

Elbasvir-Grazoprevir (*Zepatier*)

Drug Summary

Table of Contents

- [Elbasvir-Grazoprevir \(*Zepatier*\)](#)
- [Class and Mechanism](#)
- [Manufacturer for United States](#)
- [FDA Status](#)
- [Indications](#)
- [Contraindications](#)
- [Dosing](#)
- [Clinical Use](#)
- [Cost and Medication Access](#)
- [Adverse Effects](#)
- [Major Drug Interactions](#)
- [Resistance](#)
- [Full Prescribing Information](#)
- [Summary](#)

Class and Mechanism

Elbasvir-grazoprevir (*Zepatier*) ([Figure 1](#)) is an oral fixed-dose combination of an NS5A replication complex inhibitor (elbasvir), and a “later”-generation HCV NS3/4A protease inhibitor (grazoprevir). Elbasvir (formerly MK-8742) is a small-molecule inhibitor of nonstructural protein 5A and possesses in vitro activity against most major HCV genotypes and some viral variants resistant to earlier NS5A inhibitors. Grazoprevir (formerly MK-5172) is a macrocyclic compound that reversibly binds to the HCV NS3/4A protease, an enzyme responsible for cleaving and processing the HCV-encoded polyprotein. It is distinct from earlier-generation protease inhibitors in its potent in vitro activity against a broader array of HCV genotypes, as well activity against some of the major resistance-associated variants (R155K and D168Y) resulting from failure with first-generation protease inhibitors.

Manufacturer for United States

The fixed-dose combination medication elbasvir and grazoprevir (*Zepatier*) is manufactured by Merck & Co., Inc.

FDA Status

On January 28, 2016, the fixed-dose combination elbasvir-grazoprevir (*Zepatier*) was approved by the United States FDA for the treatment of chronic hepatitis C genotypes 1 or 4 infection in adults.

Indications

The fixed dose combination elbasvir-grazoprevir (50 mg/100 mg) is FDA-approved for the treatment of chronic hepatitis C genotypes 1 or 4 with the following specific requirements based on genotype, prior treatment experience, and presence of baseline polymorphisms at amino acid positions 28, 30, 31, or 93. It is recommended that patients with HCV genotype 1a infection undergo resistance testing prior to initiation of treatment with elbasvir-grazoprevir for the presence of virus with NS5A resistance-associated polymorphisms, as this will determine the duration and addition of ribavirin to the treatment regimen. For patients with HCV/HIV-1 coinfection, the dosage and duration are the same as listed below.

Elbasvir-Grazoprevir for Genotypes 1 or 4 (with or without cirrhosis)

- Genotype 1a, treatment-naïve or peginterferon/ribavirin-experienced* (without baseline NS5A polymorphisms[^]): Elbasvir-grazoprevir for 12 weeks
- Genotype 1a, treatment-naïve or peginterferon/ribavirin-experienced* (with baseline NS5A polymorphisms[^]): Elbasvir-grazoprevir plus ribavirin for 16 weeks
- Genotype 1b, treatment-naïve or peginterferon/ribavirin-experienced*: Elbasvir-grazoprevir for 12 weeks
- Genotype 1a[#] or 1b, peginterferon/ribavirin/protease inhibitor-experienced⁺: Elbasvir-grazoprevir plus ribavirin for 12 weeks
- Genotype 4, treatment-naïve: Elbasvir-grazoprevir for 12 weeks
- Genotype 4, peginterferon/ribavirin-experienced*: Elbasvir-grazoprevir plus ribavirin for 16 weeks

*Patients who have failed therapy with peginterferon alfa plus ribavirin

[^]One or more polymorphisms at the amino acid positions 28, 30, 31, or 93.

The optimal treatment duration for peginterferon/ribavirin/protease inhibitor-experienced patients with genotype 1a and one or more baseline NS5A resistance-associated polymorphisms has not been established.

⁺Patients who have failed therapy with peginterferon alfa plus ribavirin plus an HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir)

Contraindications

Elbasvir-grazoprevir is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh Class B or C). In addition, elbasvir-grazoprevir is contraindicated with concomitant use of organic ion transporter polypeptide 1B (OATP1B) inhibitors, strong inducers of cytochrome P450 3A (CYP3A), and efavirenz ([Figure 2](#)). When elbasvir-grazoprevir is coadministered with ribavirin, the contraindications for ribavirin apply to the use of the combination regimen.

