

Treatment of HCV Genotype 3

This is a PDF version of the following document:

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

Topic 3: [Treatment of HCV Genotype 3](#)

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<https://www.hepatitisc.uw.edu/go/treatment-infection/treatment-genotype-3/core-concept/all>.

Introduction

Background

In the United States, among all persons living with hepatitis C virus (HCV) infection, approximately 10% have HCV genotype 3 infection, with an even higher proportion of HCV genotype 3 among persons who inject drugs.[1,2,3] Individuals with HCV genotype 3, when compared with persons infected with other HCV genotypes, have relatively faster rates of fibrosis progression, higher prevalence of severe (Grade 3) steatosis, and a higher incidence of hepatocellular carcinoma.[4,5,6,7] In the current direct-acting antiviral (DAA) therapy era, HCV genotype 3 infection has been relatively difficult to treat compared with other HCV genotypes, especially in persons with cirrhosis or prior HCV treatment failure. The following discussion regarding initial treatment and retreatment of HCV genotype 3 assumes the person with HCV and their clinician have already made the decision to initiate HCV treatment. This topic review does not address the treatment of HCV genotype 3 in persons with decompensated cirrhosis, renal impairment, acute HCV infection, or post-liver transplantation.

Medications used to Treat Hepatitis C

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 DAAs exert their action at specific steps in the HCV life cycle. There are three major classes of DAA 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.[8,9] Adherence with the treatment regimen is of paramount importance. Thus, individuals should receive detailed counseling regarding the importance of adherence prior to starting therapy, as well as intensive monitoring and follow-up during therapy.

Approach to Choosing HCV Genotype 3 Treatment Regimen

When considering treatment of persons with chronic HCV genotype 3, five major factors influence the choice and duration of therapy: (1) cirrhosis status, (2) prior treatment experience, (3) coexistent renal disease, (4) drug interactions, and (5) medication cost and/or insurance considerations. With certain regimens for treatment-experienced and/or cirrhotic patients, pre-treatment NS5A resistance may also influence both the choice of regimen, duration or inclusion of ribavirin. The following treatment recommendations are based on the AASLD-IDSAs HCV Guidance for persons with HCV genotype 3 infection.[10,11]

- [AASLD-IDSAs HCV Guidance for Treatment-Naïve Patients with Genotype 3 HCV](#)
- [AASLD-IDSAs HCV Guidance for Treatment-Experienced Patients with Genotype 3 HCV](#)

HCV Genotype 3: Initial Treatment

Background

Treatment of HCV genotype 3 infection has emerged in the DAA era as the most treatment-refractory of all the HCV genotypes. The sustained virologic response rates at 12 weeks post treatment (SVR12) with sofosbuvir plus weight-based ribavirin given for 12-16 weeks was substantially lower SVR rates in persons with HCV genotype 3 than with HCV genotype 2.[12,13] The relatively lower SVR12 rates with HCV genotype 3 were improved by using a 12-week course of sofosbuvir plus ribavirin plus peginterferon,[14] or extending the all-oral sofosbuvir plus ribavirin regimen to 24 weeks.[15,16] The dual DAA combination of daclatasvir plus sofosbuvir proved more efficacious than sofosbuvir plus ribavirin combination, but required a longer duration (16 or 24 weeks) in patients with HCV genotype 3 infection and cirrhosis; the role of ribavirin remained unclear when duration was extended.[17,18,19,20] Glecaprevir-pibrentasvir and sofosbuvir-velpatasvir have become the mainstay of DAA therapy for treatment-naïve patients with HCV genotype 3 infection, including those with compensated cirrhosis.[21,22,23,24,25]

Factors to Consider Prior to Choosing Initial Treatment Regimen

For persons chronically infected with genotype 3 hepatitis C, five factors should be considered when choosing the initial treatment regimen and duration: (1) the presence of baseline NS5A resistant variant Y93H (screening required for patients with cirrhosis or prior treatment experience in whom sofosbuvir-velpatasvir or daclatasvir plus sofosbuvir is being considered), (2) presence or absence of cirrhosis and (3) coexistent renal disease, (4) drug interactions, and (5) cost and/or insurance considerations.

