Mitigating Progression of Liver Fibrosis in HIV/HCV Coinfection

CMEO Podcast Transcript

Nancy Reau:

Hello, and welcome. On behalf of CME Outfitters, thank you for joining us for today's CMEO Briefcase, titled mitigating progression of liver fibrosis and HIV hepatitis C coinfection. Today's program is supported by an educational grant from Gilead Sciences. I'm Dr. Nancy Reau from Rush University Medical Center, and I'll be the moderator for today's briefcase.

Christian Ramers:

Hi. I'm Christian Ramers, Chief of Population Health at Family Health Centers at San Diego and Associate Clinical Professor at UC San Diego School of Medicine. And I'll be presenting our patient case today.

Nancy Reau:

The goal of this educational activity is to empower learners to apply efficacy and safety data to treatment decisions for optimal management of hepatitis C with HIV. Let's get started with our patient case. Alonzo Martinez is a 37-year-old Hispanic male with HIV. He is presenting to his treating physician, Dr. Ramers, for a telehealth review of his annual labs.

Christian Ramers:

Hey, Alonzo. It's Dr. Ramers. Nice to see you again. How are you feeling today?

Alonzo Martinez:

Hey, Dr. Ramers. It's nice to see you, too. I'm doing okay. No complaints.

Christian Ramers:

All right. It's good to hear. Now, listen. The purpose of the visit today was really to share some of the results from your annual assessment that we did last week. We ran some of those tests and it looks like you have contracted the hepatitis C virus, and I wanted to talk to you about some treatment options.

Alonzo Martinez:

Treatment? But I already take antivirus for HIV. I don't even feel sick right now.

Christian Ramers:

Yeah. A lot of the times that we see hepatitis C, people don't have symptoms, actually. You can have hepatitis C and really not have any symptoms, especially in the early stages. It's often called the silent killer sometimes

because the symptoms can show up a lot later and really sneak up on you. But the risk of complications really increases the longer you've had it, and it goes up especially if it's been left untreated.

Alonzo Martinez:

Well, how did this even happen? I thought people got HCV from injecting drugs and sharing needles. I haven't touched a needle in 15 years.

Christian Ramers:

Yeah. There's actually several ways that you can get hepatitis C and you're correct that sharing needles is one of them. But it's not the only way, unfortunately. One of the other ways it can be transmitted is actually through sexual activity. Can I ask you a little bit about your relationships? I know you've said before that you may have a couple of different partners. Is that the case now?

Alonzo Martinez:

Yeah, I do have multiple partners. But they all take PrEP, so why does that even matter?

Christian Ramers:

Yeah. You asked about how could I get this if I'm taking my antivirals? The antivirals that we use for HIV and the antivirals that we use for PrEP also really are targeted against HIV, and they don't necessarily protect from other sexually transmitted diseases like syphilis or gonorrhea or chlamydia. Then even for hepatitis C as well.

Unfortunately, HIV antivirals, and then the antivirals used for PrEP don't protect against hepatitis C. What's possible is what happened in your case is that this could have been sexually transmitted. The good news is that there are medications that can clear the virus from your bloodstream and cure your hepatitis C, which we can't do with a lot of other infections. It is a curable disease.

Alonzo Martinez:

See, Dr. Ramers, that makes me very nervous, because I had a friend who took the hepatitis C shots years ago and I remember how sick he got from it. I don't want go through that, so I don't know.

Christian Ramers:

Yeah. I understand your concerns. Believe me, the treatment that I think you're referring to is something called interferon. That was the only injectable medicine that we used to use. I used to treat patients with it and I understand how many side effects that has. You had to take it for a long time, sometimes up to a year. It had really pretty bad side effects like you mentioned, and thank goodness we don't really use that at all anymore.

There's been a whole new generation of hepatitis C treatments that are very different from interferon. Today, it's just pills. You just take pills, just like you're taking for your HIV, usually in as few as two to three

months. The effectiveness and the cure rates are way higher than they were with interferon and the side effects are really way less.

