

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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<http://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 infections. Given the relatively high sustained virologic response (SVR) rates with the treatment of genotype 2 historically, the data regarding retreatment of patients with genotype 2 in whom prior therapy failed is somewhat limited. The following discussion regarding initial treatment and retreatment of patients with genotype 2 chronic hepatitis C assumes the patient and their clinician have already made the decision to proceed with hepatitis C therapy. For the regimens included as preferred or alternative in the 2016 American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD/IDSA) guidance for genotype 2 infection, the cost of the preferred and alternative treatment regimens, when including initial treatment and retreatment, range from approximately \$75,000 to \$294,000 ([Figure 1](#)). Although some company-related drug assistance programs provide free medication to certain low-income patients, getting medications paid for remains problematic for many clinicians and patients.

Medications Used to Treat HCV: 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. 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.

Genotype 2: Initial Treatment

Background: Historically, treatment of genotype 2 infection achieved higher sustained virologic response (SVR) rates than with genotype 1 infection, even with a shorter duration of therapy and lower doses of ribavirin. Prior to the availability of direct-acting antiviral agents, the standard of care for treatment-naïve patients with genotype 2 hepatitis C consisted of a 24-week course of peginterferon plus fixed-dose ribavirin, with SVR rates of 75 to 85%. In 2013, the FDA approved a 12-week course with the all-oral regimen of sofosbuvir plus ribavirin for the treatment of genotype 2 infection based on data from several studies showing SVR rates of approximately 95% with this regimen. Several studies reported SVR rates greater than 90% with daclatasvir plus sofosbuvir, thereby providing a ribavirin-free option for patients unable to tolerate ribavirin. Most recently, SVR rates greater than 99% have been observed with a 12-week course of sofosbuvir-velpatasvir, making this regimen the preferred regimen for the treatment of patients with genotype 2 HCV.

Factors to Consider Prior to Choosing Initial Treatment Regimen: For patients chronically infected with genotype 2 hepatitis C, three major factors determine the optimal treatment regimen: (1) whether the patient has previously received and failed therapy, (2) the presence or absence of cirrhosis, and (3) cost. Hepatitis C therapy in patients with decompensated cirrhosis, renal impairment, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD/IDSA Guidance (see [Initial Treatment of HCV Infection](#)): The following is a summary of joint recommendations issued by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). The recommendations listed below are for initial treatment of patients with chronic hepatitis C genotype 2 infection ([Table 1](#)).

Key Studies to Support Recommendations: The following key studies support the recommendations for treatment of patients with chronic hepatitis C and genotype 2 infection who are treatment naïve or who have previously received treatment and had virologic relapse with a regimen that included peginterferon and ribavirin. Click on the study name (blue) to see more details and to view a PowerPoint slide summary.

- [A1444040](#): In study A1444-040, a phase 2 trial involving patients with genotypes 1, 2, and 3, patients received daclatasvir plus sofosbuvir, with or without ribavirin. A total of 44 treatment-naïve patients with genotype 2 or 3 were enrolled in the study, including 26 with genotype 2 infection. The patients with 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 patients with genotype 2 infection 24 (92%) of 26 achieved an SVR12. For the 2 patients 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 patient 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 patients with chronic HCV genotype 1-4 and HIV coinfection, including treatment-naïve and experienced patients. The treatment-naïve patients received an 8-week or 12-week course of daclatasvir plus sofosbuvir. The treatment-naïve group included 17 patients with genotype 2 infection. The SVR12 rates for the treatment-naïve genotype 2 patients were 11 (100%) of 11 in those who received the 12-week course and 5 (83%) of 6 in those treated with an 8-week course of therapy.
- [FISSION](#): This phase 3 trial enrolled 499 treatment-naïve patients with genotype 2 or 3 HCV infection and randomized treatment to 12 weeks of sofosbuvir plus weight-based ribavirin versus 24 weeks of peginterferon plus fixed-dose ribavirin. For patients with genotype 2 infection, 68 (97%) of 70 achieved an SVR12 with sofosbuvir plus ribavirin compared with only 78% with peginterferon plus ribavirin.
- [<POSITRON](#): Patients in this multinational phase 3 trial were enrolled if they had genotype 2 or 3 infection and were (a) not willing to receive interferon, (b) not able to receive interferon,

