Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/cme/long-term-cardiovascular-risk-reduction-with-evolocumab-insights-from-fourier-ole-at-aha-2026/85394/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Long-Term Cardiovascular Risk Reduction With Evolocumab: Insights From FOURIER-OLE at AHA 2026

Announcer:
You're listening to GLC on ReachMD. This activity, titled 'Long-Term Cardiovascular Risk Reduction With Evolocumab: Insights From FOURIER-OLE at AHA 2026' is provided by Global Learning Collaborative.

Dr. Sabatine:
Hi, I'm Marc Sabatine from TIMI Study Group and Brigham and Women's Hospital at Harvard Medical School, and I'm here at AHA 2026 and wanted to share some exciting data that's going to be presented here at this congress. There's going to be data presented on the external control arm analysis from FOURIER-OLE.

It seems like a complicated topic, but it's really fundamental to our understanding for lipid lowering. To take a step back, we know that LDL cholesterol lowering reduces the risk of cardiovascular events. We also know it takes time for that clinical benefit to kick in after we reduce levels of LDL cholesterol.

And of course, that stands to reason. If we lower someone's LDL cholesterol today, we don't expect their risk of a myocardial infarction to be lower tomorrow. Rather, the lower levels of LDL cholesterol will lead to healthier arteries, but that takes months to develop. It's those healthier arteries that will then translate into a lower risk of myocardial infarction, a lower risk of stroke, but that's over months to years. And then it's the lower risk of those events that then translates into lower risk of cardiovascular death.

And so in the FOURIER trial, that trial was shorter than we had hoped for. It only lasted a median of 2.2 years. If we know from the statin trials that the benefit is about half as much in the first year as subsequent years, then the effects we saw in FOURIER were likely an underestimate of the true benefit.

And in fact, that's what we saw in FOURIER. There was a 20% risk reduction for CV death, MI, or stroke, but that was 16% in the first year and 25% after the first year. How can we gain more information about that? Well, a couple of different ways. One way is there was the FOURIER open-label extension in which everyone in the trial who was still alive and on study drug in certain regions of the world that were participating in the open label extension all transitioned over to evolocumab, and we followed those individuals for 5 years.

Now, what's interesting for that group is that even though in the open-label extension everyone was getting evolocumab, everyone's LDL cholesterol levels were super low, there was still a difference in cardiovascular risk for the people who had started evolocumab earlier. So those people whose arteries had been marinating in lower levels of LDL cholesterol had about a 20% lower risk during the open-label extension. So that's the so-called legacy effect for statins.

That's one way to look at it. Another way to look at it, to ask the counterfactual, is what happens if the placebo arm didn't switch to evolocumab? What if they had stayed on placebo? And so the statistical group at Amgen led a very nice analysis that then tried to model out using external controls what that event rate would be in the placebo arm if they had stayed on placebo.

This requires very careful matching of patient characteristics and then making sure that the event rates in your external control seem to match the event rates in the trial, which we had the benefit of a placebo arm in FOURIER to do that matching, and they did a good job

© 2026 ReachMD

with reasonably close event rates.

And those analyses suggested that had we compared evolocumab to placebo over about 8 years, we would have seen a 29% risk reduction, and those are through modeling exercises. The third, and perhaps the best way to do it, is just to do a trial that lasts a long time, and that's what we did with VESALIUS.

That trial had a median follow-up approaching 5 years, and in that trial, there was a 27% risk reduction for CV death, MI, or stroke. So all these data are really highly consistent. And I would say the take-home point is that for lipid lowering, you can't start early enough, that the benefit grows over time, and we have data now from FOURIER, from FOURIER open-label extension, from the external control analysis, and from VESALIUS that all point to really the robust clinical benefits over time with intensive LDL cholesterol lowering.

So hope you found this interesting. It's been a very exciting AHA, and thanks so much for joining me.

Announcer:
You have been listening to GLC on ReachMD. This activity is provided by Global Learning Collaborative. Thank you for listening!

© 2026 ReachMD