AASLD-IDSA HCV Guidance for Initial Treatment of HCV Genotype 3

The following is a summary of recommendations issued in the AASLD-IDSA HCV Guidance. The recommendations listed below are for persons with hepatitis C genotype 3 infection who are treatment naïve.[26,27] 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 1. AASLD-IDSA HCV Guidance for Genotype 3: Initial Treatment Treatment-Naïve Genotype 3 Patients Without Cirrhosis

Recommended and alternative regimens listed alphabetically

Recommended for Treatment-Naïve Genotype 3 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 3 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 Treatment-Naïve Genotype 3 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 I](#), [Level A](#)

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.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 3 without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Table 2. AASLD-IDSA HCV Guidance for Genotype 3: Initial Treatment Treatment-Naïve Genotype 3 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Treatment-Naïve Genotype 3 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 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 3 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

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

Resistance-associated substitution (RAS) testing for Y93H is recommended for cirrhotic patients. If present, ribavirin should be included in the regimen or sofosbuvir-velpatasvir-voxilaprevir should be considered.

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

Alternative for Treatment-Naïve Genotype 3 Patients With 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

This regimen is appropriate to consider for patients with cirrhosis and Y93H.

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

Alternative for Treatment-Naïve Genotype 3 Patients With Compensated Cirrhosis[^]

Daclatasvir	+	Sofosbuvir	±	Ribavirin
<i>*(60 mg) one tablet once daily for 24 weeks</i>		<i>(400 mg) one tablet once daily for 24 weeks</i>		<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>

Resistance-associated substitution (RAS) testing for Y93H is recommended for cirrhotic patients. If present, ribavirin should be included in the regimen or sofosbuvir-velpatasvir-voxilaprevir should be considered.

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.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 3 with compensated cirrhosis [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Studies of Initial Treatment of Adults with HCV Genotype 3

The following key studies support the recommendations for initial treatment of patients with chronic hepatitis C and genotype 3 infection. The medications are listed in alphabetical order.

Daclatasvir plus Sofosbuvir

- [ALLY-3](#): The phase 3 ALLY-3 trial enrolled 152 adults with genotype 3 infection (101 treatment-naïve and 51 treatment-experienced).[17] All persons enrolled received a 12-week course of the oral regimen of daclatasvir (60 mg once daily) plus sofosbuvir (400 mg once daily). Individuals with compensated cirrhosis were allowed in the trial. Among the treatment-naïve participants, SVR12 was achieved in 89% (84 of 94) achieved and SVR12 (97% in those without cirrhosis and 58% in those with cirrhosis).

Glecaprevir-Pibrentasvir

- [ENDURANCE-3](#): In this phase 3 randomized study, investigators compared the efficacy and safety of 8 or 12 weeks of glecaprevir-pibrentasvir versus 12 weeks of sofosbuvir and daclatasvir in non-cirrhotic treatment-naïve adults with HCV genotype 3 infection; 348 individuals were randomized in 2:1 ratio to receive 12 weeks of either glecaprevir-pibrentasvir or sofosbuvir plus daclatasvir whereas 157 were assigned to 8 weeks of glecaprevir-pibrentasvir.[25] For individuals in the 8-week arm, 95% (149 of 157) achieved an SVR12. Similar results were observed in the 12-week arm—95% (222 of 233) achieved an SVR12.
- [SURVEYOR-II \(Part 3\)](#): In this partially randomized, open-label, phase 3 trial, the safety and efficacy of glecaprevir-pibrentasvir was evaluated in treatment-naïve and treatment-experienced adults with HCV genotype 3.[28] Enrollment included 40 treatment-naïve adults with cirrhosis who received or 12 weeks of glecaprevir-pibrentasvir. For the treatment-naïve participants 98% (39 of 40) achieved an SVR12.

Sofosbuvir-Velpatasvir

- [ASTRAL-3](#): The ASTRAL-3 trial was a randomized, open-label phase 3 study that compared sofosbuvir-velpatasvir for 12 weeks with sofosbuvir plus ribavirin for 24 weeks in adults with HCV genotype 3 infection.[22] Of the 552 persons enrolled in the study, 30% had compensated cirrhosis and 26% were treatment-experienced. For the treatment-naïve participants who received sofosbuvir-velpatasvir, 97% (200 of 206) achieved an SVR12, which was significantly better than the 87% (174 of 201) SVR12 rate in treatment-naïve participants who received sofosbuvir plus ribavirin (P

HCV Genotype 3: Retreating Persons who Failed Prior Therapy

Background

Treatment of HCV Genotype 3 infection can be particularly challenging in persons with prior treatment failure, especially those with cirrhosis. Sofosbuvir-velpatasvir is currently the main recommended option for peginterferon plus ribavirin-experienced persons without cirrhosis based on the latest AASLD-IDSA HCV Guidance. In peginterferon plus ribavirin-experienced persons with compensated cirrhosis, the AASLD-IDSA HCV Guidance recommends using triple-class DAA therapy that includes an NS5A, NS3/4 protease inhibitor and NS5B inhibitor, in the form of either elbasvir-grazoprevir plus sofosbuvir or sofosbuvir-velpatasvir-voxilaprevir.

