Transcript Details

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Building Bridges, Closing Gaps in NASH Care: The Pivotal Role of Gastroenterologists

Announcer:
Welcome to CME on ReachMD. This activity, titled “Building Bridges, Closing Gaps in NASH Care: The Pivotal Role of Gastroenterologists” is provided by Prova Education.

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Dr. Brown:
Welcome. This is CME on ReachMD, and I'm Dr. Kimberly Brown. Today I will be highlighting the key messages and clinical data presented at a satellite symposium by Prova Education at ACG [American College of Gastroenterology] 2023 in Vancouver. This presentation focused on nonalcoholic steatohepatitis, or NASH, and was entitled “Building Bridges, Closing Gaps in NASH Care: The Pivotal Role of Gastroenterologists.” I presented at this symposium along with my esteemed colleagues Dr. Alina Allen and Dr. Mazen Noureddin.

So the global prevalence of NAFLD [nonalcoholic fatty liver disease] worldwide is about 30%. This is very similar to what we see here in North America. In the red circle, you see about 31%. This is a bit higher than in Western Europe, which is about 25%.

The prevalence of NASH, of course, is somewhat less, NASH being the inflammatory component of NAFLD. Worldwide, about 5.3% of patients are expected to have NASH. In North America, it's about 5%. But again, the highest is where we see it in Latin America; about 7% of patients have NASH, which is the component of NAFLD that progresses to fibrosis and further damage in the liver.

The problem that we see is that it's only going to get worse. In the United States, NAFLD is projected to increase about 21% from 2015 to 2030, and NASH in the US is projected to increase 63%.

So where are our patients with NAFLD? Well, typically, these are patients who have obesity, they have diabetes, they may have metabolic syndrome. And so when we look for them, we see them in many of our clinics, primary care clinics, in our endocrinology clinics, but also in our gastroenterology clinics. And it's important to take action because, as I stated before, NASH is a progressive disease.

So if we start with the patients who have NAFLD, and again, we talked about 30% of the people in the United States expected to have NAFLD, about a quarter of those will progress to develop a worse form, which would be additional fibrosis; that would be considered NASH. And of those patients, that is a risk factor for developing advanced fibrosis or cirrhosis, which would be F4. And once a patient has cirrhosis, they then become at risk of more advanced complications, such as liver cancer, liver failure, or even liver transplantation.

There are care pathways that have been designed to try to assess the enormous number of patients that have or potentially have NAFLD. So we see here, the care pathway that has been very nicely designed, looking at the steps that we can take both for identification, as well as testing, as well as further testing to try to stratify patients into low, intermediate, or high risk, such that we know how best to manage those individuals. And we'll go through each of those steps.

Step 1 is really to identify patients at risk for clinically significant fibrosis. We need to identify clinical risk factors for NAFLD, so those patients who are obese particularly those patients who have diabetes, but also those who have additional metabolic disease, such as hypertension or dyslipidemia or the configuration or the constellation of symptoms that we call metabolic syndrome. Patient presentation is often a clue as well. Does the patient have elevated liver tests? Although it is important to note that not all patients with NAFLD present with elevations in AST and ALT. Sometimes we'll find these patients with imaging. They've had imaging of the abdomen for

another reason and we find steatosis, and those patients are then identified at risk for fibrosis.

Step 2, we of course need to conduct standard history and blood tests to obtain some of the key measures we can use to assess our patients. Screening adult patients for the amount of alcohol that they use. Alcohol looks very similar to NAFLD under the microscope. Alcohol intake is very important. Traditionally, it is assumed that patients have significant increased risk if they drink more than 14 drinks if they're a woman, per week, or 21 drinks for a man, but the amount of alcohol that patients take is very important, because patients may have obesity and other risk factors in addition to alcohol use, and all of this plays an important role in our assessment of patients. Basic laboratory testing such as aminotransferases and CBC [complete blood count] should be done. Patients should have other forms of chronic liver disease excluded, and they should be evaluated for liver masses. If we're seeing someone for the first time, we need to screen them for malignancy as well.

Step 3 is to progress to conducting some kind of noninvasive test to look for liver fibrosis. And the easiest and the simplest method that we can use is what's called the FIB-4. So FIB-4 is really calculated from 4 very easy to obtain variables: the age of the patient, the AST, the platelet count, and the ALT. These are commonly found in the clinical medical record or can be obtained when you see a patient. And patients can be risk stratified using the FIB-4, looking for clinically significant fibrosis or damage in the liver.

