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Clinical Perspectives on Prioritizing LDL-C Management After a Recent Coronary Event

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Clinical Perspectives on Prioritizing LDL-C Management After a Recent Coronary Event,” is sponsored by Novartis Pharmaceuticals Corporation. This program is intended for US health care professionals.

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

Moderator:
Thanks for tuning in to ReachMD. I’m your host for this program featuring an interview with Dr Kathleen Drinan, a clinical cardiologist at the University of Chicago in Illinois.

In today’s program, Dr Drinan will discuss low-density lipoprotein cholesterol, or LDL-C, management in patients who have had a recent coronary event. She will share her clinical perspectives on data that highlight the importance of starting patients early on a non-statin lipid-lowering therapy or (LLT) after failure to reach target LDL-C levels on a maximally tolerated statin therapy.

Before we dive into today’s discussion about LEQVIO, inclisiran, an siRNA lipid-lowering therapy that directly targets the liver, let’s go over the indication for LEQVIO.

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 Drinan:
Hello, thank you for having me. I’m Dr Kathleen Drinan. I’m a clinical cardiologist committed to LDL cholesterol management in patients with ASCVD, especially those high-risk patients who, after a recent coronary event, need to take action to achieve the guideline-recommended LDL Cholesterol targets.

We have lots to talk about, and I’m really looking forward to sharing my clinical experience with you.

Moderator:
Thank you, Dr Drinan. We’re happy to have you here today. So, we’re here to talk about managing LDL-C levels in patients who have experienced a recent coronary event and why you believe it’s important to start a non-statin LLT early in patients who are not at goal on a statin.

So, to begin, can you tell us a little about why LDL-C management in this patient population is such an important topic?

Dr Drinan:
Of course. For some background, atherosclerotic cardiovascular disease, or ASCVD, is a progressive disease characterized by the formation and buildup of atherosclerotic plaques. ASCVD is the primary contributor to cardiovascular disease and includes coronary artery disease, or CAD, peripheral artery disease, and cerebrovascular disease.[2-6]

It’s important to keep in mind that LDL cholesterol is the most abundant form of atherogenic cholesterol[7] and LDL cholesterol level is one of the most readily modifiable risk factors for ASCVD.[8-9] Therefore, taking swift action to manage these LDL cholesterol levels in a patient with a recent coronary event is imperative. I like to think of it as a golden moment when I see that patient, after having a recent coronary event, they’re very engaged, they’re very motivated, they’re very concerned. They'll frequently present with family’s support. There is a short window of time when we are able to take meaningful action to help lower their LDL cholesterol levels to guideline-

recommended targets. This is where we, as cardiologists, may be able to address this unmet need and help our patients.

Moderator:
Thank you for that introduction on our topic for today.

Now, as a clinical cardiologist understanding the burden of ASCVD, how do you manage LDL-C levels in your patients, and what challenges do you face?

Dr. Drinan:
Well for management of LDL cholesterol I start patients on statin therapy. I repeat LDL cholesterol levels every time I either start a statin or change a dose of a statin, or add a non-statin lipid lowering agent, trying to evaluate with each step whether they're reaching guideline recommended targets. This kind of routine testing isn't necessarily common practice in many cardiology practices, and there are patients that struggle frequently to reach their LDL cholesterol goals even after years of titrating and cycling through multiple statins.

It's been a challenge for us as cardiologists—Studies show that up to 80% of patients with ASCVD remain on the same statin regimen despite LDL cholesterol levels above 70 mg/dL. This data is based on 2 years of real world and electronic health record data from 2017 to 2018 in over 300,000 patients with ASCVD.[10]

After a recent coronary event, reaching and remaining below LDL cholesterol targets is especially critical.[2,11] Based on claims data from the Family Heart Database, we know that there were 49% more total cardiovascular events observed in the patients who did not achieve their LDL cholesterol goals or targets.[12] The effect of LEQVIO on cardiovascular morbidity and mortality has not been determined. In addition, underutilization of guideline recommended lipid lowering therapy is one contributor to suboptimal LDL cholesterol levels in patients. This is not something we should be taking lightly. This is our golden moment with the patient who's very concerned, after a coronary event, and wants to create a long-term plan to get to and stay below guideline recommended LDL cholesterol goals.

So, for example, in my clinical experience, if I have a patient with a recent coronary event who is already on a statin and has LDL cholesterol levels around 100 mg/dL, I will begin exploring incorporation of a non-statin lipid-lowering therapy with proven efficacy in their treatment regimen so that I can get their LDL cholesterol to 70 mg/dL or below. In my practice, I often use LEQVIO for my statin-treated patients who are in immediate need of additional lipid lowering of their LDL cholesterol levels because it's proven efficacy and safety data and is dosed only twice a year after 2 initial doses.[1] Recommendations for using LEQVIO are often a relief for many of my patients when they find out that there are other options—besides taking another pill—that may help them reach their goals. I urge my colleagues to consider LEQVIO for their appropriate patients as well.

Moderator:
That's all very interesting. Now, can you please tell us more about what specific clinical data support your choice of LEQVIO for your patients?