Dosing

Elbasvir-grazoprevir is available as a fixed-dose, coformulated tablet that contains 50 mg of elbasvir and 100 mg of grazoprevir ([Figure 3](#)).

- The recommended dose is one tablet taken orally once daily, with or without food.
- No dosage adjustment is recommended for elbasvir-grazoprevir in patients with renal insufficiency, including patients with end-stage renal disease or patients on hemodialysis.
- For patients with mild hepatic impairment (Child-Pugh Class A), no dose adjustment of elbasvir-grazoprevir is recommended. Elbasvir-grazoprevir is contraindicated for use in patients with moderate to severe hepatic impairment (Child-Pugh Class B or C).
- When ribavirin is used with elbasvir-grazoprevir in patients with a CrCl greater than 50 mL/min, it should be given as weight-based dosing in two divided doses with food (weight less than 66 kg=800 mg/day; 66 to 88 kg=1000 mg/day; 81 to 105 kg=1200 mg/day; greater than 105 kg=1400 mg/day). For patients with CrCl less than 50 mL/min, the dose of ribavirin should be adjusted to be consistent with the recommendations in the ribavirin package insert.

Clinical Use

Elbasvir-grazoprevir has primarily been studied as an all-oral (interferon-free) combination regimen in treatment-naïve and treatment-experienced patients with genotype 1 or 4 chronic HCV infection. The phase 3 C-EDGE trials have evaluated elbasvir-grazoprevir, with or without ribavirin (typically given for 12 weeks) and have demonstrated SVR12 rates in the 92 to 97% range. This combination elbasvir-grazoprevir appears to have comparable efficacy in patients with HCV and HIV coinfection as those with HCV mono-infection. The C-SURFER study demonstrated excellent SVR12 rates in patients with Stage 4 or 5 kidney disease, including those on hemodialysis. Elbasvir-grazoprevir has similar efficacy in patients with or without cirrhosis, but it should not be used in patients with moderate to severe hepatic impairment (Child-Pugh Class B or C).

Cost and Medication Access

Merck has established a list price of \$54,600 for a 12-week treatment course. For patients needing a 16-week course, the list price is \$72,800.

- Merck has an active Patient Assistance Program for patients who cannot obtain or afford elbasvir-grazoprevir. Information on the program can be obtained at Merck Patient Assistance Program ([Merck Helps](#)) website or by calling 1-800-405-5810.
- Merck has also developed a co-pay assistance program. There are specific conditions that apply. Information to help patients get access and support to elbasvir-grazoprevir is available on the [Merck Access and Support Services](#) website.

Adverse Effects

Using pooled data from phase 2 and 3 trials (N=834), the most common adverse observed in

patients receiving elbasvir-grazoprevir were fatigue (11%), headache (10%), and nausea (5%). Elevations in alanine aminotransferase levels (ALT) to greater than 5 times the upper limit of normal occurred in 1% of subjects, typically occurring at or after 8 weeks of therapy, with most resolving at or after the completion of therapy. To date, the rash and photosensitivity noted with earlier protease inhibitors has not been a problem in patients receiving elbasvir-grazoprevir.

Major Drug Interactions

Concomitant use of elbasvir-grazoprevir with OATP1B inhibitors can cause significant increases in the plasma levels of grazoprevir; thus, these combinations are contraindicated. The concomitant use of elbasvir-grazoprevir with strong CYP3A inducers or efavirenz can result in significant lowering of elbasvir and grazoprevir plasma levels, which may result in reduced efficacy of elbasvir-grazoprevir; accordingly, these combinations are contraindicated. Use of elbasvir-grazoprevir is not recommended with moderate CYP3A inducers or with certain strong CYP3A inhibitors. See the elbasvir-grazoprevir (*Zepatier*) [Full Prescribing Information](#) for a detailed description of drug-drug interactions that may occur when using elbasvir-grazoprevir.

