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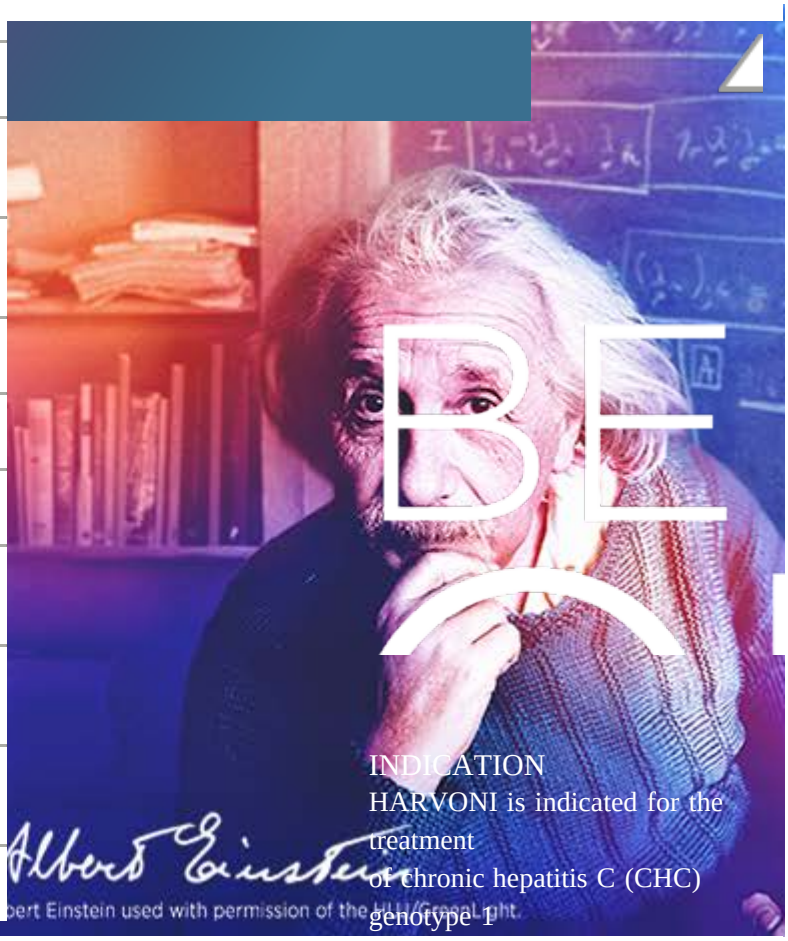


HCV cure can start with you and a once-daily, single-tablet regimen

The goal of HCV therapy is cure, or sustained virologic response (SVR), which is defined as undetectable HCV RNA at 12 or more weeks after the end of treatment.[1,2] Click here to learn more about results from HARVONI clinical studies.

Review hypothetical patient cases and HARVONI clinical study outcomes

Register to learn more about HARVONI and receive updates

References:

1. US Department of Health and Human Services, Center for Drug Evaluation and Research. Draft Guidance for Industry. Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment. October 2013.

Important Safety Information

2. AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed January 5, 2015.

3.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Risk of Serious Symptomatic Bradycardia When Coadministered with Amiodarone:
  Amiodarone is not recommended for use with HARVONI due to the risk of symptomatic bradycardia, particularly in patients also taking beta blockers or with underlying cardiac comorbidities and/or with advanced liver disease. In patients without alternative, viable treatment options, cardiac monitoring is recommended. Patients should seek immediate medical evaluation if they develop signs or symptoms of bradycardia.
- Risk of Reduced Therapeutic Effect of HARVONI Due to P-gp Inducers:
  Rifampin and St. John's wort are not recommended for use with HARVONI as they may significantly decrease ledipasvir and sofosbuvir plasma concentrations.
- Related Products Not Recommended:
  HARVONI is not recommended for use with other products containing sofosbuvir (SOVALDI®).

HARVONI OVERVIEW

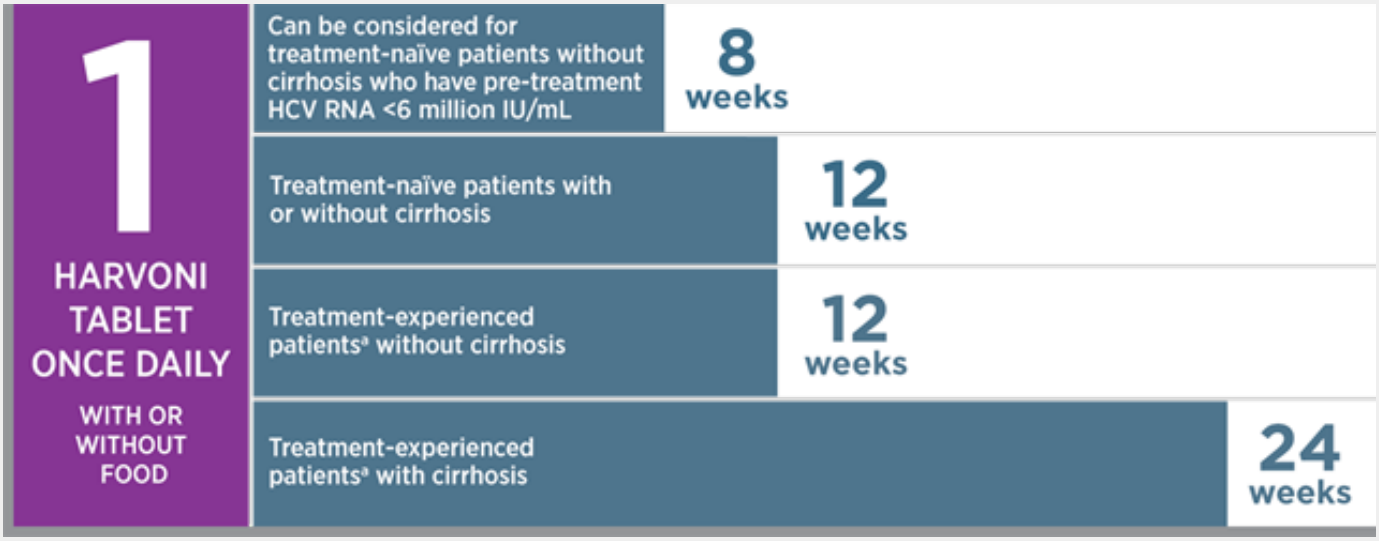
Dosing | Study Results | Safety Information

Pill not actual size

HCV patients can now benefit from the simplicity of a single-tablet regimen[1]

HARVONI delivers the simplicity of a complete regimen with one tablet, once daily to treat your HCV genotype 1 patients.[1]

Recommended treatment duration for HCV genotype 1 patients[1]



[a] Treatment-experienced patients who failed treatment with either peginterferon (Peg-IFN) alfa + ribavirin (RBV) or an HCV protease inhibitor + Peg-IFN alfa + RBV.[1]

- HARVONI is interferon- and ribavirin-free for genotype 1 treatment-naïve and treatment-experienced patients with or without cirrhosis[1]
- Each HARVONI tablet contains 90 mg of ledipasvir and 400 mg of sofosbuvir[1]
- Relapse rates are affected by baseline host and viral factors and differ between treatment durations for certain subgroups[1]
- No dose adjustments are required based on advanced age, mild or moderate renal impairment, or mild, moderate, or severe hepatic impairment. The safety and efficacy of HARVONI have not been established in patients with decompensated cirrhosis[1]
- No dose recommendations can be given for patients with severe renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73m^2) or with end stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite[1]

Register to learn more about HARVONI and receive updates

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

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  Amiodarone is not recommended for use with HARVONI due to the risk of symptomatic bradycardia, particularly in patients also taking beta blockers or with underlying cardiac comorbidities and/or with advanced liver disease. In patients without alternative, viable treatment options, cardiac monitoring is recommended. Patients should seek immediate medical evaluation if they develop signs or symptoms of bradycardia.
- Risk of Reduced Therapeutic Effect of HARVONI Due to P-gp Inducers:
  Rifampin and St. John's wort are not recommended for use with HARVONI as they may significantly decrease ledipasvir and sofosbuvir plasma concentrations.
- Related Products Not Recommended:
  HARVONI is not recommended for use with other products containing sofosbuvir (SOVALDI®).

