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Observational Multicenter Cohort Study Examining Pharmacogenomic Factors Influencing Rosuvastatin Discontinuation across Diverse Ethnic Groups

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ABSTRACT

Despite its widespread use for cardiovascular risk management, rosuvastatin's long-term effectiveness is often limited by treatment cessation. Genetic differences, particularly in ABCG2 and SLCO1B1, can alter drug transport, efficacy, and side-effect profiles. The ABCG2 rs2231142 variant increases drug exposure, which may enhance lipid-lowering effects but also raises the likelihood of adverse events, especially muscle-related complications. Investigating these genetic influences in a real-world, ethnically diverse population is critical for improving adherence and enabling tailored therapy. This study evaluated the roles of ABCG2 rs2231142 (G>T; Q141K) and SLCO1B1 rs4149056 (T>C; V174A) variants in rosuvastatin discontinuation and LDL cholesterol response in a multiethnic cohort from the United Arab Emirates. A total of 422 adult patients prescribed rosuvastatin were enrolled in this multicenter prospective cohort and monitored over 12 months. Information on therapy discontinuation was collected from clinical records and patient follow-ups. Genotyping was performed using TaqMan SNP assays. Discontinuation risks associated with each genotype were analyzed using Cox regression and Kaplan-Meier survival curves, while changes in LDL cholesterol were evaluated with descriptive statistics and logistic regression models. Individuals carrying the T/T genotype of ABCG2 rs2231142 exhibited the highest likelihood of stopping therapy (HR = 4.40, $p < 0.001$), followed by heterozygotes (G/T, HR = 1.75). LDL cholesterol changes were markedly different between those who continued treatment (−17.86 percent) and those who discontinued (+21.89 percent, $p < 0.001$). The ABCG2 variant was significantly more frequent in discontinuers (30.6 percent vs. 17.4 percent, $p = 0.0026$), whereas the SLCO1B1 rs4149056 variant showed no significant impact on therapy cessation. Carriers of the ABCG2 minor allele are at elevated risk of discontinuing rosuvastatin due to side effects. Incorporating ABCG2 genotyping into clinical practice may support individualized dosing strategies and enhance patient adherence.

Keywords: Statin discontinuation, Rosuvastatin, Personalized medicine, Pharmacogenomics, ABCG2 rs2231142

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Introduction

Statins, which inhibit HMG-CoA reductase, are among the most widely prescribed medications worldwide for the prevention of cardiovascular disease (CVD) [1]. Robust evidence from both primary and secondary prevention trials consistently demonstrates their efficacy in reducing cardiovascular events [2]. The 2018 ACC/AHA guidelines recommend moderate- to high-intensity statin therapy for individuals at elevated risk of atherosclerotic cardiovascular disease (ASCVD), with each 1 mmol/L reduction in LDL cholesterol linked to an approximately 20% relative reduction in major vascular events [3]. Despite this compelling evidence, real-world adherence remains poor in most populations, primarily due to adverse effects that lead to premature discontinuation [4].

Cardiovascular disease is the leading cause of morbidity and mortality globally, including in the Middle East, a region projected to experience one of the sharpest increases in ASCVD burden over the next decade [5]. The 2022 Saudi Guidelines for Dyslipidaemia highlight the earlier onset and greater clustering of risk factors in Middle Eastern populations and advocate more intensive, regionally tailored lipid-lowering strategies [6]. However,

adherence to statin therapy in routine clinical practice across the Gulf Cooperation Council (GCC) countries is low, and high-quality, region-specific adherence data remain scarce [7].

Statin-associated musculoskeletal symptoms (SAMS) represent the most common reason for treatment interruption [8]. An increasing body of evidence underscores the clinical significance of SAMS, even when creatine kinase levels are normal (Davis and Weller, 2021). Although severe myopathy and rhabdomyolysis are rare [9], milder muscle symptoms are a major driver of non-adherence [10]. Observational studies and registries report SAMS incidence of 17–30%, whereas randomised controlled trials show rates around 5%, likely reflecting under-reporting among highly motivated trial participants [11-13]. Systemic statin exposure, modulated by both drug-drug interactions (DDIs) and drug-gene interactions (DGIs), is a key determinant of tolerability [14, 15].

