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Prioritizing LDL-C Reduction for Established CVD Patients in Primary Care

Announcer:
Welcome to *Heart Matters* on ReachMD. This medical industry feature, titled "Prioritizing LDL-C Reduction for Established CVD Patients in Primary Care," is sponsored by Amgen. Here's your host, Dr. Mary Katherine Cheeley.

Dr. Cheeley:
This is *Heart Matters* on ReachMD, and I'm Dr. Mary Katherine Cheeley. Joining me today is Dr. Leah Cordovez to discuss how primary care physicians can lead the management of LDL-C in patients with established cardiovascular disease, or CVD for short. We'll examine how Repatha®, or evolocumab, can lower LDL-C to reduce the risk of MI, stroke, and coronary revascularization for these patients with established CVD.

Dr. Cordovez is a distinguished physician with triple board certification in Internal Medicine, Integrative Medicine, and Obesity Medicine. She's also a fellow of the American College of Physicians. In addition to her clinical practice, she also holds a Master of Healthcare Management. Dr. Cordovez, thank you so much for being here today.

Dr. Cordovez:
Thank you for having me, Dr. Cheeley. I'm delighted to be here and bring a little more attention to this topic.

Dr. Cheeley:
Before we begin, let's take a moment to review some important safety information about Repatha®.

Announcer:
Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to it. Serious hypersensitivity reactions including angioedema have occurred.

If signs or symptoms of serious hypersensitivity reactions occur, discontinue Repatha, treat according to standard of care, and monitor until resolved.

Dr. Cheeley:
We'll cover more important safety information later in the podcast too. But for now, Dr. Cordovez, let's jump in! Can you provide some insights into the current landscape of ASCVD management and how we're doing in terms of patient outcomes?

Dr. Cordovez:
Of course! So, over the years, the incidence of ASCVD hasn't improved at all; in fact, it's been on the rise.[1]

In 2019, there were approximately 2.8 million new ASCVD cases.[1] And, nearly half of all ASCVD patients are considered to be at very high risk for a cardiovascular event to occur.[2] These are patients who've already suffered multiple major ASCVD events, or those who've previously experienced a major ASCVD event and have additional high-risk factors, for example those who are 65 years or older, have diabetes, or have hypertension.[3,4] Therefore, they could've been more appropriately managed.

So what this tells us unfortunately, is that despite advances in treatment and updated guideline recommendations on risk factor modification,[3,4] ASCVD-related outcomes aren't declining because we haven't been doing as well at managing risk factors that lead to cardiovascular events in these patients.[1]

Dr. Cheeley:
So then what treatment strategies can primary care physicians use to improve clinical outcomes and reduce the risk of cardiovascular events, such as MI and stroke, in ASCVD patients?

Dr. Cordovez:
Well, from my perspective, lipid management is one of the most impactful and modifiable approaches for ASCVD patients to reduce their risk of cardiovascular events. It's more impactful than managing smoking, all psychological risk factors, abdominal obesity, hypertension, fruit and vegetable intake, exercise, diabetes, and alcohol.[5]

But sadly, we're still falling short. Despite years of having this data, patients may not be receiving appropriate treatment to reach the recommended LDL-C level by us, their primary care physicians or specialists. Even with treatment using a high-intensity statin and/or ezetimibe, 74 percent of very high-risk ASCVD patients in the U.S. haven't reached the recommendation by the American College of Cardiology's 2022 Expert Consensus Decision Pathway, also known as ECDP, of an LDL-C below 55 milligrams per deciliter.[2,4] So, it's clear we *need* to do better. Study after study has shown that lowering a patient's LDL-C reduces secondary cardiovascular events.[6]

So, whether you're a primary care physician or a cardiologist, there's room for improvement in managing lipid levels for our very high-risk ASCVD patients. We must help our patients who remain vulnerable because their LDL levels exceed the guideline or ECDP recommendations. Also, patients often visit their primary care physicians more frequently than specialists, and considering the potential wait times for specialist appointments, primary care physicians have a significant opportunity to directly treat at-risk ASCVD patients without needing the referral to the specialist in the first place.

Dr. Cheeley:
With this in mind, are there very high-risk ASCVD patients who may be under-recognized for the intensified LDL-C management needed to lower their cardiovascular event risk?

Dr. Cordovez:
In my experience, when a patient has a major cardiovascular event, they're closely managed by their healthcare providers and, generally, the patient and their loved ones are very motivated to do what's needed to recover.

