Treatment of HCV Genotype 2

Introduction

Background

In the United States, genotype 2 accounts for approximately 13-15% 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 patients with genotype 2 chronic HCV assumes the patient 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, renal impairment, acute HCV infection, or post-liver transplantation.

Medications Used to Treat HCV Genotype 2

The HCV Medications section on this web site provides detailed information for each of the 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: nonstructural proteins 3/4A (NS3/4A) protease inhibitors, NS5A inhibitors, and 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 patients with genotype 2 HCV.[4,5]

- AASLD-IDSA HCV Guidance for Treatment-Naïve Patients with Genotype 2 HCV
- AASLD-IDSA HCV Guidance for Treatment-Experienced Patients with Genotype 2 HCV
HCV Genotype 2: Initial Treatment

Background

Historically, in the interferon era, treatment of HCV genotype 2 infection resulted in higher sustained virologic response (SVR) rates than 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%. In 2013, the combination of sofosbuvir with peginterferon and ribavirin showed greater than 90% SVR12 rates in HCV genotype 2 infection. Later that year, the United States Food and Drug Administration (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 92-97% with this regimen. 

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%. Subsequently, SVR rates of 99% have been reported with sofosbuvir-velpatasvir or glecaprevir-pibrentasvir for initial treatment of individuals with HCV genotype 2.

Factors to Consider Prior to Choosing Initial Treatment Regimen

For initial treatment of persons with chronic HCV genotype 2 infection, four major factors influence the choice of regimen and duration of therapy: (1) the presence or absence of cirrhosis, (2) coexistent renal disease, (3) drug interactions, and (4) medication cost and/or insurance considerations. The treatment regimens and duration of therapy for patients with HCV-HIV coinfection are the same as for those for HCV monoinfection, with the exception that 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. 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

<table>
<thead>
<tr>
<th>Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis</th>
<th>Rating: Class I, Level A</th>
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<tbody>
<tr>
<td>Glecaprevir-Pibrentasvir</td>
<td>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks</td>
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<tbody>
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<td>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks</td>
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</table>
Alternative for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

**Daclatasvir** *(60 mg) one tablet once daily for 12 weeks*

**Sofosbuvir** *(400 mg) one tablet once daily for 12 weeks*

**Rating:** Class IIa, Level B

**Note:** *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.


### 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 12 weeks*

**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).*

#### Alternative for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis

**Daclatasvir** *(60 mg) one tablet once daily for 16-24 weeks*

**Sofosbuvir** *(400 mg) one tablet once daily for 16-24 weeks*

**Rating:** Class IIa, Level B

**Note:** *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.
For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

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.

**Daclatasvir plus Sofosbuvir**

- **AI444040**: In study AI444040, a phase 2 trial involving adults with HCV genotypes 1, 2, or 3, all participants received daclatasvir plus sofosbuvir, with or without ribavirin. A total of 44 treatment-naïve adults with genotype 2 or 3 were enrolled in the study, including 26 with HCV genotype 2.[14] The participants with HCV genotype 2 or 3 received one of three 24-week regimens: (1) daclatasvir plus sofosbuvir, with the first week consisting of sofosbuvir alone, (2) daclatasvir plus sofosbuvir, and (3) daclatasvir plus sofosbuvir plus ribavirin. Among the treatment-naïve adults with HCV genotype 2 infection, 92% (24 of 26) achieved an SVR12. For the 2 individuals with genotype 2 who were classified as not having an SVR12, one was lost to follow-up (but had an undetectable HCV RNA at treatment week 14) and the other did not return for all of the post-treatment visits (but had an undetectable HCV RNA level at post-treatment week 24). All regimens were well tolerated and safe.

- **ALLY-2**: This phase 3 trial enrolled treatment-naïve and treatment-experienced adults with chronic HCV genotype 1, 2, 3, or 4 and HIV coinfection.[15] The treatment-naïve participants received an 8-week or 12-week course of daclatasvir plus sofosbuvir. For the 17 treatment-naïve HCV genotype 2 participants, the SVR12 rates were 100% (11 of 11) in those who received 12 weeks of therapy and 83% (5 of 6) with the 8-week course of therapy.

