[1] Effect of ETC-1002 on Serum Low-Density Lipoprotein Cholesterol in Hypercholesterolemic Patients Receiving Statin Therapy. Ballantyne CM, McKenney JM, MacDougal DE et al. The American journal of cardiology 2016.ETC-1002 is an oral, once-daily medication that inhibits adenosine triphosphate citrate lyase, an enzyme upstream of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, to reduce cholesterol biosynthesis. ETC-1002 monotherapy has demonstrated significant reduction in low-density lipoprotein cholesterol (LDL-C) compared with placebo in phase 2 studies. The objective of this study was to compare the lipid-lowering efficacy of ETC-1002 versus placebo when added to ongoing statin therapy in patients with hypercholesterolemia. This phase 2b, multicenter, double-blind trial (NCT02072161) randomized 134 hypercholesterolemic patients (LDL-C, 115 to 220 mg/dl) on stable background statin therapy to 12 weeks of add-on treatment with ETC-1002 120 mg, ETC-1002 180 mg, or placebo. The primary efficacy end point was the percent change in calculated LDL-C from baseline to week 12. For LDL-C, the least-squares mean percent change +/- standard error from baseline to week 12 was significantly greater with ETC-1002 120 mg (-17 +/- 4%, p = 0.0055) and ETC-1002 180 mg (-24 +/- 4%, p <0.0001) than placebo (-4 +/- 4%). ETC-1002 also dose dependently reduced apolipoprotein B by 15% to 17%, non-high-density lipoprotein cholesterol by 14% to 17%, total cholesterol by 13% to 15%, and LDL particle number by 17% to 21%. All these reductions in ETC-1002-treated cohorts were significantly greater than those with placebo. Rates of adverse events (AEs), muscle-related AEs, and discontinuations for AEs with ETC-1002 were similar to placebo. In conclusion, ETC-1002 120 mg or 180 mg added to stable statin therapy significantly reduced LDL-C compared to placebo and has a similar tolerability profile. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27138185

[2] Brown urine : Myoglobin-induced renal failure after concomitant administration of simvastatin and amiodarone. Pietsch U, Muller-Hocker C, Filipovic M. Der Anaesthesist 2016; 65:366-368. Rhabdomyolysis is a rare but well-known complication of statin therapy. The risk is considerably increased when concomitant drugs are administered that inhibit metabolism and breakdown via the cytochrome CYP3A4. We report a case of myoglobin-induced acute renal failure secondary to the concomitant use of simvastatin and amiodarone. The risk of rhabdomyolysis is mainly determined by the statin dose; in the case of the concomitant use of CYP3A4 inhibitors, a maximal daily dose of 20 mg is recommended to avoid harmful drug interactions. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27142363

[3] Endothelial Effect of Statin Therapy at a High Dose Versus Low Dose Associated with Ezetimibe. Garcia MM, Varella CG, Silva PF et al. Arquivos brasileiros de cardiologia 2016; 106:279-288. BACKGROUND: The effect of statins on the endothelial function in humans remains under discussion. Particularly, it is still unclear if the improvement in endothelial function is due to a reduction in LDL-cholesterol or to an arterial pleiotropic effect. OBJECTIVE: To test the hypothesis that modulation of the endothelial function promoted by statins is primarily mediated by the degree of reduction in LDL-cholesterol, independent of the dose of statin administered. METHODS: Randomized clinical trial with two groups of lipid-lowering treatment (16 patients/each) and one placebo group (14 patients). The two active groups were designed to promote a similar degree of reduction in LDL-cholesterol: the first used statin at a high dose (80 mg, simvastatin 80 group) and the second used statin at a low dose (10 mg) associated with ezetimibe (10 mg, simvastatin 10/ezetimibe group) to optimize the hypolipidemic effect. The endothelial function was assessed by flow-mediated vasodilation (FMV) before and 8 weeks after treatment. RESULTS: The decrease in LDL-cholesterol was similar between the groups simvastatin 80 and simvastatin 10/ezetimibe (27% +/- 31% and 30% +/- 29%, respectively, p = 0.75). The simvastatin 80
group presented an increase in FMV from 8.4% +/- 4.3% at baseline to 11% +/- 4.2% after 8 weeks (p = 0.02). Similarly, the group simvastatin 10/ezetimibe showed improvement in FMV from 7.3% +/- 3.9% to 12% +/- 4.4% (p = 0.001). The placebo group showed no variation in LDL-cholesterol level or endothelial function. CONCLUSION: The improvement in endothelial function with statin seems to depend more on a reduction in LDL-cholesterol levels, independent of the dose of statin administered, than on pleiotropic mechanisms.Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27142792

[4] Efficacy and safety of the cholesteryl ester transfer protein inhibitor anacetrapib in Japanese patients with heterozygous familial hypercholesterolemia. Arai H, Teramoto T, Daida H et al. Atherosclerosis 2016.BACKGROUND AND AIMS: This multicenter, randomized, double-blind, placebo-controlled study assessed the lipid-modifying efficacy/safety profile of anacetrapib 100 mg added to ongoing statin +/- other lipid-modifying therapies (LMT) in Japanese patients with heterozygous familial hypercholesterolemia (HeFH). METHODS: Patients 18-80 years with a genotype-confirmed/clinical diagnosis of HeFH who were on a stable dose of statin +/- other LMT for >=6 weeks and with an LDL-C concentration >=100 mg/dL were randomized to anacetrapib 100 mg (n = 34) or placebo (n = 34) for 12 weeks, followed by a 12-week off-drug reversal phase. The primary endpoints were percent change from baseline in LDL-C (beta-quantification method [BQ]) and safety/tolerability. RESULTS: At Week 12, treatment with anacetrapib reduced LDL-C (BQ) compared to placebo and resulting in a between-group difference of 29.8% (95% CI: -38.6 to -21.0; p < 0.001) favoring anacetrapib. Anacetrapib also reduced non-HDL-C (23.6%; p < 0.001), ApoB (14.1%; p < 0.001) and Lp(a) (48.7%; p < 0.001), and increased HDL-C (110.0%; p < 0.001) and ApoA1 (48.2%; p < 0.001) versus placebo. Anacetrapib 100 mg added to ongoing therapy with statin +/- other LMT for 12 weeks was generally well-tolerated. There were no differences between the groups in the proportion of patients who discontinued drug due to an adverse event or abnormalities in liver enzymes, creatinine kinase, blood pressure, electrolytes or adjudicated cardiovascular events. CONCLUSIONS: In Japanese patients with HeFH, treatment with anacetrapib 100 mg for 12 weeks resulted in substantial reductions in LDL-C and increases in HDL-C and was well tolerated. (ClinicalTrials.govNCT01824238).Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27131642

