## Transcript Details

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Confronting the Complexities of Reaching LDL-C Thresholds in Patients with Primary Hyperlipidemia

**ReachMD Announcer:**
Welcome to ReachMD. This medical industry feature, titled “Confronting the Complexities of Reaching LDL-C Thresholds in Patients with Primary Hyperlipidemia” is sponsored by Novartis Pharmaceuticals Corporation and is intended for US health care professionals. The speaker has been compensated by Novartis Pharmaceuticals Corporation to conduct this presentation.

**OHS Announcer:**
Thanks for tuning in to ReachMD. I am your host for this program that features an interview with Dr Michael Bloch, a vascular medicine specialist and clinical lipidologist who directs a large
multidisciplinary vascular medicine and lipid clinic in Reno, Nevada. In today's program Dr Bloch will discuss low-density lipoprotein cholesterol (or LDL-C) management in patients with primary hyperlipidemia and share his clinical considerations in recognizing appropriate patients for treatment with LEQVIO (inclisiran). Before we begin, let’s go over the indication for LEQVIO.

INDICATION: 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 low-density lipoprotein cholesterol (LDL-C).[1]

**Dr Bloch:**
Thank you so much for having me! This discussion on recognizing the appropriate patients with primary hyperlipidemia for treatment with LEQVIO is important, given the increasing number of patients with established ASCVD or increased risk of CVD and the struggle that some of these patients have to reach their recommended LDL-C target.[2,3] CVD remains the leading cause of death in the United States, accounting for greater than 900,000 deaths annually.[2] And as we are well aware, patients with or at risk for CVD may have several modifiable risk factors, such as elevated LDL-C, low physical activity, diabetes, poor dietary habits, and high systolic blood pressure that contribute to their CVD risk.[3-5] However, I want to note here at the outset that the effect of LEQVIO on cardiovascular morbidity and mortality has not yet been determined. For patients with ASCVD or at increased risk of CVD, LDL-C is a modifiable therapeutic target[1,6,7]; however, many patients continue to struggle to lower their LDL-C levels, even with maximally tolerated statin therapy.[8-10]

**OHS Announcer:**
Thank you for that insight, Dr Bloch! What led to your interest in LEQVIO as a treatment option for your patients?

**Dr Bloch:**
When I learned about the data from the Phase 3 trials, it really piqued my interest in LEQVIO. The trials demonstrated powerful and consistent LDL-C reduction throughout each of the 6-month dosing intervals after 2 initial doses.[1] It was also well tolerated in these clinical trials, with the most common adverse reactions being injection site reaction, arthralgia, and bronchitis.[1,11] I’m also aware that in July 2023, the FDA approved an expanded indication for LEQVIO, which is great because it enables a broader use of treatment including in primary hyperlipidemia patients with an increased risk of CVD.[1]

**OHS Announcer:**
Thank you for that overview, Dr Bloch! Based on your clinical experience, can you share a patient case in which you considered LEQVIO as a treatment option?

**Dr Bloch:**

Absolutely! So, I have an ASCVD patient, a 62-year-old woman, who had her first myocardial infarction at 55 years old and came back to the catheterization laboratory at 60 years of age to have 2 vessels stented, after she experienced recurrent angina. Her baseline LDL-C was over 200 milligrams per deciliter, when she first presented with her initial MI at age 55.

The patient has a family history of premature coronary disease and, despite following a Mediterranean diet and exercising regularly, the patient had persistently high LDL-C levels. After the initial myocardial infarction event, she was treated with atorvastatin 80 milligrams daily and her LDL-C levels came down to around 110 milligrams per deciliter. However, on persistent statin therapy, no further reduction was seen in her LDL-C levels, and I started discussing the potential addition of a nonstatin lipid-lowering medication with her. I offered her a PCSK9 monoclonal antibody, but she was hesitant to self-inject.

**OHS Announcer:**
So, why did you consider LEQVIO as a treatment option for this patient?

**Dr Bloch:**
Well, I think the clinical evidence really demonstrates that LEQVIO could be a potential treatment option for patients with ASCVD given the powerful and consistent LDL-C reduction.[1] To begin, LEQVIO was studied in the ORION-10 Phase 3 multicenter, double-blind, randomized, placebo-controlled 18-month trial.[1] ORION-10 enrolled patients with ASCVD.[1] The primary end point of this study was percentage change in LDL-C from baseline to day 510 or month 17.[1] In ORION-10, there was a 52% 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 ezetimibe.[1,12]

**OHS Announcer:**
That's interesting to hear, Dr Bloch. Regarding patients who achieved guideline-recommended LDL-C thresholds, was that also an end point studied in ORION-10 trial?

**Dr Bloch:**
Yes, it was! In ORION-10, 84% of LEQVIO-treated patients with ASCVD achieved LDL-C levels less than 70 milligrams per deciliter at month 17, compared with 18% of placebo-treated patients.[1,13]

**OHS Announcer:**
Nice! The data from ORION-10 look very promising. Now, can you tell me what were some of the safety and tolerability data from LEQVIO that motivated you to choose this therapy?

