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HEPATITIS C TREATMENT

Andrew Aronsohn, MD, FAASLDIPCE

2/22/2022

Hepatitis C Treatment

[video transcript]

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Dr. Aronsohn, who will be speaking with us today about Hepatitis C treatment. Dr. Aronsohn is a specialist in the diagnosis and treatment of liver disease, including the medical management of liver transplantation. He's an associate professor at the University of Chicago Medical Center for for liver diseases, a multidisciplinary center that is nationally known for its research discoveries and treatment innovations related to liver disease and transplantation. He's also a faculty member of the McLean center for clinical medical ethics. Dr. Aronsohn, His research interests involve the investigation of ethical issues surrounding Hepatitis C therapy, which include the fair distribution of resources and linkage to care. He leads the Hepatitis curriculum of echo Chicago, which aims to educate and empower primary care providers to effectively manage Hepatitis C in the local primary care setting. Turn it over to you, Dr. Aronsohn.

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All right. Thanks so much, Dr. Weiss, I really appreciate it. It's great to be here. It's a we were just talking, it's a rainy day here in Chicago, rainy and cold, but at least it's not snowing, which means it'll probably be rainy and cold for you guys in a couple of days. I don't have any disclosures to report for this for this talk. So a couple of the learning objectives. Today, we're going to discuss the eligibility recommended regimens for treatment for Hepatitis C, including some of the simplified regiments, we'll discuss a the therapeutic regimen and monitoring plan for Hepatitis C, adverse effects, contraindications, drug interactions, and then we'll talk a little bit about prior authorization as well. And we'd like to invite you to certainly post questions in the chat in the q&a. And I will leave time at the end to be able to get to all your questions, so please ask them as they come to mind. So we will talk about some of the epidemiology of hep C diagnosis and screening, staging, and then get into the therapy, the first couple was going to be pretty quick. So we'll have time for therapy. This is I'd like to start off with some of the enhanced data looking at positivity rates for in RNA positivity rates for Hepatitis C over the years, it's an enhanced data, which takes us up to 202,016. It's a little dated. But what's important to see here is that, you know, when you look at the RNA positive people in the green bars, you know, we still have quite a few people to treat. So even though we have these great therapies that are available for treatment, and curing Hepatitis C, which we'll spend the most of our time today talking about, certainly we have a long way to go. The other interesting thing is is divided out by males and females, but I want to really draw your attention to the bimodal distribution of Hepatitis C, amongst amongst people in the United States. And initially, you know, Hepatitis C was seen as a disease that affects people born between 1945 and 1965, the so called Baby Boomers, but we're seeing a huge increase in younger patients. And I know we have an audience today. Some of it some of you are very familiar with management of Hepatitis C and treatment of Hepatitis C. So this is no news to you. But for those of you that are less familiar, we're starting to see a huge increase in younger patients. And this is closely linked to the opioid epidemic and people who are being infected with Hepatitis C, through drug use. We're not really

making a huge dent, as far as deaths related to Hepatitis C, we are seeing I'm not showing this data, but we are seeing downtrending in transplants for Hepatitis C since 2013, when the DEA is became available. But certainly, although the number is going down, we're still seeing quite a few people dying each year of Hepatitis C and, you know, 14,000, I think in the era of COVID, I think our meter sticks for for infections and deaths have really gotten really blown, you know, we're looking at such higher numbers with that, you know, but 14,000 people in a disease that is curable, you know, nearly 100% of the time with minimal input is is still way, way, way too high. You really can't have a conversation about Hepatitis C without thinking about and describing some of the disparities in care. This is death rates caused by Hepatitis C where you can see American Indian Alaskan natives and black and Hispanic people are much more likely to die of Hepatitis C than white people are. So this is a disparity that we're seeing throughout the cascade of care. in treatment of Hepatitis C, okay, so just wanted to give a flavor and just a background of the epidemiology and then move on this is really geared towards this next two or three slides is geared towards those that are a little less familiar with Hepatitis C, of just how we staged the disease. And by staging, you know, this is really answering the question when a patient says How bad is my Hepatitis C. And what we're really answering with is really has to do with how much fibrosis is in the liver. And that is the staging. Excuse me, to make the diagnosis of Hepatitis C, our screening test is a Hepatitis C antibody test, if it is available, always order the reflex. Because if the reflex if the antibody is positive, that will reflect to an RNA test. And that's how you confirm your infection. Somebody with a positive RNA has a current Hepatitis C infection, these are the folks that need to be linked to care. If the antibody is negative, this patient's very unlikely to have Hepatitis C, if it's reactive, in the RNA is negative. This is somebody that either has been cure already, potentially a false positive, or somebody that spontaneously resolved their Hepatitis C infection. Staging is really important, because it's very variable over time, we know that there are various factors that will affect the progression of disease, like HIV co infection, alcohol use immune suppression, and certain genetic factors. But you know, we've all seen patients and you know, anyone that has seen patients with Hepatitis C, who have had this disease for 50 years and may have very minimal fibrosis, and there are certainly people that have had it for far shorter periods of time that have very advanced fibrosis at that time. So staging can be tricky, and is important to do for every patient that has Hepatitis C, the various staging systems that we use the sort of the quick and dirty one, the easiest one and the least expensive. One is called the FIB four. And this is important because this is usually part of most prior authorizations, you have to have some staging workup done as you submit for a prior authorization. For some patients with Hepatitis C. This is used when a really helpful website is from the University of Washington Hepatitis see website, which is has a lot of really useful tools on it. And this is called the FIB for this uses the age the ASC, the ALP and the platelet count, and this gives you a very sort of dichotomous view of whether somebody has cirrhosis or not, it's not going to give you different stages like whether it's stage three or stage two or whatever. But it will tell you if it's advanced fibrosis or cirrhosis or not. And it can use a cutoff of you know 1.45, which would be negative high negative predictive value for advanced fibrosis if it's less than that. And a fib for score greater than 3.25 has a very high specificity for somebody that has advanced fibrosis. So you know, if you're working in a center and a setting, where resources are limited, and you would like to stage a patient and really know just whether

