Patients still needed for HCV study

A clinical trial designed exclusively for people with inherited bleeding disorders and chronic HCV infection (either mono-infected or HIV-1/HCV co-infected) is currently recruiting patients.

The specific purpose of the study, which first began in the spring of 2014 and will be concluding enrollment in December 2014, is to determine the efficacy, safety and tolerability of treatment with ledipasvir (LDV)/sofosbuvir (SOF), fixed-dose combination for participants with genotypes 1 or 4 HCV infection, and SOF + ribavirin for participants with genotypes 2 or 3 HCV infection.

The Phase 2b, multicenter trial, “Efficacy and Safety of Ledipasvir/Sofosbuvir Fixed-Dose Combination and Sofosbuvir + Ribavirin for Subjects with Chronic Hepatitis C Virus and Inherited Bleeding Disorders,” is being sponsored by Gilead Sciences.

In February 2014, Gilead filed a New Drug Application with the U.S. Food and Drug Administration for LDV/SOF, a fixed-dose combination therapy for genotype 1 HCV. SOF was approved by the FDA in December 2013 for use with other anti-virals for treatment of chronic HCV with genotypes 1, 2, 3 and 4. Both drugs are direct-acting antivirals. LDV is an NSSA inhibitor, a drug that disrupts a nonstructural protein HCV needs to replicate. SOF is a nucleotide analog polymerase inhibitor, which blocks polymerase, an enzyme that provides instructions for making copies of HCV RNA.

There are 13 trial sites across the U.S. actively recruiting patients in states such as Georgia, California, Minnesota, North Carolina, Pennsylvania, New York, Washington D.C. and Massachusetts. The study is taking place at Georgetown University Hospital and the contact is Gayle Balba.

Those interested in enrolling are encouraged to access clinicaltrials.gov for more information such as eligibility criteria, trial locations and questions to consider before enrolling in a trial.

According to Gilead, bleeding disorders patients may be eligible to enroll in other ongoing hepatitis C studies. Patients and treaters should check with their hepatologists for current and future hepatitis C studies.


Please note that the clinicaltrials.gov identifier for this study is NCT02120300.

New newsletter format coming soon!

Starting with the January issue, the HCV/HIV News will be distributed via email. This format will allow us to bring you more up-to-date articles from many more sources.

A recent poll of HCV/HIV Today readers showed an overwhelming majority prefer the idea of a paperless edition. Look for the new and improved issue to hit your email box in January.
FDA approves elvitegravir and cobicistat booster

The U.S. Food and Drug Administration (FDA) recently approved Gilead Sciences next-generation HIV integrase inhibitor elvitegravir (brand name Vitekta) and pharmacoenhancer cobicistat (Tybost) as stand-alone agents to be used in combination antiretroviral therapy. The 2 drugs were already available as part of the Stribild single-tablet regimen.

Elvitegravir
The FDA-approved indication for elvitegravir is for use with a ritonavir-boosted protease inhibitor plus at least one other antiretroviral for treatment-experienced patients. In a Phase 3 trial of treatment-experienced adults with drug-resistant HIV, elvitegravir worked as well as the approved integrase inhibitor raltegravir (Isentress) when combined with a fully active ritonavir-boosted protease inhibitor and other antiretroviral drug(s).

Like raltegravir and the other approved integrase inhibitor, dolutegravir (Tivicay, also in the recently approved Triumeq single-tablet regimen), elvitegravir is generally well-tolerated and side effects are uncommon. The most frequently reported adverse events in clinical trials were diarrhea, nausea, and headache. Elvitegravir will be sold as 85 mg and 150 mg tablets and should be administered once-daily with food. It is not yet approved for use with cobicistat outside the Stribild regimen, and the FDA states that "elvitegravir coadministered with protease inhibitors and cobicistat is not recommended."

Administering elvitegravir with other drugs that act as CYP3A inducers could reduce elvitegravir to subtherapeutic levels. It should not be administered with numerous drugs for various conditions, should be taken 2 hours apart from antacids, and women should use non-hormonal contraception.

Cobicistat
Cobicistat increases blood levels of elvitegravir and certain other antiretrovirals by interfering with the drug-processing CYP3A enzyme in the liver, but it is not itself active against HIV. Studies have found that cobicistat worked as well as ritonavir as a booster for atazanavir (Reyataz) or darunavir (Prezista).

