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Targeting Mixed Hyperlipidemia with APOC3 Inhibition

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Dr. Taub:
This is CME on PACE-CME and ReachMD and I'm doctor Pam Taub and here with me today is my good friend and colleague Dr. Kosh Ray.

Dr. Ray:
Pam, great to be with you.

Dr. Taub:
Well, I can't think of anybody better to talk to hypertriglyceridemia about than you. And so let's start with reviewing some of the data on the clinical trials with APOC3 inhibition in patients with mixed hyperlipidemia.

Dr. Ray:
OK, so I think we want to start by defining mixed dyslipidemia. So these are patients who essentially have a high LDL and also a high triglyceride typically in that 150 to 500 milligrams per deciliter rate despite usually being on statin therapy and they're not uncommon. And some of this will be driven by obesity, diabetes. So we see this quite regularly.

And one of the issues that we've had is that a lot of the medications that we've had haven't really translated into reductions in clinical events. And these patients are not only at risk of cardiovascular disease, but also pancreatitis, not as much as the really, really high levels. So one of the trials that I want to talk about is a trial, called the MUIR trial, and there are others I'll mention as well and what we've now really realized is that triglyceride metabolism is a lot more complex.

And what MUIR did was study the population with this mixed hypertriglyceridemia in that in that range around about 300 or so and then with a dose finding study, typically 10/25/50, actually lowered the triglycerides down to somewhere between 100 and 150 and the dosing schedule was every three months. And this is a new class of drug, but it's not one that in terms of mechanism of action that we've not seen before. Inclisiran was a prototype and this is now just targeting a different protein, but with that same siRNA-based approach. And in the open label extension, typically when we do these shorter studies, because of the long duration of action, you've only got so many doses you've given. So what was seen in the open label extension is that this dosing frequency could be maintained with additional doses not causing any adverse effects. So it gives you that safety side of things as well.

I want to mention also another approach which is antisense oligonucleotide. And that was studied in the BRIDGE-TIMI 73a study. That produced similar-ish results. The dosing frequency is more often, it's more frequent, every month, but again the results looked very similar in terms of reductions in triglycerides. So that really now sets us up nicely for something that's potentially to be transformative in our clinical practice.

Dr. Taub:
Well, I think these patients with mixed hyperlipidemia are often overlooked in terms of triglycerides and LDL is what we focus on. But now we have so many incredible agents for LDL lowering so that residual risk is from triglycerides and we need to do more because our patients are still having high event rates.

Dr. Taub:
And so this has been brief, but a great discussion. And before we wrap up, what's your take home message?

Dr. Ray:
Well, the take home message of these exciting therapies for people with mixed dyslipidemia so that triglyceride in the 150 to 500 range requires infrequent dosing, looks to be very well tolerated and really provides quite marked reductions in triglyceride levels. You know the order of 50, 60, 70%. These are really effective treatments.

Dr. Taub:
Well, thank you for your insights, Kosh. I always learn something from you.

Dr. Ray:
That's very kind. Thank you.

Announcer:
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