Physician Perspectives on Rosuvastatin in Cardiovascular Disease Management

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Background and Objective of the Survey

Physicians hold a favorable view of rosuvastatin in cardiovascular disease (CVD) management, considering its potent lipid-lowering effects and proven benefits in reducing cardiovascular events. As a high-potency statin, rosuvastatin is often seen as an effective first-line therapy for lipid management, particularly in patients with high cardiovascular risk or those with elevated LDL cholesterol levels despite lifestyle modifications. Clinical trials, such as JUPITER and CRESTOR, have demonstrated significant reductions in major cardiovascular events, including myocardial infarction, stroke, and cardiovascular mortality, in patients with and without pre-existing CVD. While rosuvastatin is generally well-tolerated, physicians remain vigilant for potential adverse effects, such as myopathy, liver enzyme elevations, and new-onset diabetes, particularly in high-risk patient populations. Treatment with rosuvastatin is individualized based on each patient's cardiovascular risk profile, comorbidities, and preferences, with dosage selection and monitoring of lipid levels and liver function being key considerations. Ensuring patient adherence and persistence to rosuvastatin therapy through education regarding its benefits, potential side effects, and the importance of long-term adherence is essential in achieving optimal outcomes in CVD management.

The objective of the survey is:

To understand the physician perspectives on rosuvastatin in cardiovascular disease management

Methodology of the Survey

A survey was conducted to understand the physician perspectives on rosuvastatin in cardiovascular disease management. A total of 150 doctors from India participated in the survey.

Step 1: A literature search was done on the topic. Below topics were covered in the literature search

- Introduction
- Mechanism of action of statins
- HMG-CoA reductase inhibitors
- Pharmacology of Rosuvastatin
- The “pleiotropic effects” of rosuvastatin
- Role of Rosuvastatin in Primary and Secondary Prevention
- Rosuvastatin vs Other Statins
- Rosuvastatin in High CV Risk Patients
- Rosuvastatin in patients withzdiabetes
- Rosuvastatin in atrial fibrillation patients
- Rosuvastatin for prevention in special populations
- Resistance to statin use in the elderly
- Effect of rosuvastatin on lipid profile and atherosclerosis
- Safety and Tolerability of Rosuvastatin
- Rosuvastatin: Economic Evaluation in Cardiovascular High-Risk Patient
- Abstracts

Step 2: A survey questionnaire was prepared based on the literature search. The survey form was shared through the digital medium with physicians across India.

Step 3: Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

Introduction[1]

Ischaemic heart disease (IHD) is the leading cause of mortality worldwide and constitutes a major health burden. According to World Health Organisation (WHO) statistics, it accounts for 12.8% of deaths, with stroke and other cerebrovascular diseases accounting for a further 10.8%. In the United Kingdom, data from the Health Surveys for England suggest that while mortality may be declining, cardiovascular disease morbidity continues to rise. Epidemiological studies have established a strong correlation between cholesterol and the incidence of cardiovascular disease. The associated morbidity and mortality are positively correlated to low-density lipoprotein cholesterol (LDL-C) and inversely related to high-density lipoprotein cholesterol (HDL-C).

Statins are 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors that are effective in the reduction of total and LDL cholesterol. A number of large randomized control trials have demonstrated unequivocally that lowering LDL-C, particularly with statins reduces the risk of cardiovascular deaths and events. HMG CoA inhibitors have been shown to prevent initial cardiovascular events and subsequent cardiovascular events in ischaemic heart disease patients, irrespective of the cholesterol concentration. In addition to the beneficial cholesterol-lowering effects, statins improve endothelial function, enhance the stability of atherosclerotic plaques, and inhibit inflammatory as well as thrombogenic responses in arterial walls. Furthermore extensive post-marketing surveillance has shown that long-term statin therapy is generally well tolerated.

The lipid-lowering arms of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) and Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) showed the benefit of statin therapy in primary prevention of cardiovascular events. The 4S study was the first study conclusively linking a statin with improved outcomes in patients with coronary heart disease. It established simvastatin as the most common LDL-C lowering treatment for patients with CHD in northern Europe.[11] Subsequently, more studies including results of the Treating to New targets (TNT) trial have shown that intensive lipid-lowering (atorvastatin 80 mg) significantly reduces the risk of recurrent cardiovascular events compared to standard lipid-lowering (atorvastatin 10 mg) in stable CHD patients. Other clinical trials using various statins have confirmed similar beneficial effects for ameliorating cardiovascular risk in specific groups such as patients with diabetes, heart failure, and

renal failure. Early detection and treatment with statins have been shown to reduce morbidity and mortality in those with heterozygous familial hypercholesterolemia.

The reduction in cardiovascular events from statin therapy is proportional to the LDL-C reduction. A 1.0 mmol/L reduction in LDL-C results in a 20% decrease in major coronary events and revascularization. Larger reductions in LDL-C are associated with greater reductions in cardiovascular events, so more potent statins result in greater cardiovascular risk reduction. The drive towards more stringent goals for LDL-C lowering in cardiovascular risk prevention has brought high-impact statin therapy into focus. Different statins have varying effects on LDL-C reduction with rosuvastatin producing the greatest reduction and fluvastatin the least. Statins vary in their lipophilicity and metabolism. These affect their extrahepatic tissue penetration and drug interactions with potential safety implications.

Mechanism of action of statins[2]

Statins competitively inhibit hydroxy methylglutaryl coenzyme A (HMG CoA) reductase, the enzyme involved in cholesterol endogen production that regulates its formation velocity, thereby increasing the availability of cholesterol low-density lipoproteins (LDL-C) in the cell membrane and allowing for its levels to decrease.

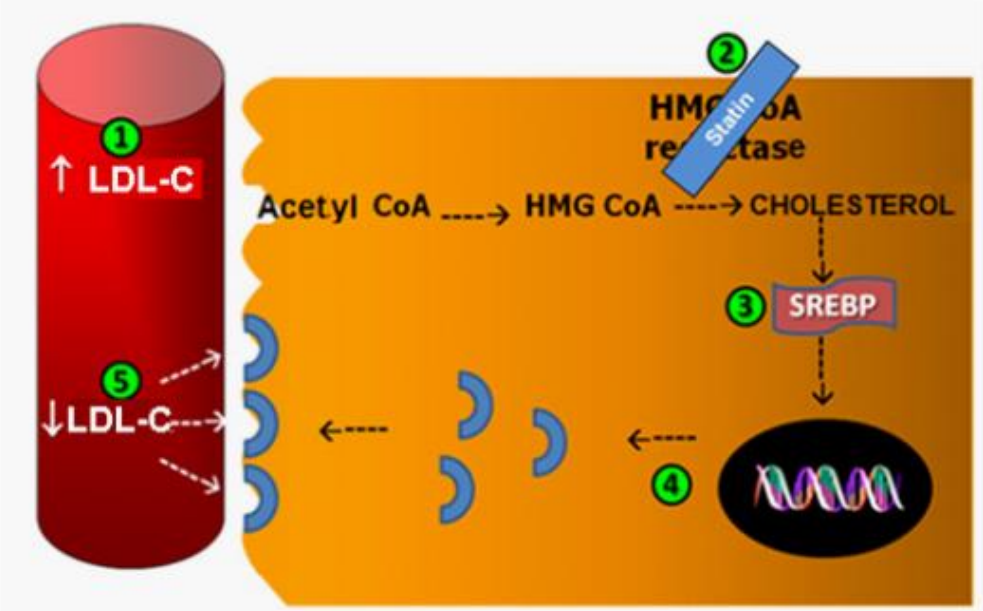

Figure 1. 5-Step statin action mechanisms: When LDL-C levels are high (1), a statin is given in order to inhibit the HMG-CoA reductase in the hepatocyte (2). This leads to intracellular cholesterol reduction thereby eliciting the activation of a transcription factor named SREBP (Sterol and Retinol Binding Protein) and its translocation to the nucleus (3). This way, LDL-C receptors expression is promoted (4) and its removal from circulation is increased.

HMG-CoA reductase inhibitors[2]

HMG-CoA reductase inhibitors are the first-choice drugs (against other lipid-lowering drugs such as the bile acids sequestering agents) in hypercholesterolemia and mixed dyslipidemia patients with predominance of increased cholesterol. The decision for use, according to the addenda of NCEP-ATP III (National Cholesterol Educational Program–Adult Treatment Panel III) clinical guidelines recommendations is dependent on the cardiovascular risk, specified in four levels.

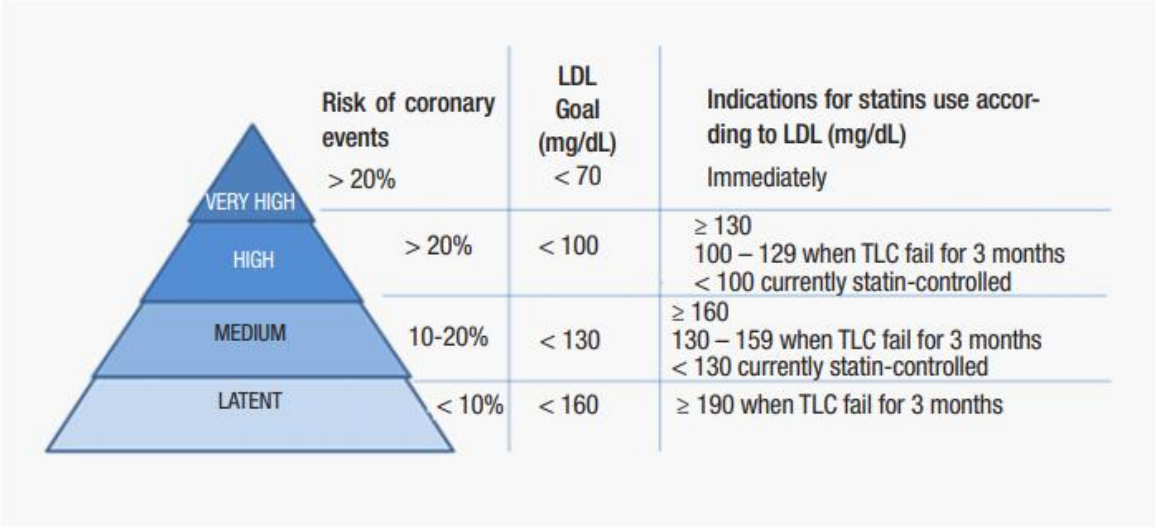

Figure 2. LDL-C goal levels and recommendations for use of statins for each of four (coronary) cardiovascular risk levels. TLC: Therapeutic Lifestyle Changes.

Very high risk

It occurs when there exists a previous cardiovascular episode (myocardial infarction), stable or instable angina, coronary artery procedure such as angioplasty or bypass, of otherwise clinically significantly myocardial ischemia evidence) involving more than one risk factor (e.g. diabetes, hypertension, persistent smoking).

High risk

It occurs under prior coronary disease conditions or its equivalent (peripheral artery disease, aneurism of abdominal aorta, carotid disease (including transient ischemic attack or apoplexy of carotid origin or >50% obstruction of any carotid artery) or primary atherogenic dyslipidemia), as well as in those people which multiple risk factors involve >20% risk of 10 years coronary disease.

Intermediate risk

Occurs in people with metabolic syndrome or which multiple risk factors involve 10 to 20% coronary disease 10-year risk.

Latent risk

Exists in those people which risk factors involve.

Pharmacology of Rosuvastatin[1]

Rosuvastatin which is a new-generation HMG-CoA reductase inhibitor exhibits some unique pharmacologic and pharmacokinetics properties. It has low extrahepatic tissue penetration, low potential for CYP3A4 interactions, and substantial LDL-C lowering capacity and may therefore have some advantages. Its potential impact in primary and secondary prevention of cardiovascular disease in different groups including heart failure, elderly, renal failure, and diabetes, and also in combination with other lipid-lowering drugs is the subject of ongoing clinical studies.

Rosuvastatin is a fully synthetic HMG-CoA reductase inhibitor. Other HMG-CoA reductase inhibitors are either natural, mevinic acid derived (lovastatin, simvastatin pravastatin) or synthetic, heptenoic acid derived (atorvastatin, fluvastatin). Rosuvastatin belongs to a new generation of methane-sulphonamide pyrimidine and N-methane sulfonyl pyrrole-substituted 3, 5- dihydroxy-heptenoates. Although the characteristic statin pharmacophore remains similar to other statins, the addition of a stable polar methane-sulphonamide group provides low lipophilicity and enhanced ionic interaction with HMG-CoA reductase enzyme thus improving its binding affinity to this enzyme.

Pharmacodynamics[1]

Rosuvastatin competitively inhibits the HMG-CoA reductase enzyme selectively and reversibly. This enzyme converts HMG-CoA to mevalonic acid in the cholesterol biosynthetic pathway which is the rate-limiting step in cholesterol synthesis. Rosuvastatin therefore decreases hepatic sterol synthesis, which, in turn, leads to a decreased concentration of hepatocellular cholesterol. Hepatocytes respond to this decreased intracellular cholesterol concentration by increased synthesis of LDL receptors to enhance hepatic LDL reuptake from the circulation. The net result of this process is increased fractional catabolism of LDL which reduces serum LDL-C concentration and total cholesterol. Statins also reduce production of ApoB leading to reduced hepatic output of very low-density protein cholesterol (VLDL-C) and triglycerides. In patients with homozygous familial hypercholes-terolaemia, rosuvastatin decreases LDL-C despite absence of functional LDL receptors. This may be sec-ondary to marked inhibition of cholesterol synthesis which decreases LDL production. Rosuvastatin has demonstrated comparable reductions in triglyceride (TG) concentrations to other statins with the greatest benefit seen in patients with high baseline TG levels. Studies have shown rosuvastatin to increase HDL-C by 8–12%

with no clear relationship between the dose and response, although the increase is greatest in patients with low baseline HDL-C levels. This may be due to reduction of cholesterol ester transfer protein (CETP). The affinity of rosuvastatin for the active site of the enzyme is four times greater than the affinity of HMG-CoA for the enzyme. It has the highest affinity for HMG-CoA reductase among statins marketed in Europe. This high affinity coupled with tight ionic interaction result in a slow recovery of enzyme activity after removal of rosuvastatin. Since it is a hyhydrophilictatin, rosuvastatin relies on the organic anion transporting polypeptide-1B1 (OATP-1B1), which is strongly expressed on the hepatocyte basolateral membrane, as the key mechanism for active transport into hepatocytes. Its affinity for OATP-1B1 is comparable to atorvastatin but significantly greater than pravastatin or simvastatin. Rosuvastatin is therefore primarily distributed to hepatocytes while peripheral concentrations are low. As observed with other statins, rosuvastatin has pleiotropic effects independent of HMG-CoA reductase inhibition. These include improvements in endothelial function, anti-inflammatory, antithrombotic and anti-oxidant effects. Rosuvastatin and other statins improve endothelial function by increasing the production of endothelial nitric oxide and reducing the production of oxygen-derived free radicals. This in turn reduces endothelial dysfunction that has been implicated in atherosclerosis. Rosuvastatin reduces high sensitivity C reactive protein (hsCRP) which is a marker of inflammation and an independent cardiovascular risk predictor and other inflammatory markers. Rosuvastatin inhibits platelet aggregation to leukocytes which inhibit formation of clots in injured endothelium.

