Original Article

# Efficacy and safety of the intensive dose of rosuvastatin 40 mg/day in patients with acute coronary syndrome and at high risk of cardiovascular disease-ROSUVEES-2 ☆

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## ARTICLE INFO

## ABSTRACT

Background: Randomized clinical trials have established the benefits of statin therapy in acute coronary syndromes (ACS) via their pleiotropic effects.

Aim of the study: This was a 12-week, open-label, multicenter, postmarketing observational study evaluating the efficacy and safety of rosuvastatin 40 mg/day in very high-risk or high-risk Indian patients according to NCEP ATP III guidelines.

Methodology: One hundred and sixty two patients (age: 30 to 69 years) with evidence of coronary artery disease, hospitalized with chest pain with/without electrocardiogram changes and with non-ST segment elevation ACS and ST segment elevation ACS who received optimal reperfusion therapy were enrolled. The primary endpoint was the percent change from baseline in low-density lipoprotein cholesterol (LDL-C) levels at 6 and 12 weeks of treatment. Other lipid parameters, high sensitive C-reactive protein (hsCRP), glycosylated hemoglobin, and clinical biochemical parameters were also assessed.

Results: At 12 weeks, intensive therapy with rosuvastatin 40 mg/day significantly reduced LDL-C ($p < 0.001$), total cholesterol (TC) ($p < 0.001$), triglyceride ($p < 0.01$), TC/high density lipoprotein cholesterol (HDL-C) ratio ($p < 0.001$), non-HDL-C ($p < 0.001$), LDL-C/HDL-C ratio ($p < 0.001$), and hsCRP ($p = 0.034$) in very high-risk and high–risk patients with ACS. Overall, 54.5% (61/112) patients achieved LDL-C goal of <70 mg/dL. However, the change in HDL-C and very low density lipoprotein cholesterol (VLDL-C) were not significant. Few adverse events including myalgia were reported during the study.

Conclusion: Results of this study showed that 40 mg dose of rosuvastatin, initiated early and continued for 12 weeks, was effective in terms of reducing LDL cholesterol and was well tolerated.

## 1. Introduction

Acute coronary syndromes (ACS) result from acute obstruction of a coronary artery and may lead to consequences varying from unstable angina to sudden death.[1] Statins have emerged as the most effective lipid-lowering agents in preventing cardiovascular (CV) events in patients with established coronary heart disease (CHD).[2] Evidence accumulated over 20 years shows that statins can lower the long-term CV risk by reducing elevated low-density lipoprotein cholesterol (LDL-C), small-dense LDL-C, and C-reactive protein.[2,3]

The available evidence supports the beneficial effects of the regular use of statins in ACS, and highlights association between early initiation and reductions in recurrent coronary events and

mortality.[4] Numerous pleiotropic effects of statins play a vital role in prevention of CV events.[5] Statins increase the release of endothelial nitric Oxide (NO) independent of cholesterol levels, thus increasing the NO production and reversing endothelial dysfunction.[1,2,6] Statins have been shown to modulate several mechanisms involved in the pathogenesis of ACS, such as stabilizing plaque and decreasing thrombogenicity and inflammation.[1,2]

The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III guidelines recommend that intensive statin treatment should be used in patients admitted with ACS. As per guidelines, setting an 'optional' target of LDL-C goal <70 mg/dL for 'very high-risk' patients must be left as a therapeutic option on the basis of clinical trial evidence, whereas a LDL-C goal of <100 mg/dL can be retained as a strong recommendation for 'high-risk patients'.[7] Increasing evidence suggests that early administration of high dose statins in patients with ACS, aggressively lowers LDL-C and decreases morbidity and mortality.[8]

Randomized clinical trials evaluating statin therapy started early after ACS onset have clearly shown that administration of statins have beneficial effect on CV events at 6 months which persisted for 2 years of follow-up.[2] A meta-analysis of statin use in patients with ACS confirmed the benefits of early high-dose statin administration in decreasing recurrent myocardial ischemia and possibly coronary revascularization. A mortality benefit in patients with ACS was observed over the long term (24 months).[9] Additionally PRISM (The Platelet Receptor Inhibition in Ischemic Syndrome Management) study demonstrated that early withdrawal of statin treatment shortly after onset of ACS symptoms increases the risk of cardiac events.[6]