HARVONI was evaluated in 3 pivotal clinical trials that included 1952 adult subjects[1]

Patient types	Study name	Treatment arms and durations
Treatment-naïve subjects with or without cirrhosis (N=865)[a]	ION-1	A randomized, open-label trial that evaluated 12 and 24 weeks of treatment with HARVONI with or without ribavirin
Treatment-naïve subjects without cirrhosis (N=647)	ION-3	A randomized, open-label trial that evaluated 8 weeks of treatment with HARVONI with or without ribavirin and 12 weeks of treatment with HARVONI
Treatment-experienced subjects with or without cirrhosis (N=440)	ION-2	A randomized, open-label trial that evaluated 12 and 24 weeks of treatment with HARVONI with or without ribavirin in genotype 1 subjects who failed prior therapy with IFN-based regimens, including regimens containing an HCV protease inhibitor (PI)

[a] SVR rates for all treatment-naïve subjects enrolled in the 24-week treatment groups in ION-1 (N=434) were not available at the time of the interim analysis.[1]

- In all trials, sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA

<25 IU/mL at 12 weeks after the end of treatment[1]

- Relapse was a secondary endpoint, which was defined as HCV RNA ≥25 IU/mL with 2 consecutive values or last available post-treatment measurement during the post-treatment period after achieving HCV RNA <25 IU/mL at the end of treatment[1]
- The HARVONI studies are part of the first Phase 3 clinical trial program to evaluate a once-daily, single-tablet regimen for the treatment of HCV genotype 1

Baseline characteristics for subjects in HARVONI clinical trials[1-4]

Total subjects	N=1952[a]
Compensated cirrhosis	n=224
HCV genotype 1b	n=497
IL28B non-C/C alleles	n=1466
Mean BMI	26 to 29 kg/m² (range: 18 to 56 kg/m²)
Mean age	52 to 57 years (range: 18 to 80 years)
Previously failed an HCV protease inhibitor–containing regimen	n=231
Black subjects	n=308
Hispanic or Latino subjects	n=181

[a] SVR rates for all subjects enrolled in the 24-week treatment groups in ION-1 (N=434) were not available at the time of the interim analysis.[1]

- HARVONI clinical studies did not exclude patients taking diabetes medications or patients who were stable on an anticoagulant regimen[2-4]

HARVONI cured nearly all treatment-naïve, treatment-experienced, and cirrhotic genotype 1 subjects[1]

The overall SVR rate was 97% (n=1042/1079) across HARVONI Phase 3 clinical trials.[1-4]

HARVONI treatment by patient type based on clinical studies[2-4]

Patient characteristics	No cirrhosis	Cirrhosis	Weeks of treatment	SVR
Treatment-naïve with pre-treatment HCV RNA <6 million IU/mL	X		8	97% (n=119/123)
Treatment-naïve	X		12	96% (n=208/216) 99% (n=176/177)
Treatment-naïve		X	12	94% (n=32/34)
Treatment-experienced	X		12	95% (n=83/87)
Treatment-experienced		X	24	100% (n=22/22)

Primary Endpoint

In all trials, sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA <25 IU/mL at 12 weeks after the end of treatment.[1] Achieving SVR12 is considered a virologic cure.[5]

Register to learn more about HARVONI and receive updates

IMPORTANT SAFETY INFORMATION

Adverse Reactions

Most common (≥10%, all grades) adverse reactions were fatigue and headache.

Drug Interactions

- In addition to rifampin and St. John's wort, coadministration of HARVONI is also not recommended with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir. Such coadministration is expected to decrease the concentration of ledipasvir and sofosbuvir, reducing the therapeutic effect of HARVONI.
- Coadministration of HARVONI is not recommended with simeprevir due to increased concentrations of ledipasvir and simeprevir. Coadministration is also not recommended with rosuvastatin or

co-formulated elvitegravir/ cobicistat/ emtricitabine/ tenofovir disoproxil fumarate due to increased concentrations of rosuvastatin and tenofovir, respectively.

Consult the full Prescribing Information for HARVONI for more information on potentially significant drug interactions, including clinical comments.

SAFETY INFORMATION

Warnings and Precautions

- Risk of Serious Symptomatic Bradycardia When Coadministered with Amiodarone: Amiodarone is not recommended for use with HARVONI due to the risk of symptomatic bradycardia, particularly in patients also taking beta blockers or with underlying cardiac comorbidities and/or with advanced liver disease. In patients without alternative, viable treatment options, cardiac monitoring is recommended. Patients should seek immediate medical evaluation if they develop signs or symptoms of bradycardia.

  To learn more about counseling and the cardiac monitoring of patients, as well as the signs and symptoms of bradycardia, click here.

- Risk of Reduced Therapeutic Effect of HARVONI Due to P-gp Inducers: Rifampin and St. John's wort are not

recommended for use with HARVONI as they may significantly decrease ledipasvir and sofosbuvir plasma concentrations.

- Related Products Not Recommended: HARVONI is not recommended for use with other products containing sofosbuvir (SOVALDI®).

Warnings & Precautions | Adverse Reactions | Discontinuations | Drug Interactions

HARVONI demonstrated tolerability with low discontinuation rates and does not require IFN or RBV for genotype 1 patients[1]

Adverse reactions (all grades) reported in ≥5% of subjects receiving 8, 12, or 24 weeks of treatment with HARVONI[1]

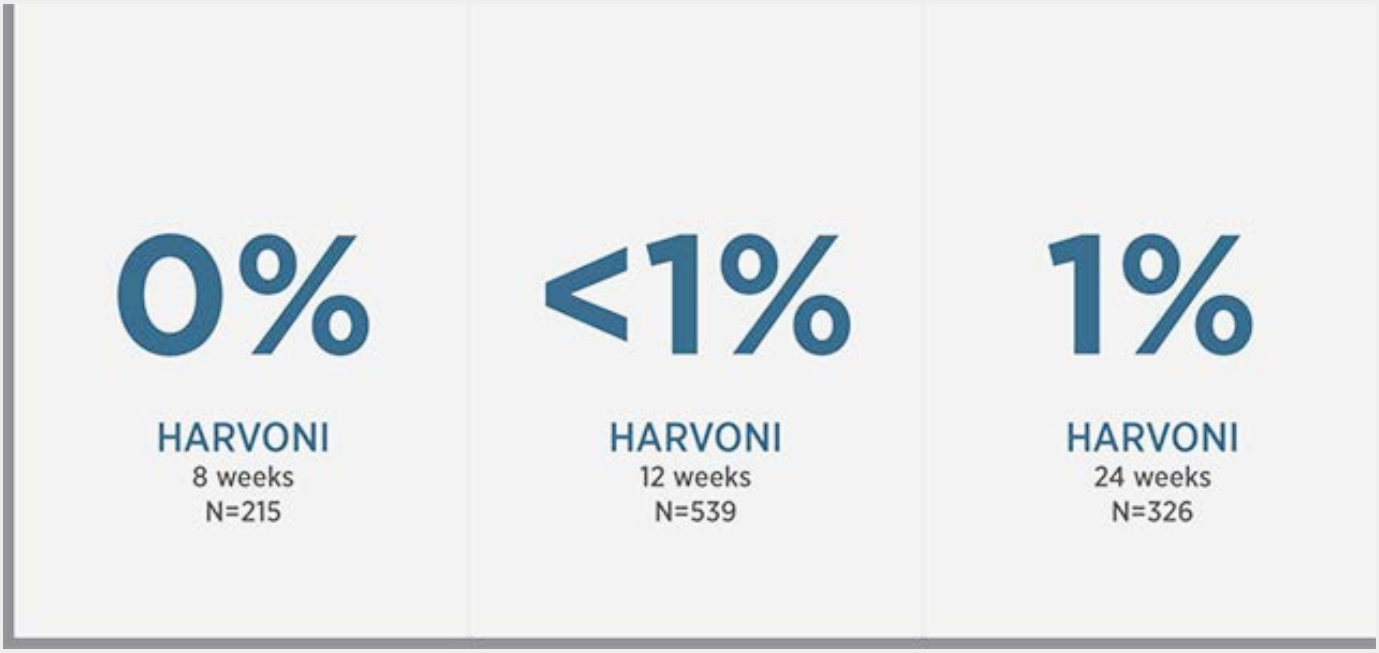
	HARVONI 8 weeks	HARVONI 12 weeks	HARVONI 24 weeks
	N=215	N=539	N=326
Fatigue	16%	13%	18%
Headache	11%	14%	17%
Nausea	6%	7%	9%
Diarrhea	4%	3%	7%
Insomnia	3%	5%	6%

