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Efficacy and safety of switching to ezetimibe 10 mg/rosuvastatin 2.5 mg in Korean patients with type 2 diabetes mellitus and dyslipidaemia: A multicentre, prospective study (EROICA study)

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Abstract

Aims: To evaluate the lipid-lowering efficacy, safety, and adherence of switching from moderate- or low-intensity statin monotherapy to ezetimibe 10 mg/rosuvastatin 2.5 mg in Korean patients with type 2 diabetes mellitus (T2DM) and dyslipidaemia.

Materials and Methods: This multicentre, open-label, single-arm, prospective study enrolled adults with T2DM and LDL-C ≥70 mg/dL despite ≥12 weeks of moderate or low-intensity statin therapy. Participants received ezetimibe 10 mg/rosuvastatin 2.5 mg once daily for 12 weeks. The primary endpoint was the proportion achieving LDL-C <70 mg/dL at Week 12. Secondary endpoints included changes in lipid and glycaemic parameters, subgroup analyses, and safety outcomes.

Trial registration number: Clinical Research Information Service: KCT0008224 (https://cris.nih.go.kr).

Results: Of 639 screened patients, 586 were included in the full analysis set (FAS). At Week 12, 62.3% (95% CI 58.4–66.2) achieved LDL-C <70 mg/dL. Mean LDL-C decreased by 26.0% from 90.9 ± 17.2 to 67.3 ± 19.3 mg/dL ($p < 0.001$). Total cholesterol, non–HDL-C, and apoB decreased significantly (all $p < 0.001$); HDL-C and triglycerides were unchanged ($p = 0.914$ and $p = 0.393$, respectively). HbA1c increased by 0.15 ± 0.53% and fasting glucose by 3.6 ± 24.7 mg/dL (both $p < 0.001$). HOMA-IR decreased by −0.22 ± 3.09, not significant ($p = 0.085$). Subgroup analyses showed greater LDL-C reductions in patients with BMI <23 kg/m^2, prior low-intensity statin use, or pravastatin therapy, and smaller reductions in those receiving GLP-1 receptor agonists or thiazolidinediones. Adherence averaged 97.5% (97.4%, ≥80%). Among 591 participants, 9.8% had at least one adverse event, mostly mild and not clinically significant.

Conclusions: Switching to ezetimibe 10 mg/rosuvastatin 2.5 mg achieved substantial LDL-C reductions, high goal attainment, excellent adherence, and good tolerability in Korean T2DM patients with dyslipidaemia.

KEYWORDS

cardiovascular Risk, dyslipidaemias, ezetimibe, lipid management, rosuvastatin, type 2 diabetes mellitus

1 | INTRODUCTION

Atherosclerotic cardiovascular disease (ASCVD) is a leading cause of death in patients with diabetes in Korea.[1] Compared with those without diabetes, individuals with diabetes have about a twofold higher risk of ASCVD and a two to fourfold higher ASCVD-related mortality.[2,3] Dyslipidaemia, a key modifiable risk factor, accelerates atherosclerosis in diabetes through adverse lipid profile changes. In Korea, 72% of adults aged ≥30 years with diabetes had hypercholesterolemia between 2016 and 2018 (Diabetes Fact Sheet in Korea 2020).[4] Current guidelines recommend strict low-density lipoprotein cholesterol (LDL-C) targets and moderate to high-intensity statins as first-line therapy in patients with diabetes and dyslipidaemia.[5–7] The Korean Diabetes Association and Korean Society of Lipid and Atherosclerosis set LDL-C goals in patients with diabetes and dyslipidaemia at 100, 70, or 55 mg/dL, based on cardiovascular risk, and advise adding ezetimibe or a PCSK9 inhibitor if goals are not achieved with the maximum tolerated statin dose.[8]

