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Original Research

Efficacy and Safety of Fimasartan, Atorvastatin, and Ezetimibe Combination Therapy in Patients With Hypertension and Dyslipidemia: A Randomized, Double-Blind, Multicenter, Therapeutic Confirmatory, Phase III Clinical Trial

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ABSTRACT

Background: Essential hypertension and primary hypercholesterolemia are common and independent cardiovascular risk factors that frequently coexist and warrant integrated management. This study aimed to evaluate the efficacy and safety of triple combination therapy (FMS + ATO/EZE) with Fimasartan (FMS), atorvastatin (ATV), and ezetimibe (EZE) compared with atorvastatin/ezetimibe (ATO/EZE) dual therapy or Fimasartan (FMS) monotherapy in patients with hypertension and hypercholesterolemia.

Methods: This multicenter, randomized clinical trial was conducted across 25 clinical trial institutions in the Republic of Korea. A total of 315 participants were screened, of whom 148 eligible participants were randomized to receive FMS + ATO/EZE ($n = 49$), ATO/EZE ($n = 49$), or FMS ($n = 50$). The primary efficacy endpoints were the change in mean sitting systolic blood pressure (msSBP) from baseline to week 8 in the FMS + ATO/EZE group compared with that in the ATO/EZE group and the percentage change in low-density lipoprotein cholesterol (LDL-C) from baseline to week 8 in the FMS + ATO/EZE group compared with that in the FMS group. Safety was assessed based on treatment-emergent adverse events (TEAEs).

Results: In the full analysis set, the FMS + ATO/EZE group demonstrated superior reduction in msSBP compared to the ATO/EZE group (least squares [LS] mean difference: -7.26 ± 2.84 mm Hg; 95% confidence interval [CI]: $-12.91, -1.61$; $P = 0.0124$). Similarly, the percentage reduction in LDL-C was significantly greater in the FMS + ATO/EZE group than in the FMS group (LS mean difference: $-58.02\% \pm 4.03\%$; 95% CI: $-66.03, -50.02$; $P < 0.0001$). The incidence of TEAEs was comparable across treatment groups: FMS + ATO/EZE (20.83%), ATO/EZE (22.45%), and FMS (16.00%) ($P = 0.7030$). Serious adverse events occurred in 1.36% of the total safety population, without significant difference between the groups ($P = 0.5480$).

Conclusions: Triple combination therapy with FMS + ATO/EZE was superior to dual therapy or monotherapy in reducing both BP and LDL-C levels in patients with essential hypertension accompanied by primary hypercholesterolemia. The safety profile was comparable with that of the individual components, confirming the tolerability and safety of FMS + ATO/EZE therapy. However, the 8-week follow-up period and enrollment of an exclusively Korean cohort may limit the assessment of long-term effects and generalizability to other ethnic populations.

Introduction

Hypertension and dyslipidemia frequently coexist as major cardiovascular risk factors, presenting a significant challenge requiring comprehensive management.^{1–4} In the Republic of Korea, among 9.8 million patients with hypertension, approximately 3.4 million (34.6%) receive concurrent treatment for both conditions.^{5,6} Current guidelines recommend simultaneous treatment of both conditions to comprehensively reduce overall cardiovascular risk.^{3,7}

Angiotensin II receptor blockers (ARBs) have emerged as effective antihypertensive agents, with Fimasartan (FMS) demonstrating particular efficacy across Asian populations.^{8–12} FMS, an angiotensin II type-1 receptor blocker, lowers blood pressure (BP) by inhibiting vasoconstriction and aldosterone-mediated effects within the renin-angiotensin system, showing rapid and sustained BP reductions in randomized trials.^{12,13} Atorvastatin (ATO) reduces hepatic cholesterol synthesis via HMG-CoA reductase inhibition, while the addition of ezetimibe (EZE)—a selective intestinal NPC1L1 cholesterol absorption inhibitor—provides incremental low-density lipoprotein cholesterol (LDL-C) lowering and improved cardiovascular outcomes compared to statin monotherapy in high-risk populations.¹⁴

In patients with concomitant hypertension and dyslipidemia, coadministration of FMS with a statin has been shown to improve control of both BP and LDL-C, with a safety profile comparable to that of monotherapy. Furthermore, triple combination regimens incorporating a renin-angiotensin system blocker with a statin + ezetimibe have demonstrated significant additive reductions in BP and atherogenic lipids without an increase in adverse events.^{15–18}

However, the management of these coexisting conditions typically requires multiple medications, increasing regimen complexity and potentially reducing patient adherence. In this context, treatment simplification through single-pill fixed-dose combinations (FDCs) has been associated with improved adherence and more effective risk-factor control. Korean hypertension and dyslipidemia guidelines emphasize the importance of aggressive, integrated management in high-risk patients, underscoring the clinical utility of combination therapies that are both efficacious and conducive to simplified dosing regimens.^{19,20}

Despite these advances, robust randomized data specifically comparing the FMS + ATO + EZE triple regimen against ATO/EZE dual ther-

apy or FMS monotherapy in patients with essential hypertension and primary hypercholesterolemia remain limited; the recently completed Phase 3 study was designed to address this evidence gap.²¹

Therefore, this study aimed to compare and evaluate the efficacy and safety of a triple combination therapy with FMS, ATO, and EZE versus ATO/EZE dual therapy or FMS monotherapy in patients with essential hypertension and primary hypercholesterolemia. The primary objectives were to assess BP control and cholesterol-lowering effects, and the overall safety profile of these therapeutic approaches was evaluated.

Methods

This multicenter phase III clinical investigation employed a randomized, double-blind, parallel-group design to assess the therapeutic efficacy and safety profile of a triple combination regimen comprising FMS, ATO, and EZE (ClinicalTrials.gov identifier: NCT05930028).

Study Population

This study enrolled men and women aged ≥ 19 years who were diagnosed with primary hypercholesterolemia accompanied by essential hypertension and required medical treatment. At screening, eligible participants had triglyceride (TG) and LDL-C levels of <400 and ≤ 250 mg/dL, respectively. After providing written informed consent, participants underwent a washout period of 4 weeks (extended to 6 weeks for those previously treated with fibrates), during which all lipid-lowering and antihypertensive medications were discontinued, and therapeutic lifestyle changes were implemented. At baseline, participants were eligible for randomization if they met two major criteria as follows: (1) uncontrolled hypertension, defined as mean sitting systolic BP (msSBP) ≥ 140 and <180 mm Hg with mean sitting diastolic BP (msDBP) <110 mm Hg, and (2) LDL-C levels meeting the cardiovascular risk criteria based on the Korean guidelines for the management of dyslipidemia (**Supplemental [Online Only] Appendix Table S1**).