Factors to Consider Prior to Choosing Retreatment Regimen

For retreatment of adults with HCV genotype 3 infection, several factors influence the regimen choice, including (1) the prior regimen (categorized as prior peginterferon plus ribavirin or DAA experience [with or without prior receipt of an NS5A inhibitor]), (2) presence of NS5A resistance-associated substitution Y93H if sofosbuvir-velpatasvir or daclatasvir plus sofosbuvir is being considered, (3) presence or absence of cirrhosis, and (4) medication cost or insurance considerations. The retreatment of individuals with HCV genotype 3 and decompensated cirrhosis, renal impairment, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD-IDSA HCV Guidance for Retreatment of HCV Genotype 3

The following is a summary of AASLD-IDSA HCV Guidance for adults with hepatitis C genotype 3 infection who are treatment-experienced and failed prior therapy with either (1) peginterferon plus ribavirin or (2) DAA (including NS5A inhibitors sofosbuvir).^[29,30,31] 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 3: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically,

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

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

Baseline resistance-associated substitution (RAS) testing for Y93H is recommended. If the Y93H substitution is identified, a different regimen should be used, or weight-based ribavirin should be added as an alternative option.

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

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

<p>Daclatasvir <i>*(60 mg) one tablet once daily for 12 weeks</i></p>	+	<p>Sofosbuvir <i>(400 mg) one tablet once daily for 12 weeks</i></p>
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Baseline RAS testing for Y93H is recommended. If the Y93H substitution is identified, a different regimen should be used, or weight-based ribavirin should be added as an alternative option.

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

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 detailed information.

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

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

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).

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

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

This regimen is appropriate to consider for patients with Y93H.

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 3 patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Table 4. AASLD-IDSA HCV Guidance for Genotype 3: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

<p>Elbasvir-Grazoprevir <i>Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks</i></p>	+	<p>Sofosbuvir <i>(400 mg) one tablet once daily for 12 weeks</i></p>
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Rating: [Class I](#), [Level B](#)

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With 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

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

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

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

+

Ribavirin

1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)

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

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

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

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).

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

Source: AASLD-IDSAs. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 3 patients with compensated cirrhosis. [[AASLD-IDSAs Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Table 5. AASLD-IDSAs HCV Guidance for Genotype 3: Retreatment DAA-Experienced (Including NS5A Inhibitors), Genotype 3 Patients With or Without Compensated Cirrhosis[^]

Recommended for DAA-Experienced (Including NS5A Inhibitors), Genotype 3 Patients 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

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

Recommended for DAA-Experienced (Including NS5A Inhibitors), Genotype 3 Patients 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

1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)

For patients with prior NS5A inhibitor failure and cirrhosis, weight-based ribavirin is recommended.

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

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

Source: AASLD-IDS A. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A inhibitors), genotype 3 patients with or without compensated cirrhosis. [[AASLD-IDS A Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Studies of Retreatment of Adults with HCV Genotype 3

The following key studies support the recommendations for treatment of persons with chronic hepatitis C and genotype 3 infection who are treatment-experienced. The medications are listed in alphabetical order.

Daclatasvir plus Sofosbuvir

- [ALLY-3](#): The phase 3 ALLY-3 trial enrolled 152 adults with HCV genotype 3 infection (101 treatment-naïve and 51 treatment experienced).[17] All participants received a 12-week course of daclatasvir (60 mg once daily) plus sofosbuvir (400 mg once daily). Participants with compensated cirrhosis were allowed in the trial. Overall, SVR12 was achieved in 86% (44 of 51) of the treatment-experienced participants, including a 94% SVR12 rate in those without cirrhosis and 69% in those with cirrhosis.