The FDA approved cobicistat specifically as a booster for 300 mg atazanavir or 800 mg darunavir when taken once-daily with food. It is approved for both treatment-naive and treatment-experienced patients. The FDA cautions that cobicistat "is not interchangeable with ritonavir" to boost 600 mg twice-daily darunavir or other HIV protease inhibitors, and its interactions with other drugs are unpredictable. As noted above, cobicistat is not yet approved as a booster for elvitegravir outside the Stribild regimen. It should not be used in addition to ritonavir.

Ritonavir -- the only other approved pharmacoenhancer -- is itself active against HIV and was initially used as a stand-alone protease inhibitor, but its use is limited by toxicity and unwanted drug interactions at higher doses. Cobicistat is generally safe and well-tolerated. It increases blood levels of serum creatinine, a kidney biomarker, but does not affect actual glomerular filtration. The most common adverse effects of cobicistat in combination with atazanavir are jaundice and yellowing of the eyes.

Complete labeling information for Vitekta and Tybost will be posted soon at Drugs@FDA.

Press release from the U.S. Food and Drug Administration
First combination pill to treat HCV is approved

The U.S. Food and Drug Administration recently approved Harvoni (ledipasvir and sofosbuvir) to treat chronic hepatitis C virus (HCV) genotype 1 infection.

Harvoni is the first combination pill approved to treat chronic HCV genotype 1 infection. It is also the first approved regimen that does not require administration with interferon or ribavirin, two FDA-approved drugs also used to treat HCV infection.

Both drugs in Harvoni interfere with the enzymes needed by HCV to multiply. Sofosbuvir is a previously approved HCV drug marketed under the brand name Sovaldi. Harvoni also contains a new drug called ledipasvir.

"With the development and approval of new treatments for hepatitis C virus, we are changing the treatment paradigm for Americans living with the disease," said Edward Cox, M.D., M.P.H., director of the Office of Antimicrobial Products in the FDA’s Center for Drug Evaluation and Research. "Until last year, the only available treatments for hepatitis C virus required administration with interferon and ribavirin. Now, patients and health care professionals have multiple treatment options, including a combination pill to help simplify treatment regimens."

Harvoni is the third drug approved by the FDA in the past year to treat chronic HCV infection. The FDA approved Olysio (simeprevir) in November 2013 and Sovaldi in December 2013.

According to the Centers for Disease Control and Prevention, about 3.2 million Americans are infected with HCV, and without proper treatment, 15-30 percent of these people will go on to develop cirrhosis.

Harvoni’s efficacy was evaluated in three clinical trials enrolling 1,518 participants who had not previously received treatment for their infection (treatment-naive) or had not responded to previous treatment (treatment-experienced), including participants with cirrhosis. Participants were randomly assigned to receive Harvoni with or without ribavirin. The trials were designed to measure whether the hepatitis C virus was no longer detected in the blood at least 12 weeks after finishing treatment (sustained virologic response, or SVR), indicating that a participant’s HCV infection has been cured.

In the first trial, comprised of treatment-naive participants, 94 percent of those who received Harvoni for eight weeks and 96 percent of those who received Harvoni for 12 weeks achieved SVR. The second trial showed 99 percent of such participants with and without cirrhosis achieved SVR after 12 weeks. And in the third trial, which examined Harvoni’s efficacy in treatment-experienced participants with and without cirrhosis, 94 percent of those who received Harvoni for 12 weeks and 99 percent of those who received Harvoni for 24 weeks achieved SVR. In all trials, ribavirin did not increase response rates in the participants. The most common side effects reported in clinical trial participants were fatigue and headache.

Harvoni is the seventh new drug with breakthrough therapy designation to receive FDA approval. The FDA can designate a drug as a breakthrough therapy at the request of the sponsor if preliminary clinical evidence indicates the drug may demonstrate a substantial improvement over available therapies for patients with serious or life-threatening diseases. Harvoni was reviewed under the FDA’s priority review program, which provides for an expedited review of drugs that treat serious conditions and, if approved, would provide significant improvement in safety or effectiveness.

Harvoni and Sovaldi are marketed by Gilead, based in Foster City, California. Olysio is marketed by Janssen Pharmaceutical based in Raritan, New Jersey.

Press release from the U.S. Food and Drug Administration
Gilead Sciences, Inc. recently announced that two Phase 3 clinical trials (Studies 104 and 111) evaluating an investigational once-daily single tablet regimen containing tenofovir alafenamide (TAF) for the treatment of HIV-1 infection in treatment-naïve adults met their primary objectives.

The studies demonstrated that the single tablet regimen comprising elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg and TAF 10 mg (E/C/F/TAF), was non-inferior to Gilead’s Stribild (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) based on the proportion of patients with HIV RNA levels (viral load) of less than 50 copies/mL at 48 weeks of therapy. In addition, E/C/F/TAF demonstrated more favorable renal and bone safety compared to Stribild.