[5] The relative bioavailability of 2 prototype fixed-dose combination formulations for amlodipine and rosuvastatin in healthy white and Chinese subjects. Nwe HH, Bullman JN, Joshi SM et al. Clinical pharmacology in drug development 2016; 5:131-140. A fixed-dose combination (FDC) may improve patient compliance and clinical outcomes in the management of cardiovascular risk in hypertensive and dyslipidemomic patients. The study (NCT02075619) evaluated the bioavailability of 2 prototype FDC tablet formulations (FDC1 and FDC2) of amlodipine/rosuvastatin (10 mg/20 mg) compared with coadministered reference tablets. It was a randomized, single-dose, 3-way crossover pilot study in healthy white (n = 12) and Chinese (n = 12) adults. Three treatments (FDC1, FDC2, and reference) were administered after fasting with a washout period of 12-17 days. The pharmacokinetics of amlodipine and rosuvastatin were studied for all subjects (pooled) and by ethnicity. Safety and tolerability were also evaluated. Both FDCs met the bioequivalence criteria (90% confidence intervals falling within the range of 0.80-1.25) for AUC0-t and Cmax for amlodipine and rosuvastatin. Intrasubject variability (AUCO-t and Cmax ) was in the region of 23%-25% for rosuvastatin and 7%-10% for amlodipine. The FDC formulations demonstrated similar bioavailability to coadministered commercially available amlodipine and rosuvastatin. All treatments were generally well tolerated.Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27138026
*Current cardiology reviews* 2016. HMG CoA reductase inhibitors, or statins, are standard of care for preventing cardiovascular disease in at-risk populations. Statins are a well-established therapy proven to reduce long-term cardiovascular mortality and morbidity for prevention of secondary cardiovascular events and have become guideline-recommended therapy following acute myocardial infarction. Emerging data from clinical trials over the last decade indicates that statin therapy may provide broad beneficial effects beyond their primary lipid lowering mechanisms. In coronary heart disease, statins have demonstrated a unique ability to target several cellular pathways, which appear to play an underappreciated role in acute inflammation and subsequent thrombosis. Herein, we review the potential mechanisms where statins may act as antithrombotic agents in the setting of acute coronary syndromes and discuss the clinical implications of these findings. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27142048

[7] Non-cholesterol Sterols in the Diagnosis and Treatment of Dyslipidemias: A Review. Baila-Rueda L, Cenarro A, Civeira F. *Curr Med Chem* 2016. Non-cholesterol sterols have been used as markers of cholesterol intestinal absorption and hepatic synthesis, leading to a better understanding of cholesterol homeostasis in humans. This review discusses the main non-cholesterol sterols that are clinically useful, different methods to quantify the factors associated with blood concentration, and the potential role of non-cholesterol sterols in the diagnosis and treatment of different types of dyslipidemia. The main indication is the use of non-cholesterol sterols for the diagnosis of rare diseases associated with defects in cholesterol synthesis or anomalies in the absorption and/or elimination of phytosterols. However, other potential uses, including the diagnosis of certain hypercholesteroleemias and the individualization of lipid-lowering therapies, are promising as they could help treat a wider population. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27142287

[8] Relation between plasma and brain lipids. Wellington CL, Frikke-Schmidt R. *Current opinion in lipidology* 2016; 27:225-232. PURPOSE OF REVIEW: This article evaluates recent experimental and human evidence regarding the involvement of lipids, lipoproteins, and apolipoproteins in neurodegenerative diseases, and reviews the current literature of the effects of cholesterol-lowering treatment on cognition. RECENT FINDINGS: Plasma levels of traditional lipids and lipoproteins are not consistently associated with risk of dementia even though low plasma levels of apolipoprotein E, through unknown mechanisms, robustly predict future dementia. Experimental evidence suggests neuroprotective roles of several brain and cerebrospinal fluid apolipoproteins. Whether plasma levels of apolipoprotein E, or any other apolipoprotein with possible central nervous system and/or blood-brain barrier functions (apolipoproteins J, A-I, A-II, A-IV, D, C-I, and C-III) may become accessible biomarker components that improve risk prediction for dementia together with genetic risk variants and cardiovascular risk factors remains to be determined. SUMMARY: Apolipoproteins with well-established functions in peripheral lipid metabolism may play important roles for brain vascular health and Alzheimer's disease pathophysiology. Experimental work on lipids, lipoproteins, and apolipoproteins in the central nervous system together with robust prospective human studies will help to substantiate the drug target potential of these lipid components. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27149391

(DILIN) in their most recently updated registry include a 1- to 3-week delay in the appearance of acute DILI from short-course antibiotics such as cefazolin. They corroborated the finding that acute DILI in patients with underlying liver disease was far more severe and potentially fatal than in patients without liver disease. The only drug that seemed to have an increased risk of hepatotoxicity in these patients was azithromycin. While nearly one in six patients with acute DILI had persistently elevated liver tests at 6 months, and results for 75% of these patients continued to be abnormal at 12 months, most of these "chronic" injury cases were relatively minor and the result of cholestatic hepatotoxins. Newly described DILI agents include tolvaptan, as well as some new direct-acting antiviral protease inhibitors for chronic hepatitis C. The latter have been associated with serious acute hepatitis, hyperbilirubinemia, and decompensation. Herbal hepatotoxicity continues to be increasingly reported, although applying causality assessment to these cases can, in fact, be more challenging than with prescription drugs. As important as cases with DILI, the class of PCSK9 inhibitors used to lower low-density lipoprotein (LDL) cholesterol have not been associated with significant liver injury, in contrast with other lipid-lowering agents. With respect to pharmacologic DILI risk factors, new data show that drugs metabolized by cytochrome P450 enzymes had a nearly four times higher likelihood of causing DILI. Interestingly, high lipophilicity, which was previously felt to be a risk factor for DILI, was not found to be associated, although more study is needed to confirm this observation. While human leukocyte antigen (HLA) genotypes have been linked to several specific agents, the role of such testing in the general population remains undefined due to the currently low positive and negative predictive values of the available tests. New DILI biomarkers, specifically microRNA-122 and keratin-18, among others, appear to have the necessary predictive value to determine the prognosis and outcome of patients with paracetamol (acetaminophen [AAP])-induced acute liver failure (ALF), and may be of great benefit in deciding who requires N-acetylcysteine (NAC), and for what duration. Treatment options for other forms of DILI remain limited; no firm conclusions can currently be drawn for the use of NAC in non-AAP ALF. PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27142208