they're cirrhotic or not, this can be really helpful. Other markers of fibrosis, like the Fibro tests, these are direct markers of fibrosis, these are serologic tests. And these give you a score and they're all calibrated a little bit differently between zero and one. And then you can see if somebody is cirrhotic, or how close they are to being erotic based on this score. So that's another marker. And then there is transient elastography or the fiber scan. And this is the reason I have the picture of the cheese's. I'll digress for a minute or two to tell you the story of the fiber scan if you don't already know it and the urban the urban legend or the urban myth is that this technology was invented in France where they would, you know, in France, when the cheese becomes ripe and ready to go, it becomes harder and harder. So we used to have to kind of just poke all the cheeses to see if they were ready to be sold as they as they became more ripe. And someone came up you know there was a physicist around there that said hey, you know, you know sound waves go really fast through hard things and slow through soft things. And then they started scanning all the cheese and they would be able to find out when when the velocity of the sound waves got fast enough they know that cheese was ready to go and southern came to us. You know the same thing happens in the liver. When the liver becomes neurotic, it becomes stiffer and stiffer. So it turns out this technology works quite well for livers too in addition to cheese, and the faster the sound waves go, the more fibrosis or the stiffer the liver is, and those are the patients that are more likely to have cirrhosis. So what you see here is transient elastography or a FibroScan. This is not an all Your sound is just basically measuring sound waves, the test takes about five or 10 minutes, and you'll get an answer back and kilopascals that will show you how fast the sound waves are going through the liver. And the ones that move quite fast are more synonymous with cirrhosis. So if the speed is greater than 12 and a half, this is a patient that likely has cirrhosis, and in this lower ones are going to be more synonymous with patients that have earlier stages or no fibrosis at all. So this is a very great way that we can

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find that level of cirrhosis or whether a patient has cirrhosis or not. And then the last thing, this isn't as common as a fibro scan, or transient elastography Magnetic Resonance Elastography or an MRE is doing sort of the same thing by measuring waves going through the liver, but you're doing it in cross section. This works a little bit better in patients that are obese, and also has the added benefit of measuring fatty liver disease and can take pretty accurate measurements of fat. So, you know, at the end of the day, you know if you're interested in treating Hepatitis C in a primary care setting, there's lots of different ways where you can stage a patient if you've noticed, I didn't even mention a biopsy. So biopsies are not standard of care at all, to treat Hepatitis C. And there's all these non invasive ways from sort of a low tech approach using a fib four all the way to some of these higher tech scans that you can use. All right, so I'm going to shift gears and we'll get to the bulk of this talk, which is looking at treatment of Hepatitis C. So Hepatitis C is a very curable disease. And when we talk about cure, we talked about sustained virologic response or SVR. And when a patient is cured of their Hepatitis C, a number of things happen. The first is the virus is eradicated. So unlike other viral illnesses like HIV, or Hepatitis B, where our medications suppress the virus, Hepatitis C is very different in that the virus is cured. And even in patients that may have cirrhosis, you're we're seeing improved clinical outcomes in

patients who are cured. This includes improving the histology, so the liver will get better after a cure, and also decrease rates of decompensation decrease rates of developing liver cancer and improvement in lifespan and decrease of mortality. So here is you know, we've come quite a long way in treatment of Hepatitis C, over the years, and you can see on the on the y axis is SVR percentage or percentage of patients that was cured. And it's really been quite a revolution in our therapeutics. So if you go back to the early 1980s, interferon was used as a monotherapy. In this treatment for either six or 12 months, was pretty ineffective you if you were lucky you and cure 10% of the patients. And you know if there was anyone that's on this webinar that remembers treating patients with interferon, this is a really, really difficult treatment patients became quite ill, you really couldn't treat a lot of sick patients that had a lot of comorbidities, or advanced fibrosis, flu like symptoms, depression, really patients pretty terrible taking these injections, Rive of iron was added, which improved some of the cure rates. And then things really changed around 2013, when the first direct acting antiviral agents or DHEA, is were added to the mix. And now things are quite different. So in 2022, this is just an example. But then we're going to go in a little bit more detail of the actual treatments. But treatments now are anywhere from two to three months. They're all oral therapies, we don't use interferon at all anymore. The cure rates are close to 100% for most patients, and one of the things I would like to focus on over the next couple of minutes is talking about sort of some of the expanded indications for treatment, and most importantly, the simplification of the treatment. So you know, Hepatitis C treatment is something that is quickly moving out of the hands of specialists, and into hands of primary care because this is more accessible for patients. And honestly, when working with primary care providers, treating Hep C could be the easiest thing you guys do all day. It's pretty straightforward. And hopefully I can give you for those of you that are less familiar with it and give you a good flavor for it. So what are the medications that we use to treat there's really three basic categories or three classes of drugs that we use to treat Hepatitis C. The first one is the polymerase inhibitor and one of the examples is a medication called sofosbuvir. There. This is actually the coolest slide that I have. So if you're planning on logging out soon, you can just watch this slide and then feel free to log off after that just And, but this is this is all I got this is the best I got. So this is the primary strand being built onto the template slant strand as a polymerase is going along. And sofosbuvir is a molecule that looks like this, which kind of has a stopper on the end of it. And do it again, here we go one more time, in case you missed it, here's the next nucleotide trying to be added on to it, and it's not able to do it. So this is a train a chain Terminator that ends the primer, Stan prematurely and effectively kills the virus. And then it makes it unable to replicate. So that's how things like polymerase inhibitors work. The second is a protease inhibitor, and this is an example of this is called Cat probeer. And the way that the Hepatitis C virus replicates is that it's translated into a very long poly protein in that poly protein needs to be cleaved into different pieces in order to perform its daily activities and to replicate. And the protease inhibitor or the protease is the scissors that cuts this long poly protein into smaller pieces. protease inhibitor inhibits this molecule, so you're unable to cut this long strand of protein into the smaller pieces. And it's pretty useless as a long strand. And this also stops the replication of the virus. And then the final thing is NS five A inhibitors like Dipa spheres as a as a example of that. The NS five a domain is implicated in replication of the virus. And this is a molecule that sort of fits into that replication complex, and renders it useless so that the violent

