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Support@ceitraining.org

PRE-TREATMENT EVALUATION OF THE PATIENT WITH HEPATITIS C VIRUS INFECTION

Speaker: Oluwaseum Falade-Nwulia, MBBS, MPH

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Pre-Treatment Evaluation of the Patient with Hepatitis C Virus Infection
[video transcript]

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Without further ado, we're going to start with Dr. Falade-Nwulia who's going to talk to us about pre-treatment evaluation of patients with hepatitis C and what are the things we need to do to get ready for treatment. Thank you so much.

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Thank you. Good afternoon. It's such a pleasure to be here this afternoon talking about hepatitis C, a disease that affects many of our patients, but I think more importantly, a disease that we can now treat and care in our patients.

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I have no disclosures.

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And these are the objectives we're going to be covering today. Quick show of hands. How many of us currently treat hepatitis C in our practices? OK so perfect. It's very encouraging to see so many of us treating hepatitis C.

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So, we'll start the talk by going over the epi of hepatitis C in HIV.

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It's believed that somewhere between 10 to 25 percent of individuals infected with HIV are also infected with hepatitis C and this is not surprising due to shared modes of transmission. The prevalence of hepatitis C in HIV-infected populations varies by the risk factor for HIV acquisition. So, if you look on this graphic, you see on the Y axis the percentage that is Hepatitis C co-infected of the HIV total. In those that acquired HIV through injection drug use, it's thought about 65 percent and in some populations up to 90 percent, are co-infected with hepatitis C. If you acquired HIV through heterosexual sex, the prevalence of Hepatitis C is about 15 percent. And if you are a man who has sex with men who acquired HIV that way, the prevalence of hepatitis C in this population is thought to be about 8 percent.

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Not only is Hepatitis C common, it is also associated with significant mortality. This is data from the D:A:D. The D:A:D is a cohort of HIV-infected individuals. And this particular study looks at over 33,000 participants followed between 1999 and 2008. A large proportion were infected with hepatitis C, 15.3 percent. And 11.5 percent either had current or prior Hepatitis B infection. In this period of follow up, there were about 2,400 deaths and you see that the second leading cause of death was liver-related. 13.7 percent of deaths were directly related to viral hepatitis infection.

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In the next slide we're going to go over the natural history of hepatitis C. This is important because it's important that our patients understand the natural history because as we all know, information is power. I tell my patients that they likely acquired hepatitis C because blood from someone infected with hepatitis C got into their body. This could occur in a number of ways. The most common way is through injection drug use. If individuals inject and share needles, syringes, cotton, cooker, water. So many patients know about not sharing needles but are not as aware about the risk of hepatitis C transmission with sharing other drug use paraphernalia. When patients first acquire hepatitis C, they have acute hepatitis C infection. About 15 percent of patients will clear the infection, meaning their immune system controls viral replication and they resolve hepatitis C. Of the 85 percent that go on to chronic hepatitis C, a majority will have stable disease, meaning that their liver does not have progressive damage. However, over the next 20 years, 20 percent will progress to cirrhosis. The challenge is that we have no way of knowing who will progress and who will not progress. Once you develop cirrhosis, about 6 percent of patients per year who progress to end stage liver disease and another 4 percent per year who progress to hepatocellular cancer. I tell my patients that if they have hepatitis C, they could very well develop end stage liver disease or hepatocellular cancer, outcomes that we would prefer to avoid. Once patients have either of these options are dead or liver transplant and I am sure we all agree that we want to prevent that in our patients.

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Now, this is a schematic of what I just went over and I put it up here to highlight some factors that will accelerate the progression from chronic liverdisease to cirrhosis. If you are older, your rate of progression is much faster. If you have HIV, have hepatitis B, drink alcohol, or are obese, the risk of progression of liver disease can occur much faster. Obesity is linked to fatty liver disease, which we know is associated with progression of liver disease. When the patient first develops cirrhosis, all the majority of the liver has been replaced by scar tissue. The liver is still able to perform its function and in those patients we see they have compensated cirrhosis. As liver damage progresses, they become decompensated. We say a patient is decompensated when they have symptoms and the symptoms we see most commonly are the presence of viruses, ascites, encephalopathy, jaundice, and they at that point can also and they also remain at risk for hepatocellular cancer.