The ABCG2 rs2231142 (c.421C>A; Q141K) variant impairs BCRP efflux transporter function, resulting in higher rosuvastatin plasma concentrations and increased risk of muscle-related adverse effects [16, 17]. The 2022 Clinical Pharmacogenomics Implementation Consortium (CPIC) guidelines recommend rosuvastatin dose adjustment in carriers of ABCG2 loss-of-function variants [18]. Nevertheless, evidence linking this variant to rosuvastatin discontinuation, particularly in multi-ethnic populations with widely varying allele frequencies, remains limited.

Previous pharmacogenomic studies in the Emirati population have identified distinctive allele frequencies for statin-related genes, emphasising the importance of population-specific data to enhance safety and inform clinical decisions in understudied groups [19-21].

The current study examines the association of ABCG2 rs2231142 (G>T; Q141K) and SLCO1B1 rs4149056 (T>C; V174A) variants with rosuvastatin discontinuation in a genetically diverse, real-world cohort from the United Arab Emirates. By investigating the influence of these pharmacogenomic markers on adverse effects and treatment persistence, this research seeks to advance personalised statin therapy in high-diversity populations.

Materials and Methods

Participants and study setting

This multicentre observational study was performed in Al Ain, United Arab Emirates, within the framework of the previously described EmHeart multicentre interventional cohort [22]. Data were gathered between January 2021 and June 2023 from several healthcare facilities in the UAE, including Tawam Hospital (a public tertiary centre – Cardiology Department), Mediclinic Hospital (a private multispecialty hospital – Cardiology Unit), The Heart Medical Center in Al Ain (a private specialised cardiovascular facility), and Burjeel Hospital in Abu Dhabi (a private tertiary hospital).

Of 500 initially eligible individuals, 78 were excluded because of incomplete follow-up. Baseline characteristics (age, sex, and genotype distribution) of excluded participants were comparable to those who completed the study. Reasons for exclusion were: (i) 40 patients formally withdrew or could not be contacted despite multiple attempts; (ii) 20 patients missed scheduled appointments and no further clinical information was available; and (iii) 18 patients either never started rosuvastatin or stopped it within the first 7 days, precluding their classification as continuers or discontinuers. Such attrition is typical in real-world observational research.

The final cohort comprised 422 participants who fulfilled all inclusion criteria and were followed for 12 months. Data on rosuvastatin discontinuation were obtained from electronic medical records (EMRs) and supplemented by scheduled telephone follow-up. Discontinuation was defined as cessation of rosuvastatin for >30 consecutive days without initiation of another lipid-lowering agent. Persistence was measured as the number of days of continuous rosuvastatin use. Telephone follow-ups, performed by trained healthcare staff using a standardised questionnaire, occurred at 1, 3, 6, and 12 months after treatment initiation (or recruitment for prevalent users). These calls collected self-reported information on discontinuation reasons, adverse effects, and any alternative therapies. Discontinuation rates were derived from the proportion of patients who stopped rosuvastatin, verified by cross-referencing self-reports with pharmacy refill data.

The cohort included both statin-naïve patients (72% of participants, newly started on rosuvastatin at enrolment) and prevalent statin users already on treatment at recruitment. This design enabled assessment of early adverse events and discontinuation in new users as well as longer-term persistence and cumulative tolerability in prevalent users.

Data collection, ethics, and follow-up procedures

The study was conducted in accordance with the Declaration of Helsinki and received ethical approval from the Abu Dhabi Department of Health Research and Technology Committee (reference nos. DOH/CVDC/2020/1187, DOH/CVDC/2021/1519, DOH/CVDC/2022/1458, DOH/CVDC/2023/1952, MCME.CR.213.MAIN.2021, and SNA/FA/2020-14) under the overarching EmHeart pharmacogenomics project. One related substudy focusing on statin-related adverse effects, with different objectives and methodology, has been published separately.