virus can't replicate anymore. So the important thing isn't exactly how these things work. But just understanding that similar to HIV therapy and other kinds of antiviral therapies, you're using different classes of drugs that have very, very different approaches, and in terminating viral replication, and these all will work together to be highly effective. So couldn't resist using the word old reference. If anyone's keeping track at home, I don't think you can use exclamation points on word I've tried it doesn't work. But if you want to sound smart and want to know what all these drugs are, just have to look at the generic names for them. And if they have a premiere at the end of them, they are protease inhibitors like cat Premier, and they have an asphere. At the end of them. That's an NS five A inhibitor like velpatasvir. And if it has a booth here, at the end of them, it's a polymerase inhibitor like sofosbuvir Vir. So all Hepatitis C drugs are going to be combinations of at least two classes of drugs, and in one instance, three classes of drugs, but you never use one alone. Again, it sounds a lot like HIV therapy, because there are some similarities. So here they are. And you can see here on the column, on the left, you have protease inhibitors, you have NS five A inhibitors and you have polymerase inhibitors. And then you have these different combinations. So the ones that we're really going to focus on the most the one, you're going to use 99% of the time, 95% of the time, are going to be these two sofosbuvir, there are no pedosphere. This is Epclusa in ghlac Kappa via pibrentasvir, which is NAB red, this is really doing the lion's share of the work. So I've given similar Hep C talks for many years. And this table used to be quite big when there was lots and lots of different therapies out there. And it was pretty difficult to navigate. And now this has kind of been shortened because these are really the most highly effective ones that you're going to see the most. And if you're really going to focus on these two. This really is the ones that you're going to see the most and I'm certainly going to use the most. So understanding that most of our viewers of this webinar are in New York State I wanted, I went back and reviewed some of the drug utilization programs for the New York State. And these are the drugs that are approved in New York State on the preferred agents. So now I've read article a cap bm pibrentasvir sofosbuvir and velpatasvir Epclusa. And this is one we'll talk about in a moment. This is vosevi, which is sofosbuvir, co-chair, velpatasvir and voxilaprevir. And this is a three drug combination. And this is using all three classes of drugs the protease inhibitor, the NS five inhibitor, and the polymerase inhibitor. This is a special category of a drug that's really used just for people who have failed a prior DEA regimen. So some people who need to be retreated. And we'll go through an example of those patients. So you know, one of the biggest roadblocks ensuring Hep C and eliminating Hep C has been needs for prior authorizations. These can be although the medications themselves are pretty simple to use, which I'll show you in the treatment regimen. quite easy. The the hoops to jump through in order to get these medications available over the years and get them into patients hands has been quite, quite difficult. I'm really happy to say that New York is one of the, you know, growing number of states that are starting to eliminate prior authorizations for many patients. So as of I believe it's October of 2020, although I could be wrong in New York, excuse me.

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Prior Authorization is not needed for treatment, naive net New York Medicaid patients, okay, so if you're looking to put patients on treatment, this makes things a whole lot easier. Prior

Authorization is still needed, as far as I could tell, based on the New York state websites for retreatment prescribing a non preferred drug or when there is no evidence of an FDA approved diagnosis and a history. So you know, understandably, they have to have hep C in order to treat them first. So you know, if anybody has comments on that, or, or if that's incorrect, please, please let me know, because I'm still living in a state where you need prior authorization for everything. So notice a little bit of jealousy in my voice. Okay. So if there's one thing if you're new to Hepatitis C, or gaining more experience with Hepatitis C, the HCV guidelines is a really, really helpful tour tool, excuse me, because this is kind of the one stop shopping this is the way that you know, if you really need one place to go to, to know who to treat and understand some of the data behind these treatment regimens. And even things like treatment, monitoring, and other issues, this is the place to go. There's really three things you need to know about your patient in order to start them on treatment. The first is their genotype. The second is whether they are treatment experienced or treatment naive. And the third is whether they have cirrhosis or not. So, you know, of course, the genotype is pretty easy to get just from a lab test. I will argue, though, that the genotype I'm going to show you some data is nibm, maybe on its way and becoming obsolete based on the pan genotypic nature of most of our treatments. Certainly, it's pretty easy to figure out if somebody has been treated before when you take your history. Easier said than done sometimes, but most of the time you can get it and then the cirrhosis or not, which is why I wanted to spend just a few minutes early. Earlier on talking about cirrhosis and staging. When you go to HCV guidelines, I would invite you to scroll down at the bottom for the simplified treatments for treatment naive patients and again, most of the patients we're going to be seeing our treatment naive patients. There'll be a few treatment experience and those details you can find on the website. But this is I feel very, very helpful because this is these are one pagers Okay, so this is everything you need to know and how to treat someone with hep C on one page. Excuse me, this is going fast. Both patients without cirrhosis and those with compensated cirrhosis. And you can download PDFs for both of these and print them out. And I wanted to you know, I'm not going to spend the entire hour kind of going through each step. But I just kind of wanted to show you what this looks like and give you an example of the simplified regimen for adults without cirrhosis. These are patients can have any genotype. They don't have cirrhosis and their treatment naive and it kind of tells you what the you know who is not eligible. People that have had liver transplants have liver cancer people who are pregnant things like that. And this will take you through step by step. So it'll tell you to calculate the FIB four score so And it even tells you the cut offs for the fibs four score or these other kind of non invasive tests that I've already shown you medication reconciliation, and we're going to talk a little bit about that potential drug interactions. Using the Liverpool drug interaction checker, there's really, really helpful. This is a publicly available website. If you Google University of Liverpool drug interaction, there's a Hepatitis C site that you can just enter in the medications that they're taking and the medicines that you want to start them on. And it's going to spit out whether there's any drug interactions, educating the patient, here are the tests that you need to take to give to have done before treatment, pretty obvious things like a CBC, Patek function panel, check their GFR and then of course, screening the patient for Hepatitis B and HIV and making sure they're not pregnant. So this is this is pretty much it, this is all you need. And then I want to get into a little bit of the therapies themselves. So these simplified treatment regimens

