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ACHIEVED SVR, WHAT'S NEXT? HCV POST TREATMENT OUTCOMES AND MANAGEMENT

David E. Bernstein, MD, MACG, FAGA, FACP, FAASLD

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Dr. David Bernstein is an internationally known gastroenterologist hepatologist and is currently the president of JSDB medical consulting LLC and David Bernstein, MD PC. Dr. Bernstein graduated from SUNY Stony Brook School of Medicine completed his medical medical residency at Montefiore Medical Center and his fellowship in Gastroenterology and Hepatology at the University of Miami affiliated hospitals he has served as chief of gastroenterology at Winthrop hospital and chief of gastroenterology for the Long Island Jewish Hospital and North Shore University Hospital. Most recently, he was the head of the liver sub specialty service line, Vice Chair of clinical trials chief division of hepatology and director of the Sandra Atlas Bass Center for liver diseases for the Northwell Health System. Dr. Bernstein's research focuses primarily on the management and treatment of liver diseases, with most of his work concentrated on developing new treatments for viral Hepatitis, primary biliary, biliary, colonitus, and fatty liver disease. He has authored or co authored more than 300 original scientific manuscripts, reviews, book chapters and abstracts, including the monthly column liver lines, which has been published in the Anton community newspaper for the past 25 years. He also has served as a special consultant, then to the New York State Department of Health, and in that role helped develop and implement New York State's five year strategic plan for viral Hepatitis, as well as guidelines used for the treatment of Hepatitis C in New York State. Happy to turn it over to you Dr. Bernstein.

01:50
Jeff, thank you very much. Thank you all for coming to this. It's actually an exciting talk for me because it sort of highlights a career. Just to put this in perspective. I remember being in the room when the first serum was sent out to California to evaluate for this new antibody, which has Hepatitis C. And then I remember the first trials of interferon, back in the mid 90s. When we could cure almost nobody for many years, and the side effects were just so horrible. And now what we really focus on is after we cure people what to do, and what are the effects of cure. And so it's really been incredible. And I I think it's highlighted by the fact that three of my colleagues two years ago won the Nobel Prize for their work on this, and it remains one of the few viruses you can actually treat and cure chronic viruses. So with that said, let's talk a little bit about today's topic, which is a you have achieved SVR sustained virologic response, what do we do next? These are my disclosures. So and these are the objectives for today, and you can read them. And we can talk about some of the questions that you may have, you know, towards the end, but I'd like to get into the heart of the matter. And since we're going to be talking about this concept called sustained virologic response, which is synonymous with cure, and it took a very long time before FDA allowed us to use the word cure and now we do regularly because we can, let's define SVR before we do that, let me ask you what you think it is. So this is a

polling question. How do you define SVR sustained virologic response, negative Hepatitis C viral load at the end of treatment, normalization of at the end of treatment, negative Hepatitis C viral load at 12 weeks post treatment completion, negative viral load at 24 weeks post treatment completion, immunity to reinfection with Hepatitis C in the future, negative Hepatitis C viral load at four weeks after treatment initiation. The good news is everybody got it? Right. The bad news is a lot of you didn't vote, but those who voted voted correctly. So the answer is see a negative viral load 12 weeks after completing treatment. And that's the goal. It doesn't matter what the treatment is, if the treatment is interferon if the treatment is any of the different direct acting antiviral therapies. The definition of sustained virologic response is undetectable virus 12 weeks at least 12 weeks after the completion of therapy, meaning patient comes in 16 weeks later, 20 weeks later and you get it that's all fine. It doesn't have to be done right at 12 weeks, anytime after that 12 weeks is important. Why don't we feel comfortable using that? Time? Because if you remember back in the interferon days, we use 24 weeks. The reason is, is that much fewer than 1% of people will actually experience a relapse between weeks 12 and 24. And many of those are reinfection, meaning they were re exposed to the virus. So we feel comfortable using the term sustained virologic response and cure. If someone has undetectable virus, at least 12 weeks, you know, after completing therapy. And that's good news for us. Since more than 95% of all patients who undergo therapies with the currently available oral direct acting antiviral treatments will be cured with timeframes of either a 12 or 16 weeks. So this has been a revolution in our treatment of viral Hepatitis. And there's once you're negative, you know, it's really get through that period, only about two to 3%. Within the end of therapy, and 12 weeks, we'll have detectable virus again. So if you reach that point, you're cured. So it's very important that you become negative on treatment. But interestingly enough, even if you become negative at 10 weeks of a 12 week course, you will still have the same chance of earning negative with a curator more than 95%. So you just have to get to that negative. What is sure mean? Then what what does it not mean? If you had Hepatitis C, were treated and cured, you can still get it again, because the Hepatitis C antibody is not protected. So it's important then to counsel patients that they're at risk for reinfection that we're going to talk about that a little bit later. So people can get it again, and again and again. And we do see that in very few people, mostly young people who are caught up in the opioid epidemic and have risks. But it's very important to have a discussion with the patient, that cure doesn't mean that you're immune. There is no immunity to Hepatitis C. And there is no vaccine for Hepatitis C, there are some in the works, but nothing's close. So we need to know what SVR does mean, and what it doesn't mean, and you can sort of see that here. What are then some of the effects of having a cure? Well, first and foremost, you've gotten rid of a chronic disease, which is always a good thing. We know that Hepatitis C is a systemic disease. So within the liver, if you cure the disease to decrease inflammation, I'll show you that you've decreased by Groasis. I'll show you that in some patients, even cirrhosis can be reversed. And if patients have not had complications of portal hypertension, it's unlikely that they will develop