The exclusion criteria included severe hypertension (msSBP ≥ 180 mm Hg or msDBP ≥ 110 mm Hg) in the reference arm, significant BP differences between arms (msSBP ≥ 20 mm Hg and msDBP ≥ 10 mm Hg measured three times), secondary hypertension or dyslipidemia, significant cardiovascular/hepatic/renal disorders (estimated glomeru-

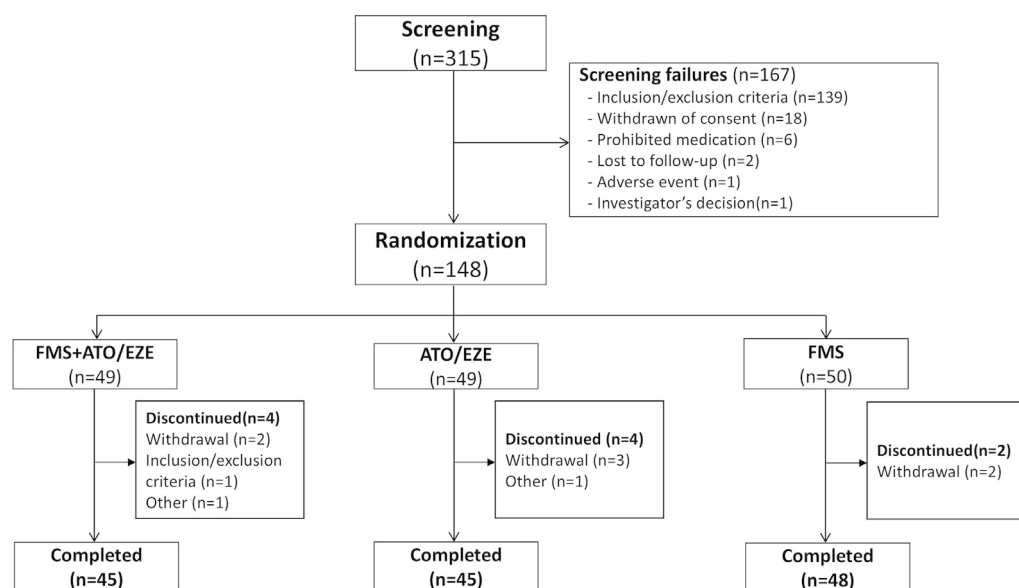


Figure 1. Flowchart of participant disposition. ATO = atorvastatin; EZE = ezetimibe; FMS = Fimasartan.

lar filtration rate < 30 mL/min/1.73 m²), abnormal laboratory values (glycated hemoglobin ≥9%, aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ≥2× the upper limit of normal, serum creatinine ≥2 mg/dL), malignancy within 5 years, positive for hepatitis B or C virus, pregnancy/nursing, recent clinical trial participation (within 4 weeks), or known hypersensitivity to study medications.

Study Design

This multicenter investigation was conducted in 25 medical institutions across the Republic of Korea between July 2023 and September 2024. This study was performed in accordance with the International Conference on Harmonization-Good Clinical Practice guidelines and the ethical principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ministry of Food and Drug Safety and respective institutional review boards of each participating center.

Eligible participants with concurrent hypertension and hypercholesterolemia who met the inclusion criteria were randomized in a 1:1:1 ratio using the stratified block method to receive one of three treatment regimens as follows: (1) Triple combination therapy of FMS 60 mg and ATO 20 mg/EZE 10 mg (FMS + ATO/EZE group); (2) dual combination therapy of ATO 20 mg/EZE 10 mg (ATO/EZE group); or (3) FMS 60 mg monotherapy (FMS group). To maintain double-blind conditions, all participants received three investigational tablets daily, with matching placebos identical in appearance to the corresponding active tablets. Participants were instructed to take the study medication once daily at the same time each day. The treatment period was 8 weeks, with no dose adjustments permitted. Medication adherence was assessed at each visit based on pill count and participant interviews conducted by investigators. The study design is illustrated in Figure 1.

Study Outcomes

The primary efficacy endpoints were the mean changes in msSBP compared between the FMS + ATO/EZE and ATO/EZE groups, and the mean percentage change in LDL-C compared between the FMS + ATO/EZE and FMS groups at week 8 compared to the baseline for each.

The secondary efficacy endpoints were the percentage change in LDL-C from baseline to week 4, mean change in msSBP from baseline to week 4, mean change in msDBP from baseline to weeks 4 and 8, and

the percentage changes in TG, total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) from baseline to weeks 4 and 8.

Safety endpoints were evaluated based on treatment-emergent adverse events (TEAEs), laboratory assessments (from both central laboratory and clinical trial institutions), vital signs (pulse), physical examinations, electrocardiograms, and changes in body weight. The occurrence of adverse events and abnormal changes in clinical laboratory values was compared between the treatment groups using appropriate statistical methods according to the characteristics of each variable.

Measurement of Efficacy Parameters

To evaluate the primary and secondary efficacy endpoints, measurements of BP (msSBP and msDBP) and lipid parameters were performed. Blood pressure was measured in the upper arm that exhibited no functional or anatomical abnormalities. At the screening visit (Visit 1), BP was assessed in both upper arms, and the reference arm was determined based on the mean of three consecutive measurements. The arm with the higher mean sitting systolic blood pressure (msSBP) was designated as the reference arm. From subsequent visits onward, all BP measurements were performed exclusively on this designated arm. If the msSBP was identical in both arms, the arm with the higher msDBP was designated instead. If both msSBP and msDBP were equal, the arm with the highest individual sitting SBP measurement was selected. If the highest sitting SBP was also identical in both arms, the arm with the highest individual sitting DBP measurement was designated as the reference arm. Blood pressure was measured using a validated, sponsor-provided electronic sphygmomanometer. Three consecutive measurements were obtained at intervals of at least 2 minutes. The average value was calculated from these three measurements and recorded as an integer, rounded to the nearest whole number from the first decimal place.

Blood samples for lipid profile analysis, including TC, TG, LDL-C, and HDL-C, were collected in the morning after a fasting period of at least 9 hours. Lipid parameters (TC, TG, LDL-C, and HDL-C) were directly measured from blood samples at the central laboratory at prebaseline (Visit 2), week 4, and week 8.