Pharmacokinetics[1]

The oral bioavailability of rosuvastatin is 20%, which is comparable to atorvastatin, pravastatin and fluvastatin, and qualitatively higher than simvastatin and lovastatin. After a single oral dose the peak plasma concentration is reached at 5 hours. This is longer than other HMG-CoA inhibitors which achieve maximum plasma concentrations in less than 3 hours. In compiled data from pharmacokinetic trials, the peak plasma concentration and area under the concentra-tion time curve show a largely linear relationship as the dose of rosuvastatin increases from 5 to 80 mg. Food intake decreases the rate of absorption of rosuvastatin by 20% but not the extent of absorption. This does not reduce the cholesterol lowering potency; therefore rosuvastatin can be taken with or without food, and in the morning or evening. Approximately 90% of rosuvastatin is protein bound mainly to albumin; other statins have approximately 95% protein binding except pravastatin which has lower protein binding of 50%. The mean of volume distribution is 134 litres in steady state. Rosuvastatin is less lipophilic than other statins such as atorvastatin and simvastatin but more lipophilic than pravastatin. Penetration of statins into extra-hepatic tissues occurs by passive diffusion and is dependent on their lipophilicity. This has

implications on their muscle safety as increased rhabdomyolysis was reported in patients on lipophilic agents like cerivastatin and lovastatin. Human hepatocyte studies indicate that rosuvastatin is a poor substrate for metabolism by cyto-chrome P450 and hence 90% of the drug is excreted unchanged. CYP2C9 is the main isoenzyme involved in metabolism with minimal effect from CYP2C19. Rosuvastatin is metabolised to an N-desmethyl metabolite which is less potent than the parent drug in inhibiting HMG-CoA reductase activity. The parent drug rosuvastatin is responsible for approximately 90% of plasma HMG-CoA inhibitor activity. Rosuvastatin is less likely to cause metabolic drug to drug interactions since it has limited metabolism by CYP isoenzymes. Other HMG-CoA reductase inhibitors such as atorvastatin and simvastatin are metabolised via CYP3A4. Their plasma concentrations are increased by inhibitors of CYP3A4 such as itraconazole, protease inhibitors and macrolide antibiotics. Rosuvastatin has a plasma half-life of 19 hours which is longer than atorvastatin (15 hours) and simvastatin (2–3 hours). It is primarily eliminated in the faeces (90%) compared with 10% renal excretion. Approximately 72% of absorbed rosuvastatin is eliminated in bile and 28% via renal excretion.

The "pleiotropic effects" of rosuvastatin[3]

Like other drugs of this class, the benefits of rosuvastatin are independent of LDL-C baseline levels but they even exceed the predicted lowering effect of plasma LDL-C, suggesting other significant clinical beneficial effects in addition to the cholesterol-lowering one. These ancillary properties, other than those for which statins were specifically developed, are known as "pleiotropic effects" and significantly contribute to the statin efficacy in CV disease prevention and treatment. Atherosclerosis represents an inflammatory disease associated in its earliest phase with endothelial dysfunction and a higher risk of CV events. Statins ancillary properties are involved in all the CV diseases pathophysiological stages: initially by the reducing the oxidative stress and inflammation and improving endothelial function; then acting on the progression and rupture of plaque by inhibiting smooth muscle cell proliferation, promoting the stability of atheroma and inhibiting the thrombogenic response.

The pleiotropic effects of statins may be linked or not to the primary mechanism of action of these drugs. In fact, an association has been demonstrated with the faculty to inhibit the formation of mevalonate and its downstream products, the isoprenoid molecules. The non-sterol intermediates of the cholesterol synthesis pathway, farnesylpyrophosphate (FPP) and geranylgeranylpyrophosphate (GGPP), play important roles as regulators of essential signaling proteins in vascular cells.

They represent lipid binding sites for transmembrane movement and activity of several proteins including Rho and Ras, which are crucial components of various protein kinase signaling patways. In fact while Ras system is essential for cell growth and intracellular signaling, Rho proteins have a crucial role in the inflammatory process at the base of atherosclerosis pathophysiology.

Rho kinase (ROCK) are serine/threonine kinases, downstream effectors of the small GTPase Rho. They play key roles in a variety of cellular functions, and are also involved in basic processes of atherosclerosis. ROCK is able to promote the contraction of vascular smooth cell, through the stimulation of the myosin light chain phosphorylation. It can acts by directly phosphorylate the myosin light chain or alternatively by phosphorylating and then inactivating the myosin light chain phosphatase, an enzyme responsible for the dephosphorylation of the activated myosin light chain and consequently able to determine the relaxation of smooth muscle cells. ROCK activity is therefore responsible for the persistence of a state of smooth muscle cells contraction, closely related to the onset and development of CV diseases. Furthermore, evidences suggest that statins are able to determine an increased production of nitric oxide (NO) through the inhibition of the ROCK system that, by decreasing post-transcriptional stabilization of endothelial NO synthase (eNOS) mRNA, down-regulates eNOS expression. In vitro trials demonstrated that the increased NO production in cultured cells incubated with HMG-CoA inhibitors was completely reversed by the presence of L-mevalonate, trought the activation of the ROCK system.

Furthermore experiments with human vascular smooth muscle and mononuclear cells showed a great reduction, induced by statins, of interleukin-6 (IL-6) synthesis, a key molecule in chronic inflammation, strongly involved in atherosclerotic development and progression.

The inhibition of the ROCK system induced by statin treatment has proven to positively modulate the prothrombotic condition associated with atherosclerosis. In vivo and in vitro studies showed the ability of HMG-CoA reductase inhibitors to improve the fibrinolytic activity: on the one hand, the administration of statins is in fact associated with an increase of tissue plasminogen activator inhibitor, and with a reduction of activator inhibitor type-1 levels on the other hand. Moreover, clinical concentrations of statins showed to determine a reduction of matrix metalloproteinase-1 expression in human and animal cells, influencing plaque stability and progression of coronary artery disease.

Role of Rosuvastatin in Primary and Secondary Prevention[1]

There have been a number of clinical studies evaluating rosuvastatin on its own, against placebo and against other statins in various clinical settings.

Rosuvastatin in primary prevention

Clinical studies have demonstrated the benefits of statins in primary prevention. This is believed principally to be secondary to reduction in LDL-C, high sensitivity C-reactive protein (hsCRP) and elevation of HDL-C though other effects are recognised. The Cholesterol Treatment Trialists' Collaborators (CTT) meta-analysis established that a 1 mmol/L reduction in LDL cholesterol results in a 20% reduction in cardiovascular risk. The benefit of statins in low risk populations was demonstrated in the Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese (MEGA) study where reduction of cholesterol using pravastatin 10 mg reduced cardiovascular events by 33%.

JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) marked an important juncture in primary cardiovascular disease prevention with statins. The participants had a mean Framingham risk score at baseline of 11.6% and would otherwise not have qualified for lipid lowering therapy. They were apparently healthy individuals with normal levels of LDL-C (<3.4 mmol/L) and increased hsCRP (>2 mg/L). The hsCRP threshold value of 2 mg/L is the approximate median hsCRP value after 30 days of statin therapy. It originated from secondary prevention trials and in particular the PROVE-IT-TIMI-22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy Thrombolysis In Myocardial Infarction) and A to Z (Aggrastat to Zocor) which showed that achieving this level of hsCRP was associated with improved cardiovascular outcomes. JUPITER was a randomised, double blind, placebo-matched, multicentre trial conducted at 1315 sites in 26 countries. 17,802 participants received either 20 mg of rosuvastatin, or matched placebo, and were followed up every six months. 12 months into the study, the rosuvastatin group had a 50% lower median LDL-C, 37% lower median hsCRP and 17% lower median triglyceride level ($P < 0.001$ for all three comparisons) which persisted to study completion. The observed increase in HDL-C was transient. Results showed that rosuvastatin was associated with a significant reduction in first major cardiovascular events (HR 0.56; 95% CI, 0.46 to 0.69; $P < 0.00001$) which was the primary endpoint. Reductions were further seen in the incidence of the individual components of the trial end point including myocardial infarction (54%), stroke (48%), arterial revascularisation (47%), unstable angina and death from cardiovascular causes. This is important as up to 50% of all myocardial

infarctions and strokes occur in patients with LDL cholesterol concentrations that are considered normal. The benefits were largely similar for men and women, and were observed in all subgroups including age, ethnicity, region and cardiovascular risk score. Previously, there has been limited data on statin benefits in women, black and Hispanic patients.

Since the results of JUPITER were initially published, several secondary subgroup analyses of the study population have been reported. Participants with a 10 year low baseline risk (<5%) benefited less than those with risk >5%. Participants with a 10 year intermediate baseline risk by Framingham (5%–20%) experienced incremental absolute risk reductions that were proportional to their global risk. In a different subgroup analysis, participants at high global risk (10 year Framingham score >20%) showed no additional benefit for the combined endpoint of myocardial infarction, stroke and cardiovascular death (HR 0.50; 95% CI, 0.27 to 0.93) when compared with subjects who had an intermediate Framingham risk score.

Another series of sub analyses have looked at lipid profiles and hsCRP particularly in relation to residual cardiovascular risk. In all of them, participants who achieved low concentrations of hsCRP in addition to low values of the lipid parameters of interest had the best outcome. When hsCRP is included in enrolment of primary prevention, rosuvastatin produced greater benefit when compared with other statins.

These results compare favourably with other primary prevention trials using different statins. WOSCOPS (West of Scotland Coronary Prevention Study) showed that pravastatin 40 mg in men with moderate hypercholesterolaemia reduced incidence of myocardial infarction and cardiovascular death by 31%. Similarly, AFCAPS (Air Force/Texas Coronary Atherosclerosis Prevention Study) demonstrated that lovastatin 20–40 mg daily reduced risk of first major coronary event by 37% in men and women with average LDL-C and below average HDL-C when compared with placebo.[42] In the ASCOT lipid lowering arm, atorvastatin 10 mg reduced the incidence of myocardial infarction, stroke and cardiovascular death by 36% compared to placebo.

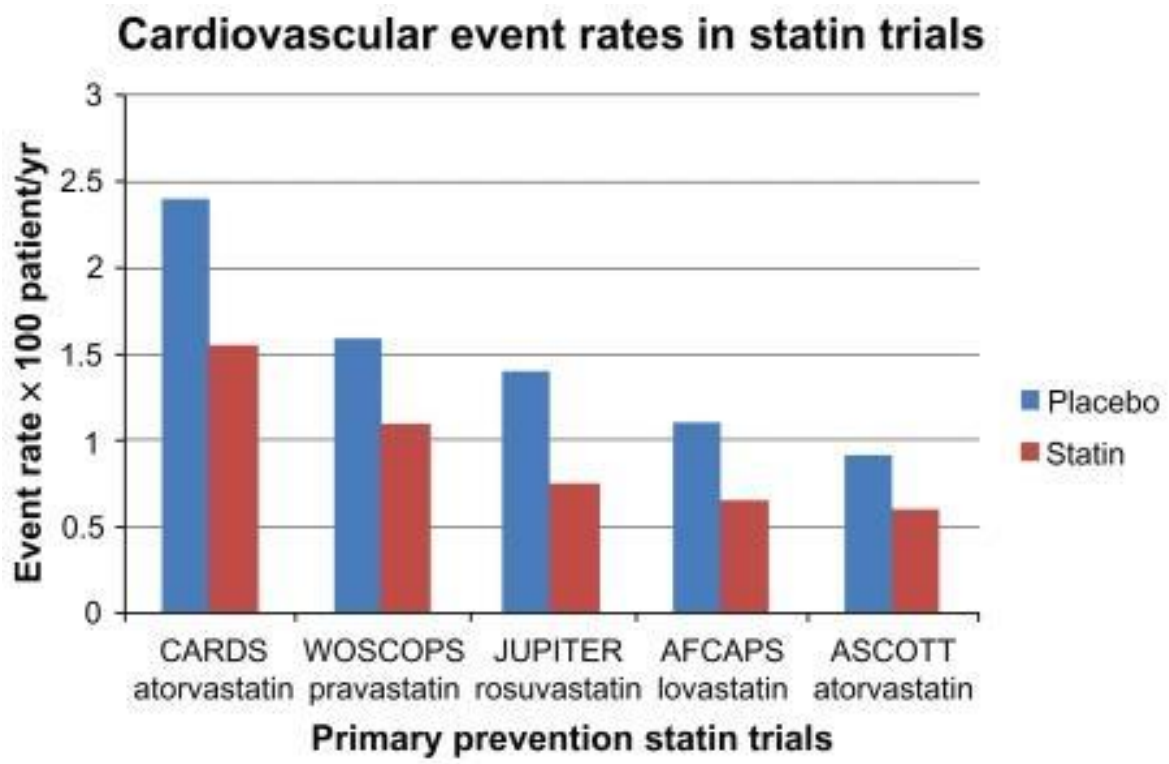

Figure 3. CHD event rate in primary prevention trials.