All data were entered into the Castor EDC platform (Castor EDC, Netherlands; www.castoredc.com). Baseline demographics, comorbidities, indication for statin therapy, and relevant clinical variables (e.g., thyroid disease) were extracted from EMRs using ICD coding. Concomitant medications, laboratory results, confirmed diagnoses, and drug allergies were also recorded. Statin discontinuation dates and documented reasons were primarily sourced from EMRs, with missing information completed via follow-up telephone interviews. Statin-associated muscle symptoms (SAMS) within the first year were verified by combining medical record review and patient interviews.

To reduce bias, only participants with complete genetic and clinical datasets were retained. Misclassification and recall bias were minimised by cross-validating self-reported discontinuation with objective EMR and pharmacy records. Reported reasons for discontinuation included SAMS, cost barriers, perceived lack of need, safety concerns, and preference for non-pharmacological management. Because these reasons were not uniformly documented for all discontinuers, no subgroup analyses by reason were performed.

LDL-cholesterol measurements

LDL-cholesterol (LDL-C) levels were recorded at baseline and after 12 months of follow-up. Baseline LDL-C was represented by a single measurement for all patients. At the 12-month visit, the average of two or three available LDL-C values was used to obtain a more stable estimate and reduce measurement variability.

The efficacy analysis of LDL-C response was restricted to a subset of 100 participants who had complete paired (baseline and follow-up) LDL-C data. This limitation arose from inconsistent timing of routine lipid profiling across UAE clinical practices; the subgroup was defined purely by data availability rather than by any pre-specified selection criteria. Percentage change in LDL-C from baseline to follow-up was calculated and compared between continuers and discontinuers. All LDL-C measurements were performed using standardized enzymatic colorimetric assays to ensure uniformity across study sites.

Genotyping

All participants were genotyped for two single-nucleotide polymorphisms: ABCG2 rs2231142 (G>T, p.Q141K) and SLCO1B1 rs4149056 (T>C, p.V174A). Peripheral blood was collected in EDTA tubes and stored at −20 °C. Genomic DNA was isolated using either the FlexiGene DNA Kit or QIAamp DNA Blood Kit (Qiagen, Germany). Genotyping was carried out with predesigned TaqMan SNP genotyping assays on the QuantStudio 7 Flex Real-Time PCR System (Applied Biosystems, Thermo Fisher Scientific). Genotype calling was performed with TaqMan Genotyper Software, and a random subset of samples was confirmed by Sanger sequencing, achieving 100% concordance.

For ABCG2 rs2231142, results are reported using the forward (plus) strand notation G>T (Q141K), consistent with major pharmacogenomics databases (PharmGKB, CPIC) and most published literature on rosuvastatin pharmacokinetics, even though the coding-strand change is technically c.421C>A.

Statistical analysis

Rosuvastatin discontinuation was analyzed using Kaplan-Meier survival curves and Cox proportional-hazards regression to compare discontinuation-free survival across ABCG2 rs2231142 genotypes (G/G, G/T, T/T). Discontinuation-free survival represents the proportion of patients remaining on rosuvastatin without interruption throughout the 12-month period. Patients who persisted until the end of follow-up were censored at their last contact date. Hazard ratios (HRs) with 95% confidence intervals were calculated to quantify risk differences.

Descriptive statistics (mean, standard deviation, range) were computed for percentage LDL-C change in continuers versus discontinuers. Between-group comparisons of LDL-C reduction, stratified by statin intensity and genotype, were performed using Student's t-tests and one-way ANOVA as appropriate. Normality of LDL-C percentage change was confirmed prior to parametric testing. Univariate and multivariable analyses were conducted in SPSS version 29.0 (IBM Corp., Armonk, NY, USA), with adjustment for age, sex, and statin intensity. Statistical significance was defined as $p < 0.05$.