Statins are first-line therapy for patients with diabetes and dyslipidaemia; however, meta-analyses have shown a modestly increased risk of new-onset diabetes (~9–13%), with more intensive regimens carrying a higher risk.[9,10] Concerns about dose-related adverse effects, coupled with the need for potent LDL-C lowering, have led many clinicians in Korea to favour low-dose statin/ezetimibe fixed-dose combinations as a treatment option. However, evidence on LDL-C target attainment with low-dose statin/ezetimibe therapy in type 2 diabetes mellitus (T2DM) is scarce. One small randomised study demonstrated that rosuvastatin 2.5 mg plus ezetimibe 10 mg achieved significantly greater LDL-C reduction (−31% vs. −12%) compared to rosuvastatin dose escalation.[11] A recent meta-analysis found rosuvastatin 5 mg plus ezetimibe 10 mg offered lipid-lowering efficacy and tolerability comparable to rosuvastatin 20 mg.[12] To date, no large, prospective, real-world studies have evaluated the efficacy and safety of the specific low-dose ezetimibe 10 mg/rosuvastatin 2.5 mg combination in Korean patients with T2DM inadequately controlled on moderate- or low-intensity statins. Thus, this study aims to evaluate the lipid-lowering efficacy, lipid profile improvements, and safety of the fixed-dose combination ezetimibe 10 mg/rosuvastatin 2.5 mg (Rosuzet® 10/2.5 mg) in these patients—particularly those who did not achieve LDL-C <70 mg/dL on moderate or low-intensity statin monotherapy.

2 | METHODS

2.1 | Study design and participants

This was a single-arm, open-label, multicentre, prospective study evaluating the efficacy and safety of a fixed-dose combination of ezetimibe 10 mg/rosuvastatin 2.5 mg (Rosuzet® 10/2.5 mg) in patients with T2DM and dyslipidaemia whose LDL-C levels were inadequately controlled with moderate- or low-intensity statin monotherapy. This study was conducted at 10 hospitals in the Republic of Korea between January 2023 and January 2025. Eligible participants were aged ≥19 years, diagnosed with T2DM, and had been receiving moderate- or low-intensity statin monotherapy for at least 12 weeks prior to enrolment. Additional inclusion criteria included baseline LDL-C ≥70 mg/dL, glycated haemoglobin (HbA1c) <9%, and either a T2DM duration ≥10 years or at least one major cardiovascular risk factor (male ≥45 years, female ≥55 years, family history of premature

cardiovascular disease, hypertension, smoking, or low high-density lipoprotein cholesterol [HDL-C; below 40 mg/dL in men or below 50 mg/dL in women]). Key exclusion criteria included hypersensitivity to study drug components, active liver disease, myopathy, concomitant cyclosporine use, severe renal impairment (creatinine clearance <30 mL/min), pregnancy or lactation, and any condition deemed inappropriate by the investigator, such as uncontrolled hyper- or hypothyroidism, or a history of malignant tumours within the past 5 years.

2.2 | Compliance with ethics guidelines

This study was conducted in accordance with the principles of the International Declaration of Helsinki 2013[13] and the International Conference on Harmonization Good Clinical Practice guidelines.[14] The study protocol was approved by the relevant institutional review board or independent ethics committee at each study site. The protocol for this study was prospectively registered with clinical research information service (KCT0008224; https://cris.nih.go.kr). All patients provided written informed consent before enrolment.

2.3 | Comorbidities and risk factor assessment

Comorbidities were assessed at baseline based on documented medical history and clinical evaluation. Hypertension was defined as a prior physician diagnosis, current antihypertensive treatment, or blood pressure ≥140/90 mmHg. Dyslipidaemia was defined as a prior diagnosis or ongoing lipid-lowering therapy, with eligibility requiring LDL-C ≥70 mg/dL despite ≥12 weeks of low- to moderate-intensity statin monotherapy. Current smoking was defined as self-reported active smoking at the time of enrolment, while former smokers and non-smokers were categorised separately. Additional comorbidities of interest included coronary artery disease, cerebrovascular disease, peripheral vascular disease, carotid artery disease, and abdominal aortic aneurysm, which were recorded if present.