or (c) were intolerant to a previous course of interferon. A total of 278 patients were randomized to receive a 12-week course of sofosbuvir plus weight-based ribavirin versus placebo. For patients with genotype 2 infection, 101 (93%) of 109 achieved an SVR12 with sofosbuvir plus ribavirin.

- [VALENCE](#): In this phase 3 trial, investigators enrolled 419 treatment-naïve or treatment-experienced patients with genotype 2 or 3 HCV infection. Patients with genotype 2 received a 12-week course of sofosbuvir plus weight-based ribavirin versus placebo. For the treatment-naïve patients with genotype 2 infection, 31 (97%) of 32 who received sofosbuvir plus ribavirin achieved an SVR12.
- [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 patients with chronic HCV genotype 2 infection, including treatment-naïve and treatment-experienced patients. Patients with compensated cirrhosis were permitted and comprised 14% of the total 266 patients enrolled in the study. The SVR12 rate among sofosbuvir-velpatasvir recipients was 99% and was superior to the SVR12 rate of 94% among those who received sofosbuvir plus ribavirin, P-value=0.02. In the treatment-naïve patients who received sofosbuvir-velpatasvir, 114 (99%) of 115 achieved an SVR12. Also, the single patient who did not achieve SVR12 in the sofosbuvir-velpatasvir group had received only one dose of the drug and discontinued after experiencing headache and anxiety. Patients with compensated cirrhosis did equally well as those without cirrhosis.

Genotype 2: Retreating Persons who Failed Prior Therapy

Background: Prior to the introduction of direct-acting antiviral agents, the SVR rates with treatment of genotype 2 infection was approximately 75% to 85%. Accordingly, less 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. With a 12-week course of the dual regimen of sofosbuvir plus ribavirin, the SVR12 rates with retreatment have generally been higher than 85%. Recent results with sofosbuvir-velpatasvir have shown 20 (100%) of 20 treatment-experienced patients with genotype 2 achieved an SVR 12.

Factors to Consider Prior to Choosing Retreatment Regimen: For retreatment of patients with genotype 2 hepatitis C, several major factors influence the optimal regimen for retreatment, including (1) the prior regimen the patient failed, (2) presence or absence of cirrhosis, and (3) cost. 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 Guidance (see [Retreatment of Persons in Whom Prior Therapy has Failed](#)): The following is a summary of joint recommendations issued by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). The recommendations listed below are 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.

Genotype 2: Retreatment

Table 2. Peginterferon plus Ribavirin Treatment-Experienced Patients

Recommended for Retreatment of 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 Retreatment of Genotype 2 patients without Cirrhosis

Daclatasvir <i>60 mg* once daily for 12 weeks</i>	+	Sofosbuvir <i>400 mg once daily for 12 weeks</i>
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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.

Not recommended

Recommended for Retreatment of 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](#)

Alternative for Retreatment of Genotype 2 patients with Compensated Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 16 to 24 weeks* *400 mg once daily for 16 to 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.

Alternative

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 2: Retreatment

Table 3. Sofosbuvir plus Ribavirin Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for Retreatment of Genotype 2 patients regardless of cirrhosis status

Daclatasvir + **Sofosbuvir** ± **Ribavirin**
60 mg once daily for 24 weeks* *400 mg once daily for 24 weeks* *1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks*

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

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.

