You know, one of the things that we find in patients who have this high burden of athero-- they have a lot of comorbidities, they have polyvascular disease-- they tend to be patients that, despite being on high intensity statin therapy, even when you've ezetimibe, they tend to be the patients who don't have very low LDLs despite maximal therapy. So these aren't patients that just on a statin, you drive their LDL to 40.

So they're often in this gray zone. Maybe they're somewhere between 70 to 100, where a lot of people say, well, that's pretty good. But actually, for that patient, that's not very good.

And so if they're on a high intensity statin and their LDL is still somewhere between 70 and 100, maybe even they're above 100, those are patients that you really want to escalate therapy. And certainly, adding ezetimibe is great. And I do that often to many of my patients.

The problem is that it's a relatively modest reduction. And so I do add that, the high intensity statin therapy. But if you really want to lower their risk substantially, and we know that risk is driven by their LDL, that often those patients are really going to benefit from a PCSK9 inhibitor. Because you really want to take that patient from 75, 80 down to 40, 35. And with a PCSK9 inhibitor, it's really the only way to do that. Because the absolute event rates in these patients, even with an LDL of 75, is actually still quite high.

On the flip side, if you have younger patients who have early disease, who have a family history, these patients often have a genetic predisposition to elevated cholesterol levels. Some of them we may be able to diagnose with heterozygous FH. But it's actually-- frequently these patients have elevated LDLs, but they don't really fall into any clear genetic diagnosis.

To be honest, even on high intensity statin therapy, these patients, their LDLs are often still significantly elevated-- well above 70. And because their lifetime risk over many decades is so high, in these patients who are young, who have early thrombotic events, really the only way to substantially lower their risk over the lifetime of that patient is a PCSK9 inhibitor.

So I think whether you're looking at patients who are already on maximal therapy, who have a lot of comorbidities, you really want their LDLs more to be in the 40s and 50s. But these younger patients, who people say, well, they've just had one MI-- but they're 42, they're 45. Having an LDL of 75 for 35 years is not going to get it done. That we know from really genetic studies looking at LDL from birth that that cumulative area under the curve, that's a huge burden of athero over a long period of time. And those patients are going to have poor outcomes when they get to their 60s and 70s.