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Personalizing LDL-C Treatment—Novel Options That Align With Patient Preferences

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 novel non-statin therapies for atherosclerotic cardiovascular risk reduction. And again, as I've shared previously, we have a wide array of therapies at our disposal to help in lowering LDL cholesterol. In terms of non-statin therapy, we've talked about ezetimibe and the PCSK9 inhibitor monoclonal antibodies, but there are two additional therapies that we have available as options to reach for. First is the drug inclisiran, which is a PCSK9 inhibitor, but it's a small interfering RNA molecule that actually is administered in health care settings. You have an initial dose up front, a second dose 90 days thereafter, and then you're dosed every 6 months in healthcare settings beyond that. On average, you get about a 50, or 5-0% reduction in LDL cholesterol. And obviously, there are pros and cons to every therapy that we have, but for someone who may be reticent to self-administer the drug, or have loved ones, neighbors, family that are helping in terms of the injecting, this may be an option for them overall.

At present time, we don't have cardiovascular outcomes trial data presented or published for inclisiran, and we eagerly await that data to help better round out our understanding of the effects of this drug.

The other option is bempedoic acid, which is an oral non-statin therapy. It works as what's referred to as an ATP-citrate lyase inhibitor, sort of thinking about this as working upstream through the statin pathway, but is not a statin, and on average, achieves lesser degrees of LDL cholesterol lowering, upwards of about 18 to 20% reduction in LDL cholesterol with a magnitude dependent upon whether someone's on background therapy with a statin or not. Obviously, an advantage afforded by this is its oral formulation overall. The limiting factor being that it achieves lesser degrees of LDL cholesterol lowering. But we do have favorable cardiovascular outcomes trial data actually in a trial that was dedicated to evaluating patients with stat intolerance, both in secondary prevention and primary prevention.

And so building off of this in 2022 the American College of Cardiology and its Expert Consensus Decision Pathway did create a space for the use of both bempedoic acid and/or inclisiran, essentially in our patient who is an adult with atherosclerotic cardiovascular disease at very high risk. The recommendation is to be on maximally tolerated, ideally high-intensity statin therapy to achieve a 50% reduction in LDL cholesterol and get their LDL less than 55. Beyond maximally tolerated statin therapy, would still consider ezetimibe and/or a PCSK9 inhibitor monoclonal antibody first, but in individuals who either can't access those therapies or fail to achieve their LDL

cholesterol goals, you may consider bempedoic acid, or inclisiran in this patient population.

Rishi, maybe you could just sort of speak to sort of how you may think about contextualizing the use of bempedoic acid and/or inclisiran, particularly in rural settings.

Dr. Wadhera:
Yeah, I think it's a great question, Ty. In terms of bempedoic acid, oral agent, so easier for patients to take as long as, again, they have access to a pharmacy and access to a provider that can provide them with prescriptions for these medications. And I think you've spoken to the fact that our repertoire of medications to target dyslipidemias has grown, and inclisiran is another great agent. I think one of the challenges with inclisiran is that it's an injectable, but it's an injectable that's administered, as you pointed out, first after 90 days and then in 6-month intervals. So although there may be upfront challenges, particularly for patients in rural settings who need this therapy in terms of teaching and counseling and coming into the office to get this medication, the intervals, the spaced-out intervals, I think, diminish access concerns, but something we do need to think about as our portfolio of lipid-lowering agents expands with these agents.

Dr. Gluckman:
Those are great points. I love them a lot. So this has been a great discussion, but unfortunately, our time is up. Thanks so much for listening.

Announcer:
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