

Treatment of HCV Genotype 2

This is a PDF version of the following document:

Module 5: [Treatment of Chronic Hepatitis C Infection](#)

Lesson 2: [Treatment of HCV Genotype 2](#)

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<https://www.hepatitisC.uw.edu/go/treatment-infection/treatment-genotype-2/core-concept/all>.

Introduction

Background

In the United States, genotype 2 accounts for approximately 13 to 15% of all hepatitis C virus (HCV) infections.[1] In the era before direct-acting antiviral agents (DAAs), sustained virologic response rates at 12 weeks post-treatment (SVR12) were relatively higher in persons with genotype 2 HCV than those with genotype 1, 3, or 4 HCV. Thus, data regarding retreatment of individuals with genotype 2 in whom prior therapy failed are limited. The following discussion regarding initial treatment and retreatment of persons with genotype 2 chronic HCV assumes the individual and their clinician have already made the decision to proceed with hepatitis C therapy. This topic review does not address the treatment of HCV genotype 2 in persons with decompensated cirrhosis, severe renal impairment (or end-stage renal disease), or post-liver transplantation.

Medications Used to Treat HCV Genotype 2

The [HCV Medications](#) section on this website provides detailed information for each of the Food and Drug Administration (FDA)-approved medications listed in the treatment recommendations, including links to the full prescribing information and to patient assistance programs. The direct-acting antiviral agents exert their action at specific steps in the HCV life cycle. There are three major classes of direct-acting antiviral medications: (1) nonstructural proteins 3/4A (NS3/4A) protease inhibitors, (2) NS5A inhibitors, and (3) NS5B polymerase inhibitors ([Figure 1](#)); the NS5B polymerase inhibitors include the nucleoside analogs and nonnucleoside analogs.[2,3] Adherence with the treatment regimen is of paramount importance. Accordingly, patients should receive detailed counseling regarding the importance of adherence prior to starting therapy and clinicians should provide intensive follow-up during therapy.

Approach to Choosing HCV Genotype 2 Treatment Regimen

For patients chronically infected with genotype 2 HCV, two key factors influence the choice and duration of therapy: cirrhosis status and prior treatment experience. In addition, the cost of the regimen, insurance coverage, concurrent medications, and patient and provider preference can play a major role in the regimen choice. The following treatment recommendations are based on the AASLD-IDSA HCV Guidance for initial treatment of adults with HCV genotype 2 and for retreatment of adults in whom prior therapy failed, including those with HCV genotype 2.[4,5]

- [AASLD-IDSA HCV Guidance for Treatment-Naïve Patients with Genotype 2 HCV](#)
- [AASLD-IDSA HCV Guidance for Retreatreatment of Persons in Whom Prior Therapy Failed](#)

HCV Genotype 2: Initial Treatment

Background

Historically, in the interferon era, treatment of persons with HCV genotype 2 infection achieved higher sustained virologic response (SVR) rates than those with HCV genotype 1 infection, even with a shorter duration of therapy and lower doses of ribavirin. Prior to the availability of DAAs, the standard of care for treatment-naïve patients with HCV genotype 2 consisted of a 24-week course of peginterferon plus fixed-dose ribavirin, with SVR rates of 75 to 85%.[\[6,7,8,9\]](#) In 2013, the combination of sofosbuvir with peginterferon and ribavirin showed greater than 90% SVR12 rates in HCV genotype 2 infection.[\[10\]](#) Later that year, the FDA approved a 12-week course with the all-oral regimen of sofosbuvir plus ribavirin for the treatment of HCV genotype 2 infection based on data from several studies showing SVR rates of approximately 92 to 97% with this regimen.[\[11,12,13\]](#) In 2015, daclatasvir plus sofosbuvir was FDA-approved as the first interferon- and ribavirin-free combination for HCV genotype 2 infection and this 12-week combination produced SVR rates of greater than 95%.[\[14,15\]](#) Subsequently, SVR rates of 99% have been reported with sofosbuvir-velpatasvir or glecaprevir-pibrentasvir for initial treatment of individuals with HCV genotype 2.[\[16,17,18,19\]](#)

Factors to Consider Prior to Choosing Initial Treatment Regimen

For initial treatment of persons with chronic HCV genotype 2 infection, three major factors influence the choice of regimen and duration of therapy: (1) the presence or absence of cirrhosis, (2) drug interactions, and (3) medication cost and/or insurance considerations. The treatment regimens for persons with HCV genotype 2 and HIV coinfection are the same as for those for HCV genotype 2 monoinfection, with the following exceptions: (1) persons with HIV-HCV coinfection and compensated cirrhosis should receive a 12-week course of glecaprevir-pibrentasvir versus an 8-week course with HCV monoinfection and (2) additional drug interactions between DAAs and antiretroviral medications need to be taken into consideration.