Dr. Drinan:
Yes, so LEQVIO was evaluated in two Phase 3, multicenter, double-blind, randomized, placebo-controlled, 18-month trials, ORION-10 and ORION-11.[1] ORION-10 enrolled patients who had ASCVD. ORION-11 also enrolled patients with ASCVD and included patients with increased risk of ASCVD.[1] Factors that increased risk of ASCVD included heterozygous familial hypercholesterolemia or FH, type 2 diabetes mellitus, or 10-year risk scores of greater than 20%.[13] All patients were receiving maximally tolerated statin therapy with or without ezetimibe and still required additional LDL cholesterol lowering.[1,13] In terms of the efficacy data in patients that have already had a cardiovascular event in ORION-10, there was a 52% LDL cholesterol reduction with LEQVIO compared to placebo groups from baseline to Month 17, when LEQVIO was administered in patients on a maximally tolerated dose of statin, with or without ezetimibe.[1,13] 84% of LEQVIO-treated patients with ASCVD achieved guideline-recommended LDL cholesterol levels of lower than 70 mg/dL at Month 17, compared with 18% of placebo-treated patients.[14] We know that the results were similar in ORION-11.[13]

Moderator:
Thank you, Dr Drinan, for sharing those insights on the efficacy data for LEQVIO.

So, tolerability is always an important consideration when it comes to getting patients on a long-term treatment plan. Can you briefly tell us about how this plays a role in your treatment decision and what we know about the tolerability and safety profile of LEQVIO?

Dr. Drinan:
What we know is that LEQVIO was well tolerated in Phase 3 clinical trials. The most common adverse reactions included injection site reaction, arthralgia, and bronchitis.[1] Adverse reactions leading to discontinuation occurred in 2.5% of patients treated with LEQVIO vs

1.9% of patients treated with placebo.[1] Injection site reactions were the most common cause of discontinuation, occurring in 0.2% in the LEQVIO group vs 0% in the placebo group.[1] And the majority of adverse events were mild to moderate.[14,15] In my clinical experience, it's exciting to be able to introduce something that's well tolerated.

Moderator:
Thank you for sharing those insights on the Phase 3 clinical trials with LEQVIO.

Now, are there any other data that you consider when treating patients who are not yet at LDL-C goals, specifically in patients who have experienced a cardiovascular event?

Dr. Drinan:
Yes, I also consider data from studies based in a real-world clinical setting, like we see in V-INITIATE. V-INITIATE was a 12-month, randomized, open-label, real-world Phase 3b clinical trial in 450 patients who had ASCVD.

The study evaluated the efficacy and safety of early initiation with LEQVIO immediately after failure to reach LDL cholesterol levels below 70 mg/dL on maximally tolerated statin vs usual care. "Usual care" was physician determined based on the 2018 AHA/ACC guidelines.[16] Early initiation of LEQVIO, immediately upon failure to reach LDL cholesterol levels of <70 mg/dL on maximally tolerated statin, reduced LDL cholesterol consistent with the pivotal trials and demonstrated 53% LDL cholesterol reduction difference from usual care, for which 73% of the patients remained on statins only at Day 330. And the safety profile of LEQVIO in V-INITIATE was also consistent with pivotal trials, with no new safety signals.[16] I do want to quickly note some study limitations. "Usual care" did not reflect best practice, with little use of guideline-recommended non-statin therapy. Therefore, a comparison of efficacy or safety of LEQVIO vs other non-statin therapies cannot be made. Use of LEQVIO was permitted in the usual care arm with 10 patients or 4% of the usual care participants receiving LEQVIO. This may impact the effectiveness of comparisons. Although the study was designed to mimic clinical practice, statin discontinuation rates may not reflect the real world due to the participants' potential behavioral changes as a result of being part of a study. The open-label design has a potential for bias and may present difficulties in the interpretation of results.[16]

Overall, these data support the early initiation of LEQVIO after patients experience a coronary event and do not reach LDL cholesterol targets with statin therapy alone. And for health care professionals, these data showed that we need to take additional action. We need to more diligently uptitrate statins, use non-statin lipid-lowering therapy, and take advantage of these moments following a cardiovascular event when there is urgency for us to take action to help our patients reach their LDL cholesterol goals.

Moderator:
Thank you, Dr Drinan, for talking with me today and sharing your perspectives on managing LDL cholesterol levels in patients with ASCVD and your experience with LEQVIO.

Are there any final thoughts or takeaways you'd like to share with listeners?

Dr. Drinan:
After 2 initial doses, LEQVIO is dosed twice a year,[1] which I think is a particularly great option for my patients and me. The fact that patients come to a clinic to get their injections instills confidence in us clinicians that they are staying adherent to their treatment plan. It's also nice for my patients who prefer to come to the clinic to have their medication administered—they don't have to worry so much about remembering to take an additional lipid-lowering therapy at home, they just need to come in every 6 months, which is typically when my patients come in for their regular check-ins. LEQVIO is a unique therapy that I find has been very well received by my patients. Its powerful, consistent efficacy on top of maximally tolerated statin through the 6-month dosing period and proven safety profile based on pivotal Phase 3 trials were reassuring. Also, the data on early use of LEQVIO after failure to reach target LDL cholesterol levels on a maximally tolerated statin help provide a glimpse of LEQVIO in the real world.

As these final thoughts bring us to the end of our program, I'd like to thank all of you for joining us.

Announcer:
For more information about LEQVIO, please visit LEQVIOHCP dot com slash expert hyphen perspectives.

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 full LEQVIO 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 dot com slash Industry Feature. This is ReachMD. Be Part of the Knowledge.

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