- Based on pooled data from three Phase 3 clinical trials in genotype 1 subjects with compensated liver disease with or without cirrhosis[1]
- The majority of the adverse events presented in the table occurred at a severity of grade 1 (mild, transient, and did not require treatment modification)[1]

Warnings & Precautions | Adverse Reactions | Discontinuations | Drug Interactions

Discontinuation rates due to adverse events were 1% or less in subjects receiving HARVONI[1]

Discontinuations due to adverse events in subjects treated with HARVONI[1]



Warnings & Precautions | Adverse Reactions | Discontinuations | Drug Interactions

HARVONI drug interaction profile[1]

Coadministration not recommended[a]

Coadministration of HARVONI with the following drugs is not recommended:

- Antiarrhythmics: amiodarone[b]
- Anticonvulsants[c]: carbamazepine, phenytoin, phenobarbital, oxcarbazepine
- Antimycobacterials[c]: rifabutin, rifampin,[d] rifapentine
- HCV product: simeprevir[d,e]
- Herbal supplement: St. John's wort[c]
- HIV antiretrovirals: elvitegravir/ cobicistat/ emtricitabine/ tenofovir disoproxil fumarate (DF),[f] tipranavir/ritonavir[c]
- Statin: rosuvastatin[g]

[a] This information is not all inclusive and is based on drug interaction studies or predicted interaction.

[b] Coadministration of amiodarone with HARVONI may result in serious symptomatic bradycardia. The mechanism of this effect is unknown. If coadministration is required, cardiac monitoring is recommended.

[c] Coadministration of HARVONI with these medications is expected to decrease concentrations of ledipasvir and sofosbuvir, leading to a reduced therapeutic effect.

[d] This interaction has been studied in healthy adults.

[e] Concentrations of ledipasvir and simeprevir are increased when simeprevir is coadministered with ledipasvir.

[f] The safety of increased tenofovir concentrations in the setting of HARVONI and elvitegravir/ cobicistat/ emtricitabine/ tenofovir DF has not been established.

[g] Coadministration of HARVONI with rosuvastatin may significantly increase the concentration of rosuvastatin, which is associated with increased risk of myopathy, including rhabdomyolysis.

Other potentially significant interactions[a]

No clinically significant interaction with HARVONI

Other DDI information

References:

1. HARVONI US full Prescribing Information. Gilead Sciences, Inc. Foster City, CA. March 2015.
2. Afdhal N, Zeuzem S, Kwo P, et al; for the ION-1 Investigators. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *N Engl J Med.* 2014;370(20):1889-1898.
3. Kowdley KV, Gordon SC, Reddy KR, et al; for the ION-3 Investigators. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. *N Engl J Med.* 2014;370(20):1879-1888.
4. Afdhal N, Reddy KR, Nelson DR, et al; for the ION-2 Investigators. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. *N Engl J Med.* 2014;370(16):1483-1493.
5. US Department of Health and Human Services, Center for Drug Evaluation and Research. Draft Guidance for Industry. Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment. October 2013.

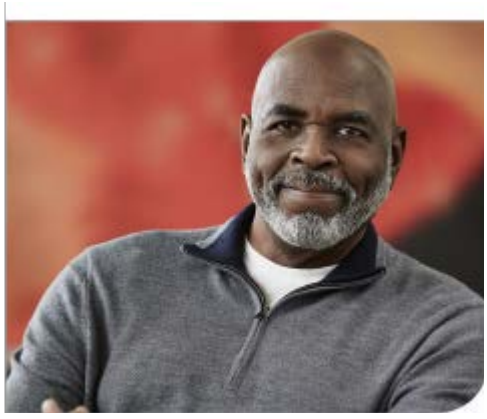
HYPOTHETICAL PATIENT CASES

HARVONI delivered high cure (SVR) rates across a broad range of genotype 1 patients, including those with cirrhosis, previous treatment experience, advanced age, and high BMI[1-4]

These hypothetical profiles of patients may help you identify patients in your own practice who could be evaluated by an HCV specialist for HARVONI treatment.

Sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA less than LLOQ (25 IU/mL) at 12 weeks after the cessation of treatment.[1] Achieving SVR is considered a virologic cure.[5]

Click the photos below to learn more about each type of HCV genotype 1 patient and the corresponding results from HARVONI clinical trials.



IMPORTANT SAFETY INFORMATION

Drug Interactions

- In addition to rifampin and St. John's wort, coadministration of HARVONI is also not recommended with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir. Such coadministration is expected to decrease the concentration of ledipasvir and sofosbuvir, reducing the therapeutic effect of HARVONI.

- Coadministration of HARVONI is not recommended with simeprevir due to increased concentrations of ledipasvir and simeprevir. Coadministration is also not recommended with rosuvastatin or co-formulated elvitegravir/ cobicistat/ emtricitabine/ tenofovir disoproxil fumarate due to increased concentrations of rosuvastatin and tenofovir, respectively.

Consult the full Prescribing Information for HARVONI for more information on potentially significant drug interactions, including clinical comments.

Treatment-Naïve Non-Cirrhotic | Treatment-Naïve Cirrhotic | Treatment-Experienced Non-Cirrhotic | Treatment-Experienced Cirrhotic

HARVONI is the only HCV treatment that offers an 8-week course of therapy[1]

WENDY[a]: A 43-year-old female who was recently diagnosed with chronic hepatitis C infection

PATIENT CHARACTERISTICS

Age	43
Race/ethnicity	Caucasian
Date of diagnosis	March 2014
Genotype	1
Cirrhosis status	Non-cirrhotic
BMI	23 kg/m^2
HCV RNA	5.2 x 10^6 IU/mL
Treatment history	Treatment-naïve

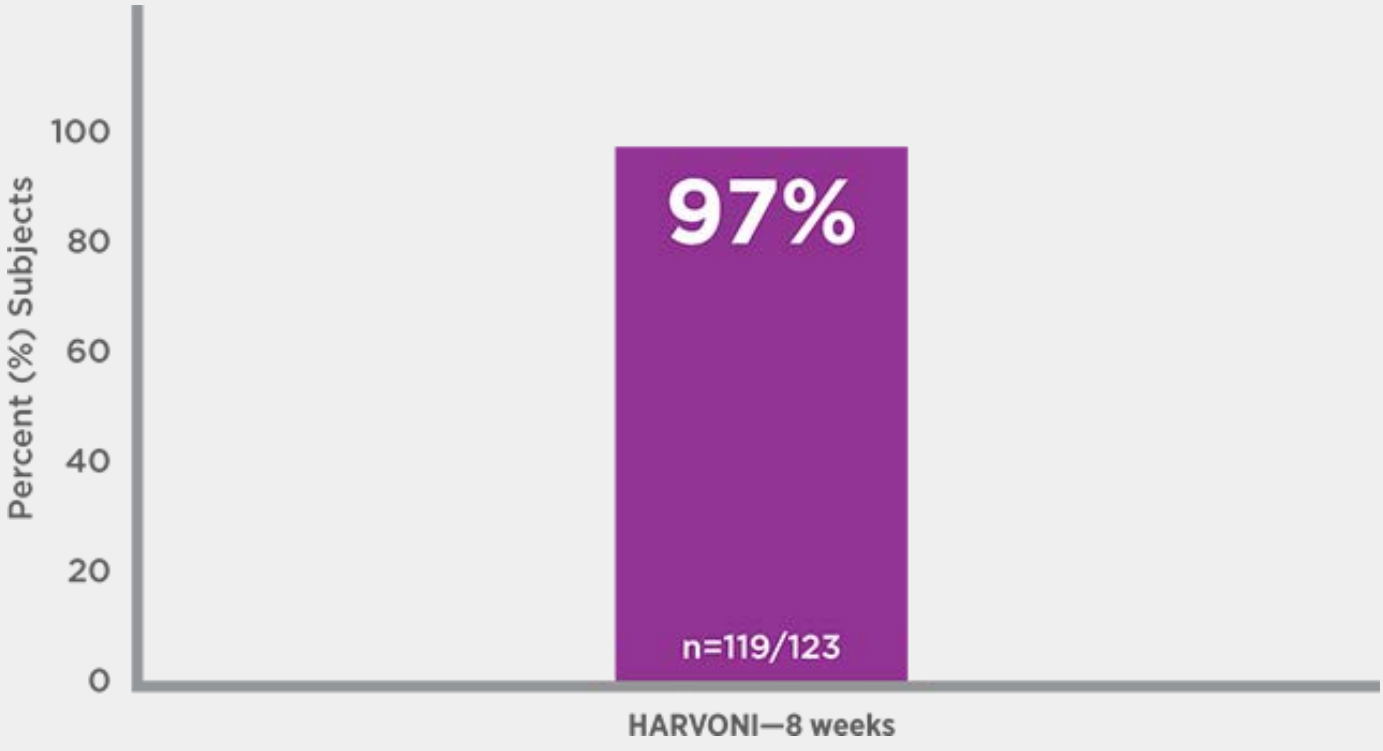
[a] Not an actual patient. Profile is based on published data from clinical studies.

