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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Taking Ownership Over Cholesterol Management: Multidisciplinary Expert Perspectives

Announcer Introduction:
This medical industry feature, titled "Taking Ownership Over Cholesterol Management: Multidisciplinary Expert Perspectives" is sponsored by Amgen. This program is intended for healthcare professionals.

Here's your host, Dr. Charles Turck

Dr. Turck:
In select high-risk patients who have suffered a recent myocardial infarction, or MI, even high intensity statins may not be able to control LDL cholesterol levels to the guideline-recommended thresholds to help prevent a future MI, stroke, or coronary vascularization.1 How should cardiologists and primary care physicians coordinate care for these high-risk patients? And is there a treatment option that can help achieve reductions in LDL-C levels?

This is ReachMD and I'm Dr. Charles Turck. Joining me to discuss multi-disciplinary collaborations in cholesterol management are Dr. Janki B. Shah and Dr. J. Kyle Turnbo. Dr. Shah is an Associate Professor of Cardiology at UCLA Health. She is a preventive and invasive cardiologist with a busy clinical practice. Dr. Shah, thanks for being here today.

Dr. Shah:
Thank you Dr. Turck, it's my pleasure to be here.

Dr. Turck:
And Dr. Turnbo is a Family Practice Provider, who is also board certified in preventive and occupational medicine. He is also the CEO and Medical Director of HealthWorks Medical LLC in Paducah, Kentucky. Dr. Turnbo, it's great to have you with us.

Dr. Turnbo:
Thank you Dr. Turck for that introduction. I'm glad to be here.

Dr. Turck:
Dr. Shah, let's jump right in. From your perspective as a cardiologist, when a patient who has had a recent MI comes to meet with you, what are the immediate concerns that you want to address?

Dr. Shah:
First of all, I want to point out that the estimated annual incidence of myocardial infarctions is 605,000 new attacks and 200,000 recurrent attacks.[2] So, when I meet a patient who has had a recent MI, my first concern is how can I help him or her prevent a future MI, stroke or coronary revascularization. About one in five patients who have had an myocardial infarction will have another cardiovascular event within one year, making these patients very vulnerable.[3] So, I work hard to make sure that they understand what has happened so far, what their future risks are, and what we're going to do together to minimize them. We go through lifestyle changes that they'll need to make and we also review their medications and ensure that their blood pressure, blood sugar, and cholesterol goals are being met.

Dr. Turck:
Coming over to you Dr. Turnbo, let's get your vantage point within primary care. What do you prioritize when a patient of yours who has suffered a recent MI comes in to see you?

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Dr. Turnbo:
Same for me, for a patient who's had a recent MI, my goal is to do what it takes to help prevent a future MI. So, lipid testing and management are top of mind for me since they're some of the most impactful, important factors that can contribute to reducing the future risk of myocardial infarction.[4] There are several risk factors that can be modified to reduce the risk of future MI, such as lack of exercise, hypertension, smoking, but lipid management is one of the most impactful.[4] For patients at high-risk for cardiovascular events, especially for patients who have recently experienced an MI, early and intensive LDL-C lowering is recommended.[1,5]

Dr. Turck
And staying with you Dr. Turnbo, what are the biggest gaps in care that you see in the treatment of high cholesterol in your highest risk patients?

Dr. Turnbo:
One of the gaps that I see in managing cholesterol for patients who've had a recent MI is that even though statins play a key role in lowering cholesterol, in select high-risk patients, statins are not enough. They need more than statins. Despite the use of high-intensity statins, about half of patients with acute coronary syndrome, or ACS, don't reach guideline-recommended threshold LDL-C levels.[6,7]

Additionally, recent evidence from the prospective GOULD Registry evaluated the LDL's treatment patterns over time in about 5,006 patients with clinical atherosclerotic cardiovascular disease in the United States, and found that at two years, only 32% of all subjects achieved the LDL-C less than 70 mg/dL. Yet only 17.1% of those patients received some type of lipid-lowering therapy intensification.[8] The findings also highlighted how infrequently lipid panels are performed. I believe that poor LDL-C management is contributing to higher incidence of myocardial infarction in many patient populations. After adjusting therapy, lipid levels should be reassessed every four to twelve weeks and repeated every three to twelve months, as needed.[1]

Dr. Turck
Dr. Shah, let me get your take on this same question about care gaps. What are you seeing in practice?

Dr. Shah:
Well, from my perspective, hospitals may not be seeing LDL cholesterol reduction as an acute priority. I'm thinking that they may not be prescribing an appropriate lipid-lowering therapy in the hospital because discharge protocols have not yet been updated to reflect new clinical guidelines and medications. Data from the same GOULD Registry that Dr. Turnbo discussed also showed that lipid-lowering therapy intensification and achievement of LDL cholesterol levels less than 70 mg/dL were both more common at sites where lipid protocols were in place.[8] This care gap leaves highly vulnerable patients without the lipid testing needed to address a significant risk factor affecting their health.