Results and Discussion

Baseline characteristics

Of the 500 initially enrolled individuals, 422 (84.4%) completed the 12-month follow-up and were included in the final analysis; 78 (15.6%) were lost to follow-up but had comparable baseline characteristics to the retained cohort.

Among the 422 analyzed participants, 298 (70.6%) continued rosuvastatin (continuers) and 124 (29.4%) discontinued (discontinuers) during the study period **(Table 1)**. Factors significantly associated with discontinuation were: statin-naïve status at enrollment ($p = 0.0038$), younger age ($p < 0.0001$), presence of statin-associated muscle symptoms (SAMS; $p = 0.00572$), and carriage of the ABCG2 rs2231142 variant ($p = 0.00257$). Discontinuers were more often new statin users (82.3% vs. 68.5%), younger (mean age 47.5 vs. 53.6 years), and more frequently carried at least one ABCG2 variant allele (30.6% vs. 17.4%).

SAMS occurred in 111 patients overall (26.3%), with higher prevalence among discontinuers (35.5%) than continuers (22.5%). High-intensity rosuvastatin was prescribed to 42.7% of the cohort, with no significant difference between continuers and discontinuers ($p = 0.648$). Sex, ethnicity, smoking, thyroid disease, and SLCO1B1 rs4149056 carrier status did not differ significantly between groups.

Univariate analysis showed no significant association between SLCO1B1 rs4149056 and discontinuation ($p = 0.617$); therefore, this variant was not included in multivariable models.

Table 1. Baseline characteristics and univariate association with rosuvastatin discontinuation.

Characteristic	Overall cohort (n = 422)	Continuers (n = 298)	Discontinuers (n = 124)	*P-value* continuers vs. discontinuers
Satin usage status				
Statin initiators	303 (71.8%)	204 (68.5%)	102 (82.3%)	0.0038
Pre-existing Statin User	119 (28.2%)	94 (31.5%)	22 (17.7%)	
Demographics				
Age, mean (SD)	51.84 (11.67)	53.64 (11.34)	47.53 (11.34)	<0.0001
Female, sex	161 (38.2%)	110 (36.9%)	51 (41.1%)	0.416
Arab Ethnicity	186 (44.1%)	135 (45.3%)	51 (41.1%)	0.431
Smokers	101 (23.9%)	74 (24.8%)	27 (21.8%)	0.502
Rosuvastatin dose				
High intensity	180 (42.7%)	125 (41.9%)	55 (44.4%)	0.648
Moderate intensity	242 (57.3%)	173 (58%)	69 (55.6%)	
Hypothyrodism	37 (8.87%)	27 (9%)	10 (8%)	0.741
SAMS	111 (26.3%)	67 (22.54%)	44 (35.5%)	0.00572
ABCG2 rs2231142 (G>T) Carriers	87 (20.6%)	52 (17.4%)	38 (30.6%)	0.00257
SLCO1B1 rs4149056 (T>C) Carriers	116 (27.5%)	84 (28.2%)	32 (25.8%)	0.617

Bold values indicate statistical significance.

Primary outcome: rosuvastatin discontinuation

The Kaplan-Meier survival curves for discontinuation-free persistence are presented in **Figure 1**. The orange curve, corresponding to the ABCG2 rs2231142 T/T genotype, shows the most rapid decline in the proportion of patients remaining on rosuvastatin over the 12-month follow-up period. In contrast, the green curve representing the G/G (wild-type) genotype exhibits the slowest decline. Patients carrying the heterozygous G/T genotype demonstrated an intermediate trajectory. This pattern is reflected in a hazard ratio of 1.75, indicating a 75% increased risk of rosuvastatin discontinuation in G/T heterozygotes compared with G/G homozygotes **(Figure 1)**.

