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Overcoming Real World Challenges of LDL-C Management: Looking Beyond Statin Therapy

Announcer
Welcome to ReachMD. This medical industry feature, titled "*Overcoming Real World Challenges of LDL-C Management: Looking Beyond Statin Therapy*" is sponsored by Novartis Pharmaceuticals Corporation. This program is intended for US healthcare professionals.

The speakers have been compensated by Novartis Pharmaceuticals Corporation to conduct this presentation.

Dr Budoff
Thanks for tuning into ReachMD. I'm your host Dr Matthew Budoff, a preventive cardiologist from Los Angeles. In this episode, Dr Ambreen Mohamed, a noninvasive cardiologist from San Diego, and I will discuss clinical perspectives on LDL-C management in patients with primary hyperlipidemia, including those with ASCVD or increased risk of CVD as well as discuss how LEQVIO, inclisiran, can benefit these patients.

Previously, LEQVIO injection was indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with clinical atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of low-density lipoprotein cholesterol (LDL-C).[1]

As many of us may be aware, FDA expanded indication of LEQVIO in July 2023.[1] LEQVIO injection is indicated as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C.[1] This enables broader use of LEQVIO in primary hyperlipidemia patients as an adjunct to diet and statin therapy. These are patients with elevated LDL-C and ASCVD or patients with increased risk of CVD including those with additional factors such as HeFH, type 2 diabetes mellitus, or 20% or greater risk of a CV event based on the Framingham risk score or equivalent.[1] So, Dr Mohamed, before we discuss LEQVIO why don't we talk about some of the current challenges you are facing in LDL-C management in getting your patients to goal?

Dr Mohamed
Hey Dr Budoff!

So in my practice, I deal with a lot of patients with ASCVD or increased risk of CVD who both struggle with their LDL-C, levels. Many times diet and statins just aren't enough.[2-5] Some of my patients simply just don't believe in the efficacy of treatment, because although they do see some improvement, they are still not reaching their target levels, which becomes super frustrating and then it further demotivates them towards treatment.[6] Some patients also run into tolerability issues or find the treatment regimen for current standard of care too overwhelming as many of them manage multiple comorbidities.[7]

So how would you approach a situation like this?

Dr Budoff
I completely agree that managing LDL-C levels in primary hyperlipidemia can be a clinical challenge. I realize that as health care professionals, the majority of us don't prioritize LDL-C management due to other comorbidities among our patients. Keeping in mind these challenges, I continue to advocate for and manage my own patients towards guideline-recommended LDL-C threshold because it's the most modifiable risk factor in patients with ASCVD or increased risk of CVD.[8,9]

Studies show that patients with ASCVD or at risk for CVD continue to have elevated LDL-C levels despite statin therapy. More than 70 percent of these patients do not reach the guideline-recommended LDL-C levels.[10,11] LDL-C threshold for patients with ASCVD is less than 70 milligrams per deciliter while that for patients with increased risk of CVD is less than 100 milligrams per deciliter.[12] So in my patients with suboptimal control of LDL-C level and ASCVD or increased risk of CVD, I do not hesitate to add an additional LLT to their statin therapy to help me get to their target LDL-C levels. This is where I consider a therapy like LEQVIO or a PCSK9 monoclonal antibody.

Dr Mohamed
So in my experience, I have used add-on LLT like PSCK9 monoclonal antibodies in my patients that are already on statins. But many of my patients struggle with adherence to at-home injections of CSK9 monoclonal antibodies. This seems to be a challenge for many clinicians, including myself. So, for example, I have a patient I have particularly been struggling with.

I recently prescribed her PCSK9 monoclonal antibodies. She is absolutely refusing to take this medication at home. She is really scared to give herself the injections, she doesn't have any friends or family that can help her with this treatment. She has even asked us, as her health care practitioners if we can give it to her in the office. So, clearly, this is a very challenging patient and an example that many of us are dealing with.

So, what are your suggestions?