Elbasvir-Grazoprevir plus Sofosbuvir

- [C-ISLE](#): In this randomized, open-label phase 2 trial, the safety and efficacy of elbasvir-grazoprevir plus sofosbuvir with or without ribavirin was evaluated in treatment-naïve and peginterferon/ribavirin-experienced adults with HCV genotype 3 and compensated cirrhosis.[32] Among the treatment-naïve participants, 23 received 8 weeks of elbasvir-grazoprevir plus sofosbuvir plus ribavirin and 24 received 12 weeks of elbasvir-grazoprevir plus sofosbuvir. The 53 treatment-experienced participants were randomized 1:1:1 to receive (a) elbasvir-grazoprevir plus sofosbuvir for 12 weeks, (b) elbasvir-grazoprevir plus sofosbuvir plus ribavirin for 12 weeks, or (c) elbasvir-grazoprevir plus sofosbuvir for 16 weeks. In an intent-to-treat analysis, the SVR12 rates ranged from 94 to 100% among the treatment arms, with only 2 viral relapses occurring and both were in the 8-week arm. Among the treatment-experienced participants, the SVR12 rates ranged from 94 to 100%, with the only study failures involving 1 person who withdrew consent and 1 who discontinued due to an adverse event.

Glecaprevir-Pibrentasvir

- [SURVEYOR-II \(Part 3\)](#): In this partially randomized, open-label phase 3 trial, 44 treatment-experienced adults with HCV genotype 3 infection (without cirrhosis) were randomized 1:1 to receive either 12 or 16 weeks of glecaprevir-pibrentasvir.[28] In addition, 47 treatment-experienced adults with HCV genotype 3 who had compensated cirrhosis received 16 weeks of glecaprevir-pibrentasvir. Prior treatment experience was with (1) peginterferon (or interferon), with or without ribavirin or (2) sofosbuvir plus ribavirin, with or without peginterferon. An SVR12 was achieved in 96% (45 of 47) of treatment-experienced of the cirrhotic participants who were treated with 16 weeks of glecaprevir-pibrentasvir. In the non-cirrhotic, treatment-experienced group, 91% (20 of 22) of treatment-experienced participants achieved an SVR12 with 12 weeks of glecaprevir-pibrentasvir, compared with 95% (21 of 22) in the 16-week arm.

Sofosbuvir-Velpatasvir

- [ASTRAL-3](#): The ASTRAL-3 trial was a randomized, open-label phase 3 study that compared sofosbuvir-velpatasvir for 12 weeks with sofosbuvir plus ribavirin for 24 weeks in adults with HCV genotype 3 infection.[22] Of the 552 participants enrolled in the study, 26% were treatment-experienced with a prior interferon-containing regimen. For the treatment-experienced recipients of velpatasvir-sofosbuvir 90% (64 of 71) achieved an SVR 12, which was significantly better than the 64% (44 of 69) in the treatment-experienced participants who received sofosbuvir plus ribavirin. For the treatment-experienced persons who received

velpatasvir-sofosbuvir, the SVR12 rates were similar without cirrhosis (91%) and with compensated cirrhosis (89%).

Sofosbuvir-Velpatasvir-Voxilaprevir

- [POLARIS-3](#): In this phase 3, open-labeled trial, adults with HCV genotype 3 infection and compensated cirrhosis who were DAA naïve (prior peginterferon and ribavirin experience permitted) were randomized to receive 8 weeks of sofosbuvir-velpatasvir-voxilaprevir or 12 weeks of sofosbuvir-velpatasvir.^[23] Thirty-one percent were treatment-experienced. For the treatment-experienced participants, the SVR12 rate was 97% (34 of 35) for the sofosbuvir-velpatasvir-voxilaprevir arm and 91% (29 of 32) for the sofosbuvir-velpatasvir arm. All persons with baseline NS5A resistance-associated substitutions achieved an SVR12.
- [POLARIS-4](#): In this phase 3, active-comparator, open-labeled trial, 314 adults with chronic HCV genotype 1, 2, or 3 with prior DAA therapy (but without an NS5A inhibitor) were randomized to receive 12-weeks of therapy with either sofosbuvir-velpatasvir-voxilaprevir or sofosbuvir-velpatasvir. Compensated cirrhosis was present in 46% and prior sofosbuvir exposure in 80% of participants. A total of 104 of enrollees had HCV genotype 3. For these individuals with HCV genotype 3, the SVR12 rates were 94% (51 of 54) for the sofosbuvir-velpatasvir-voxilaprevir group and 85% (44 of 52) for the sofosbuvir-velpatasvir group. Virologic relapse was confirmed at week 4 for 8 individuals with HCV genotype 3 who received sofosbuvir-velpatasvir. Eight of the 16 virologic failures had genotype 3; all 8 had detectable Y93H mutation at the time of treatment failure and were in the sofosbuvir-velpatasvir arm.

