

**PAUL RIDKER:** So the patients who in my clinic I'm most worried about are really in two categories. One are the genetically affected patients. We have a fair number of heterozygous FH patients with very high LDL levels. They're obviously going to develop disease 10, 15 years earlier in life. They do respond to statins. But getting their LDLs down much more aggressively is what we've been doing for quite a while. And those patients have been candidates for PCS9 inhibitors frankly for many years.

The second group, and the group I worry about much more actually because they're far more common, are what I consider my progressors, patients who just keep coming back with more disease. All cardiologists, all internists, see these patients. They're that group in our practice who have had, say, a stent, a second stent. They go on to have bypass surgery. They go on to have myocardial infarction. They go on to have a stroke.

They're telling us something profound about their biology. Having their LDL at 100 is not going to be good enough. So if the statin has not gotten it down below 70, we're going to go a lot lower. And many of those patients are going to say, look, why don't we take it down as low as we can possibly go.

Again, what's been wonderful about the data from ODYSSEY, from FOURIER, and then from SPIRE is the safety side. If we can take LDLs down to 25 or 30 and not have to worry about endocrine effects, not have to worry about any other issues, then we need to be considering these drugs.

Now, another simple way of doing this is to say, if the on-treatment LDL, past a high intensity statin, is above 100, that's a patient who I think we would all agree more LDL lowering should be initiated. And like anything else, it's diet, exercise, smoking cessation. You might want to go with ezetimibe. You might want to consider a PCSK9 inhibitor.

I think the challenge has obviously been access. How do we get these drugs to our patients? And how do we get past the frustration that a lot of cardiologists feel writing these prescriptions?