Let’s explore the clinical trial data that support the use of HARVONI in a patient like Wendy.

The ION-3 study was a randomized, open-label trial evaluating 8 weeks of treatment with HARVONI with or without ribavirin (RBV) and 12 weeks of treatment with HARVONI in treatment-naïve, non-cirrhotic subjects (N=647) with HCV genotype 1.[1] For more information on HARVONI clinical trials, including the ION-3 study, click here.

Treatment for 8 weeks can be considered for treatment-naïve patients without cirrhosis and with baseline HCV RNA <6 million IU/mL[1]

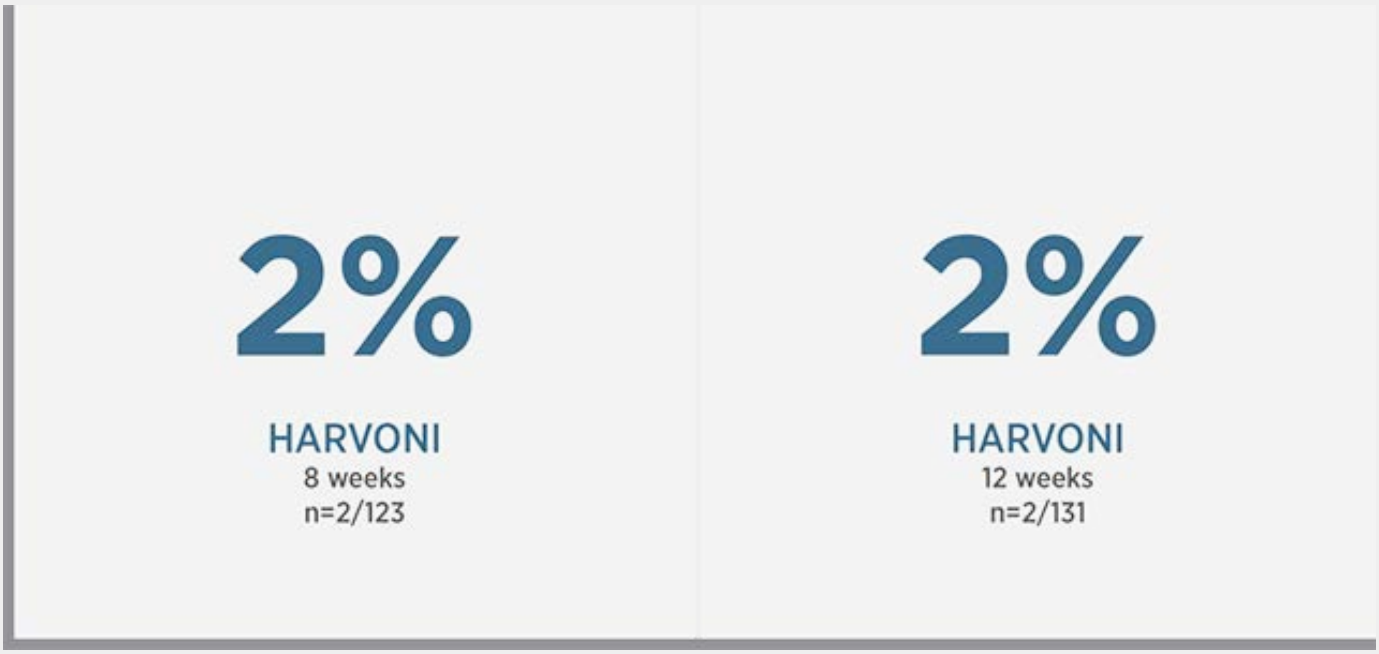
% SVR12 among treatment-naïve subjects without cirrhosis who had baseline HCV RNA <6 million IU/mL[1]



- Many treatment-naïve patients without cirrhosis may qualify for an 8-week HARVONI regimen[1,6]

- 59% of subjects taking HARVONI in ION-3 had baseline HCV RNA <6 million IU/mL[1]
- Sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA less than LLOQ (25 IU/mL) at 12 weeks after the cessation of treatment.[1] Achieving SVR is considered a virologic cure[5]

Relapse rates among subjects with baseline HCV RNA <6 million IU/mL in ION-3[1,a]



[a] HCV RNA values were determined using the Roche TaqMan® Assay; a subject's HCV RNA may vary from visit to visit.

- Among patients with baseline HCV RNA ≥6 million IU/mL, relapse rates were 10% (n=9/92) with 8 weeks of HARVONI and 1% (n=1/85) with 12 weeks[1]
- HCV RNA values were determined using the Roche TaqMan® Assay; a subject's HCV RNA may vary from visit to visit
- Relapse was a secondary endpoint, which was defined as HCV RNA ≥25 IU/mL with 2 consecutive measurements or last available post-treatment measurement taken after achieving HCV RNA <25 IU/mL at the end of treatment[1]

IMPORTANT SAFETY INFORMATION

Drug Interactions

- In addition to rifampin and St. John's wort, coadministration of HARVONI is also not recommended with

carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir. Such coadministration is expected to decrease the concentration of ledipasvir and sofosbuvir, reducing the therapeutic effect of HARVONI.

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Consult the full Prescribing Information for HARVONI for more information on potentially significant drug interactions, including clinical comments.

HARVONI consistently delivered high cure (SVR) rates across a wide range of treatment-naïve HCV genotype 1 subjects[1]

MARIA[a]: A 56-year-old female who was recently diagnosed with chronic hepatitis C infection and compensated cirrhosis

PATIENT CHARACTERISTICS

Age	56
Race/ethnicity	Hispanic
Date of diagnosis	May 2014
Genotype	1
Cirrhosis status	Compensated cirrhosis
BMI	27 kg/m^2
HCV RNA	6.5 x 10^6 IU/mL
Treatment history	Treatment-naïve

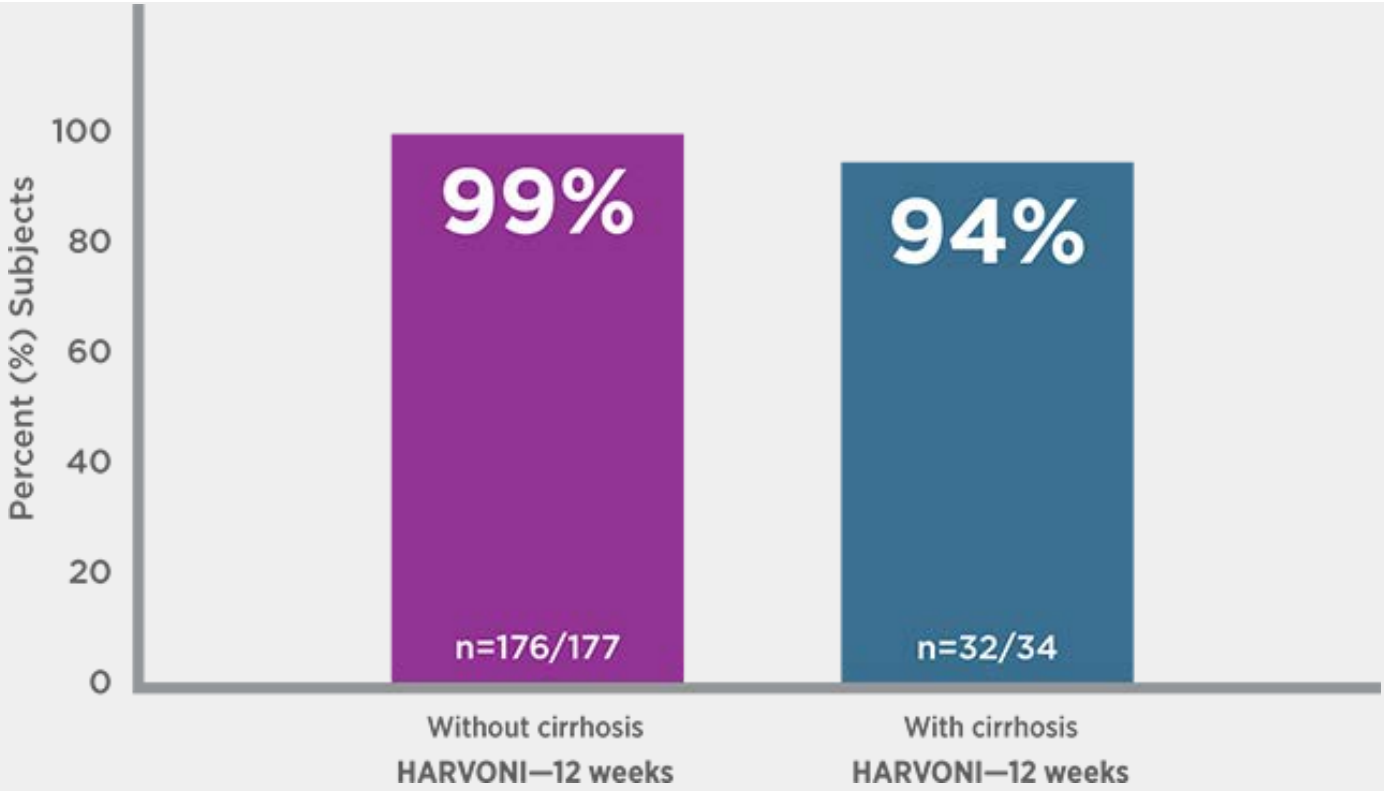
[a] Not an actual patient. Profile is based on published data from clinical studies.