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So, we all now know everything there is to know about hepatitis C. Let's treat our first patient, Mr. A. So, he's a 67 year-old African-American man. He has HIV, well-controlled on HAART, hypertension, diabetes, and prior injection drug use. He was recently transferred into your care and on initial review of the record, you see that his HIV is very well-controlled, CD4 628, HIV RNA less than 20 copies, and you see that he tested positive for hepatitis C antibody over 10 years ago. These are his medications. I bring this up to highlight a point.

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The very first thing you need to do in a patient who has an antibody test that's positive for hepatitis C is confirm infection. You do this by testing for HCV RNA and you want to use a quantitative assay that

actually gives you a number for the HCV RNA viral load. In a proportion of patients, they will have a positive antibody test but a negative RNA test. And this would happen if the patient has either resolved infections spontaneously or if they have gotten previously treated and cured of their hepatitis C. Once a patient is tested and found to be RNA negative, it's very important that we counsel patients and let them know that the antibody is a mark of exposure but because they do not have virus, they do not have active ongoing current infection. I can't tell you the number of patients who have gone to testing event, had an antibody test performed after being cured of hepatitis C and then are told that they have hepatitis C and they get confused all over again.

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So, it's important that we educate our patients and let them know that the antibody will always be positive but if the HCV RNA is not present, they do not have active ongoing infection. For patients that have ongoing risk factors for re-infection, they also need to know that previous Kern's (?) or previous care does not prevent risk of infection. And if there are ongoing risk factors for re-infection, we screen for re-infection with an HCV RNA because the antibody will always be positive so you just go straight to the HCV RNA to screen for infection.

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So, let's go back to our patient. We get our HCV RNA and it's 6.4 million international units per mil. So, this is my first question for you. What is your next step? Get additional tests, screen for alcohol, do a brief intervention and referral for alcohol treatment if indicated, treat with sofosbuvir/ledipasvir to just get the show on the road and cure him of hepatitis C, or you refer to a gastroenterologist for further evaluation and management? Please vote. By show of hands, who wants to get additional testing? Awesome. Who wants to treat immediately? Awesome. Who wants to refer to a gastroenterologist immediately? Even more awesome. We got this! We can do this! Okay.

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So, the very first thing you need to do is understand a little bit more about your patient's hepatitis C. And so some of the things you want to assess are the risk factors for acquiring hepatitis C, not so much because of the past but more because of the future because those same risk factors can put them at risk for re-infection. You also want assess for significant medical co-morbidities. So, hepatitis B is one and we know that co-infection with hepatitis B can accelerate the progression of liver disease. And there's also some emerging data that treating hepatitis C in patients that have hepatitis B can lead to reactivation of hepatitis B. Other reasons to assess for co-morbidities is because these co-morbidities may impact your treatment choice. So for example, some of our oral DAA therapies cannot be used in patients that have advanced kidney disease. Ribavarin causes anemia which might not be tolerable in some patients, for example patients with severe coronary artery disease. You want to assess for a history of complications of liver disease, complications such as hepatic encephalopathy, jaundice, gastrointestinal bleeding, or ascites because this gives you a sense of how sick your patient may be upfront. And then you also want to know if the patient has been previously treated. We know that patients who have been previously treated and failed hepatitis C treatment have something about them that may make it a little more difficult to cure them of their Hep C, so you also want to know that upfront.