2.4 | Study procedures

Following screening and baseline assessments, eligible participants were switched from their current statin regimen to ezetimibe 10 mg/rosuvastatin 2.5 mg once daily for 12 weeks. Study visits were conducted at baseline and at Week 12 (±2 weeks) for efficacy and safety evaluations.

2.5 | Study endpoints

The primary endpoint was the proportion of participants achieving LDL-C <70 mg/dL at Week 12. Secondary endpoints included changes from baseline to Week 12 in lipid parameters (total cholesterol [TC], LDL-C, HDL-C, non-HDL-C, triglycerides [TG], apolipoprotein A1 [ApoA1], apolipoprotein B [ApoB]), glycaemic parameters (HbA1c, fasting plasma glucose [FPG], homeostasis model assessment of insulin resistance [HOMA-IR]), and safety outcomes (adverse events [AEs], serious AEs, and laboratory abnormalities).

2.6 | Laboratory tests

All laboratory assessments were performed at the certified local laboratories of each participating institution according to standard operating procedures. Venous blood samples (≤10 mL) were collected after an overnight fast of at least 8 h at baseline and at Week 12 (±2 weeks). The following parameters were measured:

1. Lipid profile included as TC, LDL-C, HDL-C, non-HDL-C, TG, ApoA1, and ApoB.
2. Glycaemic parameters included HbA1c, FPG, and fasting serum insulin. HOMA-IR was calculated using the formula: HOMA-IR = fasting glucose (mg/dL) × fasting insulin (mU/L)/405.[15]
3. Liver function tests included aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (γ-GTP), and total bilirubin.
4. Renal function tests included blood urea nitrogen (BUN) and serum creatinine. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI equation.[16]

Laboratory results obtained within 4 weeks prior to baseline or within 2 weeks prior to the end-of-study visit were accepted as valid. Clinically significant abnormalities identified at baseline were recorded as medical history, whereas abnormalities observed after study drug administration were documented as adverse events.

2.7 | Statistical analysis

The full analysis set (FAS) included all participants who received at least one dose of the study drug and had at least one post-baseline LDL-C measurement. The per-protocol set (PPS) excluded participants with major protocol deviations, poor medication adherence (<80%), or missing primary endpoint data. Primary endpoint analysis was based on the FAS, with supplementary analysis using the PPS to evaluate robustness. Continuous variables were summarised as mean ± standard deviation (SD) and categorical variables as counts and percentages. Within-group changes from baseline were analysed using paired t-tests or Wilcoxon signed-rank tests, as appropriate. All statistical analyses were performed using a two-sided significance level of 0.05.

3 | RESULTS

3.1 | Patient disposition

The patient flow throughout the study is presented in Figure 1. A total of 639 patients with type 2 diabetes mellitus and concomitant

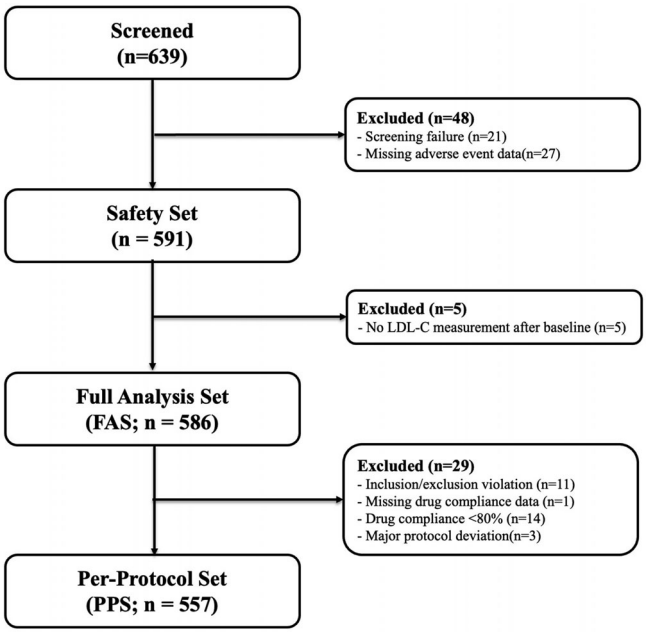

FIGURE 1 Patient disposition of the study.

