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Rethinking Disease Monitoring in Primary Biliary Cholangitis

Announcer:
You're listening to *GI Insights* on ReachMD, and this episode is sponsored by Ipsen Biopharmaceuticals, Inc. Here's your host, Dr. Alexandria May.

Dr. May:
This is *GI Insights* on ReachMD and I'm Dr. Alexandria May. Today, we'll be examining the intersection of biomarkers and non-invasive tools for monitoring disease progression in primary biliary cholangitis, or PBC for short. And joining me in this conversation is Dr. Vinod Rustgi, who's a Distinguished Professor of Medicine and the Associate Program Director for the Gastroenterology Fellowship at Rutgers Health Robert Wood Johnson Medical School in New Jersey.

Dr. Rustgi, thanks for being here today.

Dr. Rustgi:
My pleasure.

Dr. May:
Well, let's dive right in, Dr. Rustgi. When it comes to disease progression in PBC, what's the role of traditional biochemical markers like alkaline phosphatase and bilirubin in predicting long-term outcomes?

Dr. Rustgi:
What we've used over the years is alkaline phosphatase primarily. It's a measure that we use to monitor therapy and progression of disease. There are two, formulae—the UK PBC scale and also the global PBC scale—that have been very helpful in prognosticating which patients are going to run into trouble, and they use the variables of age, bilirubin, alkaline phosphatase, albumin, and platelets.

So those are things that I think people should be aware of. It's hard to carry around a lot of this in your head, so I will recommend an app called Hep Calc: H-E-P-C-A-L-C. And for all things hepatology, it's very useful, particularly for PBC, because rather than having to remember these variables, these are ordinary blood tests, and you can put in values and it'll help you assess who's going to run into trouble and what their future holds for them.

Dr. May:
Now, even with those markers available, how has our approach evolved from relying on individual values to taking a more composite, longitudinal view of disease activity?

Dr. Rustgi:
I think that's where the UK PBC score and the global PBC score are very helpful, along with things like the PBC 40 questionnaire, because, this is a very slowly progressive disease. Until the bilirubin starts to climb, it may last for decades. And so the things that bother people are their quality-of-life issues, so fatigue symptoms, their mental status, emotional status, and also how much they're itching are things that are captured by the PBC 40 questionnaire.

So I think in the totality of things, looking at the blood tests that we just mentioned and also this questionnaire is something that, on a periodic level—if not every time—you should check on a patient that you're following in clinic.

Dr. May:
And building on that, where does risk stratification fit into this evolving framework, and how do you use it to identify patients who may be at higher risk of progression?

Dr. Rustgi:
The goal of therapy is really to have, of course, medications that are free of side effects that patients can tolerate—adherence is easy, they're not difficult for the patient to carry forth with—because this is obviously a chronic therapy, a long-term therapy.

People should be monitoring the alkaline phosphatase. And, by the way, the lower the level, the better down into the normal range is the desired. But most studies look at bringing it down to at least 1.5 times the upper limit of normal, roughly around 200 IUs per milliliter. This is the goal. Now, if that isn't achieved, then you have to look at, perhaps, second-line therapies.

Those non-responders to URSO, of whom there are many, are people that we do want to monitor more closely, perhaps every three months. If somebody is fairly stable on URSO, then they should just be followed every six months or so.

Dr. May:
For those just tuning in, you're listening to *GI Insights* on ReachMD, and this episode is sponsored by Ipsen Biopharmaceuticals Incorporated. I'm Dr. Alexandria May, and today I am speaking with Dr. Vinod Rustgi about how we can track disease progression in primary biliary cholangitis.

So, Dr. Rustgi, I'd like to zero in on transient elastography. How is this non-invasive technique changing the way you assess fibrosis and disease trajectory in PBC, particularly as a compliment to traditional approaches?

Dr. Rustgi:
So fibroscan and transient elastography among other technologies have become sort of an extension of the physical exam for a hepatologist. For those of you who are familiar with it, obviously, it's a daily tool. For those who perhaps don't have access to it, it is a method of looking at both the fat content of the liver, as well as the amount of scarring, or the stiffness of the liver.

The stiffness is actually expressed in kilopascal units, and a value of less than eight kilopascals is a good prognostic sign in primary biliary cholangitis. When the values get higher—particularly over a value of 14—that's when it's commensurate with cirrhosis, and those are the patients that you want to be especially careful of.

In between, you have some indeterminate values, and F2 and F3 are sometimes hard to differentiate, but less than eight kilopascals is a very good prognostic sign.

Dr. May:
Now, when you're integrating biochemical markers with tools like elastography, what's your approach when the data don't align?

Dr. Rustgi:
When they don't align, and that can happen, you really do have to assess whether the study is a good study, meaning that the fibroscan is something that not only gives you the value of the steatosis and of fibrosis, but there is a value given on the report called the IQR median. It doesn't always get reported out, but if you look at the original report, it should be there.

That is a measure of the statistical dispersion of the signals you're getting. There are 10 values that are average to get us the final numbers, and if those are less than 15 percent, then that means the data are very good—that they're reproducible. And if they're more than that—the manufacturer actually allows up to 30 percent—the wider the data, that means the less reproducible it is. If it's a good study and there's still discordance such as a low kilopascal value but a patient who has thrombocytopenia or other signs of portal hypertension, then you know that there's something amiss. More concerning is when a patient has indeterminate values, and yet you're seeing things that maybe are more concerning, such as, again, a low albumin or a high bilirubin.

Those are patients where sometimes you may have to do a liver biopsy for clarity, especially if you're considering adding second-line therapy.

Dr. May:
Before we come to the end of our program, Dr. Rustgi, let's look at this from a practical standpoint. How do you incorporate these monitoring strategies into routine care, and how does this help you identify patients who may need closer follow up or treatment adjustments?

Dr. Rustgi:
So, again, the alkaline phosphatase is probably the most important value to follow, as long as the bilirubin is within the range of normal and even the low range of normal. If somebody has prognostic factors that you worry about—it's a diagnosis of somebody who's less than 45 years of age, somebody whose alkaline phosphatase stays above the 1.5 times the upper limit of normal on URSO, and even a mild elevation in total bilirubin, and greater than two times the upper limit of normal in a bilirubin is a value that's greater than two

milligrams per deciliter—those are the patients you want to worry about. And those are the patients that you should be following every three months. If they're stable on URSO alone, then those patients can be seen every six months.

There is a role for second-line therapy in those patients that we just mentioned that are more worrisome, and those include the PPAR agonists that we have available to us.

Dr. May:
With those important insights in mind, I want to thank my guest, Dr. Vinod Rustgi, for joining me to discuss the role of biomarkers and non-invasive tools in monitoring PBC progression. Dr. Rustgi, it was great having you on the program.

Dr. Rustgi:
Well, thank you. It was my pleasure.

Announcer:
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