[10] The Treatment of Disorders of Lipid Metabolism. Parhofer KG. Deutsches Arzteblatt international 2016; 113:261-268.BACKGROUND: Disorders of lipid metabolism are very common. They play an important role in the pathogenesis of atherosclerosis and can be effectively treated by lifestyle changes and drugs. METHODS: This review is based on pertinent literature retrieved by a selective search. RESULTS: The main disorders of lipid metabolism are LDL-hypercholesterolemia, hypertriglyceridemia, mixed hyperlipoproteinemia, and low HDL cholesterol. The lipoprotein(a) level can also be elevated either in isolation or in combination with other disorders of lipid metabolism. According to the current European recommendations, an LDL-cholesterol target value should be defined on the basis of the overall cardiovascular risk. If this risk is very high, as in patients with documented atherosclerosis, the target value should be set at <70 mg/dL (<1.8 mmol/L). If the risk is lower, higher target values can be set: <100 mg/dL (<2.6 mmol/L) or <115 mg/dL (<3.0 mmol/L). Lifestyle changes are an effective treatment mainly for patients with hypertriglyceridemia and mixed disorders of lipid metabolism. Lowering the LDL-cholesterol concentration with statins is by far the most important type of pharmacotherapy. Patients who cannot tolerate statins or whose cholesterol level is not adequately lowered can be given ezetimibe instead. PCSK9 antibodies have been available since the autumn of 2015; they can apparently lower the LDL-cholesterol level by more than 50%, but no endpoint trials have yet been reported. At present, they should only be given to carefully selected patients. Fibrates and omega-3 fatty acids have been found to prevent cardiovascular events in monotherapy trials but yield no added benefit when given together with statins. The design of these trials was faulty, however,
and the utility of such combinations in patients with mixed disorders of lipid metabolism or hypertriglyceridemia cannot yet be definitively assessed. CONCLUSION: There is a causal relationship between hypercholesterolemia and the risk of vascular and cardiovascular events. A reduction of LDL cholesterol lessens the risk of cardiovascular events.


[12] No effects of pantoprazole on the pharmacokinetics of rosuvastatin in healthy subjects. Huguet J, Lu J, Gaudette F et al. Eur J Clin Pharmacol 2016. PURPOSE: Rosuvastatin disposition is modulated by the expression and activity of several membrane transporters including BCRP (ABCG2). The objective of our study was to investigate the effects of pantoprazole, a previously proposed BCRP inhibitor, on the disposition of rosuvastatin. METHODS: The impact of pantoprazole (40 mg ID for 2 days) on rosuvastatin pharmacokinetics was evaluated in healthy volunteers (n = 16) who received a single oral dose of rosuvastatin (10 mg) either alone or with pantoprazole. Rosuvastatin, N-desmethylosuvastatin, and rosuvastatin lactone levels were quantified in plasma while rosuvastatin and N-desmethylosuvastatin excretion were measured in urine. RESULTS: Ratios and 90% standard confidence interval of geometric means for C max (1.03 [0.91-1.16]), AUC0-infinity (1.03 [0.89-1.19]) and renal clearance (0.96 [0.85-1.09]) were all within the pre-specified range of 0.8-1.25, indicating a lack of drug-drug interaction between pantoprazole and rosuvastatin. CONCLUSIONS: Concomitant administration of pantoprazole with rosuvastatin did not affect rosuvastatin plasma concentrations. The use of pantoprazole as a BCRP inhibitor should be revisited when characterizing BCRP-mediated transport in humans. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27146814

[13] Statin non-adherence: clinical consequences and proposed solutions. Rosenson RS. F1000Research 2016; 5. Large controlled clinical trials have demonstrated reductions with statin therapy in cardiovascular events in patients presenting with acute coronary syndromes and stable coronary heart disease and individuals at high risk of a cardiovascular event. In trials of acute coronary syndromes and stable coronary heart disease, high-intensity statin therapy is more effective in the prevention of recurrent cardiovascular events than low-intensity statin therapy. Thus, evidence-based guidelines recommend in-hospital initiation of high-intensity statin therapy for all acute coronary syndrome patients. Clinical trials report high adherence to and low discontinuation of high-intensity statin therapy; however, in clinical practice, high-intensity statins are prescribed to far fewer patients, who often discontinue their statin after the first refill. A coordinated effort among the patient, provider, pharmacist, health system, and insurer is necessary to improve utilization and persistence of prescribed medications. The major cause for statin discontinuations reported by patients is perceived adverse events. Evaluation of potential adverse events requires validated tools to distinguish between statin-associated adverse events versus non-specific complaints. Treatment options for statin-intolerant patients include the use of a different statin, often at a lower dose or frequency. In order to lower LDL cholesterol, lower doses of statins may be combined with ezetimibe or bile acid sequestrants. Newer treatment options for patients with statin-associated muscle symptoms may include proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27134737
[14] **Chronic oral administration of low-dose combination of fenofibrate and rosuvastatin protects the rat heart against experimentally-induced acute myocardial infarction.** Garg M, Khanna D, Balakumar P, Kalra S. *Fundamental & clinical pharmacology* 2016. Fenofibrate and rosuvastatin at low-doses might have experimental pleiotropic benefits. This study investigated the combined effect of low-doses of fenofibrate and rosuvastatin in isoproterenol-induced experimental myocardial infarction. Rats administered isoproterenol (85 mg/kg/day, s.c.) for 2 days (day 29 and day 30) of 30 days experimental protocol developed significant myocardial infarction that was accompanied with high myocardial oxidative stress and lipid peroxidation, elevated serum markers of cardiac injury, lipid abnormalities, and elevated circulatory levels of C-reactive protein. Pretreatment with low-doses of fenofibrate (30 mg/kg/day p.o., 30 days) and rosuvastatin (2 mg/kg/day p.o., 30 days) both alone or in combination markedly prevented isoproterenol-induced myocardial infarction and associated abnormalities while the low-dose combination of fenofibrate and rosuvastatin was more effective. Histopathological study in isoproterenol control rat heart showed necrosis with edema and acute inflammation at the margins of necrotic area. The rat heart from low-dose fenofibrate and rosuvastatin pre-treated group showed scanty inflammation and no ischemia. In conclusion, fenofibrate and rosuvastatin pretreatment in low-doses might have a therapeutic potential to prevent the pathogenesis of myocardial infarction. Moreover, their combined treatment option might offer superior therapeutic benefits via a marked reduction in myocardial infarct size and oxidative stress, suggesting a possibility of their pleiotropic cardioprotective action at low-doses. This article is protected by copyright. All rights reserved. Pubmed ID: http://www.ncbi.nlm.nih.gov/pubmed/?term=27148865