dyslipidaemia were screened for eligibility. Of these, 48 were excluded from the Safety Set (SS) because of screening failure ($n = 21$) or missing adverse event data ($n = 27$), leaving 591 patients in the SS. An additional five patients were excluded from the Full Analysis Set (FAS) due to the absence of any post-baseline LDL-C measurement, resulting in 586 patients (99.15% of SS) in the FAS. Among these, 29 patients were excluded from the per-protocol set (PPS) owing to violations of inclusion or exclusion criteria ($n = 11$), missing drug compliance data ($n = 1$), drug compliance <80% ($n = 14$), or major protocol deviations ($n = 3$). The final PPS consisted of 557 patients (95.05% of FAS) who completed the study without major protocol deviations.

3.2 | Baseline characteristics

Baseline demographic, clinical, and laboratory characteristics for the FAS are summarised in Table 1. The mean (±SD) age was 62.9 ± 9.7 years, with 42.8% of participants being male. Hypertension was present in 56.8% of patients, 15.9% were current smokers, and 4.9% had a family history of premature cardiovascular disease. The mean baseline LDL-C was 90.9 ± 17.2 mg/dL. Mean HDL-C and non–HDL-C levels were 51.8 ± 11.6 mg/dL and 115.6 ± 22.5 mg/dL, respectively, while the mean triglyceride level was 133.1 ± 71.0 mg/dL. The mean apolipoprotein A1 and apolipoprotein B levels were 141.8 ± 22.3 mg/dL and 90.6 ± 17.4 mg/dL, respectively. Mean HbA1c was 6.85 ± 0.77%, mean fasting plasma glucose was 129.0 ± 25.3 mg/dL, and the mean HOMA-IR was 3.36 ± 5.11. Baseline characteristics for the SS and PPS are presented in Tables S1 and S2, respectively, and were generally consistent with those observed in the FAS. Treatment compliance was high throughout the study. In the FAS, the mean (±SD) compliance rate over 12 weeks was 97.5 ± 8.1%, with a median of 100%. Overall, 97.4% of participants achieved a compliance rate of ≥80%.

TABLE 1 Baseline demographics and clinical characteristics of the study population (full analysis set, $n = 586$).

Characteristic	Mean ± SD, median (range), or *n* (%)
Age, years	62.9 ± 9.7
Sex	
Male	251 (42.83)
Female	335 (57.17)
Body weight, kg	66.7 ± 13.3
Height, cm	161.7 ± 9.0
Hypertension	333 (56.8)
The duration of diabetes, years	11.19 ± 8.19
Current smoker	93 (15.9)
Family history of premature ASCVD	29 (4.9)
Baseline lipid profile	
Total cholesterol, mg/dL	167.4 ± 24.2
LDL-C, mg/dL	90.9 ± 17.2
HDL-C, mg/dL	51.8 ± 11.6
Non–HDL-C, mg/dL	115.6 ± 22.5
Triglycerides, mg/dL	133.1 ± 71.0
Apolipoprotein A1, mg/dL	141.8 ± 22.3
Apolipoprotein B, mg/dL	90.6 ± 17.4
HbA1c, %	6.85 ± 0.77
Fasting plasma glucose, mg/dL	129.0 ± 25.3
HOMA-IR	3.36 ± 5.11

Note: Data are presented as mean ± SD, median (range), or *n* (%).
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein.