Sample Size Calculation

This study aimed to simultaneously demonstrate the superiority of the FMS + ATO/EZE group over the ATO/EZE group in msSBP reduction

and over the FMS group in LDL-C reduction as coprimary endpoints. Since both coprimary endpoints should meet the superiority hypothesis concurrently, no multiplicity adjustment was made, and a significance level of 5% with 95% power was set for each endpoint, achieving an overall power of 90%.

The mean difference in SBP change after 8 weeks between FMS + ATO/EZE group and ATO/EZE group was -12.46 mm Hg, and the standard deviation was assumed to be 15.6 mm Hg. Based on these assumptions, 42 participants were needed per treatment group. The mean difference in LDL-C level after 8 weeks between FMS + ATO/EZE group and FMS group was -47.36%, and the standard deviation was assumed to be 16.85%. Based on these assumptions, 4 participants were needed per treatment group.

Finally, a total sample size of 150 patients (50 patients per group) was determined, considering a 15% dropout rate and a 1:1:1 randomization ratio. The following formula was used to determine sample size for two independent means; $n = 2\sigma^2 (Z_{\alpha/2} + Z_{\beta})^2 / (\mu_t - \mu_c)^2$, where n : sample size required in each group, $\mu_t - \mu_c$: mean difference between treatment and control group, σ : standard deviation, $Z_{\alpha/2}$: significance level, Z_{β} : power.

Statistical Analysis

The full analysis set comprised all randomized participants receiving at least one dose of the study treatment and assessed at least once for primary efficacy variables after administration. The coprimary efficacy endpoints and continuous variables among secondary endpoints were compared between the groups using an analysis of covariance model, with baseline values and cardiovascular risk categories as covariates. Categorical secondary endpoints were compared using logistic regression, with baseline values and cardiovascular risk categories as covariates. For within-group comparison, paired t tests or Wilcoxon signed-rank tests were used for continuous variables.

Safety analyses were performed on the safety set, defined as the participants who received at least one dose of the investigational drug after randomization. Adverse events were coded using the MedDRA version 27.0.

Data were summarized using descriptive statistics for continuous variables and counts and proportions for categorical variables. For between-group comparison, continuous variables were assessed using ANOVA or Kruskal-Wallis tests, and for categorical variables, χ^2 or Fisher's exact tests were used. All statistical tests were two-sided, with $P < 0.05$ considered statistically significant. Statistical analyses were performed using the SAS software (version 9.4; SAS Institute, Inc., Cary, NC, USA).

Results

Baseline Characteristics

A total of 315 participants were screened, and 148 were randomly assigned to receive FMS + ATO/EZE ($n = 49$), ATO/EZE ($n = 49$), or FMS ($n = 50$) therapy (Figure 2). During the 8-week treatment period, 10 participants discontinued the study, and 138 completed the treatments (45 in the FMS + ATO/EZE, 45 in the ATO/EZE, and 48 in the FMS group). Among the 148 randomized participants, 147 (99.32%) received at least one dose of the study medication and were included in the safety analysis (48 [97.96%] in the FMS + ATO/EZE group, 49 [100%] in the ATO/EZE group, and 50 [100%] in the FMS group). For efficacy evaluation, 143 (96.62%) participants were included in the full analysis set (47 [95.92%] in the FMS + ATO/EZE group, 47 [95.92%] in the ATO/EZE group, and 49 [98.00%] in the FMS group), with exclusions primarily due to the lack of primary endpoint measurement after the baseline visit. Demographic and baseline clinical characteristics, including baseline BP and lipid profiles, were similar among all groups (Table I). No significant differences were observed between the groups.

Efficacy

The mean changes in msSBP from baseline after 8 weeks of treatment were -17.45, -10.04, and -21.31 mm Hg in the FMS + ATO/EZE, ATO/EZE, and FMS groups, respectively (Table II). Treatment with FMS + ATO/EZE resulted in a significantly greater reduction in msSBP compared to treatment with ATO/EZE (least squares [LS] mean difference, -7.26 mm Hg [95% confidence interval, CI: -12.91 to -1.61 mm Hg], $P = 0.0124$) (Figure 3A). The mean changes in msDBP from baseline to 8 weeks were -5.94, -2.26, and -8.90 mm Hg in the FMS + ATO/EZE, ATO/EZE, and FMS groups, respectively. DBP reduction was significantly greater in the FAE group than in the AE group (LS mean difference, -3.97 mm Hg [95% CI: -6.82 to -1.12 mm Hg], $P = 0.0068$). Regarding target BP achievement, the FMS + ATO/EZE group demonstrated an achievement rate of 38.30% (18 participants) at week 8, which was significantly higher than that in the ATO/EZE group (21.28%, 10 participants) (Figure 3B). Although the FMS group showed the highest achievement rate (51.02%, 25 participants) compared to the FMS + ATO/EZE group, this difference was not statistically significant.

The LS mean percentage changes in LDL-C at 8 weeks compared with baseline values were -51.12% in the FMS + ATO/EZE group and 6.91% in the FMS group (Table III). Treatment with FMS + ATO/EZE had significantly greater effects on LDL-C reduction than FMS alone (LS mean difference, -58.02% [95% CI: -66.03% to -50.02%], $P < 0.0001$) (Figure 4A). The LS percentage changes in the TC after the 8-week treat-

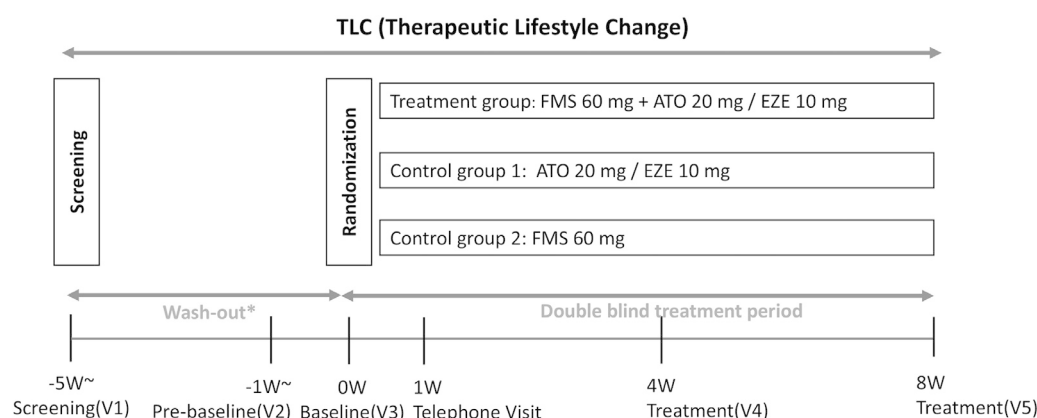


Figure 2. Study design. ATO = atorvastatin; EZE = ezetimibe; FMS = Fimasartan; V = visit; W = week. *For fibrates, patients would have a wash-out period for 6 weeks prior to prebaseline (Visit 2).