Alonzo Martinez:

Oh, okay. Well, that doesn't sound too bad, Dr. Ramers. As long as you promise no needles, I say let's do it. I'll tell my partners. They probably should get tested for HCV, too.

Christian Ramers:

That's a great idea. Sounds good.

Nancy Reau:

According to expert guidelines, how often should sexually active HIV positive men who have sex with men be screened for hepatitis C infection? Christian, so we just met Alonzo. Do you want to tell us a little more about your history of him and how he ended up in this screening program?

Christian Ramers:

Sure. Thanks, Nancy. As you can see, he's a 37-year-old Hispanic male and really presenting with new HCV infection that was picked up on really a standard annual screen. You can see his medical history. He's been HIV positive since 2012, so at least 10 years. He does already have resistance to tenofovir with a mutation called a K65R mutation. One of the more common ones that we see that has required him to be on a second line regimen.

Knows his hyperlipidemia and his body mass index is above 30. In terms of his social history, he is a man who has sex with other men and does have multiple partners, as we identify in the case history. He also has a history of injection drug use, but has not injected at all since 2007 and has had subsequent negative hep C screenings since then. He does drink occasional alcohol and denies tobacco.

You can see on the screen, his recent labs. These were fasting. He was hepatitis C antibody positive, hepatitis B surface antigen negative. His CD4 count is nice and high, 800, and as HIV RNA is undetectable. His transaminases are listed there with an AST of 55 and an ALT of 221, and his lipids show an LDL of 98, HDL 46, triglyceride is 144, and a normal glucose at 92.

His current medications for his HIV involve the darunavir, cobicistat, emtricitabine, and tenofovir alafenamide combination. He takes that once daily, and again, that's a second line regimen for him. He is also on rosuvastatin at 10 milligrams once a day.

Nancy Reau:

Thank you. Alonzo's liver test numbers are clearly not normal. And that should not be the only trigger for hepatitis C screening, right? Even if his numbers had been normal, you still would've advocated for hepatitis C screening?

Christian Ramers:

Yeah, that's right. With our new recommendations, first of all, all adults should have hepatitis C screening, but Alonzo does fall into a category where he should have annual screening. That's because really, all HIV positive men, especially HIV positive men who have sex with men, or even HIV negative men who have sex with men who are accessing PrEP should get annual hepatitis C screening, because this is one of the populations where sexual transmission can occur. In his case, this is how this was actually picked up.

Nancy Reau:

Our patient seemed a little mystified. Do you think that there's awareness in this population that there could be liver risk for hepatitis C?

Christian Ramers:

Yeah. He had a common misperception, which is that this is only something that you get from injection drug use. In fact, hepatitis C, as we know, is a relatively robust virus and it could be transmitted through tattoo needles, through close contact with blood, and then also through sexual transmission.

There are even some populations where sexual transmission makes up the majority of hepatitis C transmission. I think there is a growing awareness, but really it's not where it needs to be in terms of screening adequately in this population.

Nancy Reau:

Epidemiology of hepatitis C has definitely been changing to be more bimodal, in that a younger population is higher risk because of injection drug use. What about in our coinfection individuals, as their demographics and risk factors are a little bit different as you outlined?

Christian Ramers:

That's a good point, Nancy. I think that it's actually much more homogeneous than what we see with this bimodal distribution in the older baby boomers that maybe have gotten exposed long in their past from injection drug use or tattoos or from the blood supply. The younger, we're talking about mono infected populations, where it is primarily injection drug use, really it's anyone who is sexually active in this category. So any men who have sex with men of any age.

One of the things that PrEP has really infused into this epidemiology is that condom use is on the decline I would say, because people are using PrEP as their preferred method of preventing HIV infection. That does put our populations at risk of bacterial STDs, as well as of sexual transmission of hepatitis C, which can occur at any age across the spectrum.

Nancy Reau:

I think that there are always really important tidbits for awareness, and this is definitely something that I think clinicians that are not familiar with a coinfected population or MSM, probably are hesitant to talk to other patients about. Our primary care providers do have a big burden of discussing lots of things, and this probably does follow in a little under the threshold of what they're used to.

