PAUL RIDKER: I think most of us in the lipid community have made the assumption, for 20 years frankly, that lower is better for LDL cholesterol. Our own JUPITER trial-- remember, designed in 2001, at a time when the LDL guidelines said, take it very aggressively in primary prevention, from 160 all the way down 130. That's where we were in 2001.

And back then, my group said, well, we're going to give a high-intensity statin, rosuvastatin at 20 milligrams, to people whose LDLs were already at 100. But they were at risk because they had an elevated C-reactive protein. And, of course, JUPITER gave the largest relative risk reduction of any statin trial done.

Now, admittedly, I see the world through inflammation-colored glasses. It's the biology that we're interested in. And the interface between lipids and inflammation is terribly interesting. But the fundamental finding, that we could take with a statin, LDLs down in the 30s and 40s and the patients did very well, was a signal that all the PCSK9 trials had to follow.

Now, when we designed the SPIRE trials, SPIRE-2, the entry criterion was, you're on a high-intensity statin but the LDL is still above 100. Remember, that's the one trial that gave the largest risk reduction in the PCSK9 arena. And we've gotten replication of that effectively now in ODYSSEY outcomes, saying, in the group where the LDLs are in that-- above 100, 110 range, is really where the sweet spot clearly is.

These patients need more ApoB reduction. They need more LDL reduction. And we can get down there.

I think the challenge has been with expensive drugs, how do you figure out who needs that the most? And I've said this many times. So I'm turning 60. Reality is, I'd rather be 60 years old with heterozygous FH than 60 years old, having had a myocardial infarction, bypass surgery, and two stents. Because that latter patient is very aggressively progressing their disease. And the former might get away with other issues.

Probably I'm going to treat both in my clinic. But my concern has been, particularly with payers, I'm allowed to push on the genetic side. But I'm having a hard time pushing on what I consider very high risk clinical side.