Intensive lipid-lowering statin regimen during ACS provides greater protection against death or major CV events, and rosuvastatin is the most potent statin currently available with the highest efficacy in decreasing LDL-C compared with other statins. Several studies have demonstrated the higher lipid-lowering efficacy of rosuvastatin over other statins. Compared with other potent statins, rosuvastatin has longer half-life of 20 hours with favorable safety profile in the dose range of 5 to 40 mg.[3,10] Rosuvastatin in the dose range of 5 to 40 mg has also shown reduction in LDL-C levels in range of 38.8–54.7 mg/dL.[10]

The results from SATURN (Study of Coronary Atheroma by Intravascular Ultrasound: Effect of Rosuvastatin versus Atorvastatin) showed that change in primary efficacy end point percent atheroma volume (PAV), was comparable between atorvastatin and rosuvastatin. However, effect on normalized total atheroma volume (TAV), a secondary end point, was significantly more with rosuvastatin as compared to atorvastatin.[11] The CENTAURUS (Comparison of the Effects Noted in The ApoB:ApoA-1 ratio Using Rosuvastatin or Atorvastatin in Patients with Acute Coronary Syndrome) study demonstrated that rosuvastatin 20 mg produced similar changes in ApoB:ApoA-1 ratio at 3 months when compared with atorvastatin 80 mg. The study showed that rosuvastatin 20 mg is as effective as atorvastatin 80 mg in intensive statin treatment.[12]

There is dearth of data on effect of high dose rosuvastatin in Indian 'high' risk and 'very high' risk patients. This study was undertaken to explore the efficacy and safety of the intensive dose of rosuvastatin 40 mg/day, initiated early and continued for 12 weeks, in 'very high' or 'high' risk Indian patients, identified as per NCEP ATP III guidelines.

## 2. Methods

### 2.1. Trial design

This was a 12-week, open-label, multicenter study (CTRI/2014/01/004269) evaluating the efficacy and safety of the intensive dose of rosuvastatin, 40 mg/day, initiated early and continued for 12-weeks, in a very high risk or high risk Indian patients, according to NCEP ATP III guidelines. Study was conducted in 12 centers spread across 6 cities in India.

Enrolled patients were prescribed and advised to self-administer commercially available rosuvastatin 40 mg orally once daily (OD) for the period of 12 weeks as per discretion of treating physicians. During the 2nd visit (after 6 weeks of treatment) and 3rd visit (after 12 weeks of treatment), patients were evaluated if he/she could tolerate rosuvastatin 40 mg and assessed history of myalgia/myopathy with increased creatine phosphokinase (CPK) enzyme levels. At the end of 12 weeks of treatment with rosuvastatin 40 mg, all patients were titrated to rosuvastatin 20 mg and continued at the discretion of the investigator. Patients, whose dose titration to rosuvastatin 20 mg was made at 2nd visit or 3rd visit, were to continue with the same dosage of rosuvastatin 20 mg at the discretion of the investigator. In addition to rosuvastatin treatment, patients were advised for therapeutic lifestyle changes (diet, exercise). All concomitant medications taken by the patient were noted in the case report form. This study did not interfere with any therapeutic or diagnostic measures taken by the treating physicians and patients were recruited regardless of past or present therapeutic regimens.

The study was conducted in accordance with the principles of the Declaration of Helsinki and in compliance with Good Clinical Practice guidelines. Written informed consent was obtained from all study participants before being examined for eligibility criteria. The study protocol and the informed consent form were reviewed and approved by relevant Institutional Review Board before initiation of study.

### 2.2. Patients

Men and non-pregnant women aged ≥30 to ≤69 years, with evidence of coronary artery disease, who were hospitalized with recent chest pain (ischemic symptoms) with or without ECG changes; or with non-ST segment elevation acute coronary syndrome (ACS) and ST segment elevation ACS were eligible for enrollment in study.