Resistance

Patients with HCV genotype 1a infection should undergo HCV RNA NS5A resistance testing prior to initiation of treatment with elbasvir-grazoprevir, since results of the resistance testing will determine treatment duration and the addition of ribavirin. This recommendation is based on data that patients with HCV genotype 1a with one or more of the HCV NS5A baseline polymorphisms at positions M28, Q30, L31, or Y93 have reduced efficacy with a 12-week treatment course of elbasvir-grazoprevir. Specifically, with the presence of one or more of these four polymorphisms in patients with genotype 1a, the SVR12 rates were 70% (39/56) with a 12-week course of elbasvir-grazoprevir. In contrast, in patients with genotype 1a (and one or more of the the four polymorphisms) the SVR rates were 100% (6/6) with a 16-week course of elbasvir-grazoprevir plus ribavirin. Accordingly, based on available data, in the presence of one or more of these polymorphisms in a patient with genotype 1a warrants the addition of ribavirin to elbasvir-grazoprevir, and extending therapy from 12 to 16 weeks. Among patients in the United States with genotype 1a enrolled in the clinical trials, the prevalence of one or more of these polymorphisms (at positions 28, 30, 31, or 93) was 12%.

Pooled analysis of drug resistance among the 50 patients who experienced treatment failure in the registration studies for elbasvir-grazoprevir revealed that treatment-emergent NS3 substitutions occurred in 78% of genotype 1a patients, 25% of genotype 1b patients, and 40% of genotype 4, with A156T and D168A occurring as the most frequent mutations in patients with genotype 1a. These two resistance-associated variants can confer resistance to grazoprevir and other protease inhibitors. Specific NS5A substitutions occurred in 81% of patients with genotype 1a who failed therapy, 88% of genotype 1b, and in all of those with genotype 4. Elbasvir remains active in vitro against M28V and Q30L genotype 1a NS5A variants and L28M/V, R30Q, L31V, and Y93C, which can confer resistance to other NS5A inhibitors. Other NS5A substitutions aside from those mentioned can reduce the activity of elbasvir against genotype 1a or 1b.

Several commercial laboratories offer HCV RNA NS5A resistance testing, including [Quest](#) and [Monogram \(Labcorp\)](#) and [Mayo Medical Laboratories](#).

Full Prescribing Information

Elbasvir-grazoprevir (Zepatier) [Full Prescribing Information](#).

Summary

Elbasvir-grazoprevir provides a safe, very effective, well-tolerated, all oral, one-pill once-daily option for the treatment-naïve and treatment-experienced patients with genotype 1 or 4 infection. Patients with genotype 1a will need resistance testing prior to initiation of therapy and presence of a polymorphism at amino acid positions 28, 30, 31, or 93 requires addition of ribavirin and extension of therapy from 12 to 16 weeks. Based on the C-SURFER data, this regimen is particularly attractive for HCV-infected patients with advanced kidney disease. Although data are limited, the triple combination of elbasvir-grazoprevir plus sofosbuvir may provide an additional potent ribavirin-free 12-week regimen for genotype 3 patients, but more data are needed to establish whether this 12-week triple regimen is effective in cirrhotic patients with genotype 3 infection. The announced list price for elbasvir-grazoprevir (\$54,600) is significantly lower than other first-line regimens and should enable broad patient access from private insurance companies and federally-funded programs.

Clinical Trials

C-EDGE CO-STAR

In this randomized, phase 3, placebo-controlled trial, investigators enrolled 301 treatment-naïve patients with chronic HCV genotype 1, 4, or 6 to receive a 12-week course of elbasvir plus grazoprevir; all subjects enrolled had a history of injection drugs and all were receiving opiate agonist therapy. In the trial, 201 subjects received elbasvir plus grazoprevir at enrollment (immediate treatment arm) and 100 subjects received placebo for 12 weeks, followed by treatment with elbasvir plus grazoprevir (deferred treatment arm). At baseline, 58% of the patients in the study had a positive urine drug screen (for a substance other than an opioid agonist). Most of the patients (76%) had genotype 1 infection and 21% had cirrhosis. The SVR12 results were available only for the immediate treatment group and 95% of patients achieved an SVR12 (when excluding patients who discontinued the trial for non-treatment related reasons). The results were similar regardless of whether the baseline urine drug screen was positive. Adherence with medications was excellent, with 99% of patients taking at least 90% of the medication.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-EDGE Coinfection