Let’s explore the clinical trial data that support the use of HARVONI in a patient like Maria.

The ION-1 study was a randomized, open-label trial evaluating 12 and 24 weeks of treatment with HARVONI with or without ribavirin (RBV) in treatment-naïve subjects (N=865) with HCV genotype 1.[1] SVR rates for all subjects enrolled in the 24-week treatment groups (N=434) were not available at the time of interim analysis. For more information on HARVONI clinical trials, including the ION-1 study, click here.

HARVONI was effective in treatment-naïve HCV genotype 1 subjects with cirrhosis[1]

% SVR12 among treatment-naïve HCV genotype 1 subjects with and without cirrhosis in ION-1[1]



- Sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA less than LLOQ (25 IU/mL) at 12 weeks after the cessation of treatment[1]

Relapse rates were low among subjects with or without compensated cirrhosis receiving HARVONI in ION-1[1]

	HARVONI 12 Weeks (N=214)
Relapse[a,b,c]	<1% (n=1/212)

[a] Excluding one subject with genotype 4 infection.

[b] Relapse was a secondary endpoint.

[c] The denominator for relapse is the number of subjects with HCV RNA <25 IU/mL at their last on-treatment assessment.

Register to learn more about HARVONI and receive updates

IMPORTANT SAFETY INFORMATION

Drug Interactions

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HARVONI delivered high cure (SVR) rates in genotype 1 subjects who failed prior therapy[1]

KEVIN[a]: A 55-year-old male who was diagnosed with chronic hepatitis C infection in 2009 and previously received treatment.

PATIENT CHARACTERISTICS

Age	55
Race/ethnicity	Caucasian
Date of diagnosis	December 2009
Genotype	1
Cirrhosis status	Non-cirrhotic
BMI	29 kg/m^2
HCV RNA	5.8 x 10^6 IU/mL
Treatment history	Peg-IFN + RBV + HCV PI

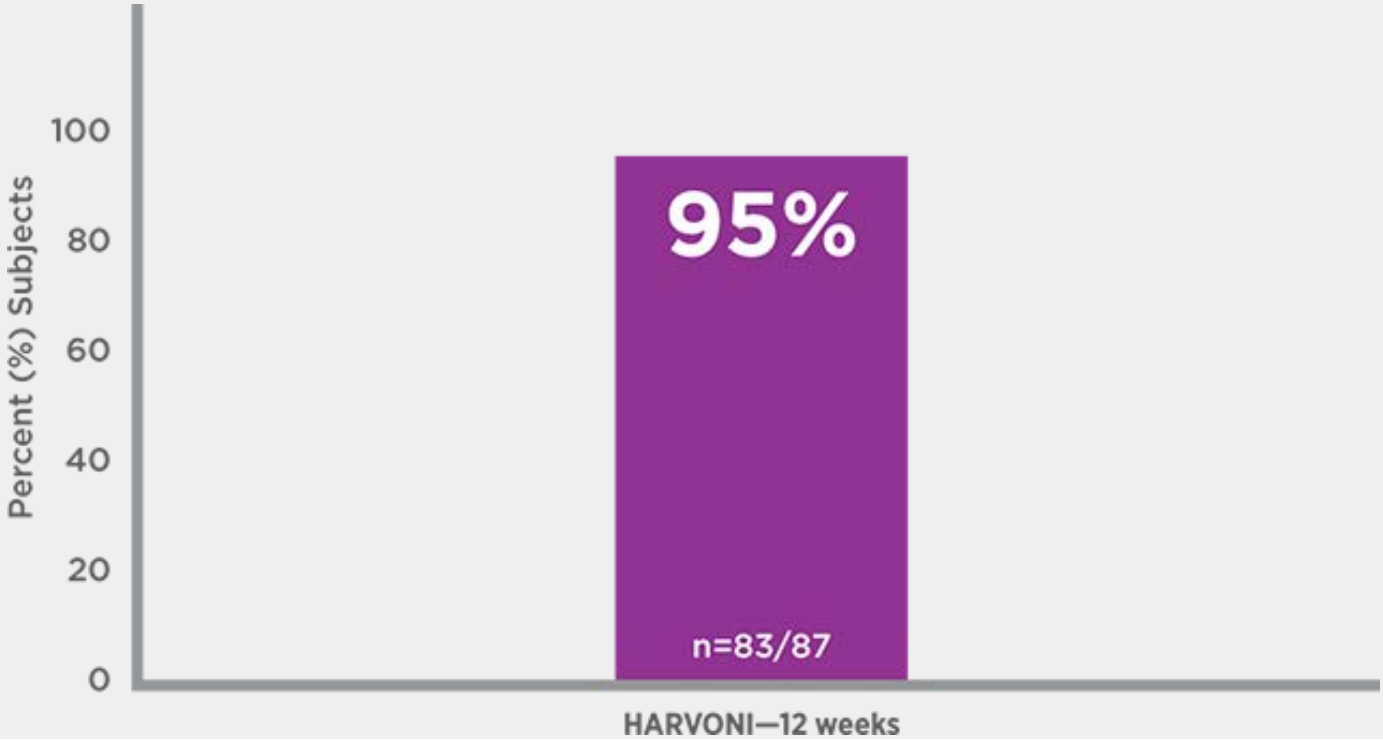
[a] Not an actual patient. Profile is based on published data from clinical studies.

Let’s explore the clinical trial data that support the use of HARVONI in a patient like Kevin.

The ION-2 study was a randomized, open-label trial evaluating 12 and 24 weeks of treatment with HARVONI with or without ribavirin (RBV) in genotype 1 HCV-infected subjects with or without cirrhosis (N=440) who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.[1] For more information on HARVONI clinical trials, including the ION-2 study, click here.

HARVONI delivered high cure (SVR) rates in HCV genotype 1 treatment-experienced adult subjects[1]

% SVR12 among treatment-experienced HCV genotype 1 subjects without cirrhosis in ION-2[1]



- Sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA less than LLOQ (25 IU/mL) at 12 weeks after the cessation of treatment.[1] Achieving SVR is considered a virologic cure[5]

Relapse rates were low for treatment-experienced non-cirrhotic HCV genotype 1 ION-2 subjects[1]

	HARVONI 12 Weeks
Relapse[a,b,c]	5% (n=4/86)[d]

[a] The denominator for relapse is the number of subjects with HCV RNA <25 IU/mL at their last on-treatment assessment.

[b] Relapse was a secondary endpoint.

[c] Subjects with missing cirrhosis status were excluded from this subgroup analysis.

[d] These 4 non-cirrhotic relapsers all had baseline NS5A resistance–associated polymorphisms.