[15] **Statins for the treatment of depression: A meta-analysis of randomized, double-blind, placebo-controlled trials.** Salagner E, Fernandes BS, Dodd S *et al.* *Journal of affective disorders* 2016; 200:235-242. BACKGROUND: In epidemiological studies, statins appear to benefit mood, and there are now some randomized controlled trials examining the efficacy of statins. However, the role of statins in depression remains uncertain. Thus the aim of this paper was to assess the effect of statins on depressive symptoms by performing a meta-analysis of all double-blind, randomized, placebo controlled clinical trials (RCT) conducted in subjects with depression. METHODS: A systematic search was executed using PubMed and ClinicalTrials.gov in November 30th, 2015 for all double-blind, RCT of statins versus placebo in persons with depressive symptoms. Sixty-seven potential articles were identified through search of electronic databases, of those three met inclusion criteria and were included in the meta-analysis. The outcome measure was change in Hamilton Depression Rating Scale (HDRS) scores associated with statin use. A meta-analysis was conducted and standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated. GRADE was used to assess study quality. RESULTS: The three articles included provided data on 165 participants with moderate to severe depression. Of these, 82 were randomized to statins as an adjuvant therapy to antidepressant treatment (i.e., citalopram or fluoxetine) and 83 to the placebo arm. All studies were double-blind RCTs, with a follow-up of 6-12 weeks. The statin agents evaluated were lovastatin, atorvastatin, and simvastatin. When compared to placebo, statins, as add-on to treatment as usual, largely improved depressive symptoms as assessed by the HDRS (SMD=-.73, 95% IC -1.04 to -0.42, p<0.001, 3 between-group comparisons, n=165). No serious adverse effects were reported. CONCLUSIONS: Our results suggest that adjunctive treatment with statins could be useful for the treatment of depressive symptoms. Additional double-blind, randomised, placebo-controlled trials are necessary to settle the matter. Pubmed ID: http://www.ncbi.nlm.nih.gov/pubmed/?term=27148902
[16] Accuracy of the Atherosclerotic Cardiovascular Risk Equation in a Large Contemporary, Multiethnic Population. Rana JS, Tabada GH, Solomon MD et al. Journal of the American College of Cardiology 2016; 67:2118-2130.BACKGROUND: The accuracy of the 2013 American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Risk Equation for atherosclerotic cardiovascular disease (ASCVD) events in contemporary and ethnically diverse populations is not well understood. OBJECTIVES: The goal of this study was to evaluate the accuracy of the 2013 ACC/AHA Pooled Cohort Risk Equation within a large, multiethnic population in clinical care. METHODS: The target population for consideration of cholesterol-lowering therapy in a large, integrated health care delivery system population was identified in 2008 and followed up through 2013. The main analyses excluded those with known ASCVD, diabetes mellitus, low-density lipoprotein cholesterol levels <70 or >/=190 mg/dl, prior lipid-lowering therapy use, or incomplete 5-year follow-up. Patient characteristics were obtained from electronic medical records, and ASCVD events were ascertained by using validated algorithms for hospitalization databases and death certificates. We compared predicted versus observed 5-year ASCVD risk, overall and according to sex and race/ethnicity. We additionally examined predicted versus observed risk in patients with diabetes mellitus. RESULTS: Among 307,591 eligible adults without diabetes between 40 and 75 years of age, 22,283 were black, 52,917 were Asian/Pacific Islander, and 18,745 were Hispanic. We observed 2,061 ASCVD events during 1,515,142 person-years. In each 5-year predicted ASCVD risk category, observed 5-year ASCVD risk was substantially lower: 0.20% for predicted risk <2.50%; 0.65% for predicted risk 2.50% to <3.75%; 0.90% for predicted risk 3.75% to <5.00%; and 1.85% for predicted risk >/=5.00% (C statistic: 0.74). Similar ASCVD risk overestimation and poor calibration with moderate discrimination (C statistic: 0.68 to 0.74) were observed in sex, racial/ethnic, and socioeconomic status subgroups, and in sensitivity analyses among patients receiving statins for primary prevention. Calibration among 4,242 eligible adults with diabetes was improved, but discrimination was worse (C statistic: 0.64). CONCLUSIONS: In a large, contemporary "real-world" population, the ACC/AHA Pooled Cohort Risk Equation substantially overestimated actual 5-year risk in adults without diabetes, overall and across sociodemographic subgroups. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27151343

