SPEAKER: For the many years where our strongest medications were statins, high potency statins, and maybe combination of statins with ezetimibe, was very rare the situation where you were driving somebody's LDL to uncomfortably low zones. Now, with PCSK9 inhibitors, it's pretty much the standard. So the majority of patients who are taking a statin or statin plus ezetimibe and then they add a PCSK9 inhibitor, they are likely to get below 30, and sometimes below 20, sometimes below 15.

And so there are questions of, how safe is that for me? Or should I worry? Should I back titrate? What we know is that there are no signals out there from extremely low LDL reduction. You have to keep in mind that driving LDL down doesn't mean eliminating cholesterol from the blood. The VLDL cholesterol still provide plenty for the distribution in the circulation.

So there were concerns many years ago. The two people that won the last Nobel Prize for cholesterol, Goldstein and Brown, they predicted that it would be not safe to reduce LDL below 25 in the sense that cells need to get some cholesterol from the outside, and when the threshold is below 25 they may not get enough of a concentration. This has not translated into any signals in terms of cognition, memory, and other types of side effects. So we are at a different stage today, where we believe that there is no need to have any conversations about, warnings, or concerns for patients who happen to fall with their LDL below 30 or 25 or 20, unless of course there are reports from patients that must be explored.