AASLD-IDSA HCV Guidance for Initial Treatment of HCV Genotype 2

The following is a summary of the AASLD-IDSA HCV Guidance for initial treatment of persons with chronic HCV genotype 2 infection.[\[20,21\]](#) For individuals with cirrhosis, the AASLD-IDSA HCV Guidance defines compensated cirrhosis as Child-Turcotte-Pugh class A and decompensated cirrhosis as Child-Turcotte-Pugh class B or C. The recommended regimens are listed by evidence level; when the evidence level is considered equivalent, the regimens are listed alphabetically.

Table 1. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 2 without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed October 11, 2020.

Table 2. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

For HIV/HCV-coinfected patients, a treatment duration of 12 weeks is recommended.

Rating: [Class I](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

[^]For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 2 with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed October 11, 2020.

Studies of Initial Treatment of Adults with HCV Genotype 2

The following key studies support the recommendations for treatment-naïve adults with chronic hepatitis C and genotype 2 infection. The medications are listed in alphabetical order.

Glecaprevir-Pibrentasvir

- [ENDURANCE-2](#): This phase 3, randomized, double-blind, placebo-controlled trial evaluated the safety and efficacy of 12 weeks of therapy with glecaprevir-pibrentasvir in adults with HCV genotype 2 infection, without cirrhosis.[17] Among those enrolled, 70% percent were HCV treatment naïve. Overall, when excluding 6 sofosbuvir-experienced participants, 99% (195 of 196) achieved an SVR12 by intent-to-treat analysis. There were no serious adverse events related to glecaprevir-pibrentasvir.[17]
- [EXPEDITION-1](#): This phase 3, single-arm, open-label trial evaluated the safety and efficacy of a 12-week course of glecaprevir-pibrentasvir in treatment-naïve and treatment-experienced adults with compensated cirrhosis and HCV genotype 1, 2, 4, 5, or 6 infection.[16] A total of 31 participants with HCV genotype 2 received treatment and 100% (31 of 31) achieved an SVR12.[16]
- [EXPEDITION-8](#): This single-arm, multicenter, phase 3b trial evaluated the efficacy of glecaprevir-pibrentasvir for 8 weeks in treatment-naïve adults with compensated cirrhosis and HCV genotype 1, 2, 3, 4, 5, or 6.[22] For the purposes of this trial, participants with HIV coinfection, HBV coinfection, or decompensated cirrhosis were excluded.[22] Twenty-six genotype 2 individuals were included, among whom 100% achieved an SVR12.[22] It is worth noting that despite the high proportion of participants who achieved an SVR12 in this study, due to the overall small number of individuals with compensated cirrhosis in clinical trials, some experts continue to recommend 12 weeks of glecaprevir-pibrentasvir in those with underlying compensated cirrhosis, regardless of genotype.[22]
- [SURVEYOR-II \(Part 4\)](#): This phase 3, single-arm, open-label trial evaluated the safety and efficacy of 8 weeks of glecaprevir-pibrentasvir in 203 adults with HCV genotype 2, 4, 5, or 6 infection without cirrhosis.[17] Among those enrolled, 71% (145 of 203) had HCV genotype 2 and 67% (137 of 203) were sofosbuvir naïve. In the subset of sofosbuvir-naïve genotype 2 participants, 99% achieved an SVR12.[17] In this trial, the presence of baseline resistance-associated substitutions had minimal effect on SVR12 rates, with 96% (51 of 53) of persons with an underlying L31M RAS mutation achieving an SVR12.[17]

