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ROSENSON:**

The clinical trials with PCSK9 inhibitors-- FOURIER, SPIRE-2 showed a reduction in myocardial infarction, stroke, and cardiovascular events, but no change in mortality. These were very short-term studies. And typically when we evaluate mortality, the studies are designed to last for a period of five to six years. Mortality reduction seen in the 4S trial, the Lipid trial, and borderline significance in the West of Scotland trial, these changes were seen at about five to six years.

The ODYSSEY Outcome study, which lasted longer, and FOURIER SPIRE-2 showed a reduction in all cause mortality, which is favorable. However, in the statistical plan, they did a hierarchical analysis that mortality could only be evaluated if there was a reduction in coronary heart disease, deaths, and cardiovascular deaths. And there were no reduction in those deaths. And so according to the statistical plan, the mortality should not have been analyzed.

However, apart from the clinical trialists, the fact that people actually live longer after receiving alirocumab is a very favorable finding. Of course, we remember shortly after the release of the PCSK9 inhibitors, there were certain skeptics who said, well, there was no change in survival. I'm going to wait. I'm not going to use these therapies. Well, there was a reduction in mortality.

Clearly, we need to understand the non-cardiovascular deaths that contribute to the reduction in total deaths. But no one needs to look at the bottom line. People actually did live longer, and that's encouraging. And hopefully we'll see further reduction in mortality with the FOURIER Open Label Extension that is following individuals for another three to five years after the end of the trial.