WEBINAR VIDEO TRANSCRIPT

Partnership for Care HIV TAC

Hepatitis C Virus (HCV) Treatment Guidelines

Speaker: **Stacey Trooskin, M.D., Ph.D.**

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STEVE LUCKABAUGH: Good afternoon. My name is Steve Luckabaugh and I'd like to welcome you to the hepatitis C virus treatment guidelines webinar. This webinar is brought to you by the Partnerships for Care HIV Training, Technical Assistance, and Collaboration Center, HIV TAC. The Partnerships for Care project is a three-year, multi-agency project funded by the Secretary's Minority AIDS Initiative Fund and the Affordable Care Act.

The goals of the project are to expand provision of HIV testing, prevention, care, and treatment in health centers serving communities highly impacted by HIV; to build sustainable partnerships between health centers and their state health department; and to improve health outcomes among people living with HIV, especially among racial and ethnic minorities. The project is supported by the HIV Training, Technical Assistance, and Collaboration Center, HIV TAC.

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Our speaker today is Dr. Stacey Trooskin. Dr. Trooskin is the director of viral hepatitis programs at Philadelphia FIGHT Community Health Centers. She received her MPH from Yale University School of Public Health and her medical degree from Robert Wood Johnson Medical School, and her PhD from Rutgers School of Public Health. She completed her internal medicine residency and infectious disease fellowship at the Hospital of the University of Pennsylvania. Dr. Trooskin's primary research interests focus on health disparities in developing and evaluating models of HCV care. Dr. Trooskin serves as the chief medical advisor to the National Viral Hepatitis Roundtable, as a member of the American Association of the Study of Liver Diseases, and the Infectious Disease Society of America's HCV Guidelines Committee. Please join me in welcoming Dr. Trooskin.

STACEY TROOSKIN: Thank you. Thank you for that introduction. It's a pleasure to be with you all over this, ah, this lunch hour, for those of you that are on the east coast, and a little bit earlier if those of you listening are further to the west. Today we're going to spend the next hour talking about the AASLD IDSA HCV treatment guidelines, and we're really going to focus on the coinfected patient. And I think that–I don't want anyone to participate the next hour thinking that you're going to walk away knowing everything there is to know about how to treat patients, but really what I'd like to do is give you an overview of the resources that are available to you, and give you the tools to help you navigate through the ASL, the IDSA website treatment guidelines, so that you can feel much more comfortable as you move forward and treat this population.

So, the objectives in the next hour are to discuss the treatment guidelines that are recommended by AASLD and IDSA, and describe the main treatment options for HCV infection among HIV-infected patients, which you will see is identical to those who are HCV monoinfected, and list both host and viral factors that influence the duration and/or type of antiviral treatment that we choose. So, I think it's really important to recognize here that the AASLD, IDSA guidance really should be considered a living and breathing document, and it's updated frequently. In fact, we just updated the website within the last two to three weeks.

We have both on their FDA-approved regimens, but we may also recommend off-label use of certain drugs or tests. And there is this disclaimer that's on the website, this guidance for the hepatitis C treatment and developed is changing constantly. And we actually recommend that you view the guidance through www.HCVguidelines.org for the latest recommendations, and urge people who are using this as a resource to not print it out and use it as a manual, because we do update them quite often. And so, what you may have one day could be outdated a week later. And so, definitely use the web version as the reference.

This is what the home page looks like, and this is revamped–just rolled out a few weeks ago. And I actually really think that the committee members did a tremendous job. I think, for those of you that can remember the Hardy Boys choose-your-own-adventure type of model, we have a little bit of that now on the website. If you look at the bar across the top, there's Home, with a little arrow next to it, the Test, Evaluate, and Monitor, and then Treatment-naive, Treatment-experienced, Unique Populations. And so basically what it allows you to do is say, well, am I

here to talk about how to test, evaluate, or monitor my patient? Then you can pull down that menu.

But the next two bars are perhaps the most important. You either need to know whether your patient is treatment-naive, so, never experienced any treatment in the past for hepatitis C, versus treatment-experienced. And now, treatment-experienced can be defined as an interferon-based regimen, or any DAA regimen that was either used with or without interferon. And then, it pulls it down, and you determine whether or not your patient is cirrhotic, and what genotype they have. And then it takes you to the page that is specifically designed to address the patient with those specific characteristics. So, again, treatment-experienced versus not, cirrhotic versus not, and then what genotype they have. And then you can really hone in on what are the current recommended treatments for your specific patient. So, it's a much more user-friendly model of guidance. And I think–we're quite proud of that, and I hope you all find it easy to navigate moving forward.

