Transcript Details
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The Lp(a)-Lowering Landscape: Navigating Current and Future Therapeutic Options

Dr. Michos:
Welcome to Lipid 360. I'm Dr. Erin Michos. I'm a professor of medicine and cardiology at Johns Hopkins University, part of our Advanced Lipid Clinic, and I'm our associate director of Preventive Cardiology.

So severe hypertriglyceridemia is defined by triglyceride levels above 500, and once they get above 1000—or extreme hypertriglyceridemia—we see chylomicronemia in the blood, and patients are very at risk for pancreatitis, which is a disorder that has significant morbidity and even mortality associated with it.

There is a rare genetic disorder called familial chylomicron syndrome—or FCS—that is manifest by having monogenetic biallelic mutations in lipoprotein lipase. And these individuals have very severely elevated triglyceride levels, develop early-onset pancreatitis at a young age. And unfortunately, up until very recently, there was no available pharmacotherapy that they responded to because the traditional therapies to treat triglycerides, such as fibrates, omega-3 fatty acids, statins, they all require a functioning LPL enzyme, and patients with FCS don't have LPL.

But this year, we have our first agent available to treat FCS called olezarsen. It's an APOC3 inhibitor. APOC3 inhibits LPL, but there is other mechanisms that are independent of LPL, which is why inhibiting APOC3, even in FCS, can have substantial triglyceride lowering and reduce the risk of pancreatitis. And we have a second agent in this class, plozasiran, which is a small interfering RNA targeting APOC3, that hopefully is undergoing FDA review very shortly, and hopefully we will have a second agent for FCS.

But much more commonly in clinical practice is multifactorial chylomicron syndrome. Patients can also have very severe triglyceride levels, but they often have comorbidities such as diabetes and obesity. But often this is either from being heterozygous—maybe they only have one genetic defect in LPL—so there's a genetic risk plus environmental factors or polygenetic risk. And they can still be challenging to treat, even though they do have some response to traditional therapies.

So here at the American Heart Association, we saw the results of the CORE trial, results of olezarsen—that's that ASO inhibitor of APOC3—applied specifically to a severe hypertriglyceridemia population. And what was really remarkable is that when you look at those in the subset that had triglycerides above 880, again, substantial reduction in pancreatitis risk, and really a number needed to treat of only 1 in 4 with this agent to reduce a pancreatitis event.

So I'm very excited that we have new therapies for patients who are suffering from the more severe forms of hypertriglyceridemia.

Thank you for listening to Lipid 360. I'm Dr. Erin Michos.