



HCSP FACT SHEET

• HCV DRUGS IN DEVELOPMENT •

Drugs in Development: Phase 3 Genotype 1 – Sovaldi (sofosbuvir)/ledipasvir

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Foreword

The studies below are from Gilead's Phase 3 clinical trial development of sofosbuvir and ledipasvir with and without ribavirin to treat HCV genotype 1. The data for this fact sheet is taken from an article published in the *New England Journal of Medicine* (NEJM).

These journal articles provide the best type of information since the papers were peer-reviewed and have been published in a prestigious medical journal.

There were three medications used in these studies:

- Sovaldi (sofosbuvir) – polymerase inhibitor, 400 mg
- Ledipasvir – NS5A inhibitor, 90 mg
- Ribavirin – when used it is dosed twice a day based on body weight

*Sofosbuvir and ledipasvir are co-formulated into one pill, taken once a day. Ribavirin is dosed twice a day.

Note: A comprehensive chart that lists the Phase 3 studies of sofosbuvir and ledipasvir with and without ribavirin is included on page 5.

ION-1:

Patient Population:

A total of 865 treatment-naïve patients were treated with ledipasvir and sofosbuvir with and without ribavirin. There were 4 treatment arms—2 arms in the 12-week groups and 2 arms in the 24-week treatment groups. The patient population across all of the treatment arms was similar: Male (55 - 64 yo), mean age (52% - 53%), White (82% - 87%), genotype 1a (66% - 68%), genotype 1b (31% - 33%), and cirrhosis (15% - 17%).

Results:

The overall cure rates were 97 to 100%.

Side effects:

The most common side effects were fatigue, headache, insomnia, and nausea. There were no treatment discontinuations.

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The information in this fact sheet is designed to help you understand and manage HCV and is not intended as medical advice. All persons with HCV should consult a medical practitioner for diagnosis and treatment of HCV.

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Genotype 1 – Sovaldi (sofosbuvir)/Ledipasvir

ION-2:

Patient Population:

There were a total of 440 treatment-experienced patients who were treated with the combination of ledipasvir and sofosbuvir with and without ribavirin. There were 4 arms—2 arms in the 12-week groups and 2 arms in the 24-week groups. The patient population was similar across all treatment arms: male (68% - 75%), age (~55 - 57 yo), White (77% - 85%), genotype 1a (78% - 79%), genotype 1b (21% - 22%), and cirrhosis (20% in all treatment arms).

The types of prior non-response—relapse or breakthrough, non-response to pegylated interferon, ribavirin therapy with and without protease inhibitor therapy—were similar within all arms.

Results:

The cure rates across all arms were very high—87% to 99% regardless of type of prior response.

Side Effects:

The most common side effects were fatigue, headache and nausea. There were no treatment discontinuations due to side effects.

ION-3:

In this study ledipasvir and sofosbuvir with and without ribavirin was given for 8 or 12 weeks.

Patient Population:

There were 647 treatment-naïve patients without cirrhosis randomly assigned to 3 treatment arms. The patient population was similar across all treatment arms: male (54% - 60%), mean age (51-53 yo), White (76% - 81%), genotype 1a (80%), genotype 1b (20%). F0-F2 (50-59%), and F-3 (13%)

- Arm 1: Sovaldi (sofosbuvir) and ledipasvir (215 pts) treated for 8 weeks

- Arm 2: Sovaldi, ledipasvir, ribavirin (216 pts) treated for 8 weeks
- Arm 3: Sovaldi, and ledipasvir (216 pts) treated for 12 weeks

Results:

The overall cure rates were 92% to 98%.

Side Effects:

Fatigue, headache and nausea were the most common side effects especially in the ribavirin containing group. There were 3 treatment discontinuations, but there were no treatment discontinuations in the 8-week sofosbuvir/ledipasvir (no ribavirin) arm.

Comments:

The high cure rates, shorter treatment duration, lower side effects and small pill count make the combination of sofosbuvir plus ledipasvir with and without ribavirin a promising future treatment option for people with HCV genotype 1. Gilead has stated that the approval by the Food and Drug Administration (FDA) is expected by October 10, 2014.