Christian Ramers:

Yeah. My comment on that is that in an HIV clinic or in an STD clinic, sexual health really needs to be part of primary care. We should just get a little bit more used to it and more comfortable with it. In this case, it's generally part of what we should be offering. In fact, many of our systems have this as a popup for all HIV positive patients to get an annual hepatitis C. That's really the way it should be to pick this up.

As we mentioned, all people with HIV should be screened for hepatitis C at entry into care, and then annual screening really is recommended for these key populations. Then finally, periodic testing, when you have a specific activity or exposure that increases the risk is another good practice. What we see a lot in our own clinical practice is the presentation of acute hepatitis C.

For that reason, sometimes checking the antibody and the RNA, as well as the ALT are all necessary to pick up that acute infection, because it can take several weeks to months for that antibody actually to convert to being positive. And if you only send the antibody when you have a suspicion of acute hepatitis C, you might miss it.

Nancy Reau:

Well, why don't I let you review just a little bit, the epidemiology of coinfection, to drive that message home; that we do have to be comfortable with these discussions because the epidemiology definitely warrants this being part of the conversation with our patients.

Christian Ramers:

Globally, HIV positive individuals are five to eightfold more likely to be hep C antibody positive compared to the general population or HIV negative individuals. In my opinion, this is probably just because of shared routes of transmission. I like to think of HIV as a sexually transmitted infection that sometimes can be bloodborne and hepatitis C is a bloodborne pathogen that sometimes can be sexually transmitted, and so there's that overlap in people who inject drugs or in men who have sex with men, where they are really at risk for both infections.

Among men who have sex with men, hepatitis C infections markedly increased since the 2000s in the US, Europe, Asia, and Australia, and there are some theories of why this may be. I think the onset of PrEP may have had something to do with that, with perhaps decreased condom use. Hepatitis C infection amongst HIV positive MSM and HIV negative MSM accessing PrEP appear to be similar in the studies that have been done in parts of the US and Europe. Then unfortunately, we don't really have a vaccine for hepatitis C and infection does not really provide long lasting immunity.

Those who either clear the infection spontaneously or are treated and cured are actually at ongoing risk for reinfection. On the right-hand side, you can see the results of a meta-analysis of the odds of hepatitis C in selected HIV populations versus HIV negative population groups. You can see something quite striking, which is the prison population actually has the highest odds ratio here. But several other groups, including MSM, those who inject drugs, those who are participating in sex work or other high-risk activities do have close to a five or over a fivefold risk of hepatitis C infection.

Nancy Reau:

Christian, I'll ask you, before we turn to the next audience response question, if you have a person who's either spontaneously cleared the infection or has been treated and cured, how do you screen them or do you still need to screen them?

Christian Ramers:

That's a great question, Nancy, and it really hits on the idea that hepatitis C antibody generally stays positive for life. And once somebody has been exposed, that then becomes a useless test, because it does not provide you any new information. In order to see if somebody who has already cleared hepatitis C has been re-exposed or reinfected, you really have to use that HCV RNA. Then if you're suspicious of acute infection, maybe with a symptomatic or icteric illness, then you have to send that ALT as well.

Nancy Reau:

Thank you. All right. I'm going to poll our audience now. Which of the following concerning patient outcomes results from the natural history of HIV hepatitis C coinfection. Christian, why is coinfection so important? Why do we emphasize this even above and beyond mono infection?

Christian Ramers:

Thanks for the question, Nancy. There are a lot of aspects of treating coinfected patients that are not very different between hepatitis C mono infection and HIV hep C coinfection, such as the effectiveness of the drugs and things like that. But there are some aspects that are really strikingly different between the mono infected population and the coinfected population. The main thing that really bothers or scares me a little bit more is the rapidity with which progression can occur. From being infected to getting cirrhosis, we generally think in the mono infected population, this is a process that takes decades, and yet in some coinfected populations, it seems to be very, very rapid.