3.3 | Primary outcome

In the FAS, 365 participants (62.29%, 95% CI 58.36–66.22) achieved LDL-C <70 mg/dL at Week 12 after switching from moderate-intensity or lower-dose statin monotherapy to fixed-dose rosuvastatin 2.5 mg/ezetimibe 10 mg (Figure 2). Similar results were observed in the PPS, with 355 participants (63.73%) attaining the LDL-C goal (Figure 2).

3.4 | Secondary outcomes

In the FAS, mean LDL-C decreased significantly from 90.9 ± 17.2 mg/dL at baseline to 67.3 ± 19.3 mg/dL at Week 12, representing a mean change of −23.66 ± 20.93 mg/dL (−26.02%; $p < 0.001$; Table 2). Total cholesterol decreased by −25.18 ± 24.97 mg/dL (−15.04%; $p < 0.001$), non–HDL-C by −25.15 ± 24.02 mg/dL (−21.75%; $p < 0.001$), and

apolipoprotein B by −13.31 ± 16.76 mg/dL (−14.68%; $p < 0.001$; Table 2). Apolipoprotein A1 increased by 1.53 ± 14.76 mg/dL (1.11%; $p = 0.012$). There were no statistically significant changes in HDL-C (−0.03 ± 6.71 mg/dL; $p = 0.914$) or triglycerides (−7.87 ± 94.08 mg/dL; $p = 0.393$; Table 2). For glycaemic parameters in the FAS, mean HbA1c increased from 6.85 ± 0.77% at baseline to 7.01 ± 0.91% at Week 12 (0.15 ± 0.53%; $p < 0.001$), fasting plasma glucose increased from 128.95 ± 25.31 mg/dL to 132.52 ± 30.61 mg/dL (3.59 ± 24.69 mg/dL; $p < 0.001$), and HOMA-IR decreased slightly from 3.36 ± 5.11 to 3.13 ± 3.85 (−0.22 ± 3.09; $p = 0.085$; Table 2). Findings in the PPS were consistent with those in the FAS for both lipid and glycaemic parameters (Table S3).

3.5 | Subgroup analysis

In the FAS population, subgroup analyses demonstrated consistent LDL-C–lowering effects across most demographic and clinical categories (Table S4). Patients aged ≥65 years experienced a mean LDL-C reduction of −28.3%, compared with −24.4% in those aged <65 years ($p = 0.010$ for between-group difference), with corresponding LDL-C target attainment rates (<70 mg/dL) of 65.4% and 60.1%, respectively ($p = 0.195$). Participants with BMI <23 kg/m^2 achieved the greatest LDL-C reduction (−30.5%; baseline LDL-C 89.5 ± 16.6 mg/dL) and highest attainment rate (75.3%), whereas those with BMI ≥25 kg/m^2 showed smaller reductions (−23.9%; baseline LDL-C 92.0 ± 17.9 mg/dL) and lower attainment rates (56.8%; both $p < 0.001$; Table S4). Other ASCVD risk factors, including family history of premature ASCVD, hypertension, current smoking, low HDL-C, and number of ASCVD risk factors, did not significantly modify LDL-C–lowering efficacy.

Subgroup analyses for diabetes medications and prior statin therapy are summarised in Tables S5 and S6. LDL-C reduction was attenuated in patients receiving thiazolidinediones (−18.7%) or GLP-1 receptor agonists (−14.5%) compared with those not on these agents (−26.7% and − 26.3%, respectively), with statistically significant between-group differences ($p = 0.004$ and $p = 0.025$). Correspondingly, LDL-C target attainment rates were lowest in the GLP-1 RA (50.0%) and thiazolidinedione (51.0%) subgroups. Prior statin type, intensity, and dose also influenced outcomes. Pravastatin users achieved the greatest LDL-C reductions (−37.5% overall; −33.9% with 40 mg) and the highest target attainment rate (74.2%), whereas rosuvastatin users had the smallest reduction (−16.6%) and lowest attainment rate (42.4%). Low-intensity statin users exhibited greater LDL-C reductions and higher attainment rates (−39.3%, 78.0%) than moderate-intensity (−23.4%, 59.5%) or high-intensity users (+20.6%, 25.0%). Within the same statin type and intensity, lower doses generally yielded larger percentage reductions; for example, atorvastatin 10 mg achieved a greater reduction than atorvastatin 20 mg (−24.5% vs. −21.7%), and rosuvastatin 5 mg outperformed rosuvastatin 10 mg (−22.9% vs. −7.0%).

