Lecture Abstract or Synopsis for publication

PCSK9 INHIBITION AFTER ACUTE CORONARY SYNDROME: WHO SHOULD BE TREATED?

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Abstract

Patients with acute coronary syndrome (ACS) face a high risk of recurrent ischemic cardiovascular events. Some of this risk is attributable to lipoprotein abnormalities and may be modified by lipid-lowering interventions. Statins have been the cornerstone of this approach for two decades and are applied almost universally for patients with ACS. Now, PCSK9 inhibitors have the potential to lower levels of LDL cholesterol to unprecedented low levels, particularly on a background of statin therapy.

The ODYSSEY OUTCOMES trial (clinicaltrials.gov NCT01663402) compared the effects of the PCSK9 inhibitor alirocumab with placebo on cardiovascular outcomes in 18,924 patients with recent ACS and elevated levels of atherogenic lipoproteins despite intensive or maximal tolerated statin treatment. Median follow-up was 2.8 years, with 8242 patients eligible for follow-up of 3 to 5 years. Alirocumab reduced the primary endpoint of coronary heart disease death, non-fatal myocardial infarction, ischemic stroke, or hospitalization for unstable angina (9.5% vs 11.1%, HR 0.85, 95% confidence interval [CI] 0.78-0.93, P<0.001). All-cause death, a secondary endpoint, was also reduced (3.5% vs 4.1%, HR 0.85, 95% CI 0.73-0.98). Adverse events were similar in both groups except for an excess of injection site reactions, usually minor, with alirocumab.

Since PCSK9 inhibitors are injectable biological agents, it is important and practical to identify patients most likely to benefit from treatment. Among prespecified subgroups of the trial population that were at high absolute risk for recurrent cardiovascular events and accordingly derived a large absolute benefit of treatment with alirocumab were those with baseline LDL cholesterol of at least 2.6 mmol/L; with diabetes, polyvascular disease, or prior coronary artery bypass surgery; with statin intolerance; or with high levels of lipoprotein (a). Data from each of these subgroups will be presented and discussed.