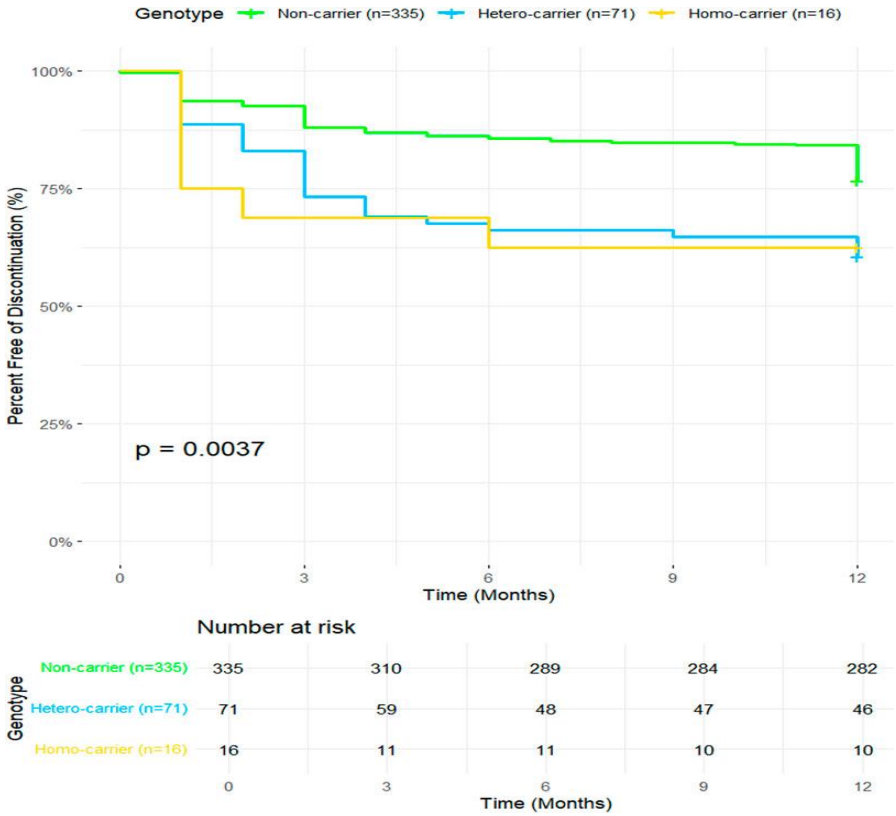

Figure 1. Kaplan-Meier curves depicting discontinuation-free survival on rosuvastatin over 12 months, stratified by ABCG2 rs2231142 genotype. The y-axis shows the percentage of patients remaining free from discontinuation, and the x-axis indicates follow-up time in months. Three genotype groups are displayed: non-carriers (G/G; n = 335, green line), heterozygous carriers (G/T; n = 71, blue line), and homozygous carriers (T/T; n = 16, yellow line). A log-rank test revealed statistically significant differences across genotypes (p = 0.0037). The number-at-risk table beneath the plot indicates the number of participants still under observation at each time point.

The yellow line corresponding to the T/T genotype exhibits the steepest decline, consistent with a hazard ratio of 4.40, meaning homozygous T/T individuals had a more than fourfold higher risk of discontinuing rosuvastatin compared with G/G individuals ($p < 0.001$). This visual pattern strongly supports the overall genotypic effect on treatment persistence **(Figure 1)**.

Multivariate analysis of predictors of rosuvastatin discontinuation

Multivariate logistic regression was performed to identify independent predictors of discontinuation, adjusting for ABCG2 rs2231142 genotype, presence of statin-associated muscle symptoms (SAMS), statin initiation status (new vs. prevalent user), and age.

Carriage of the ABCG2 c.421C>A (rs2231142) variant allele was independently associated with higher odds of discontinuation (adjusted OR 1.861, 95 percent CI 1.114–3.110, p = 0.018). Experiencing SAMS also significantly increased the likelihood of stopping treatment (adjusted OR 1.925, 95 percent CI 1.189–3.118, p = 0.008). Being a statin initiator (newly prescribed at enrollment) was a strong independent risk factor (adjusted OR 2.168, 95 percent CI 1.275–3.687, p = 0.004). In contrast, older age was protective, with each additional year reducing the odds of discontinuation by approximately 4% (adjusted OR 0.958, 95 percent CI 0.939–0.978, $p < 0.001$) **(Table 2)**.