Dr Budoff
I'd have to agree that you're not alone in seeing patients facing challenges with PCSK9 monoclonal antibodies. Nevertheless, I must emphasize that PCSK9 is an excellent therapeutic target. I strongly believe in empowering patients to be a part of the decision making process because ultimately the best therapy is the one that the patient actually takes.

So, while I have a lot of confidence in treatments acting against PCSK9, I needed a way to bring my patients along in this belief because I have heard from many of them that they prefer fewer injections. LEQVIO as an option for my patients provided me with that possibility. I've integrated twice-yearly injection therapy with LEQVIO, after two initial doses, in my practice to manage LDL-C levels as an adjunct to diet and statin in my appropriate patients.[1]

Dr Mohamed
So, I was introduced to LEQVIO not too long ago. It was introduced to me as a first-in-class small interfering RNA, or siRNA, therapy that selectively targets the liver to prevent production of PCSK9 protein and therefore regulate LDL-C levels.[1] I know you mentioned earlier that the use of LEQVIO has been expanded to primary hyperlipidemia patients as a statin add-on therapy, such as those with ASCVD or patients with increased risk of CVD.[1] With the ability to use LEQVIO in a broader patient population, I'd love to hear your experience with it! What do you and your patients think about LEQVIO?

Dr Budoff
It's a truly unique option that resonates with both me and my patients. My patients like LEQVIO because it's only dosed twice a year, they don't need to inject it themselves. When they start LEQVIO as an adjunct to statin therapy, they get an initial dose, another at three months, and then every six months.[1] As their doctor, I like LEQVIO because it can integrate seamlessly into patients' existing healthcare regimen, usually every six months. I can have confidence that they are receiving their doses because it's HCP administered and is happening in my own practice.[1] I also appreciate the close partnership I build with my patients when they come in to get LEQVIO dose and the continuity of care when they come back for their dose. We get to see patients play an active role in their treatment, and our patients get to see us delivering the treatment at each LEQVIO injection visit. But none of this would matter if LEQVIO wasn't delivering the efficacy my patients need.

Announcer
For those just joining us, you're listening to a medical industry feature on ReachMD. I'm your host, Dr Matthew Budoff, and I'm speaking with Dr Ambreen Mohamed on managing LDL-C levels in patients with ASCVD or increased risk of CVD.

Dr Mohamed
So, I am somewhat familiar with their efficacy data based on their website and I thought that the data showed impactful results! ORION-10 and ORION-11 were Phase III multicenter, double-blind, randomized, placebo-controlled 18-month trials.[1,13] ORION-10 enrolled patients with ASCVD. ORION-11 enrolled patients with ASCVD and also patients at increased risk of ASCVD. In ORION-11, there was a 50% LDL-C reduction with LEQVIO compared to placebo groups from baseline to month 17, when LEQVIO was administered in patients on maximally tolerated dose of statin with or without other lipid modifying therapy.[1] Similar results were observed in ORION-10

trial, with a 52 percent LDL-C reduction difference from placebo at month 17 from baseline.[1]

Does your real-world experience reflect these trial data?

Dr Budoff
Yes! But before we talk about my own experience, I want to highlight 3 key data points that resonate with me and my patients. First, I often highlight to my patients that LDL-C reduction was apparent within 14 days after the first dose of LEQVIO in a Phase II trial.[1,14] Patients are particularly motivated when they learn about such a response in LDL-C reduction. Second, my patients are happy to hear that LEQVIO may help get them to guide line recommended target, which is LDL-C levels below 70 milligrams per deciliter for ASCVD patients and below 100 milligrams per deciliter for those with increased risk of CVD.[12] Finally, both my patients and I feel more comfortable knowing that there is long-term data for LEQVIO from the ORION-8 open label extension trial.[15] The powerful, proven, and sustained LDL-reduction through each 6 month dosing really make a difference to patients, especially after all the struggles they've been through to get to LDL-C goals.[1] So I think that the results from LEQVIO trials are overall consistent with my own experience with LEQVIO in appropriate patients.