As you can see on the left-hand graph here, the percentage of people with cirrhosis is extremely high in this HIV hep C coinfected population that's followed through time, and much higher than the HCV mono infected population. I don't think we know exactly why this is, but it may have to do with immune-mediated damage, with the way that the hep C virus behaves in the livers of HIV coinfected patients. The studies done to date have shown that HCV infection progresses to cirrhosis two to seven times more often and two to three times more quickly than HIV HCV coinfected individuals.

The other important aspect here is, what is the burden of HCV coinfection in the HIV population? You can see, it really causes the majority of liver related problems. On the graphic on the right-hand side, you can see HCV infection is by far the greatest risk factor for liver related death in people infected with HIV. So a huge burden in terms of liver related death among the HIV population who with our antiretrovirals, otherwise can have long, full lives, and so this is a very important aspect to address. Up to 90% of liver related deaths in people with HIV are actually attributable to HCV infection, and endstage liver disease predominantly due to HC is a leading cause of mortality in people with HIV infection.

Nancy Reau:

Our HIV medicines do, or at least HIV itself might have some association with steatosis. Do you think that this is contributing or are HIV therapies sub hepatoxic?

Christian Ramers:

That's a really good question. The toxicity of HIV medicines in terms of general drug-induced liver injury, don't seem to be more common in coinfected individuals, but the first part of your question, I think is a little bit less understood. We are seeing incidents of fatty liver in HIV patients, which seems to be above the general population.

And it's not exactly clear whether that's due to the virus itself, whether it's due to some of the therapies, including some of the older therapies that we think were much more toxic than our current therapies. Or whether it's due to weight gain, which has been loosely, but consistently associated with antiretroviral therapy, and there are very smart people still trying to work this out.

Nancy Reau:

Well, we'll stay tuned for that then, I guess. When we talk about evaluation, you alluded to the fact that we often lump coinfection in with mono infection and efficacy. So we should not be telling our patients that they are less likely to be cured. But their evaluation might be a little bit different. Is that correct?

Christian Ramers:

We generally hit a lot of the same things, which includes genotype for the hepatitis C, hepatitis C RNA. Then we really want to pay attention to the other hepatitis, such as hepatitis A and hepatitis B. There are very important reasons to know somebody's hepatitis B status, whether they have HIV or not, but in particular with HIV, some of our medicines that we use to treat HIV also treat hepatitis B. So we really want to have a solid idea of where somebody is in terms of that.

Then a lot of the other tests that we use are very similar. The biomarker tests or transient elastography are what we use to stage the fibrosis. It's important to know that the fibro scan or the scales that we use have been developed in specific cohorts of HIV and hep C coinfected people. When we're interpreting fibro scans, let's make sure that we use the right scales and the right data here. Then there are a couple of nuances here, and that is that some of our calculated indices, such as the APRI and the FIB-4 depend heavily on platelet count.

There is an entity called HIV related thrombocytopenia or even HIV related ITP or immune-mediated thrombocytopenia purpura, which may falsely lower the platelets or lower the platelets and give a false interpretation of the APRI and the FIB-4. So I tell providers just to pay extra attention to that. They may be tricked by thinking the fibrosis is a little more advanced than it actually is, because of a lower-than-average platelet count due to HIV causes that aren't necessarily related to the liver disease.

Nancy Reau:

Do you still advocate at all for a liver biopsy in this population? Because if they have significant fibrosis, that's going to impact how you would follow them longitudinally, I imagine.

Christian Ramers:

I generally do not, and the reason is because patients don't generally like it. It's invasive, and we have very good tools that as I mentioned, have been very well-validated in HIV hep C coinfected populations, most specifically the fibro scan or the transient elastography. I generally rely on that, plus or minus an additional serological measure.

Nancy Reau:

Excellent. Thank you. Well, let's follow up now with Alonzo to see the results of his hepatitis C workup.

Christian Ramers:

Okay. Welcome back, Alonzo. I wanted to go over some of the results of your HCV evaluation.