them after cure even if the patient has cirrhosis. We'll talk a little bit about liver cancer, because if you cure someone who's cirrhotic who has Hepatitis C, they're still at risk for developing liver cancer, but the risk is lower. What about extra hepatic manifestations? Well, this is equally important, I would say, if not more, so since Hepatitis C is associated with many other conditions. So if you cure Hepatitis C, you usually get rid of it, they had cryoglobulinemia, you decrease the chance someone will develop non Hodgkins lymphoma, kidney disease may get better. Diabetes certainly gets better. And interestingly enough, for unclear reasons. The risk of stroke and the risk of having a heart attack, go way down. If someone is cured, overall neurocognitive function gets better. And patients routinely report improved quality of life, and better work productivity. So cure is a good thing. And there's absolutely no reason in 2022 that anyone with Hepatitis C shouldn't be treated, because there are all possible folks who can be cured. So there are a lot of benefits that we see from therapy. So this is sort of just the list, right? I would say most important is your decreased liver related complications and death. And we can see that as with the new therapies and the high levels of cure, the number of patients actually being transplanted for Hepatitis C has gone way down where it used to be the number one indication, it no longer is, as an aside, the top two are alcohol and fatty liver. In addition, overall, all cause mortality in these patients gets better. diabetes, high blood pressure, stroke, risk, risk of heart attack, all go down. So that's really important. And as I said earlier, you can see an improvement in overall quality of life. So here's another question. Which of the following is not a benefit of sustained virologic response, reduction in labor Related Compensation, reduction in bacterial infections, reduction in the risk of hepatocellular carcinoma, short and weightless time on liver transplant improvement and all cause mortality? Or a decrease in fibrosis? Okay, so we have a smattering of answers, the correct answer here would be D. All of the others, things that are listed here get better and are correct with sustained virologic response, shorten weightless time for liver transplant actually doesn't and paradoxically, it actually makes it longer, which we'll go over. And so that's something that we need to consider when we treat patients who are on a transplant list who are going for a catabolic transplant. So all the other things listed here do benefit from patients having a sustained virologic response. This is a very important study to show you and it's been replicated. Many times this is small, it's just an example. But the key here is these are patients that had Hepatitis C, and had cirrhosis as a result of Hepatitis C. And you can see in the top right, photograph B, a typical cirrhotic liver with those nodules, patients were treated.

11:44
This is in a interferon era, right because it's 2012. And what you can see from this is in the patients that had sustained virologic response or cure, they will fall for at least four years out, and there was a significant decrease in the amount on the number of patients that had cirrhosis. You can see it there. All 38 had cirrhosis beforehand. Only 15 of the 38 had cirrhosis when this was done. So the cirrhosis actually got better now I was taught in medical school the

