed necessary (eg. more advanced liver disease)

HAV: hepatitis A virus; HBV: hepatitis B virus.
Additional Case Scenarios
64-Year-Old Male; Recently Diagnosed with HCV Genotype 1a

- Recently received cohort screening (b. 1952)
- Alcohol x 40 yrs, stopped with diagnosis of HCV
- No swelling, jaundice, GI bleeding or confusion
- Normal PE
- HTN, BPH
- Tattoos in his youth

Non-invasive assessment
- FIB-4 score: 2.87 (indeterminate)
- Ultrasound result:
  - borderline hepatic enlargement
  - mild coarsening of the echotexture
  - borderline splenomegaly (spleen at 12.6cm)

What should you do next?
38-Year-Old Male; Diagnosed Several Years Ago with HCV Genotype 1a; Treatment-Naive

- Chronic lower back pain
- Depression, untreated
- PTSD
- Opioid abuse – ~17 yr history, multiple detox stays
- Stopped heroin 2 months ago, has been buying buprenorphine on the street
- Laboratory values
  - AST/ALT – 96/112
  - Coags/CBC – nl
  - Hep C Ab – positive
  - VL/genotype (857,342/1a)
  - HIV – neg

What should you do next?
62-Year-Old Male; Newly Diagnosed with HCV Genotype 1b

- Hypertension
- Current alcohol use (~1 pint of vodka/day)
- IV heroin ~40 years ago
- Remote history of cocaine abuse
- ROS: fatigue, RUQ pain
- Additional information
  - Viral load 1 million
  - No coinfection
  - WBC 8, Hct 40, plts 155
  - AST 84, ALT 52
  - INR 1
  - Abdominal US – no cirrhosis

What should you do next?
44-Year-Old Female; Newly Diagnosed with HCV

- Medical history remarkable for injection drug use, but abstinent from illicit drugs (including injection drug use), tobacco, and alcohol for 10 years
- No current medications
- Vital signs and PE normal
- Additional information:
  - HCV viral load 1 million IU/mL
  - HCV genotype 1b
  - stage-2 fibrosis
  - up to date with all vaccines (including hepatitis A and hepatitis B)

What should you do next?
58-Year-Old Female; 20 Year History of HCV

- Treatment-naïve; previously refused treatment with peg-interferon (PEG-IFN) or ribavirin
- Now expresses interest in being treated with the “one-pill-a-day” regimen.
- Laboratory studies reveal HCV genotype 1a and normal liver function tests.
- Liver biopsy performed 1 year ago was significant for mild liver fibrosis; viral load level obtained 2 months ago was 8 million IU/mL.

What should you do next?
Please remember to complete and submit your Post-Test and Evaluation for CME credit.

**Missed anything?**

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- If you have any additional questions, please contact Patricia Siple at patricia.siple@peerview.com.

*Thank you and have a good day!*