Table I
Baseline demographic and clinical characteristics of the full analysis set.

	FMS + ATO/EZE (N = 47)	ATO/EZE (N = 47)	FMS (N = 49)	P value
Age (years)	64.15 ± 11.30	63.43 ± 10.61	62.47 ± 9.26	0.7304 ^A
Male, n (%)	30 (63.83)	36 (76.60)	32 (65.31)	0.3438 ^C
Current smoker, n (%)	12 (25.53)	9 (19.15)	7 (14.29)	0.3800 ^C
BMI, (kg/m ²)	26.55 ± 3.44	26.54 ± 3.15	26.12 ± 2.99	0.7800 ^K
Duration of essential hypertension (years)	8.92 ± 8.31	7.84 ± 6.68	6.41 ± 5.53	0.3937 ^K
Duration of primary hypercholesterolemia (years)	5.42 ± 5.23	5.91 ± 4.50	5.01 ± 4.37	0.4808 ^K
Drug therapy before enrollment				
Antihypertensive	35 (74.47)	35 (74.47)	37 (75.51)	0.9908 ^C
Lipid-lowering	38 (80.85)	36 (76.60)	35 (71.43)	0.5542 ^C
Statin	37 (78.72)	33 (70.21)	35 (71.43)	0.5990 ^C
Ezetimibe	16 (34.04)	9 (19.15)	12 (24.49)	0.2475 ^C
Fibrates	3 (6.38)	4 (8.51)	1 (2.04)	0.3560 ^F
Omega-3	3 (6.38)	2 (4.26)	0	0.2029 ^F
Cardiovascular risk categories, n (%)				0.9998 ^F
Very high	16 (34.04)	15 (31.91)	16 (32.65)	
High	10 (21.28)	10 (21.28)	11 (22.45)	
Moderate	18 (38.30)	19 (40.43)	20 (40.82)	
Low	3 (6.38)	3 (6.38)	2 (4.08)	

A = ANOVA test; ATO/EZE = atorvastatin/ezetimibe dual therapy; BMI = body mass index; C = Chi-square test; F = Fisher's exact test; FMS + ATO/EZE = Fimasartan, atorvastatin, and ezetimibe triple combination therapy; FMS = Fimasartan; K = Kruskal–Wallis test.

Table II
Changes in blood pressure from baseline to week 8.

	FMS + ATO/EZE (N = 47)	ATO/EZE (N = 47)	FMS (N = 49)
Sitting SBP			
Baseline	152.04 ± 9.36	151.74 ± 10.10	148.82 ± 7.80
Week 8	134.60 ± 15.09	141.70 ± 14.68	127.51 ± 12.88
Change from baseline to week 8	-17.45 ± 14.71	-10.04 ± 13.25	-21.31 ± 12.44
LS mean	-16.98 ± 2.30	-9.72 ± 2.30	
LS mean	-16.77 ± 2.30		-21.96 ± 2.33
LS mean difference [95% CI]		-7.26 [-12.91, -1.61]	5.19 [-0.34, 10.73]
P value for LS mean difference		0.0124	0.0656
Sitting DBP			
Baseline	91.00 ± 9.08	92.34 ± 10.40	92.37 ± 9.17
Week 8	85.06 ± 9.30	90.09 ± 11.15	83.47 ± 9.22
Change from baseline to week 8	-5.94 ± 6.96	-2.26 ± 7.41	-8.90 ± 8.34
LS mean	-5.90 ± 1.16	-1.93 ± 1.16	
LS mean	-6.05 ± 1.22		-8.49 ± 1.24
LS mean difference [95% CI]		-3.97 [-6.82, -1.12]	2.45 [-0.47, 5.36]
P value for LS mean difference		0.0068	0.0989

ATO/EZE = atorvastatin/ezetimibe dual therapy; DBP = diastolic blood pressure; FMS + ATO/EZE = Fimasartan, atorvastatin, and ezetimibe triple combination therapy; FMS = Fimasartan; LS = least squares; SBP = systolic blood pressure.

ment were -36.08% in the FMS + ATO/EZE group and 5.01% in the FMS group ($P < 0.0001$). TG levels were significantly decreased in the FMS + ATO/EZE group compared to that in the FMS group (LS mean difference, -18.26% [95% CI, -32.88% to -3.64%], $P = 0.0150$). The percentage changes in the HDL-C levels in the FMS + ATO/EZE, ATO/EZE, and FMS groups were 6.33%, 6.40%, and 2.65%, respectively. No statistically significant difference in HDL-C levels was observed between the groups; however, all groups demonstrated increased HDL-C levels after treatment.

The FMS + ATO/EZE group demonstrated significant lipid-lowering efficacy, with 65.96% (31 participants) of patients reaching their LDL-C targets at week 8, which was comparable to the achievement rate of 70.21% (33 participants) in the ATO/EZE group (Figure 4B). Both the FMS + ATO/EZE and ATO/EZE groups substantially outperformed the FMS group, which showed a minimal lipid-lowering effect, with only 4.08% (two participants) achieving their LDL-C goals at week 8.

Safety

Safety analyses were performed on the safety set, defined as the 147 participants who received at least one dose of the investigational drug

after randomization (FMS + ATO/EZE group, 48 participants; ATO/EZE group, 49 participants; FMS group, 50 participants). TEAEs occurred in 29 patients (19.73%), with a total of 40 events. Most of the 40 adverse events had mild-to-moderate severity (26 mild, 13 moderate, and 1 severe). In the treatment group, TEAEs were reported in 10 participants (20.83%), with 16 events in the FMS + ATO/EZE group, 11 participants (22.45%) with 13 events in the ATO/EZE group, and 8 participants (16.00%) with 11 events in the FMS group. The difference in the AE incidence rates between the treatment groups was not statistically significant (Table IV).