Summary Points

- In the DAA era, HCV genotype 3 has emerged as the most difficult HCV genotype to treat.
- For treatment-naïve adults without cirrhosis, two regimens are recommended with equal evidence rating: (1) glecaprevir-pibrentasvir for 8 weeks, or (2) sofosbuvir-velpatasvir for 12 weeks.
- For treatment-naïve adults with compensated cirrhosis, two regimens are recommended: (1) glecaprevir-pibrentasvir for 12 weeks or (2) sofosbuvir-velpatasvir for 12 weeks. Baseline NS5A genotype 3 resistance testing should be performed, and ribavirin should be added to sofosbuvir-velpatasvir if the Y93H mutation is detected.
- For retreatment of HCV genotype 3 in adults without cirrhosis, the recommended regimen is sofosbuvir-velpatasvir for 12 weeks. Baseline NS5A genotype 3 resistance testing should be performed, and ribavirin should be added to sofosbuvir-velpatasvir if the Y93H mutation is detected.
- For retreatment of HCV genotype 3 in adults with compensated cirrhosis and prior peginterferon plus ribavirin experience, two regimens are recommended: (1) elbasvir-grazoprevir plus sofosbuvir for 12 weeks or (2) sofosbuvir-velpatasvir-voxilaprevir for 12 weeks.
- The recommended regimen for retreatment of HCV genotype 3 infection in adults who have failed prior DAA treatment (including with an NS5A inhibitor) consists of sofosbuvir-velpatasvir-voxilaprevir for 12 weeks. In this situation, weight-based ribavirin should be added to this regimen for those with cirrhosis and prior failure with an NS5A inhibitor.
- Treatment of HCV genotype 3 in treatment-naïve adults with compensated cirrhosis and treatment-experienced non-cirrhotic adults, baseline NS5A genotype resistance testing should be performed if treatment with sofosbuvir-velpatasvir or sofosbuvir plus daclatasvir is being considered. Ribavirin should be added to sofosbuvir-velpatasvir or sofosbuvir plus daclatasvir if the Y93H mutation is detected.

Citations

1. Robaey G, Bielen R, Azar DG, Razavi H, Nevens F. Global genotype distribution of hepatitis C viral infection among people who inject drugs. *J Hepatol*. 2016;65:1094-1103.
[\[PubMed Abstract\]](#) -
2. Gordon SC, Trudeau S, Li J, et al. Race, Age, and Geography Impact Hepatitis C Genotype Distribution in the United States. *J Clin Gastroenterol*. 2019;53:40-50.
[\[PubMed Abstract\]](#) -
3. Germer JJ, Mandrekar JN, Bendel JL, Mitchell PS, Yao JD. Hepatitis C virus genotypes in clinical specimens tested at a national reference testing laboratory in the United States. *J Clin Microbiol*. 2011;49:3040-3.
[\[PubMed Abstract\]](#) -
4. McMahon BJ, Bruden D, Townshend-Bulson L, et al. Infection With Hepatitis C Virus Genotype 3 Is an Independent Risk Factor for End-Stage Liver Disease, Hepatocellular Carcinoma, and Liver-Related Death. *Clin Gastroenterol Hepatol*. 2017;15:431-437.e2.
[\[PubMed Abstract\]](#) -
5. Kanwal F, Kramer JR, Ilyas J, Duan Z, El-Serag HB. HCV genotype 3 is associated with an increased risk of cirrhosis and hepatocellular cancer in a national sample of U.S. Veterans with HCV. *Hepatology*. 2014;60:98-105.
[\[PubMed Abstract\]](#) -
6. Bochud PY, Cai T, Overbeck K, et al. Genotype 3 is associated with accelerated fibrosis progression in chronic hepatitis C. *J Hepatol*. 2009;51:655-66.
[\[PubMed Abstract\]](#) -
7. Nkontchou G, Ziou M, Aout M, et al. HCV genotype 3 is associated with a higher hepatocellular carcinoma incidence in patients with ongoing viral C cirrhosis. *J Viral Hepat*. 2011;18:e516-22.
[\[PubMed Abstract\]](#) -
8. Manns MP, Buti M, Gane E, et al. Hepatitis C virus infection. *Nat Rev Dis Primers*. 2017;3:17006.
[\[PubMed Abstract\]](#) -
9. Scheel TK, Rice CM. Understanding the hepatitis C virus life cycle paves the way for highly effective therapies. *Nat Med*. 2013;19:837-49.
[\[PubMed Abstract\]](#) -
10. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Treatment-Naive Genotype 3.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
11. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Treatment-Experienced Genotype 3.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
12. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. *N Engl J Med*. 2013;368:1878-87.
[\[PubMed Abstract\]](#) -
13. Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in

