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PBC Target Practice: Normalization Is the New Norm

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Kowdley:
Hi, this is CME on ReachMD, and I'm Dr. Kris Kowdley, Director at Liver Institute Northwest and Professor at Elson S. Floyd College of Medicine Washington State University. In this brief discussion, I'll discuss consideration for assessing response to first-line therapy in PBC.

Here are some of the topics that we'll cover: assessing biochemical treatment targets for disease activity and response to first-line therapy, defining what is a treatment response, and focusing on some of the emerging data suggesting that we should really be opting to maintain bilirubin less than 0.6 times upper limit of normal and strive for normal alkaline phosphatase.

So it's important to just take a minute and discuss risk and stage in PBC. So assessment of stage, of course, can be done via liver biopsy or transient elastography or MR elastography. And there, what we're really doing is assessing where the patient is at now. Risk assessment is really the risk of the patient developing future complications down the road.

And so a variety of prognostic models have been developed, and they have helped us understand that the alkaline phosphatase and bilirubin level after a year or at least 6 months of therapy with ursodeoxycholic acid, which is our first-line therapy, can help determine prognosis over the long term. And so this has led to using alkaline phosphatase and bilirubin as surrogate endpoints to predict clinical outcomes. And based on this, several clinical trials have been constructed that have aimed at trying to evaluate the patient's response to therapy with second-line treatment as the rate at which patients achieved an alkaline phosphatase less than 1.67 times upper limit of normal and maintained a normal bilirubin level with at least a 15% reduction.

So several clinical trials have used this composite endpoint as a guide to determine whether patients are likely to have a better outcome down the road if they respond to these second-line treatments and consider second-line treatment for patients who meet these criteria.

So what is the reason for this? As I mentioned, it is clear that patients with elevated alkaline phosphatase that is above 1.67 or above twice upper limit of normal, or even 1.5 times the upper limit of normal, are at increased risk down the road, and sometimes years down the road, for needing a liver transplantation or having a liver-related serious adverse event such as variceal bleeding, jaundice, etc.

So now that we have a number of approved therapies for second-line treatment, it is important for us to be able to monitor patients after they've completed at least 6 months and likely 1 year of urso therapy to determine what is the need for that patient to need second-line therapy.

It's also important to take into account the disease stage, either by transient elastography, where more than 10 kPa is associated with an increased risk of complications and would be associated with a higher rate of advanced fibrosis. So in the clinic, we use a combination of disease stage and the alkaline phosphatase and bilirubin at the end of some period of treatment with urso to determine

whether the patient is at risk for further complications and whether they should be considered for second-line therapy.

Now, more recent data and emerging data has shown us that any elevation of alkaline phosphatase is associated with an increased risk of adverse liver events. And independent of that, patients who have advanced stage also, of course, are at increased risk for adverse liver events. Furthermore, a bilirubin of 0.6 times upper limit of normal, or 0.6 mg/dL, which would be associated with one being the upper limit of normal, is associated with a higher risk of adverse events, where patients who maintain a bilirubin less than 0.6 times upper limit of normal have better outcomes. So as our treatment paradigms are gradually shifting and we want to achieve the best possible outcomes for our patients, our goal is increasingly focused on lowering the alkaline phosphatase as low as possible and trying to achieve a bilirubin to less than 0.6 times upper limit of normal.

Well, unfortunately our time is up. Thanks for listening to this mini lecture.

Announcer:_
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