are really recommending two therapies sofosbuvir beer and lipid sphere angler kappa via prevent pibrentasvir. So I want to give you a little bit of information about these. The nice thing about these medications is now how I Absolutely boring in the best possible way they are. And the reason I'm saying that is because they're highly effective, they pretty much work for everybody. And you can pretty much use them in almost any circumstance, except for a few tiny exceptions, which I want to go over. So the first is sofosbuvir velpatasvir. So this is Epclusa. This is pan genotyping. And what that means is if you send the genotype on your patients, you're gonna get something back from one to six. This works equally well on all genotypes for your patient. So, you may ask why you even need to send the genotype and I would tell you that that's a pretty good question. But for most patients, it's not going to matter because this is going to work for all of them. The second is this is safe and effective in patients with cirrhosis, including decompensated. cirrhosis, you're going to see a little difference when we talk about glecaprevir and pibrentasvir. Because this is a drug that you cannot be using in decompensated cirrhosis. But for this drug, you can see this is safe and effective in all patients with cirrhosis. Relatively new data has shown safety in patients with chronic kidney disease and in end stage renal disease who are on dialysis. I'm putting this in here because there's not a ton of big drug drug interactions that you can really harm somebody with except for this one. This is kind of the main one that I always watch out for is amiodarone. And it's been linked to fatal arrhythmias. So you really want to watch out for a patient who's on amiodarone that you're going to treat with a sofosbuvir based regimen. And most of the treatment for this is going to be 12 weeks, it's one pill a day. And here's where the data is, is unbelievably in a great possible way boring, because this is data from Astro one published in the New England Journal now over five years ago with a sofosbuvir and velpatasvir treated for 12 weeks. And I'll take you just to the top line data here. And of 624 patients enrolled in this study 618 are cured. And you can see that this was throughout all the genotypes highly, highly effective. Some of these patients actually were treatment experience with interferon based regimens and about 20% Worse erotic in this study. So this was one of the initial registration trials, just showing high efficacy and a pan genotypic way for this for this drug. I'm not going to spend a ton of time talking about side effects because they are relatively minimal for these drug regimens. And this was a highly well tolerated medication with I think zero discontinuations for adverse events. The next drug is called Kappa, Vir and pibrentasvir. So this is Navarette. This is also pan genotypic. So this is going to work on all the genotypes. Although this is safe and effective in cirrhosis. This is not to be used in decompensated cirrhotic patients, you don't want to use the protease inhibitor, the CLA kappa Vir and a patient that has decompensated cirrhosis as there's data linking this to further decompensation. So you want to make sure that they're pretty well compensated or not cirrhotic at all. This is a safe and effective. And people with chronic kidney disease, including those with dialysis, without any dose adjustments, many of the treatment naive patients is going to be eight weeks, and there is some data showing efficacy in da experienced patients as well. This is a little bit of a busy slide, but this is some of the data and the important thing I want to show you is just the intention to treat or the modified intention to treat analysis. We're at a 1064 patients 1060 word cure. So you know at the end of the day, if you're able to get somebody on therapy, and they're able to take their medication reliably, this is somebody that is going to almost certainly be cured of their disease. So I thought what I do for the remainder of the talk is go

through a couple of cases that will highlight, you know, for especially for some of the more experienced traders, the types of patients that we're seeing a lot of and also some of the new nuances of treatment, especially in a setting like New York where you can get a lot of people on treatment, you don't need prior authorizations. So the first case is our t who's 22 years old and he was referred from a primary care physician. This gentleman has had a history of IV drug use for two years and is currently in a methadone program. There has been multiple slips in the past and patient doesn't have an upcoming court date. He has Hepatitis C positive and he has never been treated before. Further testing reveals that he is HIV negative is negative for Hepatitis B and he's a genotype three patient. His viral loads about 4 million you can see a mild elevation of his al T. His bilirubin is normal as INR is normal and his platelet count is normal. Okay. 289,000. So this is a very common patient that we're seeing as we're noticing increases of acute Hepatitis C In patients who are using people who are using drugs, this is someone that's very unlikely to have any forms of advanced fibrosis, just because he's likely hasn't had the Hepatitis C for very long.