Dr Mohamed
What about the safety and tolerability of LEQVIO? Is there anything I particularly need to discuss with my patients?

Dr Budoff
Well, I really like the safety and tolerability profiles of LEQVIO because my conversation with patients about what to expect in terms of possible side effects is very straightforward. Adverse reactions in clinical trials (in greater than or equal to 3 percent of patients treated with LEQVIO and more frequently than placebo) were injection site reaction (which included terms like injection site pain, erythema and rash), arthralgia, and bronchitis.[1] I reassure my patients that LEQVIO was well tolerated in clinical trials.[1] LEQVIO has no warnings and precautions included in the Prescribing Information.[1] No clinically significant drug-to-drug interactions are expected with LEQVIO.[1] The majority of adverse events in each trial were mild or moderate.[16,17]

LEQVIO had low discontinuations due to adverse reactions.[1] Injection site reactions were the most common cause of discontinuation.[1,17] All treatment-emergent adverse events at the injection site were localized, predominantly mild or occasionally moderate, and none were severe.[16,17]

The safety profile was consistent across all subgroups of patients, including elderly, mild-tomoderate hepatic impairment, and mild-to-severe renal impairment patient populations.[1] In addition long term safety data is also available from the ORION-8 trial.[15]

Dr Mohamed
This is really encouraging to hear. Referring to the patient I was telling you about earlier, she is unable to take her PCSK9 monoclonal antibody injections herself. And she even came to us and asked if we can give her the injections in the office. I would think the twice-yearly dosing of LEQVIO would work so well for such a patient. Of course, the comparison here pertains only to differences in dosing and administration, and should not be considered a comparison of efficacy and safety.

Would you use LEQVIO for her? How would you decide who the appropriate patient for LEQVIO is?

Dr Budoff
Initially, I used LEQVIO only in a small subset of patients that did not meet their LDL-C lowering goals similar to the ASCVD patient not at goal that you just mentioned. I have now come to appreciate just how many patients LEQVIO may benefit. I do NOT "reserve" it for specific patient types, but use it in a wide variety of approved patient types, that is, those with ASCVD and also patients at increased risk of ASCVD to lower LDL-C as an adjunct to diet and statin therapy.[1]

Dr Mohamed
This is so helpful and I can clearly see LEQVIO's unique clinical value for patients. Thank you, Dr. Budoff, for talking with me and sharing your experience on managing LDLC levels in patients with primary hyperlipidemia and your experience with LEQVIO.

Dr Budoff
Any time, Dr. Mohamed. LEQVIO is truly unique therapy due to its mechanism of action and twice yearly dosing. Its powerful, sustained efficacy and proven safety profile in addition to the long-term data are reassuring. The twice-yearly dosing regimen resonates tremendously with my patients and myself. I build strong partnership in LDL-C management with my patients as a result of seeing them twice yearly for the administration of LEQVIO. And with the expanded indication for LEQVIO, I am happy to see that even patients with increased risk of CVD can benefit from it. As these final thoughts bring us to the end of our program, I would like to thank all of you for

joining us as well.

Announcer
INDICATION
LEQVIO (inclisiran) injection is indicated as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C).

IMPORTANT SAFETY INFORMATION
LEQVIO is contraindicated in patients with a prior serious hypersensitivity reaction to inclisiran or any of the excipients in LEQVIO. Serious hypersensitivity reactions have included angioedema. Adverse reactions in clinical trials (≥3% of patients treated with LEQVIO and more frequently than placebo) were injection site reaction, arthralgia, and bronchitis.

Please see LEQVIO full Prescribing Information available on this site or at LEQVIOHCP.com.

Important Safety Information for LEQVIO is available underneath the player of this audio presentation.

This program was sponsored by Novartis Pharmaceuticals Corporation. If you missed any part of this discussion, visit ReachMD.com/Industry Feature. This is ReachMD. Be Part of the Knowledge.

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