

Dr. BHATT: For NRAC, were both very well-conducted cardiovascular outcome trials examining PCSK9 inhibitors versus placebo. In the case of FOURIER, it was evolocumab. In the case of ODYSSEY, it was alirocumab. And as far as the primary endpoint, which was a conglomerate of different ischemic events-- important ischemic events-- remarkably, both trials showed approximately a 15% relative risk reduction. So it provides great reassurance that there is something going on in terms of a class effect of PCSK9 inhibition producing important cardiovascular events in patients who are already being well-treated with statins, but as well, other good background therapy.

So in toto, incremental advance here in our knowledge of risk reduction, of reducing residual risk-- in particular, with the LDL lowering axis. And much like the IMPROVE-IT trial had moved the field forward showing that lower is better-- in that case, with exetimibe added to statin-- now we have two large well-done outcome trials showing the same with PCSK9 inhibition that is even further LDL lowering, provides clinical benefit. It does so safely without any major side effects, other than slight excesses in things like injection site reactions, and is incremental to other established therapies-- so really, another tool in our toolkit, another trick up our sleeve to help reduce residual risk in patients and elevated risk.

And what do I mean by elevated risk? Well, between the two trials, it covers a large part of the atherosclerosis universe. FOURIER examined patients with stable atherosclerosis in the coronaries, the peripheral arteries, or cerebral arteries. The ODYSSEY trial examined ACS patients who'd had an ACS-- I'll say, recently, but it was actually 1 to 12 months, so even kind of remote from their ACS. And both trials showed a 15%-ish reduction in MACE. So that's really reassuring to see that sort of concordant result. And the degree of risk reduction, I think, is clinically important. Because this is above and beyond what we can achieve with contemporary therapies such as statins, including high intensity, high potency statins.