So I wanted to just start off by setting the table here with a little bit of a review about hepatitis C. We're not going to spend too much time on that, but I think reviewing the natural history of hepatitis C reminds us, and really informs the conversation around, testing for hepatitis C as well. So, we know that in individuals who are exposed to hepatitis C, about 75% to 85% will go on and develop chronic infection. And for reasons that are not completely understood, but related to both host and viral factors, 15% to 25% will have spontaneous resolution. Those individuals will have antibodies to hepatitis C, but they will not have a viral load, or a viral RNA present, in their blood.

For those that go on and develop chronic hepatitis C, it causes inflammation within the liver, hepatic fibrosis. This can be accelerated by alcohol, HIV coinfection hepatitis B as well. And over time–it can be as short as 20 years, but sometimes quicker than that, even–and the literature has further increased the percentage that will go on and develop cirrhosis of the liver to as high as 40%, in some publications. So anywhere from 20% to 40% will go on and develop cirrhosis in the decades following infection. And that, of course, is not a good thing, because it puts individuals at risk for hepatocellular carcinoma and hepatic decompensation.

We know that the prevalence of HIV, hepatitis C coinfection is high, and this is because of shared routes of transmission. We know that about 30% of individuals living with HIV are coinfected with hepatitis C, and that amounts to around 400,000 in the United States. And the prevalence varies based on the likely mode of acquisition. So, we know that among HIV-positive individuals that got their HIV through a history of injection drug use, 90% will be coinfected with hepatitis C; anywhere from 60% to 85% will be infected if it was through a blood transfusion; and 4% to 8% among men who have sex with men will be coinfected with hepatitis C.

Antiretroviral therapy has really revolutionized the life span and the quality of life that our patients with HIV now experience. But it also has impacted the morbidity and mortality that we now see in our coinfected patients that is associated with hepatitis C. So, antiretroviral therapy

has caused a huge decrease in AIDS-related complications, allowing our patients to live longer, but that allows more time for hepatitis C to do its work. And liver disease is now the second leading cause of death in our HIV patients, and it's primarily caused by chronic hepatitis C. I think this is really important for us to remember, because we can now cure hepatitis C, and we'll talk a little bit about that as the hour goes on. So really, there should be no reason why, in our HIV patients, we are not working towards elimination of hepatitis C in this population, and as a result, really reducing the morbidity and mortality related to hepatitis C in our coinfected patients.

Hepatitis C and HIV have a complex interplay with each other. For those that are exposed to hepatitis C and go on and develop chronic infection, we know that HIV accelerates the rates and the risk of developing cirrhosis, as well as hepatocellular carcinoma and end-stage liver disease. And in fact, HIV coinfection decreases the rates of clearance of hepatitis C, so coinfected individuals are going to be less likely to clear hepatitis C on their own. They're going to have higher rates of hepatitis C RNA levels, increased risk of cirrhosis, increased risk of end-stage liver disease and hepatic decompensation, and increased risk of hepatocellular carcinoma.

And I think the other really important thing here that we tend to forget is that 30% to 50% of coinfected individuals have alcohol use disorders. And we know that alcohol and hepatitis C don't mix. They each individually can cause cirrhosis of the liver. And what I tell my patients is that when you drink alcohol in the setting of hepatitis C, it's like pouring gasoline on fire–that the rates of fibrosis and development of cirrhosis are going to be accelerated substantially. And so, we know there's no safe amount of alcohol use in the setting of hepatitis C; that abstaining from alcohol use is best, although for many of our patients that have addiction, co-morbid conditions, that's not realistic. And then, that's where harm reduction and modifying the amount of alcohol, at least, will try to come into play.

So, when we think about the recommendations for testing that are put forth by AASLD IDSA, these are the recommendations that are published in, really, last week's version of the guidelines, which are still accurate today. But again, I remind you that moving forward in time, these may, of course, change. So you always want to use the website as the reference. The AASLD IDSA guidelines committee recommends and supports the CDC'S guidelines, which are that all individuals born between 1945 and 1965 be tested without prior risk ascertainment.