Alonzo Martinez:

Oh, I can't handle too much bad news right now. Is there something wrong?

Christian Ramers:

Well, your workup so far has showed what's called hepatic fibrosis. In order to describe this, we use a scale of zero through four, and you're actually all the way up at a stage three by that scale.

Alonzo Martinez:

Fibrosis? What does that even mean? It sounds bad.

Christian Ramers:

Yeah. Fibrosis is another word for scarring, and what it means is that you've built up quite a bit of scar tissue trying to fight off the hepatitis C infection. It's making your liver getting to the point where it's making your liver not function correctly. Usually, it takes a lot of years to get to this point, but sometimes fibrosis progresses much more quickly when you have both HIV and hepatitis C at the same time. There's even a form of fibrosis that could

be related to HIV itself. It's actually a really good thing that we caught this when we did, because getting you treated for hep C is the best way we have to really stop the fibrosis from getting any worse.

Alonzo Martinez:

Okay. Is my liver ruined forever? What happens next? Please help me through this, Dr. Ramers.

Christian Ramers:

Yeah. Really good questions. It's very clear what we need to do next, and that is to get your hep C treated and cured, and we have an excellent chance of doing that. The good news is that your liver can heal. It's one of the only organs in your body that actually can heal once we get rid of what's irritating it right now. Like I said, the next step right in front of us is to get you treated and cured of that hepatitis C, and to give your liver a chance to get better.

Okay. As you can see, we have the results back from Alonzo's workup here, and his genotype is 3A, HCV RNA is 1.3 million. He has relatively preserved kidney function with a GFR of 62 mills per minute. Platelets are a little bit on the low side, 130, and his repeat ALT is, looks like on the way down at 190 IUs per liter. He did have liver elastography consistent with Metavir stage three fibrosis. His main question is, is my liver ruined forever?

As I mentioned to him, I would say, never say never. The liver can regenerate. For patients that present already with cirrhosis, if they're in an F4 category, it's a little bit of a more difficult answer, because there's less recovery. It's still estimated to be maybe half of patients that can recover. But probably more than half, if they're stage two or stage three or even lower are able to recover their liver function.

Nancy Reau:

I just had a question, because we think that he's got acute or recently acquired hepatitis C. Is it common that you would see someone that has already progressed to stage three? I know you did already warn us that this is more aggressive than mono infection.

Christian Ramers:

Yeah. If I could make a best guess about what's happening here, he may have had HIV associated liver disease or fibrosis at baseline, and somebody who's had HIV for more than 10 years maybe was treated with some older therapeutics. Maybe it is the HIV medicines that have been causing a little bit of irritation. It is unusual in the face of acute hepatitis C that we didn't know about.

Presumably he'd been screened at least every year or so, if we were following guidelines. So yes, that is a bit of a surprise. Most what I'm seeing in clinical practice is that there are more than one liver disease happening at the same time. It may be that he had underlying fatty liver or HIV associated liver disease, and then on top of that, has this acute hepatitis C infection.

Nancy Reau:

Yeah. Thank you for that. I know that in my population where I don't see as many coinfected, alcohol use disorder is often a driver for fibrosis. And so it's important to recognize if we believe our non-invasive test, but also if we believe the accuracy of it, to not necessarily ascribe it to only one condition.

Christian Ramers:

That's a great point.

Nancy Reau:

All right. Let's turn now to some of the safety and the efficacy. Alonzo was really worried because he had heard bad things about hepatitis C treatment. You and I are both old enough that we had been treating hepatitis C with pegylated interferon, with or without first generation protease inhibitors, which was definitely a particularly toxic and not always effective treatment. How about today?

Christian Ramers:

Yeah. Alonzo's concerns are very common in clinical practice, especially in people who are acquainted with, or knew someone who took older interferon therapies, because they witnessed those side effects firsthand. I see a lot of patients who may have been incarcerated and if their cellmate ever went through interferon therapy, they saw it up close and personal how difficult it was to get through that therapy. This is a great opportunity for a lot of education about the fact that we're in a completely new era really since 2015 or so. The DAA era not involving interferon at all in therapy, and it's really a good message to give to patients, that they don't have those side effects to worry about.