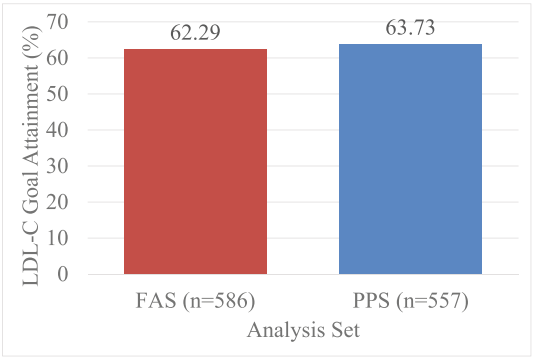

FIGURE 2 Proportion of patients achieving the LDL-C treatment goal (<70 mg/dL) at Week 12 following the switch to fixed-dose rosuvastatin 2.5 mg/ezetimibe 10 mg in the full analysis set (FAS) and per-protocol set (PPS).

3.6 | Safety

In the Safety Set ($N = 591$), 58 participants (9.81%) experienced at least one adverse event (AE), and 5 participants (0.85%) reported

TABLE 2 Baseline values, Week 12 values, and changes in lipid profile, glycaemic parameters, and insulin resistance in the full analysis set (FAS).

Parameter	Baseline (Mean ± SD)	Week 12 (Mean ± SD)	Change (Mean ± SD)	% Change	*p*-value
LDL-C (mg/dL)	90.9 ± 17.2	67.3 ± 19.3	−23.66 ± 20.93	−26.02	<0.001
Total cholesterol (mg/dL)	167.4 ± 24.2	142.2 ± 25.5	−25.18 ± 24.97	−15.04	<0.001
HDL-C (mg/dL)	51.8 ± 11.6	51.8 ± 11.7	−0.03 ± 6.71	0.02	0.914
Non–HDL-C (mg/dL)	115.6 ± 22.5	90.4 ± 23.3	−25.15 ± 24.02	−21.75	<0.001
Triglycerides (mg/dL)	133.1 ± 71.0	125.2 ± 61.8	−7.87 ± 94.08	−5.92	0.393
Apolipoprotein A1 (mg/dL)	141.8 ± 22.3	143.4 ± 22.5	1.53 ± 14.76	1.11	0.012
Apolipoprotein B (mg/dL)	90.6 ± 17.4	77.3 ± 17.5	−13.31 ± 16.76	−14.68	<0.001
HbA1c (%)	6.85 ± 0.77	7.01 ± 0.91	0.15 ± 0.53	2.19	<0.001
Fasting plasma glucose (mg/dL)	128.95 ± 25.31	132.52 ± 30.61	3.59 ± 24.69	2.78	<0.001
HOMA-IR	3.36 ± 5.11	3.13 ± 3.85	−0.22 ± 3.09	−6.55	0.085

TABLE 3 Summary of adverse events (safety set, $N = 591$).