Rosuvastatin in secondary prevention

The beneficial effects of statin therapy in patients with ischaemic heart disease are well known. The 4S study showed that simvastatin 20 mg to 40 mg daily significantly reduced major coronary events, coronary death and overall mortality in patients post-MI or those with ischaemic heart disease. In the LIPID study (Long-term Intervention with Pravastatin in Ischaemic Disease), pravastatin 40 mg reduced cardiovascular events and mortality in patients with history of myocardial infarction or unstable angina with different baseline lipid profiles. Other studies have also established the benefits of treatment after myocardial infarction.

a) Stable coronary heart disease (CHD)/Arrest and regression of atherosclerosis

The TNT trial comparing atorvastatin 80 mg with atorvastatin 10 mg, investigated whether intensive treatment to achieve LDL-C <1.81 mmol/L was associated with better outcomes. Mean LDL-C of 2 mmol/L was realised with intensive treatment. A relative risk reduction of 22% was achieved for the primary outcome which was the occurrence of a first major cardiovascular event. The IDEAL study (Incremental Decrease in Endpoints through Aggressive Lipid Lowering) compared the effect of

atorvastatin 80 mg and simvastatin 20 mg on cardiovascular outcomes. There were significant reductions in non-fatal acute myocardial infarction and in other secondary composite endpoints, with no difference in cardiovascular or all-cause mortality. Statistical significance was not demonstrated for the prespecified primary clinical outcome which was time to first occurrence of major coronary event. In as much as there have been no clinical outcome data for secondary prevention with rosuvastatin, a number of studies have compared their effect on surrogate markers and achievement of treatment goals. The STELLAR study (Comparison of the Efficacy and Safety of Rosuvastatin Versus Atorvastatin, Simvastatin, and Pravastatin Across Doses) showed that at different doses, rosuvastatin reduced total cholesterol better than other statins, and triglycerides better than simvastatin and pravastatin. Additionally a larger proportion of rosuvastatin patients achieved National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) LDL-C targets when compared with atorvastatin. PULSAR (Prospective Study to Evaluate Low Doses of Atorvastatin and Rosuvastatin) showed that in hypercholesterolaemic patients with vascular occlusive disease rosuvastatin 10 mg was better than atorvastatin 20 mg at reducing LDL-C, improving other lipid parameters and enabling achievement of US and European treatment goals.

Several studies have suggested that reduction in plaque volume is linked to the clinical outcome. ASTEROID (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-derived Coronary Atheroma Burden) investigated the impact of high dose rosuvastatin on regression of atherosclerosis. The results showed that rosuvastatin 40 mg produced significant reduction in LDL-C (53% from baseline; $P < 0.001$), increase in HDL-C (14.7% from baseline; $P < 0.001$) and regression of atheroma volume in the most diseased coronary arteries in 78% of participants. A median reduction of 6.8% in atheroma volume was recorded by IVUS (intravascular ultrasound). It must be noted that the study was non-comparative and open label. Other studies including ORION (Outcome of Rosuvastatin Treatment on Carotid Artery Atheroma: a Magnetic Resonance Imaging Observation) and METEOR (Measuring Effects on Intima Media Thickness: an Evaluation of Rosuvastatin) demonstrated that rosuvastatin 40 mg achieved a 49% LDL-C reduction and slowed progression of atherosclerosis as assessed by carotid intima-media thickness (CIMT) but did not result in regression of CIMT. The lack of plaque regression may have occurred because low risk patients with minimal subclinical carotid atherosclerosis were used in the study. The COSMOS (Coronary Atherosclerosis Study Measuring Effects of Rosuvastatin Using Intravascular Ultrasound in Japanese Subjects) study found that rosuvastatin achieved significant reduction of coronary plaque volume with good safety in stable Japanese CHD patients. The recently concluded SATURN (Study of Coronary Atheroma by Intravascular Ultrasound: Effect of Rosuvastatin versus Atorvastatin) study compared maximal doses of rosuvastatin and atorvastatin on coronary atheroma. It reported that although rosuvastatin achieved

lower LDL-C and higher HDL-C, both agents produced similar percentage reduction in atheroma volume.

b) Acute coronary syndrome (ACS)

The NCEP ATP III guidelines recommend that intensive statin treatment should be used in patients admitted with acute coronary syndrome. The European Society of Cardiology (ESC) and the American College of Cardiology (ACC) have recommended LDL-C levels of 1.8 mmol/L as the optimal target for very high risk patients (established CHD, type I diabetes with end organ damage, moderate to severe chronic kidney disease (CKD) or a SCORE level >10%). Several studies have provided evidence of the additional LDL-C lowering achieved by intensive statin therapy.

The PROVE-IT study found that intensive treatment with atorvastatin 80 mg was better than pravastatin 40 mg at preventing death and major cardiovascular events following ACS. The A to Z study which compared 40 mg and 80 mg of simvastatin demonstrated a benefit which did not reach statistical significance, while the MIRACL (Myocardial Ischaemia Reduction with Aggressive Cholesterol Lowering) study showed that early intensive treatment with atorvastatin 80 mg after ACS led to a 16% reduction in death, acute MI, unstable angina and cardiac arrest, compared with placebo. Meta-analyses of intensive statin trials have also shown that intensive treatment provides benefit above lower intensity treatment in prevention of myocardial infarction and strokes in patients with known coronary disease irrespective of the baseline LDL-C. The CENTAURUS (Comparison of the Effects Noted in The ApoB:ApoA-1 ratio Using Rosuvastatin or Atorvastatin in Patients with Acute Coronary Syndrome) study showed that 20 mg rosuvastatin produced similar changes in ApoB:ApoA-1 ratio at 3 months when compared with atorvastatin 80 mg. Previous studies have identified ApoB:ApoA-1 ratio as an important predictor of myocardial infarction. In the same study rosuvastatin 20 mg achieved similar LDL-C reduction as atorvastatin 80 mg. This study therefore showed that rosuvastatin 20 mg is as effective as atorvastatin 80 mg in intensive statin therapy. In SPACEROCKET (Secondary Prevention of Acute Coronary Events—Reduction of Cholesterol to Key European Targets Trial), a larger proportion of patients on rosuvastatin 10 mg achieved ESC, ACC and American Heart Association (AHA) optimal LDL-C target of less than 1.81 mmol/L when compared to those on simvastatin 40 mg. A crucial observation of this study was that in both treatment arms, most patients did not achieve these targets, highlighting the importance of intensive statin therapy to meet these goals. The superior lipid lowering effect of rosuvastatin makes it a good candidate for intensive lipid lowering.

Rosuvastatin vs Other Statins[2]

Statins show similar chemical structures as they all show an analogy similar the radical beta-hydroxyl-beta methyl glutaryl (HMG). Rosuvastatin, however, has a methyl-sulfonamide group which allows more interaction with some amino acid residues of the MHG CoA reductase, and this way to have a high affinity for the active site of the enzyme. Additionally, rosuvastatin hepatic selectivity shall be taken into account as it is a relatively hydrophilic (the same as pravastatin), compared to other statins, and therefore its uptake by other type of different cells would be limited. In fact, classic head-to-head randomized controlled clinical trials (RCT) such as STELLAR (Statin Therapies for Elevated Lipid Levels compared Across doses to Rosuvastatin), have shown rosuvastatin to be the inhibitor of HMGCoA reductase significantly achieving greater LDL-C decreases.

Characteristics Statin	Min Dose	% LDL-C Reduction	% HDL-C Increase	% TG Reduction	Cytochrome P450 Metabolism	Half-life (hrs)
Fluvastatin	20 mg	17%	1%	5%	2C9	1-3
Pravastatin	10 mg	20%	3%	8%	---	1-3
Simvastatin	10 mg	28%	5%	12%	3 A4	2-5
Lovastatin	20 mg	29%	7%	12%	3 A4	2-5
Atorvastatin	10 mg	37%	6%	20%	3 A4	14
Rosuvastatin	10 mg	46%	8%	20%	2C9/2C19	20

Statin	Rosuvastatin				Atorvastatin				Simvastatin			
Dose	5 mg	10 mg	20 mg	40 mg	10 mg	20 mg	40 mg	80 mg	10 mg	20 mg	40 mg	80 mg
LDL-C	-38.8 ± 0.9	-44.1± 0.6	-49.5± 0.5	-54.7 ± 0.4	-35.5± 0.6	-41.4 ± 0.5	-46.2 ± 0.5	-50.2 ± 0.4	-27.4 ± 1.4	-33.0 ± 0.6	-38.9 ± 0.9	-45.0 ± 1.0
Non HDL-C	-35.4 ± 0.8	-40.2 ± 0.5	-45.1 ± 0.4	-49.9 ± 0.3	-32.8 ± 0.5	-38.2 ± 0.5	-42.6 ± 0.5	-46.6 ± 0.4	-24.8 ± 1.2	-30.1 ± 0.5	-35.0 ± 0.8	-40.5 ± 0.9
TG	-15.2 ± 1.4	-18.7 ± 0.5	-20.1 ± 0.7	-21.9 ± 1.0	-16.4 ± 0.5	-18.9 ± 0.6	-20.7 ± 1.2	-25.0 ± 1.1	-9.3 ± 2.5	-12.7 ± 0.7	-13.3 ± 1.4	-14.5 ± 1.8
% patients with LDL-C < 70 mg/ dL *	3.2%	11.4%	20.5%	31.7%	2.0%	4.1%	9.8%	18.1%	0%	1.6%	1.5%	4.0%
% patients with LDL-C < 70 mg/ dL**	0%σ	33.0%	57.2%	67.6%	8.8%	26.2%	45.2%	52.4%	0%σ	7.0%	19.9%	ND
% patients with LDL-C < 100 mg/ dL *	38.0%	56.8%	64.5%	74.1%	28.7%	45.0%	56.6%	71.4%	8.8%	24%	34.2%	38.5%
% patients with LDL-C < 100mg/ dL**	66.7%σ	75.9%	90.1%	95.4%	62.1%	83.8%	91.1%	86.4%	50.0%σ	57.3%	76.7%	ND

Rosuvastatin ensures HMG CoA reductase sustained inhibition as it has more extended half-life (20 hrs) among statins. This characteristic makes it to outstand as a valuable therapeutic option in the intolerance context of statins as described in several case report and retrospective studies where up to

72.5% of patients with intolerance resolve their symptoms by delivering rosuvastatin once every other day such dosing (5.6mg mean) reducing LDL cholesterol by 34.5%. In fact, two controlled clinical studies assessed rosuvastatin 10 or 20 mg once every other day versus rosuvastatin 10 mg/daily during six weeks, resulting in LDL-C reduction up to 48.5%for daily dose and up to 40.9% for 20 mg once every other day (p=0.012).

Rosuvastatin also is advantageous because of its minimum metabolism through P450 cytochrome (CTP), especially through CYP2C9 and CYP2C19 isoenzyme CYP3A4, as most of the statins (simvastatin, lovastatin and atorvastatin), which is involved in a broad variety of drug interactions. Such drugs usually present in patients under therapy with verapamil, diltiazem, and macrolides, such as erythromycin or clarithromycin, among others.

Statins are usually well tolerated. Most common adverse effects include myalgia, constipation, asthenia, abdominal pain, and nausea. Several meta-analysis have found all statins to have a similar safety profile, the most frequent adverse effects occurring with higher doses of statins. Someone could believe, however, that rosuvastatin could have difference related to adverse as against other statins. Notwithstanding, a meta-analysis of four pharmacoepidemiological studies conducted on several international databases that evaluated rosuvastatin safety profile versus other statins, evidenced that there was no higher incidence of rare adverse events such as hospitalizations due to myopathies (0.5 episodes per 10000 years-patient; IC95%: -0.6 a 1.6), rhabdomyolysis (0.7 episodes per 10000 years-patient; IC95%: -0.3 a 1.6), acute renal failure (-0.2 episodes per 10000 years-person; IC95%:-2.9 a 2.5) or acute hepatic damage (-0.8 cases per 10000 years-person; IC95%: -1.8 a 0.2) with the use of rosuvastatin. What certainly was found is that the therapy with most of statins can impair glycemic control, or slightly increase diabetes mellitus risk by 9% average (OR=1.09; IC95%: 1.02 a 1.17). Due to occurrence, FDA (US Food and Drug Agency) has added up a warning in the labeling from all statins advising that they may increase glycemia and hemoglobin A1c levels, recognizing, however, statins cardiovascular benefits overweight such mildly increases.

Rosuvastatin in High CV Risk Patients

Rosuvastatin in patients with HF[3]

It is well known the positive prognostic impact of rosuvastatin in primary and secondary prevention of CAD in patients at high CV risk. Also in the HF management the role of statins seems to be crucial, as

showed by several observational studies in which incident statin administration, in patients with no prior statin use, was related with lower risks of death and hospitalization, independently of cholesterol levels, age and a history of ischemic heart disease. In patients with nonischemic HF atorvastatin 20 mg/day for 1 year increased left ventricular ejection fraction from 0.33 +/- 0.05 to 0.37 +/- 0.04 (p = 0.01) compared to placebo, in addition to effects on soluble inflammatory markers (increase erythrocyte superoxide dismutase activity and reduction in serum levels of hs-CRP, IL-6 and tumor necrosis factor-alpha receptor II). Neverthless the small sample (108 subjects) and the short follow-up period, the study suggests the role of statins in this subpopulation of patients. In a large randomized controlled trial (CORONA) which recruited 5011 elderly patients with ischemic disease and systolic HF, rosuvastatin 10 mg/day compared to placebo, over a median follow-up of 32.8 months, reduced the number of CV hospitalizations but not death from CV causes, nonfatal MI or stroke, death from any cause and any coronary event. Moreover, patients in the rosuvastatin group showed lower serum levels of LDL-C and hsCRP (P <0.001) with no significant rate of adverse events.

Similar findings emerged from GISSI-HF trial that enrolled patients with chronic HF of any etiology: in a median follow-up of 3.9 years, rosuvastatin 10 mg (2285 subjects) per day did not influence primary endpoints (time to death, and time to death or admission to hospital for CV reasons) and showed a good safety (the most frequent adverse reaction reported were gastrointestinal disorders with no statistically significant difference between rosuvastatin and placebo groups). Furthermore, an interesting result of GISSI-HF trial was the effectiveness of n-3 polyunsaturated fatty acids in decreasing the endpoint death or admission to hospital for CV reasons. The disappointing results of these two trials give rise to several interpretations. May exist varying extra-hepatic effects of statins due to their lipophilicity/hydrophilicity. Therefore, hydrophilic statins, to which the rosuvastatin belongs, could exert their effects especially in the liver, instead lipophilic statins, such as atorvastatin, affect also myocardium.

Moreover, the benefits of rosuvastatin may occur only for particular subgroups of HF patients, or for different degree of disease severity, and thus it could be a specific clinical and histopathological stage of cardiac pathology, previously or after which, rosuvastatin is ineffective.