There is sometimes a concern that, well, since I have HIV, maybe my cure rate is not going to be as good. But the literature's been quite consistent and very striking about the safety and efficacy of DAAs amongst coinfected patients, that they're equal. In fact, some cases, some of the publications you see at the bottom of a slide, the efficacy was in fact better. I attribute that to the fact that adherence may have been better amongst HIV patients who literally take a pill every day to keep themselves alive. They really understand what good adherence means.

But the SVR or the sustained virological response or cure rate was achieved in greater than 95% of patients across multiple studies, whether it be sof-vel, glecaprevir-pibrentasvir, sof-ledipasvir or grazoprevir-elbasvir over different durations of therapy. Very, very encouraging, and it's a great message to give to our patients that they have a high probability of being treated. A couple of additional therapies that you can see down on the bottom here that are just interesting side notes is that we now are able to treat people with minimal monitoring. This study, giving people really the whole course of therapy, many of whom were coinfected in this clinical trial without doing genotyping and without doing scheduled monitoring, also achieve this really amazing 95% SVR rate.

Then in terms of a public health perspective here, an ongoing transmission, which is really a key issue in the MSM population, again, because they remain at risk if they are sexually active, is that after two years of unrestricted access to DAAs in the Netherlands, 76% of the HIV positive MSM, whoever had hepatitis C were cured, and the acute HCV infections were reduced by 51%. Implying that the idea of treatment as prevention is a way to decrease the rates of additional HCV infection in a population.

Nancy Reau:

Thank you. That's incredibly encouraging, especially for some of us that might be a little bit biased by historical, or our patients are biased even by historical treatments. Let's poll the audience. Alonzo has three potential reasons that you might choose one treatment over another. He's genotype 3A, he's currently taking darunavir, cobi, FTC, and TAF, as well as rosuvastatin 10 milligrams a day. Which DAA regimen is the best choice for treating his hepatitis C infection.

Christian Ramers:

If we take a look at the section in the AASLD IDSA guidelines, there are specific recommendations on which DAA regimen to use. Several of these are pangenotypic, and the general trend in HCV therapy has been to move towards pangenotypic regimens. One of the main considerations is drug-drug interactions. We want to choose regimens that have high efficacy, and thankfully, we now have multiple regimens that are high efficacy across different genotypes.

But really, the most important consideration here is what's going to work with the ART regimen that particular patient is on. I really don't like to change a regimen that a patient is comfortable with, that's working for their HIV. It just introduces more complexity and the possibility of more problems. So we try to make the hepatitis C regimen fit into what he is already taking for his HIV.

Nancy Reau:

Christian, I have a question. Some of my patients, when they present are newly diagnosed with coinfection, and their CD4 count is not as robust as this patient's. What do you do then?

Christian Ramers:

Yeah. The recommendation is generally to focus on the HIV first, and get that viral load undetectable. When you do that, the T cells are generally going to increase and make the immune system just a little bit stronger. It also gives you a chance to get to know the patient, get them comfortable with your clinic, and really get a nice pattern going.

Hepatitis C is rarely an emergency, so you can develop a rapport. And after a couple of months, usually you'll have that virally undetectable. The CD4 cell count will be on the way up. You can have a stable regimen and then really jump right on the hepatitis C treatment right after that.

Nancy Reau:

We do have multiple choices for hepatitis C therapy. Are there some that you find are easier to integrate, or do you just know that you have multiple treatments that work well, and you're going to match those up with the HIV treatment as you need to?

Christian Ramers:

Yeah. It's important to integrate patient choice in here as well, but I would say that the drug interactions trump the patient choice in a lot of cases. Because if somebody wants to take a particular regimen, but it interacts heavily with their antiretroviral therapy, we generally will steer them towards one that has fewer interactions. Thankfully, there's a lot of really good resources in terms of looking up these interactions, and we're going to see on the next couple of slides, what some of these charts actually look like.

