ROBERT S. ROSENSON: The question of, how low should the LDL cholesterol be is an important question, and the PCSK9 inhibitors have allowed us to explore this hypothesis. In a recent paper that I led in collaboration with Sergio Fazio, Rob Hegele and Chris Cannon, we identified individuals who would require more aggressive LDL cholesterol lowering based on randomized clinical trial. Who are those individuals? Individuals on maximally tolerated statin plus ezetamibe who we have multivessel disease, a recent myocardial infarction, lower extremity arterial disease.

And in those individuals, we advocate an LDL cholesterol level less than 50 mg per deciliter. Why did we select a number of 50 milligram per deciliter? Well, this concentration was chosen because of the FOURIER trial and the ODYSSEY Outcome study, which both had up-titration at an LDL cholesterol 50 to 55 milligram per deciliter. So we feel that, based on the data, that these high risk individuals would drive more benefit from lowering LDL cholesterol to less than 50 mg per deciliter.

I think it's important also to say that the PCSK9 inhibitors have allowed us to explore the lower end of the LDL cholesterol. And it turns out there is no lower threshold. These concerns that were present from the statin trials, that there might be increased risk of side effects-- such as suicide, homicide, hemorrhagic events-- were not seen with the PCSK9 inhibitors. And so I think it's important for all of us as clinicians who guide our patients to provide the current information that indicates that these therapies are highly effective and very safe, with regards to the concerns that were raised with previous agents such as the statins.