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ODYSSEY Outcomes Trial: Does Reduction of Lipoprotein Reduce Cardiovascular Risk?

Lipoprotein is believed to possess pro-atherogenic, pro-thrombotic, pro-inflammatory, and pro-oxidative properties. High levels of lipoprotein have been associated with incident cardiovascular disease in population-based epidemiological analysis and in patients with coronary heart disease (CHD). There is also a linear relationship between lipoprotein concentration and incident CHD. European guidelines recommend that lipoprotein should be a potential target for treatment if concentrations are ≥50 mg/dl.

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While observational data suggest a potential benefit of lipoprotein lowering on cardiovascular outcomes, there are currently no randomized data that would indicate that medications that are used to lower lipoprotein also reduce cardiovascular risk. For example, Niacin reduces lipoprotein by 15 to 25% but is not known to reduce death or ischaemic cardiovascular events. Similarly, anacetrapib lowers lipoprotein by 25% but has only modest benefits when it comes to preventing cardiovascular events or providing cardiovascular benefits.

In the **ODYSSEY Outcomes: Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab** trial, researchers tested the hypothesis that baseline lipoprotein predicted recurrent major adverse cardiovascular events following an acute coronary syndrome in patients who received statin therapy. The researchers also evaluated whether the decrease in lipoprotein concentration with alirocumab, a PCSK9 inhibitor, was associated with a decreased risk of major cardiovascular events independent of LDL-C reduction.

The ODYSSEY outcomes trial included 18,9254 patients aged 40 years or older who had experienced an acute coronary syndrome 1 to 12 months before randomisation and who had an LDC-level of ≥70 mg/dl, non-HDL-C level of ≥100 mg/dl, or an apolipoprotein B level of ≥80 mg/dl on high-intensity statin therapy. Study participants were randomly assigned to treatment with alirocumab 75 mg subcutaneously every 2 weeks or placebo. The primary endpoint of the study was coronary heart disease death, nonfatal myocardial infarction, ischaemic stroke, or unstable angina that required hospitalisation. Secondary endpoints included coronary heart disease death or nonfatal myocardial infarction, fatal or non-fatal ischaemic stroke, cardiovascular death, and all-cause death. Lipoprotein was measured at 4 and 12 months.

Results of the study show that baseline lipoprotein levels and LDL-C predicted major cardiovascular events. Alirocumab reduced lipoprotein, corrected LDL-C, and reduced the risk of major cardiovascular events. Overall, lipoprotein lowering by alirocumab was found to be an independent

contributor towards the reduction of major cardiovascular events. This suggests that lipoprotein should be an independent target after an acute coronary syndrome, as already recommended by major European guidelines.

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