- patients without treatment options. *N Engl J Med.* 2013;368:1867-77.
[\[PubMed Abstract\]](#) -
14. Gane EJ, Stedman CA, Hyland RH, et al. Nucleotide polymerase inhibitor sofosbuvir plus ribavirin for hepatitis C. *N Engl J Med.* 2013;368:34-44.
[\[PubMed Abstract\]](#) -
 15. Zeuzem S, Dusheiko GM, Salupere R, et al. Sofosbuvir and ribavirin in HCV genotypes 2 and 3. *N Engl J Med.* 2014;370:1993-2001.
[\[PubMed Abstract\]](#) -
 16. Foster GR, Pianko S, Brown A, et al. Efficacy of sofosbuvir plus ribavirin with or without peginterferon-alfa in patients with hepatitis C virus genotype 3 infection and treatment-experienced patients with cirrhosis and hepatitis C virus genotype 2 infection. *Gastroenterology.* 2015;149:1462-70.
[\[PubMed Abstract\]](#) -
 17. Nelson DR, Cooper JN, Lalezari JP, et al. All-oral 12-week treatment with daclatasvir plus sofosbuvir in patients with hepatitis C virus genotype 3 infection: ALLY-3 phase III study. *Hepatology.* 2015;61:1127-35.
[\[PubMed Abstract\]](#) -
 18. Kowdley KV, Nelson DR, Lalezari JP, et al. On-treatment HCV RNA as a predictor of sustained virological response in HCV genotype 3-infected patients treated with daclatasvir and sofosbuvir. *Liver Int.* 2016;36:1611-1618.
[\[PubMed Abstract\]](#) -
 19. Hézode C, Lebray P, De Ledinghen V, et al. Daclatasvir plus sofosbuvir, with or without ribavirin, for hepatitis C virus genotype 3 in a French early access programme. *Liver Int.* 2017;37:1314-24.
[\[PubMed Abstract\]](#) -
 20. Sundaram V, Kowdley KV. Dual daclatasvir and sofosbuvir for treatment of genotype 3 chronic hepatitis C virus infection. *Expert Rev Gastroenterol Hepatol.* 2016;10:13-20.
[\[PubMed Abstract\]](#) -
 21. Everson GT, Towner WJ, Davis MN, et al. Sofosbuvir With Velpatasvir in Treatment-Naive Noncirrhotic Patients With Genotype 1 to 6 Hepatitis C Virus Infection: A Randomized Trial. *Ann Intern Med.* 2015;163:818-26.
[\[PubMed Abstract\]](#) -
 22. Foster GR, Afdhal N, Roberts SK, et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med.* 2015;373:2608-17.
[\[PubMed Abstract\]](#) -
 23. Jacobson IM, Lawitz E, Gane EJ, et al. Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials. *Gastroenterology.* 2017;153:113-22.
[\[PubMed Abstract\]](#) -
 24. Kwo PY, Poordad F, Asatryan A, et al. Glecaprevir and pibrentasvir yield high response rates in patients with HCV genotype 1-6 without cirrhosis. *J Hepatol.* 2017;67:263-271.
[\[PubMed Abstract\]](#) -
 25. Zeuzem S, Foster GR, Wang S, et al. Glecaprevir-Pibrentasvir for 8 or 12 Weeks in HCV

Genotype 1 or 3 Infection. N Engl J Med. 2018;378:354-69.

