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Advances in the Treatment of Hepatic Encephalopathy

Announcer:

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Dr. Brown:

This is CE on ReachMD, and I'm Dr. Robert Brown from Weill Cornell in New York. Here with me today is Dr. Steven Flamm from Rush University in Chicago.

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

Dr. Flamm:

Bob, that's an excellent question, and one that's very important for providers who care for patients with cirrhosis to know the background in. Why is it important? Because the therapies we have now for encephalopathy, Bob, are not ideal. Lactulose, for instance, has a lot of side effects. It has very poor tolerability. We don't have a regimen that works for everybody. We don't have regimens that are known to be effective in patients with minimal hepatic encephalopathy. We don't yet know if a medicine can prevent a first bout of encephalopathy. Rifaximin has been shown to prevent recurrent encephalopathy, but what about the first bout?

There are trials ongoing now with various different agents that are looking to address these unmet needs. There is one gigantic trial that providers should be aware of called the RED-C trial. This is a trial where patients have advanced liver disease and borderline decompensated disease. They have medically controlled ascites, but they've not had any bouts of encephalopathy. And this large trial is randomizing patients to receive rifaximin versus placebo to see if an initial bout of encephalopathy can be prevented. This study has been fully enrolled, and hopefully within the next year or so, we'll start to get top-line data in to see if we might have a product that prevents the first bout of encephalopathy.

Now, there is a new second-generation rifaximin called SSD. It's a different formulation of the product with immediate release. And hopefully that drug will also show high efficacy in this very, very important medical problem that patients with cirrhosis experience.

Bob, what about any new medicines that you're aware of that are in the pipeline?

Dr. Brown:

Well, I think we're all awaiting the data from RED-C, as well as seeing whether the novel formulation of rifaximin, SSD, will improve the results we've seen with rifaximin, which obviously was the first major step forward in HE since we started using lactulose.

I've been intrigued by—we know that the fecal microbiome plays a key role in HE, and there's been some really intriguing data on the use of fecal microbiota transplantation to change the microbiota. And you can imagine we could put in less ammonia-producing bacteria, and perhaps that would make a difference. So obviously relatively easy to do, but likely would need to be repetitive.

And then obviously we want to use disease-modulating agents in the future that will lower HE, improve liver function, and decrease portal hypertension. Some of those, I think, like FGF21 are intriguing, but we'll need more data. I think the ability to change the overall condition of the liver, particularly in patients with metabolic-associated steatotic liver disease, may be there because they have a fatty component as well as a fibrotic component. Perhaps that would be there.

We'll see what happens with GLP-1s, but the loss of muscle mass with GLP-1s may end up being a problem with HE. And as we see more patients with cirrhosis on GLP-1s, that's something we're going to have to take into consideration.

So I think there's a lot of exciting things out there, but we still got a lot of things to do.

Dr. Flamm:

We do, Bob. And a lot of work to be done in this field, but fortunately, that work is ongoing.

Dr. Brown:

Yep, I think it's better to have encouraging signs than no signs at all. So be sure to keep an eye on the emerging data. And thank you for listening.

Announcer:

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