Serious TEAEs were reported in two participants (1.36%), with a total of two events. The FMS + ATO/EZE group had one case of appendicitis (2.08%), and the ATO/EZE group had one case of humerus fracture (2.04%).

Among the TEAEs, ADRs that could not exclude a causal relationship occurred in 14 (9.52%), with a total of 20 events. ADRs were observed in five participants (10.42%) with seven events in the FMS + ATO/EZE group, four participants (8.16%) with six events in the ATO/EZE group, and five participants (10.00%) with seven events in the FMS group ($P = 0.9410$). The most frequently reported ADRs were dizziness in five participants (3.40%) with five events, ALT increase and

Table III

Percent changes in lipid variables from baseline to week 8 (mg/dL).

	FMS + ATO/EZE (N = 47)	ATO/EZE (N = 47)	FMS (N = 49)
LDL-cholesterol			
Baseline	146.81 ± 34.61	156.53 ± 34.70	151.22 ± 33.32
Week 8	69.66 ± 23.40	69.33 ± 24.63	155.65 ± 37.10
Percent change from baseline to week 8	-50.44 ± 18.94	-53.63 ± 19.16	6.34 ± 24.98
LS mean	-50.00 ± 2.82	-51.18 ± 2.89	
LS mean	-51.12 ± 3.34		6.91 ± 3.44
LS mean difference [95% CI]		1.18 [-5.85, 8.21]	-58.02 [-66.03, -50.02]
P value for LS mean difference		0.7392	<0.0001
Total cholesterol			
Baseline	217.13 ± 37.79	228.51 ± 38.96	222.86 ± 37.49
Week 8	137.36 ± 25.89	136.96 ± 26.44	228.40 ± 43.47
Percent change from baseline to week 8	-35.37 ± 14.39	-38.64 ± 14.25	4.48 ± 19.27
LS mean	-35.72 ± 2.01	-36.89 ± 2.07	
LS mean	-36.08 ± 2.50		5.01 ± 2.58
LS mean difference [95% CI]		1.18 [-3.85, 6.21]	-41.09 [-47.08, -35.09]
P value for LS mean difference		0.6431	<0.0001
Triglyceride			
Baseline	160.45 ± 60.69	165.66 ± 70.78	166.41 ± 65.20
Week 8	121.21 ± 67.14	115.91 ± 50.42	160.50 ± 74.40
Percent change from baseline to week 8	-18.55 ± 40.36	-26.94 ± 22.72	-1.28 ± 33.79
LS mean	-20.03 ± 5.18	-27.49 ± 5.20	
LS mean	-20.71 ± 6.12		-2.46 ± 6.24
LS mean difference [95% CI]		7.46 [-5.30, 20.22]	-18.26 [-32.88, -3.64]
P value for LS mean difference		0.2486	0.0150
HDL-cholesterol			
Baseline	48.89 ± 13.74	49.09 ± 10.10	49.31 ± 11.75
Week 8	50.81 ± 11.21	51.65 ± 10.57	50.42 ± 13.42
Percent change from baseline to week 8	6.33 ± 19.71	6.40 ± 17.38	2.65 ± 13.32
LS mean	5.30 ± 2.89	5.58 ± 2.92	
LS mean	7.22 ± 2.72		4.15 ± 2.80
LS mean difference [95% CI]		-0.28 [-7.32, 6.76]	3.07 [-3.39, 9.52]
P value for LS mean difference		0.9371	0.3475

ATO/EZE = atorvastatin/ezetimibe dual therapy; DBP = diastolic blood pressure; FMS + ATO/EZE = Fimasartan, atorvastatin, and ezetimibe triple combination therapy; FMS = Fimasartan; LS = least squares; SBP = systolic blood pressure.

Table IV

Summary of treatment-emergent adverse events (TEAE) in the safety set.

	FMS + ATO/EZE (N = 48)	ATO/EZE (N = 49)	FMS (N = 50)	P value
TEAEs	10 (20.83), [16]	11 (22.45), [13]	8 (16.00), [11]	0.7030 ^C
Severity				
Mild	9	9	8	
Moderate	7	3	3	
Severe	0	1	0	
Serious TEAEs	1 (2.08), [1]	1 (2.04), [1]	0 (0.00), [0]	0.5480 ^F
ADRs	5 (10.42), [7]	4 (8.16), [6]	5 (10.00), [7]	0.9410 ^F
Nervous system disorders				
Dizziness	3	0	2	
Headache	0	2	0	
Investigations				
Alanine aminotransferase increased	1	1	1	
Aspartate aminotransferase increased	1	1	1	
Blood creatine phosphokinase increased	0	1	0	
Gastrointestinal disorders				
Abdominal distension	1	0	1	
General disorders and administration site conditions				
Chest discomfort	1	0	0	
Chest pain	0	0	1	
Musculoskeletal and connective tissue disorders				
Musculoskeletal stiffness	0	1	1	

Numbers are “number of subjects (%), [number of events].”

ADR = adverse drug reaction; ATO/EZE = atorvastatin/ezetimibe dual therapy; C = Chi-square test; F = Fisher's exact test; FMS + ATO/EZE = Fimasartan, atorvastatin, and ezetimibe triple combination therapy; FMS = Fimasartan; TEAE = treatment-emergent adverse event.