[\[PubMed Abstract\]](#) -

26. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 3 without cirrhosis.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
27. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 3 with compensated cirrhosis
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
28. Wyles D, Poordad F, Wang S, et al. Glecaprevir/Pibrentasvir for HCV Genotype 3 Patients with Cirrhosis and/or Prior Treatment Experience: A Partially Randomized Phase III Clinical Trial. Hepatology. 2017 Sep 19. [Epub ahead of print]
[\[PubMed Abstract\]](#) -
29. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 3 patients with compensated cirrhosis.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
30. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 3 patients without cirrhosis.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
31. 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 3 patients with or without compensated cirrhosis.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
32. Foster GR, Agarwal K, Cramp ME, et al. Elbasvir/grazoprevir and sofosbuvir for hepatitis C virus genotype 3 infection with compensated cirrhosis: A randomized trial. Hepatology. 2018;67:2113-2126.
[\[PubMed Abstract\]](#) -

References

- European Association for Study of the Liver. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J Hepatol. 2014;60:392-420.
[\[PubMed Abstract\]](#) -
- Gane EJ, Pianko S, Roberts SK, et al. Safety and efficacy of an 8-week regimen of grazoprevir plus ruzasvir plus uprifosbuvir compared with grazoprevir plus elbasvir plus uprifosbuvir in participants without cirrhosis infected with hepatitis C virus genotypes 1, 2, or 3 (C-CREST-1 and C-CREST-2, part A): two randomised, phase 2, open-label trials. Lancet Gastroenterol Hepatol. 2017;2:805-13.
[\[PubMed Abstract\]](#) -
- Gane EJ, Schwabe C, Hyland RH, et al. Efficacy of the Combination of Sofosbuvir, Velpatasvir, and the NS3/4A Protease Inhibitor GS-9857 in Treatment-Naïve or Previously Treated Patients With Hepatitis C Virus Genotype 1 or 3 Infections. Gastroenterology. 2016;151:448-456.e1.
[\[PubMed Abstract\]](#) -
- Hagan LM, Yang Z, Ehteshami M, Schinazi RF. All-oral, interferon-free treatment for chronic

hepatitis C: cost-effectiveness analyses. J Viral Hepat. 2013;20:847-57.

[\[PubMed Abstract\]](#) -

- 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.
[\[PubMed Abstract\]](#) -
- Lawitz E, Lalezari JP, Hassanein T, et al. Sofosbuvir in combination with peginterferon alfa-2a and ribavirin for non-cirrhotic, treatment-naive patients with genotypes 1, 2, and 3 hepatitis C infection: a randomised, double-blind, phase 2 trial. Lancet Infect Dis. 2013;13:401-8.
[\[PubMed Abstract\]](#) -
- Lawitz E, Poordad F, Brainard DM, et al. Sofosbuvir with peginterferon-ribavirin for 12 weeks in previously treated patients with hepatitis C genotype 2 or 3 and cirrhosis. Hepatology. 2015;61:769-75.
[\[PubMed Abstract\]](#) -
- Lonardo A, Loria P, Adinolfi LE, Carulli N, Ruggiero G. Hepatitis C and steatosis: a reappraisal. J Viral Hepat. 2006;13:73-80.
[\[PubMed Abstract\]](#) -
- Pianko S, Flamm SL, Shiffman ML, et al. Sofosbuvir Plus Velpatasvir Combination Therapy for Treatment-Experienced Patients With Genotype 1 or 3 Hepatitis C Virus Infection: A Randomized Trial. Ann Intern Med. 2015;163:809-17.
[\[PubMed Abstract\]](#) -
- Poordad F, Landis CS, Asatryan A, et al. High antiviral activity of NS5A inhibitor ABT-530 with paritaprevir/ritonavir and ribavirin against hepatitis C virus genotype 3 infection. Liver Int. 2016;36:1125-32.
[\[PubMed Abstract\]](#) -
- Shiffman ML, Ghany MG, Morgan TR, et al. Impact of reducing peginterferon alfa-2a and ribavirin dose during retreatment in patients with chronic hepatitis C. Gastroenterology. 2007;132:103-12.
[\[PubMed Abstract\]](#) -
- Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. N Engl J Med. 2014;370:211-21.
[\[PubMed Abstract\]](#) -
- Wyles D, Wedemeyer H, Ben-Ari Z, et al. Grazoprevir, ruzasvir, and uprifosbuvir for hepatitis C virus after NS5A treatment failure. Hepatology. 2017;66:1794-1804.
[\[PubMed Abstract\]](#) -
- Zeuzem S, Hultcrantz R, Bourliere M, et al. Peginterferon alfa-2b plus ribavirin for treatment of chronic hepatitis C in previously untreated patients infected with HCV genotypes 2 or 3. J Hepatol 2004;40:993-9.
[\[PubMed Abstract\]](#) -

Figures

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

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

Figure 2 Cost of Medication Regimens used for Initial Treatment Genotype 3 Chronic HCV

This figure shows the approximate cost of a treatment course with AASLD-IDSA recommended regimens for treatment-naïve adults with genotype 3 HCV, including those without cirrhosis and those with compensated cirrhosis. The cost listed is based on available wholesale acquisition price data.