Sofosbuvir-Velpatasvir

- [ASTRAL-1](#): This phase 3, double-blind, placebo-controlled study randomized treatment-naïve and treatment-experienced adults with HCV genotypes 1, 2, 4, 5, or 6, including those with and without compensated cirrhosis, to receive sofosbuvir-velpatasvir versus placebo for 12 weeks.[18] Of the 624 participants, 104 with HCV genotype 2 received sofosbuvir-velpatasvir and 100% of these individuals achieved an SVR12.[18] In a pooled analysis of genotype 2 participants from ASTRAL-1 and ASTRAL-2, 100% (29 of 29) with compensated cirrhosis achieved an SVR12, and 99% (194 of 195) of treatment-naïve participants achieved an SVR12.[18,19]
- [ASTRAL-2](#): The ASTRAL-2 trial was a randomized, open-label, phase 3 study that compared the safety and efficacy of the fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks with sofosbuvir plus ribavirin for 12 weeks in treatment-naïve and treatment-experienced adults with chronic HCV genotype 2 infection.[19] Participants with compensated cirrhosis comprised 14% of the total 266 population enrolled in the study.[19] In the HCV treatment-naïve participants who received sofosbuvir-velpatasvir, 99% (114 of 115) achieved an SVR12 compared with 95% (106 of 111) in those who received sofosbuvir plus ribavirin.[19] The one individual who did not achieve an SVR12 in the sofosbuvir-velpatasvir group had received only one dose of the drug and discontinued after experiencing headache and anxiety. For HCV treatment-naïve participants in the sofosbuvir-velpatasvir group, there was no difference in SVR12 rates between those without cirrhosis and those with compensated cirrhosis (99% versus 100%).

- [POLARIS-2](#): The POLARIS-2 trial was a phase 3, open-label trial for treatment-naïve and treatment-experienced adults with chronic HCV genotypes 1, 2, 3, or 4 infection who were randomized to receive either 8 weeks of sofosbuvir-velpatasvir-voxilaprevir or 12 weeks of sofosbuvir-velpatasvir.[\[23\]](#) Compensated cirrhosis was present in 18% of the participants. For the HCV genotype 2 recipients of 12 weeks of sofosbuvir-velpatasvir, 100% (53 of 53) achieved an SVR12.[\[23\]](#)

HCV Genotype 2: Retreating Persons who Failed Prior Therapy

Background

Prior to the introduction of direct-acting antiviral agents, the SVR rates with treatment of HCV genotype 2 infection were approximately 75 to 85%. Accordingly, less clinical experience exists with retreatment of patients with genotype 2 than with genotype 1 infection. In particular, very limited data exist with retreatment of genotype 2 patients with cirrhosis. Recent trial data suggest either of the pangenotypic combinations of sofosbuvir-velpatasvir, sofosbuvir-velpatasvir-voxilaprevir or glecaprevir-pibrentasvir are highly effective in treatment-experienced persons with HCV genotype 2 infection.[[16,17,18,19](#)]

Factors to Consider Prior to Choosing Retreatment Regimen

For retreatment of adults with HCV genotype 2, four major factors influence the optimal regimen for retreatment, including (1) the prior regimen the patient failed, including whether there was prior exposure to an NS5A inhibitor, (2) the presence or absence of cirrhosis, (3) cost or insurance considerations. The retreatment of persons with HCV genotype 2 patients who have decompensated cirrhosis, severe renal impairment (or end-stage renal disease), or post-liver transplantation is not addressed in this lesson.

Baseline Resistance Testing

Baseline resistance testing is not routinely recommended for treatment-experienced patients with genotype 2 infection.

AASLD-IDSA HCV Guidance for Retreatment of HCV Genotype 2

The following is a summary of the AASLD-IDSA HCV Guidance for adults with HCV genotype 2 infection who failed prior DAA therapy, including those without cirrhosis and those with compensated cirrhosis.[[24,25,26](#)] For these purposes, compensated cirrhosis is defined as Child-Turcotte-Pugh class A and decompensated cirrhosis as Child-Turcotte-Pugh class B or class C. The AASLD-IDSA HCV Guidance for retreatment is no longer genotype specific, but instead emphasizes a pangenotypic approach to retreatment based on the prior treatment regimen. In addition, the AASLD-IDSA HCV Guidance no longer includes recommendations for the retreatment of persons who experienced prior treatment failure with interferon-based therapy, including interferon plus first-generation protease inhibitors (telaprevir, boceprevir); these individuals have robust cure rates with modern DAA regimens similar to that observed with treatment-naïve persons. The recommended retreatment regimens are based on prior regimen failure and listed by evidence level; when the evidence level is considered equivalent, the regimens are listed alphabetically.

Table 3. AASLD-IDSA HCV Guidance: Retreatment Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[^]

Recommended for Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks

Ribavirin: For persons with genotype 3 and cirrhosis, add weight-based ribavirin if there are no contraindications to ribavirin.

