Transcript Details
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Managing Statin Intolerance: Practical Approaches and Emerging Non-Statin Options

Announcer:
You're listening to *Heart Matters* on ReachMD. On this episode, Dr. Matthew Sorrentino, a Professor of Medicine and Vice Chair for Clinical Operations in the Section of Cardiology at the University of Chicago Medicine. He'll discuss how to manage statin intolerance and utilize alternative lipid-lowering therapies. Here's Dr. Sorrentino now.

Dr. Sorrentino:
Statin tolerance usually means that a patient is having side effects that they believe are due to the statin. Fortunately, it's fairly uncommon. But there are some patients who just do not tolerate statins. So in terms of non-statin therapy, we always first want to look at why the patient is not tolerating the statin. Many patients will come to us and say, "Since I've been on the statin, I have cramps at night," or "My knee hurts," or they're having some side effects of the statin.

So before we completely abandon the statin subgroup, we look to see if there's a different statin that somebody may be able to tolerate. Three of the statins are metabolized by the same enzymatic system in the liver. These are lovastatin, simvastatin, and atorvastatin. And some patients may have muscle symptoms with that class of statins, but not with some of the others, such as pravastatin, pitavastatin, or rosuvastatin.

So our first step is alternate statins or even alternate dosing schedules where we'll dose every other day instead of every day and see if they will tolerate that. So let's say we've tried that. Let's say we've tried one or two alternative statins, and they're still all the same muscle aches. Let's say we've tried every other day statin dosing, and they're still having side effects. We have to abandon the class.

Then, there are really three other major classes that we use. The first are intestinal agents. The most common is a medication called ezetimibe. Ezetimibe does not get into the systemic circulation, so there are no muscle symptoms. The only trouble with that medication is it only lowers cholesterol about 15 to 20 percent, and we usually want a more robust LDL lowering, so it won't get to the target goal we want for many of our patients.

The next group of agents are PCSK9 inhibitors. These are agents that target a molecule that's involved in the LDL receptor and in cholesterol uptake at the liver. Very effective class of agents. They can lower LDL in the 50 to 60 percent range, and they have virtually no muscle side effects. The main PCSK9 inhibitors that we have are twice a month subcutaneous injection. So they're usually pretty easy to take, and we've got some really good secondary prevention trials showing that they reduce cardiovascular risk.

The newest agent is an agent called bempedoic acid, a medication that also works in the liver, works in cholesterol biosynthesis, works upstream from the statins, and has very little muscle uptake. And so it is being released as a statin alternative for patients who can't take a statin. They're not quite as effective as statins. They lower LDL in the 40 to 50 percent range, but they usually are better tolerated. And when you mix bempedoic acid with ezetimibe, you can get a good LDL lowering and usually no muscle problems.

The next area is looking at other lipid particles that we haven't targeted so far. I think the most interest is in lipoprotein (a) or Lp(a). Lp(a) is a variant of LDL. It's LDL with an extra protein attached to it. And at high levels, it is not only atherogenic, but it also causes thrombogenesis. It can cause heart attacks and strokes and other problems.

Up to now, we've had no effective medicines that lower lipoprotein (a), and so if patients have very high Lp(a), we try to target all the other risk factors. But there are two molecules that are near the time they should be coming on the market. They've pretty much finished up phase three trials. One of them is a small interfering RNA. The other is a ASO or an antisense oligonucleotide. And again, by giving

these as a subcutaneous injection, they can lower Lp(a) values as much as 80, 90, 95 percent. So they seem to be highly effective. And so far, at least in the data that we have, they seem to have very few side effects. We are expecting that these will be approved within the next year or so. So I think that'll be probably the biggest thing we'll see on the market—medications that target Lp(a).

Announcer:
That was Dr. Matthew Sorrentino talking about current and emerging non-statin therapies. To access this and other episodes in our series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!