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As part of your history, you want to assess how much alcohol your patient is drinking. Alcohol accelerates liver disease. And this is an opportunity to address problematic alcohol use in our patient population. Assess for use of other liver toxic substances. I tell my patients there are many medications that are marketed as herbs, vitamins, libido supplements, over-the counter supplements. Most of them are harmless but some of them have ingredients in them that can be very toxic to your liver and so we talk about avoiding those medications. We also assess for Tylenol use. You'd be amazed at how much Tylenol some patients are using. You want to keep Tylenol use at less than 2 grams per day. I'm preaching to the audience here, but it's important again to assess for barriers to hepatitis C treatment adherence. Stable housing. My patients that I get on some of the drugs I get in a mini Cadillac Escalade. Given the cost of those regimens, I want to show you know where you're going to be keeping the Cadillac Escalade so that your pills don't get lost. We assess for ongoing substance abuse. And I think we're very lucky because our patients already have practice with treatment adherence. Patients that are doing well on HIV therapy, who are adherent to their therapies, we know are likely going to do well. Patients that are not doing as well with HIV therapies we know will need additional care and support to be successful with hepatitis C therapy. We assess for risk factors for re-infection upfront so we can address them. Assess for injection drug use that individuals can be linked to needle exchange or opioid treatment as needed. Also assess for high-risk unprotected sex amongst men who have sex with men because we know that increasingly, even in the US, this is a source for hepatitis C infection.

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In your clinical exam, you want to do a complete exam, starting from knowing what your patient's BMI is and addressing obesity if it's present and encouraging maintenance of a healthy weight because this also has implications for maintaining liver health. You evaluate for stigmata of chronic liver disease. So, these pictures show you spider nevi, which you see most prominently on shoulders, palmar erythema, ascites, splenomegaly, encephalopathy. These are all signs of advanced liver disease.

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For laboratory testing we get the general tests we usually will get but sometimes for a somewhat different reason, your complete blood count gives you the patient's hemoglobin so you have a sense of whether the patient can tolerate ribavirin. It also gives you the patient's platelets. A platelet count that is lower than normal may be an indication of portal hypertension from advanced liver disease. You want to get a serum creatinine for for a number of reasons. One, because it might determine your agent choice, but also because we know that Hepatitis C is associated with some kidney diseases and that might be an indication to accelerate access to Hepatitis C therapy for those patients. Ribavirin is teratogenic so you want to get a pregnancy test in all women in whom you are considering using ribavirin. You want to assess for hepatic inflammation. You do this through the ALT and AST tests. You want to look at hepatic synthetic function. You want to know whether the patient's liver is still able to do its job. And you do that through bilirubin PT, INR, and albumin testing. You want to get a baseline HCV RNA, you want the genotype because not all oral DAA is effective against all genotypes and so the genotype might determine your hepatitis C treatment choice. And then you also want to be aware about co-infections. I am stressing the viral co-infections because we know they have shared modes of

transmission with both HIV and hepatitis C and this is a great opportunity to assess for immunity and immunize patients if they are not already immune to both hepatitis A and B. We'll talk about hepatitis B briefly again because it has been brought to light that patients that have a history of current or prior hepatitis B can reactivate their hepatitis B during oral DAA therapy. And by re-activation I mean that they have marked Hepatitis B viral replication which leads to inflammation in the liver and there have been cases of liver transplant and even death reported in the setting of oral DA therapy in patients who had previous Hepatitis B infection.

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So, how do you assess for hepatitis B? You do this using three tests. You want to get a hepatitis B surface antigen, the antibody-- the surface antibody and the core antibody. And these are a couple of the scenarios you might come across. If all three test results are negative, this means the patient has not previously been exposed to hepatitis B and susceptible. You want to vaccinate these patients. If the antibody, the surface antibody is positive, this patient is immune and there's nothing to do with regards to hepatitis C. If the surface antigen is positive, that means the patient has ongoing hepatitis B infection. And so these are the patients that are at particular risk of hepatitis B re-activation during oral DAA therapy. Now, if only the core antibody is positive, this is where you sometimes have some challenges because we're not really sure what that means. It's referred to as being isolated core body positive. In these patients, you would consider getting hepatitis B DNA. You would consider vaccination because this could mean that the patient had previously had hepatitis B and recovered but do not have detectable detectable levels of antibody. You're hoping that vaccination will wake up the immune system and they will develop protected levels of antibody. I mean, the thought-- we don't know a lot about hepatitis B re-activation but the thought is that these patients are at risk for re-activation but that risk is low.