[17] Remnant Lipoprotein Cholesterol and Incident Coronary Heart Disease: The Jackson Heart and Framingham Offspring Cohort Studies. Joshi PH, Khokhar AA, Massaro JM et al. Journal of the American Heart Association 2016; 5.BACKGROUND: Remnant lipoproteins (RLPs), the triglyceride-enriched precursors to low-density lipoprotein, are an emerging risk factor for coronary heart disease (CHD). We sought to determine the association of RLP cholesterol (RLP-C) levels with incident CHD in 2 diverse, prospective, longitudinal observational US cohorts. METHODS AND RESULTS: We analyzed cholesterol levels from serum lipoprotein samples separated via density gradient ultracentrifugation in 4114 US black participants (mean age 53.8 years, 64% women) from the Jackson Heart Study and a random sample of 818 predominantly white participants (mean age 57.3 years, 52% women) from the Framingham Offspring Cohort Study. Multivariable-adjusted hazard ratios (HRs) for RLP-C (the sum of very low-density lipoprotein3 cholesterol and intermediate-density lipoprotein cholesterol) were derived to estimate associations with incident CHD events consisting of myocardial infarction, CHD death, and revascularizations for each cohort separately and as a combined population. There were 146 CHD events in the combined population. After adjustments for age, sex, body mass index, smoking, blood pressure, diabetes, and lipid-lowering therapy for the combined population, RLP-C (HR 1.23 per 1-SD increase, 95% CI 1.06-1.42, P<0.01) and intermediate-density lipoprotein cholesterol (HR 1.26 per 1-SD increase, 95% CI 1.08-1.47, P<0.01) predicted CHD during an 8-year follow-up. Associations were
attenuated by high-density lipoprotein cholesterol and ultimately lost significance with inclusion of real low-density lipoprotein cholesterol, which excludes Lp(a) and IDL cholesterol fractions. Similar associations were seen in multivariable analyses within each cohort. CONCLUSION: RLP-C levels are predictive of incident CHD in this diverse group of primary prevention subjects. Interventions aimed at reducing RLP-C to prevent CHD warrant further intensive investigation. CLINICAL TRIAL REGISTRATION: URL: http://www.clinicaltrials.gov/. Unique identifier: NCT00415415. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27130348

[18] HIV and Hepatitis C-Coinfected Patients Have Lower Low-Density Lipoprotein Cholesterol Despite Higher Proprotein Convertase Subtilisin Kexin 9 (PCSK9): An Apparent "PCSK9-Lipid Paradox". Kohli P, Ganz P, Ma Y et al. Journal of the American Heart Association 2016; 5.BACKGROUND: Proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors reduce low-density lipoprotein cholesterol (LDL-C) and improve outcomes in the general population. HIV-infected individuals are at increased risk for cardiovascular events and have high rates of dyslipidemia and hepatitis C virus (HCV) coinfection, making PCSK9 inhibition a potentially attractive therapy. METHODS AND RESULTS: We studied 567 participants from a clinic-based cohort to compare PCSK9 levels in patients with HIV/HCV coinfection (n=110) with those with HIV infection alone (n=385) and with uninfected controls (n=72). The mean age was 49 years, and the median LDL-C level was 100 mg/dL (IQR 77-124 mg/dL); 21% were taking statins. The 3 groups had similar rates of traditional risk factors. Total cholesterol, LDL-C, and high-density lipoprotein cholesterol levels were lower in coinfected patients compared with controls (P<0.001). PCSK9 was 21% higher in HIV/HCV-coinfected patients versus controls (95% CI 9-34%, P<0.001) and 11% higher in coinfected individuals versus those with HIV infection alone (95% CI 3-20%, P=0.008). After adjustment for cardiovascular risk factors, HIV/HCV coinfection remained significantly associated with 20% higher PCSK9 levels versus controls (95% CI 8-33%, P=0.001). Interleukin-6 levels increased in a stepwise fashion from controls (lowest) to HIV-infected to HIV/HCV-coinfected individuals (highest) and correlated with PCSK9 (r=0.11, P=0.018). CONCLUSIONS: Despite having lower LDL-C, circulating PCSK9 levels were increased in patients coinfected with HIV and HCV in parallel with elevations in the inflammatory, proatherogenic cytokine interleukin-6. Clinical trials should be conducted to determine the efficacy of targeted PCSK9 inhibition in the setting of HIV/HCV coinfection. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27130349


[20] Risk factors of transient ischemic attack: An overview. Khare S. Journal of mid-life health 2016; 7:2-7. Transient ischemic attack (TIA) is a transient episode of neurologic dysfunction caused due to loss of blood flow to the brain or spinal cord without acute infarction. Depending on the area of the brain involved, symptoms of TIA vary widely from patient to patient. Since the blockage period in TIA is very short-lived, there is no permanent damage. Risk factors for TIA include family history of stroke or TIA, age above 55 years or older, higher risk of TIA in males than females, high blood pressure, diabetes mellitus, and tobacco smoking. Genetics, race, and imbalance in lipid profile are other risk factors of TIA. TIA is usually diagnosed after taking a thorough history and a physical examination. Several radiological tests such as computed tomography and magnetic resonance imaging are useful in the evaluation of patients who have had a TIA. Ultrasound of the neck and an echocardiogram of the heart are other tests useful in the diagnosis and evaluation of the attack. The treatment following acute recovery from a TIA
depends on the underlying cause. Patients who have more than 70% stenosis of the carotid artery, removal of atherosclerotic plaque is usually done by carotid endarterectomy surgery. One-third of the people with TIA can later have recurrent TIAs and one-third can have a stroke because of permanent nerve cell loss. Having a TIA is a risk factor for eventually having a stroke. Educating the patients and inculcating lifestyle modifications in them are initial steps to minimize the prevalence of transient ischemic attack. 

[21] Cholesterol Absorption and Metabolism. Howles PN. Methods in molecular biology (Clifton, N.J.) 2016; 1438:177-197. Inhibitors of cholesterol absorption have been sought for decades as a means to treat and prevent cardiovascular diseases (CVDs) associated with hypercholesterolemia. Ezetimibe is the one clear success story in this regard, and other compounds with similar efficacy continue to be sought. In the last decade, the laboratory mouse, with all its genetic power, has become the premier experimental model for discovering the mechanisms underlying cholesterol absorption and has become a critical tool for preclinical testing of potential pharmaceutical entities. This chapter briefly reviews the history of cholesterol absorption research and the various gene candidates that have come under consideration as drug targets. The most common and versatile method of measuring cholesterol absorption is described in detail along with important considerations when interpreting results, and an alternative method is also presented. In recent years, reverse cholesterol transport (RCT) has become an area of intense new interest for drug discovery since this process is now considered another key to reducing CVD risk. The ultimate measure of RCT is sterol excretion and a detailed description is given for measuring neutral and acidic fecal sterols and interpreting the results. 

