Ezetimibe/Simvastatin (MK-0653A) Versus Rosuvastatin Versus Doubling Statin Dose in Participants With Cardiovascular Disease and Diabetes Mellitus (MK-0653A-133)(COMPLETED)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00862251

First received: March 12, 2009
Last updated: October 12, 2015
Last verified: October 2015
History of Changes

Purpose

The purpose of this study is to determine the efficacy of switching to a combination tablet ezetimibe/simvastatin (10mg/20mg) versus rosuvastatin (10 mg) versus doubling the statin dose in those patients who have cardiovascular disease and diabetes mellitus not adequately controlled on simvastatin 20 mg or atorvastatin 10 mg.

Condition	Intervention	Phase
Cardiovascular Disorder Diabetes Mellitus	Drug: ezetimibe (+) simvastatin Drug: simvastatin 40 mg or atorvastatin 20 mg Drug: Rosuvastatin Drug: atorvastatin 10 mg or simvastatin 20 mg	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Official Title: A Randomized, Double-Blind, Active-Controlled Study of Patients With Cardiovascular Disease and Diabetes Mellitus Not Adequately Controlled With Simvastatin or Atorvastatin: Comparison of Switching to Combination Tablet Ezetimibe/Simvastatin Versus Switching to Rosuvastatin or Doubling the Statin Dose

Resource links provided by NLM:

MedlinePlus related topics: Statins

Drug Information available for: Simvastatin Atorvastatin Atorvastatin calcium Rosuvastatin calcium Ezetimibe Rosuvastatin

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Statin (Simvastatin or Atorvastatin). [Time Frame: Baseline and Week 6] [Designated as safety issue: No]

Secondary Outcome Measures:

- In Participants Treated With Simvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Simvastatin [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- In Participants Treated With Atorvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Atorvastatin [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Switching Treatment to Rosuvastatin [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [Time Frame: Week 6] [Designated as safety issue: No]
- In Participants Treated With Simvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [Time Frame: Week 6] [Designated as safety issue: No]
- In Participants Treated With Atorvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [Time Frame: Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in Total Cholesterol (TC) [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in Triglycerides [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C) [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in Non-high-density Lipoprotein Cholesterol (Non-HDL-C) [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in LDL-C/HDL-C Ratio [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in TC/HDL-C Ratio [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in Non-HDL-C/HDL-C Ratio [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in Apolipoprotein B (Apo B) [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline Apolipoprotein A-I (Apo A-I) [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in Apo B/Apo A-I Ratio [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Percent Change From Baseline in High-sensitivity C-reactive Protein (Hs-CRP) [Time Frame: Baseline and Week 6] [Designated as safety issue: No]

Enrollment:	808
Study Start Date:	April 2009
Study Completion Date:	March 2011
Primary Completion Date:	March 2011 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Ezetimibe/simvastatin	Drug: ezetimibe (+) simvastatin ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks. Other Name: Vytorin Drug: atorvastatin 10 mg or simvastatin 20 mg All patients will take atorvastatin 10 mg tablets OR simvastatin 20 mg tablets, taken once daily in a 6-week screening/stabilization period prior to randomization. Other Name: Lipitor, Zocor
Active Comparator: Doubling statin dose	Drug: simvastatin 40 mg or atorvastatin 20 mg simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks. Other Name: Lipitor, Zocor Drug: atorvastatin 10 mg or simvastatin 20 mg All patients will take atorvastatin 10 mg tablets OR simvastatin 20 mg tablets, taken once daily in a 6-week screening/stabilization period prior to randomization. Other Name: Lipitor, Zocor

Active Comparator: Rosuvastatin	Drug: Rosuvastatin rosuvastatin 10 mg tablets, taken once daily for six weeks. Other Name: Crestor Drug: atorvastatin 10 mg or simvastatin 20 mg All patients will take atorvastatin 10 mg tablets OR simvastatin 20 mg tablets, taken once daily in a 6-week screening/stabilization period prior to randomization. Other Name: Lipitor, Zocor