Variable	Number of persons (%)	Number of events (%)
Total number of AEs		86
Participants with ≥1 AE	58 (9.81)	
Serious adverse events	12 (2.03)	12
Severity		
Mild (Grade 1)	48 (8.12)	73 (84.88)
Moderate (Grade 2)	12 (2.03)	12 (13.95)
Severe (Grade 3–5)	1 (0.17)	1 (1.16)
Relationship to study drug		
Certain	0 (0.00)	0
Probable/likely	0 (0.00)	0
Possible	5 (0.85)	8
Unlikely	49 (8.29)	73
Conditional/unclassified	1 (0.17)	2
Unassessable/unclassifiable	3 (0.51)	3
Fatal adverse events	1 (0.17)	1

treatment-related AEs (Table 3). Serious AEs occurred in 12 participants (2.03%). One death (0.2%) was reported during the study. Most AEs were mild in severity (84.88%), with 13.95% classified as moderate and 1.16% as severe. The most frequently affected system organ classes (SOCs) were gastrointestinal disorders (3.21%), musculoskeletal and connective tissue disorders (1.18%), and nervous system disorders (1.69%; Table S7). The most common preferred terms (PTs) were nausea (0.85%), headache (0.68%), and dizziness (0.51%; Table S7). Changes in vital signs and laboratory parameters from baseline to Week 12 are presented in Table S8. Mean heart rate increased slightly (1.09 ± 11.41 beats/min; $p = 0.020$), whereas systolic and diastolic blood pressure showed no statistically significant changes. Liver enzymes, including AST, ALT, and γ-GTP, showed modest but statistically significant increases without clinical significance (Table S9), whereas total bilirubin and BUN exhibited small yet statistically significant decreases. Serum creatinine remained stable throughout the study period. None of these changes were considered clinically significant.

4 | DISCUSSION

In this multicentre, prospective study of Korean patients with T2DM and dyslipidaemia inadequately controlled on moderate- or low-intensity statin monotherapy, switching to a fixed-dose combination of ezetimibe 10 mg/rosuvastatin 2.5 mg for 12 weeks resulted in substantial improvements in atherogenic lipid parameters. Nearly two-thirds of participants in the full analysis set achieved the LDL-C target of <70 mg/dL, with a mean LDL-C reduction of 26% from baseline. These findings provide real-world evidence supporting the use of low-dose statin/ezetimibe therapy as an effective lipid-lowering strategy in this population, and further confirm the favourable safety profile of the fixed-dose combination over 12 weeks of treatment.

Treatment adherence in this study was excellent, with a mean 12-week compliance rate of 97.5% and almost all participants (97.4%) achieving adherence ≥80%. This high level of adherence likely contributed to the robust LDL-C reductions observed and underscores the feasibility of implementing low-dose rosuvastatin/ezetimibe combinations in routine practice, where long-term statin persistence can be challenging.

Our findings are consistent with prior randomised controlled trials (RCTs) conducted in Korean populations. In the I-ROSETTE trial, Lee et al. demonstrated that low-intensity rosuvastatin/ezetimibe (2.5/10 mg) achieved significantly greater LDL-C reduction and higher goal attainment rates compared with moderate-intensity rosuvastatin monotherapy, without compromising safety or adherence.[17] Similarly, Ahn et al. compared rosuvastatin 2.5 mg/ezetimibe 10 mg with rosuvastatin 5 mg in Korean patients with hypercholesterolemia and found that the combination provided greater LDL-C reduction (−48.6% vs. −36.6%) and higher goal attainment rates without compromising safety or adherence.[18] Although the absolute LDL-C reductions in our study were smaller—likely due to differences in baseline LDL-C levels, prior statin regimens, and inclusion criteria—our results reinforce that adding ezetimibe to a low-dose statin can achieve substantial lipid-lowering while potentially minimising dose-related statin adverse effects.