Rating: [Class I](#), [Level A](#)

Alternative for Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks*

This regimen is not recommended for persons with (1) prior failure with a NS3/4 protease inhibitor-containing combination regimens, or (2) persons with genotype 3 infection with sofosbuvir and NS5A inhibitor experience.

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy failed: Sofosbuvir-Based and Elbasvir/Grazoprevir Treatment Failures. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed September 18, 2023.

Table 4. AASLD-IDSA HCV Guidance: Retreatment Elbasvir-Grazoprevir Treatment Failures, With or Without Compensated Cirrhosis[^]

Recommended for Elbasvir-Grazoprevir Treatment Failures, With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks

Ribavirin: For persons with genotype 3 and cirrhosis, add weight-based ribavirin if there are no contraindications to ribavirin.

Rating: [Class I](#), [Level A](#)

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy failed: Sofosbuvir-Based and Elbasvir/Grazoprevir Treatment Failures. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed September 18, 2023.

Table 5. AASLD-IDSA HCV Guidance for All Genotypes: Retreatment

Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Recommended for Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir <i>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks</i>	+	Sofosbuvir <i>(400 mg) one tablet once daily for 16 weeks</i>	+	Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)</i>
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For patients with or without compensated cirrhosis

Rating: [Class IIa](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg)

Recommended for Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir
Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks

For patients without cirrhosis

Rating: [Class IIa](#), [Level B](#)

Recommended for Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir <i>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks</i>	+	Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)</i>
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For patients with compensated cirrhosis

Rating: [Class IIa](#), [Level C](#)

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: glecaprevir/pibrentasvir treatment failure (all genotypes). [[AASLD-IDSA](#)] - Accessed September 18, 2023.

Table 6. AASLD-IDSA HCV Guidance for All Genotypes: Retreatment Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir-Velpatasvir-Voxilaprevir or Sofosbuvir Plus Glecaprevir-Pibrentasvir[^]

Recommended for Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir-Velpatasvir-Voxilaprevir or Sofosbuvir Plus Glecaprevir-Pibrentasvir[^]

<p>Glecaprevir-Pibrentasvir <i>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks#</i></p>	+	<p>Sofosbuvir <i>(400 mg) one tablet once daily for 16 weeks#</i></p>	+	<p>Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 16 weeks# (the daily dose is given in two divided doses)</i></p>
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#Extension of treatment to 24 weeks should be considered in extremely difficult cases (eg, genotype 3 with cirrhosis) or failure following sofosbuvir plus glecaprevir-pibrentasvir.

Rating: [Class IIa](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg)

Recommended for Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir-Velpatasvir-Voxilaprevir or Sofosbuvir Plus Glecaprevir-Pibrentasvir[^]

<p>Sofosbuvir-Velpatasvir-Voxilaprevir <i>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 24 weeks</i></p>	+	<p>Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks (the daily dose is given in two divided doses)</i></p>
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Rating: [Class IIa](#), [Level B](#)

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: sofosbuvir/velpatasvir/voxilaprevir treatment failure (all genotypes) [[AASLD-IDSA](#)] - Accessed September 18, 2023.

Studies of Retreatment of Adults with HCV Genotype 2

The following key studies support the recommendations for retreatment of adults with chronic HCV genotype 2 infection who previously failed therapy. The medications are listed in alphabetical order.

Glecaprevir-Pibrentasvir

- [ENDURANCE-2](#): This phase 3, randomized, double-blind, placebo-controlled trial evaluated the safety and efficacy of 12 weeks of therapy with glecaprevir-pibrentasvir in adults with HCV genotype 2 without cirrhosis.[17] Thirty percent were treatment-experienced; most (91%) had previously received interferon-based therapy while the remainder had received sofosbuvir-based therapy. Among DAA-naïve participants who received glecaprevir-pibrentasvir, 99% (195 of 196) achieved an SVR12 by intent-to-treat analysis.[17] None of the 61 treatment-experienced participants had virologic failure. There were no serious adverse events related to glecaprevir-pibrentasvir.[17]
- [EXPEDITION-1](#): This phase 3, single-arm, open-label trial evaluated the safety and efficacy of a 12-week course of glecaprevir-pibrentasvir in treatment-naïve and treatment-experienced adults with compensated cirrhosis and HCV genotype 1, 2, 4, 5, or 6 infection.[16] Prior treatment experience included (1) interferon (or peginterferon) with or without ribavirin, or (2) sofosbuvir plus ribavirin, with or without peginterferon.[16] A total of 31 participants with HCV genotype 2 received treatment and 100% (31 of 31) achieved an SVR12.[16]
- [SURVEYOR-II \(Part 4\)](#): This phase 3, single-arm, open-label trial evaluated the safety and efficacy of 8 weeks of glecaprevir-pibrentasvir in 203 adults with HCV genotype 2, 4, 5, or 6 infection without cirrhosis.[17] Among those enrolled, 71% (145 of 203) had HCV genotype 2 infection and 12% of those with HCV genotype 2 were treatment experienced. For all participants with HCV genotype 2 infection, 98% (142 of 145) had an SVR12.[17]