Eligibility

Ages Eligible for Study: 18 Years to 79 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Patient has not taken common statins or ezetimibe within 6 weeks of study screening or patient is currently taking a daily dose of the following statins for 6 weeks prior to study screening: simvastatin, atorvastatin, pravastatin, fluvastatin, ezetimibe, lovastatin, or ezetimibe + fluvastatin
- Patient is willing to go on a cholesterol and glucose lowering diet for the duration of the study
- Patient is willing to remain abstinent or use birth control for the duration of the study
- Patient has Diabetes Mellitus with cardiovascular disease

Exclusion Criteria:

- Patient has sensitivity to certain common statin drugs
- Patient is Asian and would not be able to start taking the higher doses of rosuvastatin necessary for the study design
- Patient consumes more than 2 alcoholic drinks per day
- Patient is pregnant or breast-feeding
- Patient has been treated with other investigational drugs within 30 days of first visit
- Patient is currently on prohibited doses of the following statin drugs: rosuvastatin, simvastatin, atorvastatin, and pravastatin
- Patient has congestive heart failure
- Patient has uncontrolled high blood pressure
- Patient has kidney disease
- Patient has uncontrolled endocrine or metabolic disease which are known to possibly increase blood lipoproteins
- Patient has diabetes mellitus that is not well controlled
- Patient is human immunodeficiency virus (HIV) positive
- Patient is currently taking medications that inhibit Cytochrome P450 3A4 (CYP3A4)
- Patient is currently taking therapies that would increase the risk of muscle weakness
- Patient has been taking certain over- the-counter lipid-lowering agents within 6 weeks prior to visit 1
- Patient is currently taking psyllium or other fiber-based laxatives

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT00862251

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Monitor Merck Sharp & Dohme Corp.

More Information

No publications provided by Merck Sharp & Dohme Corp.

Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Le NA, Tomassini JE, Tershakovec AM, Neff DR, Wilson PW. Effect of Switching From Statin Monotherapy to Ezetimibe/Simvastatin Combination Therapy Compared With Other Intensified Lipid-Lowering Strategies on Lipoprotein Subclasses in Diabetic Patients With Symptomatic Cardiovascular Disease. J Am Heart Assoc. 2015 Oct 20;4(10):e001675. doi: 10.1161/JAHA.114.001675.

Rosen JB, Jimenez JG, Pirags V, Vides H, Massaad R, Hanson ME, Brudi P, Triscari J. Consistency of effect of ezetimibe/simvastatin compared with intensified lipid-lowering treatment strategies in obese and non-obese diabetic subjects. Lipids Health Dis. 2013 Jul 16;12:103. doi: 10.1186/1476-511X-12-103.

Rosen JB, Jimenez JG, Pirags V, Vides H, Hanson ME, Massaad R, McPeters G, Brudi P, Triscari J. A comparison of efficacy and safety of an ezetimibe/simvastatin combination compared with other intensified lipid-lowering treatment strategies in diabetic patients with symptomatic cardiovascular disease. Diab Vasc Dis Res. 2013 May;10(3):277-86. doi: 10.1177/1479164112465212. Epub 2013 Jan 3.

Jimenez JG, Rosen JB, Pirags V, Massaad R, Hanson ME, Brudi P, Triscari J. The efficacy and safety of ezetimibe/simvastatin combination compared with intensified lipid-lowering treatment strategies in diabetic subjects with and without metabolic syndrome. Diabetes Obes Metab. 2013 Jun;15(6):513-22. doi: 10.1111/dom.12059. Epub 2013 Jan 25.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00862251 History of Changes
Other Study ID Numbers:	**0653A-133** 2009_559
Study First Received:	March 12, 2009
Results First Received:	February 23, 2012
Last Updated:	October 12, 2015
Health Authority:	United States: Food and Drug Administration

Keywords provided by Merck Sharp & Dohme Corp.:
cardiovascular disorder

Additional relevant MeSH terms:

Cardiovascular Diseases	Anticholesteremic Agents
Diabetes Mellitus	Antimetabolites
Endocrine System Diseases	Enzyme Inhibitors
Glucose Metabolism Disorders	Hydroxymethylglutaryl-CoA Reductase Inhibitors
Metabolic Diseases	Hypolipidemic Agents
Atorvastatin	Lipid Regulating Agents
Ezetimibe	Molecular Mechanisms of Pharmacological Action
Rosuvastatin	Pharmacologic Actions
Simvastatin	Therapeutic Uses

ClinicalTrials.gov processed this record on March 30, 2016

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First received: March 12, 2009
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History of Changes

Results First Received: February 23, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Conditions:	Cardiovascular Disorder Diabetes Mellitus
Interventions:	Drug: ezetimibe (+) simvastatin Drug: simvastatin 40 mg or atorvastatin 20 mg Drug: Rosuvastatin Drug: atorvastatin 10 mg or simvastatin 20 mg

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Participant Flow: Overall Study

	Ezetimibe/Simvastatin	Doubling Statin Dose	Rosuvastatin
STARTED	**322**	**162**	**324**
COMPLETED	**303**	**157**	**315**
NOT COMPLETED	**19**	**5**	**9**
Adverse Event	**8**	**3**	**1**
Lost to Follow-up	**0**	**0**	**1**
Protocol Violation	**2**	**0**	**1**
Withdrawal by Subject	**9**	**2**	**6**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.
Total	Total of all reporting groups

Baseline Measures

	Ezetimibe/Simvastatin	Doubling Statin Dose	Rosuvastatin	Total
Number of Participants [units: participants]	**322**	**162**	**324**	**808**
Age [units: years] Mean (Standard Deviation)	**64.1 (8.8)**	**64.7 (8.3)**	**63.6 (8.4)**	**64.0 (8.5)**

Gender [units: participants]				
Female	**162**	**82**	**142**	**386**
Male	**160**	**80**	**182**	**422**

Outcome Measures

Hide All Outcome Measures

1. Primary: Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Statin (Simvastatin or Atorvastatin). [Time Frame: Baseline and Week 6]

Measure Type	Primary
Measure Title	Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Statin (Simvastatin or Atorvastatin).
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**
Number of Participants Analyzed [units: participants]	**314**	**159**
Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Statin (Simvastatin or Atorvastatin). [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-23.13 (-25.95 to -20.31)**	**-8.37 (-12.32 to -4.41)**

Statistical Analysis 1 for Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Statin (Simvastatin or Atorvastatin).

Groups [1]	All groups

Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Percent change in least-square means [4]	-14.76
95% Confidence Interval	-19.61 to -9.91

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: In Participants Treated With Simvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Simvastatin [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	In Participants Treated With Simvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Simvastatin
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis performed on subpopulation of participants who were previously treated with simvastatin 20 mg and were switched to either Ezetimibe/simvastatin or had simvastatin dose doubled to 40 mg

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Simvastatin Dose	simvastatin 40 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Simvastatin Dose**
Number of Participants Analyzed [units: participants]	**158**	**78**

In Participants Treated With Simvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Simvastatin [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-21.59 (-25.54 to -17.65)**	**-7.98 (-13.57 to -2.38)**

Statistical Analysis 1 for In Participants Treated With Simvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Simvastatin

Groups [1]	All groups
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Percent change in Least Square Means [4]	-13.62
95% Confidence Interval	-20.44 to -6.79

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: In Participants Treated With Atorvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Atorvastatin [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	In Participants Treated With Atorvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Atorvastatin
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis performed on subpopulation of participants who were previously treated with atorvastatin 10 mg and were switched to either Ezetimibe/simvastatin or had atorvastatin dose doubled to 20 mg

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six

	weeks
Doubling Atorvastatin Dose	atorvastatin 20 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	Doubling Atorvastatin Dose
Number of Participants Analyzed [units: participants]	**156**	**81**
In Participants Treated With Atorvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Atorvastatin [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-24.58 (-28.63 to -20.53)**	**-8.85 (-14.47 to -3.23)**

Statistical Analysis 1 for In Participants Treated With Atorvastatin at Baseline, Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Doubling the Dose of Atorvastatin