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So what is the approach to this patient? Is it somebody that we would treat now? Is this somebody that should even be eligible on treatment? What are the things otherwise that we should address for this patient? So a lot of questions come up. And I think that our, our way of thinking through this and offering help to somebody like this has evolved in a very good way over the years. So what do we know about Hepatitis C infection and injection drug use, we know that Hepatitis C prevalence among people who are injecting drugs, or people who use drugs, is estimated to be anywhere from 70 to 77%. One in three people who inject drugs are going to require Hepatitis C within the first year of injecting. So this is one of the reasons why we're seeing such a high rate of people who are even new to injection injecting drugs. And what's following this is we're seeing such an increase in an O N, acute Hepatitis C, in people who are injecting drugs, especially amongst younger patients, and anywhere from 45 to 85% of patients who are infected with Hepatitis C are going to be unaware of their of their status. I showed you this data, this is some data from Chicago, just and I think it's just just kind of amazing to see how quickly things have changed. This is from back in 2007, where you can see just the classic kind of baby boomer peak of people of newly reported Hepatitis seats. So these are people that are were just being diagnosed with Hepatitis C. And now, you know, fast forward about eight years later, we're seeing this huge peak, and people aged 20 to 30, in our age, and I expect that there's something this is going on around the country, I'm certain this is the same thing in New York as well. And these are predominantly people who are using drugs or seeing this high rate of this. So this really changes everything. I mean, this is changing the algorithms of how we're treating and the ways that we're going to effectively reach folks like this, and get them help and get them the treatment that they that they require. So can you treat these patients? I mean, what happens if you try to treat patients who are using drugs? Or what about to start with people who are on opioid substitution therapy? This is data that is a little older and has been reproduced a lot. But this is one of the original studies that I wanted to show you. These are people being treated with sofosbuvir and lipid sphere, showing very, very high SVR rates or cure rates who are enrolled in opioid substitution therapy settings or, or methadone programs

and things like that. And this, you know, the reason I'm showing you this is this really kind of set off, you know, a very vigorous motion to start thinking about treating these patients being more aggressive. We're treating people we're using drugs and sort of pushing the envelope is, how many people can we treat on despite using drugs? And how successful can we be, which is really leading us to these novel treatment environments. And I call this this is called the test and treat that was presented at our liver meeting just a couple of years ago. And this is really getting away from the standard of care approach, I'll direct your attention to the bottom part of this slide first. So this is also a little bit novel testing in a harm reduction or addiction Center, which is great, getting the test. And but then when someone becomes positive, saying, Okay, go to the brick and mortar doctor's office. And then once you get there, they'll make that they'll send the RNA, they'll start showing treatment, they'll follow you up, they'll do all those other things. That's how kind of medicine has been sort of built in our country. But what about if we flip that around a little bit? So what happens if we do all those things at the Harm Reduction Center? So what happens if we meet the patients where they're at? And now that this treatment is so simple, and it's eight to 12 weeks, and it's a you know, it's one, you know, daily medication with very little follow up? Why don't we just do that right all at the Harm Reduction Center, what happens if we do that, so the testing and diagnosis, the treatment and the follow up all at the same place? And what they found was not surprisingly, when you use the standard of care, which is these yellow bars, you have a huge loss of patients when we talk about treatment and SVR, so meaning that they never make it to that place, despite everyone's best intentions. Getting into, you know, the barriers of getting into a clinic, establishing care, following through with all the things that are needed, just doesn't work well. And then if you look at the experimental group, which is looking at this point of care testing, a 57% increase in treatment and a 41% increase in SVR Now, mind you, no one's doing anything different. This is the same treatment This is the same everything, you're just co locating it at a place where patients are already going to be like the methadone clinic like the addiction treatment center and just offering them an extra service, which ultimately would be would be life saving. So this is one of just the novel ways of colocation, which I think is important for treatment. And also, we start thinking the next. The next step, which is elimination strategies is really important. So you know, I put difficult to treat populations because I would argue that there are no more difficult to treat populations, because everybody is easy to treat. And this is looking at people who are actively using drugs, people who are using drugs, people with psychiatric disorders, people who are using alcohol, unemployed, low to no education, and even using illicit drugs, cocaine, heroin, marijuana. This is real world data of patients who are enrolled in centers where they're getting treatment. And this is really proofs in the pudding here. And this is real world data that you're able to cure nearly 100% of these patients who in the past I think would have been stigmatized as people who would not be able to be treated and when do poorly of a treatment. These are really safe and effective treatments and are, should be very available to these folks. So this is reflected in our guidelines in the HCV guidelines. And I'll direct your attention to the section which talks about recommendation for screening and treatment of hep C people who inject drugs, and it says active or recent drug use are a concern for reinfection should not be a contraindication for Hepatitis C treatment. So it's important to say that Hepatitis C treatment should not be done in a vacuum. Certainly people who are struggling with addiction need access to a lot of other services, including harm reduction services. But

incorporating Hepatitis C treatment into these services, has been shown now with lots of good data to be highly effective. Alright, so let's continue with this case, our T is treated with low kappa beer and pibrentasvir. And he's very adherent to treatment although he is arrested at week three of his therapy and spends two weeks in jail where he was not able to access treatment. He gets out of jail and then he completes his therapy. But and his SVR check is 12 weeks off with therapy, his viral load is 1.2 million. So this is somebody who was a non responder or relapsed to therapy, likely because of the two weeks where he was unable to get treatment. So can you treat this retreat this patient, and how, and this is the segue into sofosbuvir, velpatasvir and voxilaprevir or vosevi. This was also a pan genotypic regimen. So this is using a drug from each of the three categories and shows a very high SPR and people who have failed D A's. It's effective and cirrhosis. But again, since there is a protease inhibitor it should not be used in patients with decompensated cirrhosis. And since this is sofosbuvir based, should not be used in conjunction with medications like amiodarone, and usually best with patients that do not have renal failure.