Nancy Reau:

Why don't we address the fact that he's genotype 3A? Again, like historical bias might have more thought that he would have more side effects or less efficacy. Now, genotype three is no longer the Achilles heel as much when we're talking about pangenotypic treatments, but it is still a factor.

It does increase steatosis, might have more aggressive disease, might increase liver cancer rates a little bit. And we do find that our genotype three patients fail a little more frequently some of our other genotypes, even though efficacy is still well above 95%.

Christian Ramers:

Nancy, it's a really good point. I think the modern era is just so different than it was, even as few as five years ago, where we're talking about a little bit of a decrease in efficacy, but still, we're above 90% in all cases. I guess it depends if you're a glass half full or a glass half empty kind of person. There are some treaters that do look for resistance in cases when you have genotype three and cirrhosis also present. In Alonzo's case, I probably wouldn't go that far. I would just proceed more with an attention to the drug-drug interactions, which are so important.

Nancy Reau:

Why don't you tell us a little bit about how to pick that, based on HIV treatment?

Christian Ramers:

Yeah. As you can see on the chart here, there are many resources that you really need to develop a table, based on what regimen he is actually on, and then you can see all of the hepatitis C regimens really across the board here. The patterns that we see really obey a couple of important trends here. The first is that a lot of the red is in places where you have protease inhibitors on both sides of the regimens; meaning the HIV side and the hepatitis C side. We've already gone through the fact that Alonzo has some drug resistance in his HIV, and he's had to be placed on a second line regimen, which includes darunavir and cobicistat, which are proteases inhibitors.

As you can see, when that lines up with several of the regimens, whether it be glecaprevir-pibrentasvir, elbasvir-grazoprevir, or sofosbuvir-velpatasvir-voxilaprevir, that's where those reds really pop up there, because of the degree of interaction between the two different protease inhibitors. On the bottom, you can see that there is some consideration for TAF or TDF, and that has to do with the idea of increasing the levels of TDF, if that happens to be in his HIV regimen. That's an interaction with velpatasvir, actually, and ledipasvir. Thankfully, in his case, he's on an HIV regimen that has TAF instead of TDF, and so we don't really have to worry too much about that.

As long as we're in any of these green zones, I think we're okay. I would say that, as I mentioned, his HIV regimen takes precedent because I don't want to change that. Lining these up, it looks like sofosbuvir-velpatasvir is a regimen that has minimal interactions with his current HIV regimen.

Nancy Reau:

Before we leave DDIs, what would you do with his rosuvastatin?

Christian Ramers:

That's a really good point, Nancy. I do this a lot, almost all day every day with treating patients with hepatitis C, and I still do not like to commit the statin drug interactions to memory. That's an encouragement for you to look it up every single time, and part of that is because the statins actually behave very differently with respect to drug-drug interactions in hep C therapeutics.

With rosuvastatin, he's on a 10-milligram dose, which actually is compatible with sofosbuvir/velpatasvir, even though you will increase that dose a little bit with the drug-drug interaction. I probably would leave it right where it is, but I would be conscious of it. I would make the patient aware that he may have slightly increased levels of rosuvastatin during the time that he is taking hepatitis C therapy, and so be a little bit more vigilant for any symptoms which may indicate early rhabdomyolysis.

Nancy Reau:

Let's turn now to an audience response question. What continued hepatitis C related monitoring is recommended for Alonzo, after he's cured of his hepatitis C infection? Christian, I'm going to turn to you a little bit about the hepatitis C care continuum. You've identified him as stage three and he has genotype three, and so there is some risk. If you believe your fibrosis testing before you treated him, how would you monitor this patient, even after his cure?

Christian Ramers:

Yeah. This is where it's critical to have a really good and reliable fibrosis assessment before you treat the patient. Most of these measures have been validated in people with chronic and active hepatitis C, and it doesn't quite work if you wait till after you've treated them to do that fibrosis assessment. So I'm very glad we did it. And I'm glad that we discovered he was F3, because anybody who's F3 or F4 is actually going to need biannual monitoring for hepatocellular carcinoma with an AFP in the blood, as well as a ultrasound test.