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Now, the patients that really are a at risk for re-activation are those that are surface antigen positive. In patients that are surface antigen positive, you want to test for HBV DNA. Luckily, most of our patients will be on hepatitis B active therapy but in patient who is not, you really do want to consider starting hepatitis B therapy. In HIV-infected patients, you would definitely start hep B therapy if the patient met criteria for (?) active HBV and (?) will talk about this some more. You monitor patients that have hepatitis B with low or undetectable HBV DNA prior to treatment at regular intervals. And the thought is that you do this at a frequency that's less than every four weeks. And if your patient on treatment begins to develop elevations in their ALT and AST, then you should think about the possibility of Hepatitis B reactivation in a patient that was known to have a history of current or prior hepatitis B prior to hep C treatment initiation.

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It's important to remember that there are other things that will lead to AST and ALT elevations in our patients. And to think about things such as alcoholic liver disease, nonalcoholic fatty liver disease, alpha-1 antitrypsin deficiency, hemochromatosis, and autoimmune hepatitis. So, you don't study full on work up for these conditions but something to keep at the back of your mind.

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So, liver disease staging.

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I tell my patients that their hepatitis C progresses and we assess how much damage there has been to the liver on a scale where zero is no damage and four is a lot of damage. This graphic shows you the varying stages, so stage zero you see a normal, healthy liver, no fibrosis. Stage 1, you have some fibrosis around the portal areas. By stage 2, the fibrosis is expanding with occasional abrasion of portal areas. Stage 3, there is a lot of fibrosis with bridging of portal areas and central areas, and by stage 4, a majority of the liver has been replaced by fibrosis and we see a patient has cirrhosis. Now these pictures are very pretty and we have these pictures from an era where patients would come to me and they would say, "Dr. Falade, I would like you to treat my hepatitis C." and I would say to them, "Yes, I would be happy to, but before we do that I would like you to please give me a piece of your liver." And they would say to me, "No, thank you," and I would never see them again. Now luckily, I don't have to ask people for pieces of their liver anymore. Now we have excellent staging tests that are based purely on blood tests and liver ultrasound-like tests.

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I also want to bring to your attention that all the insurance companies will tell us differently. The real critical goal for staging is to assess whether a patient has cirrhosis or not. That's the only question that we really need to clinically answer through our staging tests.

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It's important to know if he has cirrhosis because they are at risk of hepatic decompensation. They also have an increased risk of liver cancer. So, that if a patient has cirrhosis, you want to get imaging to assess for hepatocellular cancer prior to hep C treatment initiation in most cases. And even after the patient has been treated and cured of their hepatitis C, they will require ongoing hepatocellular cancer screening every six months. From what we know, for the rest of their life. Things may change but for now, if a patient has cirrhosis prior to hepatitis C treatment and care, they require ongoing hepatocellular cancer surveillance every six months. Cirrhosis may impact your hepatitis C treatment choice and duration. And patients with cirrhosis are at risk for viruses, dilated blood vessels in the esophagus, which can burst and lead to upper GI bleeds. And so we need to assess for these viruses and treat as needed by getting an EGD.

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So, let's go back to our case. So, we have more history, we know he acquired HIV and hepatitis C through injection drug use. He has never previously been treated for hepatitis C, his review of systems is positive for fatigue. Social history, he's drinking two to three beers daily, he reports intermittent drug use and denies sharing drug use paraphernalia. His physical exam is positive for cardiac murmurs and we say on lab testing that he has genotype 1 disease. His ALT is elevated at 48, AST elevated at 90. Platelets 125,000, so a little low. INR is 1.0, total bilirubin 1.2, albumin 3.3, hemoglobin 13.6, and his creatinine elevated at 1.4.

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And so, we actually do have enough information to begin to stage this liver disease. These are screen shots from the amazing University of Washington website that Nina Kim works on. And these are two simple algorithms that you can use to begin to determine how much disease your patient has at that first visit. So, we have the APRI, the AST to platelet ratio index. And it just uses the AST and the platelet count. So, if you remember, I showed you our patient's values and what I have done here is just put in his numbers, his AST of 90, the upper limit of AST of 40, and his platelet count of 125, and it gives me an APRI score of 180. We know that an APRI greater than one has a 76 percent sensitivity and a 72 percent specificity for cirrhosis. So, this APRI score would suggest this patient has cirrhosis. A similar marker is the FIB-4, again using things that are easily available to us. The patient's age, AST, platelet count, and ALT. And we have a score of 6.96, which is greater than 3.25, which has a 97 percent specificity for cirrhosis.