While this patient does need close follow-up, patients who are *more* likely to fall through the cracks, and are also very high-risk, are many of those patients we see daily in our practice during routine visits. These patients may have had major cardiovascular events, such as a heart attack or stroke, at some point in their medical history, although not recently, and have other risk factors. Another very high-risk patient profile includes those who have evidence of atherosclerotic disease as demonstrated by a history of stable or unstable angina, peripheral artery disease, and/or percutaneous coronary intervention or coronary artery bypass graft, with other risk factors.[3]

Now, primary care physicians may have more patients who fit this profile and are undertreated for the recommended LDL-C level than they think. These patients also depend on us, their primary care providers, to manage their LDL-C, so it's important that we know which patients to monitor more closely.[7] And even if we're unable to reach the recommended LDL-C level with the highest-tolerated dose of a statin and/or ezetimibe, there's still more we can do.[3] We don't need to wait until an at-risk ASCVD patient is discharged from the hospital after a cardiovascular event to take action. We should immediately be doing everything possible to lower their LDL-C.[8]

Dr. Cheeley:
For those just tuning in, you're listening to ReachMD. I'm Dr. Mary Katherine Cheeley. Today, I have the pleasure of speaking with Dr. Leah Cordovez about LDL-C management, focusing on the use of Repatha in established CVD patients at high risk of secondary cardiovascular events, like MI or stroke.

So let's move onto strategy, Dr. Cordovez, how can we further lower LDL-C for patients who are unable to reach the ECDP recommendation on the highest-tolerated dose of statin and/or ezetimibe?

Dr. Cordovez:
So in addition to a statin, we can now add a PCSK9 inhibitor monoclonal antibody, like Repatha, for those patients. The "PCSK9" stands for proprotein convertase subtilisin/kexin type nine. It's administered as a subcutaneous injection of 140 milligrams every two weeks. Patients can administer the medication at home, which in my practice, many patients say is convenient for them.[9] In fact, in a study where patients received injection training from a healthcare professional, 94 percent of patients were successfully able to self-administer Repatha using the SureClick® Autoinjector.[10] Additionally, more than 80 percent of prescriptions for Repatha cost $50 or less for the patients using Commercial, Medicare, and Medicaid data.[11]

Dr. Cheeley:

Thank you for that overview. Now, if we zero in on this treatment option in particular, could you share with us the evidence that supports Repatha's clinical efficacy and safety?

Dr. Cordovez:
Absolutely. The FOURIER Cardiovascular Outcomes Trial was a double-blind, randomized, placebo-controlled, event-driven trial. It looked at over 27 thousand patients with established CVD and:

- an LDL-C of at least 70 milligrams per deciliter
- and/or non-HDL-C of at least 100 milligrams per deciliter,
- who remained at risk despite moderate or high-intensity statin.

Patients were randomly assigned one-to-one to receive either subcutaneous injections of Repatha or placebo, with both groups also taking a statin medication.[9] The median LDL-C at baseline was 92 milligrams per deciliter.[9,12] A secondary composite endpoint in the trial was the time to first cardiovascular-related death, heart attack, or stroke.[9]

Now if we turn our attention to the results, the FOURIER trial found that the addition of Repatha to statin treatment resulted in a 20 percent relative risk reduction of this composite endpoint in a median of 2.2 years in adult patients with established CVD as compared to placebo, and this benefit improved over time in the study. Note that these results were driven by a reduction in the risk of MI and stroke. The hazard ratio for CV death was 1.05 with a 95 percent confidence interval of 0.88 to 1.25.[9]

Additionally, treatment with Repatha lowered LDL-C by an average of 63 percent in 12 weeks.[9] And, 84 percent of patients taking Repatha achieved LDL levels below the recommended 55 milligrams per deciliter in just four weeks. Remember that patients were already on a stable dose of statin when the trial began, so these are the LDL-C reductions achieved by Repatha.[13] And so, Repatha can dramatically reduce LDL-C to help lower the risk of another MI.

