

## FUTURE TREATMENTS

The future of treatment options for dyslipidemia will most likely involve the evaluation of other parameters besides LDL-C. Advanced lipid testing that evaluates LDL particle size, HDL particle size, direct measured LDL, homocysteine, lipoprotein (a), and CRP are gaining popularity. Additionally, the measurement of apoB may eventually overtake LDL as the primary monitoring parameter for dyslipidemia. ApoB is the primary lipoprotein in LDL-C and is indicative of the amount of small dense LDL particles that are known to be more atherogenic and are more commonly present in patients with CHD, than that of the large buoyant LDL particles. Some of the new innovative drug therapies such as torcetrapib (cholesteryl ester transfer protein inhibitor) and lapaquistat (a squalene synthase inhibitor) have failed to reach the market due to increases in mortality and liver toxicity, respectively. However, another cholesteryl ester transfer protein inhibitor, anacetrapib is still being investigated. Darapladib, a selective lipoprotein-associated phospholipase A2 (Lp-PLA2) inhibitor, is also being studied. Lp-PLA2 is a marker of vascular inflammation, produced by macrophages, within the atherosclerotic plaque itself. This substance attaches to LDL-C and is responsible for the hydrolysis of oxidized phospholipids on LDL-C particles. It is considered an emerging risk factor for CHD.

The most promising drugs to lower LDL levels are inhibitors of proprotein convertase subtilisin/kexin type 9 (PCSK9). Normally, LDL receptors bind LDL and internalize it for subsequent lysosomal degradation, and then the receptors return to the plasma membrane to repeat the process. The enzyme PCSK9 prevents LDL receptors from returning to the cell surface by facilitating their degradation. Monoclonal antibodies (evolocumab, alirocumab, and bococizumab) that inhibit PCSK9 activity are in various stages of new drug development. Successful inhibition of PCSK9 allows continuous LDL receptor recycling and dramatic reductions in plasma LDL levels.

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