definition of cirrhosis is is an IR reversible fibrosis. And it's a process that couldn't get better. We now know that's not true. If you take away the stimulus, in this case, Hepatitis C and give the liver time, it will actually recover. And you can see a sample biopsy be the cirrhotic I showed you in the bottom right you can see see the patient no longer has cirrhosis just has minimal fibrosis. We see this frequently. Patients are still at risk for liver cancer. However, if they had cirrhosis beforehand, so they need to be screened. But this is really dramatic. And so just look at this for a moment. The fact that you can reverse the roses is incredible as we go forward. This is a Spanish study, it looked at similar things, patients who were treated with sofosbuvir Vir based regimen. So these are all oral regimens. Those that bridging fibrosis or cirrhosis and 40% of the folks were co infected with Hepatitis C and HIV. In these patients, the same thing was seen 40% of the patients had a significant reduction in fibrosis, but many of them no longer cirrhotic. And HIV wasn't the fact that didn't matter if you had HIV or didn't. If you have this response, deliver got better. And so this study showed it from Da air, but there are many others that you can say this looks at improvement of the Child Pugh score. And here's where you wonder if you're doing good or bad based on moral and ethical. So if you look at patients who had child's class, c, significant numbers of those patients had dramatic improvement in their child's P score with a sustained virologic response. Now, one of the issues that comes up is, these are patients that are also likely on a liver transplant list and I'll show you how you can bring the MELD score down and then what do you do for them, because they're no longer higher up on the list for liver transplantation. But I think that's a separate issue. But if you treat patients and this is with DEA therapy, so this is all oral. The nice thing about the oral oral therapy is that it allows us to treat sicker patients. If you remember, we couldn't really treat the compensated cirrhotics with interferon because you could make things much worse and push them over the edge with the DEA therapy as you can. And so we are now treating sicker people those we never could treat before. And that's important when we look at data sets especially when we talk about concerns about liver cancer following cure of Hepatitis C. This is a very important study by Vandermeer still quoted, it's 10 years old at this point, it looked at patients who were treated in the interferon era, those who had a sustained virologic response, and those that didn't. And you can see all the way to the right, the dramatic effect CQR had on developing liver failure, over one column to the left, the dramatic effect of decreasing the risk of hepatocellular carcinoma. And the dramatic effect on liberated mortality or the need for liver transplant between two are non cured. But focus on the first Iron all cause mortality. Those who were killed, were significantly less likely to die for any reason, that those who weren't. And so that's really, we still don't understand it. But it's really important when we talk about things. And you can see here, very, very confusing slides. So I'll apologize. But this comes from the VA is over 55,000 patients that were treated with oral therapies. And what it essentially shows all these nice funky graphs, is that they're significantly decreased all cause mortality in the patients who were cured versus the patients who were not given a strong argument that pretty much all patients with Hepatitis C shouldn't be treated, because you can the effects of getting rid of the

virus are really tremendous as an impacts many other systems. What about the need for liver transplantation? Well, prior to the oral therapies, we could not treat patients who had more advanced disease and the results of treatment, we're not going to be cured about 40%. So the transplant list of Hepatitis C patients went up if you introduced them the era of direct acting antivirals, and see as soon as those oral agents become available, the number of patients on weightless for liver transplant went way down because you're you're curing patients earlier, and preventing their progression. So that's critically important. When we look at these patients populations, what about meld scores, and here's where we can really have a long discussion. If we look to the left those that have meld scores of less than 16, those that you wouldn't consider evaluating for transplant, you treat those patients, almost all will have an improvement in their MELD score by at least two points, but many greater than than four. What if we look to the right, you have this patient population with a slightly higher MELD score in this study 16 to 20, those that are starting to be evaluated for liver transplant. And you would expect that over time, they would get worse and need a transplant. Well, if you treat these patients are even higher up to 2425. Mel, their MELD score is going to come down, it's going to come down considerably. They're still going to have cirrhosis, they still have advanced liver disease, but they're MELD score has come down so much that it's gonna be hard for them to ever get a liver transplant. And we use this scientific term that's called Mel purgatory in these patients. So you really have to think long and hard and some of the sicker patients are being evaluated for transplant and you want to treat them before transplantation or after. If the patient is going to have a living related transplant, there's no question you just treat. But if you need to wait for them to progress and in some areas like ours, where the median Melvin's 3435 These patients that you treat, they never get a transplant. And then the question you have to ask is have we done him a favor. And so there are a lot of discussions ethically, you know, that we have to have. This study is interesting, this looked at overall quality of life benefit and patients that had a sustained virologic response, and almost everything gets better. And we would expect that in all studies that we've seen that before, this study is a little skewed because these are all patients that were treated with soft l box. And if you remember, that's the therapy for those patients who have already failed one round of direct acting antiviral therapies. So this is the most resistant patients and even they, you know, report this so if you extrapolate back and can imagine the effects and the patients who are your garden variety, you know, they just do well So I thought a lot about the upsides of treatment and cure. What about the potential downsides? Are there downsides? You know, as we go forward? Well, one thing that we learned is, is that Hepatitis B, Hepatitis C and Hepatitis B can live together in a patient. Usually, when they live together, Hepatitis C is the dominant virus, and it suppresses Hepatitis B. We did not in the past routinely check patients being treated for Hepatitis C for Hepatitis D. Because we didn't really there wasn't a reason other than me make sure they didn't have the two infections. What was found out is early on with the direct acting antiviral therapies that if you start treatment for Hepatitis C, and the patient has underlying Hepatitis B, they can