38:18
Sorry, I got away from me. I'll trigger happy there. Okay. So here is the data for da therapy for retreatment. This is a Polaris studies showing people that have been previously treated with DHEA based treatment, have high SVR rates. So this is kind of a nice thing to have in the armamentarium. I will tell you, you know, we don't use it a whole lot, because in most cases, most people are cured. So if you think about the first line data, which is probably 95 or so percent of patients are going to be cured. That doesn't leave a whole lot of people that are going to need this, but it's there if you need it, and these patients will likely be cured the second time around. Alright, so case number two. This is a 53 year old gentleman who was recently diagnosed with HIV. He has not yet been started on antiretroviral therapy and some baseline labs are sent this patient was appropriately screened for Hepatitis C, and found to be co infected with hep C and what Hepatitis C agents can use, and well, this work isn't even worth doing and somebody that's already has HIV, and when should you do the treatment? So a note about coinfection is people who are co infected with HIV and Hepatitis C are going to have a faster progression to cirrhosis than people who are mono infected with Hepatitis C alone. Okay, so you can see here this is everybody in this graph has Hep C, those that are HIV positive have a much higher percentage of cirrhosis over the years than those who do not have Hepatitis who do not have HIV. This is even the stood true when patients are on antiretroviral therapy and are well controlled with good CD four accounts and low viral loads. The bottom line here is they all work and they all work really well. So if you look at sofosbuvir, velpatasvir, le dip is ver sofosbuvir, le Kappa, Vir pibrentasvir, they all work quite well, with with essentially equivalent cure rate as those that have mono infection. The one thing and I mentioned this a little earlier in the talk that you really want to make sure you check into is this website, the University of Liverpool hep drug interactions website, I encourage you to do that every time you start somebody on therapy, because this is just a very quick, it'll take you like less than two minutes to search for their Hepatitis C drugs and then no set search for their CO medications. But with antiretroviral therapies and HIV therapies, you are going to see a little bit more crossover in some drug drug interactions because you're having similar drugs of similar categories like

protease inhibitors, and things like that. So you will want to make sure that you're not going to be double dipping, and putting people on too much of the same type of drug. I will say that is pretty rare now with modern HIV therapies that they're usually pretty friendly to all of our Hep C therapies. And it's pretty rare that you would have to switch somebody around, we usually recommend either is getting somebody sort of stable, you know, there's never a huge urgency to treat somebody I'm talking, you know, in the matter of weeks, not years. So it's always helpful to get somebody you know, started on there, HIV therapy, stable and HIV therapy. And then as soon as they're stable on that, go ahead and get them treated with their Hepatitis C. Okay. So next case is, you're called by a general surgeon who just had a needle stick, and then with HIV, Hepatitis C positive patient, he asked you about prophylactic therapy, and how should you evaluate him? So you know, I use kind of the easy example, which was a needle stick because you knew exactly when the time of infection was, but acute Hepatitis C is on the rise. And I sound like a broken record. And I realized that but, you know, because of the increase in injection drug use, especially amongst young people, we're seeing more and more acute Hepatitis C. So this is something I think you're likely to see a lot of if it's not from a general surgeon, with a flying needle. So when you you know, a week later, this page, the surgeon has his labs drawn, he's got an incredible, incredibly high viral load of load of 45 million as a CNA, LT are elevators Billy's up a little bit as INR is normal, feels a little tired, but otherwise, he is doing well. So should you start treatment. So there's data of treatment and acute Hep C, and there's even data of shortening the treatment, although this isn't quite ready for primetime yet. This is looking at six weeks of therapy with high SVR rates. But you can see here this is rather than 12 weeks, but you can see this as a pretty small study. But certainly, these patients are very people are very, very responsive to this. But the recommendations right now is to not wait it out. That was an old recommendation, the new recommendations are to if somebody has acute Hepatitis C, go ahead and treat them with the standard regimen, there is no such thing is pre exposure, or post exposure prophylaxis for Hepatitis C doesn't really exist, just go ahead and treat them. And the medications are so effective that you shouldn't have shouldn't have any, any problems. All right, my last example, before I'll open it up for questions, is a you know, you can't can't have a whole talk for an hour without mentioning COVID whines, right. So you're seeing a new telehealth visit of a 35 year old man with a history of hypertension, and is referred to you with for a new diagnosis Hepatitis C, viral load is 2.3 million and no other evaluation is done. And as you're talking to him, just like everything these days, patient says, you know, I'm gonna wait till COVID kind of dies down before coming in, in person. And you're kind of like, well, you know, should I just like see him in six months? Like, what do we what do we do, I've heard this treatment, it's pretty easy. So this is a great study called the min mon approach. And I call it the kiss or the keep it simple, stupid. And it's great because it really I think is going to be where Hepatitis treat, see treatment is going, especially with our simplified regimens. And I think it's kind of it just takes it even a step further. This was a little bit almost before its time with COVID. But I think it's something that you know, we're doing in our, in our clinics here, and it's been really, it's been really helpful. So the way that this goes is rather than somebody coming into the clinic and getting their labs drawn and having to come back to the pharmacy and doing all that gotten rid of the genotype altogether, because remember, all of our treatments are pan genotypic giving all the treatment at the point of entry. So one time just show up and get your