So once you know the FIB-4 score, what do you do next? Well, if a patient has a score less than 1.3, this is low risk. It really excludes advanced fibrosis, and no further evaluation is needed. But it is important that we continue to monitor that patient over time and repeat the FIB-4 in 2 to 3 years. In patients who have a FIB-4 score greater than 2.67, this is a patient with a very high risk for advanced fibrosis, and that patient needs to be referred to a hepatologist. And then those patients who have an intermediate score, the next step is really to do a secondary noninvasive test, typically a liver stiffness measurement, and if one is concerned or if one doesn't have that available to them, that would be when you might consider a liver biopsy, MR elastography, or another evaluation to try to get a secondary assessment to best risk stratify your patient.

So how do we obtain a liver stiffness measurement? Well, the FibroScan or elastography is now widely used across the United States. This methodology uses a shear wave which is introduced through the skin, travels through the liver, and then is retrieved back to the transducer, and it gives us an idea of the stiffness or the pliability of the liver. So a liver stiffness measurement which is denoted as kPa less than 8, that patient is really at low risk for significant fibrosis. We have liver stiffness measures greater than or equal to 12; that would be a patient likely to have very significant fibrosis. And then of course, we have those patients who land between 8 and 12. Those are patients who have intermediate risk, likely have stage 2 or above fibrosis. But again, these measurements can be very, very helpful in trying to risk stratify this large group of patients.

For those just joining, you're listening to CME on ReachMD. I'm Dr. Kimberly Brown, and today, we're discussing NASH and the role of gastroenterologists.

So we know weight loss can work. So if you look at this study, these were patients who had biopsies before and after what we would consider lifestyle intervention to promote weight loss. And you can see that a significant percentage of patients were able to have improvements in their biopsies, both in terms of the steatosis or fat, the ballooning or inflammation, and even the resolution of the features that we call NASH, as well as fibrosis. But if you look at the top of the pyramid, it really required 10% or more weight loss to achieve that significant fibrosis regression. And less than 10% of patients were able to achieve this in the year that they were undergoing lifestyle intervention. So we know it works, but it is very difficult for patients to achieve.

So do we have any medications right now that we can use? The answer is no. The FDA has determined that there are very strict endpoints for the approval of medications that will in the future hopefully be used for NASH. So if you look at the efficacy endpoints that have been used in the clinical trials, either the phase 2B or 3 trials, one has to see either NASH resolution, which is defined as the resolution of steatohepatitis on the overall histopathologic reading, in addition to no worsening of fibrosis. So you have to have NASH resolution with no worsening of fibrosis. Or the secondary endpoint can be fibrosis improvement, which is improvement of 1 or more fibrosis stages with no worsening in steatohepatitis. So those are the endpoints that the FDA has given us for our clinical trials.

So let's go through a few of the clinical trials of the medications that I think are the closest to being approved. The first we'll discuss is resmetirom. And this was a phase 3 trial called the MAESTRO-NASH trial. The endpoints, again, were a NASH resolution and fibrosis improvement. And what this study showed is that they achieved both. So when one looks at the results for NASH resolution, both the 80-mg as well as the 100-mg doses of resmetirom achieved NASH resolution, again, significant as compared to placebo. But similarly, improvement in fibrosis was seen as well. You can see that, again, the 80- or the 100-mg, those patients achieved significant fibrosis improvement as compared with placebo. In addition, there appeared to be a favorable impact on the lipid profile in this patient population.

The next study looks at lanifibranor, which is a different medication which was used in the phase 2b study called the NATiVE3 study.

And when one looks again at those FDA endpoints, lanifibranor was given at an 800-mg as well as a 1200-mg dose. And when one looks at the results from the 1200-mg dose, one can see, again, resolution of NASH with no worsening fibrosis was significant. Resolution of NASH and improvement of fibrosis was seen as well. And improvement of fibrosis by at least 1 stage with no worsening of NASH was seen as well. So again, another promising therapy that may be available to us in the future.

And then the last study we'll look at is a medication that is currently available but not available for treatment of NASH. This is a phase 2 study looking at semaglutide at 72 weeks of treatment. And one can see in the various doses of semaglutide that was used – 0.1 mg, 0.2 mg, and 0.4 mg – that resolution of NASH with no worsening fibrosis, again, one of the FDA endpoints, was seen in the patient population who received semaglutide at the 0.4-mg dose. This study, however, did not show the secondary endpoint, which was improvement in fibrosis with no worsening of NASH; those were not significantly different from placebo. But again, further studies with this medication and others will be ongoing, and hopefully, these medications for use in our patients with NASH will be soon to come hopefully in 2024.

So in summary the noninvasive tests are available to really allow us to risk stratify this very large group of patients who have NAFLD and to identify those patients who likely have NASH, the inflammatory component, fibrosis, and more progressive disease. There are several options that are available today to manage patients, typically targeting weight loss, including lifestyle interventions as well as bariatric surgery. And what's exciting is that new drugs are currently in late-phase development, and hopefully, some will be available to us as early as 2024 in helping us manage our patient population with NASH.

That's all the time we have today, so I want to thank our audience for listening. It was great speaking with you today.

Announcer:
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