SPEAKER: We now have two completed trials with PCSK9 inhibitors. First, we had the FOURIER trial with evolocumab, and more recently we have the results of the ODYSSEY outcomes trial with alirocumab. So Fourier took 27,000 patients with stable coronary disease, randomly assigned them to the addition of either evolocumab or placebo on top of their statin therapy.

Overall, there was a significant 15% reduction in the primary mace plus outcome and a 20% reduction in the key principal endpoint, which was the more traditional mace, that is CV mortality, MI, and stroke. Importantly as well, there were no new safety issues that emerged.

ODYSSEY outcomes took a somewhat different population. They took patients with a relatively recent acute coronary syndrome, 4 to 12 months prior to randomization. Again, very large trial, 17,000 patients, who had either alirocumab or placebo, again, added to statin therapy. Although, in this case, the vast majority of patients were indeed on high dose statin therapy.

The dose of alirocumab was titrated to get patients into the desired range of LDL. And again, very low LDL levels were achieved. Again, a highly statistically significant 15% reduction in the primary endpoint.

One difference between the outcomes, however, was that in order to see outcomes, there was a significant reduction in total mortality observed. Both of these trials included a large proportion of patients with diabetes, as you would expect for patients with cardiovascular disease.

In the Fourier trial, about 40% of the patients had diabetes at baseline. There was similar LDL reduction, similar relative risk reduction, and a greater absolute risk reduction, given the fact that these are higher risk patients.

The ODYSSEY outcome's diabetes subset data were presented at the American Diabetes Association meeting. And again, showed similar efficacy, similar safety, and greater absolute risk reduction in their diabetic cohort, which was about 25% of the total population.