[22] Perioperative Rosuvastatin in Cardiac Surgery. Zheng Z, Jayaram R, Jiang L et al. The New England journal of medicine 2016; 374:1744-1753. BACKGROUND: Complications after cardiac surgery are common and lead to substantial increases in morbidity and mortality. Meta-analyses of small randomized trials have suggested that perioperative statin therapy can prevent some of these complications. METHODS: We randomly assigned 1922 patients in sinus rhythm who were scheduled for elective cardiac surgery to receive perioperative rosuvastatin (at a dose of 20 mg daily) or placebo. The primary outcomes were postoperative atrial fibrillation within 5 days after surgery, as assessed by Holter electrocardiographic monitoring, and myocardial injury within 120 hours after surgery, as assessed by serial measurements of the cardiac troponin I concentration. Secondary outcomes included major in-hospital adverse events, duration of stay in the hospital and intensive care unit, left ventricular and renal function, and blood biomarkers. RESULTS: The concentrations of low-density lipoprotein cholesterol and C-reactive protein after surgery were lower in patients assigned to rosuvastatin than in those assigned to placebo (P<0.001). However, the rate of postoperative atrial fibrillation did not differ significantly between the rosuvastatin group and the placebo group (21.1% and 20.5%, respectively; odds ratio 1.04; 95% confidence interval [CI], 0.84 to 1.30; P=0.72), nor did the area under the troponin I-release curve (102 ng/hour per milliliter and 100 ng/hour per milliliter, respectively; between-group difference, 1%; 95% CI, -9 to 13; P=0.80). Subgroup analyses did not indicate benefit in any category of patient. Rosuvastatin therapy did not result in beneficial effects on any of the secondary outcomes but was associated with a significant absolute (+/-SE) excess of 5.4+/-1.9 percentage points in the rate of postoperative acute kidney injury (P=0.005). CONCLUSIONS: In this trial, perioperative statin therapy did not prevent postoperative atrial fibrillation or perioperative myocardial damage in patients undergoing elective cardiac surgery. Acute kidney injury was more common with rosuvastatin. (Funded by the...
Variants with large effects on blood lipids and the role of cholesterol and triglycerides in coronary disease. Helgadottir A, Gretarsdottir S, Thorleifsson G et al. *Nature genetics* 2016. Sequence variants affecting blood lipids and coronary artery disease (CAD) may enhance understanding of the atherogenicity of lipid fractions. Using a large resource of whole-genome sequence data, we examined rare and low-frequency variants for association with non-HDL cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides in up to 119,146 Icelanders. We discovered 13 variants with large effects (within ANGPTL3, APOB, ABCA1, NR1H3, APOA1, LIPC, CETP, LDLR, and APOC1) and replicated 14 variants. Five variants within PCSK9, APOA1, ANGPTL4, and LDLR associate with CAD (33,090 cases and 236,254 controls). We used genetic risk scores for the lipid fractions to examine their causal relationship with CAD. The non-HDL cholesterol genetic risk score associates most strongly with CAD (P = 2.7 x 10^-28), and no other genetic risk score associates with CAD after accounting for non-HDL cholesterol. The genetic risk score for non-HDL cholesterol confers CAD risk beyond that of LDL cholesterol (P = 5.5 x 10^-8), suggesting that targeting atherogenic remnant cholesterol may reduce cardiovascular risk. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27135400

ESSENS dyslipidemia: A placebo-controlled, randomized study of a nutritional supplement containing red yeast rice in subjects with newly diagnosed dyslipidemia. Kasliwal RR, Bansal M, Gupta R et al. *Nutrition* 2016. OBJECTIVE: Evidence suggests prolonged exposure to lower levels of low-density lipoprotein cholesterol (LDL-C), starting at a younger age, substantially lowers cardiovascular (CV) risk. Accordingly, the CV pandemic affecting younger population in low- to low-middle-income countries, where statin usage is poor even in secondary prevention, may benefit from lipid-lowering nutritional products, as nutritional intervention is generally preferred in these cultures. However, the safety and efficacy of such preparations have not been systematically tested. METHODS: In this multicenter, double-blind study, 191 statin-free subjects with newly-diagnosed hyperlipidemia (LDL-C >120 mg/dL, 3.11 mmol/L) and no evidence of CV disease were randomized to one capsule of a proprietary bioactive phytonutrient formulation containing red yeast rice, grape-seed, niacinamide, and folic acid (RYR-NS) or matched placebo twice daily, along with lifestyle modification, for 12 wk. RESULTS: Mean baseline LDL-C levels were 148.5 +/- 24.0 mg/dL (3.85 +/- 0.62 mmol/L) and 148.6 +/- 21.9 mg/dL (3.85 +/- 0.57 mmol/L) in the RYR-NS and placebo groups respectively. Compared with placebo, RYR-NS resulted in a significant reduction in LDL-C (~29.4% versus -3.5%, P < 0.0001) and non-high-density lipoprotein cholesterol (non-HDL-C; -29.8% versus -10.3%, P < 0.0001) at 12 wk. With RYR-NS, 43.4% individuals attained desirable LDL-C levels and 55.4% desirable non-HDL-C levels by week 12, compared to only 0% and 1.1%, respectively, at baseline. No safety issues were observed. CONCLUSION: This study demonstrates the efficacy and safety of RYR-NS in lowering LDL-C and non-HDL-C after 12 wk, with magnitude of LDL-C reduction being comparable to that seen with moderate-intensity statin therapy. Further long-term studies are required to determine the impact of RYR-NS on treatment adherence and clinical outcomes. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27143594