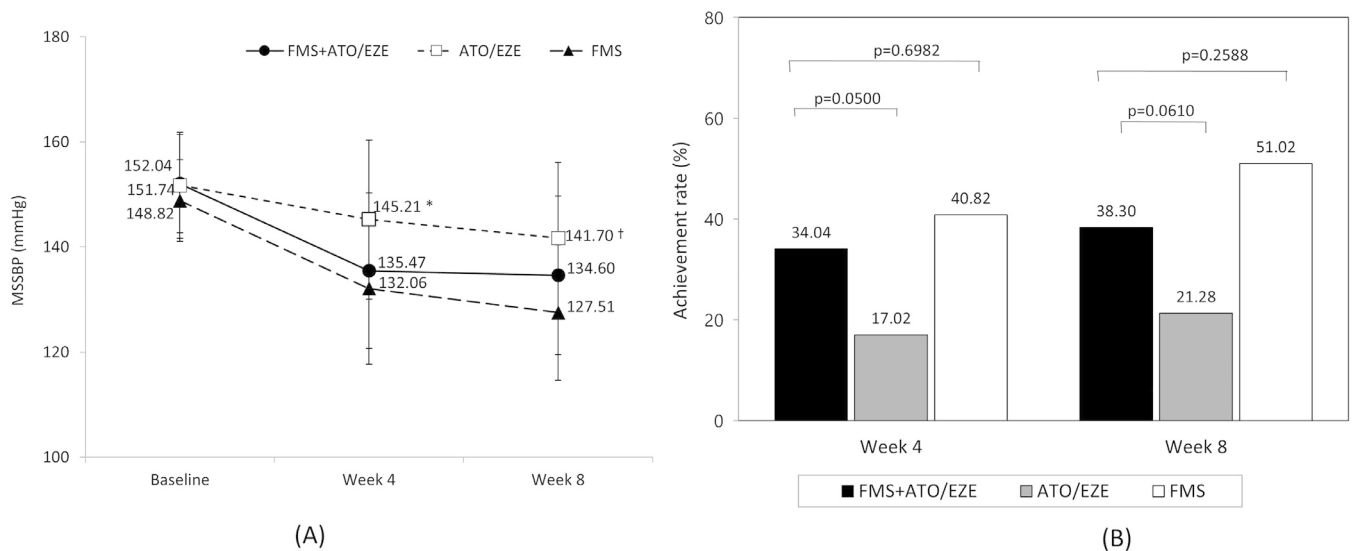


Figure 3. (A) The mean msSBP from baseline to 4 and 8 weeks of treatment. (B) Proportion of subjects achieving target blood pressure at week 4, week 8 (%).

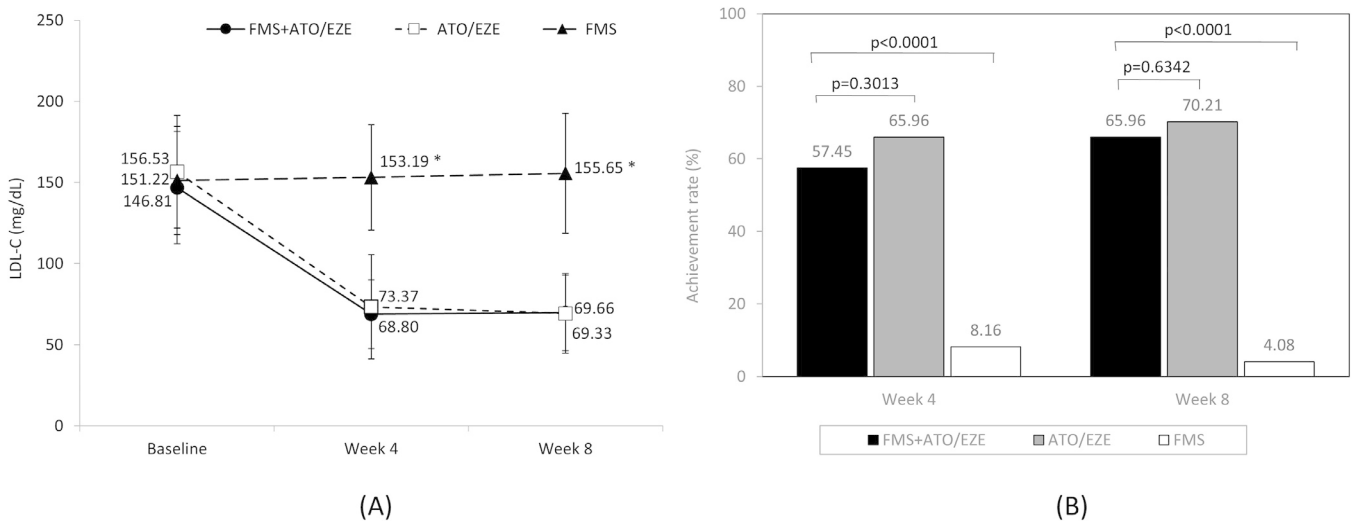


Figure 4. (A) The mean LDL-C from baseline to 4 and 8 weeks of treatment. (B) Proportion of subjects achieving LDL-C treatment goals at week 4, week 8 according to cardiovascular risk categories (%).

AST increase, each occurring in three participants (2.04%) with three events.

Discussion

Our study was a randomized, double-blind, multicenter, phase III trial that evaluated the efficacy and safety of a triple combination of FMS + ATO/EZE in patients with concurrent hypertension and dyslipidemia. After 8 weeks, the FMS + ATO/EZE group demonstrated a significantly greater reduction in msSBP than the ATO/EZE group and a substantial LDL-C reduction compared to FMS monotherapy group. The triple combination preserved a robust antihypertensive efficacy equivalent to FMS monotherapy, despite the incorporation of lipid-lowering components. The safety profile remained consistent across all treatment arms, without significant differences in TEAE incidence. Previous evidence has demonstrated that concurrent management of BP and lipid profiles yields superior cardiovascular outcomes compared to addressing single risk factors. The Anglo-Scandinavian Cardiac Outcomes Trial–

Lipid Lowering Arm study showed that adding statin therapy to antihypertensive treatment reduced major cardiovascular events by 36% in patients with hypertension.²² In fact, the combination of an ARB and lipid-lowering agents is frequently prescribed for their additive risk reduction of cardiovascular disease.^{23,24} Moreover, FDCs with ARBs and statins could have additional beneficial effects beyond apparent BP reduction and lipid profile control.^{25,26} The FMS + ATO/EZE triple combination therapy may offer clinically meaningful benefits for patients with concomitant hypertension and hypercholesterolemia.

Statins may enhance the antihypertensive effects of ARBs through several mechanisms.^{27–29} Indeed, meta-analyses of randomized controlled trials have reported that statins modestly but significantly reduce systolic BP in hypertensive patients.³⁰ However, the magnitude of this effect can vary across studies, and its clinical significance is still a matter of discussion. Furthermore, this additive benefit may not be consistent across all statin-ARB combinations. These BP-lowering effects may occur through pleiotropic mechanisms, including suppression of vascular smooth muscle cell proliferation, decreased angiotensin II-type 1 re-

ceptor expression, enhanced nitric oxide bioavailability, and improved arterial compliance.^{31,32} Favorable pharmacokinetic interactions may also contribute, as some studies have shown increased ARB concentrations when coadministered with statins.^{33,34} These findings provide a rationale for investigating the triple combination of FMS + ATO/EZE in patients with concurrent hypertension and hypercholesterolemia.