develop reactivation B, and even former liver failure. So in the first couple of years, 29 cases around the world are identified two died, one needed a transplant, because the Hepatitis B wasn't looked for. And so this is a lesson we learned, right? We didn't know first, the reality is you should always be checking for Hepatitis B before you start any of these patients even before that we knew this data, but most people don't.

21:25
But because of this, FDA changed the labeling for all direct acting antiviral agents, and say that all patients with Hepatitis C should be evaluated for Hepatitis B before treatment. And that evaluation is the Hepatitis B surface antigen, the Hepatitis B core antibody, total Hepatitis B surface antibody. And if you have other concerns, or the service engine is positive, and HCV, RNA, and so you get these tests forever, right? If people do not have Hepatitis B and have no markers that they have had previous vaccination or an immune, they should be vaccinated. If they're surface antigen positive, with detectable virus, you have to make a decision as whether you're going to treat or not nude follow the ASL D guidelines. The reality is you would at least put these patients on treatment for the course of the Hepatitis C therapy and probably three to six months afterwards. And so that's if there's any virus present. If there's no virus, but the surface antigen and as positive, you have a choice, you can monitor them and you need to monitor them closely every four to six weeks with surface antigen ALP and HPV DNA, or you can just start therapy. So the key point here is that it's very important to look for those vital markers for Hepatitis D, before you start treatment for Hepatitis C, because the last thing you want to do is have a catastrophe. What about liver cancer risk in patients that have been treated and have had a cure? Well, we know that all ceramics, regardless of etiology, have about a one to 4% chance of developing liver cancer each year. That doesn't change that doesn't go away, quite honestly, if someone is treated for Hepatitis C and cured. So the best way to think about it is once a cirrhotic always is survived even if there has been regression of the degree of fibrosis. So the risk of liver cancer remains and the risk of liver cancer is also present in those that have bridging fibrosis or f3 disease. So in those patients with baseline, bridging fibrosis or f3, before therapy, once they're treated and cured, they also after treatment, will have to go into a program for screening for for liver cancer. And we're routinely unfortunately seeing people six 810 years out from cure, who are coming in with liver cancer. And if you check them every six months, you'll catch it when it's small. If you don't check in at all, that's when you see very large tumors that we can't really do much about. This is all data from the interferon era, but it just helps us understand a little bit the long term risks of developing hepatocellular carcinoma in patients with cirrhosis, who have had a sustained virologic response and it's about 10% at 10 years. So the lower end of what I showed you before 1% per year, but remember, these were less six Roddick's, these were not those ceramics that were trialed A minus B or C because you couldn't use interferon. So there's a skill, right? These are the healthier patients there's a greater risk of developing C See in those