Fish oil and fenofibrate inhibit pancreatic islet hypertrophy, and improve glucose and lipid metabolic dysfuntions with different ways in diabetic KK mice. Nakasatomi M, Kim H, Arai T et al.
Obesity research & clinical practice 2016. We examined the effects of fish oil and fenofibrate (FF) on the pancreatic islet hypertrophy, and on the modification of glucose and lipid metabolic dysfunctions in KK mice with insulin resistance. The mice were fed one of four diets [25% lard/safflower oil (LSO), 25% fish oil (FO), or each of these diets plus 0.1wt% FF (LSO/FF, FO/FF)] for 9 weeks. FO group and both FF groups had significantly lower final body and adipose tissue weights than LSO group. Pancreatic islet hypertrophy was observed only in LSO group but not in the other groups with fish oil or FF. And, it is likely that fish oil has a stronger therapeutic effect on islet hypertrophy. Plasma adiponectin level was significantly higher in FO group but not in both FF groups. Expression of hepatic lipogenic enzyme genes such as fatty acid synthase (FAS) and stearoyl-CoA desaturase-1 (SCD-1) was lower in FO groups with or without FF, whereas fatty acid oxidation-related mRNAs such as acyl-CoA oxidase (AOX) and uncoupling protein-2 (UCP-2) were more abundant in FF groups with or without fish oil. Our results suggest that both fish oil and FF improve pancreatic islet hypertrophy with the amelioration of insulin resistance. Fish oil enhances insulin sensitivity by increasing plasma adiponectin; however, the beneficial effect of FF on insulin resistance seems to be independent of the plasma adiponectin level. These results mean that improvement of glucose and lipid metabolic dysfunctions in diabetic KK mice are independently approached by fish oil and FF. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27130153

[27] Diabetic dyslipidaemia and the atherosclerosis. Mark L, Dani G. Orvosi hetilap 2016; 157:746-752. The incidence and the public health importance of diabetes mellitus are growing continuously. Despite the improvement observed in the latest years, the leading cause of morbidity and mortality of diabetics are cardiovascular diseases. The diagnosis of diabetes mellitus constitutes such a high risk as the known presence of vascular disease. Diabetic dyslipidaemia is characterised by high fasting and postprandial triglyceride levels, low HDL level, and slightly elevated LDL-cholesterol with domination of atherogenic small dense LDL. These are not independent components of the atherogenic dyslipidaemia, but are closely linked to each other. Beside the known harmful effects of low HDL and small dense LDL, recent findings confirmed the atherogenicity of the triglyceride-rich lipoproteins and their remnants. It has been shown that the key of this process is the overproduction and delayed clearance of triglyceride-rich lipoproteins in the liver. In this metabolism the lipoprotein lipase has a determining role; its function is accelerated by ApoA5 and attenuated by ApoC3. The null mutations of the ApoC3 results in a reduced risk of myocardial infarction, the loss-of-function mutation of ApoA5 was associated with a 60% elevation of triglyceride level and 2.2-times increased risk of myocardial infarction. In case of diabetes mellitus, insulin resistance, obesity, metabolic syndrome and chronic kidney disease the non-HDL-cholesterol is a better marker of the risk than the LDL-cholesterol. Its value can be calculated by subtraction of HDL-cholesterol from total cholesterol. Target values of non-HDL-cholesterol can be obtained by adding 0.8 mmol/L to the LDL-cholesterol targets (this means 3.3 mmol/L in high, and 2.6 mmol/L in very high risk patients). The drugs of first choice in the treatment of diabetic dyslipidaemia are statins. Nevertheless, it is known that even if statin therapy is optimal (treated to target), a considerable residual (lipid) risk remains. For its reduction treatment of low HDL-cholesterol and high triglyceride levels is obvious by the administration of fibrates. In addition to statin therapy, fenofibrate can be recommended. Orv. Hetil., 2016, 157(19), 746-752. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27133274


Statin and other lipid-lowering drugs have dominated the market for many years for achievement of recommended levels of low-density lipoprotein cholesterol (LDL-C). However, a substantial number of high-risk patients are unable to achieve the LDL-C goal. Proprotein convertase subtilisin/kexin 9 (PCSK9) has recently emerged as a new, promising key therapeutic target for hypercholesterolemia. PCSK9 is a protease involved in chaperoning the low-density lipoprotein receptor to the process of degradation. PCSK9 inhibitors and statins effectively lower LDL-C. The PCSK9 inhibitors decrease the degradation of the LDL receptors, whereas statins mainly interfere with the synthetic machinery of cholesterol by inhibiting the key rate-limiting enzyme, the HMG CoA reductase. PCSK9 inhibitors are currently being developed as monoclonal antibodies for their primary use in lowering LDL-C. They may be especially useful for patients with homozygous familial hypercholesterolemia, who at present receive minimal benefit from traditional statin therapy. The monoclonal antibody PCSK9 inhibitors, recently granted FDA approval, show the most promising safety and efficacy profile compared to other, newer LDL-C lowering therapies. This review will primarily focus on the safety and efficacy of monoclonal antibody PCSK9 inhibitors in comparison to statins. The review will also address new, alternative PCSK9 targeting drug classes such as small molecules, gene silencing agents, apolipoprotein B antisense oligonucleotides, and microsomal triglyceride transfer protein inhibitors. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27133571


Metabolic syndrome (MetS) is a complicated health problem that encompasses a variety of metabolic disorders. In this study, we analyzed the relationship between the major biochemical parameters associated with MetS and circulating levels of microRNA (miR)-33, miR-103, and miR-155. We found that miRNA-33 levels were positively correlated with levels of fasting blood glucose, glycosylated hemoglobin A1c, total cholesterol, LDL-cholesterol, and triacylglycerol, but negatively correlated with HDL-cholesterol levels. In the cellular study, miR-33 levels were increased in macrophages treated with high glucose and cholesterol-lowering drugs atorvastatin and pitavastatin. miR-33 has been reported to play an essential role in cholesterol homeostasis through ATP-binding cassette transporter A1 (ABCA1) regulation and reverse cholesterol transport. However, the molecular mechanism underlying the linkage between miR-33 and statin treatment remains unclear. In the present study, we investigated whether atorvastatin and pitavastatin exert their functions through the modulation of miR-33 and ABCA1-mediated cholesterol efflux from macrophages. The results showed that treatment of the statins up-regulated miR-33 expression, but down-regulated ABCA1 mRNA levels in RAW264.7 cells and bone marrow-derived macrophages. Statin-mediated ABCA1 regulation occurs at the post-transcriptional level through targeting of the 3'-UTR of the ABCA1 transcript by miR-33. Additionally, we found significant down-regulation of ABCA1 protein expression in macrophages treated with statins. Finally, we showed that high glucose and statin treatment significantly suppressed cholesterol efflux from macrophages. These findings have highlighted the complexity of statins, which may exert detrimental effects on metabolic abnormalities through regulation of miR-33 target genes. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27139226
[31] **Neuroprotective Effects of Low-Dose Statins in the Retinal Ultrastructure of Hypercholesterolemic Rabbits.** Fernandez-Navarro J, Aldea P, de Hoz R et al. *PloS one* 2016; 11:e0154800. To evaluate the pleiotropic effects to statins, we analyze the qualitative and quantitative retinal changes in hypercholesterolemic rabbits after a low-dosage statin treatment. For this purpose, New Zealand rabbits were split into three groups: control (G0; n = 10), fed a standard diet; hypercholesterolemic (G1; n = 8), fed a 0.5% cholesterol-enriched diet for 8 months; and statins (G2; n = 8), fed a 0.5% cholesterol-enriched diet for 8 months, together with the administration of statin (pravastatin or fluvastatin sodium) at a dose of 2 mg / kg / day each diet. The retinas were analyzed by transmission electron microscopy and immunohistochemistry (glial fibrillary acidic protein). The retinal thickness of nuclear and plexiform layers were quantified in semi-thin sections. The results revealed that the low-statin-treated rabbits in comparison with the hypercholesterolemic group showed: i) a more preserved structure in all retinal layers; ii) a significant reduction in retinal thickness; iii) a decrease in cell death in the nuclear-and ganglion-cell layers; iv) a reduction of hydropic degeneration in the plexiform and nerve-fiber layers; v) a preservation of astrocytes and of the retinal area occupied by them; and vi) a better-preserved retinal vascular structure. Our findings indicate that low doses of statins can prevent retinal degeneration, acting on retinal macroglia, neurons and retinal vessels, despite that hypercholesterolemia remained unchanged. Thus, the pleiotropic effects of the statins may help safeguard the retinal ultrastructure. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27144842