In terms of safety, the FOURIER clinical trial followed patients for more than two years on average. The most common adverse events in the trial were diabetes, nasopharyngitis, and upper respiratory tract infection.[9]

Plus, a subsequent open-label extension of the study, called FOURIER-OLE, followed over 6,000 patients who participated in FOURIER. All patients were treated with Repatha, regardless of what treatment group they were originally randomized to in FOURIER. The median follow-up time for FOURIER-OLE was 5 years, and some patients were followed for up to 8.4 years across FOURIER and FOURIER-OLE. No new safety signals were found from treatment with Repatha. And of note, the incidence of serious adverse events didn't increase over time in the study.[14,15] Lastly, I also want to point out that the discontinuation rate due to adverse events by Repatha during the FOURIER-OLE trial was 0.1 percent.[15]

So, this clinical trial data on Repatha speaks to the opportunity for primary care providers to effectively help established CVD patients to lower their LDL-C.

Dr. Cheeley:
I appreciate that amazing perspective and your deep dive into the literature for us. However, can you speak to the patient safety of using Repatha to lower LDL-C below the guideline recommended level of 55 milligrams per deciliter for these very high-risk ASCVD patients?[4]

Dr. Cordovez:
Great question. Patients in the FOURIER-OLE trial that achieved very low LDL-C, at less than 20 milligrams per deciliter, had a similar incidence of serious adverse events as compared to those with higher LDL-C levels.[14]

Dr. Cheeley:
Thank you for explaining that. Now, as we discuss LDL-C reduction in the context of established CVD patients, this raises the question of whether there's data available on Repatha's impact on atherosclerotic plaque burden itself?

Dr. Cordovez:
I'm glad you asked that. In a prior study, called the Glagov Trial, the effect of Repatha on plaque was studied in 968 patients with coronary artery disease for 78 weeks using intravascular ultrasound. Atherosclerotic plaque burden was measured as percent atheroma volume, or PAV. In this double-blind study with one-to-one randomization, the patients treated with Repatha and statin not only showed a 61 percent greater reduction in LDL-C than those treated with statin alone, but also showed about a one percent greater reduction in PAV. And while it's great to understand the impact of Repatha on PAV, it's important to note that the GLAGOV trial was not designed to assess a correlation between a change in PAV and cardiovascular events using intravascular ultrasound.[16]

Dr. Cheeley:
Wonderful. And to wrap up our discussion today, Dr. Cordovez, what are some of the key lessons that you would like to emphasize for our listeners?

Dr. Cordovez:
So, I'd like to highlight this call to action for primary care physicians to really own the early management of these ASCVD patients with a prior history of a cardiovascular event. Because we know that by lowering their LDL-C, we can reduce the risk of future cardiovascular events, like MI and stroke.[17] For so long, we've had patients we wished we could do something more for, and now we finally can!

Primary care providers can feel confident in prescribing Repatha to patients who don't meet the guideline recommended LDL-C level with maximal statin and/or ezetimibe.[4,9] Additionally, Repatha has a demonstrated safety profile in over 27 thousand patients.[9]

Ultimately, primary care physicians have the power to reduce the risk of heart attack, stroke, and coronary revascularization for their patients with established CVD. Let's not wait for these patients to have another cardiovascular event—we can act now to reduce the risk for our patients and lead the way today.

Dr. Cheeley:
Those are some amazing takeaways for us to think about as we begin to wrap up today's program. Please stay tuned to hear some important safety information for Repatha.

Announcer:
Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to it. Serious hypersensitivity reactions including angioedema have occurred.

If signs or symptoms of serious hypersensitivity reactions occur, discontinue Repatha, treat according to standard of care, and monitor until resolved.

The most common adverse reactions in primary hyperlipidemia studies were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

And in the Cardiovascular Outcomes Trial, the most common adverse reactions were diabetes mellitus, nasopharyngitis, and upper respiratory tract infection.

As a human monoclonal antibody, there is potential for immunogenicity with Repatha.

For a copy of the full Prescribing Information for Repatha, please visit www. Repatha.com/PI or call 1 – 844 – REPATHA.

Dr. Cheeley:
For ReachMD, I'm Dr. Mary Katherine Cheeley. And I would like to extend a huge thank you to our guest for igniting momentum and encouraging primary care providers to take charge of LDL-C management in our at-risk ASCVD patients. Dr. Cordovez, it has been a pleasure speaking with you today.

Dr. Cordovez:
Thank you so much. It's been a pleasure to be here. I'm delighted to talk about it!

Announcer:
This medical industry feature was brought to you by Amgen. If you missed any part of this discussion, visit *Industry Features* on ReachMD.com, where you can Be Part of the Knowledge.

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