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Target in Sight: Escalating Therapy to Reach LDL-C Goals

Announcer:
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Dr. Gluckman:
Welcome to CME on ReachMD. I'm Dr. Ty Gluckman.

Dr. Wadhera:
And I'm Dr. Rishi Wadhera.

Dr. Gluckman:
In this episode, we're going to talk about initial non-statin therapies for atherosclerotic cardiovascular disease risk reduction. And to be truthful, we are blessed to have a wide array of therapies that we can use that are not statins, that can be added on to maximally tolerated statin therapy to be able to further lower LDL cholesterol and in addition, reduce cardiovascular risk. The vast majority of these therapies work within the liver to ultimately lead to a decrease in LDL cholesterol levels. The one exception is ezetimibe that works within the intestines to inhibit the absorption of cholesterol in the body. But nonetheless, we have a wide array of therapies that are available.

We generally think about adding ezetimibe as our first non-statin therapy, principally because it's oral, it's well tolerated, it comes in a single dose, and it's able to achieve, on average, about 20 to 25% reduction in LDL cholesterol lowering on top of maximally tolerated statin therapy, and it's often our first go-to in this patient population.

But for individuals that have achieved treatment with maximally tolerated statin therapy, preferentially high-intensity statin therapy, like the patient did with our case, and we've added ezetimibe, and they still have room to move, particularly more pronounced room to move in terms of LDL cholesterol lowering, most often we will reach for the PCSK9 inhibitors, and in particular the PCSK9 inhibitor monoclonal antibodies, alirocumab and evolocumab. These are drugs that, on average, can achieve a 50 to 60% reduction in LDL cholesterol lowering on top of maximally tolerated statin therapy and other background lipid-lowering therapy. These are injectable drugs that are injected under the skin, either every other week or once a month, and have been associated with favorable cardiovascular outcomes trial data showing a significant reduction in adverse cardiovascular events.

I think this is well illustrated in the 2022 American College of Cardiology Expert Consensus Decision Pathway. And if you go back to our patient, a patient who has atherosclerotic cardiovascular disease at very high risk, that guidance document highlights that there are dual goals, both a 50% reduction in LDL cholesterol from baseline and getting their LDL cholesterol less than 55. We start with ideally high-intensity statin therapy, but on a backdrop of maximally tolerated statin therapy. This guidance document recommends that individuals consider ezetimibe and/or a PCSK9 inhibitor, all with a goal of trying to get their LDL cholesterol below that 55 mg/dL threshold. It's important to recheck their lipid panel 4 to 12 weeks thereafter to ensure that they've achieved that LDL cholesterol goal, and thereafter, you're surveying them every 3 to 12 months with a lipid panel, principally to ensure adherence.

Rishi, as we think about adding these non-statin therapies, are there access issues, other barriers that you can think about, particularly as it relates to the rural setting?

Dr. Wadhera:
Yeah, and it's a great question, Ty. I think with ezetimibe, it's a once-daily medication that's taken orally. So insofar as rural Americans face challenges accessing pharmacy or getting prescriptions for these important LDL-lowering medications, I don't view ezetimibe any differently from statin therapies. But I think it's important to remember that ezetimibe's LDL-lowering effect is more modest when compared to PCSK9 inhibitors. So in patients who need that extra LDL lowering, or more robust LDL lowering, we have to think about the PCSK9 inhibitors and how they may be difficult for patients who experience access issues, and in part because these are injectable medications. And so I think as clinicians, we just need to remember that patients that meet criteria for PCSK9 inhibitors may require X additional counseling or support to ensure that they take these medications the right way.

Dr. Gluckman:
I think well said. And I will just say, from my own experience over the years of the nearly the decade that these monoclonal antibodies, PCSK9 inhibitors, have been approved, we initially had a lot of challenges both in terms of getting access by authorization barriers and also affordability. That's gotten much, much better over time. So many patients who previously historically couldn't, can now access this both in urban and rural settings.

I love your insights, Rishi. Thanks so much for this discussion. Thanks everyone for listening.

Announcer:
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