Table 2. Logistic regression analysis of factors associated with rosuvastatin discontinuation as a dependent factor.

Independent variables	P-value	Adjusted odds ratio (OR)	95% CI (Lower)	95% CI (Upper)
ABCG2 c.421C>A (rs2231142)	0.018	1.861	1.114	3.110
SAMS	0.008	1.925	1.189	3.118

Statin Initiators	0.004	2.168	1.275	3.687
Age	<0.001	0.958	0.939	0.978

The effect of statin-associated muscle symptoms (SAMS) on rosuvastatin persistence was evaluated using Kaplan-Meier analysis **(Figure 2)**. Patients who experienced SAMS had significantly lower discontinuation-free survival than those without SAMS (log-rank p = 0.034). At 12 months, approximately 72% of patients without SAMS were still on treatment, compared with only 66% of those reporting SAMS. These results underscore the important role of muscle symptoms in reducing treatment adherence and indicate that SAMS is a major driver of early rosuvastatin discontinuation.

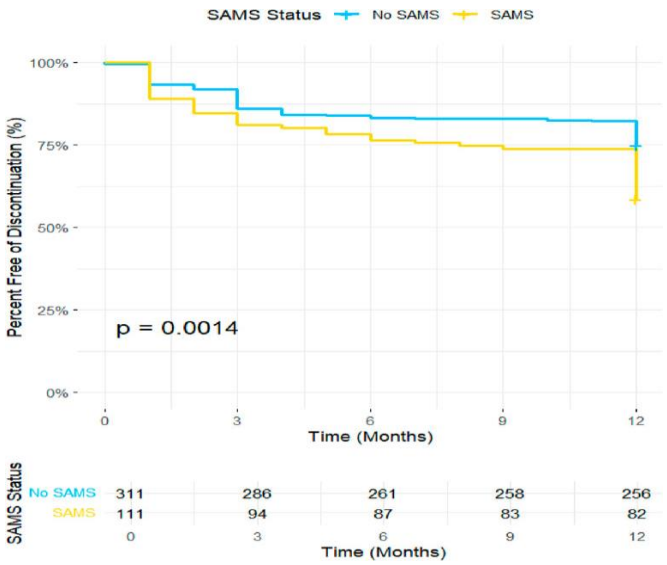

Figure 2. Kaplan-Meier curve showing discontinuation-free survival over 12 months stratified by the presence or absence of statin-associated muscle symptoms (SAMS). The y-axis indicates the percentage of patients remaining on rosuvastatin, and the x-axis denotes follow-up time in months.

Variability in LDL-C response according to discontinuation status

The mean percentage change in LDL-cholesterol was compared between continuers and discontinuers in the subset with paired lipid data (n = 100). Continuers (n = 61) achieved an average LDL-C reduction of −17.86% (SD 37.51; range −85% to +116.6%), whereas discontinuers (n = 39) showed a mean increase of +21.89% (SD 58.96; range −51% to +226%). This difference was highly statistically significant (p < 0.001). The contrasting distributions of percentage LDL-C change in the two groups are displayed in **Figure 3**.