patients with more advanced disease that we're now treating with the AAA, so you would expect higher rates of liver cancer associated with cure of Hepatitis C in these more advanced neurotics, not because there's any relationship to the therapy, but they're just sick and they remain at risk. But there was a lot of controversy when these studies where these drugs first came out, that perhaps the drugs were causing increased cancers. This is a very important study done at the VA, I bought it for a long time, it's over 10,000 patients, it essentially shows that if you're cured, and have compensated cirrhosis, your overall risk of developing parasite of the carcinoma goes way down, but does not go away. And so it's again, a strong argument for a treatment to cure, but also to continue to screen patients that have cirrhosis after cure for liver cancer, because once again, if we had small liver cancers, they're pretty easy to treat, once they're launched or spread into the vessel, and it's a different story. What predicts then the development of liver cancer after cure, having cirrhosis that would make sense being older, more than 65 and having diabetes. And if we remember, the biggest liver problem currently in the United States is actually a fatty liver. And 50 to 70% of diabetics have fatty liver disease. So get rid of the Hepatitis C, but if people are overweight or have diabetes, they're again an increased risk for the development of worsening of their liver disease and hepatocellular carcinoma. This is one of the first studies that came out after the DA therapies. And there was a concern in this that if you treated someone with the DA therapies, there was a greater risk that there will be a recurrence of liver cancer. In those patients that had already been treated. Well, you have a sick population, you have a population that already had liver cancer, right? They were treated, not necessarily cure, but treated, and then their Hepatitis C was treated. And in this study, there was a 27% recurrence risk, which is actually lower than you would expect in patients that had liver cancer and are just being filed. So this is a positive, if you will. But it's important to also remember now the therapies were treating sicker patients. Right. And so also many times we don't see these small tumors. So there was a lot of controversy. When all these therapies first came out, do da treatments increased the risk of hepatocellular carcinoma recurrence? Absolutely not. Absolutely not that that's concern has been disproved. Multiple times and here you can see, you know, what, again, you know, over 300 cirrhotic patients, and nine of the joint an 80, some odd developed liver cancer after cure, and 59 or 17, of the 59 or almost a third, develop the recurrence, it's to be expected unfortunately, that's what the data really tells us. And so, this really speaks to the importance of someone has underlying cirrhosis, they need to be screened. If someone had a pet a cellular carcinoma, they also are at higher risk, they need to be screened probably more vigorously. As an aside, if someone presents with a patent, say the carcinoma and Hepatitis C, you need to treat the parasailor carcinoma first, get rid of it as best you can, because the tumor itself is a place where the virus can hide. And so the relapse rates in people with untreated hepatocellular carcinoma are significantly higher, almost as high as 20% than those who had their Hepatitis, their hepatoma is treated. So just just another thing and here you can sort of see the overall spectrum. We've talked about what the overall risk of hepatocellular carcinoma is. We know that the six months recurrence of any

patient that has had a treated hepatocellular carcinoma is about 20%. And after the DEA therapies, it's depending upon the study anywhere from 12 to 30%. So no difference. We want someone who has had a cancer A real treatment if they have advanced diseases, transplantation, but the risks of recurrence of the parasite of the carcinoma doesn't go away. With cure of the virus, you have two separate processes that are going on. So here I'm going to show you think at least 10 studies. This is with Da therapy has the risk of de novo or new parasailor carcinomas occurring after treatment. Five good studies. I'll point out Raj Reddy study here, the second to the bottom, looking at that 35 year retrospective study. And so the answer in all of these studies is no. And if you look at the HCC recurrence rates, is the risk go up in any of these patients who were treated? No compared to other population? The answer is no. So the DEA therapies can be safely used and there is not any risk of increasing chance of getting a liver cancer or having a recurrence of an already known liver cancer.

31:07
So the AIDS do not lead to the development of parasailor carcinoma back in 2016 2017 2018. That was hotly debated. We now know that that's absolutely an incorrect statement. It does not inpatient shouldn't be treated, but they need to be continued to be followed. Critically important, they need to remain to be screened if someone has seraphic and is cured because they're going to develop these things. What are the risk factors then for the development of liver cancer those patients who a DA is in these D compensated patients. So these are patients we never would have treated in an interferon era, low platelets, right advanced portal hypertension, diabetes, again, because of the fatty liver, low albumin and any other non malignant lesions seen in the liver. And so, take home message DBAs can cure ceramics, we can treat the compensated ceramics. But also neurotics who are treated and cured still need to be evaluated and screened. For the development of hepatocellular carcinoma, that's generally an ultrasound and now feed a protein every six months. If someone is had an parasailor carcinoma, then it's an MRI, and an Alpha Theta protein every three, six or 12 months, every three or six months, depending upon the center. So now we've cured patients, how do we manage them, you know, after cure, right, and this used to be a very short discussion because almost no one got cured, but now it's a really important discussion. So let's take another case and a question. A 40 year old male with HIV and Hepatitis C genotype one A has recently completed treatment with silvassa via and the dipsea. He had F two fibrosis prior to treatment alts 45 Hepatitis B core antibody is positive and surface antigen is negative. So what's your plan? Going forward? Return to the clinic every six months for Hepatitis C screening. Check Hepatitis B surface antigen and HPV DNA refer to endoscopy for various little screening are discharged from the clinic as Hepatitis C is cured. So about half of you said, recheck the surface and you didn't get an HPV DNA. That's the correct answer. Oh, why are the others not correct? Well, the first one returned to clinic every six months for screening. We don't screen patients that have f2 fibrosis, we screen only at three or four refer to endoscopy for their cell screening.