But we also recommend that other persons outside of that birth cohort be screened based on risk factors. So, risk behaviors include a history of injection drug use or intranasal illicit drug use, and other risk exposures as well, such as people who have been on long-term hemodialysis; anyone who has had percutaneous or parenteral exposures in unregulated settings, which may include tattooing, healthcare or emergency medical or public safety workers after needle sticks; children born to HCV-infected women–this is really important as well, particularly for those of us that take care of younger individuals who have been caught up in the opiate epidemic who are of reproductive age.

We're seeing a lot of women in my own practice who are in their 20s and early 30s who may, in fact, get pregnant. Those children need to be followed, and they need to be screened for hepatitis C. We know there is a risk of perinatal transmission that has probably been unrecognized in the past. And we, as providers, need to do a better job. And then, of course, we need to be testing prior recipients of transfusions or organ transplants, and really, individuals who have received an organ or a blood component prior to 1992 need to be tested for hepatitis C, because that was the first year that we were able to screen the blood supply adequately. And then, people who have ever been incarcerated as well.

And then there are other considerations, which really influences our conversation today around HIV infection. So, for individuals who are caring for folks who are coinfected with HIV, previously we recommend testing for hepatitis C, certainly when they come into care. And then, if they have ongoing risk, I would recommend screening them annually. That's what we do in our own practice. And then, certainly, there's an additional recommendation–you can see at the bottom of the slide there–that annual HCV testing is recommended for people who inject drugs and, specifically, for HIV seropositive men who have unprotected sex with men. And periodic testing should be offered to other persons with ongoing risk factors for exposure to hepatitis C.

I work in a large FQHC system. Our HIV primary care practice has about 2,400 HIV-positive patients, and we deal with a very high-risk patient population, most of whom are ongoing engaging in some sort of risk. And so, we sort of test everybody once a year for hepatitis C as just part of their routine care, and certainly, in some cases, it may even be more frequently.

So, after somebody is tested for hepatitis C, what does the guidance recommend? And so, I put these in here because it's the same for our coinfected patient population. There isn't much difference, and where there are salient differences for treatment and other things, I will point them out. But for the most part, when we think about the coinfected patient population, we treat them very similarly, all the way from testing to cure, as we do our monoinfected patient population.

So, an anti-HCV test is recommended as the first-line test. And if the result is positive, we should be confirming with a sensitive HCV RNA test. Now, what I will tell you is that the current standard of care really is based in reflexive testing, so your major reference laboratories, Quest, LabCorp, both offer a reflexive test model. And what that means is, in one tube of blood, you draw the antibody test, it gets sent to the lab, and in that same tube of blood, if the antibody test is reactive, Quest and LabCorp will then perform a confirmatory test.

And this is really, really important, because we know that about 50% of individuals, if they just get the antibody test alone, will not get the confirmatory test done. And so we want to make sure that individuals are going forward and getting the full story of their infection, that we don't have to ask them to come back for a second blood draw. If you do this on a high volume, it would really create an unnecessary burden on your patients, but certainly on your practice, to bring individuals back for a second set of labs, or perhaps even for a second visit. And then it is

quite complicated to try to explain to a patient, you may have it, you may not have it, there's a 25% chance that you don't, but we need this other test. If you can just get the full story in one tube of blood, it makes things a lot simpler. So for all of you who are listening, if you can think about automating or eliminating an HCV antibody test alone from your orders menu, and rather substituting that with the reflexive test option, you'll be really streamlining the services that you provide to your patient population and the stressors that you put on yourselves and your own staff.

Now, the second line here is, among persons with a negative anti-HCV test who are suspected of having liver disease, testing for HCV RNA or followup testing for antibody is recommended if exposure to HCV occurred within the past six months. Because remember, they can be in a window period, and testing for HCV RNA can also be considered in persons who are immunocompromised. And this is really where your HIV patient population comes in. If we have individuals with CD4 counts of less than 200, or at some point had a CD4 count of less than 200, and they may not have been able to gender antibody, we may just want to be testing them for RNA. And I'll show you an algorithm after this slide that really sort of takes that into account. So, if somebody gives you a known exposure, or if they have transaminitis, you may want to consider just going straight to the RNA test, even in the setting of a negative antibody test.