In this prospective single-arm, open-label clinical trial, 218 patients with chronic hepatitis C genotype 1, 4, or 6 and HIV coinfection received the fixed-dose combination of elbasvir-grazoprevir once daily for 12 weeks. Nearly all (97%) patients were on antiretroviral therapy with HIV viral suppression and the median CD4 cell count was 568 cells/mm³; 86% had genotype 1a or 1b infection and 35 (16%) had compensated cirrhosis. The overall SVR12 rate was 96% by primary analysis, with the breakdown by genotype showing 96.5% for genotype 1a, 95.5% for genotype 1b and 96.4% for genotype 4. All cirrhotic patients achieved an SVR12. When patients who did not achieve an SVR12 due to treatment discontinuation or reinfection were excluded, the overall SVR12 rate was 97%.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-EDGE Treatment-Experienced

In this randomized, open-label, phase 3 trial, 420 patients with genotype 1, 4, or 6 hepatitis C infection and a history of treatment failure with peginterferon and ribavirin received elbasvir-grazoprevir (50/100 mg), with or without ribavirin, for 12 or 16 weeks. Among patients who received a 12-week regimen, the SVR12 rate was 94% for elbasvir-grazoprevir with ribavirin and 92% for elbasvir-grazoprevir without ribavirin. In the 16-week treatment arms, the SVR12 rate was 97% and 92% for elbasvir-grazoprevir, with and without ribavirin respectively. Notably, of the 12 patients with genotype 1a who experienced viral relapse, 10 had evidence of a baseline NS5A resistance-associated variant.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-EDGE Treatment-Naïve

In this randomized phase 3 trial, the safety and efficacy of the fixed-dose combination of elbasvir-grazoprevir (50/100 mg) once daily was evaluated in treatment-naïve patients with genotype 1, 4, or

6 hepatitis C infection, with or without compensated cirrhosis. Investigators randomized (in a 3:1 ratio) 421 patients to immediate versus delayed treatment arms. In the latter group, patients received a placebo for 12 weeks, followed by a 4-week interval, followed by elbasvir-grazoprevir for 12 weeks. The overall SVR12 rate was 95%, with rates of 92% for genotype 1a, 99% for genotype 1b, 100% for genotype 4, and 80% for genotype 6. Among the 70 cirrhotic patients enrolled in the trial, 97% achieved an SVR12 with no statistically significant difference compared with non-cirrhotic patients.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-SALVAGE

In this open-label, single-arm, phase 2 trial, treatment-experienced patients with genotype 1 HCV and previous failure of peginterferon/ribavirin (PR) and an earlier-generation protease inhibitor (boceprevir, telaprevir, or simeprevir) were treated with elbasvir plus grazoprevir and ribavirin for 12 weeks. Patients with compensated cirrhosis were permitted and comprised 43% of the total 79 patients enrolled in the study. At 24 weeks post treatment, SVR occurred in 76 (96%) patients. There were 3 relapses (2 in genotype 1a and 1 in genotype 1b); all 3 relapsers had experienced virologic failure on a prior PI-based regimen and had NS3 variants detected at baseline.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-SCAPE

In this phase 2, open-label, randomized trial, investigators examined the safety and efficacy of different combinations of elbasvir plus grazoprevir, with or without ribavirin, for 12 weeks in patients with HCV genotype 2 and genotypes 4, 5, or 6 infection (with and without cirrhosis). Patients with genotype 2 infection were randomized to receive (a) elbasvir 50 mg plus grazoprevir 100 mg plus ribavirin or (b) grazoprevir 100 mg on its own with ribavirin. Patients with HCV genotype 4, 5, or 6 were randomized to receive elbasvir 50 mg plus grazoprevir 100 mg, with or without ribavirin. Among patients with genotype 2 infection, 80% achieved an SVR12 with the three drug-regimen of elbasvir plus grazoprevir plus ribavirin, whereas 73% did so with dual regimen of grazoprevir plus ribavirin. In subset analysis, patients with baseline HCV RNA less than or equal to 2 million IU/mL were more likely respond than those with viral levels greater than 2 million IU/mL. The SVR12 rates were 100%, 100%, and 90% for the 18 patients with genotype 4, 5, or 6 who received elbasvir plus grazoprevir plus ribavirin (72% for the 18 patients who did not receive ribavirin).