Sofosbuvir-Velpatasvir

- [ASTRAL-2](#): The ASTRAL-2 was a randomized, open-label, phase 3 trial that compared the safety and efficacy of sofosbuvir-velpatasvir versus sofosbuvir plus ribavirin, both for 12 weeks in treatment-naïve and treatment-experienced adults with chronic HCV genotype 2 infection.[17] Individuals with compensated cirrhosis were permitted to enroll and they comprised 14% of the total 266 participants.[17] Overall, the SVR12 rate among sofosbuvir-velpatasvir recipients was 99% (133 of 134) and was superior to the SVR12 rate of 94% (124 of 132) among those who received sofosbuvir plus ribavirin.[17] For the treatment-experienced participants treated with sofosbuvir-velpatasvir, 100% (19 of 19) achieved an SVR12, including 15 without cirrhosis and 4 with compensated cirrhosis.[17]
- [POLARIS-2](#): The POLARIS-2 trial was a phase 3, open-label study of treatment-naïve and treatment-experienced adults with chronic HCV genotype 1, 2, 3, or 4 infection who were randomized to receive either 8 weeks of sofosbuvir-velpatasvir-voxilaprevir or 12 weeks of sofosbuvir-velpatasvir.[23] Prior treatment with peginterferon and ribavirin was allowed, but not prior treatment with DAAs.[23] Compensated cirrhosis was present in 18% of the participants.[23] For the HCV genotype 2 recipients of 12 weeks of sofosbuvir-velpatasvir, 100% (53 of 53) achieved an SVR12; the SVR12 rate was 97% (61 of 63) among those who received 8 weeks of sofosbuvir-velpatasvir-voxilaprevir.[23]
- [POLARIS-4](#): In this phase 3, active-comparator, open-labeled trial, 314 adults with chronic HCV genotype 1, 2, or 3 infection and prior DAA therapy (without an NS5A inhibitor) were randomized to receive a 12-week course with sofosbuvir-velpatasvir-voxilaprevir or sofosbuvir-velpatasvir.[27] Among all of the participants, compensated cirrhosis was present in 46% and prior sofosbuvir exposure in 80%.[27] For those participants with HCV genotype 2 infection, 97% (32 of 33) treated with sofosbuvir-velpatasvir achieved an SVR12.[27]

Sofosbuvir-Velpatasvir-Voxilaprevir

- [POLARIS-4](#): In this phase 3, active-comparator, open-labeled trial, 314 adults with chronic HCV genotype 1, 2, or 3 infection and prior DAA therapy (without an NS5A inhibitor) were randomized to receive a 12-week course with sofosbuvir-velpatasvir-voxilaprevir or sofosbuvir-velpatasvir. Among all participants, compensated cirrhosis was present in 46% and prior sofosbuvir exposure in 80%. For those participants with HCV genotype 2 infection, 100% (31 of 31) achieved an SVR12 with sofosbuvir-velpatasvir-voxilaprevir.

Summary Points

- The recommended regimens for initial treatment of adults with HCV genotype 2 (without cirrhosis) are glecaprevir-pibrentasvir for 8 weeks or sofosbuvir-velpatasvir for 12 weeks.
- For initial treatment of HCV genotype 2 in adults with compensated cirrhosis, the recommended regimens are sofosbuvir-velpatasvir for 12 weeks or glecaprevir-pibrentasvir for 8 weeks. If the individual has HCV-HIV coinfection, and compensated cirrhosis, the glecaprevir-pibrentasvir treatment should be extended to 12 weeks.
- For the retreatment of adults with HCV genotype 2 who were previously treated with peginterferon plus ribavirin, with or without compensated cirrhosis, the recommended and alternative regimens are the same as for initial therapy of HCV genotype 2.
- The retreatment of DAA-experienced adults with HCV genotype 2 infection depends on the prior DAA regimen that was taken.