Next Steps

There are many steps that need to be taken before treatment can be started, and it is important to be as proactive as early as possible. It is expected that most medical providers will be swamped once the new interferon-free therapies are available. Try to get ahead of the game by starting the process well in advance of the new treatments being approved.

Finances

The new interferon-free medications are expected to be very expensive. Find out how much your insurance

Genotype 1 – Sovaldi (sofosbuvir)/Ledipasvir

will cover. What will be your co-payments? How much will lab work and office visits cost? If your insurance doesn't cover all of the costs of the medications and/or co-pays, what are your options? Do you qualify for patient assistance programs? But remember you may still be responsible for laboratory work and office visits. Figure all of this into your treatment plan.

Another option is to think ahead to 2015: Next year you may have a chance to purchase "enhanced" medical insurance through your employer or the Affordable Health Care Act during the 2014 open enrollment period. Can you opt-in to an insurance policy that provides higher coverage which may provide a lower co-pay? You may have to pay higher insurance premiums for a year, but you may be able to get your HCV medications at a lower cost as well as associated office visits and laboratory work covered. Remember it all depends on what your insurance will cover, and it is difficult to know one year to the next exactly what drugs the insurance companies will cover. However, you may be able to find out in advance if they will cover HCV medications, and which ones, through your company insurance broker.

Symptoms Log

The symptoms of hepatitis C range from mild to moderate to severe. Personally, I believe that everyone with hepatitis C has symptoms, but they come on so gradually over such a long period of time that most people don't notice them or believe that they are part of the aging process. Fatigue is the most common symptom followed by "brain fog," but there are also other symptoms such as muscle and joint pain, insomnia, depression, headache and a whole spectrum of autoimmune disorders that are either linked to hepatitis C or are more common in people with hepatitis C. It is important that all of these symptoms should be evaluated by a medical specialist. In addition, ask your medical provider to test you for extrahepatic manifestations. See our fact sheet on [extrahepatic manifestations](#). In addition, it is also important that

any—and I repeat—any symptoms should be recorded in your medical records. It has been reported that some insurance companies are only providing coverage of the new medication for those who are sick or for the sickest people.

A good way to measure the symptoms is by the 1 to 10 method with 10 being the worst symptom. For example, if you could not get out of bed one day because you were so tired, rate that as a 10. If you were so very tired that you decided that you would just watch TV that night it might be a 4 or 5. It might be a good idea to start a symptom log or journal. A copy could be inserted into your medical cart. Don't be afraid to tell your doctor or nurse what symptoms you are having—most doctors and nurses welcome patient involvement in their medical care.

Support

Support is an important part of treatment even with the new medications. There are a lot of questions that may come up:

- Will the treatment work?
- What will be the side effects?
- Will I be the one person who has the worst side effects?
- What will happen if I lose my insurance when I'm on treatment?
- Will my partner understand what I'm going through?

There are many, many questions that may come up before, during and after treatment. Creating your support system will help. *If you don't already have a good support system, start now.* A really good way to begin is to find a hepatitis C support group in your area. There are over 3 million Americans with hepatitis C so there is no reason to go through treatment alone. If you can't find a group in your area there are many on the Internet.

Side Effects

There will always be side effects with any medications.

Genotype 1 – Sovaldi (sofosbuvir)/Ledipasvir

We know the newer medication will have a lot less side effects than the older medications because people will not have to take interferon. Still, be prepared for any side effects. In the clinical trials the side effects were generally mild with the most common side effects listed as fatigue, headache and nausea. Talk with your doctor and nurse about how to treat the more common ones. Be prepared to speak with your medical provider as soon as possible if any other more serious side effects occur.

It is important to know that once medications are approved and given to the general HCV population more side effects emerge that were not previously known. If this happens to you, notify you doctor or nurse right away, especially if the side effect is severe. Your medical provider will want to know so the side effect can be treated before it gets worse. It will also help other doctors and nurses so they can be on the look out to help other patients. Your medical medical provider will also report any new severe side effects to the Food and Drug Administration (FDA).

