

Comparison of Low-density Lipoprotein Cholesterol Reduction After Switching Patients on Other Statins to Rosuvastatin or Simvastatin in a Real-world Clinical Practice Setting

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Abstract

Objective: The study compared low-density lipoprotein cholesterol (LDL-C) reduction obtained after switching patients on a statin therapy to rosuvastatin or simvastatin in real-world clinical practice.

Methods: Using information from an electronic medical records database, for patients ≥ 18 years of age who received newly prescribed statin therapy during August 2003 to March 2006, who were switched to either rosuvastatin or simvastatin, and who had LDL-C values at baseline, switch and postswitch data were included ($N = 277$). Percent LDL-C reduction between patients switched to rosuvastatin ($n = 155$) and those switched to simvastatin ($n = 122$) were compared. Linear regression model was adjusted for percent LDL-C change from preswitch to switch, LDL-C at time of switch, age, sex, smoking, statin aggressiveness, and therapy duration postswitch. Percent LDL-C reduction for patients switched from atorvastatin to rosuvastatin versus atorvastatin to simvastatin was also compared.

Results: Patients switched to rosuvastatin or simvastatin were similar in age, sex, and baseline LDL-C (mean, 146 mg/dL). Patients switched to rosuvastatin from any other statin had a significantly greater percent LDL-C reduction (18.4%) postswitch than patients switched to simvastatin (5.8%; $P = .0003$). After adjusting for baseline covariates, rosuvastatin patients had a significantly greater percent LDL-C reduction postswitch than simvastatin patients (16.0% vs 8.8%, respectively; $P = .0002$). In the subgroup of patients switched from atorvastatin, patients switched to rosuvastatin ($n = 67$) had a significantly greater adjusted percent LDL-C reduction (13.6%) postswitch than patients switched to simvastatin (5.5%; $n = 75$; $P = .001$).

Conclusion: Rosuvastatin achieves greater percent LDL-C reduction than simvastatin as a switch therapy in a real-world clinical practice setting. This highlights the need to select the statin to switch to based on additional needed percent LDL-C reduction to meet individual patient targets. Availability of simvastatin (generic statin) and rosuvastatin (branded statin) as treatment options would facilitate efficient and effective management of patients with dyslipidemia.

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The importance of reducing cholesterol levels for the prevention of coronary heart disease is well recognized by US and European guidelines.¹⁻³ These guidelines recommend treatment targets and advocate the use of statins as the lipid-modifying agents of choice. Yet lipid management in clinical practice is suboptimal, with only one third to one half of patients achieving recommended cholesterol levels on lipid-lowering therapy.⁴⁻⁷ This treatment gap has considerable clinical and economic implications in terms of reduced effectiveness for preventing cardiovascular events and deaths, and increased costs to healthcare plans and payers.⁸

Healthcare plans are increasingly using formulary conversion programs and tiered pharmacy benefit designs to increase utilization of lower-cost drugs in an effort to maximize limited resources for pharmacy benefits.⁹⁻¹¹ These programs have increased the number of patients with hyperlipidemia who are switched to different statins over time.^{9,10} Additionally, some patients are switched to a different statin because of tolerability and side effects issues.^{12,13} However, little is known about the low-density lipoprotein cholesterol (LDL-C)-lowering effects in clinical practice when patients are switched from one statin to another. Several multinational clinical trials have demonstrated that switching to a more efficacious statin (eg, rosuvastatin) improved lipid goal achievement.^{14,15} A formulary conversion program within the military indicated that further LDL-C reduction can be achieved by converting patients to more effective statins.⁹

The present study was designed to assess LDL-C lowering among patients in routine clinical practice who had been switched from other statins to either rosuvastatin or simvastatin. Switches to rosuvastatin were a focal point for this study because clinical trials and observational studies have demonstrated that rosuvastatin provides the greatest LDL-C reduction in real-world clinical practice at commonly used doses compared with other statins.^{16,17} Simvastatin switches were important because simvastatin recently became available as a generic

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agent with a significantly reduced price and therefore may provide an efficient statin option for appropriate patients. The objective of this study was to compare percent LDL-C reduction observed after switching patients taking a statin therapy to either rosuvastatin or simvastatin, thereby providing evidence for healthcare administrators in making statin formulary decisions. In addition, percent LDL-C reduction observed after switching patients taking atorvastatin to either rosuvastatin or simvastatin was also examined.

Methods

A retrospective observational cohort study was conducted utilizing the General Electric Medical System (GEMS) electronic medical records database. Patients 18 years of age or older who were treated in a community-based physician practice within the GEMS and were newly prescribed statin therapy during August 2003 to March 2006 were identified from the database. From these patients, those who were switched to either rosuvastatin or simvastatin and had LDL-C values before lipid therapy initiation, switch, and postswitch were considered for inclusion in the study. Eligible patients also had to have a prescription for the initial statin for at least 3 months and could not be prescribed other antidiabetic medications (eg, bile acid sequestrants, fibrates, niacin, ezetimibe) in the 12 months before or after initiating statin therapy.