Main exclusion criteria were: patients receiving intensive lipid-lowering therapy of rosuvastatin 40 mg for >3 months before admission; alanine aminotransferase (ALT) levels >3× upper limit of normal (ULN); unexplained serum creatine kinase (CK) level >3× ULN; serum creatinine >2 mg/dL; and history of hypersensitivity to statins.

### 2.3. Endpoints

The primary endpoint was the percent change from baseline in LDL-C levels after 6 and 12 weeks of treatment. The secondary endpoints included the percent change from baseline in total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), non-HDL-C, apolipoprotein A-I (ApoA1-I), apolipoprotein B (ApoB), LDL-C/HDL-C ratio, TC/HDL-C ratio, non-HDL-C/HDL-C ratio, and ApoB/ApoA-I ratio, after 6 and 12 weeks of treatment; and the percent change from baseline in the levels of high sensitive C-reactive protein (hsCRP), an inflammatory marker, after 6 and 12 weeks of treatment. Non-HDL-C was calculated as total cholesterol from whole plasma minus HDL cholesterol.

The safety and tolerability of rosuvastatin were assessed by evaluating the incidence and severity of adverse events (AEs), serious AEs (SAEs), and abnormal laboratory values through 12 weeks of treatment.

Compliance was assessed; patients were considered non-compliant if they missed their medication for more than 5 days.

## 2.4. Assessments

Fasting blood samples were collected at baseline, and at 6 and 12 weeks, for lipid profile analysis, hsCRP, HbA1c, and biochemical parameters (ALT, aspartate aminotransferase (AST), liver enzymes, CPK, and serum creatinine) at a local laboratory. Estimated glomerular filtration rate (eGFR) was determined in a post hoc analysis using the Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI).

Safety analysis was performed on safety population, which consisted of all patients who received at least one dose of the study medication and had at least one post-baseline safety assessment.

## 2.5. Statistics

Baseline values were compared with follow-up values using repeated measures ANOVA and paired $t$-test. All statistical tests were two-sided and a '$p$' value of $<0.05$ was considered statistically significant.

## 3. Results

A total of 228 patients were screened and 162 patients (males: 123 [75.9%]; females: 39 [24.1%]) with mean ($\pm$SD) age of 53.7 ($\pm$9.0) years, were enrolled in the study. A total of 112 (69.1%) patients completed the study, 32 (19.8%) patients were lost to follow-up, and 18 (11.1%) patients were dropped out from the study. Patient characteristics at baseline are presented in Table 1.

### 3.1. Efficacy

A repeated measure ANOVA was conducted to compare the effect of rosuvastatin intensive therapy on lipid levels (Table 2). All lipid parameters improved significantly ($p < .001$) at week 12. The result of ANOVA indicated significant effect of rosuvastatin therapy on patients' LDL levels, Wilks' Lambda = 0.437, $F$ (2, 93) = 59.86. Of 112 patients who completed the study, overall 88 (78.6%) patients achieved ATP III LDL-C goal of $\leq$100 mg/dL. Out of this 61 (54.5%) patients achieved LDL-C goal of $<70$ mg/dL. Follow-up comparison indicated that each pair wise comparison was significant. LDL-C levels decreased by 46.9 mg/dL (95%CI: $-57.3$ to $-36.5$) at week 6 compared to baseline, and by 40.5 mg/dL (95%CI $-52.0$ to $-29.0$) at week 12 compared to baseline. These results suggest that rosuvastatin therapy resulted in significant decrease in LDL levels. After 12 weeks, rosuvastatin therapy had similar effect on TC, Wilks' Lambda = 0.487, $F$ (2,91) = 47.88; triglyceride, Wilks' Lambda = 0.859, $F$ (2,91) = 7.45; TC/HDL-C ratio, Wilks' Lambda = 0.529, $F$ (2,90) = 40.11; non-HDL-C, Wilks' Lambda = .469, $F$ (2,90) = 51.11 and LDL-C/HDL-C ratio, Wilks' Lambda = 0.511, $F$

(2,90) = 43.01 (Table 2). However, rosuvastatin therapy had no significant effect on HDL-C, Wilks' Lambda = 0.958, $F$ (2,92) = 2.01 and VLDL-C, Wilks' Lambda = 0.955, $F$(2,88) = 2.06. Lipid levels were also decreased from baseline after dose titration but the changes were not significant. Results for change in lipid levels at week 6 and week 12 are illustrated in Figs. 1 and 2, respectively.