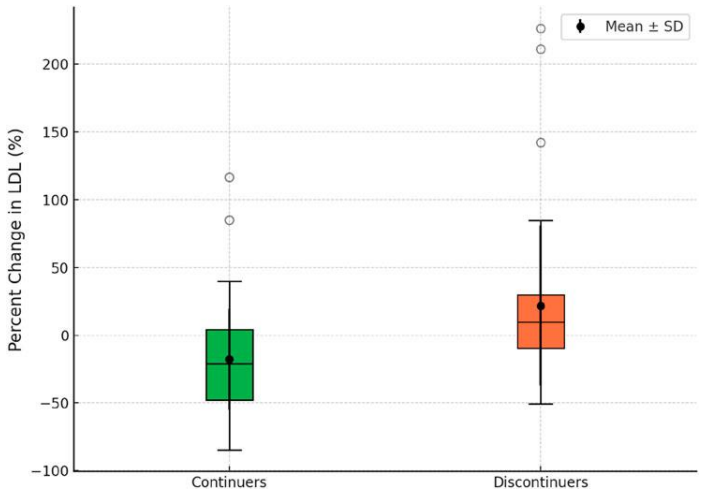

Figure 3. Box plot comparing the percentage change in LDL-cholesterol levels from baseline to 12 months between rosuvastatin continuers and discontinuers.

This study identifies the ABCG2 rs2231142 (G>T; c.421C>A) variant as an important predictor of rosuvastatin persistence, alongside statin-associated muscle symptoms (SAMS) and demographic factors. It also demonstrates the clinical consequence of discontinuation: loss of LDL-cholesterol control.

The ABCG2 rs2231142 variant reduces efflux transporter function, leading to impaired biliary excretion of rosuvastatin, elevated plasma concentrations, and greater tissue exposure [23]. A meta-analysis of eight studies involving 423 individuals confirmed that T-allele carriers exhibit significantly higher rosuvastatin plasma levels [24]. Increased drug exposure is thought to heighten the risk of adverse effects, particularly muscle symptoms, which in turn drives treatment discontinuation [17, 25].

In our cohort, Kaplan-Meier analysis revealed a clear gene–dose effect: homozygous T/T carriers (n = 16) had the lowest persistence (HR 4.40, 95% CI 2.07–9.33, p = 0.0001 vs. G/G), while heterozygous G/T individuals showed an intermediate risk (HR 1.75, 95% CI 0.99–3.09, p = 0.0547). Although the T/T group was small, the magnitude of the effect is consistent with the known pharmacokinetic impact of this variant.

Discontinuers were significantly younger (mean 47.5 vs. 53.6 years, $p < 0.0001$) and more often statin-naïve at enrollment (p = 0.0038). Younger patients may perceive lower cardiovascular risk and therefore exhibit reduced motivation for long-term therapy [26-29]. New statin users frequently encounter tolerability issues early in treatment, which further contributes to discontinuation [30].

Other factors such as rosuvastatin dose intensity, thyroid disease, and smoking status were not significantly associated with discontinuation, suggesting that genetic predisposition, muscle symptoms, and patient demographics exert stronger influence than many traditional clinical variables in this population.

Although rosuvastatin is recognized for superior LDL-lowering efficacy compared with atorvastatin [31], its real-world effectiveness is limited when patients discontinue therapy due to adverse effects or poor tolerability.

Our previous observational study investigated the relationship between muscle symptoms, elevated liver enzymes, and various factors including genetic variants. The current study builds directly on that foundation by focusing on the association between rosuvastatin discontinuation, carriage of the ABCG2 minor allele, and the occurrence of muscle pain.

Whereas the role of the SLCO1B1*5 allele in increasing the risk of statin-associated muscle symptoms (SAMS) and subsequent discontinuation is well established for atorvastatin [32], evidence for rosuvastatin has remained limited. The present work addresses this gap by examining the influence of SLCO1B1 rs4149056 and ABCG2 rs2231142 on rosuvastatin-related adverse effects and treatment persistence over 12 months.

Patients who experienced SAMS showed significantly lower treatment continuation rates than those who did not (p = 0.034). This confirms that muscle symptoms are a key clinical determinant of rosuvastatin persistence [33]. To reduce SAMS and improve adherence, clinicians should use patient-centered approaches: managing expectations, minimizing nocebo effects, emphasizing the proven benefits and safety of statins, and intensifying lifestyle interventions to potentially allow lower statin doses or switching to a better-tolerated statin. Evidence indicates that 60–80% of patients with SAMS can eventually tolerate at least one statin regimen when the appropriate agent is selected [34].

