Yuji Matsuzawa

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Exciting results of the effects of inhibiting PCSK9 on the risk of having a cardiovascular event were presented at the recent meeting of the American College of Cardiology (ACC) held in March 2017 in Washington, DC.

The FOURIER trial was the first trial to investigate the cardiovascular benefits and safety of evolocumab, a monoclonal antibody that inhibits the action of PCSK9 in plasma in an effect that increases the number of cell surface LDL receptors and thus lowers the level of LDL cholesterol in plasma. The study was conducted in more than 27,000 people who remained at high risk despite taking effective doses of statins. Evolocumab lowered LDL cholesterol levels by 59% to very low levels and reduced the risk of having a cardiovascular event by a highly significant 15%. There was a 20% reduction in the main secondary end point of cardiovascular death, myocardial infarction, or stroke. There was no evidence of any safety concerns. This trial provided clear evidence of both the cardiovascular benefits and the safety of reducing the level of LDL cholesterol to very low levels.

A group of participants in the FOURIER trial was included in a study named EBBINGHAUS. This study was also presented at the ACC meeting in Washington. It investigated the effects on cognitive function of lowering LDL cholesterol to very low levels in people treated with evolocumab. It was found that there were no differences between treatment with evolocumab and placebo in any of a battery of tests of cognitive function, essentially refuting earlier concerns about effects of very low levels of LDL cholesterol on cognitive function.

Another extremely interesting study of PCSK9 inhibition was the ORION-1 trial, also presented at the ACC meeting. This trial tested the effects of inhibiting the synthesis of PCSK9 using the novel ribonucleic acid interference drug inclisiran. The drug was given either as a single injection on day one or as two injections given on day one and day ninety. PCSK9 levels in plasma were reduced by up to 74%. With the single dose (given on day one) the time-average reduction in LDL cholesterol over nine months was 41.9%. With the two doses (given on day one and on day ninety) the time-average reduction in LDL-C over nine months was more than 50%. There were no serious safety concerns. These results indicate that major sustained reductions in LDL cholesterol can be achieved with apparent safety with as few as two to three injections per year. Cardiovascular clinical outcome trials are now needed to establish the long-term benefits and safety of this drug.