Because of the variability of lipid testing in clinical practice, baseline LDL-C measurement (baseline LDL-C) was defined as the lipid value before (up to 90 days) and closest to the date of statin therapy initiation. The LDL-C measurement at the time of the statin switch (switch LDL-C) was defined as the lipid value 30 days or less before the switch to rosuvastatin or simvastatin; the postswitch (follow-up) LDL-C measurement (postswitch LDL-C) was defined as the average of LDL-C measures taken during the period from 30 days after the statin switch to the date of the last statin prescription.

Statistical Analyses. Changes in LDL-C from baseline (statin initiation) to switch and from switch to postswitch were computed for each eligible patient. The mean difference in percent LDL-C reduction between patients who were switched

from any statin to rosuvastatin versus patients who were switched from any statin to simvastatin was computed. Additionally, the mean difference in percent LDL-C reduction between patients switched from atorvastatin to rosuvastatin or to simvastatin was compared. The distribution of percent LDL-C reduction postswitch was examined and the proportion of patients whose LDL-C postswitch values decreased by 25% or more (large reduction), by 10% to 25% (moderate reduction), by 0% to 10% (minimal reduction), or increased (>0%) were calculated. Multivariate linear regression analyses compared the effectiveness of rosuvastatin to simvastatin, adjusted for age, sex, smoking, LDL-C at time of switch, percent LDL-C change from baseline to switch, initial aggressive statin, and therapy duration postswitch. All statins at particular doses giving >40% reduction, as stated in the package inserts, were considered aggressive statin treatments (all doses of rosuvastatin; 20-, 40-, and 80-mg doses of atorvastatin; and 40- and 80-mg doses of simvastatin). Standard statin therapy category included 10 mg atorvastatin, 5, 10, and 20 mg simvastatin, all doses of pravastatin, all doses of fluvastatin, and all doses of lovastatin, based on percent LDL-C reduction stated in the package inserts. The a priori 2-tailed level of statistical significance was set at $P < .05$.

Results

On application of the inclusion criteria, there were 155 patients who were switched from any statin to rosuvastatin and 122 patients who were switched from any statin to simvastatin. Patients switched to rosuvastatin were similar to patients switched to simvastatin in age, sex, aggressive versus standard initial statin, baseline LDL-C, duration of therapy from baseline to switch, and total therapy duration (Table 1). However, patients switched to rosuvastatin were prescribed a lower dose (mean, 12.9 mg) on average than patients switched to simvastatin (mean, 29.4 mg; $P < .05$). Also, a greater proportion of patients who were switched to simvastatin (61.5%) were initially taking atorvastatin than were patients who were switched to rosuvastatin (43.2%; $P < .05$) (Table 1). LDL-C at the time of switch was significantly higher among patients who were switched to rosuvastatin (mean, 133.3 mg/dL) than patients who

Table 1. Baseline Characteristics of Patients Switched From Any Statin to Rosuvastatin or Simvastatin

Characteristics	Switched to Rosuvastatin, N = 155	Switched to Simvastatin, N = 122
Age, years, mean (SD)	61.8 (10.6)	62.9 (11.9)
Male, %	50	50
Aggressive initial statin, %	30	35
Duration of therapy from start to switch, days, mean (SD)	193 (140)	176 (141)
Total duration of therapy, days, mean (SD)	466 (160)	449 (165)
Switching from atorvastatin, n (%)	67 (43.2)	75 (61.5)*
Switch statin dose, mg, mean (SD)	12.9 (7.3)	29.4 (17.6)*
Baseline lipids, mean (SD)		
Baseline LDL-C, mg/dL [†]	146.3 (43.2)	146.2 (42.6)
Switch LDL-C, mg/dL [‡]	133.3 (44.7)	118.0 (44.6)*
Total cholesterol, mg/dL [§]	225.4 (45.5)	227.7 (45.3)
HDL-C, mg/dL [§]	49.2 (12.9)	50.4 (13.4)
Triglycerides, mg/dL [§]	178.5 (86.8)	168.3 (95.2)

*P <.05 for comparison with rosuvastatin.
[†]LDL-C value before and within 90 days of statin therapy initiation.
[‡]LDL-C value ≤30 days before statin switch.
[§]Sample size varies slightly from LDL-C total.
SD indicates standard deviation; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

were switched to simvastatin (mean, 118.0 mg/dL; P <.05) (Table 1).

