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Advances in the Treatment of Overt Hepatic Encephalopathy: What's in the Pipeline?

Announcer:
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Dr. Reau:
This is CE on ReachMD, and I'm Dr. Nancy Reau. Here with me today is Dr. Arun Jesudian.

Arun, what's in the pipeline for treating overt hepatic encephalopathy?

Dr. Jesudian:
Yes, thanks for the question, Nancy. There are therapies being studied that might improve how we take care of these patients. So, for example, could we prevent the first episode of hepatic encephalopathy in patients with cirrhosis?

So we know that microbial dysbiosis in cirrhosis is associated with altered bile acids, and rifaximin is being studied in a newer preparation, the SSD—or soluble solid dispersion—preparation that was formulated specifically to increase water solubility in the GI tract of the rifaximin molecule, and also minimize systemic exposure, as is the case with the current version of rifaximin. And this is particularly important in patients with low bile flow, like our patients with advanced cirrhosis.

And so this preparation is being studied in patients with cirrhosis who have not yet had overt hepatic encephalopathy to see if we can prevent them from having that first episode of overt hepatic encephalopathy and potentially other complications of cirrhosis, because we know that microbial dysbiosis is so important in the pathophysiology of many complications of cirrhosis. So that's one exciting study that's ongoing, and we should be hearing those results soon.

Dr. Reau:
That is really exciting. Now, in our pool of patients that have cirrhosis, many of which have compensated or asymptomatic cirrhosis, some are going to be a little higher risk for decompensation with that first episode of HE, and I think that the RED-C trial pulled a little bit of that in.

So some of the criteria to be a participant in that study included signs of, I think, portal hypertension, right? So that you can take the messaging away from the RED-C trial enrollment and also look at the patient sitting in front of you.

Can you review a little bit of just the very general criteria to participate in RED-C?

Dr. Jesudian:
Yes. These were patients who not only had cirrhosis but they clearly had clinically significant portal hypertension in that they had to have medically controlled ascites. So they were patients who had demonstrated that their portal hypertension was severe enough to cause ascites, but they weren't a patient who was very decompensated. Those patients probably would be difficult to study for this

indication, which is prevention of that first episode of overt hepatic encephalopathy.

So medically controlled ascites, and I think what that means for us in practice is that certain patients with cirrhosis don't have any portal hypertension, and certain patients have really severe portal hypertension, refractory ascites, and hepatorenal syndrome, and they really need a transplant more than anything.

But there are these patients who, just as you mentioned, are at such high risk of developing that first episode of overt hepatic encephalopathy, and I think that's who this trial tried to enroll and focus on.

Dr. Reau:
Yeah, so preventative strategies are really important, but we also know we have some patients with encephalopathy who are difficult to control despite using first-line therapy with combination lactulose and rifaximin, so not necessarily in clinical trials. But what are some of the things that you try when you have a patient where standard of care just isn't quite enough?

Dr. Jesudian:
Yes, so we do have some third-line therapies that you could consider. So zinc is one of those. Many of these patients can be deficient in zinc, or even if they're not, zinc is thought to decrease some of the ammonia neurotoxicity. We could also potentially use ammonia scavengers, like those used for urea cycle disorders, to try and decrease the ammonia in the body in general. We've talked about increasing protein intake. And you could also look for spontaneous portosystemic shunts if the patient has those, to close those in certain situations.

Dr. Reau:
If you take one thing away, be aware of treatment options in the pipeline. Every step towards addressing unmet needs counts, and this was one of them.

Thanks so much, and we'll see you next time.

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