medication There's no scheduled on treatment clinics or labs and a remote contact visit at least four and 24. Okay, so this is just taking it to the ultimate step, you determine if somebody is sporadic by just checking a fib for and then they're off and running. Okay. And the only reason you want to know if there's cirrhosis, have cirrhosis is to know if you need any kind of monitoring after their cure. And what this showed was very, very high SVR rates without us messing with people just send people home, let them take their medications, and they did quite well. So the eligibility for the study was, they had to be 18, they had to have active Hep C infection, they couldn't be pregnant, they couldn't be be compensated cirrhosis, things like that. And what this study showed was relatively large study was an SVR rate of 95%, they're able to cure 95% of people just by giving them the medicine, send them home, it was we'll see it 12 weeks after you're done, and check for SBR. So out of the 383 samples collected and week, 24 379 of them were were were positive were negative. So this is really pretty good. And I think I wanted to show you this study, because I think that this is highly predictive of I think, a very forward thinking way of starting to treat Hep C with really minimal FaceTime, and just sending patients home and letting them take their meds. So I did want to leave a little bit of time for questions, I think we'll have about 10 minutes or so, you know, there has been tremendous advances of anti retro antiviral treatment of hep C in the last five years, really with high high treatment rates, and cure rates, SVR cure rates are over seven, and 95%. In most patients with eight to 12 weeks of therapy. There really isn't any more special populations, we used to think of people with kidney disease and people with HIV and people who use drugs as special populations and had difficulties in getting treated and cured. But I think that doesn't exist anymore. Now it's really all about public health. It's about diagnosis, access, and removing coverage limitation so people can get rid of the barriers and get their Hepatitis C cure. So with that, I'll stop. I want to thank everybody for their attention. And Dr. Weiss. I don't know if you want to read questions or how you'd like to do it. Sure. Thank

47:24
you so much, Dr. Aronson. We do have some questions and encourage others to please continue to put questions either in the q&a or in the chat. And we will ask Dr. Aronson to take them on. So the first question is about, you know, just using PIP for fibrosis staging, as opposed to the need to do other serologic testing. And, you know, I think, in the context of your presenting Minnemann, and wanting to do simplify treatment, I think a lot of providers are not certain if it's okay, just to use the IP for so please. Elaborate on that, if you would?

48:06
Yeah, I absolutely agree. I think that, you know, the only risk, you know, I think the risk of that the fit for isn't going to be in the treatment itself, because the treatments are going to be pretty much the same whether someone has cirrhosis or not, the only risk would be missing somebody that has cirrhosis and doesn't get appropriate cirrhosis, follow up after treatment. So what I think I would, I would, you know, I agree with it that a fit for is is the only way is really the vast majority of time, the only thing you need. But if there's something about the patient that stands out as a little questionable in terms of how much fibrosis they have, platelet counts a little bit low. If they maybe gave you a history of maybe having a ascites. And you're not sure or you know, there

was a GI bleed and you didn't know, you know, if those those cases of what I'm doing in my practice is those are the ones that I'm going to, you know, a little bit little bit more testing just to know because again, you don't want to you know, and I didn't go into a lot of detail during my talk. But if you hear somebody that doesn't have cirrhosis, they're sort of done as long as they don't have ongoing risk factors. But if they have cirrhosis, you're going to require ongoing treatment and ongoing monitoring, looking for liver cancer screening for viruses and things like that. So you know, you don't want to miss those people. But But again, I think in the vast majority of cases times it's good for us is the way to go.

49:31
Thank you. Next question is to talk about COVID infection in terms of its impact on Hep C prognosis, progression, treatment success, and you know, the relationship with any COVID complications in terms of treatment.

49:49
Yeah, that's a great question. I mean, I think that the data is still young for this. So far, there hasn't been any signals that COVID it adversely affects treatment outcomes for patients, you know, or COVID complications. So certainly, you know, I would still in the era of COVID, I would still certainly don't want to treat people that's having active symptoms, because they just don't want, you know, you want to make sure someone is going to be adherent and be able to take their medications and things like that. But, you know, I would sort of as long as they're doing okay, I would just go ahead and treat them either before someone would get COVID or after they have COVID, as long as they don't have severe complications that, you know, sometimes it becomes an issue of, you know, if somebody is suffering from COVID pneumonia and still having symptoms and having issues with that, I don't know if I'd want to start a whole new regimen of drugs, but but then again, you know, I think it shouldn't impact. Interestingly, though, COVID has, you know, we do have data that COVID has, has caused a decrease in diagnosis and overall treatment. So not surprising sort of stating the obvious, but, you know, people are table their Hep C infection, patients have tabled it, providers have tabled it to kind of deal with COVID, because of staffing because of everything going on. And even for patients that are doing kind of simplified approaches, we're seeing less people now. And we haven't even quite reached the levels. We were at, you know, pre COVID and starting to come up, it really came down at the beginning, just like everything else that's starting to come up, we still haven't reached that area yet. So still still a lot to be done with that.

51:36
Thank you, Dr. Aaron's. Next question is to briefly discuss considerations for a patient who's reinfected after having been cured several years prior?