**Glecaprevir-Pibrentasvir**

- **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.

- **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.

**Sofosbuvir-Velpatasvir**

- **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. 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. 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.[22] 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.[22]
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 75-85%. 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 or glecaprevir-pibrentasvir are highly effective in treatment-experienced patients 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, five major factors influence the optimal regimen for retreatment, including (1) the prior regimen the patient failed, (2) presence or absence of cirrhosis, (3) coexistent renal disease, (4) drug interactions, and (5) cost or insurance considerations. The retreatment of genotype 2 patients with decompensated cirrhosis, renal impairment, HIV coinfection, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD-IDSA HCV Guidance for Retreatment of HCV Genotype 2

The following is a summary of the AASLD-IDSA HCV Guidance for patients with hepatitis C genotype 2 infection in whom (1) prior peginterferon and ribavirin therapy failed, or (2) prior sofosbuvir plus ribavirin therapy failed.\[23,24,25\] 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 class C. The recommended regimens are listed by evidence level; when the evidence level is considered equivalent, the regimens are listed alphabetically.

Table 3. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

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**Recommended for Peginterferon plus Ribavirin-Experienced, 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 Peginterferon plus Ribavirin-Experienced, 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**
Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Daclatasvir *(60 mg) one tablet once daily for 12 weeks*  +  Sofosbuvir *(400 mg) one tablet once daily for 12 weeks*

Rating: **Class IIa, Level B**

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.


### Table 4. AASLD-IDSA HCV Guidance for Genotype 2 Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis^

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Peginterferon plus Ribavirin-Experienced, 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 Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis^**

**Glecaprevir-Pibrentasvir**

*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

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).“

**Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis^**

Daclatasvir *(60 mg) one tablet once daily for 16-24 weeks*  +  Sofosbuvir *(400 mg) one tablet once daily for 16-24 weeks*
Rating: Class IIa, Level B
Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

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


Table 5. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^

Recommended regimens listed by evidence level.

**Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without 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 B

**Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^**

**Glecaprevir-Pibrentasvir**
*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks
Rating: Class IIb, 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. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A Inhibitors), genotype 2 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance] - Accessed April 28, 2019.
Table 6. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment
Sofosbuvir plus NS5A-Experienced, Genotype 2 Patients, With or Without
Compensated Cirrhosis

Recommended regimens listed by evidence level.

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A Inhibitors), genotype 2 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance](#) - Accessed April 28, 2019.
Studies of Retreatment of Adults with HCV Genotype 2

The following key studies support the recommendations for retreatment of adult 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. None of the 61 treatment-experienced participants had virologic failure. There were no serious adverse events related to glecaprevir-pibrentasvir.

- **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.

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 of the participants. 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. 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.

- **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.[22] Prior treatment with peginterferon and ribavirin was allowed, but not prior treatment with DAAs. 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; the SVR12 rate was 97% (61 of 63) among those who received 8 weeks of 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.[26] Among all of the participants, compensated cirrhosis was present in 46% and prior sofosbuvir exposure in 80%. For those participants with HCV genotype 2 infection, 97% (32 of 33) treated with sofosbuvir-velpatasvir achieved an SVR12 and 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; the alternative is daclatasvir plus sofosbuvir for 12 weeks.
- For initial treatment of HCV genotype 2 in adults with compensated cirrhosis, the recommended regimens are glecaprevir-pibrentasvir or sofosbuvir-velpatasvir for 12 weeks; the alternative, daclatasvir plus sofosbuvir, should be given for 16-24 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.
- For retreatment of adults with HCV genotype 2 who previously failed therapy with sofosbuvir plus ribavirin, the recommended regimens are (1) glecaprevir-pibrentasvir for 12 weeks or (2) sofosbuvir-velpatasvir for 12 weeks; the same regimens are used in persons with or without compensated cirrhosis.
Citations


4. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Treatment-Naive Genotype 2. [AASLD-IDSA Hepatitis C Guidance] -

5. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Treatment-Experienced Genotype 2. [AASLD-IDSA Hepatitis C Guidance] -


20. AASLD-IDSA. 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]

21. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 2 without cirrhosis. [AASLD-IDSA Hepatitis C Guidance]


23. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A Inhibitors), genotype 2 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

24. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 patients without cirrhosis [AASLD-IDSA Hepatitis C Guidance]

25. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-
experienced, genotype 2 with compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance] -


References


- Lawitz E, Buti M, Vierling JM, et al. Safety and efficacy of a fixed-dose combination regimen of grazoprevir, ruzasvir, and uprifosbuvir with or without ribavirin in participants with and without cirrhosis with chronic hepatitis C virus genotype 1, 2, or 3 infection (C-CREST-1 and C-CREST-2, part B): two randomised, phase 2, open-label trials. Lancet Gastroenterol Hepatol. 2017;2:814-23. [PubMed Abstract] -


# Figures

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

<table>
<thead>
<tr>
<th>NS3/4A Protease Inhibitors</th>
<th>NS5A Inhibitors</th>
<th>NS5B Polymerase Inhibitors</th>
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Table 2. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment
Treatement-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 12 weeks*

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).

**Alternative for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis^**

**Daclatasvir**

*(60 mg) one tablet once daily for 16-24 weeks*

**Sofosbuvir**

*(400 mg) one tablet once daily for 16-24 weeks*

Rating: **Class IIa, Level B**

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

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

Table 3. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

<table>
<thead>
<tr>
<th>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glecaprevir-Pibrentasvir</strong></td>
</tr>
<tr>
<td><em>Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks</em></td>
</tr>
<tr>
<td><strong>Rating:</strong> Class I, Level A</td>
</tr>
<tr>
<td><strong>Note:</strong> <em>This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).</em></td>
</tr>
</tbody>
</table>

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<tr>
<th>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sofosbuvir-Velpatasvir</strong></td>
</tr>
<tr>
<td><em>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks</em></td>
</tr>
<tr>
<td><strong>Rating:</strong> Class I, Level A</td>
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<tr>
<th>Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daclatasvir</strong> <em>(60 mg) one tablet once daily for 12 weeks</em> + <strong>Sofosbuvir</strong> <em>(400 mg) one tablet once daily for 12 weeks</em></td>
</tr>
<tr>
<td><strong>Rating:</strong> Class IIa, Level B</td>
</tr>
<tr>
<td><strong>Note:</strong> <em>The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.</em></td>
</tr>
</tbody>
</table>

Table 4. AASLD-IDSA HCV Guidance for Genotype 2 Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

### Recommended for Peginterferon plus Ribavirin-Experienced, 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 Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis

**Glecaprevir-Pibrentasvir**
*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks

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).

### Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis

**Daclatasvir** *(60 mg) one tablet once daily for 16-24 weeks* + **Sofosbuvir** *(400 mg) one tablet once daily for 16-24 weeks*

Rating: **Class IIa, Level B**
Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

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

Table 5. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment
Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or
Without Compensated Cirrhosis

Recommended regimens listed by evidence level.

<table>
<thead>
<tr>
<th>Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir-Velpatasvir</td>
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<td>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks</td>
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<td>Rating: <strong>Class I, Level B</strong></td>
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<tr>
<td>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks</td>
</tr>
<tr>
<td>Rating: <strong>Class IIb, Level B</strong></td>
</tr>
<tr>
<td>Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).</td>
</tr>
</tbody>
</table>

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A Inhibitors), genotype 2 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance] - Accessed April 28, 2019.
Table 6. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Sofosbuvir plus NS5A-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^  

Recommended regimens listed by evidence level.

<table>
<thead>
<tr>
<th>Recommended for Sofosbuvir plus NS5A-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^</th>
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^For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A Inhibitors), genotype 2 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance] - Accessed April 28, 2019.