LDL-C Reduction Postswitch. Patients switched to rosuvastatin from any other statin had a significantly greater percent LDL-C reduction postswitch (18.4%) than patients switched to simvastatin (5.8%; P <.05) (Figure 1). A similar difference in LDL-C reduction was estimated after adjusting for age, sex, smoking, initial statin aggressiveness, LDL-C at switch, percent LDL-C reduction from baseline to switch, and therapy duration postswitch. Patients switched to rosuvastatin had an estimated 16.0% LDL-C reduction postswitch compared with an estimated 8.8% reduction among patients switched to simvastatin (Figure 1). Little percent LDL-C reduction occurred before patients were switched to rosuvastatin (6%) and the difference in preswitch percent LDL-C reduction compared with patients switched to simvastatin (14.6%) was significantly lower (P <.05).

A significantly greater proportion of patients switched to rosuvastatin had a greater than 25%

LDL-C reduction (44%) than patients switched to simvastatin (29%; P <.05) (Table 2). Furthermore, a significantly larger percent of patients who were switched to simvastatin (38%) experienced LDL-C elevation (increase in LDL-C) postswitch compared with those who were switched to rosuvastatin (21%) (Table 2).

LDL-C Reduction When Switched From Atorvastatin to Rosuvastatin or Simvastatin. The majority of patients who were switched to rosuvastatin or simvastatin were initially prescribed atorvastatin (43% [n = 67] of those who were switched to rosuvastatin and 61% [n = 75] of those who were switched to simvastatin; Table 1). The mean ending dose of atorvastatin before switching to rosuvastatin was higher (20.7 mg) than the average dose before switching to simvastatin (15.2 mg; P <.05). Also, the average dose of rosuvastatin postswitch was 12.0 mg, compared with 25.3 mg of simvastatin. Patients switched from atorvastatin to rosuvastatin had significantly greater observed percent LDL-C reduction postswitch (14.6%) than patients switched

Comparison of Low-density Lipoprotein Cholesterol Reduction After Switching Patients on Other Statins

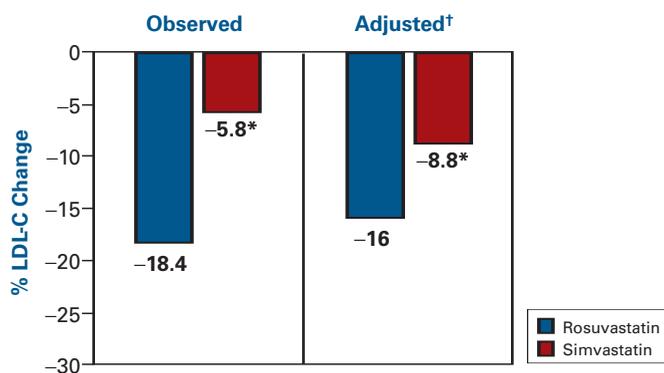
from atorvastatin to simvastatin (4.6%; $P < .05$) (Figure 2). When adjusted for baseline characteristics, a similar difference was documented; patients switched from atorvastatin to rosuvastatin had significantly greater estimated percent LDL-C reduction (13.6%) than patients switched from atorvastatin to simvastatin (5.5%; $P < .05$) (Figure 2).

Discussion

Patients who were switched from any statin to rosuvastatin or simvastatin did experience an additional percent reduction in LDL-C postswitch. Furthermore, a switch from atorvastatin to rosuvastatin or simvastatin provided additional percent LDL-C reduction for both patient switch groups. However, rosuvastatin achieved a significantly greater average percent LDL-C reduction than simvastatin as a switch therapy in real-world clinical practice. Rosuvastatin patients achieved a greater LDL-C reduction even with a higher LDL-C at the time of switch and with being switched to a lower dose than simvastatin patients. For patients switched from atorvastatin, the average doses went from 20.7 mg of atorvastatin to 12.0 mg of rosuvastatin versus 15.2 mg of atorvastatin to 25.3 mg of simvastatin, and the switch to rosuvastatin produced a greater average LDL-C reduction than simvastatin.

With the introduction of simvastatin as a generic statin, health plan administrators would have opportunities to provide more efficient care by encouraging simvastatin use in a patient segment with lower percent LDL-C reduction need and by encouraging use of more effective statins like rosuvastatin in patients with a higher percent LDL-C reduction requirement. This study provides useful data from real-world clinical practice to help clinicians and health providers make patient treatment and policy decisions. The study results indicate that it is possible to derive additional percent LDL-C reduction by switching patients to rosuvastatin or simvastatin from any other statin or from atorvastatin specifically. However, pharmacy administrators and physicians may need to consider the differential lipid management needs of their patients. Switching to simvastatin may be appropriate for patients who need to maintain their LDL-C level on another statin and for patients who need a

Figure 1. Percent LDL-C Change Among Patients Switched to Rosuvastatin Compared With Simvastatin



* $P < .05$ compared with rosuvastatin.