Rosuvastatin in patients with chronic renal failure[3]

Likewise, in patients with end-stage renal disease on chronic haemodialysis, who represent a category of subjects at high CV risk, rosuvastatin is effective in decreasing LDL-C and CRP levels with no significant effects on death from CV causes, nonfatal MI infarction or nonfatal stroke. These were the

conclusions of AURORA trial, performed on 2776 patients undergoing hemodialysis and treated with rosuvastatin 10 mg daily over a median follow-up period of 3.8 years compared to placebo. However, this study enrolled patients aged between 50 to 80 years old, omitting younger hemodialytic patients which, anyway, represent a subclass at high CV risk. Furthermore, the mean baseline LDL-C levels within the study population were not high (99 mg/dl), so we can conclude that in renal failure patients, unlike general population, the CV disease is attributable also to non-traditional risk factors such as arterial calcification and arrhythmias. These reasons may be adduced to explain the disappointing results of this trial and to support the primary prevention and statin use in these patients, on the basis of magnitude of CV risk factors and of specific pathophysiology of uremia. This concept is in accordance with a post hoc analysis of AURORA trial that showed in participants with DM (n=731) a 32% reduction in fatal and nonfatal cardiac events rates with rosuvastatin therapy. Nevertheless, in patients at high CV risk rosuvastatin showed reno-protective effects, evaluated by means of GFR, compared to placebo treated subjects.

However dose adjustment is necessary in patients with kidney disease. In particular, while no modifications are needed in presence of mild renal impairment (GFR ≥60 mL/min/1.73 m2), 40 mg dose is contraindicated in presence of GFR ranging from 30 to 60 mL/min/1.73 m2 (moderate renal impairment), and finally no administration is permitted in presence of severe renal impairment (GFR 80 mL/min/1.73 m^2).

In hemodialytic patients rosuvastatin contraindicated but caution is needed as steady-state plasma concentrations are approximately 50% greater compared with subjects with normal renal function.

Rosuvastatin in patients with diabetes[1]

Type 2 diabetes is associated with increased risk of coronary heart disease. In the UK Prospective Diabetes Study (UKPDS), every 1 mmol/L increment in LDL-C was associated with a 57% increase in relative risk of coronary heart disease. Furthermore, the LDL-C of diabetic patients predicted their risk of stroke. CARDS (Collaborative Atorvastatin Diabetes Study) showed that atorvastatin 10 mg led to a reduction in cardiovascular events and strokes in diabetes patients without high HDL-C and no prior history of cardiovascular disease. This has strengthened the need for statin therapy for primary prevention in diabetes patients. Sub-group analyses of 4S showed the benefits of simvastatin in reducing major coronary events and revascularisation in diabetic patients with coronary heart disease. However, the reduction in total and cardiovascular mortality was not significant due to the small sample size.

A randomised double blind double-dummy, multicentre, phase IIIb, parallel-group study to compare the efficacy and safety of rosuvastatin (10 mg and 20 mg), and atorvastatin (10 mg and 20 mg) in patients with type 2 diabetes mellitus (ANDROMEDA) showed that rosuvastatin produced greater reductions in LDL-C, ApoB and total cholesterol when compared with equal doses of atorvastatin. A greater proportion of patients on rosuvastatin achieved European LDL-C goals compared to those on atorvastatin. The CORALL (Cholesterol Lowering Effects of Rosuvastatin compared with Atorvastatin in patients with type 2 diabetes) study showed that rosuvastatin produced greater reductions in ApoB:ApoA-1 ratios, LDL-C and total cholesterol in diabetic patients with moderate dyslipidaemia. The superior effect of rosuvastatin compared with atorvastatin in reduction of LDL-C was also demonstrated in the URANUS (Use of Rosuvastatin versus Atorvastatin in type 2 diabetes mellitus) study.

Rosuvastatin in atrial fibrillation patients[3]

Patients suffering from atrial fibrillation (AF), the most common cardiac arrhythmia and important risk factors for ischemic stroke, benefit from treatment with rosuvastatin. Data from several trials show that statin therapy determines a 50-60% decrease of recurrent AF risk and incidence of postoperative AF, but it is not significantly effective in preventing new-onset AF. These benefits occur in a dose-independent manner, and seem attributable to well-known anti-inflammatory and antioxidant properties of this statin able to counteract atrial structural remodeling. In fact, in subjects with high hsCRP serum value (> 2 mg/l), a further increase has been associated with a 36% higher risk of developing AF, and administration of rosuvastatin 20 mg once a day has been shown to reduce the relative risk of new AF of 27% compared with placebo group. Furthermore, in AF patients, rosuvastatin, administrated before elective electrical cardioversion, was able to reduce the risks of AF recurrence during the following 3 months. This antiarrhythmic action is due to the reduction of serum asymmetric dimethylarginine levels, a marker associated with higher risk of early recurrence of AF after electrical cardioversion, and the impaired endothelium-dependent vasodilatation. The GISSI-HF trial also demonstrated the favorable effect of rosuvastatin 10 mg once daily in preventing new-onset and recurrent AF (13% relative risk reduction, 2.1% absolute risk reduction) in patients with HF. At any rate, as the weight of the evidences is weak, the 2012 European Guidelines for the management of AF do not recommend the use of statins in the “upstream therapy” of AF, the nonantiarrhythmic treatment able to prevent its recurrence.

Rosuvastatin for prevention in special populations[4]

On the other hand, two important studies, ie, AURORA (A study evaluating the Use of Rosuvastatin in patients requiring Ongoing Renal dialysis: an Assessment of survival and cardiovascular events) and CORONA (Controlled Rosuvastatin Multinational Trial in Heart Failure), evaluating the efficacy of rosuvastatin in specific populations found that while rosuvastatin did reduce the levels of LDL-C and hsCRP, there was no difference in the rate of primary endpoints in the rosuvastatin groups compared with placebo.

Several studies have shown that patients undergoing maintenance hemodialysis have an increased risk of CVD, and observational studies have suggested that statin therapy can have survival benefits in patients undergoing hemodialysis. AURORA was a prospective trial that randomized 2776 patients, aged 50–80 years (mean baseline age 64 years), who were undergoing maintenance hemodialysis for advanced renal failure to receive rosuvastatin 10 mg daily or placebo. After three months of treatment, patients randomized to the rosuvastatin group had LDL-C levels that were 43% lower than their baseline level as compared with only a 2% reduction from baseline in the placebo group. The median hsCRP level decreased by 12% in the rosuvastatin group (by 0.65 mg/L, versus an increase of 0.21 mg/L in the placebo group, $P < 0.001$).

After a median follow-up of 3.8 years, the primary endpoint of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke occurred in 396 patients in the rosuvastatin group (0.2 events per 100 patient-years) versus 408 patients in the placebo group (9.5 events per 100 patient-years), with no significant effect of treatment (HR 0.96, 95% CI 0.84–1.11, $P = 0.59$). The lack of an effect of rosuvastatin therapy on the primary endpoint was consistent in all the pre-specified subgroups, including patients younger than 65 years and those aged ≥65 years.

These findings suggest that the CVD process in patients undergoing hemodialysis differs from that in other patient populations. In the general population, a majority of cardiovascular events are coronary events such as myocardial infarctions. In the hemodialysis population, however, only approximately 25% of cardiovascular events are myocardial infarctions. Rather, heart failure, sudden cardiac death, and arrhythmias predominate in this population. Therefore, the anti-inflammatory and lipid-lowering effects of statins may not benefit a population in which myocardial infarctions do not predominate.

CORONA investigated the use of rosuvastatin in older patients with systolic heart failure, a population also generally excluded from statin trials. The study randomized 5011 patients aged at least 60 years (mean baseline age 73 years, with 41% at least 75 years) with New York Heart Association Class II, III, or IV ischemic systolic heart failure to rosuvastatin 10 mg daily or placebo. After a median follow-up of 32.8 months, patients in the rosuvastatin group had decreased levels of LDL-C (45% difference between groups, $P < 0.001$) and hsCRP (37% difference between groups) compared with placebo. However, there was no statistically significant decrease in the primary outcome, that included death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke (HR 0.92, 95% CI 0.83–1.02, $P = 0.12$). On the other hand, there was a statistically significant reduction in the number of hospitalizations for cardiovascular causes in the rosuvastatin group compared with the placebo group ($P < 0.001$), which was a secondary endpoint for this trial.

The authors of the study had hypothesized that statin use would stabilize coronary plaques and reduce myocardial ischemia and infarction, and thereby decrease the rate of sudden death in patients with ischemic heart failure, a population in which half of the sudden deaths are caused by plaque rupture. While it is unclear why treatment with rosuvastatin did not decrease the rate of the primary outcome, the authors suggested that alternative mechanisms of death, such as pump failure rather than atherosclerotic causes, effects of other drugs the patients were on, and the need for a longer follow-up period to see beneficial effects of treatment as possible explanations.

A post hoc analysis from CORONA did suggest a significant interaction by hsCRP status (P interaction = 0.026) with rosuvastatin benefitting those with hsCRP ≥2 mg/L but not those with low hsCRP. Furthermore, an economic analysis of the overall CORONA cohort, including both the primary outcome and the secondary outcome of hospitalizations, did find that the overall reduction in CVD events with rosuvastatin partially offset the costs of rosuvastatin treatment by 44%, thus finding rosuvastatin treatment to be a cost-effective treatment for older patients with systolic heart failure.

Resistance to statin use in the elderly[4]

Statins have been shown to reduce CHD events and in some cases all-cause mortality. This finding applies across nearly all available studies, with the possible exception of highly specialized populations, such as systolic heart failure and end-stage renal disease requiring hemodialysis.

While the evidence for statins for secondary prevention in the elderly is more established (despite their underutilization), there are fewer primary prevention studies dedicated to enrolling large numbers of elderly patients, and thus data to support guidelines in this age group are limited. This is possibly due in part to the increasing uncertainties of risk assessment in older individuals as the predictive value of risk factors declines. Other issues to take into consideration include the increased need to balance the benefits of primary prevention with the risks of polypharmacy, health care costs, and adverse medication effects in a population with decreased life expectancy, increased number of coexisting diseases, and more difficult social and economic situations. As the population of the elderly continue to increase with medical advances, these issues are becoming more important.

Of note, a small but statistically significant increased risk of incident diabetes has been reported with statin therapy compared with placebo in a recent large meta-analysis of statin clinical trials (odds ratio 1.09, 95% CI 1.02–1.17), a risk that was highest in trials with older participants such as those in PROSPER and JUPITER. This translated to one new case of diabetes per 1000 person-years of treatment, but extended over four years, nine vascular events would be prevented for each new case of diabetes. Thus, it is generally thought that the risk of incident diabetes is low when compared with the significant reduction in CVD events. However, some authors have suggested that the risk/benefit ratio of treatment may not be as favorable in subjects with a propensity to develop diabetes, such as the elderly, and warrants further study.

Low to moderate doses of statins do appear to be well tolerated in the elderly. The safety of statin therapy in the elderly can be enhanced by avoiding concomitant use of P450 inhibitors, chronic immunosuppressive therapy (cyclosporine), or fibrates (gemfibrozil), and by limiting concomitant use of niacin and alcohol intake (less than two drinks daily). Obviously, laboratory screening for renal, liver, and thyroid function should be performed before initiation of statin therapy. Consider starting statin therapy at lower doses and titrating slowly (toxicity is dose-related). If there is severe medical illness, major surgery, or major trauma, the discontinuation of statin therapy until recovery can be considered.

Effect of rosuvastatin on lipid profile and atherosclerosis[3]

Several RCTs showed the beneficial effects of rosuvastatin on both lipid profile and atherosclerosis. Nissen SE et al. in their prospective, open-label blinded end-points trial (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden 14 [ASTEROID]) highlighted as the intensive rosuvastatin therapy (40 mg/d) performed on 507 patients

for 24 months is associated with a decline of mean LDL-C value from 130.4 mg/dL to 60.8 mg/dL with a reduction of 53.2% when compared to the baseline, a 14.7% increase of HDL-C levels (from 43.1 mg/dL, to 49.0 mg/dL), and a regression of coronary atherosclerosis assessed by IVUS imaging (a 6.8% median reduction of total atheroma volume) and by quantitative coronary angiography (decrease of mean percentage of diameter stenosis from 35.7% to 34.5%, p 2 mg/l] were treated with rosuvastatin 20 mg daily or placebo and followed for a median of 1.9 years for the occurrence of the combined primary end point of MI, stroke, arterial revascularization, hospitalization for unstable angina, or death from CV causes.

These results reinforce the axiom "lower is better" about the predictive role of LDL-C values for CV events, and confirm that the beneficial effects on CV prevention go beyond the merely lipidlowering action, as shown by a reduced rate of major CV events also in patients with acute MI and low baseline LDL-C levels. In a Korean study, in fact, 1.054 patients with acute MI and baseline LDL-C levels below 70 mg/dl were divided into two groups according to the prescribing of statins at discharge (statin group n = 607; non statin group n = 447). The one-year follow-up showed a significant reduction of major adverse cardiac events, including death, recurrent MI, target vessel revascularization, and coronary artery bypass grafting in the statin group compared to no statin one (adjusted hazard ratio [HR]: 0.56; 95% confidence interval [CI]: 0.34 to 0.89; p = 0.015); with a reduction of the risk of cardiac death (HR: 0.47; 95% CI: 0.23 to 0.93; p = 0.031) and coronary revascularization (HR: 0.45, 95% CI: 0.24 to 0.85; p = 0.013).

Safety and Tolerability of Rosuvastatin

Safety of rosuvastatin

As the other molecules of its class, treatment with rosuvastatin can be associated with myopathy and rhabdomyolysis, especially when rosuvastatin is co-administrated with other drugs. Symptoms of muscle involvement (myalgias, muscle stiffness, weakness, arthralgias and back pain or aching of the extremities) represent the main causes of treatment discontinuation in several RCTs. Pooled safety data on 12.400 patients receiving rosuvastatin 5–40 mg/day showed a safety profile similar to 10 to 80 mg of atorvastatin, 10 to 80 mg of simvastatin, and 10 to 40 mg of pravastatin. In particular the incidence of clinically significant elevations in alanine aminotransferase (>3 times the upper limit of normal) and creatine kinase (>10 times the upper limit of normal) was 10 times the upper limit of normal with muscle symptoms) 10% in patients receiving rosuvastatin. As regards to rhabdomyolysis, its incidence in patients treated with rosuvastatin does not significantly differ from those of other currently approved statins. Very few cases are reported in literature.

As regards to drug-drug interactions, although rosuvastatin is excreted mainly unchanged and plasma concentrations are not increased by cytochrome inhibitors, some cases has been observed. The inhibition of organic anion transporting polypeptide 1 and other hepatic transporters by cicliosporine and gemfibrozil, determining an increase in plasma rosuvastatin concentrations, by the inhibition of statin biliary excretion, can explain the higher risk of myotoxicity when cicliosporine and gemfibrozil are co-administered with rosuvastatin. Moreover, Merz T and Fuller SH reported an asymptomatic elevation of serum transaminase levels in a 73-year-old white woman after concomitant use of rosuvastatin and amiodarone. Other drug interactions have been rarely reported.