The post-MI care pathway may be another area that has some gaps. As I see it, the pathway is often fragmented after a patient has been discharged from the hospital and this could be contributing to poor coordination of care. The fragmentation can lead to confusion for the patient and I think as a medical community, we must get better at communicating with patients as to why they are on treatment and what the goals of those treatments are.

The GOULD Registry showed that less than 30% of patients understood that the main reason for taking cholesterol medication was to reduce the risk of another MI or stroke. And over 65% of patients did not know, either their approximate LDL cholesterol level or their LDL cholesterol goal. Patients may not even be aware of the importance of having regular follow-up visits with their providers, and thus, they can easily get lost in the shuffle and fall out of the care pathway without the needed active engagement that comes with proper education and reminders.

Dr. Turck:
Dr. Shah, I'd like to go back to what you said about very few patients being prescribed appropriate lipid-lowering therapy upon discharge. Why do you think that is?

Dr. Shah:
It's important to understand that for the patients who are hospitalized for a cardiac event or a stroke, if this is a recurrent event or if they have multiple high-risk conditions, guidelines recommend maximum tolerated statin therapy and perhaps additional lipid-lowering therapy if their LDL cholesterol remains above 70 mg/dL.1 Even beyond the guideline recommended threshold of 70 mg/dL, cardiovascular outcomes trials of statins show that continued cardiovascular event reduction is linearly related to continual reduction of LDL cholesterol, illustrating benefits of lower LDL-C levels with lipid-lowering therapy.[1]

I can propose a few reasons why lipid-lowering therapy is not being prescribed enough in appropriate high-risk patient populations. First off, the hospital physician may be assuming that the patient will be followed closely in an outpatient setting decision could be deferred to

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that setting. However, we know that all patients are not compliant with this and may fall through the cracks.

Another reason might be that the prior authorization process that is required for prescribing lipid-lowering therapy needs administrative assistance and the hospital physicians may not have the infrastructure to complete the process while the patient is hospitalized. For example, there may be additional data that is needed to put through the prior authorization, such as what prior statins the patient had been on, documentation of side effects, proof of prior labs are sometimes required to justify the use of adjunct lipid-lowering therapy.

And another contributing factor as to why physicians may not be prescribing lipid-lowering therapy to patients upon discharge could be because the conversation about starting or escalating lipid-lowering therapy is a lengthy one. The hospital physicians may be reluctant to engage at that level, particularly since they are not the ones who will be seeing that patient for long-term cardiac care.

Dr. Turck:
For those just joining us, this is ReachMD. I'm Dr. Charles Turck and today I'm speaking with Drs. Janki B. Shah and J. Kyle Turnbo about updated collaborative approaches to cholesterol management.

Dr. Turck:
So, Dr. Turnbo, let's focus for a moment on what the current cholesterol guidelines have to say about identifying and treating high-risk patients who've had a recent MI.

Dr. Turnbo:
The American College of Cardiology and the American Heart Association guidelines, the ACC and AHA, recommend optimizing LDL-C management in very high-risk atherosclerotic coronary vascular disease patients.1 These are individuals who've had multiple major atherosclerotic, or ASCVD events, or one major ASCVD event and multiple high-risk conditions, such as over 65, hypertension, diabetes mellitus, persistent elevated LDL cholesterol, in their definition greater than 100 mg/dL despite maximally tolerated statin, with or without ezetimibe therapy, HeFH, which is heterozygous familial hypercholesterolemia, chronic kidney disease, smoking, prior coronary intervention, be that catheter-based or bypass surgery, and congestive heart failure are also risk factors.[1]

In such patients, when the LDL-C exceeds 70 mg/dL on statin with or without ezetimibe, the guidelines recommend the addition of a PCSK9 inhibitor, such as Repatha®, also known as evolocumab.[1]

Dr. Turck:
Well, that gives us an opportunity to get a better understanding of Repatha® as a treatment option. But before we dive in, let's take a moment to review the indications and some important safety information for Repatha®.

Repatha® is indicated in adults with established cardiovascular disease to reduce the risk of myocardial infarction, stroke, and coronary revascularization.

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

Now let's talk about some important safety information for Repatha®. Repatha® is contraindicated in patients with a history of serious hypersensitivity to it. Serious hypersensitivity reactions include angioedema have occurred. We'll hear more about the important safety information later in today's discussion.

Dr. Turck:
Dr. Turnbo, thanks for walking us through some of those risk factors and guidelines. Turning to you, Dr. Shah, can you tell us a little about how Repatha® works?

Dr. Shah:
Essentially, Repatha® enhances the removal of LDL cholesterol.[10] It inhibits PCSK9. PCSK9 is a protein that promotes breakdown of low-density lipoprotein receptors or LDLRs resulting in fewer LDL receptors on the liver cell surface and increasing plasma LDL cholesterol levels.[10]

By inhibiting the binding of PCSK9 to LDL receptors, Repatha® allows the LDL receptors to recycle back to the liver cell surface and as a result, increase the number of LDL receptors available to clear LDL cholesterol from the blood, thereby lowering LDL-C levels.[10]

Dr. Turck:
Thanks for explaining the mechanism of action of Repatha®. Could you also speak to the role of Repatha® in treating high-risk

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established CVD patients?