The tolerability and safety of FMS + ATO/EZE combination are noteworthy because combination therapies may raise concerns regarding increased adverse events. Our study confirmed no significant differences in TEAEs across the treatment groups, with serious adverse events remaining infrequent. This safety profile was consistent with the known profiles of individual drug components, suggesting no significant pharmacological interactions between FMS, ATO, and EZE. These findings provide clinical reassurance for physicians aiming for comprehensive management of both hypertension and dyslipidemia in high-risk patients. The FMS + ATO/EZE triple combination therapy could enhance medication adherence and consequently optimize therapeutic outcomes in real-world clinical settings. This potential for improved adherence is a key advantage of FDCs, as managing multiple cardiovascular risk factors often leads to polypharmacy, which can negatively impact patient compliance. A recent large-scale, retrospective real-world analysis in Germany by Koenig et al.³⁵ provided evidence supporting this, demonstrating that patients receiving lipid-lowering therapy as an FDC had significantly better adherence and persistence over a 12-month period compared to those on multipill regimens.

Mild, transient elevations in ALT and AST were observed in a small number of participants receiving Fimasartan-containing therapy. Although the elevations were asymptomatic and resolved without intervention, prior studies have reported similar enzyme increases associated with ARBs, including Fimasartan. No participant discontinued treatment due to hepatic events, and all values remained within two times the upper limit of normal. These findings suggest a favorable hepatic safety profile, although liver enzyme monitoring may be considered in vulnerable patients.

Our study has several limitations. First, the 8-week follow-up period was insufficient to fully evaluate the long-term effects on lipid profiles and BP. Second, all participants in this study were of Asian ethnicity, which may limit the generalizability of our findings to other ethnic groups. Ethnic differences in pharmacodynamic and pharmacokinetic responses to both antihypertensive and lipid-lowering agents have been reported. For instance, the GEMINI-AALA trial demonstrated variations in the efficacy of amlodipine/atorvastatin therapy among diverse ethnic populations, and a pharmacogenetic analysis in healthy Korean subjects revealed distinct atorvastatin pharmacokinetic profiles compared with non-Asian cohorts.^{36,37} These differences underscore the need for caution when extrapolating our results to non-Asian populations and highlight the importance of conducting future large-scale, multiethnic studies to confirm these findings. Lastly, as a phase III licensing study primarily designed to assess the efficacy and safety of the FMS + ATO/EZE triple combination, we did not specifically investigate its effects in patients with comorbidities, such as diabetes mellitus or heart failure, which frequently coexist with hypertension and hypercholesterolemia. Nevertheless, FMS + ATO/EZE triple combination therapy for 8 weeks significantly improved both BP and lipid profiles in patients with essential hypertension and primary hypercholesterolemia, supporting its potential as a valuable treatment option for these coexisting conditions.

Conclusions

In Korean patients with concomitant hypertension and hypercholesterolemia, the triple combination of Fimasartan, atorvastatin, and ezetimibe achieved greater BP reduction than atorvastatin/ezetimibe and greater LDL-C reduction than Fimasartan alone, with a lipid-lowering effect similar to atorvastatin/ezetimibe. The regimen was well tolerated, supporting its use for simultaneous BP and lipid control in this population.

Declaration of competing interest

The authors declare that they have no competing financial interests or personal relationships that could have influenced the work reported in this article.

CRediT authorship contribution statement

Soon Jun Hong: Conceptualization, Investigation, Writing – original draft. **Ju Hyeon Kim:** Conceptualization, Methodology, Formal analysis, Investigation, Visualization, Writing – original draft. **Kwang Soo Cha:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jin Bae Lee:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jae Youn Moon:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Goo-Yeong Cho:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Deok-Kyu Cho:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jong-Pil Park:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jeong-Eun Yi:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Kye Hun Kim:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Hyeonju Jeong:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Moo-Yong Rhee:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jung-Hee Lee:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Kye Tack Ahn:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Young Won Yoon:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Sang-Yeub Lee:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Ki-Chul Sung:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Tae-Joon Cha:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jinho Shin:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Yoon Haeng Cho:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jang-Won Son:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jong-Hwa Ahn:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Sang-Don Park:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Woong Chol Kang:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Joo-Yong Hahn:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Jong-Won Ha:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Project administration.

Ethics Committee Approval

The study has been approved by the institutional review board of [Korea University Anam Hospital \(2023AN0182\)](#) and by the ethics committees of each participating center.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.clinthera.2025.08.012](https://doi.org/10.1016/j.clinthera.2025.08.012).