Recommended for Retreatment of Genotype 2 patients regardless of cirrhosis status

**Sofosbuvir-
Velpatasvir** + **Ribavirin**
*Fixed-dose
combination of
sofosbuvir (400* *1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks*

mg)/velpatasvir (100
mg) one tablet once
daily for 12 weeks

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

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Key Studies to Support Recommendations: The following key studies support the recommendations for retreatment of patients with chronic hepatitis C and genotype 2 infection who previously failed therapy with peginterferon and ribavirin. Click on the study name (blue) to see more details and to view a PowerPoint slide summary.

- [BOSON](#): In the randomized, open-label BOSON trial, investigators enrolled patients with genotype 2 or 3 chronic HCV infection. Those with genotype 2 infection had compensated cirrhosis and all had previously failed therapy. Patients received one of three treatment regimens: sofosbuvir plus ribavirin for 16 weeks, sofosbuvir plus ribavirin for 24 weeks, and sofosbuvir plus ribavirin plus peginterferon alfa-2a for 12 weeks. Among the 592 patients enrolled in the study, 48 (8%) had genotype 2 infection. For the patients with genotype 2 infection, the SVR 12 rates were 87% with the 16-week course of sofosbuvir plus ribavirin, 100% with 24 weeks of sofosbuvir plus ribavirin, and 94% with 12 weeks of sofosbuvir plus ribavirin plus peginterferon.
- [FUSION](#): The FUSION trial was a phase 3 trial that compared a 12-week and 16-week course of sofosbuvir plus ribavirin in treatment-experienced patients with genotype 2 or 3 HCV infection. For patients with genotype 2 infection, 31 (86%) of 36 achieved an SVR12 with the 12-week course and 30 (94%) of 32 had an SVR12 with the 16-week course. Of note, for the 19 patients with genotype 2 infection and cirrhosis, the SVR12 rates were higher with a 16-week course (76%) than with a 12-week course (60%).
- [VALENCE](#): In this phase 3 trial, investigators enrolled 419 treatment-naive or treatment-experienced patients with genotype 2 or 3 HCV infection. Patients with genotype 2 received a 12-week course of sofosbuvir plus ribavirin versus placebo. For the treatment-experienced patients with genotype 2 infection, 37 (90%) of 41 achieved an SVR12. Among these treatment-experienced patients, with genotype 2 infection, SVR12 was obtained in 7 (78%) of 9 with cirrhosis compared with 30 (94%) of 32 without cirrhosis.
- [LONESTAR-2](#): In the phase 2 LONESTAR-2 trial, treatment-experienced patients with genotype 2 or 3 infection received open-label sofosbuvir plus peginterferon plus ribavirin for 12 weeks. Among the treatment-experienced patients with genotype 2 infection, 22 (96%) of 23 achieved an SVR12. Of note, more than 50% of the patients in this study had cirrhosis and 13 (93%) of 14 patients with genotype 2 infection and cirrhosis obtained an SVR12.
- [ASTRAL-2](#): In the ASTRAL-2 trial, among the 19 treatment experienced patients who received a 12-week course of sofsobuvir-velpatasvir, 100% achieved and SVR 12.

Genotype 2: Treatment Regimens under Study

Treatment Regimens under Study for Patients with HCV Genotype 2: A variety of new combinations are currently being examined for genotype 2 infection. Most of these are interferon- and ribavirin-free and some will examine shorter-courses (6 or 8 weeks) therapy.

- **Paritaprevir-Ritonavir-Ombitasvir:** This combination has been studied in treatment-experienced Japanese patients with genotype 2 infection. Patients received ombitasvir 25 mg plus paritaprevir-ritonavir 100/100 mg or 150/100 mg for 12 weeks. The SVR24 rate was higher in patients with subtype 2a (90%) than 2b (27%). This combination is being studied further with the addition of sofosbuvir (with or without ribavirin) in 6, 8 or 12 week durations.
- **ABT-493 plus ABT-450:** ABT-493, a pangenotypic NS3/4A protease inhibitor, and ABT-530, a potent NS5A inhibitor will be studied, with or without ribavirin, in a variety of doses and durations (8 or 12 weeks) in both treatment-naïve and treatment-experienced patients with genotype 2 or 3 infection.
- **Ledipasvir-Sofosbuvir:** Ledipasvir has reduced activity against genotype 2 compared with genotype 1 but is currently being studied in genotype 2 patients for 8 or 12 weeks.