IMPORTANT SAFETY INFORMATION

Drug Interactions

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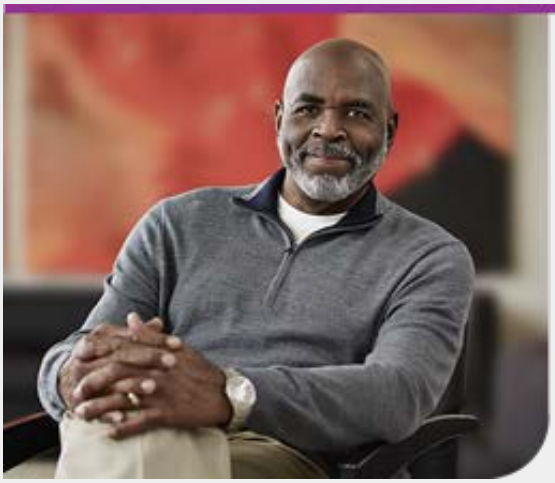
Consult the full Prescribing Information for HARVONI for more information on potentially significant drug interactions, including clinical comments.

HARVONI produced consistently high cure (SVR) rates among HCV genotype 1 treatment-experienced subjects[1]

JOE[a]: A 62-year-old male, diagnosed with chronic hepatitis C infection, who has prior treatment experience and compensated cirrhosis.

PATIENT CHARACTERISTICS



Age	62
Race/ethnicity	African-American
Date of diagnosis	November 1995
Genotype	1
Cirrhosis status	Cirrhotic
BMI	31 kg/m^2
HCV RNA	6.7 x 10^6 IU/mL
Treatment history	Peg-IFN + RBV

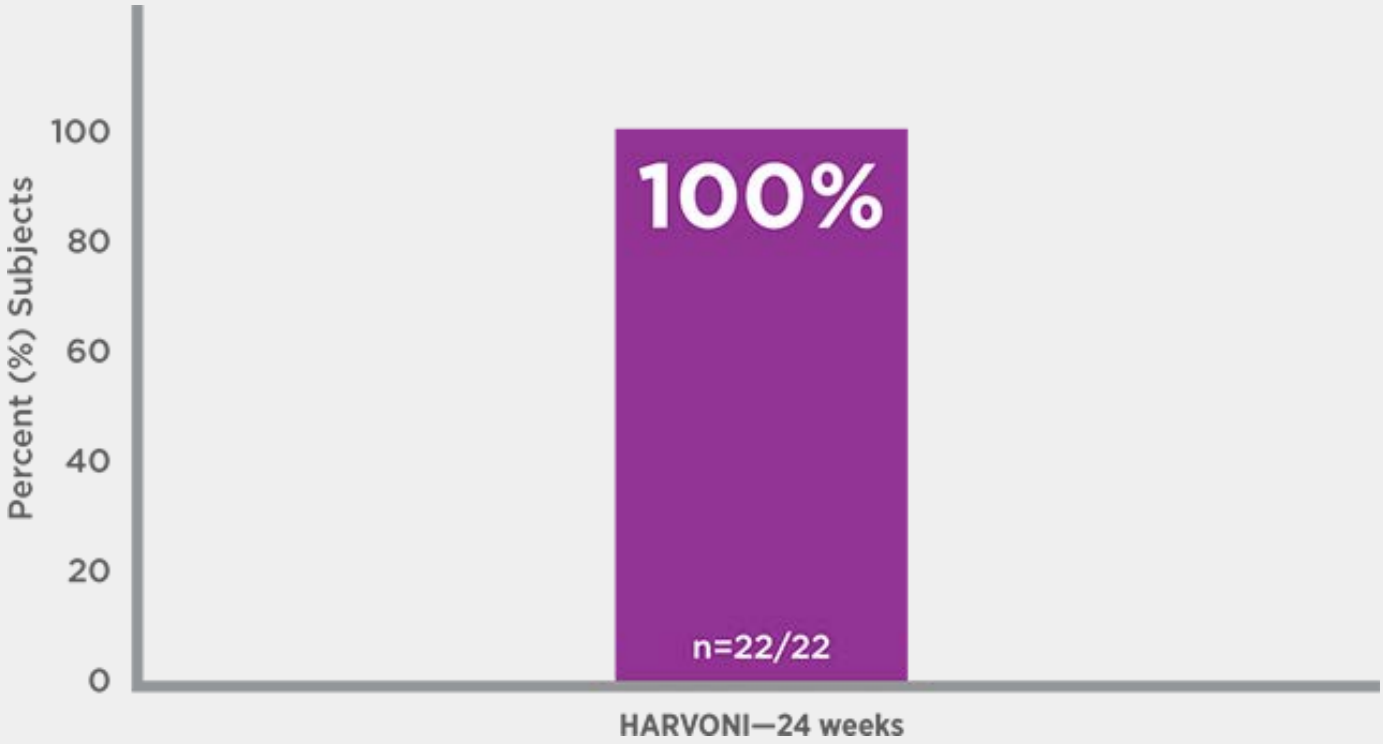
[a] Not an actual patient. Profile is based on published data from clinical studies.

Let’s explore the clinical trial data that support the use of HARVONI in a patient like Joe.

The ION-2 study was a randomized, open-label trial evaluating 12 and 24 weeks of treatment with HARVONI with or without ribavirin (RBV) in genotype 1 HCV-infected subjects (N=440) who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.[1] For more information on HARVONI clinical trials, including the ION-2 study, click here.

100% of treatment-experienced genotype 1 subjects with cirrhosis receiving HARVONI alone for 24 weeks achieved cure (SVR)[1]

% SVR12 among treatment-experienced HCV genotype 1 subjects with cirrhosis in ION-2[1]



- Sustained virologic response (SVR) was the primary endpoint and was defined as HCV RNA less than LLOQ (25 IU/mL) at 12 weeks after the cessation of treatment.[1] Achieving SVR is considered a virologic cure[5]

Relapse rates for treatment-experienced HCV genotype 1 subjects with cirrhosis in ION-2[1]

	HARVONI 12 Weeks (N=22)	HARVONI 24 Weeks (N=22)
Relapse[a,b,c]	14% (n=3/22)	0% (n=0/22)

[a] The denominator for relapse is the number of subjects with HCV RNA <25 IU/mL at their last on-treatment assessment.

[b] Relapse was a secondary endpoint.

[c] Subjects with missing cirrhosis status were excluded from this subgroup analysis.

References:

1. HARVONI US full Prescribing Information. Gilead Sciences, Inc. Foster City, CA. March 2015.
2. Afdhal N, Zeuzem S, Kwo P, et al; for the ION-1 Investigators. Ledipasvir and sofosbuvir for untreated HCV genotype 1 Infection. *N Engl J Med.* 2014;370(20):1889-1898.
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4. Afdhal N, Reddy KR, Nelson DR, et al; for the ION-2 Investigators. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. *N Engl J Med.* 2014;370(16):1483-1493.
5. US Department of Health and Human Services, Center for Drug Evaluation and Research. Draft Guidance for Industry. Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment. October 2013.
6. Ipsos HCV USA Therapy Monitor Q4 2013-Q3 2014.

IMPORTANT SAFETY INFORMATION

Drug Interactions

- In addition to rifampin and St. John's wort, coadministration of HARVONI is also not recommended with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir. Such coadministration is expected to decrease the concentration of ledipasvir and sofosbuvir, reducing the therapeutic effect of HARVONI.
- Coadministration of HARVONI is not recommended with simeprevir due to increased concentrations of ledipasvir and simeprevir. Coadministration is also not recommended with rosuvastatin or co-formulated elvitegravir/ cobicistat/ emtricitabine/ tenofovir disoproxil fumarate due to increased concentrations of rosuvastatin and tenofovir, respectively.

Consult the full Prescribing Information for HARVONI for more information on potentially significant drug interactions, including clinical comments.

YOUR ROLE IN HCV MANAGEMENT

HCV cure can start with you. Begin by screening your patients.

The initial action you can take toward HCV cure is to identify patients who are chronically infected with the disease. Screening recommendations in the US have changed in recent years, and treatment options have demonstrated cure rates above 90%.[1] Be the one to take action today. Your patients' cure can start with you.

Discover which patients have been exposed to HCV

Screening based upon several risk factors, such as past or current injection drug use and HIV infection, was the standard for many years. However, identifying all potential patients through these risk factors alone was only partially successful.

Baby boomers

People born between 1945 and 1965, also known as baby boomers, account for approximately 75% of all HCV patients, and they may have been infected for over 20 years.[2]

That's why the Centers for Disease Control and Prevention (CDC), US Preventive Services Task Force (USPSTF), and American Association for the Study of Liver Diseases (AASLD) issued updated HCV screening recommendations that include both age- and risk-based criteria.[3-5] A specific billing code (G0472) has been created for these patients.