In Study 104, 93.1 percent (n=405/435) of patients taking E/C/F/TAF compared to 92.4 percent (n=399/432) of patients taking Stribild, with 95 percent CI from -2.6% to 4.5%, achieved HIV RNA of less than 50 copies/mL at week 48. In Study 111, 91.6 percent (n=395/431) of E/C/F/TAF patients compared to 88.5 percent (n=385/435) of Stribild patients, with 95 percent CI from -1.0% to 7.1%, achieved HIV RNA of less than 50 copies/mL at week 48. Both regimens were generally well tolerated. Discontinuation rates due to adverse events, safety and resistance profiles were comparable between E/C/F/TAF and Stribild in both studies.

Laboratory abnormalities were generally similar for both regimens, with the exception of renal and bone safety indicators, which favored the TAF-based regimen. There was a statistically significant difference in the median change in estimated glomerular filtration rate (eGFR) from baseline to week 48, favoring the TAF-based regimen (-6.8 mL/min for E/C/F/TAF vs. -10.4 mL/min for Stribild in Study 104 (p<0.001); -5.7 mL/min for E/C/F/TAF vs. -11.9 mL/min for Stribild in Study 111 (p<0.001)). Additionally, patients taking the TAF-based regimen experienced a significantly smaller median percentage decrease from baseline in lumbar spine bone mineral density compared to Stribild patients (-1.19 vs. -2.67 in Study 104 (p<0.001); -1.11 vs. -2.81 in Study 111 (p<0.001)) and in hip bone mineral density (-0.77 vs. -3.24 in Study 104 (p<0.001); -0.74 vs. -2.78 in Study 111 (p<0.001)).

In Study 104, median changes from baseline in total fasting cholesterol, HDL (high-density lipoprotein or “good” cholesterol) and LDL (low-density lipoprotein or “bad” cholesterol) were, respectively, 30, 7 and 15 mg/dL for E/C/F/TAF and 12, 3 and 2 mg/dL for Stribild (total cholesterol, p<0.001; HDL, p<0.001; LDL, p<0.001). In Study 111, median changes from baseline in total cholesterol, HDL and LDL were respectively, 27, 7 and 11 mg/dL for E/C/F/TAF and 14, 4 and 2 mg/dL for Stribild (total cholesterol, p<0.001; HDL, p<0.001; LDL, p<0.001).

Gilead plans to submit data from Studies 104 and 111 for presentation to a scientific conference in early 2015.

Several additional ongoing Phase 3 studies are evaluating E/C/F/TAF among multiple HIV patient populations, including patients who switch to E/C/F/TAF from either a single tablet or multi-pill Truvada-containing regimens, patients with a history of antiviral drug resistance, patients with mild to moderate renal impairment and treatment-naïve HIV-positive adolescents. An additional Phase 3b study, WAVES, is evaluating E/C/F/TAF among HIV-positive women who switched from a multi-pill regimen.

Based on the results of Studies 104 and 111 and data from these additional ongoing studies, Gilead plans to submit regulatory applications for E/C/F/TAF in the United States and European Union in the fourth quarter of 2014.
Talking with your doctor about HCV

By Alan Franciscus
HCV Advocate

One of the most important decisions that anyone with hepatitis C (HCV) will make is about HCV treatment. In the past, it has been a difficult decision because of the significant side effects, long treatment duration and modest cure rates. We now have therapies that have fewer side effects, shorter treatment durations and high cure rates. This year we will have three new therapies to choose from to treat HCV genotype 1. The newer therapies will have higher cure rates, lower side effects and shorter treatment periods. So the time is ripe to start talking with your medical provider about treatment.

Some people find it difficult to talk with their medical provider. Being proactive and assertive can take practice, but most medical providers appreciate patients who are well prepared, ask questions and take an active role in their medical care.

Making an Appointment
Doctors are incredibly busy and rushed. Find out if you can make an appointment for a longer period of time than the usual appointment slot. Tell the scheduling person that you want to talk about HCV treatment. Ask if you need to have any tests before the appointment with your medical provider. This will save time for you and your medical provider. A medical provider will appreciate being proactive since it will save her/him time and it will also establish that you are committed to your health, medical care and treatment.

Prior to the Appointment
Make a list of questions and prioritize the most important 4 or 5 questions. For example:

- What treatments are available? Which treatment is best for me?
- Which treatment do you have the most experience treating patients with?
- What side effects have your patients reported? How severe have the side effects been and how have you treated them?
- What experience do you have with insurance companies covering these treatments? Do you work with patient assistance programs?