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-SURFER

In this phase 3, randomized study, investigators enrolled 224 patient with hepatitis C genotype 1 and chronic renal disease, including patients on hemodialysis, to receive immediate treatment with 12 weeks of therapy with elbasvir plus grazoprevir, or deferred therapy. Subjects in the deferred group received placebo during the first 12 weeks and use of placebo was considered important as a comparator for safety purposes, particularly due to safety concerns in this patient population with advanced renal disease. Overall, 80% of the patients enrolled in the trial were treatment-naïve and 76% were on hemodialysis. Among the 116 patients who completed therapy, 115 (99%) achieved an SVR12. Six patients were excluded from the modified full analysis set population, but all six had HCV

RNA levels less than 15 IU/ml at that time of study discontinuation. The safety profile observed in patients who received grazoprevir plus elbasvir was comparable to that seen in patients receiving placebo.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-SWIFT

In this open-label phase 2 trial, investigators evaluated the efficacy of shorter durations (4, 6, or 8 weeks) of fixed-dose elbasvir-grazoprevir, given in combination with sofosbuvir, in treatment-naïve patients with HCV genotype 1 (n=102) or genotype 3 (n=41) infection, with and without compensated cirrhosis. Among the genotype 1 patients without cirrhosis who were treated with 6 weeks of therapy, 87% achieved an SVR12, compared with only 33% among those who had 4 weeks of therapy. Better SVR12 rates were obtained in cirrhotic patients with genotype 1 who had 8 weeks of treatment (94%) than with 6 weeks of therapy (80%). Non-cirrhotic patients with genotype 3 infection had excellent SVR12 rates (93% with 8 weeks of therapy and 100% with 12 weeks of therapy); for the cirrhotic patients, 91% achieved an SVR12 with 12 weeks of therapy.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-WORTHY

In this open-label, phase 2 trial involving patients with genotype 1 hepatitis C, treatment-naïve patients with compensated cirrhosis (cohort 1, n=123) and treatment-experienced patients with a prior null response to peginterferon plus ribavirin (cohort 2, n=130) were randomized to receive elbasvir plus grazoprevir, with or without ribavirin, for 12 or 18 weeks. In the cirrhotic cohort, 90% to 97% of patients achieved an SVR12; in the null responder cohort, SVR12 occurred in 91% to 100% of patients. The SVR12 rate for null cirrhotics (historically the most treatment refractory) was 94% for genotype 1a and 100% for genotype 1b. A subgroup analysis did not show a significant benefit of adding ribavirin to elbasvir plus grazoprevir.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

C-WORTHY Coinfection

This was a randomized, open-label, phase 2 trial of elbasvir plus grazoprevir, with or without ribavirin, in treatment-naïve HCV monoinfected patients without cirrhosis or patients with HIV and HCV coinfection without cirrhosis; the C-WORTHY Coinfection was a substudy conducted within a larger C-WORTHY study. In the monoinfected group 159 patients received different combinations of elbasvir plus grazoprevir that varied by elbasvir dose (20 or 50 mg), duration (8 or 12 weeks), and addition of ribavirin. In the HCV-HIV coinfection group, 59 patients were randomized to receive either elbasvir (50 mg) plus grazoprevir (100 mg), with or without ribavirin, for 12 weeks. In the HCV-monoinfected patient group, SVR12 was achieved in 80% of patients who received 8 weeks of therapy (with ribavirin), 93% with 12 weeks of therapy (with ribavirin), and 98% with 12 weeks of therapy (without ribavirin). For the HCV coinfecting patients, the SVR12 rates with 12 weeks of therapy were 97% (with ribavirin) and 87% (without ribavirin). These combinations were generally well-tolerated with fatigue, headache, and nausea the most common side effects.

View Clinical Trial: [In your Browser](#) | [Download PDF](#)

Figures

Figure 1 Packaging - Elbasvir-Grazoprevir (Zepatier)

Photograph courtesy of Merck & Co., Inc.