Other high-risk populations

Besides the one-time screening of all baby boomers, the CDC, USPSTF, and AASLD recommend screening other high-risk populations.[3-5]

A simple blood test can reveal the presence of HCV antibodies

Order a simple one-time antibody test for the patient. The American Gastroenterological Association provides a list of ICD-9 and CPT billing codes for screening.

Once the screening test is performed, a negative HCV antibody test result means it is unlikely your patient has been exposed to the hepatitis C virus. If, however, you believe your patient may have been exposed in the past 6 months, consider testing for HCV antibodies again or ordering an HCV RNA test.

Once the screening test is performed, a positive HCV antibody test result means your patient has been exposed to hepatitis C and a diagnosis of chronic hepatitis C infection will need to be confirmed using an HCV RNA test.

At this point, you can refer your patient to an HCV specialist, or take the next step to confirm the diagnosis.

Counseling

When a patient presents who falls within the screening recommendations:

- Discuss screening with him/her
- Counsel him/her on HCV
- Explain why you want to run an HCV screening (antibody) test
- Tell a patient who is potentially infected with HCV about viable treatment options to help allay any

anxieties, concerns, or resistance he/she may have about being screened

To help you counsel your patients about screening, download the Hepatitis C Discussion Guide.

Register to learn more about HARVONI and receive updates

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

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- Risk of Reduced Therapeutic Effect of HARVONI Due to P-gp Inducers:
  Rifampin and St. John's wort are not recommended for use with HARVONI as they may significantly decrease ledipasvir and sofosbuvir plasma concentrations.
- Related Products Not Recommended:
  HARVONI is not recommended for use with other products containing sofosbuvir (SOVALDI®).

To determine if an HCV infection is chronic, confirm the diagnosis

A blood test that detects the presence of HCV RNA is needed to verify that your patient is chronically infected with HCV.

You or an HCV specialist can order an HCV RNA quantification/viral load test to confirm the diagnosis. Order the test yourself to potentially accelerate the specialist's evaluation and possible treatment of the patient.

If HCV RNA is not detected, your patient is not chronically infected, even though he/she has been exposed to HCV. (About 15%–25% of patients clear the virus spontaneously within the first few months following

initial infection.[6])

If HCV RNA is present, your patient should be referred to an HCV specialist for assessment and treatment evaluation.

Automate screening and diagnosis with reflex testing

If your patient's antibody test result is positive, many lab services can perform an HCV RNA test on the sample automatically, through a "reflex-testing" option. You can enhance the speed and efficiency of patient care by selecting this option on the lab order form when available. When ordering the antibody test, look for "Reflex" or "w/Reflex" in the test name.

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You can connect patients to specialist care

Patient referral can take place either once there is a positive antibody screening or once the patient is diagnosed with chronic HCV following a positive HCV RNA test. It is helpful to confirm the diagnosis, as no viral load would indicate that a referral is not needed.

Referral needs to take place regardless of viral load levels, liver enzyme levels, or absence or presence of symptoms. Studies show that none of these indicates or predicts disease severity or progression.[7] Therefore, you should refer all HCV patients to a specialist for further evaluation.

Help referred patients follow through

Between 25%–50% of referred patients miss their first specialist appointment or never see the specialist at all.[8] Below are some suggestions that can make a difference:

- When possible, confirm your patient's hepatitis C diagnosis with an HCV RNA quantification/viral load test
- If the HCV RNA quantification/viral load test is positive, counsel the patient on what the diagnosis means and that a specialist can evaluate further for treatment
- Consider ordering an additional blood test to determine the HCV genotype so treatment can be expedited once the patient reaches the specialist
- Communicate that for HCV genotype 1 patients, a once-daily, single-tablet regimen with HARVONI is available. To help you counsel your patients about HARVONI, download the Hepatitis C Discussion Guide
- Refer to a specialist who treats HCV, is accepting new patients, and has a convenient location. For tools to help find a specialist in your area, click here
- Be hands-on. Assist with scheduling the appointment for the patient and call to check if he/she went to the specialist
- After the specialist appointment has taken place, record the referral, and stay in touch with the patient and specialist as co-management needs arise

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Prepare your patients for success by counseling at every stage

When patients fully understand HCV, the screening steps, and treatment options, they are more informed and less likely to be anxious or resistant about taking steps toward possible cure. That's why counseling and guidance are so important at all stages. Key areas to cover with your patients are:

Screen

- Who should be screened
- Why they should be screened
- The treatment options like HARVONI that exist for patients who test positive for HCV genotype 1

Diagnose

- Confirming for a chronic hepatitis C infection if the screening test is positive
- What a positive diagnosis means
- The importance of being evaluated for treatment

Connect

- Finding an HCV specialist
- What to expect at the specialist's office
- Available patient support, such as Support Path®

At each stage, make sure patient questions have been answered.

To assist in your conversations with patients, the Hepatitis C Discussion Guide is available here to download.

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Related Products Not Recommended:

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From screening to referral, be the one to put it into practice

The hypothetical patient profiles in this section illustrate the types of patients with hepatitis C you may encounter in your practice and reflect common issues that can arise when addressing a patient's hepatitis C at each of the screening, diagnosis, and referral steps. Click the photos below to read each profile.

[a] Not an actual patient. Profile is based on published data from clinical studies.

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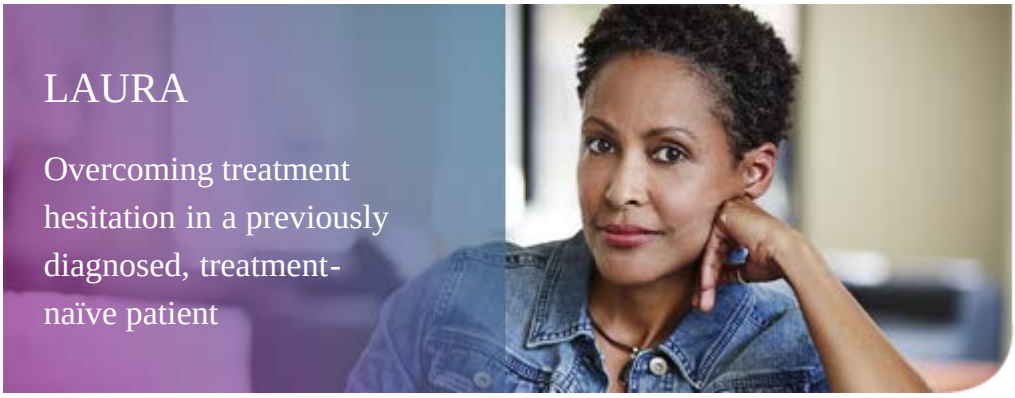
Screen | Diagnose | Connect | Counsel | Hypothetical Profiles

Laura | Carlos | Gregory



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PATIENT CHARACTERISTICS

Risk Factor	Age	Race/ethnicity	BMI	Medications	HCV Antibody Test Result	HCV RNA Test Result	Genotype
Blood transfusion prior to 1992	50	African-American	25 kg/m^2	Metformin	Positive	5.9 x 10^6 IU/mL	1

Screening and Diagnosis

1990

Laura received a blood transfusion.