Summary Points

- The recommended regimens for initial treatment of HCV genotype 2 in patients without cirrhosis consists of sofosbuvir-velpatasvir for 12 weeks; the alternative is daclatasvir plus sofosbuvir for 12 weeks. Both of these regimens typically have SVR12 rates greater than 90%.
- For initial treatment of genotype 2 patients with compensated cirrhosis, the recommended regimen is sofosbuvir-velpatasvir for 12 weeks; the alternative, daclatasvir plus sofosbuvir, should be given for 16 to 24 weeks.
- For the retreatment of genotype 2 patients, with or without compensated cirrhosis, the recommended and alternative regimens are the same as for initial therapy of genotype 2.
- For retreatment of genotype 2 patients who previously failed therapy with sofosbuvir plus ribavirin, the recommended regimens, with equal rating are (1) daclatasvir plus sofosbuvir (with or without ribavirin) for 24 weeks or (2) sofosbuvir-velpatasvir plus ribavirin for 12 weeks; the same regimens are used with or without compensated cirrhosis.
- The demand and interest for studies that examine future therapies for genotype 2 will likely be somewhat limited given the very high SVR rates with the 12-week course of sofosbuvir-velpatasvir.

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Figures

Figure 1 Cost of Medication Regimens used to Treat Genotype 2 Chronic HCV

This figure shows the approximate cost of different preferred and alternative regimens used for treatment-naive patients with genotype 2 chronic HCV, including cost in patients without cirrhosis and with compensated cirrhosis. Cost based on available wholesale acquisition price data.

Estimated Cost of Regimens for Treatment HCV GT 2 HCV	
Regimen and Duration of Therapy	Cost of Regimen*
GT 2 HCV without Cirrhosis	
Sofosbuvir-Velpatasvir x 12 weeks	\$74,760
Daclatasvir + Sofosbuvir x 12 weeks	\$147,000
GT 2 HCV with Compensated Cirrhosis	
Sofosbuvir-Velpatasvir x 12 weeks	\$74,760
Daclatasvir + Sofosbuvir x 16 weeks	\$196,000
Daclatasvir + Sofosbuvir x 24 weeks	\$294,000
*Cost estimates based on Wholesale Acquisition Cost (WAC)	

Genotype 2: Initial Treatment

Table 1. Treatment-Naive Patients

Recommended for 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 Genotype 2 patients without Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 12 weeks* *400 mg 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.

Not recommended

Recommended for 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](#)

Alternative for Genotype 2 patients with Compensated Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 16 to 24 weeks* *400 mg once daily for 16 to 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.

Alternative

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 2: Retreatment

Table 2. Peginterferon plus Ribavirin Treatment-Experienced Patients

Recommended for Retreatment of 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 Retreatment of Genotype 2 patients without Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 12 weeks* *400 mg 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.

Not recommended

Recommended for Retreatment of 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](#)

Alternative for Retreatment of Genotype 2 patients with Compensated Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 16 to 24 weeks* *400 mg once daily for 16 to 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.

Alternative

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 2: Retreatment

Table 3. Sofosbuvir plus Ribavirin Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for Retreatment of Genotype 2 patients regardless of cirrhosis status

Daclatasvir <i>60 mg* once daily for 24 weeks</i>	+	Sofosbuvir <i>400 mg once daily for 24 weeks</i>	±	Ribavirin <i>1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks</i>
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Rating: [Class IIa](#), [Level C](#)

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.

Recommended for Retreatment of Genotype 2 patients regardless of cirrhosis status

Sofosbuvir- Velpatasvir <i>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (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</i>
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Rating: [Class IIa](#), [Level C](#)

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