Figure 2 Medication Contraindications

Source: Elbasvir-Grazoprevir (Zepatier) Prescribing Information

Drugs that are Contraindicated for Use with Elbasvir-Grazoprevir*	
Organic ion transporter polypeptide 1B (OATP1B) inhibitors	
Antimycobacterials	Rifampin
HIV medications	Atazanavir Darunavir Lopinavir Saquinavir Tipranavir
Immunosuppressants	Cyclosporine
Strong CYP3A Inducers	
Anticonvulsants	Phenytoin Carbamazepine
Herbal products	St. John's Wort (<i>Hypericum perforatum</i>)
HIV medications	Efavirenz [†]
*This is not a complete list of all drugs that inhibit OAT1B or strongly induce CYP3A	
[†] Efavirenz is listed as a strong CYP3A inducer because it reduced grazoprevir exposure by ≥80%	

Figure 3 Pill - Elbasvir-Grazoprevir (Zepatier)

Photograph courtesy of Merck & Co., Inc.



References

- Brown A, Hezode C, Zuckerman E, et al. C-SCAPE: efficacy and safety of 12 weeks of grazoprevir ± elbasvir ± ribavirin in patients with HCV GT2, 4, 5 or 6 infection. Presented at the 50th Annual Meeting of the European Association for the Study of the Liver, Vienna, Austria; April 22-26, 2015. Abstract P0771.
- Buti M, Gordon SC, Zuckerman E, et al. Grazoprevir, Elbasvir, and Ribavirin for Chronic Hepatitis C Virus Genotype 1 Infection After Failure of Pegylated Interferon and Ribavirin With an Earlier-Generation Protease Inhibitor: Final 24-Week Results From C-SALVAGE. *Clin Infect Dis.* 2016;62:32-6.
[[PubMed Abstract](#)]
- Carrion AF, Martin P. Safety and efficacy of elbasvir and grazoprevir for treatment of hepatitis C. *Expert Opin Drug Saf.* 2016;15:883-90.
[[PubMed Abstract](#)]
- Coburn CA, Meinke PT, Chang W, et al. Discovery of MK-8742: an HCV NS5A inhibitor with broad genotype activity. *ChemMedChem.* 2013;8:1930-40.
[[PubMed Abstract](#)]
- Dore G, Altice F, Litwin AH, et al. C-EDGE CO-STAR: efficacy of grazoprevir and elbasvir in persons who inject drugs (PWID) receiving opioid agonist therapy. Presented at the 2015 Annual Meeting of the American Association for the Study of Liver Diseases, San Francisco; November 13-17, 2015. Abstract 40.
- Forns X, Gordon SC, Zuckerman E, et al. Grazoprevir and elbasvir plus ribavirin for chronic HCV genotype-1 infection after failure of combination therapy containing a direct-acting antiviral agent. *J Hepatol.* 2015;63:564-72.
[[PubMed Abstract](#)]
- Howe AY, Black S, Curry S, et al. Virologic resistance analysis from a phase 2 study of MK-5172 combined with pegylated interferon/ribavirin in treatment-naïve patients with hepatitis C virus genotype 1 infection. *Clin Infect Dis.* 2014;59:1657-65.
[[PubMed Abstract](#)]
- Jacobson IM, Asante-Appiah E, Wong P, et al. Prevalence and Impact of Baseline NS5A Resistance-Associated Variants (RAVs) on the Efficacy of Elbasvir/Grazoprevir (EBR/GZR) Against GT1a Infection - 16 Weeks vs 12 weeks. Presented at the 66th Annual Meeting of the American Association for the Study of Liver Diseases. San Francisco, CA. November 13-17, 2015.
- Jacobson IM, Poordad F, Firpi-Morell R, et al. Efficacy and safety of grazoprevir and elbasvir in hepatitis C genotype 1-infected patients with Child-Pugh class B cirrhosis (C-SALT). Presented at the 50th Annual Meeting of the European Association for the Study of the Liver, Vienna; April 22-26, 2015. Abstract O008.
[[PubMed Abstract](#)]
- Kwo P, Gane E, Peng CY, et al. Efficacy and safety of grazoprevir/elbasvir +/- RBV for 12 or 16 weeks in patients with HCV G1, G4, or G6 infection who previously failed peginterferon/RBV: C-EDGE treatment-experienced. Presented at the 50th Annual Meeting of the European Association for the Study of the Liver, Vienna; April 22-26, 2015. Abstract P0886.
- Lagging M, Brown A, Mantry PS, et al. Grazoprevir plus peginterferon and ribavirin in treatment-naïve patients with hepatitis C virus genotype 1 infection: a randomized trial. *J Viral Hepat.* 2015;23:80-8.
[[PubMed Abstract](#)]
- Lahser FC, Bystol K, Curry S, et al. The Combination of Grazoprevir, a Hepatitis C Virus (HCV) NS3/4A Protease Inhibitor, and Elbasvir, an HCV NS5A Inhibitor, Demonstrates a High Genetic Barrier to Resistance in HCV Genotype 1a Replicons. *Antimicrob Agents Chemother.* 2016;60:2954-64.
[[PubMed Abstract](#)]
- Lawitz E, Gane E, Pearlman B, et al. Efficacy and safety of 12 weeks versus 18 weeks of treatment with grazoprevir (MK-5172) and elbasvir (MK-8742) with or without ribavirin for hepatitis C virus genotype 1 infection in previously untreated patients with cirrhosis and