[†]Adjusted for percent LDL-C change from baseline to switch, LDL-C at time of switch, age, sex, smoking, statin aggressiveness, and therapy duration postswitch.

LDL-C indicates low-density lipoprotein cholesterol.

smaller additional LDL-C reduction to achieve individual target LDL-C goal. However, switching to rosuvastatin would be needed for those patients who require, on average, a greater LDL-C reduction than $\geq 9\%$ (Figure 1; average reduction after adjustment for simvastatin, 8.8%, in comparison with rosuvastatin, 16%) to reach and maintain individual LDL-C target goal. These data highlight the need to allow access to both simvastatin and rosuvastatin to meet individual needs of different patients based on their percent LDL-C reduction needs.

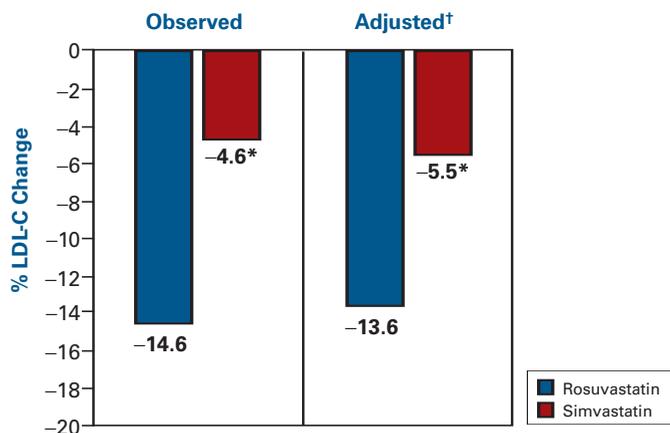
The study results also provide helpful insights for plans that are removing atorvastatin from preferred

Table 2. Distribution of LDL-C Reduction Postswitch Among Patients Switched to Rosuvastatin or Simvastatin

LDL-C Change	Switched to Rosuvastatin, N = 155	Switched to Simvastatin, N = 122
<-25%	68 (44%)	36 (29%)*
-25% to -10%	37 (24%)	26 (21%)
-10% to 0%	17 (11%)	13 (11%)
>0% (LDL-C increased)	33 (21%)	47 (38%)*

* $P < .05$ for comparison with rosuvastatin.
LDL-C indicates low-density lipoprotein cholesterol.

■ Figure 2. Percent LDL-C Change Among Patients Switched From Atorvastatin to Rosuvastatin (n = 67) or Simvastatin (n = 75)



*P < .05 compared with rosuvastatin.

†Adjusted for percent LDL-C change from baseline to switch, LDL-C at time of switch, age, sex, smoking, statin aggressiveness, and therapy duration postswitch. LDL-C indicates low-density lipoprotein cholesterol.

status to maximize efficiency by encouraging increased use of generic simvastatin. In such specific situations where patients are primarily being switched from atorvastatin to simvastatin or rosuvastatin, switching patients needing, on average, ≤6% (Figure 1; average reduction after adjustment for simvastatin, 5.5%, in comparison with rosuvastatin, 13.6%) lower additional percent LDL-C reduction to simvastatin and switching patients needing, on average, >6% additional percent LDL-C reduction to rosuvastatin may improve lipid management among these patients.

Because this was an observational database study, there are limitations that should be considered when interpreting the results. The drug information in the GEMS database is the physician prescription order and not pharmacy claims data. Therefore, it was not possible to ascertain that all statin prescription orders were filled by the patient. To reduce introduction of potential bias due to non-filling of some prescriptions, only those patients with at least a 90-day supply of statin therapy (eg, at least one 30-day prescription with 2 refills, three 30-day prescriptions, or one 90-day prescription for mail order) were included. Excluding patients who did not receive statin prescriptions for more than 3 months was done to minimize any bias due to pos-

sible inclusion of patients who were more likely to have missed filling their prescriptions. The observed frequency of statin discontinuation was similar between rosuvastatin and simvastatin patients and therefore the comparative effectiveness of the statins would not be expected to change because of this study assumption. The titration rate for all patients prescribed statin therapy was very low (<5%) and unlikely to have a significant impact on the study findings.

In conclusion, rosuvastatin achieved greater percent LDL-C reduction than simvastatin as a switch therapy in clinical practice. The study results indicate that it is possible to switch patients to simvastatin when a smaller additional percent LDL-C is required. However, rosuvastatin may be more suitable as a switch to statin option when a greater percent reduction in LDL-C is required to meet individual patient care needs. Availability of simvastatin and rosuvastatin as switch to statin options may help providers achieve effective and efficient management of dyslipidemia among patients switching from one statin treatment to another.

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