Subgroup analyses revealed consistent LDL-C–lowering effects across most demographic and clinical strata, but also highlighted clinically relevant differences. Greater reductions and higher attainment rates were observed in patients with lower BMI (<23 kg/m^2) and those previously on low-intensity statin therapy, whereas attenuated responses occurred in those receiving GLP-1 receptor agonists or thiazolidinediones. The mechanisms underlying this attenuated response remain uncertain and may reflect complex metabolic pathways, potential drug–drug interactions, or selection bias, thereby warranting further investigation. Statin type, intensity, and dose prior to switching also affected outcomes, with the most pronounced benefits seen in pravastatin users and the smallest in those previously on rosuvastatin. A potential explanation is the presence of CYP2C9 genetic polymorphisms, which affect the metabolism and pharmacologic response to rosuvastatin but not to other statins.[19] Variants in CYP2C9 can reduce enzymatic activity, potentially leading to reduced responsiveness to rosuvastatin and thereby limiting the incremental lipid-lowering effect when switching to ezetimibe 10 mg/rosuvastatin 2.5 mg. Such resistance is less relevant for other statins. This observation underscores an important clinical implication: switching within the same statin class, such as from a prior dose rosuvastatin to a relatively lower-dose rosuvastatin/ezetimibe combination, may provide less incremental benefit than switching from a different statin, such as pravastatin. Notably, within the same statin type and intensity, lower doses tended to yield greater percentage LDL-C reductions after the switch—an observation that may reflect higher relative potency gains when transitioning from a weaker regimen.

Safety outcomes were favourable. Most adverse events were mild, and laboratory changes, including modest increases in liver enzymes, were not clinically significant. These data reinforce the tolerability profile of combining ezetimibe with low-dose rosuvastatin,

which may help mitigate dose-related statin intolerance concerns. These observations are also supported by meta-analytic evidence showing that rosuvastatin 5 mg plus ezetimibe 10 mg achieves lipid-lowering efficacy comparable to high-dose rosuvastatin monotherapy, with potential tolerability advantages.[12]

We observed small but statistically significant increases in HbA1c and fasting plasma glucose, consistent with prior reports of statin-associated glycaemic effects.[20] While these changes may have little short-term clinical impact, long-term effects should be considered, especially for patients with poor baseline glycaemic control.

The strengths of this study include its prospective, multicentre design, inclusion of a large, well-characterised T2DM cohort, and comprehensive assessment of lipid, glycaemic, and safety outcomes. This study has several limitations. First, the single-arm, open-label design without a control group limits the ability to directly compare the efficacy of the fixed-dose combination with other lipid-lowering regimens. Second, the treatment period was relatively short (12 weeks), precluding assessment of long-term lipid control, safety, and cardiovascular outcomes. Third, although this was a multicentre study, the study population consisted exclusively of Korean patients with T2DM and dyslipidaemia, which may limit the generalizability of the findings to other ethnic groups or clinical settings. Fourth, all participants were required to have inadequate LDL-C control on moderate- or low-intensity statin monotherapy at baseline, and the results may not apply to statin-naïve individuals or those on high-intensity statin therapy. Finally, lifestyle factors such as diet and physical activity, which could affect lipid and glycaemic outcomes, were not controlled or systematically monitored.

In conclusion, switching from moderate- or low-intensity statin monotherapy to ezetimibe 10 mg/rosuvastatin 2.5 mg achieved substantial LDL-C reductions, high target attainment rates, and excellent adherence, with a favourable safety profile in Korean patients with T2DM and dyslipidaemia. These findings provide real-world evidence supporting this combination as an effective, well-tolerated strategy for optimising lipid management in high-risk diabetic populations, particularly when LDL-C goals are not met with statin monotherapy.

AUTHOR CONTRIBUTIONS

Sangmo Hong, Won J. Kim, and Chang B. Lee designed the trial and did data analysis. All authors interpreted data and were involved in the conduct of the trial. All authors contributed to data collection. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors contributed to the data interpretation. Sangmo Hong drafted the first and subsequent versions of the report with input and critical revisions by all authors, who reviewed and approved the final report as submitted.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.70258.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. Data will be shared with researchers who submit a research proposal approved by the independent review board after publication. Individual participant data will be shared in data sets in a de-identified and anonymised format.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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