And also, remembering to share with your patient population that if they've either spontaneously cleared a virus and have a positive antibody test, or they've been treated and cured, that antibody test may always be positive. And then they need to be screened moving forward with initial HCV RNA testing, because that anti-HCV is always going to be there. And so, really, providing some guidance to our patients, making sure they're empowered to talk with their future providers, or whoever is going to be doing their screening, to say, hey listen, that antibody test doesn't mean anything to me. I've been told it's positive in the past, but I either got rid of it on my own or I was cured, so I need the viral load test.

Always needing an RNA viral load or quantitative test prior to initiation of anti-viral therapy. We need to document that baseline level of viremia; in some cases, it impacts how we choose which regimen. There's one regimen in particular if the viral load is less than six million copies, then it can get eight weeks of treatment instead of 12, if they're not HIV coinfected and if they're not cirrhotic. In our HIV patient population, it's always 12 weeks, but it's good to have a sense of what their baseline level of viremia is.

Always need genotype as well, to guide selection of the most appropriate anti-viral regimen. Unless, of course, you're in a resource-limited setting, and you have access to a pan-genotypic regimen, which happens mostly abroad, and I could argue in some FQHC settings, if you're getting free drugs from a drug company to treat somebody who is uninsurable, then you could argue that perhaps you could treat without knowing that genotype if you're using a pan-genotypic regimen. But for the most part, the recommendation is to always know the genotype to help guide selection of the most appropriate anti-viral regimen. And most payer systems will require you to do that as well.

And then the last point here–if an individual is found to have positive results for an anti-HCV test, but is negative for viral RNA, then they should be informed that they don't have evidence of active infection. And I would even say at that point, they should receive some harm-reduction counseling as to how to keep themselves negative in the future.

This is an algorithm that is not taken from the AASLD IDSA guidance, but rather from Tersa. It's a very specific document that's geared towards coinfected individuals. And this really just sort of highlights what I mentioned before, that individuals who are immunocompromised and may not have been able to mount an antibody response to their hepatitis C infection–to consider even in the setting of a negative HCV antibody test to take a look at their transaminase is now–we all know if we treat hepatitis C, that you don't need a transaminitis, and it's not always present in the setting of a hepatitis C infection. But if somebody has an elevated ALT and their antibody test is negative, really think carefully and consider doing a quantitative RNA test. And I would even say if they've given you a very strong history or have a known exposure, and they have a very low CD4 count, or have a history of a very low CD4 count, you may want to consider screening with a viral load test just to make sure that they're not infected.

For individuals who have resolved their infection, again, remembering that you always have to do the screen with the viral load test, not the antibody test, because that will persist as a positive test result.

So when we counsel individuals with current active infection–I'm just going to walk you through here–these all can be found, again, in the guidance, but I think it's important to make sure that we know how to message to patients who are newly diagnosed with hepatitis C, or perhaps have known they've been positive for a while, but have never sought care. I think it's really important to make sure that you let them know that there is good treatment available. But we also want to make sure that we reduce the progression of liver disease and prevent transmission of hepatitis C as well. So, again, counseling around alcohol use, and then, if appropriate and the patient is open to it, facilitating cessation of alcohol consumption with referral to alcohol treatment programs.

And there are other conditions that can accelerate fibrosis, including hepatitis B. We want to make sure that we're controlling those, and we'll talk a little bit about hepatitis B and the complex interplay with hepatitis C, even more so with HIV, as we move forward. And then we need to evaluate individuals for advanced fibrosis. Now, our options are much more varied than they have been in the past. Historically, liver biopsy was considered the gold standard. It's no longer so. In fact, I have not ordered a liver biopsy on any of my patients in more than two years. Noninvasive markers are really now what we're using.

And so, strategies like a fibroscan, otherwise known as transient elastography, which really measures how much scarring is in the liver by sending a sheer wave force and seeing how it bounces off the liver–you can imagine that a cirrhotic, or a very scarred-down liver, doesn't bounce very well and absorb the shear wave. Instead, it bounces it off, and it gives you a very high reading. If someone has a nice, healthy, soft, pliable liver, a sheer wave force is nicely

absorbed by the liver, and it gives you a lower reading. And so, transient elastography has really become a great modality. It's noninvasive; it's just like an ultrasound machine, where you put some jelly on someone's belly, and they take some pictures; the patients are not uncomfortable in any way, shape, or form.