51:46
Yeah, this is a great question. So you know, there's a few things that you want to consider. The first is if you're able to, and this is not always possible is to get an understanding of what they were shared with initially. Okay. And in I usually go, you know, sometimes people don't

remember, I mean, I can't remember a medicine that was on five years ago, so I wouldn't really expect anyone else to remember it. You know, 2013 as a good cutoff date. So sometimes people remember dates, pre 2013, unless they were in a clinical trial, they probably weren't treated with TAs and post, they probably were, and everybody remembers getting a shot of interferon. Okay, so did you get a shot? And did you feel terrible after and everyone's gonna remember that? So, because the reason why you want to try to drill down on what they were treated with before is if it was an interferon in ribe of iron regimen before vas, they're effectively like a treatment naive patient, okay, their treatment outcomes are going to be you know, as going to be the same. If they were treated with Da, then you would want to know, and then the second thing that you want to know is what how did they get reinfected? Okay, so was this truly reinfection? Or was this you know, nobody checked an SVR and a number were really cured in the first place. So trying to get sort of the timeline of what that happened. But then, you know, so once you know what they were treated up if they were initially treated with a DEA, if they were truly truly reinfected. So let's say they got Navarette two or three years ago, and they demonstrated an SVR, and then they went back to using IV drugs and had a documented new exposure. That person has almost like a new treatment naive patients. So you're gonna treat them again, like they are, you're starting fresh. It's not always so easy, because sometimes they don't You don't know. And if you're in doubt, then you have to treat them as a treatment failure and use a three and three that drug regimen. Most you know, and then, you know, I think you can't have this conversation without also thinking about addressing, you know, what were their risk factors for becoming reinfected? So this gets back to not treating Hepatitis C in a vacuum, and do they have access to harm reduction? If this is someone who's using injection drugs, they have access to harm reduction services? Do they understand using clean needles? Do they you know, things like that, so they can, you know, you can prevent re infections over time. So that was a long answer. I apologize. But I think that in summary, you really want to try to drill down what they were initially treated with whether they were actually reinfected or they were just never cured in the first place. And then and then kind of looking at some of these other surrounding factors to help them from not getting reinfected again. I hope that answers your question.

54:41
Thank you. The next is more of a comment. Someone wrote in that prior authorizations are certainly a barrier to care but the exorbitant prices for these medications should be mentioned as the likely reason for much of the under treatment, especially among the uninsured.

54:59
Yeah, So literally, I'm glad you made that comment. I couldn't agree with you more. I will say that through, you know, collective negotiations with drug companies sofosbuvir and velpatasvir now has generics. So we're starting to see some of that. And I think that the, you know, I think in payers have gotten a little bit savvier on negotiating to bring down some of these costs. They're still exorbitantly expensive. But, but they're coming down. And I think that the states are starting to see this as well, because I think by them, you know, the signs, this motion, that they're coming off prior authorization is showing that they're becoming a little bit more affordable. So I

think I think there is a little bit of movement for that. But you're right. This is this is, this was for sure, a hindrance at the beginning. And this is why things were locked down. And I think what we're starting to see is a lot of people who are doing the right thing, seeing their doctors, and there were so many barriers to getting these medications, the medications were so you know, expensive in 2017 or 2018, or whatever that, you know, they were turned away, because, you know, I know in Illinois, and I don't know how it was in New York. But you know, there was many years where you couldn't treat someone unless they have cirrhosis, because the medications were so expensive if they had Medicaid. So, you know, these sort of ridiculous policies based on drug costs really, ultimately harmed a lot of patients.

56:24
Thank you. I'll just make sure everyone on the call is aware that New York State Department of Health AIDS Institute does have a special program for individuals who are uninsured to be treated for hep C called the hep CAP program. And there are 12 care and treatment programs throughout New York State that can treat individuals who are uninsured, uninsurable for hep C treatment. So we I think we have two questions on the same topic about there is a drug drug interaction on the Liverpool site. I think it's with fentanyl and GP. And the question of whether for patients using opioids, one, you've seen any drug interactions, particularly with fentanyl, and if that would be a reason to choose for Epclusa over GP?

57:11
Wow, that's a great question. You know, I haven't seen that in my practice. And, you know, I, I guess I will say that I had not seen that that's not something I've typically done. And you know, but I think theoretically, it makes sense. You know, I'm glad you brought up that question, something that I'm gonna look more into, I haven't been making choices of GP i There's no formal recommendations to pick GP over sofosbuvir. And the dip is sphere, if someone has a history of drug use, so that hasn't sort of been studied. But you know, I think most of the times these decisions are made based on the payer. And I don't think we have I think it'd be hard to make an argument to use another agent because of that, just from a from a logistics standpoint of getting it paid for. But it's a great point, it's something I look into more and have not treated based on that.

58:05
Thank you. Final question is whether you order HIV and the hep panel at the same time, and if the patient did have both HIV and Hep C, would you refer on to a specialist or cannabis patient be treated in a primary care setting?

58:18
Yeah, great question. So I order them both at the same time. I'm a hepatologist. So I'm not an HIV provider. So it's kind of I think it's a it's a kind of a cop out answer. But, you know, it depends on what your practice is set up, as I think the best care. You know, I know a lot of primary care providers are also the HIV providers. So in those cases, if you're the HIV provider, I think absolutely, absolutely, you should treat the Hep C to, since I don't treat HIV because I'm

not infectious disease, I will usually get them started on HIV therapy and get them tolerating the regimen with working closely with the ID doc to start their Hep C regimen at the same time. It's nice, you know, if you make both diagnoses at the same time, if you're if you're the one person that's doing both, that's great, that's easy, but I always will contact it the HIV provider and say, Hey, I'm looking to use these drugs. So as you're planning your HIV regimen, you know, these ones would work better, just so you don't run into any issues. And, and remember, you know, Hep C therapy is short and HIV therapy is long. So if you're going to pick an awkward regimen, you pick the awkward Hep C regimen, not the awkward HIV regimen because they're going to be on that for long periods of times.

59:32
So we're, we're actually just over time, so really want to thank you so much, Dr. Aronsohn for the presentation.

[End Transcript]