Citations

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Figures

Figure 1 Classes of Direct-Acting Antiviral Agents Used to Treat HCV

Note that all medications in gray boxes have been discontinued and are no longer manufactured in the United States.

NS3/4A Protease Inhibitors	NS5A Inhibitors	NS5B Polymerase Inhibitors
Boceprevir	Daclatasvir	Dasabuvir
Glecaprevir	Elbasvir	Sofosbuvir
Grazoprevir	Ledipasvir	
Paritaprevir	Ombitasvir	
Simeprevir	Pibrentasvir	
Telaprevir	Velpatasvir	
Voxilaprevir		

Table 1. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 2 without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed October 11, 2020.

Table 2. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

For HIV/HCV-coinfected patients, a treatment duration of 12 weeks is recommended.

Rating: [Class I](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

[^]For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 2 with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed October 11, 2020.

Table 3. AASLD-IDSA HCV Guidance: Retreatment Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[^]

Recommended for Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks

Ribavirin: For persons with genotype 3 and cirrhosis, add weight-based ribavirin if there are no contraindications to ribavirin.

Rating: [Class I](#), [Level A](#)

Alternative for Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks*

This regimen is not recommended for persons with (1) prior failure with a NS3/4 protease inhibitor-containing combination regimens, or (2) persons with genotype 3 infection with sofosbuvir and NS5A inhibitor experience.

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy failed: Sofosbuvir-Based and Elbasvir/Grazoprevir Treatment Failures. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed September 18, 2023.

Table 4. AASLD-IDSA HCV Guidance: Retreatment Elbasvir-Grazoprevir Treatment Failures, With or Without Compensated Cirrhosis[^]

Recommended for Elbasvir-Grazoprevir Treatment Failures, With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks

Ribavirin: For persons with genotype 3 and cirrhosis, add weight-based ribavirin if there are no contraindications to ribavirin.

Rating: [Class I](#), [Level A](#)

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy failed: Sofosbuvir-Based and Elbasvir/Grazoprevir Treatment Failures. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed September 18, 2023.

Table 5. AASLD-IDSA HCV Guidance for All Genotypes: Retreatment Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Recommended for Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir <i>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks</i>	+	Sofosbuvir <i>(400 mg) one tablet once daily for 16 weeks</i>	+	Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)</i>
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For patients with or without compensated cirrhosis

Rating: [Class IIa](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg)

Recommended for Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks

For patients without cirrhosis

Rating: [Class IIa](#), [Level B](#)

Recommended for Glecaprevir-Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir-Voxilaprevir <i>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks</i>	+	Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)</i>
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For patients with compensated cirrhosis

Rating: [Class IIa](#), [Level C](#)

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: glecaprevir/pibrentasvir treatment failure (all genotypes). [[AASLD-IDSA](#)] - Accessed September 18, 2023.

Table 6. AASLD-IDSA HCV Guidance for All Genotypes: Retreatment Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir-Velpatasvir-Voxilaprevir or Sofosbuvir Plus Glecaprevir-Pibrentasvir[^]

Recommended for Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir-Velpatasvir-Voxilaprevir or Sofosbuvir Plus Glecaprevir-Pibrentasvir[^]

<p>Glecaprevir-Pibrentasvir *Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks#</p>	+	<p>Sofosbuvir (400 mg) one tablet once daily for 16 weeks#</p>	+	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 16 weeks# (the daily dose is given in two divided doses)</p>
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#Extension of treatment to 24 weeks should be considered in extremely difficult cases (eg, genotype 3 with cirrhosis) or failure following sofosbuvir plus glecaprevir-pibrentasvir.

Rating: [Class IIa](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg)

Recommended for Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir-Velpatasvir-Voxilaprevir or Sofosbuvir Plus Glecaprevir-Pibrentasvir[^]

<p>Sofosbuvir-Velpatasvir-Voxilaprevir Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 24 weeks</p>	+	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks (the daily dose is given in two divided doses)</p>
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Rating: [Class IIa](#), [Level B](#)

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

Source: AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: sofosbuvir/velpatasvir/voxilaprevir treatment failure (all genotypes) [[AASLD-IDSA](#)] - Accessed September 18, 2023.