Dr. Shah:

Absolutely. Let's talk briefly about the Repatha® cardiovascular outcomes trial, also known as FOURIER, which was designed to evaluate whether addition of Repatha® to a statin would reduce major cardiovascular events compared to statin alone. It was a double-blind, randomized, placebo-controlled, event-driven trial of about 27,000 adults with established cardiovascular disease with the LDL cholesterol at the time of randomization being 70 mg/dL or higher or the non-HDL cholesterol being 100 mg/dL or greater, despite high or moderate intense statin therapy.[10,12,13]

Patients were randomly assigned to receive either subcutaneous injections of Repatha® 140 mg every two weeks, Repatha® 420 mg once monthly, or a placebo. Patients were between the ages of 40 to 85 years with prior myocardial infarction, stroke, or symptomatic peripheral arterial disease, or PAD, plus additional risk factors, such as diabetes, smoking, or hypertension.[10]

The primary endpoint was a composite of time to first occurrence of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization with the secondary endpoint being time to first occurrence of cardiovascular death, myocardial infarction, or a stroke.[10] The median LDL cholesterol at baseline was 92 mg/dL despite stable background lipid-lowering therapy. 81% of patients in the trial had previously experienced a myocardial infarction.[10,136]

Dr. Turck:

And Dr. Turnbo, what were the findings in FOURIER?

Dr. Turnbo:

The FOURIER trial found that Repatha® added to a statin reduced a risk of the key secondary composite endpoint of time to the first occurrence of cardiovascular death, MI, or stroke, by 20% in a median of 2.2 years. The hazard ratio for the key secondary composite endpoint was 0.80 and the 95th percent confidence interval was 0.73 to 0.88. Additionally, Repatha® plus a statin 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%. The hazard ratio for the primary composite endpoint was 0.85 and the 95th percent confidence interval was 0.79 to 0.92. Please note, the relative risk reductions for the primary and secondary composite endpoints were driven by a reduction in the risk of MI, stroke, and coronary revascularization. The observed hazard ratio for cardiovascular death was 1.05 with the 95th percent confidence interval of 0.88 to 1.25. The observed hazard ratio for hospitalizations due to unstable angina was 0.99 with a 95th percent confidence interval of 0.82 to 1.18.

With regards to LDL-C lowering, Repatha® plus statin lowered LDL-C by 63% at twelve weeks.

Dr. Turck:

Thank you Dr. Turnbo. I'd also like to cover some additional important safety information for Repatha®.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions: Hypersensitivity reactions including angioedema have been reported in patients treated with Repatha®. If signs or symptoms of serious hypersensitivity reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.

Adverse reactions in primary hyperlipidemia: The most common adverse reactions greater than 5% in patients treated with Repatha® and more frequently than placebo were nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions. From a pool of the

52-week trial and seven, 12-week trials, local injection site reactions occurred in 3.2% and 3.0% of Repatha®-treated and placebo-treated patients respectively. The most common injection site reactions were erythema, pain, and bruising. Hypersensitivity reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common hypersensitivity reactions were rash, eczema, erythema, and urticaria.

Adverse reactions in the cardiovascular outcomes trial: The most common adverse reactions in greater than 5% of patients treated with Repatha® and more frequently than placebo were diabetes mellitus, nasopharyngitis, and upper respiratory tract infection. Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new onset diabetes mellitus during the trial was 8.1% in patients treated with Repatha®, compared with 7.7% in patients that received placebo.

Immunogenicity: Repatha® is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity with Repatha®.

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Please see link to full prescribing information on the landing page for this episode.

Dr. Turck:
Well, given what we've learned about LDL-C management in this particular treatment option, it enables an aggressive approach to treating high LDL-C in your appropriate patient populations. Dr. Shah, what are your thoughts on the best treatment approach?

Dr. Shah:
I recommend a 'see it, treat it' philosophy. Treatment of elevated LDL cholesterol in high-risk patients is critically important. I encourage all healthcare providers to adopt the same philosophy. I understand it is often tempting for primary care providers to allow specialists to make decisions about medications related to their field, but often patients have the closest relationship with their PCP and the trust they have in them may make them more compliant with the medication if it's also recommended by them. The 'see it, treat it' philosophy is also great because it prevents delays in care.

Dr. Turck:
Clearly, the two of you have given us some meaningful insights that we can draw from in improving care for these high-risk patients. So, with that, I want to thank my guests for talking through care coordination strategies on cholesterol management.

Dr. Shah, Dr. Turnbo, it was great speaking with you both, today.

Dr. Shah:
Thank you so much for having me, Dr. Turck.

Dr. Turnbo:
It was my pleasure. Thank you, so much.

Dr. Turck:
I'm Dr. Charles Turck and thank you for joining us today.

Announcer Close:
This program was sponsored by Amgen. If you missed any part of this discussion, visit reach-m-d-dot-com-slash-industry-feature. This is ReachMD. Be Part of the Knowledge.

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