

## Atherosclerosis and Lipid Lowering: is there a Need for New Agents?

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### Editorial

Cardiovascular disease (CVD) is the leading cause of death worldwide. Among well-known risk factors, such as visceral obesity, sedentary lifestyle, metabolic syndrome, smoking, hypertension, age, gender, family history of heart attacks, diabetes, low levels HDL-C, high levels of LDL-C and total cholesterol are very strong predictors of CVD events and death [1-5].

In recent years, there have been significant advances in the elucidation of biomarkers of atherosclerotic disease, and also their pathogenesis, prevention and treatment. Atherosclerosis is a systemic inflammatory disease characterized by on-going progression in response to systemic risk factors and local pro-atherogenic stimuli that leads to acute myocardial infarction, stroke and lower limb ischemia [6].

An intriguing question is what is the real level cardio protective LDL cholesterol? Especially for patients with a history of heart attack, peripheral artery disease, or stroke: is 70 mg/dL, which is currently recommended or should go down to levels of 40 or 30 mg/dL?

Statins has substantially reduced CVD events around the world and is recommended as first-line therapy for CVD management. However, a need for other lipid-lowering agents, because some patients do not tolerate statins due to adverse events, or cannot reach LDL-C level desired because of high levels of LDL-C, or patients with very high risk cardiovascular events need more intensive reduction therapy [7-9]. Can we pay the benefits of these new agents when statins are effective and inexpensive?

Zhang et al. reported a meta-analysis study to evaluate the safety and efficacy of anti-PCSK9 antibodies in randomized, controlled trials (RCTs). Twenty-five RCTs encompassing 12,200 patients were included. The study showing largely no significant difference between anti-PCSK9 antibodies and placebo (or ezetimibe), except that alirocumab was associated with reduced rates of death (relative risk (RR): 0.43, 95 % CI: 0.19 to 0.96,  $P=0.04$ ) and an increased rate of injection-site reactions (RR: 1.48, 95 % CI: 1.05 to 2.09,  $P=0.02$ );

evolocumab reduced the rate of abnormal liver function (RR: 0.43, 95 % CI: 0.20 to 0.93,  $P=0.03$ ), both compared with placebo. Evolocumab and alirocumab substantially reduced the LDL-C level by over 50%, increased the HDL-C level, and resulted in favourable changes in other lipids [9].

New agents, as well as prevention programs should be implemented in order to decrease the morbidity and mortality caused by atherosclerotic events.

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