In addition to this, compared to baseline inflammatory marker hs-CRP decreased by 3.0 (95%CI: $-6.2$ to 0.2; $P > .05$) at week 6, and by 1.4 (95%CI: $-2.7$ to $-0.1$; $P < .05$) at week 12.

### 3.2. Tolerability

Changes from baseline to the end of treatment for all biochemical parameters were not significant. After 12 weeks of treatment, CPK levels increased marginally by 0.9 U/L; no patient

**Table 1**
Patient characteristics at baseline.

| Variable(s) | $N = 162$ |
|---|---|
| Age (years) (mean $\pm$ SD) | 53.7 $\pm$ 9.0 |
| Weight (kgs) (mean $\pm$ SD) | 72.8 $\pm$ 12.6 |
| **ATP risk category, n (%)** | |
| Very High-risk | 68 (42.0%) |
| High-risk | 94 (58.0%) |
| **Smoking history, n (%)** | |
| Smoker | 26 (16.0%) |
| Non-Smoker | 132 (81.5%) |
| Missing Data | 04 (2.5%) |
| **Concurrent illness, n (%)** | |
| Hypertension | 85 (52.5%) |
| Diabetes | 57 (35.2%) |
| Dyslipidemia | 50 (30.9%) |
| CAF | 07 (4.3%) |
| Peripheral artery disease | 02 (1.2%) |
| Missing | 46 (28.4%) |
| **Past history, n (%)** | |
| Myocardial infarction | 28 (17.3%) |
| Stable angina | 24 (14.8%) |
| Unstable angina | 14 (8.6%) |
| Heart failure | 04 (2.5%) |
| Atrial fibrillation | 01 (0.6%) |
| Missing | 102 (63.0%) |
| **Lipid profile (mg/dL), (mean $\pm$ SD)** | |
| LDL-C ($n = 162$) | 119.3 $\pm$ 37.2 |
| HDL-C ($n = 162$) | 38.1 $\pm$ 10.1 |
| Total Cholesterol ($n = 157$) | 186.3 $\pm$ 50.9 |
| VLDL-C ($n = 152$) | 30.0 $\pm$ 14.5 |
| Triglycerides ($n = 161$) | 168.2 $\pm$ 106.1 |
| Non-HDL Cholesterol ($n = 157$) | 149.1 $\pm$ 46.4 |
| TC-HDL-C ratio ($n = 155$) | 5.1 $\pm$ 1.5 |
| LDL-C/HDL-C ratio ($n = 156$) | 3.2 $\pm$ 1.2 |
| **Inflammatory marker, (mean $\pm$ SD)** | |
| hsCRP ($n = 115$) | 6.9 $\pm$ 12.0 |

