

VIVIAN

FONSECA:

There is still an unmet need for cardiovascular disease, particularly in people with diabetes. The number of trials with new drugs for diabetes, such as SGLT2 inhibitors and GLP-1 receptor agonists have shown benefits that are somewhat unexpected but very, very important for managing glucose. Despite that, if you look at the results and the curves you still see a significant number of people having cardiovascular events even on these medications. And by events here I mean atherosclerotic events like strokes and heart attacks.

We now have to go back and look at other risk factors again, blood pressure lowering and LDL lowering. And here too we have some very important clinical trial results. First of all, should we have lower goals? And the answer is very clearly, yes.

A few years ago we moved away from having fixed goals and focused on getting everybody on high intensity statins. But the improving trials showed that even people on high intensity statin, if they lowered their LDL further, had a benefit. And most of that benefit was seen in people with diabetes.

In fact, there was hardly any benefit in those without diabetes. But the benefit was small because the LDL lowering with ezetimibe on top of a statin is actually very modest. Even so, lowering the LDL to about 55 or lower led to a significant reduction in events in these people with diabetes.

So I was part of the AACE Lipid Guideline Group that came to the conclusion that there are few people who have what is called extreme risk. And I like that term because we use high risk for most people with diabetes. We've had the LDL goal of less than 70 for many, many years.

But there are people who take high intensity statins and still have events, and those people need additional LDL lowering. And the IMPROVE-IT trials showed that you can do something further for them. Then came PCSK9 inhibitors, and these were a game changer in terms of LDL lowering. They could lower LDL down to the 30s very safely in a lot of people.

And now we have outcome trials, FOURIER and ODYSSEY, showing that you can reduce cardiovascular events. With FOURIER, it with myocardial infarction and stroke. And in a very short period of time, that was a shorter duration trial than ODYSSEY, there was a significant reduction in events.

ODYSSEY was a longer duration trial, had a larger number of patients with diabetes, and showed a reduction not only in these events but also in mortality. So this is a very significant improvement beyond statin therapy. There was one other interesting finding in those trials. And that is there are some people with diabetes who, despite taking a high intensity statin still have an LDL cholesterol a little above 100. And lowering that down to not 30, but with PCSK9 you can even get it below 55, which is what the AACE goal has been recommended for people with extreme risk, led to a very significant reduction.

In fact, the best result in ODYSSEY was in people with diabetes whose LDL was a little above 100, above what their goal should be, and bringing them down to the goal that has been set for extreme risk people, less than 55. They had a very dramatic reduction in events and mortality.