**Dr Bloch:**
Absolutely. For my patient and me, the safety and tolerability profile played a significant role when considering LEQVIO as a treatment option. When I told my patient that the safety profile of LEQVIO is quite good, it was very attractive for her. Now, as I mentioned earlier, LEQVIO was well-tolerated in clinical trials.[11] In the Phase 3 clinical trials, over 18 months, the most common adverse reactions occurring in greater than or equal to 3% of patients treated with LEQVIO, and more frequently than placebo, were injection site reaction, arthralgia, and bronchitis.[1,12]

Adverse reactions led to discontinuation in 2.5% of patients treated with LEQVIO vs 1.9% of patients receiving placebo.[1] Injection site reactions were the most common causes for treatment discontinuation observed in 0.2% of patients taking LEQVIO vs 0% taking placebo.[1] And the majority of adverse events were mild to moderate.[11]

**OHS Announcer:**
Thank you for sharing your rationale and motivation for using LEQVIO in your patient. Now, Dr Bloch, based on your patient's condition, what was the impact of using LEQVIO?

**Dr Bloch:**
After the addition of LEQVIO to her treatment regimen, along with the continuation of statin therapy and diet, my patient experienced consistent reductions in her LDL-C level and achieved the guideline-recommended threshold of less than 70 milligrams per deciliter.[14] But of course, individual results may vary.

**OHS Announcer:**
That's amazing to hear that your patient was able to benefit from treatment with LEQVIO, Dr Bloch. How did your patient react to the dosing regimen of LEQVIO?

**Dr Bloch:**

That's a really great question! Before my patient began treatment with LEQVIO, she would sometimes forget to pick up her atorvastatin 80 milligrams from the pharmacy despite frequent calls and counseling efforts from the pharmacy and her provider's office. When discussing further treatment options with her, she expressed her hesitancy over having additional therapies to take at home, given the concern of a heavy medication burden. As I mentioned before, she was also hesitant to self-inject. I wanted to take her concerns seriously and find an option that would best fit her needs.

She was very receptive to the dosing regimen of LEQVIO after I explained to her it's administered as a single subcutaneous injection initially, again at 3 months, and then every 6 months.

**OHS Announcer:**
That's great to hear, Dr Bloch. Can you walk us through, in more detail, the dosing and administration of LEQVIO and how you've integrated it into your practice?

**Dr Bloch:**
Certainly. LEQVIO 284 milligrams is a single subcutaneous HCP-administered injection given initially, again at 3 months, and then every 6 months.[1] I was confident that once I administered LEQVIO, my patient would not miss a dose for the next 6 months. By injecting in our office, we make sure patients come in for their 6-month dose, and I would have our clinical pharmacist or my office manager follow up with her if she didn't show up.

I also explained to my patient that if she misses her planned dose by less than 3 months, then LEQVIO can still be administered, and the dose should be maintained according to the original dosing schedule.[1] And I said to her that if she misses her planned dose by more than 3 months, then she would have to restart with a new dosing schedule-administer LEQVIO initially, again at 3 months, and then every 6 months.[1]

**OHS Announcer:**
Thank you for sharing your insights on how you explain the dosing and administration to your patient, Dr Bloch! Are there any other types of patients that you would consider for treatment with LEQVIO?

**Dr Bloch:**
Certainly. In addition to patients with established ASCVD, like the one I just described to you, LEQVIO is a reasonable treatment option for high-risk patients without ASCVD who are at high risk for future CVD events and whose LDL-C is not optimally controlled despite statin therapy and diet. These patients include those with heterozygous familial hypercholesterolemia, type 2 diabetes, or a 10-year cardiovascular risk greater than or equal to 20%.[1,11]

For example, in my practice, we have a 55-year-old gentleman who's been seeing us for more than 5 years. He has type 2 diabetes and a family history of premature coronary artery disease and a calculated 10-year cardiovascular risk greater than or equal to 20%. We've had a lot of trouble escalating his statin dose, and he's only been able to tolerate low doses of multiple different statins.

Currently, we have him on maximally tolerated statin, which is 5 milligrams of rosuvastatin, 3 days a week, plus ezetimibe 10 milligrams a day. Despite these medications and aggressive diet and exercise, we've been unable to get his LDL-C below the recommended target of 100 milligrams per deciliter. We talked about the different options that were available to this patient and we decided that LEQVIO would be a great choice.

**OHS Announcer:**
Dr Bloch, thank you for sharing. And thank you for your time today. It definitely seems like LEQVIO may be able to benefit a broad range of patients! Any final thoughts you would like to share?

**Dr Bloch:**
Well, it's been a pleasure discussing some of the challenges related to LDL-C management and recognizing the appropriate patients that may benefit from LEQVIO as a treatment option. With the expanded indication of LEQVIO, I am confident it's a reasonable choice for patients with primary hyperlipidemia who need additional help when diet and statin therapy are not enough to lower LDL-C to its recommended target.[1]

LEQVIO has demonstrated powerful and consistent LDL-C reduction in the Phase 3 studies, and the results I shared with you are very reassuring for me and my patients.[1]

**OHS 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.

**ReachMD Announcer:**

Please see LEQVIO full Prescribing Information 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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