Finally, asymptomatic liver enzyme elevations and renal failure occur with rosuvastatin at a similarly low incidence as with other statins. Rosuvastatin treatment has been associated in a dose-dependent fashion with variable percentage of dipstick-positive (‡2+) proteinuria (from <1.2% to 12%), due to a statin-provoked inhibition of low-molecular-weight protein reabsorption by the renal tubules.

Gastrointestinal (diarrhea, constipation, nausea and dyspepsia) and neurological (headache, dizziness, and paresthesias) symptoms are commonly reported but, as generally temporary and with mild-to-moderate intensity, rarely lead to treatment discontinuation.

Tolerability of Rosuvastatin[5]

Oral rosuvastatin is generally well tolerated both as monotherapies and when coadministered as either separate tablets or a FDC, with FDC trials (i.e. ROSE, MRS-ROZE and I-ROSETTE; Sect. 3) being the focus of this section. The safety populations in ROSE , MRS-ROZE and I-ROSETTE comprised 123, 206 and 197 rosuvastatin recipients, respectively, and 121, 204 and 195 rosuvastatin monotherapy recipients, respectively.

Across the FDC trials, adverse events (AEs) and treatment-related AEs (TRAEs) occurred in 11.2–21.4% and 1.9–5.7% of rosuvastatin recipients versus 11.3–21.5% and 1.7–3.1% of rosuvastatin monotherapy recipients; the overall incidences of AEs and TRAEs did not signifcantly difer between rosuvastatin and rosuvastatin monotherapy recipients in any trial. Furthermore, rosuvastatin and rosuvastatin monotherapy recipients did not signifcantly difer with respect to the incidences of various

types of AEs. The most common AEs with rosuvastatin, where specifed, included those that were gastrointestinal (2.4% vs 4.1% of rosuvastatin monotherapy recipients in ROSE and 3% vs 0.5% in I-ROSETTE) or musculoskeletal (2.4% vs 0.8% and 2.0% vs 0.5%, with this category specifed to include connective tissue disorders in the latter study). Where reported, prespecifed TRAEs [including gastrointestinal-related AEs, musculoskeletal-related AEs, skin and subcutaneous-related AEs, and drug-related alanine aminotransferase (ALT) elevations ≥3 × upper limit of normal (ULN)] occurred infrequently in rosuvastatin and rosuvastatin monotherapy recipients (all≤1.5%), with no clinically meaningful or statistically significant between group differences.

Serious AEs (SAEs) were infrequent, occurring in 0.5–2.4% of rosuvastatin recipients versus 0.5–1.7% of rosuvastatin monotherapy recipients in the FDC trials (no signifcant between-group differences). Where specifed, no SAEs in rosuvastatin recipients were drug related (although one rosuvastatin 10 mg monotherapy recipient experienced a serious drug-related AE in I-ROSETTE). Discontinuation of rosuvastatin due to AEs occurred rarely (≤1.6% of patients in any study; no significant differences between rosuvastatin and rosuvastatin monotherapy recipients). No deaths were reported.

With respect to laboratory findings, ALT and aspartate aminotransferase (AST) elevations ≥ 3 × ULN (where specified, two consecutive times) and creatine kinase elevations ≥5 or ≥10 × ULN were infrequent, occurring in ≤0.6% of rosuvastatin recipients (vs ≤0.5% of rosuvastatin monotherapy recipients) in any trial. There were no significant differences between treatment groups.

Skeletal muscle effects (e.g. myalgia, myopathy and, rarely, rhabdomyolysis) can occur with rosuvastatin. Certain precautions thus pertain to the use of rosuvastatin; consult local prescribing information for further details.

Safety data from SP-RE-003 and the multinational ACTE and GRAVITY trials, in which rosuvastatin and ezetimibe were co-administered as separate tablets, were largely consistent with those from the FDC trials. During GRAVITY, rosuvastatin had a safety profile similar to that of simvastatin; proportions of patients experiencing AEs were comparable across treatment arms. While AEs occurred in signifcantly more rosuvastatin recipients than rosuvastatin monotherapy recipients in SP-RE-003 (19.4% vs 9.4%; p <0.01) the treatment groups did not signifcantly difer in the incidences of TRAEs or SAEs. During the 12-week extension of SP-RE-003, adverse drug reactions and SAEs were comparable

between patients who continued on rosuvastatin/ ezetimibe therapy received during the initial 8-week treatment period and patients who switched from rosuvastatin monotherapy to rosuvastatin at the start of the extension. Also of note, when rosuvastatin was compared with rosuvastatin up-titration in ACTE, rosuvastatin and rosuvastatin up-titration recipients did not significantly differ with respect to incidences of AEs, TRAEs or SAEs [based on 95% CIs of between-group differences (pooled doses); no serious TRAEs or deaths occurred during the trial]. Pre-specified AEs of special interest (including hepatitis-, gallbladder- and gastrointestinal related AEs, allergic reaction or rash, ALT or AST elevations ≥3 × ULN and creatine kinase elevations ≥10 × ULN with or without muscle symptoms) occurred infrequently (all ≤1.4% in either treatment group, except for gastrointestinal-related AEs, which were reported in 4.1% of rosuvastatin recipients vs 1.4% of rosuvastatin up-titration recipients) and with no statistically significant differences between treatment groups.

Rosuvastatin: Economic Evaluation in Cardiovascular High-Risk Patient[2]

Several economic evaluations based on STELLAR study with one year horizon time and under payer's perspective of Canada and the United States (considering the percentage of change of lipidic parameters and the people reaching LDL-C goal), have evidenced that branding rosuvastatin in 10mg/ day dosing is more cost-effective than branding atorvastatin (10 and 20 mg/day) and simvastatin (20 and 40 mg/day) and pravastatin generics (20 and 40 mg/day). In the same way, other economic evaluations made in Europe and North America have used clustered efficacy data from several rosuvastatin controlled clinical assays compared head-to-head to other statins, concluding once again that rosuvastatin 10 mg/day is more cost-effective than other therapeutic options, such as atorvastatin 10mg/day, from the primary caregivers' perspective in the United Kingdom.

It has been determined that for patients with increasingly higher coronary risk, the therapy with statins is more cost-effective. And the question raised in this connection is whether rosuvastatin is more cost-effective than other statins, specifically in cardiovascular high-risk risk patients. The answer is yes, and it was confirmed by DISCOVERY BELUX study, as did as well POLARIS study. Additionally, other study used a Markov model to Project the number of CV events and the cost associated to a high-risk population in several pharmacological treatment context, established that using rosuvastatin instead of other statins may reduce cardiovascular events in this type of population and saving cost for several US dollars of United States health systems. These results have been confirmed in other RCTs including subjects from other geographic locations, among which PULSAR study. For example, in a study using Monte Carlo probabilistic simulation model and based on JUPITER study for long-term cost-effectiveness of rosuvastatin at 20 mg/day versus simvastatin or atorvastatin generics 40 mg/day for CV

morbidity-mortality prevention in CV high-risk Sweden population (from Sweden health system payer's perspective and a permanent time-horizon), found that the higher cost-effectiveness and cost-utility of rosuvastatin was basically by the number of CV prevented.

Rosuvastatin cost-effectiveness could be determined in the context of Latin America countries, where the cost of medicinal products varies from country to country, using RCT as a basis such as STELLAR or JUPITER studies, as made by other economic evaluations or otherwise, using RCT made in South American population, such as DISCOVERY PENTA study.

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Abstracts

Rosuvastatin and cardiovascular events in patients undergoing hemodialysis

Abstract

Background

Statins reduce the incidence of cardiovascular events in patients at high cardiovascular risk. However, a benefit of statins in such patients who are undergoing hemodialysis has not been proved.

Methods

We conducted an international, multicenter, randomized, double-blind, prospective trial involving 2776 patients, 50 to 80 years of age, who were undergoing maintenance hemodialysis. We randomly assigned patients to receive rosuvastatin, 10 mg daily, or placebo. The combined primary end point was death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. Secondary end points included death from all causes and individual cardiac and vascular events.

Results

After 3 months, the mean reduction in low-density lipoprotein (LDL) cholesterol levels was 43% in patients receiving rosuvastatin, from a mean baseline level of 100 mg per deciliter (2.6 mmol per liter). During a median follow-up period of 3.8 years, 396 patients in the rosuvastatin group and 408 patients in the placebo group reached the primary end point (9.2 and 9.5 events per 100 patient-years, respectively; hazard ratio for the combined end point in the rosuvastatin group vs. the placebo group, 0.96; 95% confidence interval [CI], 0.84 to 1.11; P=0.59). Rosuvastatin had no effect on individual components of the primary end point. There was also no significant effect on all-cause mortality (13.5 vs. 14.0 events per 100 patient-years; hazard ratio, 0.96; 95% CI, 0.86 to 1.07; P=0.51).

Conclusions

In patients undergoing hemodialysis, the initiation of treatment with rosuvastatin lowered the LDL cholesterol level but had no significant effect on the composite primary end point of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

Reference: ellström BC, Jardine AG, Schmieder RE, et al. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis [published correction appears in N Engl J Med. 2010 Apr 15;362(15):1450]. *N Engl J Med*. 2009;360(14):1395-1407.

Cholesterol lowering in intermediate-Risk persons without cardiovascular disease

Background

Previous trials have shown that the use of statins to lower cholesterol reduces the risk of cardiovascular events among persons without cardiovascular disease. Those trials have involved persons with elevated lipid levels or inflammatory markers and involved mainly white persons. It is unclear whether the benefits of statins can be extended to an intermediate-risk, ethnically diverse population without cardiovascular disease.

Methods

In one comparison from a 2-by-2 factorial trial, we randomly assigned 12,705 participants in 21 countries who did not have cardiovascular disease and were at intermediate risk to receive rosuvastatin at a dose of 10 mg per day or placebo. The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included revascularization, heart failure, and resuscitated cardiac arrest. The median follow-up was 5.6 years.

Results

The overall mean low-density lipoprotein cholesterol level was 26.5% lower in the rosuvastatin group than in the placebo group. The first coprimary outcome occurred in 235 participants (3.7%) in the rosuvastatin group and in 304 participants (4.8%) in the placebo group (hazard ratio, 0.76; 95% confidence interval [CI], 0.64 to 0.91; P=0.002). The results for the second coprimary outcome were consistent with the results for the first (occurring in 277 participants [4.4%] in the rosuvastatin group and in 363 participants [5.7%] in the placebo group; hazard ratio, 0.75; 95% CI, 0.64 to 0.88; P<0.001). The results were also consistent in subgroups defined according to cardiovascular risk at baseline, lipid level, C-reactive protein level, blood pressure, and race or ethnic group. In the rosuvastatin group, there was no excess of diabetes or cancers, but there was an excess of cataract surgery (in 3.8% of the participants, vs. 3.1% in the placebo group; P=0.02) and muscle symptoms (in 5.8% of the participants, vs. 4.7% in the placebo group; P=0.005).

Conclusions

Treatment with rosuvastatin at a dose of 10 mg per day resulted in a significantly lower risk of cardiovascular events than placebo in an intermediate-risk, ethnically diverse population without cardiovascular disease.

Reference: Yusuf S, Bosch J, Dagenais G, et al. Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease. *N Engl J Med*. 2016;374(21):2021-2031.

Rosuvastatin: Role in secondary prevention of cardiovascular disease

Abstract

Cardiovascular (CV) diseases are a major cause of premature death and disability. Non-communicable diseases (NCD) are responsible for 52% of mortality amongst Indians, of these CV diseases are responsible for 66% of NCD mortality in India. We not only need widespread primary preventive strategy but also need effective secondary prevention protocols to reduce this. Secondary prevention in patients who already had myocardial infarction (MI) or revascularization is of utmost importance to reduce mortality, cardiac events and improve quality of life. Lifestyle changes and medical therapy have a very important role in secondary prevention of CVD. Optimal control of hypertension, diabetes mellitus and dyslipidemia plays a critical role in secondary prevention. Statins are one of the most commonly used drugs in secondary prevention as a part of medical therapy. Effective LDL reduction, more patients achieving LDL goals, reduction in intima thickness, improvement in endothelial dysfunction, reduction in inflammatory markers are considered to be surrogate markers of reduced risk with statins. Rosuvastatin is one of the two most commonly used statins. It is a potent, effective and safe HMG-COA reductase inhibitor. Data related to secondary prevention is limited with rosuvastatin. Most of the clinical evidences with rosuvastatin have shown more effective LDL reduction than other statins. More number of patients achieve LDL goals and reduction in intima thickness. This article attempts to explore data on role of rosuvastatin for secondary prevention.

Reference: Wander GS, Hukkeri MYK, Yalagudri S, Mahajan B, Panda AT. Rosuvastatin: Role in Secondary Prevention of Cardiovascular Disease. *J Assoc Physicians India*. 2018;66(3):70-74.

