## ERIK S. STROES:

So now that we know that LDL lowering is the key and that offers you the benefit, actually, this brings us back to how vigorous we should be in trying to lower LDL. For instance, if we get patients referred with so-called statin intolerance, and they tried everything, we often continue to try even more.

We all know about the studies that if you, for instance, give rosuvastatin, 2.5 milligrams-- which is virtually nothing-- but you're able to give 2.5 milligrams three times a week and patients really take it, you get-- not very potent-- but you get at least maybe up to 20% LDL reduction. If you add on ezetimibe and the patient tolerates it, you can go from 170 maybe to 130. And then if it's a high risk patient, you can add PSCK9 on top of this very low backbone of the statin therapy, not every day regimen, where then all of a sudden you can reach values which are very low.

And there is a strange phenomenon which we often see. If you give PCSK9, the mean reduction is 60%. But actually, there's a waterfall plot, and it can differ from 20% to 85%, and vary, where you have relatively refractory patients. And in those patients, if you succeed in striving for triple therapy-- so maximally tolerated statin therapy, whatever dose, whatever number of pill takes a week combined with the injection once every two weeks-- that actually gives you kind of a potentiation of the effect. Completely understanding, we don't do it. But the combination often resolves the issue of hyper-responsiveness. So don't give up, even if you tried four different statins.