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There are other tests we can order and pay money for. So, one of these is the FibroSURE, the fibrosis index. It's a proprietary score using different markers, GGT, bilirubin, haptoglobin, apolipoprotein A-1, and a2 macroglobulin and it too will give us a score. This graphic shows you the different cutoff points for the different stages of liver disease. It also will give you a necroinflammatory activity, which basically is just an indication of how quickly the inflammation is progressing in that specific patient's liver. There are some instances in which you would want to avoid using the ACB FibroSURE. You want to avoid it in patients with Gilbert's disease, acute hemolysis, viral hepatitis, drug-induced hepatitis, genetic liver disease, autoimmune hepatitis, or extrahepatic cholestasis.

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Now, this I think is the golden boy of liver staging, transient elastography. How many of us have access to transient elastography? It's so convenient because in under five minutes, you can tell patients how much liver disease they have. And basically, it's like an ultrasound. You put the probe over the patient's liver. It shoots a sound wave into the liver. And the probe measures how quickly the sound wave gets back into the liver. If it gets back really quickly, that suggests that the liver is stiffer and suggests that the patient has more liver disease. If it takes longer, then the liver is not as stiff and the patient has less liver disease.

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And these are the cutoffs. The fibroscan, which is what we call the transient elastogram commonly in the U.S., has cutoff points. A score less than 7.0 suggests absent or mild fibrosis. A score between 7.0 and 9.5, significant fibrosis. A score between 9.5 and 12.5, severe fibrosis. And a square above 12.5, cirrhosis. And the higher the score, the more severe the patient's liver disease is and the higher their risk of hepatitis C. There's data to suggest that patients that have really high fibroscan scores are at higher risk of developing hepatocellular cancer.

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So, in recap, in our patients with cirrhosis, it's important to screen for hepatocellular cancer. We need to screen and manage their varices. And we also need to further stage their liver disease by calculating a

Child-Pugh-Turcotte score and the MELD score. This gives us a sense of their liver-related mortality over the next six months and whether they do need to be referred for a liver transplant.

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How do we screen for HCC and in who do we scree? We screen in all patients with cirrhosis. In your patients with F3 liver disease, we also need to consider screening for liver cancer because, again, our staging tests are not perfect. So, although you're getting an F3, they may very well have cirrhosis. You do this using imaging. Most commonly we use an ultrasound. You can add on an Alpha fetoprotein but an Alpha fetoprotein alone should not be used to screen for HCC. And it's commonly done at 6 month intervals.

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So, my patient has cirrhosis. What else do I need to know? I need to know whether they are compensated, meaning they're asymptomatic, or whether they're are decompensated. And the symptoms you will see most commonly for decompensated patients are ascites and encephalopathy.

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So, how do I calculate the CTP score? Again, really helpful calculators are available online. I got this online and we'll calculate the CTP score for Mr. A. So, we know he had no encephalopathy and so his score for that is one. He had no ascites. His score for that is one. His bilirubin is 1.2, which is less than 2, so his score for that is one. His albumin was 3.3, which is somewhere between 2.8 and 3.5, so his score for that is 2. His INR was 1.2, which is less than 1.7, so his score for that is one. And so to calculate his CTP, I add up all these numbers and the total I get is six. And so, for patients with class A disease, which are patients that have compensated cirrhosis, they have a CTP score between five to six. So, Mr. A has compensated cirrhosis. Patients that have scores above six have class B and C and are thus considered to have decompensated liver disease.

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I also need to calculate his MELD. Again, online calculators and I can put in his figures. Putting in his serum bilirubin, INR, serum creatinine, whether he's been on dialysis, and his serum sodium. We get a MELD core of 10. And what that means with a MELD score of 10 is that he has a 6 percent risk of mortality over the next three months related to liver disease. We know from prospective data that patients that have a MELD score of 15 or above may benefit from liver transplants or if patients have high MELD scores, they should be referred to a liver transplant center just for evaluation.