But there are also biomarkers, too. So, some of you may have used either a HepaScore or a FibroShore in your practice, or APRI scores, which are composite measurements and calculations that you can use to estimate how much scarring is in somebody's liver. Really moving more towards those. And so, it's helpful–really the most important thing as a provider is to determine whether or not somebody is cirrhotic or not. Because if somebody is cirrhotic, they need ongoing hepatocellular carcinoma screening, and that usually needs to occur even after cure. If they have cirrhosis at the time of treatment, even after you get rid of the hepatitis C, you still need to make sure you're doing those two six-month ultrasounds, plus or minus an ASP for your patient.

For all individuals who are chronically infected hepatitis C, both monoinfected and clearly our infected patient populations, they need their hep and B vaccines. So getting serology and making sure that you immunize your patients is important. And in the guidance, it says that vaccination against pneumococcal infection is recommended to all patients with cirrhosis, but for those of us that are treating our coinfected patients, we're already needing to provide pneumococcal vaccine for all of our HIV-positive patients. So even if they're not cirrhotic, we need to be doing that anyway.

And then, of course, individuals should be counseled on how to avoid HCV transmission with others. So, harm reduction counseling around safe injection practices. And particularly among our HIV-positive positive MSM, but also patients that engage in heterosexual sex as well, harm reduction counseling–say, sex counseling–is important, so our patients can make informed decisions.

Additional laboratory testing. So, within 12 weeks prior to starting anti-viral therapy, you always want to make sure you get that complete blood count and an INR. And I think for any of you who have prescribed treatments in the past, all of these are often required by our insurance companies as well, that we need to submit these labs not just for good medical care, but also to get approval of direct acting agents. You want to check albumin, total and direct bilirubin, your transaminases and alk-phos levels. And then, of course, make sure that individuals have good creatinine clearance and GFR. Then checking genotype and subtype, as we discussed, in that baseline viral load.

I think it's really important to talk a little bit here about HBV coinfection. So, there was recently a black box warning on direct acting agents that individuals who are coinfected with hepatitis B and hepatitis C–and this is in HIV-infected or -noninfected patients–but if they're coinfected with B and C, once you are treating the hepatitis C, the hepatitis B has been documented to have the potential to flare. And in some cases, particularly abroad, there's been a fulminant liver failure associated with that. So, all individuals with HCV DAA therapies should, before they

initiate therapy, be assessed for HBV coinfection. You want to check the surface antigen, the surface antibody, and then core antibody as well. And if the core antibody is positive, I would consider checking a viral load as well, just to make sure there's no active replication presence.

And in those individuals that do have a hepatitis B coinfection, if they meet the criteria for treatment, I would go ahead and begin that treatment for hepatitis B prior to initiating each CVD AA therapy, and try to get control of the virus prior to treating the hepatitis C.

Testing for the presence of resistance-associated substitutions, otherwise known as RASs formerly called RAV–variants, V for variants–prior to starting treatment should be performed. And there are complex reasons for that, all of which you can find in the treatment guidance, but it does impact drug choice as well. And it depends on the genotype what RAS you're looking for. Most common in the United States is genotype 1a, and there are important treatment decisions that you have to make based on the presence of RASs within genotype 1a. And it can affect duration as well as drug choice.

Anyone who's scheduled to receive an NA–an NS3 protease inhibitor should also be assessed for a history of decompensated liver disease and for severity of disease, using a Child-Turcotte-Pugh score. And so, I think it's important to consider doing a CTP score on all of your patients, because if somebody is cirrhotic, and they are teetering on the verge of decompensation, you really want to make sure that they see a liver transplant specialist, and that that medication be provided in conjunction with a liver transplant specialist.

So, I just want to give that disclaimer first. But particularly for individuals who are going to be receiving protease inhibitors, they can be pretty dangerous in individuals who have a CTP score of seven or greater. It can really decompensate individuals, and we should not be using protease inhibitors in that patient population. If someone has a marginal score of five or six and can be closely monitored for a laboratory, for clinical symptoms during treatment, they should not receive treatment with a regimen that contains paritaprevir or autonomy or ritonavir. So, just a note. But for those of you that are going to be treating in a primary care setting, if somebody has either a Child-Pugh B or C score, I would recommend referring them to a liver transplant specialist or hepatologist so that they can be more closely monitored, and leave that decision-making to them, if there is one in the near vicinity.