Estimated Cost of Recommended Regimens for Initial Treatment HCV GT3	
Regimens and Duration of Therapy	Cost of Regimen*
Genotype 3 HCV Without Cirrhosis	
Glecaprevir-Pibrentasvir for 8 weeks	\$26,400
Sofosbuvir-Velpatasvir for 12 weeks	\$74,760
Genotype 3 HCV With Compensated Cirrhosis	
Glecaprevir-Pibrentasvir for 12 weeks	\$39,600
Sofosbuvir-Velpatasvir for 12 weeks	\$74,760
*Cost estimates based on Wholesale Acquisition Cost (WAC)	

Table 1. AASLD-IDSA HCV Guidance for Genotype 3: Initial Treatment Treatment-Naïve Genotype 3 Patients Without Cirrhosis

Recommended and alternative regimens listed alphabetically

Recommended for Treatment-Naïve Genotype 3 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 3 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 Treatment-Naïve Genotype 3 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 I](#), [Level A](#)

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.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 3 without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Table 2. AASLD-IDSA HCV Guidance for Genotype 3: Initial Treatment Treatment-Naïve Genotype 3 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Treatment-Naïve Genotype 3 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 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 3 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

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

Resistance-associated substitution (RAS) testing for Y93H is recommended for cirrhotic patients. If present, ribavirin should be included in the regimen or sofosbuvir-velpatasvir-voxilaprevir should be considered.

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

Alternative for Treatment-Naïve Genotype 3 Patients With 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

This regimen is appropriate to consider for patients with cirrhosis and Y93H.

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

Alternative for Treatment-Naïve Genotype 3 Patients With Compensated Cirrhosis[^]

Daclatasvir

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

+

Sofosbuvir

(400 mg) one tablet once daily for 24 weeks

±

Ribavirin

1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks (the daily dose is given in two divided doses)

Resistance-associated substitution (RAS) testing for Y93H is recommended for cirrhotic patients. If present, ribavirin should be included in the regimen or sofosbuvir-velpatasvir-voxilaprevir should be considered.

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.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 3 with compensated cirrhosis [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

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

Recommended and alternative regimens listed by evidence level and alphabetically,

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

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

Baseline resistance-associated substitution (RAS) testing for Y93H is recommended. If the Y93H substitution is identified, a different regimen should be used, or weight-based ribavirin should be added as an alternative option.

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

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

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

Baseline RAS testing for Y93H is recommended. If the Y93H substitution is identified, a different regimen should be used, or weight-based ribavirin should be added as an alternative option.

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

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 detailed information.

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

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

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).

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients Without Cirrhosis

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

This regimen is appropriate to consider for patients with Y93H.

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 3 patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Table 4. AASLD-IDSA HCV Guidance for Genotype 3: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

<p>Elbasvir-Grazoprevir Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks</p>	+	<p>Sofosbuvir (400 mg) one tablet once daily for 12 weeks</p>
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Rating: [Class I](#), [Level B](#)

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With 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

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

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

<p>Sofosbuvir-Velpatasvir Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks</p>	+	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)</p>
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Rating: [Class I](#), [Level B](#)

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 3 Patients With Compensated Cirrhosis[^]

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

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).

[^]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: peginterferon/ribavirin-experienced, genotype 3 patients with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

Table 5. AASLD-IDSA HCV Guidance for Genotype 3: Retreatment DAA-Experienced (Including NS5A Inhibitors), Genotype 3 Patients With or Without Compensated Cirrhosis[^]

Recommended for DAA-Experienced (Including NS5A Inhibitors), Genotype 3 Patients 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
 Rating: [Class I](#), [Level A](#)

Recommended for DAA-Experienced (Including NS5A Inhibitors), Genotype 3 Patients With or Without Compensated Cirrhosis[^]

<p>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></p>	+	<p>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></p>
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For patients with prior NS5A inhibitor failure and cirrhosis, weight-based ribavirin is recommended.

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

[^]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 3 patients with or without compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed April 28, 2019.