Survey Form

1) How frequently do you prescribe Rosuvastatin for cardiovascular disease management?

a) Very frequently
b) Frequently
c) Occasionally
d) Rarely

2) What factors influence your decision to prescribe Rosuvastatin over other statins for cardiovascular disease management?

a) Efficacy in lowering LDL cholesterol
b) Safety profile
c) Cost-effectiveness
d) Patient preference
e) Other

3) How effective do you find Rosuvastatin in achieving target LDL cholesterol levels in your patients?

a) Very effective
b) Effective
c) Moderately effective
d) Not very effective

4) In your clinical experience, what proportion of patients report experiencing side effects with Rosuvastatin?

a) Many patients
b) Some patients
c) Few patients
d) Rarely any patients

5) How often do you initiate Rosuvastatin therapy as primary prevention in patients without known cardiovascular disease but with elevated LDL cholesterol levels?

a) Very often
b) Occasionally
c) Rarely
d) Never

6) What role, if any, do you believe Rosuvastatin plays in reducing the risk of cardiovascular events beyond lowering LDL cholesterol levels?

a) Significant role
b) Moderate role
c) Limited role
d) Not sure

7) How often do you monitor liver function tests in patients prescribed Rosuvastatin?

a) Regularly, at least every 3 months
b) Occasionally, based on patient characteristics
c) Only when clinically indicated
d) Not applicable, I do not routinely monitor liver function

8) What patient population do you consider as the most suitable candidates for Rosuvastatin therapy?

a) Older adults with high cardiovascular risk
b) Patients with familial hypercholesterolemia
c) Individuals with statin intolerance
d) Patients with moderate LDL cholesterol elevation

9) What are the most common reasons patients cite for non-adherence to Rosuvastatin therapy?

a) Cost-related issues
b) Perceived lack of benefit
c) Side effects
d) Forgetfulness
e) Other

10) What improvements, if any, would you like to see in the current guidelines or recommendations for Rosuvastatin use in cardiovascular disease management?

a) Clearer guidance on dosage adjustments
b) More comprehensive information on drug interactions
c) Inclusion of specific patient populations
d) Other

11) How often do you discuss lifestyle modifications (e.g., diet, exercise) with patients prescribed Rosuvastatin?

a) Always
b) Often
c) Occasionally
d) Rarely or never

12) In your opinion, what are the most significant advantages of Rosuvastatin over other statins for cardiovascular disease management?

a) Potent LDL cholesterol lowering
b) Favorable safety profile
c) Cardiovascular risk reduction benefits
d) Ease of administration
e) Other

13) What considerations guide your decision to prescribe Rosuvastatin as monotherapy versus in combination with other lipid-lowering agents?

a) LDL cholesterol levels
b) Presence of other cardiovascular risk factors
c) Patient preferences
d) History of statin intolerance

14) In your clinical experience, how does Rosuvastatin compare to other statins in terms of patient tolerability and overall satisfaction?

a) Superior
b) Comparable
c) Inferior

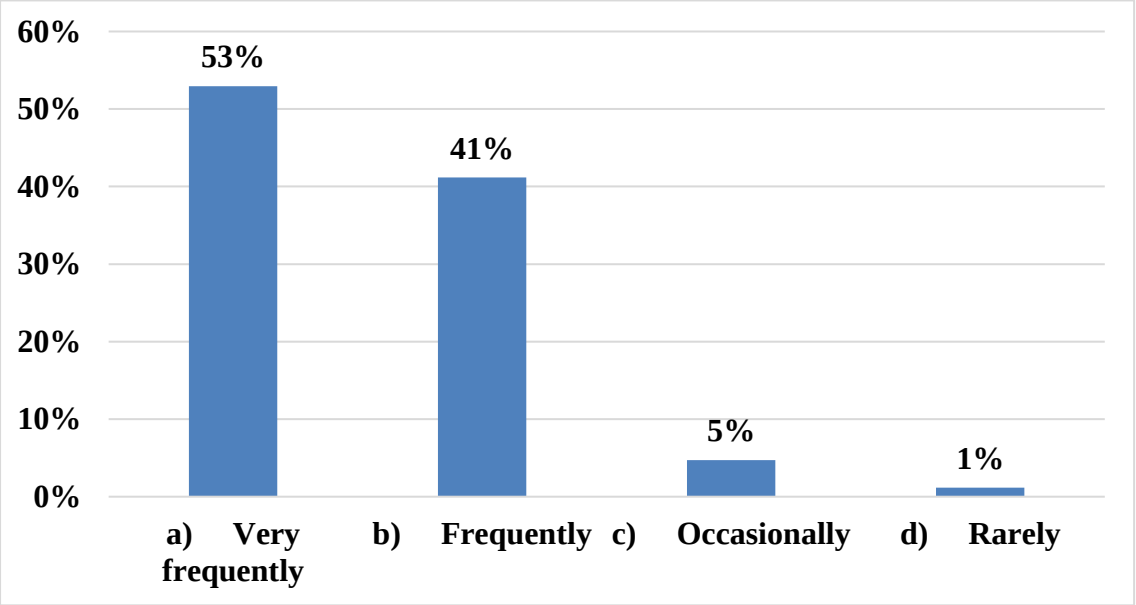
15) How often do you consider Rosuvastatin as a suitable choice for patients with comorbidities, such as diabetes or hypertension?

a) Very often
b) Occasionally
c) Rarely
d) Never

Survey Findings

1) How frequently do you prescribe Rosuvastatin for cardiovascular disease management?

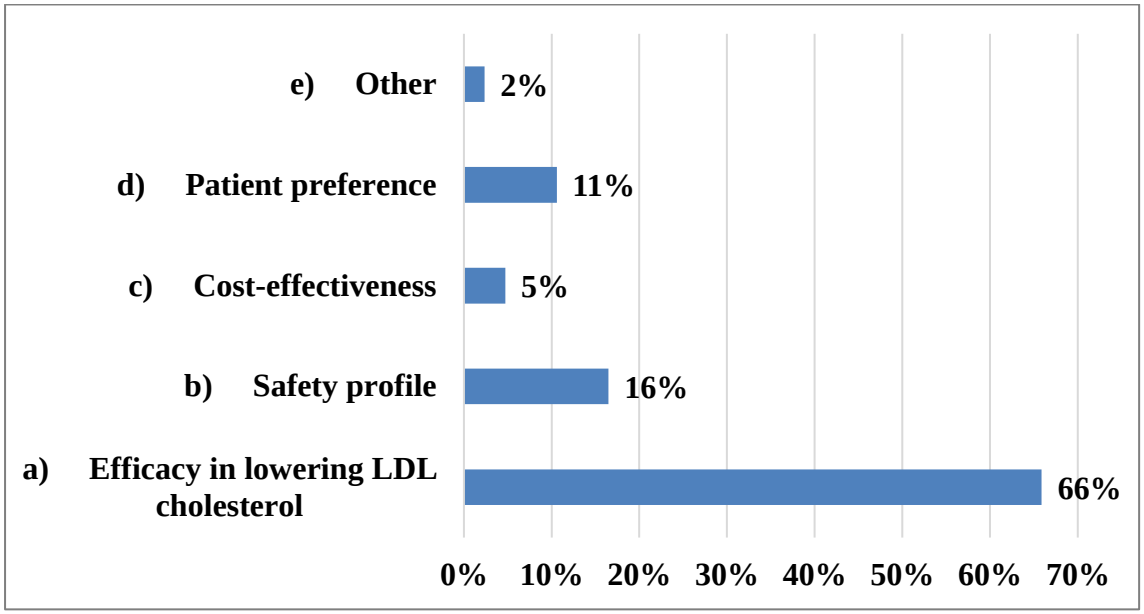
a) Very frequently
b) Frequently
c) Occasionally
d) Rarely



53% of doctors very frequently prescribe Rosuvastatin for cardiovascular disease management.

2) What factors influence your decision to prescribe Rosuvastatin over other statins for cardiovascular disease management?

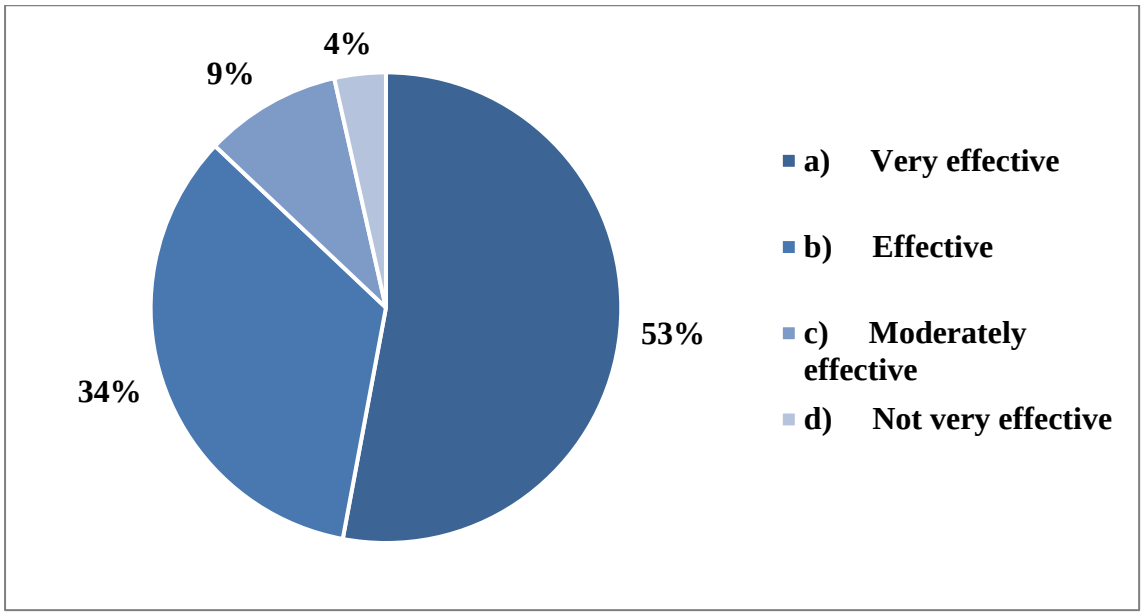
a) Efficacy in lowering LDL cholesterol
b) Safety profile
c) Cost-effectiveness
d) Patient preference
e) Other



According to majority of doctors, 66%, their decision to prescribe Rosuvastatin over other statins for cardiovascular disease management is influenced by its efficacy in lowering LDL cholesterol.

3) How effective do you find Rosuvastatin in achieving target LDL cholesterol levels in your patients?

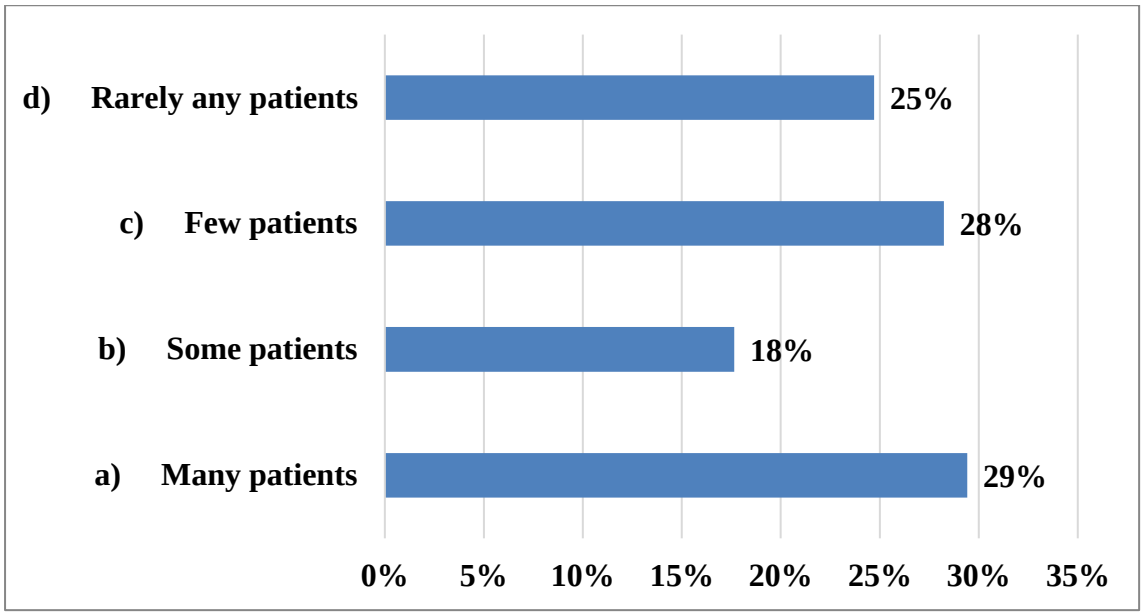
a) Very effective
b) Effective
c) Moderately effective
d) Not very effective



More than half the doctors (53%) find Rosuvastatin very effective in achieving target LDL cholesterol levels in your patients.

4) In your clinical experience, what proportion of patients report experiencing side effects with Rosuvastatin?

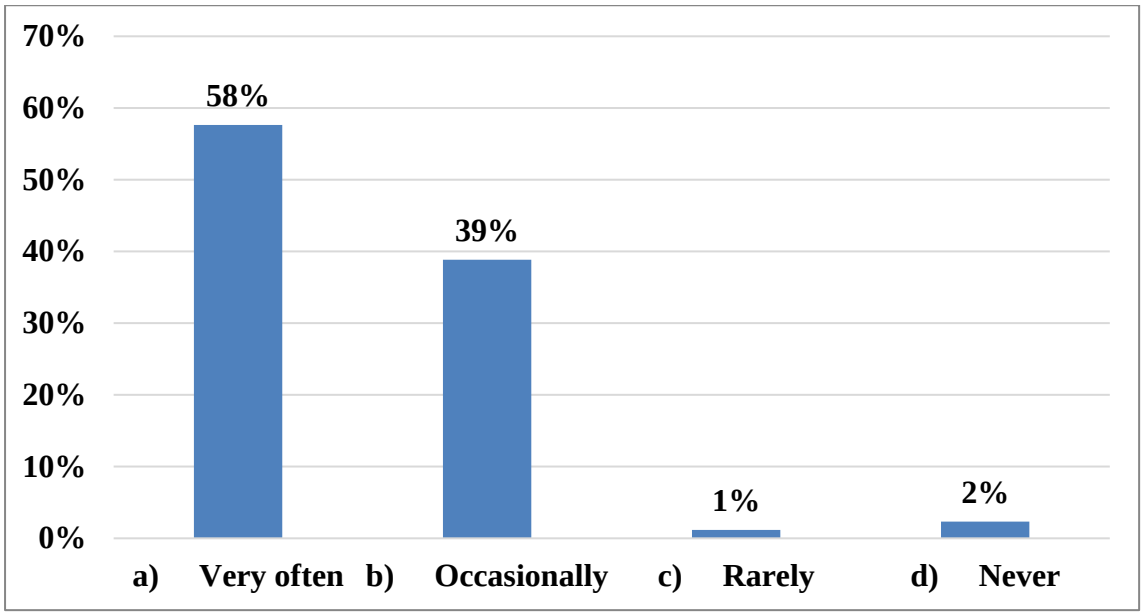
a) Many patients
b) Some patients
c) Few patients
d) Rarely any patients



In the clinical experience of 29% of doctors, many patients report experiencing side effects with Rosuvastatin.

5) How often do you initiate Rosuvastatin therapy as primary prevention in patients without known cardiovascular disease but with elevated LDL cholesterol levels?