[32] **Simvastatin offers new prospects for the treatment of Duchenne muscular dystrophy.** Whitehead NP, Kim MJ, Bible KL et al. *Rare diseases (Austin, Tex.)* 2016; 4:e1156286. Duchenne muscular dystrophy (DMD) is the most common and severe inherited neuromuscular disorder. DMD is caused by mutations in the gene encoding the dystrophin protein in muscle fibers. Dystrophin was originally proposed to be a structural protein that protected the sarcolemma from stresses produced during contractions. However, more recently, experimental evidence has revealed a far more complicated picture, with the loss of dystrophin causing dysfunction of multiple muscle signaling pathways, which all contribute to the overall disease pathophysiology. Current gene-based approaches for DMD are conceptually appealing since they offer the potential to restore dystrophin to muscles, albeit a partially functional, truncated form of the protein. However, given the cost and technical challenges facing these genetic approaches, it is important to consider if relatively inexpensive, clinically used drugs may be repurposed for treating DMD. Here, we discuss our recent findings showing the potential of simvastatin as a novel therapy for DMD. Pubmed ID http://www.ncbi.nlm.nih.gov/pubmed/?term=27141415

[33] **Targeted study to evaluate the cardiovascular risk factor status among patients and efficacy of statins in attaining goal lipid levels in a regional hospital in Sultanate of Oman.** Jose J, Al-Tamimi FA, Helal MM et al. *Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society* 2015; 23:371-376. BACKGROUND AND OBJECTIVE: Elevated LDL (Low Density Lipoprotein) cholesterol is a major cause of Coronary Heart Disease (CHD) and LDL lowering therapy reduces the risk for CHD. The study was conducted with the aim of assessing the prescribing pattern of statins based on cardiovascular risk factor category, pattern of lipid monitoring followed among the patients and extent of attainment of goal Low Density Lipoprotein (LDL-C) observed among the patients. METHODS: A group of patient files (among those on statin agent during the year 2011) from the Department of Medicine in Nizwa Hospital were selected for targeted evaluation on the risk factor status of patients and efficacy of statins in attaining goal lipid levels. Goal LDL-C levels were estimated for each patient depending on their risk factor status. Subsequent follow ups of the patients were reviewed from the patient files and
accordingly the attainment and maintenance of goal-LDL-C in the patients were evaluated. RESULTS: A total of 183 patients were identified. Mean age of the evaluated patients was 63.6 +/- 11.58 years. Evaluating the status of patients on the presence of risk factors, majority (63.9%) of them had presence of CHD. Simvastatin was the most commonly used agent and titration of dose was done in only 3.3% of patients. Mean LDL-C level of the patient before initiation of treatment was 3.74 +/- 1.9 mmol/L. Only in 59 (32.2 %) of the total evaluated 183 patients, there was evidence of attaining goal-LDL-C levels. Among them, there was evidence of maintenance of goal LDL-C in 16 (27.1%) of the patients.

CONCLUSION: Statins were used less frequently for primary prevention of CHD. Absence of lipid monitoring; base line and follow up in a good number of patients as well as lack of dose titration among the patients were observed. Importance of adequate lipid monitoring and follow up to ensure attainment of goal LDL-C needs to be stressed to serve the objective of use of statins; primary and secondary prevention of CHD.


[34] Clinical efficacy and safety of evolocumab for low-density lipoprotein cholesterol reduction. Henry CA, Lyon RA, Ling H. *Vascular health and risk management* 2016; 12:163-169. Multiple categories of medications have been developed to manage lipid profiles and reduce the risk of cardiovascular events in patients with heart disease. However, currently marketed medications have not solved the problems associated with preventing and treating cardiovascular diseases completely. A substantial population of patients cannot take advantage of statin therapy due to statin intolerance, heart failure, or kidney hemodialysis, suggesting a need for additional effective agents to reduce low-density lipoprotein cholesterol (LDL-C) levels. Proprotein convertase subtilisin/kexin type 9 (PCSK9) was discovered in 2003 and subsequently emerged as a novel target for LDL-C-lowering therapy. Evolocumab is a fully human monoclonal immunoglobulin G2 (IgG2) directed against human PCSK9. By inactivating PCSK9, evolocumab upregulates LDL receptors causing increased catabolism of LDL-C and the consequent reduction of LDL-C levels in blood. Overall, evolocumab has had notable efficacy, with LDL-C reduction ranging from 53% to 75% in monotherapy and combination therapies, and is associated with minor adverse effects. However, studies regarding the ability of evolocumab to reduce mortality as well as long-term safety concerns are limited. The fact that the drug was introduced at a cost much higher than the existing medications and shows a low incremental mortality benefit suggests that many payers will consider evolocumab to have an unfavorable cost-benefit ratio.