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a series of fact sheets written by experts in the field of liver disease

HCV ADVOCATE

HCSP FACT SHEET

•HCV DRUGS IN DEVELOPMENT•

Drugs in Development – Phase 3
AbbVie's 3 Drug Combination Therapy

Coming Soon:
VIEKIRA PAK Fact Sheet

Written by:
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Editor-in-Chief

Foreword

The studies below are from AbbVie's Phase 3 studies for the treatment of HCV genotype 1a & 1b. The data for this fact sheet is taken from various articles 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.

The medications used in the studies included:

- HCV protease inhibitor, 150mg ABT-450/r (ritonavir 100mg),
- HCV NS5A inhibitor, 25 mg ombitasvir (formerly ABT-267),
- HCV polymerase inhibitor 250mg dasabuvir (formerly ABT-333) and,
- Ribavirin dosed by body weight.

* *ABT-450/r and ombitasvir are co-formulated into one pill, taken once a day. Dasabuvir and ribavirin are taken twice daily.*

Note: A comprehensive chart that lists the Phase 3 studies of AbbVie's 3D combinations with and without ribavirin is included on page 5.

SAPPHIRE-I:

Patient Population:

There were two groups in this study—the information has been combined for this article. There was a total of 631 patients who received at least one dose of the study drugs. The majority of patients were male (344 pts), White (572 pts), and age (~50 yo). There were 427 patients with HCV genotype 1a and 204 patients with HCV genotype 1b. There were no patients with cirrhosis. The treatment duration was 12 weeks.

The two groups (group A and B) were treated at different time points—group A received the AbbVie drugs at day 1. Group B received placebo drugs at day 1 through week 12 and then received the AbbVie drugs beginning at the end

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of the 12-week placebo period. This meant that they could have a comparator arm, but it also gave the placebo group an opportunity to receive the study drugs.

Results:
Overall cure rates were 95 to 98% The cure rates were comparable within all groups (HCV genotype subtype, viral load, race, IL28B).

Side Effects:
The most common side effects were fatigue and headache. The rate of serious side effects was low (2.1%) and the rate of treatment discontinuation was also low (0.6%).

SAPPHIRE-II:

Patient Population:
There were 297 patients who received the study drug (97 patients received placebo). I am only including the information from the group that received the study drug. Most of the patients were male (167 pts), White (269 pts), age (~52 yo), genotype 1a (173 pts), and genotype 1b (123 pts). The treatment duration was 12 weeks.

Results:
The overall cure rates were 96 to 97%. Similar cure rates were seen in subtype 1a and 1b and regardless of type of prior non-response.

Side Effects:
The most common side effects reported in the group that received the study drugs vs. the placebo group were headache (36.4% vs. 35.1%) and fatigue (33.3% vs. 22.7%). Itching occurred more frequently in the group that received the study drugs (13.8% vs. 5.2%). There were 1.3% treatment discontinuations.

TURQUOISE-II:

Patient Population:
- Group A: 12 weeks of treatment—208 patients, the majority of patients were male (146 pts), White (199 pts), age (~57 yo), genotype 1a (140 pts), and genotype 1b (68 pts)
- Group B: 24 weeks of treatment—172 patients, the majority of patients were male (121 pts), White (161 pts), age (~56 yo), genotype 1a (121 pts), and genotype 1b (51 pts).

Results:
The overall cure rates were from 89% to 100%.

Side Effects:
There were more side effects in the 24-week treatment group. The most common side effects (in more than 18% of patients in both groups) were fatigue, headache, nausea and itching. Two percent of the trial participants discontinued treatment due to side effects.

PEARL-111/PEAR-IV:

Patient Population:
The patients were somewhat similar between the arms:

- Genotype 1a—male (63-70%); White (83-86%); Age (~51yo); fibrosis–F0/F1 (63 to 64%), F2 (17to 21%), F3 (16to 19%).
- Genotype 1b—male (41-51%); White (94%); age (~48-49yo); fibrosis–F0/F1 (68 to71%), F2 (18 to 23%), F3 (10 to 11%).

Results:
The overall results were 90 to 99%.

Side Effects:
The majority of side effects were mild. The most common side effects were headaches and fatigue. Two patients in the study discontinued therapy due to side effects.

Genotype 1 – AbbVie

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 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?

Genotype 1 – AbbVie

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. 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, nausea and itching. 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.

Genotype 1 – AbbVie

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.

AbbVie-Phase 3 Clinical Trial Results

Phase 3 Studies – Genotype 1 – ABT-450/r, ombitasvir, dasabuvir – with and without ribavirin						
Study name/ Treatment Period	Ribavirin Y/N	TX Naïve/ Experienced	Number of Patients	Cure Rates Overall	Cure Rates Genotype 1a	Cure Rates Genotype 1b
SAPPHIRE-1						
12 weeks	YES	naïve	473	96%	95%	98%
SAPPHIRE-II						
12 weeks	yes	experienced	297	96%	96%	97%
PEARL-III						
12 weeks	yes	naïve	210			100%
12 weeks	no	naïve	209			99%
PEARL-IV						
12 weeks	yes	naïve	100		97%	
12 weeks	no	naïve	205		90%	
TURQUOISE-II						
12 weeks	yes	both	208	92%	89%	94%
24 weeks	yes	both	172	96%	99%	100%

Genotype 1 – AbbVie

Related publications:

- **Olysio (simeprevir) Package Insert**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/Olysio_pi.pdf
- **Sovaldi (sofosbuvir) Package Insert**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/sovaldi_pi.pdf
- **Phase 3 Genotype 1 – Sovaldi (sofosbuvir)/ledipasvir**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/Phase_3_Genotype_1_SOF-LDV.pdf

For more information

- **American Association for the Study of LIver Diseases**
  www.aasld.org
- **Centers for Disease Control and Prevention**
  www.cdc.gov
- **Food and Drug Administration (FDA):**
  www.fda.gov
- **Mayo Clinic**
  www.mayoclinic.com

Visit our websites to learn more about viral hepatitis:

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HCV Drugs in Development