So, staging of liver fibrosis. So, we talked a little bit about this, and why it's important to identify cirrhotics versus non-cirrhotics. Again, in cirrhotic patients, there's an increased hepatocellular carcinoma risk. You have to screen, you have to monitor them for hepatic decompensation, and you also consider that liver transplant evaluation. And we can determine cirrhosis by the measures that I've already mentioned, either by liver biopsy, which has fallen out of favor just for the purposes of staging, and also the noninvasive tests.

Monitoring for hepatocellular carcinoma. As I mentioned, this is important to do even after a patient with cirrhosis has been cured. You want to make sure you get a hepatic ultrasound, and really a plus or minus an AFP, but really it's the imaging that's important. That should be done

every six months. Any suspicious lesion requires more specific testing with a multi-phase CT or an MRI. And remembering that AFP alone now is inadequate screening test for hepatocellular carcinoma, and routine screening for HCC without advanced fibrosis or cirrhosis is not recommended.

For our cirrhotic patients, again, considering referral to a liver transplant specialist for those who you have concern for decompensation. You always want to look for encephalopathy, presence of ascites. They may need diagnostic paracentesis or evaluation for a liver transplant. And all cirrhotic patients should have an endoscopy to evaluate for the presence of esophageal varices. They may need prophylaxis with this nonselective beta blocker.

When we talk about treatment, I think it's really critical to recognize that the goal of treatment is really to reduce all-cause mortality, liver-related adverse consequences, including end-stage liver disease, cancer. And we do this by achieving virologic cure, as evidenced by what we call a sustained virologic response, or SVR. And the AASLD IDSA guidance committee says that treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that can't be remediated by treating the hepatitis C, or a transplant, or an other directed therapy.

So, this is a critical point, because I know that there are some jurisdictions around the country that are really rationing treatment for individuals with the sickest livers, with METAVIR scores of two, three, or four. But guidance recommends that everybody with hepatitis C should be treated, unless you're going to die really with a short life expectancy, usually within a year's time.

So we've come a long way with respect to treatment. Some of you who are listening may have had experience using interferon-based regimens dating back to as far as 1986, where TRICARE rates, SVR rates, were less than 10%. With the addition of Ribavirin, there was a little bit more success for cure. When we pegylated our interferon and added Ribavirin, we could expect perhaps a 50% cure rate. And then in 2011, we had our first direct acting agent. And really, direct acting agents are exactly that. They act directly on the virus, whereas interferon and Ribavirin really act as immunomodulators, kind of revving up the immune system to try to kick the virus out. They had a lot of side effects, were poorly tolerated, and were 48 weeks of treatment. Now, we have direct acting agents, all oral regimens–gone are the days of interferon–with cure rates that now exceed 95%.

Different classes of direct acting agents now exists. There's NS3-4A inhibitors, NS5A inhibitors; there are NS5B inhibitors, and then non-nucleoside inhibitors as well. They all work at different parts of the virus. And here is a simple mnemonic to remember some of the DAAs. If they start at–if the second half of the word starts with pre-, think of those that are protease inhibitors. If there's a -uvir, in sofosbuvir, dasabuvir, they can be either nucleotide or non-nucleotide polymerase inhibitor. And if it ends in -asvir, like ledipasvir, ombitasvir, daclatasvir can be an NS5A inhibitor.

The factors associated with treatment and cure. Again, genotype, the stage of liver fibrosis, really focusing on cirrhosis versus non-cirrhosis, whether they're naive or experienced. And then there's always special populations–whether or not folks have chronic kidney disease, the children, transplants, et cetera.

There are medications that are currently FDA approved. Actually, earlier in the week, which occurred after I had to turn in my slide, there was another medication–it's actually a tripill, sofosbuvir/velpatasvir, as sof/vel/vox, is now approved. But up until a week ago, these were the medications that were currently FDA approved. And you can see that we have a lot of options at this point in time. We have options across all genotypes, and you can see that there is even a pan-genotypic regimen in sofosbuvir/velpatasvir. That allows us to treat all genotypes with one pill once a day.