Work

With the newer medications, it is unlikely that a person will require a leave of absence from their work. Some people, however, may want to take off some time at the beginning of treatment to pamper themselves. It is ok if you want to do this, but you will most likely have to take family leave, vacation or sick leave. Remember, you might want to save that time for better use since treatment for most people will only be 12 weeks and most people in the clinical trials reported that they did not miss any work.

Vaccinations

Everyone with liver disease (including hepatitis C) should be vaccinated against hepatitis A and hepatitis B if they are not already protected. Your medical provider may want you to get additional vaccinations prior to starting treatment.

Medical Tests

There are a variety of tests that will need to be performed before or right after starting treatment. A genotype test is a blood test that is given once to determine the strain of hepatitis C. This test will dictate what treatment to take and how long treatment is to be given.

A viral load—HCV RNA—test is given to confirm active infection and it is given right before treatment as a baseline test. A viral load test is also taken at the end of treatment and 12 to 24 weeks after treatment to find out if someone has been cured of hepatitis C.

There are also tests to find out if there is any damage to the liver. There is the liver biopsy and the Fibroscan. Some medical insurance companies may require one of these tests to be performed before they will provide coverage for the medications.

As mentioned above your medication provider may run a battery of tests to find out if you have any conditions related to hepatitis C.

A medical provider will require that a woman planning to undergo treatment or a female sexual partner of a male patient beginning treatment undergo a pregnancy test prior to starting treatment to make sure the female is not pregnant.

Commitment

Your medical provider will want to make sure that you are making a commitment to treatment. You are the most important part of the medical team; so tell them that you will make a commitment to take all of the medications as close to 100% of the time as possible and to keep all the medical appointments and laboratory appointments required. Additionally, you should expect your medical team to treat you with respect and do what needs to be done to help you be cured.

Remember: Everyone has the right to be treated and cured.

Genotype 1 – Sovaldi (sofosbuvir)/Ledipasvir

Genotype 1 – ledipasvir, sofosbuvir with and without ribavirin					
Study name/ Treatment Period	Ribavirin Y/N	Number of Patients	Cure Rates Overall	Cure Rates Genotype 1a	Cure Rates Genotype 1b
ION-1: Treatment Naïve					
12 weeks	no	214	99%	98%	100%
12 weeks	yes	217	97%	97%	99%
24 weeks	no	217	98%	98%	97%
24 weeks	yes	217	99%	99%	100%
ION-2: Treatment Experienced					
12 weeks	no	109	94%	95%	87%
12 weeks	yes	111	96%	95%	100%
24 weeks	no	109	99%	99%	100%
24 weeks	yes	111	99%	99%	100%
ION-3: Treatment Naïve					
8 weeks	no	215	94%	93%	98%
8 weeks	yes	216	93%	92%	95%
12 weeks	no	216	95%	95%	98%

Gilead table adapted from: Doi:10.1056/NEJMoa1402338

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Related publications:

- **Olysio (simeprevir) Package Insert**
www.hcvadvocate.org/hepatitis/factsheets_pdf/Olysio_pi.pdf
- **Phase 3 AbbVie's 3 Drug Combination Therapy**
www.hcvadvocate.org/hepatitis/factsheets_pdf/Phase_3_Genotype_1_AbbVie.pdf
- **Sovaldi (sofosbuvir) Package Insert**
www.hcvadvocate.org/hepatitis/factsheets_pdf/sovaldi_pi.pdf

For more information

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| <ul style="list-style-type: none">• American Association for the Study of Liver Diseases
www.aasld.org• Centers for Disease Control and Prevention
www.cdc.gov | <ul style="list-style-type: none">• Food and Drug Administration (FDA):
www.fda.gov• Mayo Clinic
www.mayoclinic.com |
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www.hepatitistattoos.org

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HCV Drugs in Development