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Now, of note, patients that have the decompensated liver disease should only be treated for hepatitis C in specialized centers with access to liver transplant. And the reason is because in patients have the decompensated liver disease, oral DAA treatments may make them better but in a proportion of patients it actually makes them worse. So, that you don't want a patient getting worse without having previously seen someone that could rescue them with liver transplant if that came to be.

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OK so Mr. A says, "Doc, I got this. I want to get cured. How do I stay healthy? What do I need to do?"

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So, I think the very first thing we need to do is talk about his alcohol because that's something you can intervene upon there and then. This is data showing the percentage of patients who develop cirrhosis on the Y axis over different time periods on the X axis. All these patients have hepatitis C but the ones in blue only have hepatitis C and the ones in green have hepatitis C but also drink excessive amounts of alcohol. In this study, it was defined as greater than 40 grams per day for women and greater than 60 grams per day for men. And what you see is, regardless of time period, your risk of cirrhosis goes up significantly if you have hepatitis C and also drink alcohol.

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There are so many tools we can use to screen for alcohol. I'm sure that is something we all currently do in our practice and there are lots of helpful tools online to help us gain some confidence with actually doing a brief intervention in our practice. Something as simple as, "Mr A., I'm concerned about your levels of alcohol use. They are harmful to your health. What are you willing to do to reduce or stop your alcohol use to improve your health? How can I help you?" Something as simple as that will start a discussion and you'd be surprised that a lot of patients, in fact, we actually have data to show that in clinical settings a brief intervention like that can actually reduce levels of alcohol use in patients that have harmful levels. Some of my patients have actually stopped drinking alcohol completely, amazingly, after a conversation like this.

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So, other patient education points. You need to talk about transmission because we want to be sure that our patients do not transmit to other patients. They should not share razors, nail clippers or toothbrushes. We talk about sexual transmission amongst men who have sex with men and the need to use condoms or avoid recreational drugs during anticipated sexual activity. We talk about not sharing needles and other drug use paraphernalia. If patients are injecting, we link them to harm reduction services such as opiate treatment programs and needle exchange. With regards to maintaining and liver-healthy lifestyle, I tell all my patients that there is no level of alcohol use that we know is safe. And so my recommendation is that you not drink alcohol. And I know that not every patient can achieve that goal but they know that that's the goal and I work with them to get them to what they are able to achieve, and sometimes just reducing alcohol use is all some patients can do. We talk about avoiding over-the-counter medications or complementary medications. And if they really, really feel like they need to take that over-the-counter medicine, I say bring it to me, take it to your primary care doctor, or have someone look at every single ingredient to make sure that there's nothing harmful in it. But the truth is some of those OTCs you don't even know what is in them. So, as a general rule, I encourage patients not to take herbal remedies. We talk about achieving and maintaining a normal body mass index and there is some data to suggest that drinking coffee may be beneficial. I don't know if you have many coffee drinkers in your practice. I don't have many in my practice but something to think about. And we always talk about new therapies. We talk about the fact that there are new treatments, many as simple as one pill a day, with just three months, no side effects, offering a 95 percent chance of cure. I

mean, you'd be surprised at how patients' ears perk up when they hear about curing one of their diseases. And we also start the discussion about risk of re-infection and beginning to practice the things that will prevent them from getting re-infected with hepatitis C after treatment and care.

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It takes a village. Our patients have so many interactions with so many members of the healthcare team and it's so important that we're all giving our patients the right messaging so that they can engage both in hepatitis C treatment but also in harm reduction practices that will improve their overall health outcomes.

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So, let's go back to Mr. A. I've presented his additional results. We've talked about his care. Do we have everything we need to make a treatment decision for Mr. A.? Please vote.

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Okay. It worked! Okay. So, it's looking like, okay, so most people feel like we have everything we need to make a treatment decision.

