What do we get from recent statin and CETP inhibitors trials?

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Low density lipoprotein cholesterol (LDL-C) has been well known to be a major cause of atherosclerotic cardiovascular disease (ASCVD). LDL-C lowering treatment with statin showed a significant reduction in cardiovascular event in previous clinical trials and thus LDL-C reduction is currently recommended as a primary target to prevent ASCVD. Moreover, results of clinical trials and meta-analyses indicated that high-intensive statin treatment lowers LDL-C levels and risk of nonfatal cardiovascular events compared with moderate-intensity statin treatment. However, residual risk of cardiovascular events and safety concerns of high-intensity statin treatment exist. Recently, IMPROVE-IT study showed that ezetimibe plus moderate-intensity statin therapy after acute coronary syndromes incrementally lowers LDL-C levels and improve cardiovascular outcome compared with moderate-intensity statin therapy. Consequently, the results of IMPROVE-IT study were incorporated in 2017 American Association of Clinical Endocrinologists (AACE) /American College of Endocrinology (ACE) guidelines for management of dyslipidemia and prevention of cardiovascular disease and 2017 American Diabetes Association (ADA) recommendation. However, despite these efforts of lowering LDL-C, a substantial residual cardiovascular risk still remains. Here includes other lipid abnormalities such as low high density lipoprotein cholesterol (HDL-C). Previous observational studies have reported that low HDL-C is associated with increased risk of ASCVD, while the risk of CVD decreases by 2-3% per 1mg/dL increase in HDL-C. The most representative agents to primarily increase HDL-C are cholesteryl ester transfer protein (CETP) inhibitors. CETP plays a main role in the transfer of cholesteryl ester from HDL into triglyceride-rich lipoproteins. Accordingly, inhibition of CETP results in raised HDLC and lowered LDL-C. Until now, four CETP inhibitors including torcetrapib, dalcetrapib, evacetrapib, and anacetrapib were introduced and all of them significantly raised HDLC from 30% to 133%. However, the results of CV outcome in clinical trials were different among the four agents. Torcetrapib increased the risk of cardiovascular event and total mortality in patients at high cardiovascular risk (ILLUMINATE trial). Dalcetrapib and evacetrapib also did not result in a lower rate of cardiovascular events.
in patients with recent acute coronary syndrome and high risk vascular disease, respectively (dal-OUTCOMES and ACCELERATE trials). Meanwhile, anacetrapib significantly decreased incidence of major coronary events in patients with atherosclerotic vascular disease (REVEAL trial).

This topic focuses on summarizing the major results of recent statin and CETP inhibitors trials and how to interpretate and implicate the trials’ results in real clinical practice.

References