You may have other questions or concerns so list them, but prioritize the questions. Personally, I show the list of questions to my medical provider as soon as the provider enters the room to send a message that I need time to talk.

Some medical providers (about 25%) communicate through email. If this is the case you are in luck! Send your questions in advance – your medical provider may be able to answer most of the questions via email or at least he/she can read them ahead of time and answer them quickly. This way you can ask any follow-up questions during the appointment. At the end of the appointment, ask if you can email follow-up questions.

Bring a Friend
Let’s face it: the time spent with a medical provider can be stressful. You may not remember every answer or remark. A friend or relative can take notes, help you remember and prompt you to ask questions that you may forget to ask.

The Appointment
Dress appropriately and be groomed. Arrive for your appointment early. You may have to wait — medical providers frequently run late. Review your

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Stribild works well regardless of age, sex or race/ethnicity

By Liz Highleyman
HIVandHepatitis.com

The elvitegravir-based Stribild single-tablet regimen demonstrated good long-term efficacy and tolerability -- including fewer neuropsychiatric side effects than Atripla -- with consistent results across demographic subgroups, researchers reported at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy recently in Washington, DC. Other studies showed that Stribild is a good option for black patients either initiating or switching antiretroviral therapy (ART).

Stribild -- a 1-pill-once-daily regimen containing the integrase inhibitor elvitegravir, cobicistat as a booster, tenofovir, and emtricitabine -- is a recommended regimen for initial HIV therapy.

Richard Elion from Whitman Walker Health and colleagues performed a subgroup analysis of participants in Gilead Sciences’ Phase 3 pivotal trials of Stribild known as Study 102 and Study 103.

This combined analysis included a total of 1408 people with HIV starting ART for the first time. Most (90%) were men, about 70% were white, nearly one-quarter were black, the mean age was 38 years, and the median baseline CD4 T-cell count was approximately 380 cells/mm3.

Participants were randomly assigned to receive Stribild or Gilead's older Atripla single-tablet regimen (efavirenz/tenofovir/emtricitabine) or boosted atazanavir (Reyataz) plus tenofovir/emtricitabine (the drugs in Truvada).

**Results**

The primary analysis at week 48 showed that 89% of people taking Stribild, 84% taking Atripla, and 87% taking atazanavir had undetectable viral load (<50 copies/mL).

After 144 weeks on treatment, 79% of participants taking Stribild had undetectable viral load, as did 75% of those taking either Atripla or atazanavir.

Virological response rates for the 3 regimens were statistically similar regardless of demographic factors: Age: 78%, 73%, and 69% among people <40 years vs 81%, 78%, and 81% among people >40 years. Sex: 80%, 75%, and 76% among men vs 67%, 78%, and 62% among women.

Race: 81%, 79%, and 75% among white participants vs 75%, 68%, and 73% among non-whites.

Response rates were also similar regardless of baseline viral load or CD4 cell count:

- HIV RNA: 81%, 74%, and 77% among those with <100,000 copies/mL vs 75%, 76%, and 71% among those with 100,000-400,000 copies/mL vs 80%, 83%, and 72% among those with >400,000 copies/mL.
- CD4 count: 71%, 76%, and 76% among those with <200 cells/mm3 vs 81%, 75%, and 74% among those with >200 cells/mm3.

Emergent drug resistance was uncommon (<5%) in all treatment arms. Stribild continued to be generally safe and well-tolerated at 144 weeks. Dropout rates due to adverse events were similar in the Stribild, Atripla, and atazanavir arms (6%, 7%, and 8%, respectively).

Most side effects occurred with similar frequency across treatment arms. However, efavirenz-associated neuropsychiatric symptoms such as insomnia, abnormal dreams, and dizziness were significantly more common in the Atripla arm compared with either the Stribild or atazanavir arms. Jaundice and yellowing of the eyes was more common in the atazanavir group.

Fewer than 2% or patients in any arm discontinued due to kidney-related problems, a potential adverse effect of tenofovir. Changes in serum creatinine occurred mostly within the first 4 weeks, then stabilized.

"Stribild had robust and durable efficacy through week 144," which was “consistent across demographics, HIV-1 RNA, and CD4 [count],” the researchers concluded. "Overall efficacy, safety, and tolerability support the use of Stribild as a first-line regimen in treatment-naive HIV patients."

