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### Swing for the Fences – LDL-C as the Power Hitter

#### Announcer:

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#### Dr. Malachowski:

Hello. I'm Dr. Malachowski, and here with me today is Dr. Randy Englert. Our topic today is the role of LDL-C levels in the management of patients with high-risk ASCVD.

So, Randy, in our treatment approach, LDL-C is the power hitter. What can you tell the crowd listening about why it's important to consistently track and manage LDL-C levels in patients at high risk?

#### Dr. Englert:

Well, LDL management is the cornerstone of risk reduction in management of ASCVD. So the goal is for early, aggressive LDL reduction with sustained maintenance of those low LDL levels over the patient's lifetime. And so this has been described with the cumulative-exposure hypothesis, which states that the effect of LDL on ASCVD risk reduction depends on both the magnitude as well as on the duration of that LDL lowering.

So you have LDL as well as other small ApoB-containing lipoproteins that are going to freely enter the arterial wall. These lipoproteins are going to get trapped and oxidized. This leads to an inflammatory response and atheroma formation. And with continued exposure, you have additional LDL particles that are going to accumulate, leading to progressive plaque development.

And so that time immediately following an ACSVD event represents a critical window in the intensification of lipid-lowering therapy. And so in that first 90 days, patients are at highest risk for a recurrent event. And so we want to optimize our medical therapy early and aggressively.

And so high-intensity statins are the mainstay of therapy for our patients with ASCVD. We're going to up-titrate our statin therapy to the maximal tolerated dose. And so that's going to typically be atorvastatin 40 to 80 mg daily or rosuvastatin 20 to 40 mg daily.

Based on the LDL reduction that we're able to achieve with a high-intensity statin dosing, we're going to be aiming for that target of LDL less than 55. And based on the percent reduction that we still require, if needed, to achieve that LDL target, that's going to help us in the selection of the next lipid-lowering agent to achieve our LDL goals. And so you have to be familiar with the percent reduction you're expecting with these different agents, so the PCSK9 inhibitors, ezetimibe, bempedoic acid, and inclisiran.

And so for the same LDL reduction, the longer duration of that LDL control produces greater benefit. And we've seen this consistently in lipid-lowering trials, specifically with the medications, where you see the reduction in the events early on, especially in the first year, but that widens over time. The benefit gets greater the longer you have LDL control. So be aggressive early and regularly monitor those lipids.

**Dr. Malachowski:**

Well, that's fantastic, Randy. It sounds like you've got a lot of great hitters there. And it's important not just to have those hitters that you can get to the plate but also making sure that you have a really strong treatment lineup. So I love the insight you provide there.

I think the implementation on management is just as important as making sure that you are getting enough batting practice in. So having the ability to connect your patients with those statins, to look to see where you're able to achieve those lowering strategies, and then for patients that need a designated hitter or a different medication, having a protocolized strategy that is easy to execute will help get those patients on the products that they need, make sure that it's cost-effective, started as early as possible, and that they're able to maintain that care. So as we see those LDL-C levels come down, it's able to be provided at a cost-effective therapy over the course of that treatment.

Do you have any other highlights that you would want to share with the audience today on how they can help patients achieve this goal?

**Dr. Englert:**

So going into this with a regular monitoring routine in mind, so every time you're going to intensify therapy or when you're first initiating, until you get your patient down to your LDL target is going to be key. So be aggressive. Get aggressive. Get those numbers down early and then make sure you're regularly monitoring to ensure that your patients are achieving their targets and for good adherence.

**Dr. Malachowski:**

Fantastic. So some great key takeaways there. Starting early, driving that number therapeutic, get it as low as is recommended, and then making sure that you're using all of the products that are available for your patient to make sure that they can achieve that goal.

And I think the final piece is execution, making sure that we're able to get this to the patient as seamlessly as possible, as early as possible, and that we're able to maintain this advantage as long as possible is going to help our patients achieve those long-term successful goals that are going to lead to a longer and healthier life.

Well, thank you for tuning in, and we'll hope to hear from you again soon.

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