**Table 2**
Mean change in lipid levels (mg/dL) after 6 weeks and 12 weeks of treatment compared to baseline.

| Variables | $N = 228$ | Baseline | Week 6 | Difference (95% CI) | P value | Week 12 | Difference (95% CI) | P value |
|---|---|---|---|---|---|---|---|---|
| | n | Mean $\pm$ SD | Mean $\pm$ SD | | | Mean $\pm$ SD | | |
| LDL-C | 95 | 121.1 $\pm$ 40.3 | 74.2 $\pm$ 30.8 | $-46.9^a$ ($-57.3$, $-36.5$) | 0.000 | 80.6 $\pm$ 32.8 | $-40.5^a$ ($-52.0$, $-29.0$) | 0.000 |
| TC | 93 | 189.0 $\pm$ 45.2 | 139.1 $\pm$ 39.3 | $-49.9^a$ ($-62.3$, $-37.4$) | 0.000 | 144.8 $\pm$ 41.6 | $-44.2^a$ ($-56.8$, $-31.5$) | 0.000 |
| Triglyceride | 93 | 166.8 $\pm$ 88.0 | 138.4 $\pm$ 55.6 | $-28.4^a$ ($-48.9$, $-7.8$) | 0.003 | 133.6 $\pm$ 52.6 | $-33.2^a$ ($-54.0$, $-12.3$) | 0.001 |
| HDL-C | 94 | 38.7 $\pm$ 10.0 | 37.8 $\pm$ 8.3 | $-0.9$ ($-3.3$, $1.4$)$^b$ | 0.926 | 39.4 $\pm$ 9.9 | $0.7$ ($-1.8$, $3.1$)$^b$ | 1.000 |
| VLDL-C | 90 | 30.6 $\pm$ 14.4 | 27.5 $\pm$ 11.2 | $-3.1$ ($-6.7$, $0.6$) | 0.140 | 28.4 $\pm$ 22.0 | $-2.2$ ($-8.4$, $4.1$) | 1.000 |
| TC/HDL-C ratio | 92 | 5.1 $\pm$ 1.5 | 3.7 $\pm$ 1.1 | $-1.4^a$ ($-1.7$, $-1.0$) | 0.000 | 3.8 $\pm$ 1.6 | $-1.3^a$ ($-1.7$, $-0.8$) | 0.000 |
| LDL-C/HDL-C ratio | 92 | 3.2 $\pm$ 1.2 | 2.0 $\pm$ 0.9 | $-1.2^a$ ($-1.4$, $-0.8$) | 0.000 | 2.4 $\pm$ 2.6 | $-0.8^a$ ($-1.4$, $-0.1$) | 0.029 |

*Note*: Based on estimated marginal means.
CI = confidence interval, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SD = standard deviation, TC = total cholesterol, VLDL-C = very low-density lipoprotein cholesterol.
[a] The mean difference is significant at the 0.05 level.
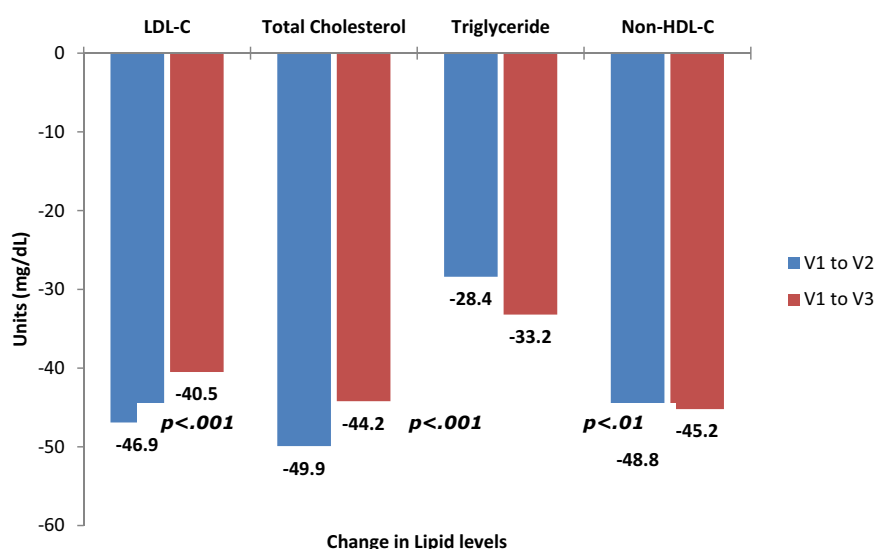[b] Adjustment for multiple comparisons: Bonferroni.