That's because even after you cure hepatitis C, there is still a risk of developing hepatocellular carcinoma. It's one of the biggest tragedies in all of hep C treatment where you cure the hep C and yet somebody still develops cancer, but this is going to be a really important part of his ongoing care. Now, in his care situation, I'm seeing him about every three to six months anyway for his HIV, so I just incorporate that into his usual care. If there isn't a concerning nodule or a mass that's detected, that's when I do bring in special expertise, such as a hepatologist.

Nancy Reau:

I think it's interesting. I've heard some of our other experts say, if you could restage this person and they are no longer advanced fibrosis, you could stop monitoring them. Do you believe that?

Christian Ramers:

All it takes is getting burned once, when you see the fiber scan look better. There's a study that was done close to me at the Scripps Clinic, where they were liver biopsies done and fiber scans done every six months, and they were paired. It turns out that the fiber scan tends to look a little bit better, much more quickly than the liver biopsies actually do. In this case, I actually choose the worst that he's ever done, and that typically is done right before the treatment occurs, and mark that as his high-water mark, so to speak, and really treat him like that for life. Because I don't want to be the one that misses somebody who does develop cancer because of lack of screening.

There's one additional thing I want to talk about, Nancy. We've mentioned this a couple of times, which is that he is at risk of reinfection. If he remains sexually active and doesn't know the status of his partners, he doesn't really have any immune protection from having that hepatitis C. It's important to talk about knowing the status of his sexual partners, as we saw from that study in the Netherlands. The more people we can identify and treat, the less likely there's going to be onward transmission. Then, monitoring for signs and symptoms of acute hepatitis C infection.

Thankfully, we do liver function tests about every six months on our HIV patients, so we will pick up on elevation in transaminases. Then finally, annual screening for reinfection is going to be, again, part of his usual care, and that's going to have to be with an HCV RNA.

Nancy Reau:

Given that you weren't 100% convinced that all of his fibrosis was related to his hepatitis C, would you continue to assess for progression and fibrosis, even after you've cured him?

Christian Ramers:

Yeah. That's a really good point, Nancy. One of the things I like to do is to watch where his transaminases fall to during and after the hepatitis C treatment. We mentioned that you don't really need to do monitoring during treatment, but I do like to see where he ends up. And if he ends up with those transaminases completely back to normal, I feel pretty good that there's not really ongoing inflammation.

But as you mentioned, I am concerned that he may have a secondary cause of liver disease. And with a BMI above 30 and having HIV, he really is a setup for having some type of fatty liver disease. Absolutely, I want to remain vigilant and watch for any further progression. That may involve another fiber scan for transient elastography in his future, a couple of years down the road, and it certainly does involve measuring transaminases at least twice a year.

Nancy Reau:

Well, thank you so much, Dr. Ramers, for your insight today. And thank you to our patient, Alonzo, for guiding us through management of HIV hepatitis C coinfection. Let's pull it all together with our smart goals to apply in practice. After today, we hope participants will screen patients with HIV for hepatitis C coinfection at guideline-recommended intervals, to optimize early detection.

Prioritize compatible ART and DAA therapy for patients with HIV hepatitis C coinfection, to improve liver related morbidity and mortality outcomes. Thoroughly evaluate DDIs of ART, DAA, and other medications when choosing DAA treatment for patients with HIV hepatitis C coinfection. Educate vulnerable patients on harm reduction strategies to reduce hepatitis C transmission and reinfection.

Be sure to check out the other activities in the CMEO Briefcase series, treatment decisions for patients with hepatitis C and CKD, and treatment selection in a patient with decompensated cirrhosis. These activities, as well as many other educational resources for clinicians and patients, can be found online at the CME Outfitters Infectious Disease and Virtual Education Hubs.

To receive continuing education credit and a principal certificate for completing today's activity, participants must complete the post test and evaluation online. Thank you all for participating and providing the best care for your patients. Take care.