So, fixed-dose combination regimens have really become the standard of care. So we are as simple now as one pill once a day, ranging anywhere from eight to 12 weeks. Again, eight weeks is not really an option for a coinfected patient population, but 12 weeks is currently.

There are some regimens, however, that are not recommended for HIV and hep C coinfected patients, and a lot of this has to do with the anti-retroviral regimens and drug-drug interactions. And I've listed them here for you; you can use this as a reference. And again, the AASLD IDSA guidance has a very thorough listing of drug-drug interactions as well. But I think that all medications, all the DAA that are available, can be used in coinfected patient populations, but we just need to be mindful as prescribers as to how the drugs interact with somebody's specific regimen. And if you can adjust their HIV regimen, if they're not limited by drug resistance, then that's the thing to do. I think it's really important to make sure that your patients are virologically suppressed in terms of their HIV. You want to get them on a regimen that works for them, that's well-tolerated, and then layer on top their hepatitis C medication.

I'll also mention that treatment interruption for HIV is not recommended to accommodate hepatitis C treatment, according to the guidance. That's important.

There are also Ribavirin drug interactions that, if those of you who have been treating for a while may be aware of, you do not want to use zidovudine with ribavirin, or didanosine with ribavirin. Not that many of us are using either of those drugs anymore, certainly not zidovudine as well, but abacavir also may compete intracellularly with ribavirin. And if you want to decrease the ribavirin using weight-based dosing, there's no decrease in SVR. So that's a good tip to know.

Instead of talking about what drugs don't work, I've tried to create for you here a little bit of a can-do sort of table; again, adapted from the treatment guidance. And so, this gives you a sense of what medications can be used with our most commonly used anti-retroviral therapies. And so, there's a lot of leeway here. This is not that hard to find a treatment regimen that works for most of our patients. So, rest assured that for the most part–except for our very complicated patients who have had a very challenging HIV treatment histories, and have developed a lot of

resistance over time–for the most part, you're going to be able to find really good modern regimens for their HIV that work very nicely with their hepatitis C direct acting agent regimens.

Here's a treat–recommended regimens according to AASLD IDSA guidance. A coinfected person should be treated and retreated the same as persons without HIV infection, of course, after recognizing and managing the interaction. So, we've already discussed that. I think that this is a nice important tip here, that daily daclatasvir plus sofosbuvir, with or without ribavirin, is a recommended regimen when anti-retroviral regimen changes cannot be made to accommodate alternative HCV direct acting anti-viral. So you always have daclatasvir plus sofosbuvir to lean on if you're in a tough spot with a lot of HIV drug resistance.

And, as I've already shared with you, treatment courses shorter than 12 weeks, such as the use of eight weeks of ledipasvir/sofosbuvir, are not recommended for coinfected patients. So right now, our coinfected patients, the shortest we can go is 12 weeks' time. And just a quick note that if you are going to use the daclatasvir-based regimen, daclatasvir would require dose adjustments with both ritonavir boosted out zanamivir, and [INAUDIBLE].

There's a couple things to note here around monitoring, according to AASLD IDSA guidance. There's some leeway, because clinic visits or telephone contact is recommended as clinically indicated. And what I will tell you is that I see my patients, and much more often than is recommended, according to the recommendations that follow here. I have a large patient population; many are homeless, many are actively using drugs. And we see them back in clinic very frequently as well. And I honestly do check the HCV viral load, not because I'm concerned, but because we check it more frequently than it's recommended by guidance, because it provides a tremendous amount of positive reinforcement for our patients, and they're excited to see how they're doing. They're excited to see their viral load go down. And so as long as they're open and they want to get their blood drawn, we're happy to do it for them, because it gives us a sense of how they're doing with adherence, and it gives them a sense of accomplishment as they're making their way through treatment.

According to guidance, the CDC creatinine level, in addition to their GFR hepatic function panel, should be checked four weeks after treatment initiation and as clinically indicated. So I use that last statement as my, as a little bit of my green light to go ahead and gauge my patients in a more regular way.

