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Bridging the Gap: Lipid Management in ASCVD Patients with Diabetes to Reduce CV Risk

ReachMD Announcer:
You're listening to ReachMD. This medical industry feature, titled "Bridging the Gap: Lipid Management in ASCVD Patients with Diabetes to Reduce CV Risk," is sponsored by Amgen. This program is intended for US healthcare professionals, and the speakers have been compensated for participating in this presentation. And now, here's your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck. Joining me to discuss how we can utilize lipid management in type 2 diabetes with ASCVD patients to reduce their cardiovascular risk is Dr. Yehuda Handelsman. He serves as the Medical Director and Principal Investigator at the Metabolic Institute of America. He's also the Chair of the Scientific Advisory Board for the Diabetes, Cardiorenal, and Metabolic Institute. Dr. Handelsman, welcome to the program.

Dr. Handelsman:
Thank you, Dr. Turck. It's a pleasure to be here.

Dr. Turck:
So let's start with some background on LDL-C management in ASCVD patients with diabetes. What are the current gaps in care and their implications for patients?

Dr. Handelsman:
Cardiovascular diseases is a leading cause of serious complications in people with type 2 diabetes.[1] The INTERHEART study showed lipids are one of the most modifiable risk factors associated with MI.[2,3] This finding is further reinforced by data from statin trials, which demonstrate a linear correlation between LDL-C lowering and reduced cardiovascular events in patients with ASCVD.[4,5]

In statin trials, we saw for every incremental reduction in LDL-C, there's a proportional decrease in the risk of major cardiovascular outcomes.[4]

But unfortunately, despite this clear evidence, significant gaps in care remain. Among adults in a US cohort with ASCVD and type 2 diabetes, 79 percent failed to achieve LDL-C targets of less than 70 milligrams per deciliter.[6]

Together, these insights underscore the critical importance of aggressively targeting LDL-C to reduce risk of major adverse cardiovascular events, especially in high-risk ASCVD patients with diabetes.

Dr. Turck:
And with that background in mind, can you give us an example of a high-risk ASCVD patient with type 2 diabetes who might need additional intervention to lower their LDL-C and risk of a cardiovascular event?

Dr. Handelsman:
Absolutely. Our hypothetical patient today is Ritesh, a 63 years old Indian male with type 2 diabetes, hypertension, obesity, and metabolic syndrome. He also has a history of NSTEMI at age 56 and a family history of cardiovascular disease as his brother had an MI at 59. Despite being on 40 milligrams of atorvastatin daily, his LDL-C remains elevated at 98 milligrams per deciliter.

Given these details, Ritesh is the definition of a very high-risk patient. He has multiple overlapping risk factors, including type 2 diabetes and a history of ASCVD from his prior NSTEMI.[7] His South Asian ethnicity is also important to consider, as it's associated with an

increased susceptibility for diabetes and risk of cardiovascular disease.[8,9,10]

Now, Ritesh's LDL-C remains high at 98 milligrams per deciliter, placing him at significant risk of recurrent events. According to the ADA's 2024 guidelines, patients like Ritesh should have an LDL-C level of less than 55 milligrams per deciliter, with at least 50 percent reduction from baseline.[11] At his current level, Ritesh is far from meeting this target, and each day, his cardiovascular risk accumulates.[12]

Dr. Turck:
And focusing in on these more aggressive LDL-C targets, can you expand upon why they're so crucial?

Dr. Handelsman:

Certainly, and the evidence here is robust and consistent. We learned from the CTTC meta-analysis, which included data from multiple secondary prevention trials with statins, that there is a clear relationship between LDL-C lowering and reduction in CV events.[4]

So to further investigate this link, the FOURIER cardiovascular outcomes trial evaluated whether the addition of Repatha®, or evolocumab, injection to a statin would reduce major cardiovascular events compared to statins alone.[13] But before we dive into the FOURIER trial, let's discuss the Indications for Repatha.

ReachMD Announcer:

Repatha is indicated to reduce the risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) in adults with established cardiovascular disease.

Repatha is also indicated as an adjunct to diet, alone or in combination with other LDL-C-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia, or HeFH, to reduce LDL-C.

Now, let's review some Important Safety Information.

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

Dr. Handelsman:
With that information in mind, let's talk about the FOURIER trial.

This trial randomized over 27,000 patients with established cardiovascular disease and LDL-C greater than or equal to 70 milligrams per deciliter, and/or non-HDL-C greater than or equal to 100 milligrams per deciliter. At baseline, in FOURIER, the median LDL-C was 92 milligrams per deciliter, despite high- or moderate-intensity background lipid therapy. Patients were randomly assigned to receive Repatha or placebo.[13]

Now if we look at the results, the trial found that, when combined with statins, treatment with Repatha reduced the risk of the key secondary composite endpoint of time to first occurrence of cardiovascular death, MI, or stroke by 20 percent over a median of 2.2 years. The absolute risk reduction for the key secondary composite endpoint was 2 percent. Repatha also reduced the risk of the primary composite endpoint of time to first occurrence of cardiovascular death, MI, stroke, coronary revascularization, or hospitalization due to unstable angina by
15 percent.[13]

The observed hazard ratio for the primary endpoint was 0.85, with 95 percent confidence interval of 0.79 to 0.92. So this was robust and statistically significant. The observed hazard ratio for cardiovascular death was 1.05 with 95 percent confidence interval of 0.88 to 1.25. And the observed hazard ratio for hospitalizations due to unstable angina was 0.99 with 95 percent confidence interval of 0.82 to 1.18.[13]

Additionally, Repatha plus statin lowered LDL-C by a mean percent change of 63 percent at 12 weeks vs statins alone.[14]

Based on this evidence, the FOURIER trial specifically demonstrated the benefits of LDL-C lowering in a high-risk established CVD population.[14]