References

- Dabrowska E, Narkiewicz K. Hypertension and dyslipidemia: the two partners in endothelium-related crime. *Curr Atheroscler Rep.* 2023;25:605–612.
- Dalal JJ, Padmanabhan TN, Jain P, et al. LIPITENSION: interplay between dyslipidemia and hypertension. *Indian J Endocrinol Metab.* 2012;16:240–245.
- Mancia G, Kreutz R, Brunstrom M, et al. 2023 ESH guidelines for the management of arterial hypertension the task force for the management of arterial hypertension of the European Society of Hypertension: endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J Hypertens.* 2023;41:1874–2071.
- Otsuka T, Takada H, Nishiyama Y, et al. Dyslipidemia and the risk of developing hypertension in a working-age male population. *J Am Heart Assoc.* 2016;5:e003053.
- Kim HC, Lee H, Lee HH, et al. Korea hypertension fact sheet 2022: analysis of nationwide population-based data with a special focus on hypertension in the elderly. *Clin Hypertens.* 2023;29:22.
- Lee J, Son H, Ryu OH. Management status of cardiovascular disease risk factors for dyslipidemia among Korean adults. *Yonsei Med J.* 2017;58:326–338.
- McEvoy JW, McCarthy CP, Bruno RM, et al. 2024 ESC guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J.* 2024;45:3912–4018.
- Chi YH, Lee H, Paik SH, et al. Safety, tolerability, pharmacokinetics, and pharmacodynamics of Fimasartan following single and repeated oral administration in the fasted and fed states in healthy subjects. *Am J Cardiovasc Drugs.* 2011;11:335–346.
- Lee H, Yang HM, Lee HY, et al. Efficacy and tolerability of once-daily oral Fimasartan 20 to 240 mg/d in Korean Patients with hypertension: findings from Two phase II, randomized, double-blind, placebo-controlled studies. *Clin Ther.* 2012;34:1273–1289.
- Rhee MY, Baek SH, Kim W, et al. Efficacy of Fimasartan/hydrochlorothiazide combination in hypertensive patients inadequately controlled by Fimasartan monotherapy. *Drug Des Devel Ther.* 2015;9:2847–2854.
- Lee H, Kim KS, Chae SC, et al. Ambulatory blood pressure response to once-daily Fimasartan: an 8-week, multicenter, randomized, double-blind, active-comparator, parallel-group study in Korean patients with mild to moderate essential hypertension. *Clin Ther.* 2013;35:1337–1349.
- Lee JH, Yang DH, Hwang JY, et al. A randomized, double-blind, candesartan-controlled, parallel group comparison clinical trial to evaluate the antihypertensive efficacy and safety of Fimasartan in patients with mild to moderate essential hypertension. *Clin Ther.* 2016;38:1485–1497.
- Seo SM, Ihm SH, Yi JE, et al. Comparative efficacy and safety of Fimasartan in patients with hypertension: a network meta-analysis of randomized controlled trials. *J Clin Hypertens (Greenwich).* 2022;24:971–983.
- Qian J, Li Z, Zhang X, et al. Efficacy and tolerability of ezetimibe/atorvastatin fixed-dose combination versus atorvastatin monotherapy in hypercholesterolemia: a phase III, randomized, active-controlled study in Chinese patients. *Clin Ther.* 2022;44:1282–1296.
- Min KL, Park MS, Jung J, et al. Comparison of pharmacokinetics and safety of a fixed-dose combination of rosuvastatin and ezetimibe versus separate tablets in healthy subjects. *Clin Ther.* 2017;39:1799–1810.
- Rhee MY, Ahn T, Chang K, et al. The efficacy and safety of co-administration of Fimasartan and rosuvastatin to patients with hypertension and dyslipidemia. *BMC Pharmacol Toxicol.* 2017;18:2.
- Jeon ES, Lim SW, Kim SY, et al. A randomized, double-blind, multicenter, phase III study on the efficacy and safety of a combination treatment involving Fimasartan, amlodipine, rosuvastatin in patients with essential hypertension and dyslipidemia who fail to respond adequately to Fimasartan monotherapy. *Clin Hypertens.* 2022;28:40.
- Song ZY, Kim MH, Lee HC, et al. Efficacy and safety of coadministered ezetimibe-rosuvastatin plus telmisartan in south Korean patients with dyslipidemia and hypertension: a multicenter, randomized, double-blind, active-controlled, phase III trial. *J Clin Med.* 2023;12:2377.
- Chung S, Ko YG, Kim JS, et al. Effect of FIXed-dose combination of ARb and statin on adherence and risk factor control: the randomized FIXAR study. *Cardiol J.* 2022;29:815–823.
- Kim H-L, Lee EM, Ahn SY, et al. The 2022 focused update of the 2018 Korean Hypertension Society Guidelines for the management of hypertension. *Clin Hypertens.* 2023;29:11.
- Catapano AL, Vrablik M, Karpov Y, et al. A phase 3 randomized controlled trial to evaluate efficacy and safety of new-formulation Zenon (rosuvastatin/ezetimibe fixed-dose combination) in primary hypercholesterolemia inadequately controlled by statins. *J Cardiovasc Pharmacol Ther.* 2022;27:10742484221138284.
- Sever PS, Dahlof B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet.* 2003;361:1149–1158.
- Ferdinand KC, Kleinpeter MA. Management of hypertension and dyslipidemia. *Curr Hypertens Rep.* 2006;8:489–496.
- Kim TS, Rha SW, Kim SY, et al. Efficacy and tolerability of telmisartan/amlodipine and rosuvastatin coadministration in hypertensive patients with hyperlipidemia: a phase III, multicenter, randomized, double-blind study. *Clin Ther.* 2019;41:728–741.
- Lee CJ, Kang WC, Ihm SH, et al. Efficacy and safety of combination therapy with telmisartan, rosuvastatin, and ezetimibe in patients with dyslipidemia and hypertension: a randomized, double-blind, multicenter, therapeutic confirmatory, phase III clinical trial. *J Clin Hypertens (Greenwich).* 2024;26:262–273.
- Lee SJ, Oh J, Hong SJ, et al. Effectiveness of Fimasartan and rosuvastatin combination treatment in hypertensive patients with dyslipidemia. *Clin Ther.* 2020;42:1058–1066.e1053.
- Kanbay M, Yildirim A, Bozbas H, et al. Statin therapy helps to control blood pressure levels in hypertensive dyslipidemic patients. *Ren Fail.* 2005;27:297–303.
- Koh KK, Quon MJ, Han SH, et al. Additive beneficial effects of losartan combined with simvastatin in the treatment of hypercholesterolemic, hypertensive patients. *Circulation.* 2004;110:3687–3692.
- Spannella F, Filippini A, Giulietti F, et al. Statin therapy is associated with better ambulatory blood pressure control: a propensity score analysis. *J Hypertens.* 2020;38:546–552.
- Briasoulis A, Agarwal V, Valachis A, Messerli FH. Antihypertensive effects of statins: a meta-analysis of prospective controlled studies. *J Clin Hypertens (Greenwich).* 2013;15:310–320.
- Strazzullo P, Kerry SM, Barbato A, et al. Do statins reduce blood pressure?: A meta-analysis of randomized, controlled trials. *Hypertension.* 2007;49:792–798.
- Oesterle A, Laufs U, Liao JK. Pleiotropic effects of statins on the cardiovascular system. *Circ Res.* 2017;120:229–243.
- Kim CH, Kang SI, Shin D. Pharmacokinetic interaction between telmisartan and rosuvastatin/ezetimibe after multiple oral administration in healthy subjects. *Adv Ther.* 2021;38:1094–1105.
- Huh KY, Lee SW, Lee SB, et al. Pharmacokinetic interaction among ezetimibe, rosuvastatin, and telmisartan. *Clin Pharmacol Drug Dev.* 2021;10:1290–1296.
- Koenig W, Lorenz ES, Beier L, Gouni-Berthold I. Retrospective real-world analysis of adherence and persistence to lipid-lowering therapy in Germany. *Clin Res Cardiol.* 2024;113:812–821.
- Erdine S, Ro YM, Tse HF, et al. Single-pill amlodipine/atorvastatin helps patients of diverse ethnicity attain recommended goals for blood pressure and lipids (the Gemini-AALA study). *J Hum Hypertens.* 2009;23:196–210.
- Kim S, Seo JD, Yun YM, et al. Pharmacokinetics and genetic factors of atorvastatin in healthy Korean subjects. *Front Genet.* 2022;13:836970.