- patients with previous null response with or without cirrhosis (C-WORTHY): a randomised, open-label phase 2 trial. *Lancet*. 2015;385:1075-86.
[[PubMed Abstract](#)]
- Manns MP, Vierling JM, Bacon BR, et al. The combination of MK-5172, peginterferon, and ribavirin is effective in treatment-naïve patients with hepatitis C virus genotype 1 infection without cirrhosis. *Gastroenterology*. 2014;147:366-76.e6.
[[PubMed Abstract](#)]
 - Poordad F, Lawitz E, Gutierrez J, et al. C-SWIFT: Grazoprevir/elbasvir + sofosbuvir in cirrhotic and noncirrhotic, treatment-naïve patients with hepatitis C virus genotype 1 infection, for durations of 4, 6, or 8 weeks and genotype 3 infection for durations of 8 or 12 weeks. Presented at the 50th Annual Meeting of the European Association for the Study of the Liver, Vienna; April 22-26, 2015. Abstract O006.
 - Rockstroh JK, Nelson M, Katlama C, et al. Efficacy and safety of grazoprevir (MK-5172) and elbasvir (MK-8742) in patients with hepatitis C virus and HIV co-infection (C-EDGE CO-INFECTION): a non-randomised, open-label trial. *Lancet HIV*. 2015;2:e319-27.
[[PubMed Abstract](#)]
 - Roth D, Nelson DR, Bruchfeld A, et al. Grazoprevir plus elbasvir in treatment-naïve and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4-5 chronic kidney disease (the C-SURFER study): a combination phase 3 study. *Lancet*. 2015;386:1537-45.
[[PubMed Abstract](#)]
 - Sulejmani N, Jafri SM, Gordon SC. Pharmacodynamics and pharmacokinetics of elbasvir and grazoprevir in the treatment of hepatitis C. *Expert Opin Drug Metab Toxicol*. 2016;12:353-61.
[[PubMed Abstract](#)]
 - Sulkowski M, Hezode C, Gerstoft J, et al. Efficacy and safety of 8 weeks versus 12 weeks of treatment with grazoprevir (MK-5172) and elbasvir (MK-8742) with or without ribavirin in patients with hepatitis C virus genotype 1 mono-infection and HIV/hepatitis C virus co-infection (C-WORTHY): a randomised, open-label phase 2 trial. *Lancet*. 2015;385:1087-97.
[[PubMed Abstract](#)]
 - Summa V, Ludmerer SW, McCauley JA, et al. MK-5172, a selective inhibitor of hepatitis C virus NS3/4a protease with broad activity across genotypes and resistant variants. *Antimicrob Agents Chemother*. 2012;56:4161-7.
[[PubMed Abstract](#)]
 - Tong X, Kwong AD. Barrier to resistance: lessons from 2 direct-acting hepatitis C virus inhibitors, MK-5172 and Sofosbuvir. *Clin Infect Dis*. 2014;59:1675-7.
[[PubMed Abstract](#)]
 - Zeuzem S, Ghalib R, Reddy KR, et al. Grazoprevir-Elbasvir Combination Therapy for Treatment-Naïve Cirrhotic and Noncirrhotic Patients With Chronic Hepatitis C Virus Genotype 1, 4, or 6 Infection: A Randomized Trial. *Ann Intern Med*. 2015;163:1-13.
[[PubMed Abstract](#)]