In a related study, David Hardy from the David Geffen School of Medicine and colleagues performed a post-hoc (after the fact) analysis of black or African-American participants, who made up about 30% of the treatment-naive participants in Study 102.

Black people account for a growing proportion of people with HIV and are more prone to kidney disease than whites, which could be a concern when using tenofovir-containing regimens.

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There were 106 black participants (out of a total 348) assigned to receive Stribild and 91 (out of 352) assigned to receive Atripla in Study 102. More of the black patients were women (about 30% vs <10% of whites), but otherwise the groups were similar.

At 144 weeks, 78% of black patients taking Stribild and 66% taking Atripla had undetectable viral load, compared with 81% and 79%, respectively, of white patients. That is, Stribild showed a stronger advantage for black participants. A significantly higher portion of black participants reported achieving adherence >90% with Stribild than with Atripla (89% vs 74%), while adherence was the same in both treatment arms for white participants (94%).

Black people taking Stribild had significantly lower rates of side effects -- including neuropsychiatric symptoms -- and adverse events leading to drug discontinuation than blacks taking Atripla. No black participants stopped Stribild due to kidney-related adverse events.

"Stribild compared to Atripla is an efficacious, durable, well-tolerated, and safe treatment regimen for HIV-1-infected, treatment naive, black adults," the researchers concluded.

Similarly, Joseph Gathe from Therapeutic Concepts in Houston and colleagues reported findings from an analysis of black patients who switched from non-nucleoside reverse transcriptase inhibitor (NNRTI)- or boosted protease inhibitor (PI)-based regimens to Stribild in the open-label STRATEGY-PI and STRATEGY-NRTI trials.

They found that black participants who switched to Stribild from a NNRTI or boosted PI had "numerically higher rates of virological success at week 48," and there were no cases of virological failure. In STRATEGY-PI, 95% of blacks on Stribild vs 89% on a boosted PI had undetectable viral load; response rates for whites were 93% vs 87%, respectively. In STRATEGY-NRTI, 95% of blacks taking Stribild vs 74% taking a NNRTI had undetectable HIV RNA; corresponding rates for whites were 94% vs 91%.

Again, Stribild was well-tolerated with infrequent discontinuations due to adverse events and no proximal renal tubulopathy.

Notes. Bring something to read. Be patient.

It is important that you treat your medical provider and the staff with respect. At the same time, you should always be treated with respect. If you feel that someone (including your medical provider) is treating you disrespectfully you should report it to someone in the medical office or to the medical provider.

If you suspect that your medical provider is annoyed with a question you asked her/him, check in with them about it. Say something like, “Is there something I said that is bothering you?” It is always good to clear the air and it could be something that is unrelated to you or the consultation. Medical providers are human and their mood can be affected by many factors unrelated to you.

If any disrespectful behavior continues you should consider changing medical providers if that is an option. If that is not an option keep making noise, but in a respectful way.

Ask Questions

If there are terms that are used that you don’t understand, ask. Some medical providers may not realize that you did not go to medical school so you may not know what a term means. I remember I read that HCV treatment could cause “myalgia” and it frightened me. I looked it up and it’s muscle pain — much less frightening than what I had imagined!

You may be given information that may bring up many questions — don’t hesitate to ask more questions. If the appointment is coming to an end, tell your provider that you have more questions and ask for a follow-up call or appointment.

Parting Words

Remember you don’t have to make a decision right away. If you are not 100% committed to starting treatment, tell your medical provider and make a follow-up appointment. Don’t let anyone talk you into it. Take the time to think over what you learned and do your research. Be prepared and do your homework before every appointment. Work closely with your medical provider — it should be a partnership. Just don’t make a habit of putting off the decision — that is a decision and it can be dangerous.

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Hemophilia Association of the Capital Area
2014 Calendar of Events

November
5  KUWYH Dinner, Navigating the Financial Aid and Scholarship Process, Joe’s Seafood, Prime Steak and Stone Crab Restaurant, Washington, DC. Biogen Idec presenting.
8  Women’s Day Out: Capitol Hill Food Tour, CSL Behring presenting.

December
1  Men’s Support Group and Dinner, Arlington, Virginia – 6:30 pm
7  Holiday Event, A Christmas Carol at Ford’s Theatre, Washington, DC. Time TBD.

All events are free to HACA members. To join or register for an event, contact us at 703-352-7641 or admin@hacacares.org

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"[Stribild] may be a viable switch option for virologically suppressed black patients on a PI + [ritonavir] or NNRTI with [tenofovir/emtricitabine] who desire a regimen modification or simplification," the researchers concluded.

References

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