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So, we have a lot of what we need. But you know this is an HIV conference and I figured this would come up. You know, we talk so much about resistance in the HIV world. Where does resistance come up in the hepatitis C world? And the good news is that when you are treating a patient that has not previously been treated for hepatitis C, majority of the time hepatitis C resistance testing should not come up. Now, the only time you really do need to think about resistance testing is if your patient has genotype 1A infection, if you are considering use of the drug Grazoprevir/Elbasvir, so that drug specifically, also referred to as Zepatier. And the reason we have to test for resistance. So, that drug is in the class of NS5A agents and we know that at baseline, 10 to 15 percent of patients will have NS5A resistance-associated substitutions. Those resistance-associated substitutions in patients with genotype 1A were linked to lower response rates with SVR with somewhere between 22 percent and 58 percent. So, that's a lot lower than the 95 percent we're used to. So that if a patient has those NS5A RAVs and you want to use this specific drug, you want to know upfront because you're going to have to extend your duration of therapy and add ribavirin.

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Okay. So, Mr. A. Let's get some more information. Genotype 1A, he has cirrhosis, he's compensated, ultrasound, no masses, EGD, small varices. These are his meds. Very standard. He's on HAART with a boosted PI, Metroprol and Lisinopril for hypertension, Metformin for diabetes, Rosuvastatin for hyperlipidemia, and Omeprazole.

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Are we ready to initiate hepatitis C therapy? Please vote.

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Okay, okay. So, it looks like a lot of people are ready to initiate hepatitis C therapy. Yeah, we're getting there.

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But there's something we need to think about: drug interactions. Okay, drug interactions.

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So, our DA therapies have some drug interactions. We need to be especially careful with HIV antiretroviral agents and some other classes. Now, this is an ARV interaction scorecard. I pulled this from the hepatitis C treatment guidelines. And the way you use this is to look at the HIV drugs on the X axis and then the oral DAA drugs on the Y axis. And the code is green, go, no drug interactions, yellow is proceed with caution, there might be some interactions, there might be some additional monitoring needed, and red is do not go there-- contraindicated. So, if I wanted to look for an interaction between Atazanavir, Ritonavir and Sofosbuvir, I would focus on this green box here. Now, the good news is that there are some ART regimens that generally don't have interactions with oral DAAs. So, Raltegravir and Dolutegravir, as you would have predicted, are green of course across the board. Now, there are some HIV antiretroviral agents that you have to make some adjustments in your oral DAA dose. So for example, if I wanted to use Atazanavir/Ritonavir with Daclatasvir, I would need to reduce the dose of the oral DAA Daclatasvir from 60 to 30 milligrams. If I wanted to use Efavirenz or Etravirine with Daclatasvir, I would need to increase the dose of Daclatasvir from 60 to 90 milligrams.

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The other classes that have drug interactions that we really do need to be aware of our and look for: acid blockers, that's a big one. There are a bunch of different things you have to do with acid blockers with different oral DAAs, anti-seizure medications, statins, and the other big class is Amiodarone. So, there are lots of drug interactions with Amiodarone that we do need to be careful about. There are so many I cannot go into them and so what I recommend is that you find a friendly neighborhood pharmacist. My pharmacist is my bestie. Now, some of us have access to friendly neighborhood pharmacists but some of us just don't. There are options. There are things we can do. You can get help with assessing for drug interactions. You can use online websites such as the Liverpool drug interaction website, you can get the app on your phone. You put in the oral DAA, you put the drug you are looking for the drug interaction with, and it provides very helpful information for both assessing and managing drug interactions in patients you want to start hepatitis C therapy on.

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So in conclusion, I have reviewed the need for a history, physical exam, and laboratory testing in our patients that we want to treat for hepatitis C. The goal of liver disease staging really is to assess for presence of liver cirrhosis. In our patients with cirrhosis, they require screening for hepatocellular cancer. And you want to do this with imaging both prior to initiation of oral DAA treatment and even after hepatitis C treatment and care, because they remain at risk for HCC even after care, if they had cirrhosis prior to treatment. You want to address alcohol use and ongoing risk factors for re-infection because we want to keep our patients held in even after we cure of them of their hepatitis C. You want

to assess for drug interactions and it takes a village. Everybody has a role to play. I mean, I will tell you in our practice, I think the biggest players in making sure that our patients succeed in their hepatitis C therapy are actually our nurses, our case managers, and our pharmacy staff because they work the closest with the patients to ensure that they have the best outcomes.

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Thank you so much for the opportunity to present. Thanks to Mark Sulkowski and thanks to the organizers for inviting me.

[Video end]