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Evaluating Biochemical Response 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. Steve Jackson.

Dr. Jackson:
This is *GI Insights* on ReachMD, and I'm Dr. Steve Jackson. Joining me to discuss biochemical response in primary biliary cholangitis, or PBC for short, and the role it plays in managing long-term disease risk is Dr. Alan Bonder. He's an Associate Professor of Medicine and the Medical Director of Liver Transplant at Beth Israel Deaconess Medical Center in Boston.

Dr. Bonder, thanks for being here today.

Dr. Bonder:
Thank you, Dr. Jackson. It's a pleasure to be with you.

Dr. Jackson:
Well, let's start with some background, Dr. Bonder. Can you outline the current management approach for PBC and the role of ursodeoxycholic acid as first-line therapy?

Dr. Bonder:
Let's just call it urso, or UDCA. So the most important thing is that UDCA is currently the only first-line therapy approved for PBC. And this is based on studies from the late nineties from Poupon in France showing that patients who got treated with UDCA improved cholestasis—which is their liver function test—they slowed disease progression, improved their stage of fibrosis, and actually reduced their mortality or the need for liver transplantation.

So once we diagnose the patient with PBC, the soonest possible you can get those patients on UDCA, the better for this patient from a response perspective.

Dr. Jackson:
Now, the American Association for the Study of Liver Diseases, or AASLD, recommends assessing biochemical response to UDCA after roughly 12 months of therapy with markers like alkaline phosphatase, also known as ALP, and total bilirubin helping to estimate long-term risk. How do clinicians use those markers in practice to determine whether treatment is achieving an adequate response?

Dr. Bonder:
I think we need to start first, Dr. Jackson, with the definition of biochemical response. In a patient who is diagnosed with PBC, and you start them on UDCA, you measure the alkaline phosphatase, or the ALP. And if that alkaline phosphatase does not go below a certain threshold after 12 months, then the patient is labeled as a non-responder.

On top of the ALP and total bilirubin, it's really important to understand that we use another marker of disease activity, such as the liver stiffness from the elastography. So those three markers are kind of the key markers that tell us if the patient is a responder or a non-responder. So if the patient basically does not go through on a certain threshold, then we start thinking about, what other options does that patient need to get into remission or to get to a normal liver function test so they can have a better outcome?

Dr. Jackson:
I'd like to take a closer look at ALP for a moment. What does persistent elevation tell us about ongoing disease activity in PBC?

Dr. Bonder:
So this is one of the most important biochemical markers, telling us the story of first response. If the alkaline phosphatase does not really improve with first-line therapy, then this is when we start thinking about adding a second-line therapy for non-responders. So I think alkaline phosphatase, up to today, is one of the key drivers for looking at responders versus non-responders and getting patients into newly approved medications.

Dr. Jackson:
For those just tuning in, you're listening to *GI Insights* on ReachMD, and this episode is sponsored by Ipsen Biopharmaceuticals, Inc. I'm Dr. Steve Jackson, and I'm speaking with Dr. Alan Bonder about evaluating treatment response in primary biliary cholangitis.

So, Dr. Bonder, even with appropriate treatment, the AASLD notes that roughly 40 percent of patients with PBC may have an incomplete biochemical response to UDCA after about a year of therapy. What does the evidence tell us about these patients, and why is it so important to recognize incomplete response early?

Dr. Bonder:
This is one of the key features of therapy in patients with PBC, I think. As you mentioned, we wait for 12 months to assess response. And if the ALK PHOS or ALP is not below a certain threshold, we start thinking about getting those patients into second-line therapies. And, currently, we have two new approved second-line therapies that have been shown in recent studies to get those patients back to below that threshold, so they can actually be considered responders. So recognizing this incomplete response will basically help us to identify what patients need to be on a second-line therapy.

Dr. Jackson:
And when clinicians see persistent elevation in markers like ALP despite treatment, how do they determine when further evaluation or adjustments to management may be warranted?

Dr. Bonder:
This is one of the key features of PBC. There's a lot of different issues why a patient's alkaline phosphatase will not go back to normal. For example, one of the main concerns that I have personally in clinics is UDCA is a weight-based therapy, and with the metabolic, epidemic and rates of obesity that we have in this country, we are seeing a lot of underdosed patients.

So if a patient is properly dosed at 13 to 15 milligrams per kilogram per body weight, then we might not see a complete response. The other part is that we do have patients who are intolerable to UDCA, so there are some side effects. They are very unusual, but GI distress, thinning of the hair, and then severe itching at the time of starting those medications can make patients very intolerable. And sometimes, as we mentioned before, 30 to 40 percent of patients who are on this first-line therapy don't really achieve biochemical response.

So, in those cases, with the new development of new medications, we can basically use those new tools to help get this patient into biochemical response with the new second-line therapies.

Dr. Jackson:
Before we wrap up, Dr. Bonder, let's think big picture for a moment. Why is it so important for clinicians to continue monitoring biochemical response and avoid therapeutic inertia in the management of chronic conditions like PBC?

Dr. Bonder:
I think this is the most important feature in patients with PBC. So looking at response based on your alkaline phosphatase is one of the key features to look for in terms of identifying patients who need only a first-line therapy or patients who will need a second-line therapy —or the newly approved medications—so we can help them get them back to a complete biochemical response.

Dr. Jackson:
With those important insights in mind, I want to thank my guest, Dr. Alan Bonder, for helping us better understand how treatment response is monitored in primary biliary cholangitis. Dr. Bonder, it was great having you on the program.

Dr. Bonder:
Thank you so much for having me, Dr. Jackson. I hope you get to enjoy the podcast.

Announcer:
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