**Fig. 1.** Mean change in LDL, TC, TG and non-HDL-C levels at week 6 and week 12.
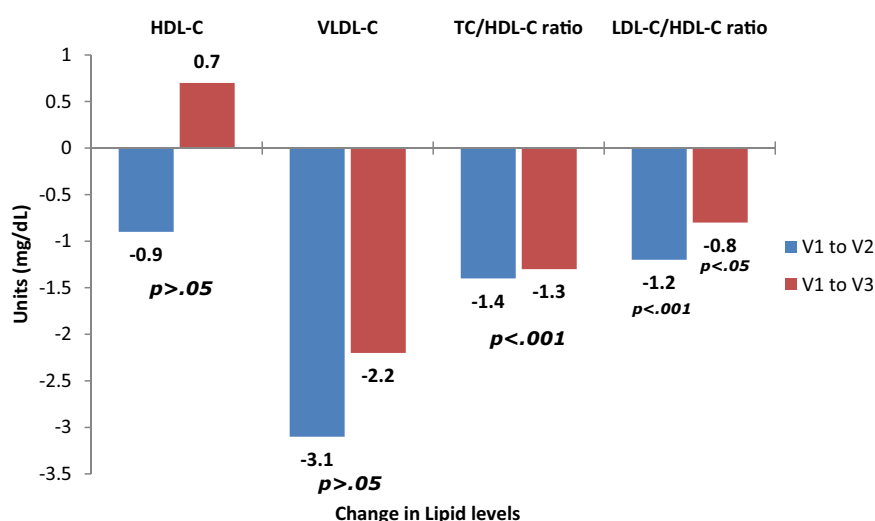


**Fig. 2.** Mean change in HDL-C. VLDL-C, TC-HDL ratio and LDL-HDL ratio at week 6 and week 12.

in the study had change in serum CPK level. SGOT levels decreased significantly by 36.5 IU/L ($P < 0.01$), and SGPT levels were non-significantly reduced by 5.3 IU/L ($P > 0.05$). Mean serum creatinine levels at baseline and week 12 remained unchanged. In a post hoc analysis, the eGFR increase between baseline and week 12 was minimal and not statistically significant. The levels of HbA1c from baseline to week 12 remained unchanged. Changes in laboratory values at week 12 from baseline are listed in Table 3.

### 3.3. Safety

A total of 8 (3.5%) AEs were reported by 8 (3.5%) patients. Myalgia was most commonly reported AE reported by 5 (2.2%) patients. Adverse events reported were considered to be treatment related and led to dose titration in all the 8 patients. None of the AEs were categorized as serious in intensity nor did patient have a CPK value outside the normal range.

**Table 3**
Assessment of tolerability parameter.

| Variable | Mean ± SD | | | Mean change from baseline to week 12 (95%CI) | P value[a] |
|---|---|---|---|---|---|
| | Baseline | Week 6 | Week 12 | | |
| CPK U/L ($n = 87$) | – | 101.7 ± 58.0 | 102.6 ± 67.6 | 0.9 (−8.4, 10.3) | >0.05 |
| SGOT U/L ($n = 73$) | 60.6 ± 98.5 | – | 24.1 ± 9.0 | −36.5 (−59.2, −13.8) | <0.01 |
| SGPT U/L ($n = 72$) | 50.0 ± 37.6 | – | 44.7 ± 19.2 | −5.3 (−11.5, 0.9) | >0.05 |
| Serum creatinine mg/dL ($n = 107$) | 1.0 ± 0.4 | – | 1.0 ± 0.3 | 0.0 (0.0, 0.1) | >0.05 |
| eGFR ($n = 107$) | 84.6 ± 32.9 | – | 85.6 ± 52.4 | 1.0 (−10.0, 12.0) | >0.05 |
| eGFR using CKD-EPI ($n = 107$) | 84.8 ± 25.3 | – | 84.9 ± 22.4 | 0.1 (−5.4, 5.6) | >0.05 |

CPK = creatinine phosphokinase, eGFR = estimated glomerular filtration rate, SGOT = serum glutamic oxaloacetic transaminase, SGPT = serum glutamic pyruvic transaminase.
[a] Paired samples t-test.

