

**PAUL RIDKER:** I think what we're talking about here is differences between biologic understanding and the practical realities of what payers are going to allow us to do. So again, yes, we have the biologic data from FOURIER, from SPIRE, from ODYSSEY, telling us that taking the LDL down extremely low is ultimately more beneficial.

The incremental benefit, however, is getting smaller as we get lower and lower. So again, I'm concerned about those patients whose LDLs are still above 100 on a high-intensity statin. If we can get the payers to at least let us start there, we'll have made a big advance in this field.

Sure, from a biologic perspective, many of us would like it below 70, below 60, perhaps below 50. But the real issue right now is getting these drugs out to at least some patients. And I'm going to start with my highest risk individuals.

The flip side of this-- and we've talked about this and published these data, as have the folks from FOURIER-- is that even if you did take the LDL down to 20, we're not addressing the other half of this disease burden. So the inflammatory part of this is very real.

The patients who have LDLs of 20 in FOURIER and in SPIRE-- and I'm sure it's also true in ODYSSEY-- the CRP levels are still giving a very clear readout of very high risk. In FOURIER, those with an LDL of 20 and a CRP above 3 had a higher absolute risk than those with an LDL of 100 when the CRP was low. It's two different biologies.

So ultimately, we're going to have to address both of them. Right now, we have the ability to address the LDL piece. And I agree, we've just got to get them lower.