ROBERT S. ROSENSON: So which patients might be considered for PSCK9 inhibitors? I must emphasize that we use a statin. We use a high intensity statin in our patients with cardiovascular disease, because we have an extensive long-term database, randomized clinical trials, that support the use of high intensity statins.

Ezetimibe also has benefit in the IMPROVE-IT trial, and it's a far less expensive alternative to a PCSK9 inhibitor, even with the price reduction. One has to be conscious about health care economics and utilize PSCK9 inhibitors appropriately. Who are the patients that I select?

These are the individuals who have cardiovascular disease, that high risk population with prior myocardial infarction, particularly in the last two years, angiographic evidence of multivessel cardiovascular disease, individuals who have lower extremity arterial disease or a prior stroke, and other individuals who have a renal impairment. We also know that certain biomarkers identify individuals who are at higher risk for cardiovascular events, such as those with elevated lipoprotein(a) levels.

So I want to focus my attention on providing PCSK9 inhibitors to those groups of individuals who have been shown in randomized clinical trials to drive the greatest benefit and where actually cost effectiveness is optimal. Maybe in the years to come, we'll learn about other groups that are not considered as high risk for PCSK9 inhibitors and expand the treatment to those individuals. Clearly, the price reduction that we've recently seen with evolocumab will change this dynamic.

And actually, the PCSK9 inhibitor has a price that's similar to other agents, such as SGLT2 agents or ticagrelor. So our whole thought process about the extremely high cost of the PCSK9 inhibitor needs to be revisited with this price reduction and based on the clinical trial data that supports the efficacy and safety of this therapy.

There's another group of individuals where I use PCSK9 inhibitors with regularity, and those are patients with familial hypercholesterolemia-- individuals who most often have an LDL receptor defect, maybe a defect in apolipoprotein(b) or a PCSK9 gain of function. These are individuals of course who had elevated LDL cholesterol levels before they were ever born. They have life long exposure to high LDL cholesterol.

And we know from prospective studies confirmed genetically, that if you have a familial hypercholesterolemia, your risk of a cardiovascular event is increased 22-fold compared to individuals with LDL cholesterol levels let's say less than 190 milligram per deciliter. Certainly, a high LDL cholesterol alone increases the risk of cardiovascular event six-fold compared to people with an LDL cholesterol level less than 190 milligram per decilter. But the genetics identify populations at particularly high risk.

Often individuals with familial hypercholesterolemia have high lipoprotein(a). And we know that our conventional therapies-- statins and ezetimibe-- do not affect the LPA level, but PCSK9 inhibitors do. We need more information about the patients with familial hypercholesterolemia to determine how important the reduction in LPA is on cardiovascular events in those individuals. And that may require a primary prevention trial to clearly elucidate those issues.