Proactively addressing both genetic and clinical risk factors can lower SAMS rates, decrease discontinuation, and improve outcomes. These results highlight the importance of personalized management of rosuvastatin therapy, especially in populations with varying allele frequencies.

The higher prevalence of the ABCG2 c.421C>A variant among discontinuers (30.6% vs. 17.4%, p = 0.0026) aligns with Kaplan-Meier findings showing most discontinuations occurring within the first 3 months, particularly in patients with adverse effects such as SAMS. A meta-analysis of 34,150 individuals has shown that the A allele is associated with lower HDL-C and higher LDL-C and total cholesterol levels, increasing dyslipidemia risk, especially in Asian populations [16]. Although the A allele reduces ABCG2-mediated efflux and thereby increases rosuvastatin exposure and lipid-lowering efficacy, the resulting higher systemic levels also elevate the risk of side effects and treatment discontinuation.

No significant differences were observed in rosuvastatin dose intensity or comorbidities such as thyroid disease or smoking status, indicating that genetic and demographic factors play a more dominant role in discontinuation than many clinical variables. Collectively, these findings support the conclusion that the ABCG2 c.421C>A variant is a critical determinant of treatment persistence, likely mediated through exacerbation of SAMS.

Discontinuation was associated with a marked rebound in LDL-C: discontinuers showed a mean 21.89% increase, compared with a 17.86% reduction in continuers. Logistic regression confirmed that discontinuation strongly increased the odds of failing to achieve >10% LDL-C reduction (OR = 4.805, $p < 0.001$), whereas rosuvastatin

intensity (OR = 0.552, p = 0.183) and muscle symptoms (OR = 0.795, p = 0.642) did not reach significance in this model.

A 21.89% rise in LDL-C is clinically meaningful. Large-scale evidence from the Cholesterol Treatment Trialists' Collaboration shows that each 1 mmol/L (≈38.7 mg/dL) increase in LDL-C raises the risk of major cardiovascular events by 20–25% [35]. From a baseline of ≈100 mg/dL, a 21.89% increase equates to ≈0.56 mmol/L, corresponding to an estimated 11–14% higher cardiovascular risk [36]. This effect is likely amplified in high-risk patients with diabetes, hypertension, or established atherosclerosis. Stopping lipid-lowering therapy can therefore accelerate plaque progression and increase the likelihood of myocardial infarction or stroke. When statins must be discontinued due to intolerance, alternative therapies such as ezetimibe or PCSK9 inhibitors should be promptly considered [37].

Clinically, the variant has been associated with greater LDL-C reduction on rosuvastatin, as shown in a study of 305 Chinese patients with hypercholesterolemia, where 421A carriers achieved larger LDL-C decreases [38].

Limitations include difficulty in determining exact discontinuation dates (many patients could not recall the precise timing), the small number of homozygous T/T individuals (n = 16), and availability of complete LDL-C data for only 100 participants. Future studies with larger cohorts and higher numbers of homozygous minor-allele carriers are needed to confirm these findings. Additional unmeasured factors such as lifestyle changes, adherence monitoring, and differences in clinical practice may also have influenced results.

Conclusion

In conclusion, although the ABCG2 c.421C>A variant can enhance rosuvastatin efficacy, it simultaneously increases the risk of discontinuation. Personalized strategies incorporating genetic information and patient education on adherence are essential to maximize therapeutic benefits in the management of hypercholesterolemia.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.The handling editor CP declared a past co-authorship with the author GP.

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Ethics Statement: The studies involving humans were approved by Ethics approval and consent to participateThe study was conducted in accordance with the Declaration of Helsinki and approved by the Department of Health-Abu Dhabi for the Data from the UAEU (DOH/CVDC/2020/1187), (DOH/CVDC/2021/1519), (DOH/CVDC/2022/1458), (DOH/CVDC/2023/1952) (MCME.CR.213.MAIN.2021), and (SNA/FA/2020-14). Written Informed consent was obtained from all subjects involved in the study. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

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