2011

Laura's primary care physician diagnosed her with chronic hepatitis C genotype 1 infection when the RNA viral load test was positive. Laura did not seek treatment because of:

- Lack of symptoms
- Fear of potential treatment side effects

Referral

2014

After Laura's primary care physician learned about treatments, like HARVONI, he suggested Laura see an HCV specialist. Her primary care physician counseled her on these points:

- Most patients remain asymptomatic until serious liver complications arise[9]
- Hepatitis C is curable
- Treatments are shorter with fewer side effects

To help Laura feel comfortable in her decision to seek treatment with an HCV specialist, her primary care physician:

- Found a conveniently located specialist experienced in treating hepatitis C
- Told Laura about Support Path®, which offers tools and guidance for diagnosed patients
- After the HCV specialist prescribed HARVONI for Laura, her primary care physician followed up with her to monitor progress and answer questions while she was on HARVONI treatment

Register to learn more about HARVONI and receive updates

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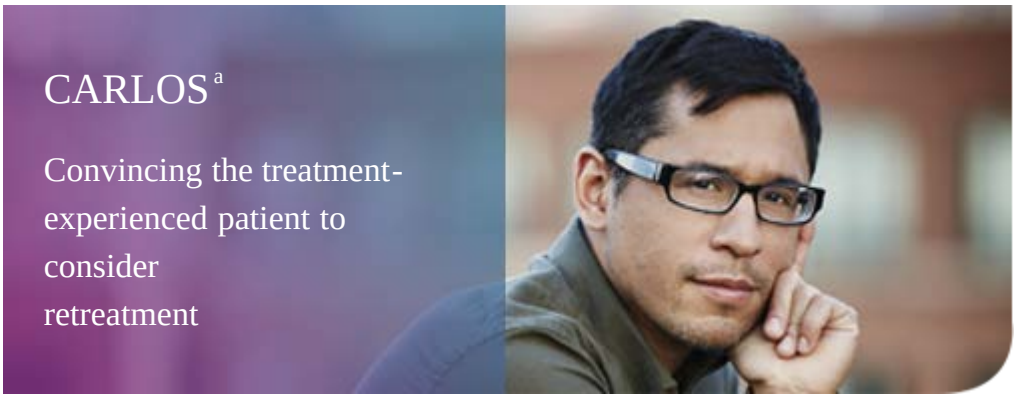

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PATIENT CHARACTERISTICS

Risk Factor	Age	Race/ethnicity	BMI	Medications	HCV Antibody Test Result	HCV RNA Test Result	Genotype
Past use of intravenous drugs	40	Hispanic	29 kg/m^2	Ibuprofen, Naproxen	Positive	6.5 x 10^6 IU/mL	1

Screening and Diagnosis

2007

Carlos' primary care physician screened him with an antibody test, which was positive. The physician then:

- Ran an HCV RNA test to confirm the diagnosis, which was positive
- Ordered a genotype test, which indicated that Carlos was genotype 1

2011

Carlos was referred to an HCV specialist who:

- Treated Carlos for chronic hepatitis C with pegylated interferon, ribavirin, and an HCV protease inhibitor for 48 weeks
- Did not attempt other options when Carlos' treatment failed to result in a sustained virologic response (SVR)

Referral

2015

Carlos' primary care physician:

- Learned of HARVONI for chronic HCV genotype 1 adult patients

Re-referred Carlos to an HCV specialist

To encourage Carlos to see the specialist and be informed about HARVONI treatment, his primary care physician:

- Explained to Carlos the SVR rates observed in the HARVONI clinical studies
- Discussed how treatments offer all-oral, simple dosing
- Told him that interferon injections are no longer needed
- Kept in contact with Carlos throughout the course of treatment with HARVONI

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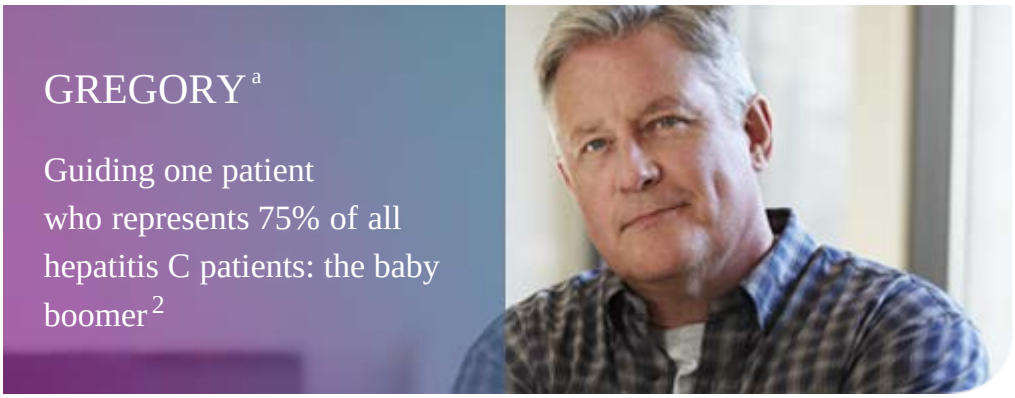

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PATIENT CHARACTERISTICS

Risk Factor	Age	Race/ethnicity	BMI	Medications	HCV Antibody Test Result	HCV RNA Test Result	Genotype
Baby boomer (born between 1945 and 1965)	60	Caucasian	31 kg/m^2	Verapamil, Metoprolol, Pravastatin	Positive	6.5×10^6 IU/mL	1

Screening and Diagnosis

2013

Because of updated screening recommendations for baby boomers (those born between 1945–1965), Gregory's primary care physician suggested he be tested for the hepatitis C virus (HCV).

After Gregory agreed to be tested, his primary care physician ordered an HCV antibody test.

After the positive antibody test result, his primary care physician counseled Gregory on these key points:

- A positive result does not prove chronic infection
- To confirm the diagnosis, Gregory needed an HCV RNA test
- If the RNA test showed chronic infection, his primary care physician would counsel Gregory on treatment options and discuss referral to an HCV specialist

Referral

2014

Based on the positive results of his HCV RNA test, his primary care physician ordered a genotype test, which showed Gregory was genotype 1. His primary care physician also began taking steps to refer Gregory to a specialist for treatment evaluation.

To help ensure he followed through with the referral and any possible treatment, Gregory's primary care physician:

- Selected a specialist experienced in treating hepatitis C and had her staff call to make the appointment for Gregory
- Explained that the specialist would likely conduct more tests and discuss treatment options with him
- Told the patient about HARVONI, which offers simple dosing and is taken once daily for 12 weeks in most patient types[1]
- Made herself available after the HCV specialist's evaluation and during treatment to answer Gregory's questions

Register to learn more about HARVONI and receive updates

References:

1. HARVONI US full Prescribing Information. Gilead Sciences, Inc. Foster City, CA. March 2015.
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9. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. *Am Fam Physician*. 2006;74(5):756-762.

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24/7 PATIENT SUPPORT

Support Path® is a suite of resources designed to help patients start with HARVONI and move toward treatment completion

GETTING STARTED

Support Path helps patients access therapy and get off to an efficient start

- Benefits investigation and prior authorization support
- Co-pay and other financial assistance
- A specialty pharmacy finder

CO-PAY COUPON

The HARVONI co-pay coupon may help eligible patients lower their out-of-pocket costs.

With a co-pay coupon, most eligible patients may pay no more than $5 per co-pay (restrictions apply)

HARVONI®
ledipasvir/sofosbuvir
90 mg/400 mg tablets

To register and read full terms and conditions, click here
Or call 1-855-769-7284

HARVONI Co-pay Registration

- Not valid for patients enrolled in government healthcare prescription drug programs, such as Medicare Part D and Medicaid. Patients in the coverage gap known as the "donut hole" also are not eligible
- The HARVONI co-pay coupon program will cover the out-of-pocket costs for HARVONI prescriptions up to a maximum of 25% of the catalog price of a 12-week regimen of HARVONI

HELP ALONG THE WAY

Support Path is ready to assist patients along the way toward treatment completion

- Educational resources, support for adherence, and progress tracking
- A 24/7 help line with nurses on call can provide answers and assistance

- Ongoing support for access and reimbursement, including help with refill authorization

Enroll

- Go to MySupportPath.com or call 1-855-7-MYPATH (1-855-769-7284) to get started

IMPORTANT SAFETY INFORMATION

Adverse Reactions

- Most common (≥10%, all grades) adverse reactions were fatigue and headache.

RESOURCE CENTER

HCV cure can start with you and these helpful tools

Register to learn more about HARVONI and receive updates

Helpful Links: Recommendations, Guidelines, and HCV Billing Codes

CDC HCV Recommendations
USPSTF HCV Recommendations
AASLD HCV Guidelines
Hepatitis C CPT Codes from the AGA
Hepatitis C ICD-9 Codes from the AGA
NY State Hepatitis C Testing Guidelines

Patient Counseling and Assistance

Hepatitis C Discussion Guide

Use this guide to plan for questions that may arise when counseling your patients about chronic HCV GT 1 and treatment with HARVONI.

Support Path®: Patient Resources

Support Path is a suite of resources designed to help your patients start HARVONI and move toward treatment completion.

Find a Specialist

AMA Doctor Finder
AGA GI Locator Service
Healthgrades Infectious Disease Specialist Directory

Additional HCV Educational Resource

ACT-on-HCV
The AASLD Curriculum & Training (ACT) provides strategies and mentoring for healthcare professionals with HCV patients.
LIVERLEARNING®
This is the AASLD's official eLearning portal with over 6300 resources—including video, audio, and slide decks specifically for primary care physicians.

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