## 4. Discussion

Statins are the drugs of first choice in treating hypercholesterolemia and have proven benefits on outcomes of CV morbidity and mortality.[10] Large secondary prevention trials have proved the efficacy of statins in preventing CV morbidity and mortality in patients with coronary heart disease.[4] Evidence from MIRACL and other studies suggest that statin treatment during ACS has beneficial effects on risk reduction in both the short term (during hospitalization) and long term (up to 1 year).[4]

Statins possesses pleiotropic effects and upregulates the expression of endothelial NO synthase, thus increasing the NO production.[4] Statins may also repair damaged endothelium by promoting mobilization of endothelial progenitor cells and accelerating re-endothelialization of injured vessels.[4] Rosuvastatin has demonstrated established clinical efficacy and safety in treating dyslipidemia in numerous clinical trials and post marketing analyses. Prolonged treatment with rosuvastatin is expected to produce pronounced benefit in patients at high risk of any major vascular event.[3]

In this post marketing observational study evaluating the clinical efficacy and safety of the intensive dose of rosuvastatin 40 mg/day in patients with ACS, encouraging results have been observed. The results showed that rosuvastatin significantly reduces mean LDL-C by 46.9 mg/dL ($P < 0.001$) after 6 weeks of treatment and by 40.5 mg/dL after 12 weeks of treatment. These results are consistent with previous established clinical studies. Dose ranging studies have proved that rosuvastatin up to 40 mg dose produces statistically significant dose-dependent decrease in LDL-C by 52–63% at 6 weeks compared with placebo.[13] Another study comparing different doses of rosuvastatin and atorvastatin showed that rosuvastatin 10–40 mg reduces LDL-C by 47–57% compared with 38–54% with atorvastatin 10–80 mg.[15] Similar results were obtained with the Statin Therapies for Elevated Lipid Levels compared Across doses to Rosuvastatin (STELLAR) study in patients with hypercholesterolemia with rosuvastatin 10–40 mg.[13]

Acute coronary syndrome significantly affects the concentration and composition of the lipids and lipoproteins in plasma. In the LUNAR (Limiting UNdertreatment of lipids in ACS with Rosuvastatin) study, the finding suggests that rosuvastatin 40 mg/day was significantly more effective than atorvastatin 80 mg/day in decreasing LDL-C and other important lipid parameters, such as apolipoprotein AI, LDL-C/HDL-C, non-HDL-C/HDL-C, TC/HDL-C, and apolipoprotein B/apolipoprotein AI, is consistent with previous data from patients without ACS and with the SATURN study.[14]

According to the NCEP-ATP III clinical guidelines, therapy is dependent on the CV risk.[10] 'Very high' risk occurs in pre-existing CV episode (myocardial infarction), stable or unstable angina, coronary artery procedure (angioplasty or bypass), or otherwise evidence of clinically significantl myocardial ischemia involving more than one risk factor (e.g., diabetes, hypertension, persistent smoking).[7,10] 'High' risk occurs in previous coronary disease conditions or its equivalent (peripheral artery disease, aneurysm 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 with >20% risk of 10 years coronary disease.[7,10]

The present study findings indicate significant decreases in TC ($P < 0.001$), triglyceride ($P < 0.01$), TC/HDL-C ratio ($P < 0.001$), and LDL-C/HDL-C ratio ($P < 0.001$) which is consistent with the findings of LUNAR study. No significant changes were observed in change in lipid levels after dose titration.

Although there is no consensus on the optimal time of administration of statins during ACS, some clinical trials and pooled analyses provide substantial support for the institution of an early therapy to improve strategies that target the pathophysiologic mechanism operating during myocardial infarction. In particular, recent findings suggest that the earlier the treatment is started after the diagnosis of ACS, the greater the expected benefit. The results of the SATURN study suggest that rosuvastatin may be preferable in 'very high' risk patients with ACS in whom a target LDL-C <70 mg/dL is desirable.[11]

In the SATURN study, HDL-C was significantly increased with rosuvastatin 40 mg and persisted over the 12-week study period.[11] However, in the present study, HDL-C increased marginally (0.7 mg/dL) in patients after 12 weeks of rosuvastatin therapy. Changes in laboratory values of CPK, SGPT, serum creatinine, eGFR, and HbA1c from baseline to week 12 was not clinically significant except for SGOT which decreased significantly by 36.5 IU/L ($P < 0.01$).

Rosuvastatin is well tolerated with lesser-known adverse events. Reporting of adverse events could be affected by patient's awareness. Myalgia is the commonest side effect with statin therapy[13] and the current study also reflects this. None of the AEs were categorized as serious in intensity. There were no deaths during the rosuvastatin treatment. These findings are consistent with the previous clinical trials with rosuvastatin.[13] Rosuvastatin exhibits a desirable pharmacologic and safety profile.