In a prespecified analysis of the FOURIER trial, 40 percent of the 27,564 enrolled patients had diabetes, as identified through medical history, clinical adjudication, or glycemic criteria. Among the 60 percent without diabetes, 38 percent of the total trial population had prediabetes, and 22 percent had normoglycemia.[15]

In a post-hoc efficacy analysis from FOURIER, LDL-C decreased by 57 percent in patients with diabetes and 60 percent in those

without diabetes compared to placebo at 48 weeks.[15]

When looking at the 5-point MACE, Repatha led to a 2.7 percent absolute risk reduction in the diabetes group, with hazard ratio of 0.83, reinforcing the cardiovascular benefit in this high-risk population.[15]

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Yehuda Handelsman about the role of LDL-C management in reducing the risk of cardiovascular events among diabetes patients with ASCVD.

So now that we've examined the gaps in care ASCVD patients with diabetes and some data for Repatha, let's return to our patient case study and explore potential treatment options. Dr. Handelsman, what interventions would you recommend to help our patient, Ritesh, achieve an LDL-C level of less than 55 milligrams per deciliter?

Dr. Handelsman:
Well, for context, the 2024 ADA guidelines emphasize starting with maximally tolerated statin therapy for patients with ASCVD and diabetes. If LDL-C hasn't dropped by at least 50 percent and remains above 55 milligrams per deciliter, the next step is adding ezetimibe or a PCSK9 inhibitor to further reduce LDL-C.[11]

For patients like Ritesh, who have established ASCVD, diabetes, and other high-risk conditions with very high CV risk, I'd consider either ezetimibe or PCSK9, but since this patient needs more than a 25 percent additional LDL-C reduction to get to 55 milligrams per deciliter, I'd go with a PCSK9 first.[16]

Repatha can reduce LDL-C by up to 63 mean percent change from baseline to 12 weeks when added to a statin. In trials like FOURIER, these therapies not only achieved profound LDL-C lowering, but also reduced major adverse CV events.[13,14] For Ritesh, combining his statin therapy with a PCSK9 inhibitor could help him meet his recommended LDL-C level of less than 55 milligrams per deciliter and reduce his cardiovascular risk.[16]

It is also important to address lifestyle factors. Ritesh could benefit from incorporating physical activity and dietary changes, such as a Mediterranean-style diet—although different from the typical Indian diet it can be modified sufficiently enough to be incorporated by Ritesh. While pharmacologic therapy is the cornerstone of LDL-C management, lifestyle interventions also play a supportive role in overall cardiovascular health.[7]

Dr. Turck:
Now with the availability of these treatment options, what are the main barriers limiting patients from achieving recommended LDL-C levels, and how can we address them?

Dr. Handelsman:
Well, there are several challenges to medical management, and they fall into three main categories: patient-level, provider-level, and systemic.[17,18]

At the patient's level, lack of education is a major challenge.[17] For patients, fear of side effects when starting a new medication is a major concern.[17,18] Paired with not being educated on the link between LDL-C and cardiovascular risk, it is very challenging to have patients start or prioritize adherence to therapy.[17,18]

Now on the provider side, clinical inertia poses a major challenge. Clinicians may not all agree on which specific guidelines or consensus statements to follow that would dictate LDL-C thresholds or treatment initiation.[17,19] This comes as no surprise, since lipid management suggestions can vary between guidelines and consensus statements. Clinical inertia may persist if the patient's primary care physicians, cardiologist, and endocrinologist each adhere to different guidelines.[7,11,16,17,20]

And systemically, gaps could exist throughout the patient journey, whether it's during follow-up with their doctor or in lipid testing. [17] Insurance may also serve as a challenge for some patients as healthcare plans may have differing requirements for coverage.[21]

Dr. Turck:
And as we approach the end of our program, Dr. Handelsman, what steps can we take to bridge the gaps in lipid management and reduce cardiovascular risk for patients like Ritesh?

Dr. Handelsman:
I'm so glad you asked this question, because there are a few management principles a clinician can implement right now.

One would be to reinforce education on the importance of cardiovascular risk in patients with ASCVD and diabetes. We talked about education being a challenge, but until patients become more aware of their risk, we cannot expect their attitudes or beliefs to change.[22]

Two, first-line high-intensity statins or the maximally tolerated statin dose should be used with escalation to therapy when needed to help patients achieve therapeutic targets.[11] When patients achieve targets faster, their results may increase feelings of control over their health and encourage them to adhere to treatment regimens.[17] As a reminder, the 2024 ADA guidelines suggest considering a PCSK9 inhibitors as an option to escalate treatment if patients like Ritesh are still unable to reach a target LDL-C level.[11] Traditional sequential therapy can contribute to clinical inertia, which may lead to longer exposure to increased LDL-C levels and a risk of recurrent CV event.[23] This reinforces the importance of identifying strategies to ensure high-quality care.

Lastly, monitor patients' adherence and response to therapy by obtaining a lipid measurement 4 to 12 weeks after lipid-lowering therapy initiation or dose adjustment.[11]

By implementing these three principles, we can help address treatment gaps at the patient, clinician, and systemic levels.

Dr. Turck:
Those are great proactive steps for us to think on as we come to the end of today's program. And I want to thank my guest, Dr. Yehuda Handelsman, for helping us better understand how to address barriers in lipid management for patients with diabetes and reduce their cardiovascular risk. Dr. Handelsman, it was great speaking with you today.

Dr. Handelsman:
Thank you for having me. It's been a pleasure.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck.

Before we close, let's take a moment to review additional important safety information for Repatha.

ReachMD Announcer:
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®.

Please see link to full Prescribing Information on the Landing Page for this episode.

This program was sponsored 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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