Patients receiving elbasvir and grazoprevir should be monitored with hepatic function panel also at eight weeks after treatment, and again at 12 weeks if they're receiving 16 weeks of treatment. And it's important to watch somebody's ALT and AST for some folks. If they have a tenfold increase at week four, or a less than tenfold increase with symptoms, then you should discontinue treatment. And really, that is one of the only circumstances where we discontinue direct acting agent therapy, because that would indicate that there could be a fulminant liver failure process happening that could be dangerous to the patient. If somebody has a less than tenfold increase in their transaminases and no symptoms, you just repeat those ALT and AST at week six and eight.

When it comes to viral load testing, the guidance recommends checking at four weeks of therapy, and then not again until you're looking for SVR, which is 12 weeks following completion of therapy. And again, my disclosure is I use this as a tool for positive reinforcement for my patients and to continue to engage them. But actually, clinically, you don't need to do it as often.

Anti-viral therapy should not be interrupted or discontinued. If viral load testing is not able to be done, either if the patient doesn't come in or if they're uninsured, you should not stop therapy. And viral load testing can be considered, both at the end of treatment and 24 weeks of longer following completion of treatment as well, but the standard is usually 12 weeks after the completion of therapy, is how we assess SVR. I also like to get a SVR check at the end of treatment, just to document that at the end of treatment, that person was still virologically suppressed.

Patients with compensated cirrhosis on paritaprevir and ritonavir based regimen should be monitored per guidelines. And that is a much more complicated thing that sort of exceeds what we're able to do in the hour today. And again, for our hepatitis B surface antigen positive patients who aren't already on HBV suppressive therapy, you want to monitor their hepatitis B DNA levels during and immediately after treatment to make sure that they're not having a surge in infection. And anti-viral treatment should be given if criteria are met for hepatitis B, and most oftentimes, they are.

And in terms of additional testing recommendations, if it's detectable at week four of treatment, you want to repeat that quantitative RNA viral load at week six. Now, if the quantitative viral load has increased by greater than tenfold at repeat testing at week six or any time thereafter, then they recommend discontinuation of HCV treatment. Because really, in my experience, that acknowledges that the patient is not taking their direct acting agents. We've had cases where the viral load is still detectable at week six, but not greater than tenfold, but very, very low level, and even at week 8. And under those circumstances, you absolutely press on and continue. Do not discontinue treatment under any circumstances.

So, at this time we'd like to open up for questions and answers.

STEVE LUCKABAUGH: OK, we have a few moments here to take some questions if you have them. Please enter your questions into the questions pane on Go To in our toolbar, and we will address those. OK, I have one. What insights do you have from your experience with HCV HIV treatment in the field?

STACEY TROOSKIN: What I can share with you all is that it's incredibly gratifying work. I think, especially when you're treating HIV patients where you can't cure their virus–at least not yet–to be able to offer them a cure for a virus that many have been living with for many decades is really, really exciting, and empowers you not only as a provider, but also the patient. And I've seen folks who have struggled with engagement, who struggled with adherence–if you promised them that if they take these hepatitis C medicines they can get rid of one of their

viruses, it actually even will push folks and motivate folks to reengage in their HIV care in a new way, with a little bit more dedication, a little more fervor, that may have gotten fatigued over time in the past.

So, I feel like if those of you who are listening haven't treated at any scale in the past, I would highly recommend doing so, because it's pretty simple, it's fun, it's exciting, and really, really gratifying for you and your patient population. And it's medically important. I shared with you that liver disease is the second leading cause of death in our HIV patient population, and that can actually be prevented by curing the hepatitis C. So, for any of you who are thinking about it, if you have clinical questions moving forward, if I can be of support in any way, I'm sure that we can get you my contact information, and feel free to reach out. I'm happy to help.

STEVE LUCKABAUGH: OK. If we have any other questions, please enter them now. And I'll remind you about the next session, Challenges in Access to HCV Care. That will be Wednesday, August 23 at 12:00 PM Eastern. The registration link is here, and if you grab the attachments–or the handouts, in the handouts section, on Go To Webinar, this information is there also.

I'm not seeing any other questions. Did you have any closing thoughts before we wrap it up?

STACEY TROOSKIN: Nope, just thanks everyone for your attention, and for logging onto today to listen. I appreciate it.

STEVE LUCKABAUGH: All right, and thank you for participating in today's webinar. We hope that you're able to find the information provided useful as you continue your P4C project. Take care, everybody, and we'll see you next time.