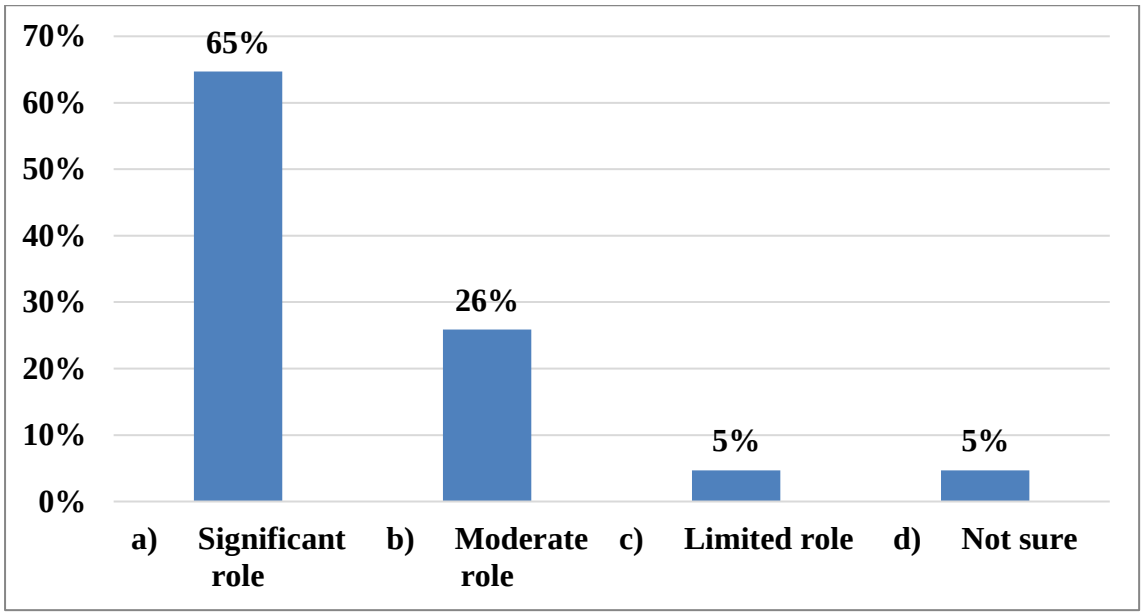
a) Very often
b) Occasionally
c) Rarely
d) Never



58% of doctors very often initiate Rosuvastatin therapy as primary prevention in patients without known cardiovascular disease but with elevated LDL cholesterol levels.

6) What role, if any, do you believe Rosuvastatin plays in reducing the risk of cardiovascular events beyond lowering LDL cholesterol levels?

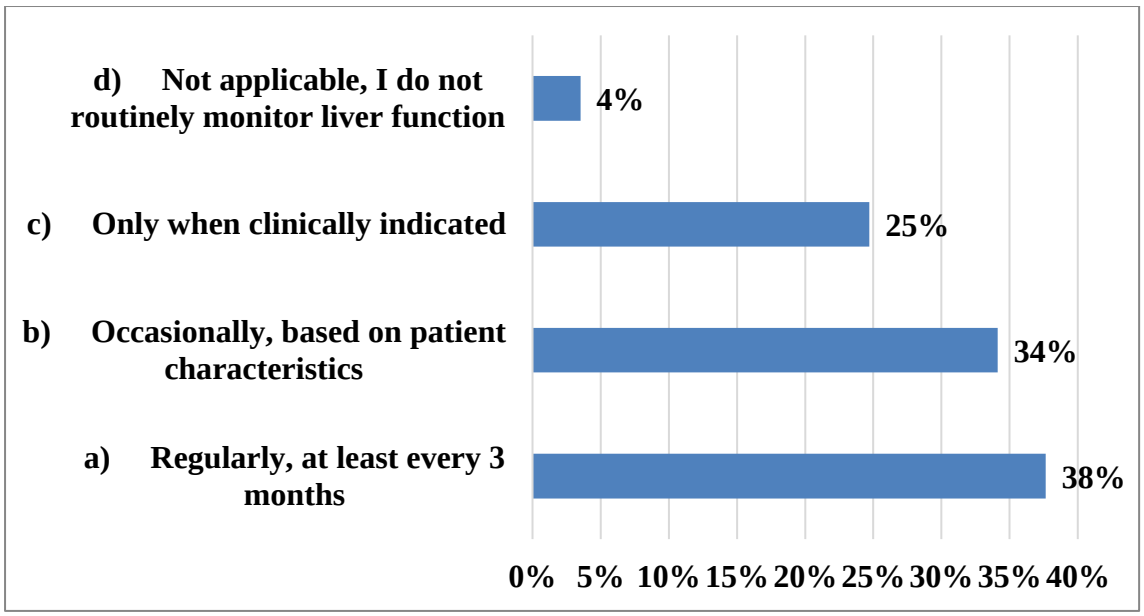
a) Significant role
b) Moderate role
c) Limited role
d) Not sure



As per 65% of doctors, Rosuvastatin plays a significant role in reducing the risk of cardiovascular events beyond lowering LDL cholesterol levels.

7) How often do you monitor liver function tests in patients prescribed Rosuvastatin?

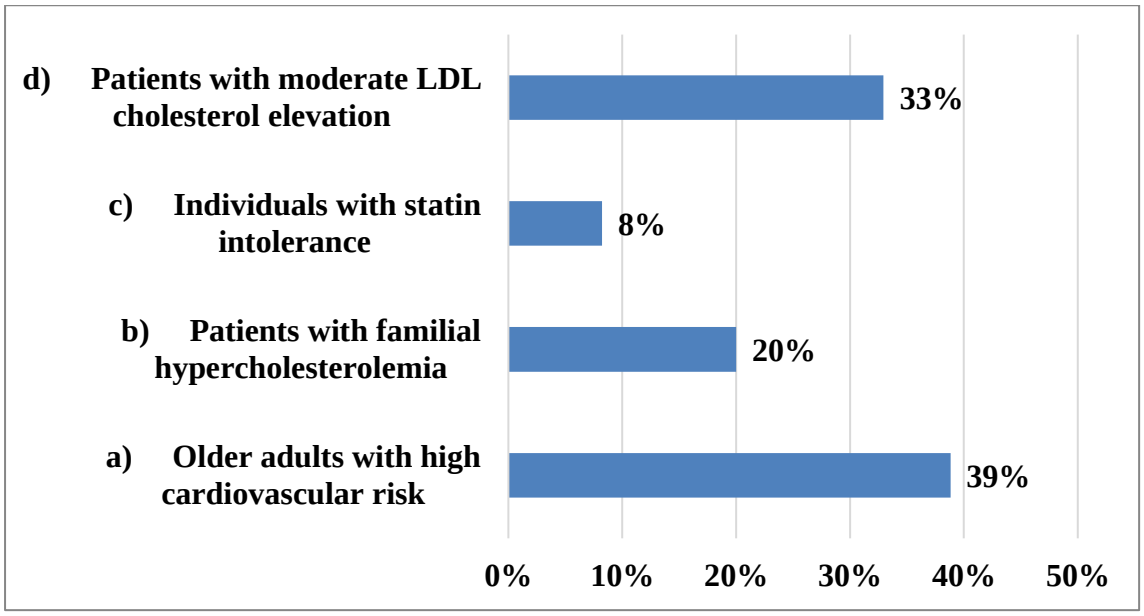
a) Regularly, at least every 3 months
b) Occasionally, based on patient characteristics
c) Only when clinically indicated
d) Not applicable, I do not routinely monitor liver function



38% of doctors monitor liver function tests regularly, at least every 3 months, in patients prescribed Rosuvastatin.

8) What patient population do you consider as the most suitable candidates for Rosuvastatin therapy?

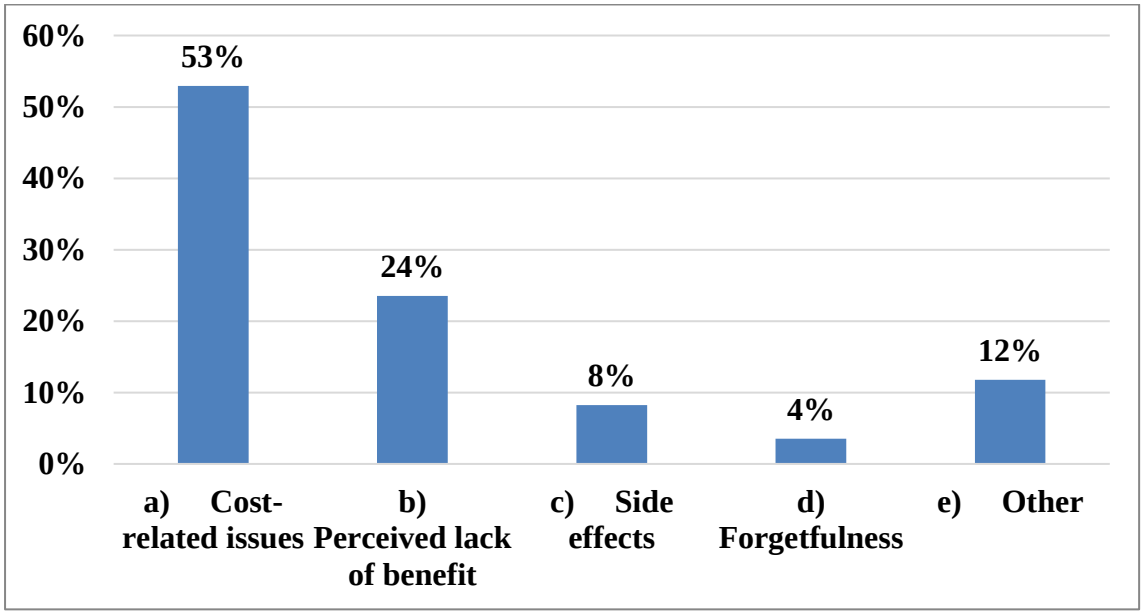
a) Older adults with high cardiovascular risk
b) Patients with familial hypercholesterolemia
c) Individuals with statin intolerance
d) Patients with moderate LDL cholesterol elevation



39% of doctors consider older adults with high cardiovascular risk as the most suitable candidates for Rosuvastatin therapy.

9) What are the most common reasons patients cite for non-adherence to Rosuvastatin therapy?

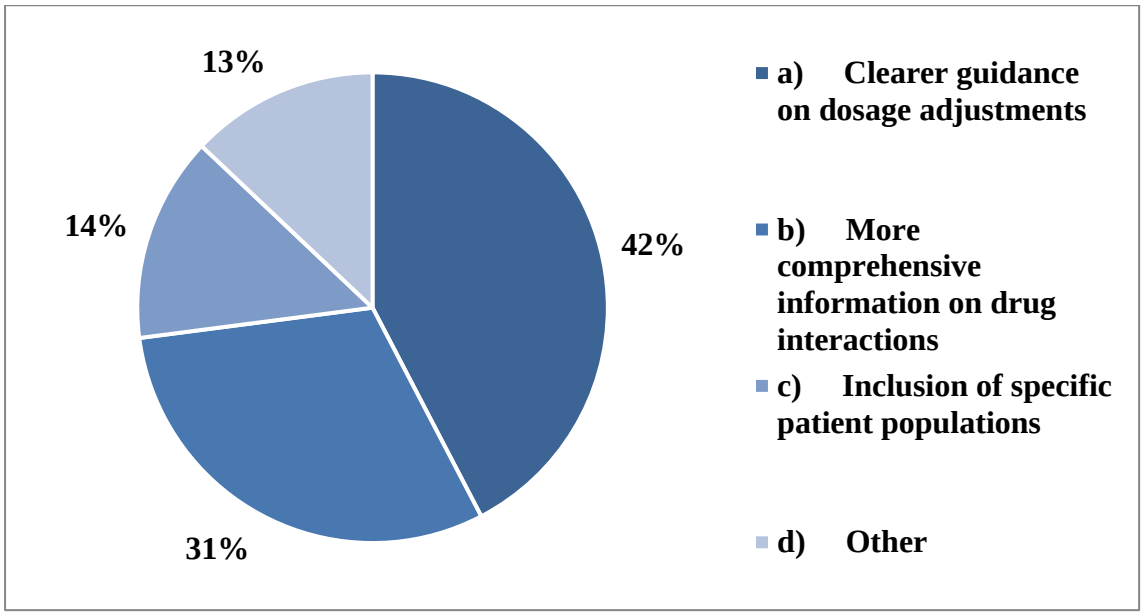
a) Cost-related issues
b) Perceived lack of benefit
c) Side effects
d) Forgetfulness
e) Other



According to 53% of doctors, the most common reasons patients cite for non-adherence to Rosuvastatin therapy is cost-related issues.

10) What improvements, if any, would you like to see in the current guidelines or recommendations for Rosuvastatin use in cardiovascular disease management?

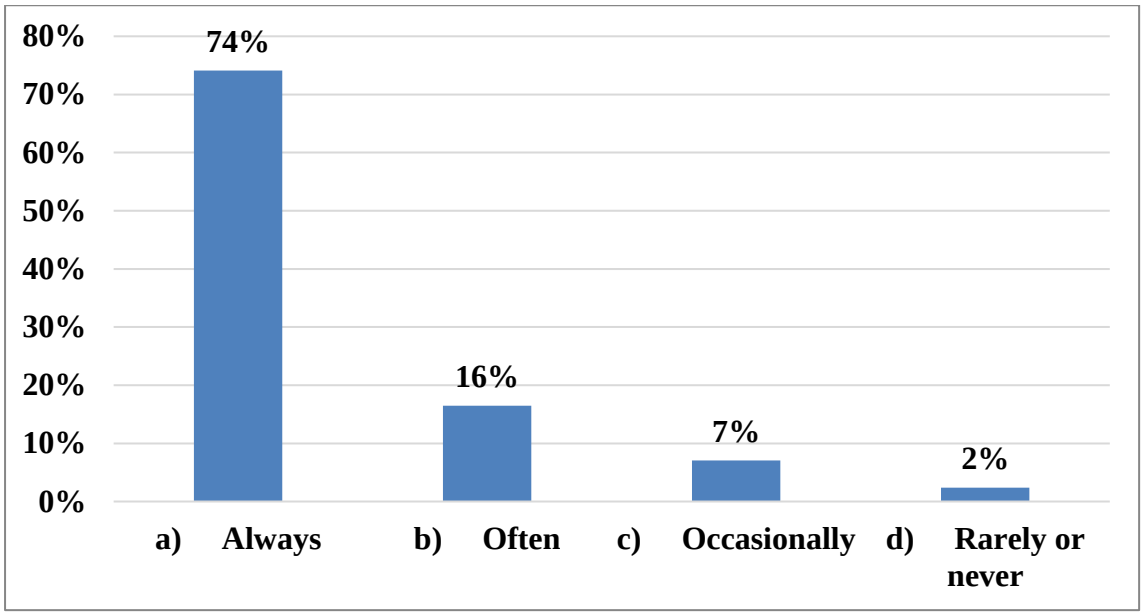
a) Clearer guidance on dosage adjustments
b) More comprehensive information on drug interactions
c) Inclusion of specific patient populations
d) Other



42% of doctors would like to see clearer guidance on dosage adjustments in the current guidelines or recommendations for Rosuvastatin use in cardiovascular disease management.

11) How often do you discuss lifestyle modifications (e.g., diet, exercise) with patients prescribed Rosuvastatin?