Recent clinical trials have generated promising results that have supported the concept of the cardioprotective effect of statin administration as first-line therapy for ACS.[2] Patients could receive a statin as early as possible following ACS.[1] Statin therapy should not be discontinued in unstable patients with ACS as it may revoke its beneficial effects.[6]

The limitation of the study is being post marketing observational study; most of the patients were lost to follow-up, due to logistical problems, or because patients were unable to follow-up on time due to their residence in remote areas.

## 5. Conclusion

The present study evaluated the safety and efficacy of high-intensity rosuvastatin therapy in Indian ACS patients. It can be concluded from the results of this study that 40 mg dose of rosuvastatin, initiated early and continued for 12 weeks, was effective in terms of reducing LDL cholesterol and was well tolerated.

### Sources

### Conflicts of interest

The authors have none to declare.

### Acknowledgements

### References

1. Warnica JW. *Acute Coronary Syndromes (ACS) (Unstable Angina; Acute MI; Myocardial Infarction)*. The Merck Manual Professional Edition; 2015 http://www.

merckmanuals.com/professional/cardiovascular-disorders/coronary-artery-disease/acute-coronary-syndromes-acs. [accessed 03.07.15].

2. Ostadal P. Statins as first-line therapy for acute coronary syndrome? *Exp Clin Cardiol.* 2012;17:227–236.

3. Rubba P, Marotta G, Gentile M. Efficacy and safety of rosuvastatin in the management of dyslipidemia. *Vasc Health Risk Manage.* 2009;5:343–352.

4. Sacks FM. Do statins play a role in the early management of the acute coronary syndrome? *Eur Heart J Suppl.* 2004;6(suppl A):A32–A36.

5. Kapur NK, Musunuru K. Clinical efficacy and safety of statins in managing cardiovascular risk. *Vasc Health Risk Manage.* 2008;4:341–353.

6. Heeschen C, Hamm CW, Laufs U, et al. on behalf of the Platelet Receptor Inhibition in Ischemic Syndrome Management (PRISM) Investigators.Withdrawal of statins increases event rates in patients with acute coronary syndromes. *Circulation.* 2002;105:1446–1452.

7. Grundy SM, Cleeman JI, Merz NB, et al. for the Coordinating Committee of the National Cholesterol Education Program; Endorsed by the National Heart, Lung, and Blood Institute, American College of Cardiology Foundation, and American Heart Association.Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation.* 2004;110:227–239.

8. Pitt B, Loscalzo J, Ycas J, et al. Lipid levels after acute coronary syndromes. *J Am Coll Cardiol.* 2008;51:1440–1445.

9. Hulten E, Jackson JL, Douglas K, et al. The effect of early, intensive statin therapy on acute coronary syndrome: a meta-analysis of randomized controlled trials. *Arch Intern Med.* 2006;166:1814–1821.

10. Feliciano-Alfonso JE. Rosuvastatin: role in cardiovascular high-risk patient. *Rev Fac Med.* 2013;61:41–51.

11. Nicholls SJ, Ballantyne CM, Barter PJ, et al. Effect of two intensive statin regimens on progression of coronary disease. *N Engl J Med.* 2011;365:2078–2087.

12. Lablanche JM, Danchin N, Farnier M, et al. Effects of rosuvastatin and atorvastatin on the apolipoprotein B/apolipoprotein A-1 ratio in patients with an acute coronary syndrome: the CENTAURUS trial design. *Arch Cardiovasc Dis.* 2008;101:399–406.

13. Brewer HB. Benefit-risk assessment of rosuvastatin 10 to 40 milligrams. *Am J Cardiol.* 2003;92(suppl):23K–29K.

14. Pitt B, Loscalzo J, Monyak J, et al. Comparison of lipid-modifying efficacy of rosuvastatin versus atorvastatin in patients with acute coronary syndrome (from the LUNAR study). *Am J Cardiol.* 2012;109:1239–1246.