Now. Because we only screen patients who have cirrhosis, so there'll be F four and discharge from the clinic as Hepatitis C is cured that could be but the first thing you need to do is recheck the Hepatitis B studies. And so for those who mentioned D, it could be but you want to make sure that it is no that is b that's present. Most commonly is going to be from fatty liver or we call fixed fibrosis. Some patients who have been cured, whose liver tests are normal but don't have any evidence of Hepatitis B infection or who are isolated Korea.

34:47
And that the Hepatitis C antibody isn't protected. And so, any patient with higher risks activities should be educated about the risk of reinfection shooting up drugs Using getting tattoos, anything with needles, or blood blood content. What else can happen after someone is cured? Well, they can acquire Hepatitis B if they're not immune. So if they're not immune, they should, you should recommend vaccination. If they had Hepatitis B as we talked about, they can reactivate, patients can have fatty liver, lots of patients drink. So alcoholic liver disease is a problem. It's from a treatment standpoint. And from a resource standpoint, alcoholic liver disease is the most expensive, and in the United States, because people drink a lot. And we've seen over the COVID year, dramatic increases in alcoholic liver disease, and autoimmune disease. So if you don't have a reason for the ALP, to be up, you need to look. So you'll check your Harvoni lockers to check your Hepatitis B studies, you'll ask about alcohol. And you'll image in some respects, looking for fatty liver. This study looked at why numbers are elevated, you know, after cure this is and the most common reason is that patients have significant fibrosis. And so that fixed fibrosis may not necessarily go away. And so you need to know the degree of fibrosis. And you need to try to explain because patients are sometimes disappointed, right when their numbers don't completely normalize. And remember, upper limit of normal for a woman 25 upper limit of normal and healthy for a man 35. And so most of the labs you get back and higher upper limit of normal is 40 or 45. So you can't just look for the red, you actually have to look for the number itself and then make that determination. And the majority of people will have fatty liver, because 1/3 of the American population has fatty liver. And so fatty liver can come from drinking that they don't tell you about. But fatty liver is the you know the biggest reason that's actually out there. So what is recommended then after cure, we talk more about lifestyle. You talk about diet, exercise and weight loss and those that need it. You talk about an appropriate diet. And usually the best recommendation we can give us either a Mediterranean diet, or to tell the patient to pretend they have diabetes and follow a diabetic type diet. Tell them to be very careful. And this really is for any patient about what over the counter things they take vitamins certain minerals, herbs can, for the most part are safe, but they can cause issues. So you need to know and they patients should almost never tell you what supplements they're taking. So you need to ask anyone with bridging fibrosis or cirrhosis? Alcohol is a no no. Anyone with bridging fibrosis or cirrhosis, cigarette smoking should be discouraged or stopped because it leads to increased fibrosis. marijuana use is not

recommended in anyone with fibrosis, because marijuana leads to the development of worsening fibrosis. We do not know if all the edibles that are currently available have an impact on the liver. It has not yet been studied. So you have to make a decision because patients ask that question a lot. And then coffee, coffee is actually really helpful. Coffee decreases the risk of developing liver cancer. So I routinely recommend my patients to drink coffee, caffeinated coffee, two to three cups a day in the morning. And it's been shown through multiple studies to be a paddle protected. So after someone's cured and what we do is really all dependent upon the degree of fibrosis. If someone had no fibrosis or grade one, they really need nothing more. They should be discharged from the specialist office and go back to the primary care doc. If they have bridging fibrosis or cirrhosis, they need to be followed long term for liver cancer. And if they have cirrhosis for variceal surveillance in the middle, difficult, right? It will just have to and nothing else going on. The reality is you wouldn't need to do anything. But you need to make sure there's no other underlying factors like fatty liver or alcohol and see whether or not they're going to progress or regress. But you don't routinely screen these patients as you go forward. What about endoscopy? Well, we only recommend screening for varices in patients with cirrhosis. If you treat someone who had small viruses and they're cured, and you repeat the endoscopy and the viruses are gone, you certainly consider stopping the beta blockers if Pharisees are are still present. We tend to repeat endoscopy but every three to four years and just evaluate these patients, about 10% of patients will develop their si cirrhotic patients will develop their says this is what the ASV recommends for patients. So as we talked about those that don't have advanced fibrosis anywhere from F zero they have to, they should be followed up as though they never had Hepatitis C. Patients should be assessed for recurrence or reinfection only if they have risk factors. Those patients with bridging fibrosis or cirrhosis even after cure should be screened for liver cancer every six months. Any cirrhotic should have a baseline endoscopy to screen for viruses. And anyone who has abnormal liver tests or is at risk of any other type of chronic liver disease should be assessed appropriately. Coming to the end, what about reinfection after? Cure? Well, it can happen. So here's a question. The 35 year old man recently diagnosed with Hepatitis C genotype three has f1 fibrosis, currently actively injecting drugs presents for an initial evaluation of Hepatitis C treatment. What would you suggest the first treatment is patient is at high risk of reinfection with Hepatitis C, or Hepatitis Hepatitis C treatment now, continue to follow up and plan to order medications in the future once the patient is no longer actively injecting drugs, or recommend drug treatment program and initiate Hepatitis C treatment once the patient is enrolled. So I'll let you guys answer that.