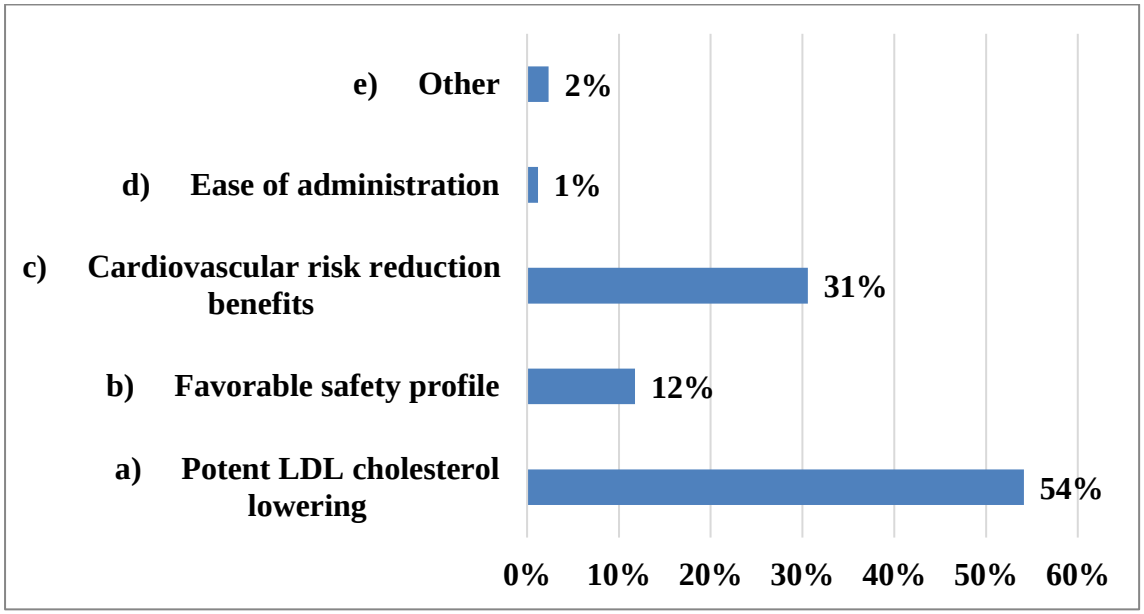
a) Always
b) Often
c) Occasionally
d) Rarely or never



Majority of doctors (74%) always discuss lifestyle modifications (e.g., diet, exercise) with patients prescribed Rosuvastatin.

12) In your opinion, what are the most significant advantages of Rosuvastatin over other statins for cardiovascular disease management?

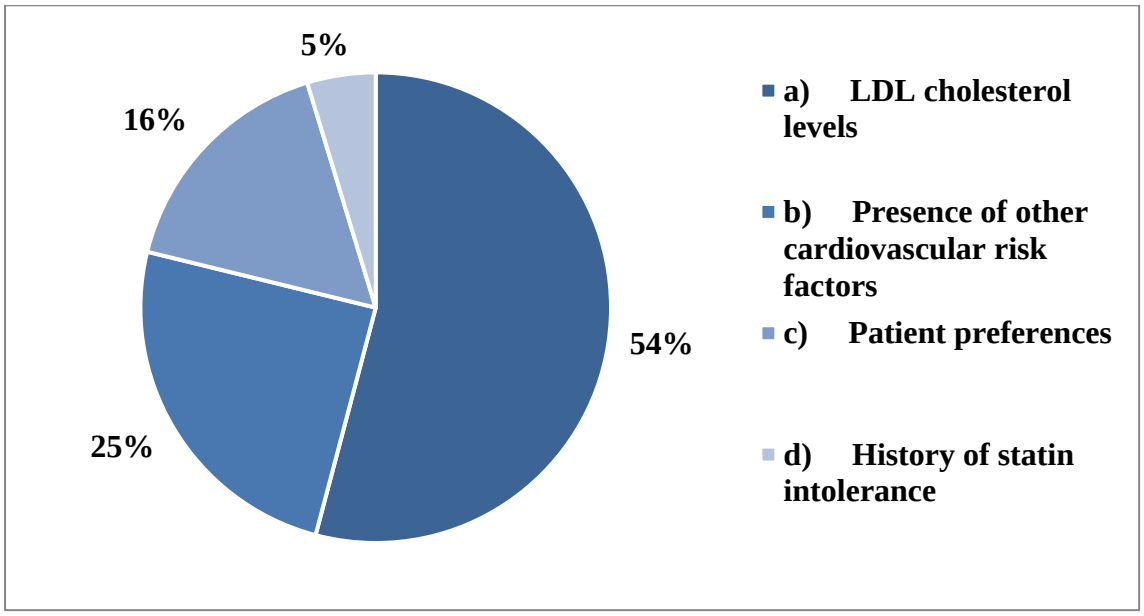
a) Potent LDL cholesterol lowering
b) Favorable safety profile
c) Cardiovascular risk reduction benefits
d) Ease of administration
e) Other



In the opinion of 54% of doctors, the most significant advantages of Rosuvastatin over other statins for cardiovascular disease management is potent LDL cholesterol lowering.

13) What considerations guide your decision to prescribe Rosuvastatin as monotherapy versus in combination with other lipid-lowering agents?

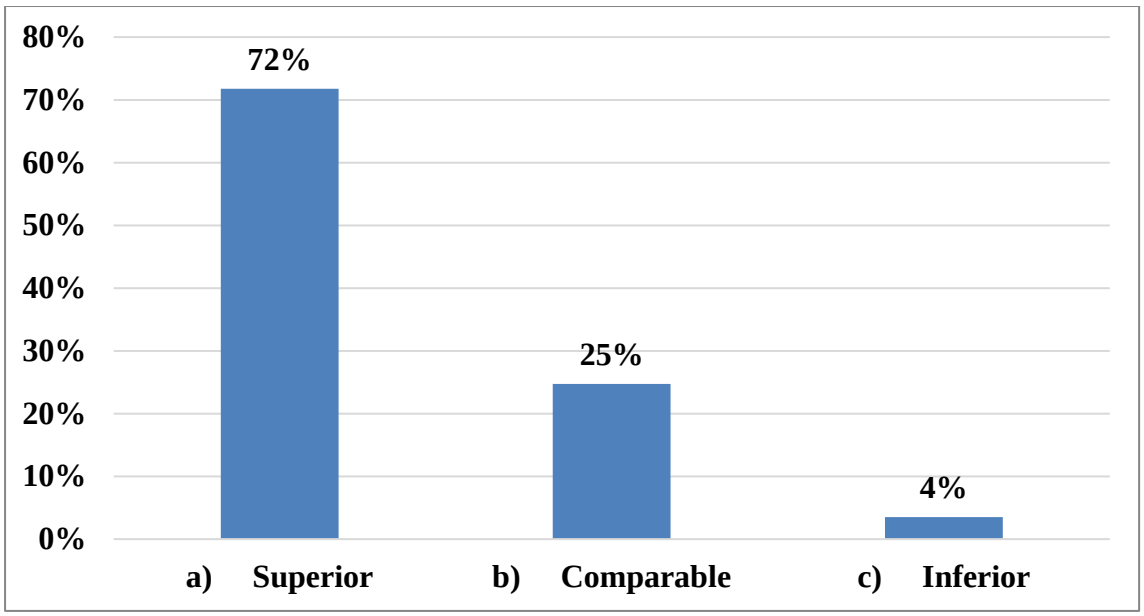
a) LDL cholesterol levels
b) Presence of other cardiovascular risk factors
c) Patient preferences
d) History of statin intolerance



According to 54% of doctors, LDL cholesterol levels guide their decision to prescribe Rosuvastatin as monotherapy versus in combination with other lipid-lowering agents,

14) In your clinical experience, how does Rosuvastatin compare to other statins in terms of patient tolerability and overall satisfaction?

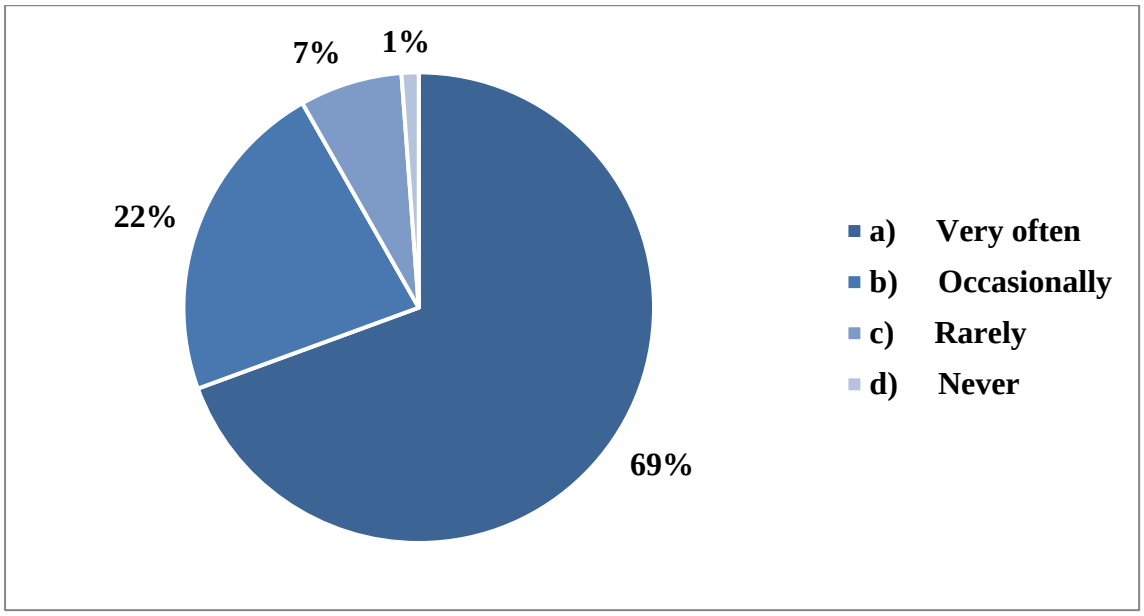
a) Superior
b) Comparable
c) Inferior



As per majority of doctors, 72%, Rosuvastatin is superior as compared to other statins in terms of patient tolerability and overall satisfaction.

15) How often do you consider Rosuvastatin as a suitable choice for patients with comorbidities, such as diabetes or hypertension?

a) Very often
b) Occasionally
c) Rarely
d) Never



Majority of doctors, 69%, very often consider Rosuvastatin as a suitable choice for patients with comorbidities, such as diabetes or hypertension.

Summary

- 53% of doctors very frequently prescribe Rosuvastatin for cardiovascular disease management.
- According to majority of doctors, 66%, their decision to prescribe Rosuvastatin over other statins for cardiovascular disease management is influenced by its efficacy in lowering LDL cholesterol.
- More than half the doctors (53%) find Rosuvastatin very effective in achieving target LDL cholesterol levels in your patients.
- In the clinical experience of 29% of doctors, many patients report experiencing side effects with Rosuvastatin.
- 58% of doctors very often initiate Rosuvastatin therapy as primary prevention in patients without known cardiovascular disease but with elevated LDL cholesterol levels.
- As per 65% of doctors, Rosuvastatin plays a significant role in reducing the risk of cardiovascular events beyond lowering LDL cholesterol levels.
- 38% of doctors monitor liver function tests regularly, at least every 3 months, in patients prescribed Rosuvastatin.
- 39% of doctors consider older adults with high cardiovascular risk as the most suitable candidates for Rosuvastatin therapy.
- According to 53% of doctors, the most common reasons patients cite for non-adherence to Rosuvastatin therapy is cost-related issues.
- 42% of doctors would like to see clearer guidance on dosage adjustments in the current guidelines or recommendations for Rosuvastatin use in cardiovascular disease management.
- Majority of doctors (74%) always discuss lifestyle modifications (e.g., diet, exercise) with patients prescribed Rosuvastatin.
- In the opinion of 54% of doctors, the most significant advantages of Rosuvastatin over other statins for cardiovascular disease management is potent LDL cholesterol lowering.
- According to 54% of doctors, LDL cholesterol levels guide their decision to prescribe Rosuvastatin as monotherapy versus in combination with other lipid-lowering agents,

- As per majority of doctors, 72%, Rosuvastatin is superior as compared to other statins in terms of patient tolerability and overall satisfaction.
- Majority of doctors, 69%, very often consider Rosuvastatin as a suitable choice for patients with comorbidities, such as diabetes or hypertension.

Consultant Opinion

Market Opportunities:

The survey reveals a significant proportion of doctors frequently prescribing Rosuvastatin for cardiovascular disease management. This indicates a robust market demand for statins, particularly Rosuvastatin, in the management of cardiovascular risk.

Value for Healthcare Professionals:

Healthcare professionals prioritize Rosuvastatin due to its efficacy in lowering LDL cholesterol levels and its significant role in reducing the risk of cardiovascular events. This highlights the value of Rosuvastatin as a preferred choice among statins for managing cardiovascular disease.

Adverse Effect Management:

A notable proportion of doctors report patients experiencing side effects with Rosuvastatin. There is an opportunity for healthcare providers to focus on proactive adverse effect management strategies, such as monitoring and addressing side effects promptly to improve patient tolerability and adherence to treatment.

Withdrawal Management:

With concerns about cost-related issues affecting patient adherence, healthcare providers can explore strategies to address affordability barriers, such as patient education on available financial assistance programs or alternative treatment options.

Market Positioning:

Pharma companies can capitalize on Rosuvastatin's superior efficacy and tolerability profile by strategically positioning it in the market as a preferred choice for cardiovascular risk management. Highlighting its benefits in reducing LDL cholesterol levels and cardiovascular events can further strengthen its market position.

Personalized Treatment Decisions:

Clearer guidance on dosage adjustments and recommendations for Rosuvastatin use in cardiovascular disease management can empower healthcare professionals to make more informed and personalized treatment decisions. This could involve developing evidence-based guidelines or tools to assist clinicians in optimizing Rosuvastatin therapy based on individual patient needs.

Improving Patient Outcomes:

Healthcare professionals play a crucial role in discussing lifestyle modifications, such as diet and exercise, with patients prescribed Rosuvastatin. Emphasizing the importance of lifestyle interventions alongside medication therapy can lead to better patient outcomes and overall cardiovascular health.

In summary, there are opportunities to enhance patient care and optimize market positioning for Rosuvastatin by focusing on adverse effect management, addressing cost-related barriers, providing clearer guidance for treatment decisions, and promoting holistic approaches to cardiovascular risk management. Pharma companies can leverage these insights to develop targeted strategies that align with healthcare professionals' priorities and improve patient outcomes.

NOTES

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