42:02
All right, everyone got an answer B, which is the correct answer. This patient should be treated. There's no There's no reason not to. And the studies have shown that people who are using drugs are not their overall cure rates are the same. And you do a lot of good for potentially society by treating people who are actually actively using injection drugs, because you'll

hopefully it will prevent the spread of the disease. So these patients should be treated right away. And so that's important, you know, and it's important for many practitioners to get over the fact that you need to treat these patients. Now reinfection occurs, but quite honestly, it's uncommon. If you treat lots of people who are high risk of recurrent disease, you're going to see reinfection. But surprisingly, the vast majority do not even if they go back to intravenous drug use. All patients who have ongoing risks for Hepatitis C should have periodic assessments for reinfection and be counseled about that risk. Remember, you never need to get an antibody again, once someone is cured only HCV RNA I can't tell you how many calls I get from patients angry because they went to see their primary care doctor or any doctor a Hepatitis C antibody was obtained was positive. And they were told the disease came back and they call up and you have to reassure them that no didn't, the antibody never goes away. And you have to get a virus to determine that someone has a flare in their enzyme you shouldn't first think about Hepatitis C you should think about all this other diseases and evaluate appropriately. And there is a higher risk of reinfection in certain populations, those of HIV who engage in activities such as men who have sex with men and patients who are actively using intravenous drugs. But if you look in the highest risk of those patients that are co infected, it's a very, very, you know, small study here, but those that are mono infected have by far the lowest risk. But overall reinfection rates in this patient population are low. What are the risk factors in the HIV positive patients who is a man had executive benefits anal intercourse with multiple having more than 10 partners and a low CD for account? And so there are specific risks and so people should be instructed or counseled about this. If reinfection occurs, you can reintroduce the same therapy they did perform the curator the same. So the good news is it's easy to treat and cure if someone is reinfected. If you look here at this is a trial of 190 people who were recently using IV drugs who received oral therapies from around the world. The overall number of cases of reinfection were low. Most of those people were young kids, teenagers 20s, who are actively using drugs. So to conclude with a couple of quick statements, although reinfection occurs, it's relatively low. It's critical to educate our patients on harm reduction strategies and safe sex. And it's important to counsel patients on the risk of reinfection prior to Hepatitis C treatment. That's important. We defined sustained virologic responses, undetectable HCV RNA at least 12 weeks after stopping treatment, and that equals cure. Once again, and I know I've said it a bunch of times, all patients who have baseline bridging fibrosis or cirrhosis, prior to cure need to be screened for parasailor carcinoma every six months for the rest of their lives. Persistently elevated liver tests after cure should be evaluated, not just poo pooed away. And Hepatitis C reinfection rates are very low, even in high risk populations, and should not be a barrier to treatment, we should be treating pretty much everyone who comes to the door unless there's have a high male that are waiting for a transplant. And then you could actually do them more harm than good because you'll prolong the wait for liver transplant or make it a point that they don't get a transplant that so called Meld purgatory. So with that, I'm going to stop. I thank you all for your attention.

46:42
Thank you so much, Dr. Bernstein. So the first question Dr. Bernstein is, you know, given the importance of establishing SVR 12 One of the challenges is that a lot of patients are not returning 12 weeks after the end of treatment. So a question from Abigail Hunter nurse practitioner is can we think about using other strategies to try to establish SVR 12 For example, dry bloodspot testing, which is qualitative, not quantitative, how can we become more innovative about documenting SVR 12 When patients are not coming back in?

47:25
practice? That's a great question. You know, can you use a dry spot if you had to shore? You know, remember, qualitative has a low picks up very low numbers. So that would actually be okay. You don't need a quantitative you just need a yes, no. And so that's helpful. The other is to if if these patients are in any type of health system, to put some sort of note in the chart, so whatever they show up to whichever physician that Hepatitis C HCV, RNA is ordered, because as I said earlier, it's not at 12 weeks, it's at least 12 weeks. So if they show up later, 16 weeks a year later, you're still going to check. You know, I think you can take some encouragement in the fact that at the end of 12 weeks of therapy, if someone is HCV, RNA negative, the chance of relapse is two to 3%. So the vast majority of the patients will not relapse, you want to document that. But that should give you some comfort, you know, to that as a strategy of how to get patients to follow up that's everywhere, you know, in every disease, you know. And so that's what I would recommend. But I think the most effective strategy in this particular difficult population that won't come back to you is still in an EMR. And if you have, for example, an Epic EMR that you can, so many different hospitals or doctors offices have, you can find the previous record from another institution. And if there's some sort of pop up or reminder, just please send it that will help.

49:16
Great, thank you for that. There's a question of whether people can donate blood after achieving SVR

49:23
Yeah, so the answer to that is no and that's a legal not a medical question, medical answer. So you know, as of now, even if someone is cured if someone has a Hepatitis C antibody, which is positive, they are not allowed to give blood and that's even in those patients that we presume had a false positive. You know, it's interesting, because we routinely use Hepatitis C positive organs, kidneys and livers and put them into HCV negative patients. So, but the end the the simple answer is no If you have the disease you can donate. So when I tell patients after they've been cured, I tell them three things that the antibody isn't protected with, they can get it again,

that they can't donate blood. And that that if they apply for life insurance, it's going to be a battle, they'll probably get up at the dock will have to write a note to take care of it. And the insurance agency who turns company who isn't your friend will prorate you at a higher rate because of that. There's no medical reason for that. So I had that I discussed those three points with everyone who's had a cure.

50:36
Thank you. Sounds like there's some room for advocacy there to change things. Yes. Okay. We have a question from Salaam Hawa, could relapse occur from intracellular viral particles that remain despite an adequate antiviral therapy and cure?

50:53
So the answer to that is probably yes, the presumption is that the people who are negative who relapsed the virus is hiding somewhere. So is it in the macro sites, the monocytes, the virus parasites, you know, we don't know. But that's the presumption it has to be somewhere. And most likely, it's in one of those three cells, but it could be in other places. We do know as I said earlier, the virus will live in hepatocellular carcinomas. And since they tend to have a decreased blood flow, if you treat someone with hepatocellular carcinoma for Hepatitis C, the relapse rate of 20% If you treat someone after the HC HCC is cured or eradicated, then the relapse rates go back to the to 3%. So the virus hide somewhere. We have a

51:46
question from Paula Bowser that I think is a great question that clinicians are really struggling with. So somebody was treated, you don't have documented SVR 12 They returned several years later with the same genotype in the setting of active injecting drug use, would you how do you decide whether to treat as a relapse or every infection, same genotype, you don't have SVR 12 documented?

52:14
So the nice thing is it doesn't matter. It doesn't matter at all. You have all the therapies we use now, a Pangea, typic. And so, and they're equally effective and patients who were worrying, they they're affected and patients who were reinfected. I would start with whatever therapy is available, you know, first, as always a de novo disease, and treat, because there's even data that shows retrieving with the same regimen and people who relapsed, you know, they do well. If they are treated and relapse, then you're going to want to move to salvage therapy, which is the saalfeld box. But I wouldn't try to get this off pillbox right away, I would go treat with what we have. It's easy to get.

53:04

And sometimes the insurance companies intervene and demand resistance testing because they say there's no documented SVR 12.

53:13
I mean, you can but the reality is, unless it's genotype three, you know, you're not going to need resistance isn't much of a problem. And I think the requirements from the insurance companies and resistance testings have gone way down, you know, because therapies become readily available and are much cheaper. Excellent.

53:38
So I really want to ask everyone to join me in thanking Dr. Bernstein for this excellent webinar.

[End Transcript]