Groups [1]	All groups
Method [2]	Longitudinal Data Analysis (LDA)
P Value [3]	<0.001
Percent change in least squares mean [4]	-15.73
95% Confidence Interval	-22.65 to -8.81

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

4. Secondary: Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Switching Treatment to Rosuvastatin [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Switching Treatment to Rosuvastatin
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed primarily based upon the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**314**	**315**
Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Switching Treatment to Rosuvastatin [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-23.13 (-25.95 to -20.31)**	**-19.32 (-22.14 to -16.51)**

Statistical Analysis 1 for Percent Change From Baseline in LDL-C After Switching to Treatment With Ezetimibe/Simvastatin vs Switching Treatment to Rosuvastatin

Groups [1]	All groups
Method [2]	Longitudinal Data Analysis
P Value [3]	0.060
Percent Change in Least Squares Means [4]	-3.81
95% Confidence Interval	-7.78 to 0.17

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [Time Frame: Week 6]

Measure Type	Secondary
Measure Title	Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)
Measure Description	No text entered.
Time Frame	Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [units: participants]	**171**	**43**	**134**

Statistical Analysis 1 for Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	3.9
95% Confidence Interval	2.5 to 6.2

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	1.9
95% Confidence Interval	1.3 to 2.6

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

6. Secondary: In Participants Treated With Simvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [Time Frame: Week 6]

Measure Type	Secondary
Measure Title	In Participants Treated With Simvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)
Measure Description	No text entered.
Time Frame	Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis performed on subpopulation of participants who were previously treated with simvastatin 20 mg and were switched to either Ezetimibe/simvastatin or had simvastatin dose doubled to 40 mg

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks

Doubling Simvastatin Dose	simvastatin 40 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	Doubling Simvastatin Dose
Number of Participants Analyzed [units: participants]	**158**	**78**
In Participants Treated With Simvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [units: participants]	**84**	**19**

Statistical Analysis 1 for In Participants Treated With Simvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)

Groups [1]	All groups
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	4.5
95% Confidence Interval	2.3 to 8.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

7. Secondary: In Participants Treated With Atorvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [Time Frame: Week 6]

Measure Type	Secondary
Measure Title	In Participants Treated With Atorvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)
Measure Description	No text entered.
Time Frame	Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or

another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis performed on subpopulation of participants who were previously treated with atorvastatin 10 mg and were switched to either Ezetimibe/simvastatin or had atorvastatin dose doubled to 20 mg

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Atorvastatin Dose	atorvastatin 20 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Atorvastatin Dose**
Number of Participants Analyzed [units: participants]	**156**	**81**
In Participants Treated With Atorvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L) [units: participants]	**87**	**24**

Statistical Analysis 1 for In Participants Treated With Atorvastatin at Baseline, Number of Participants Who Reached the Target LDL-Cholesterol Level of < 70 mg/dL (1.81 mmol/L)

Groups [1]	All groups
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	3.5
95% Confidence Interval	1.9 to 6.6

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

8. Secondary: Percent Change From Baseline in Total Cholesterol (TC) [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Total Cholesterol (TC)

Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Percent Change From Baseline in Total Cholesterol (TC) [units: Percent Change] Least Squares Mean (95% Confidence Interval)	**-13.21 (-14.99 to -11.43)**	**-4.88 (-7.37 to -2.39)**	**-10.58 (-12.36 to -8.81)**

Statistical Analysis 1 for Percent Change From Baseline in Total Cholesterol (TC)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Least Squares Mean Difference [4]	-8.33
95% Confidence Interval	-11.38 to -5.28

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:

	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in Total Cholesterol (TC)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.039
Least Squares Mean Difference [4]	-2.63
95% Confidence Interval	-5.13 to -0.13

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

9. Secondary: Percent Change From Baseline in Triglycerides [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Triglycerides
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	Doubling Statin Dose	Rosuvastatin
Number of Participants Analyzed [units: participants]	314	159	315
Percent Change From Baseline in Triglycerides [units: Percent change] Least Squares Mean (95% Confidence Interval)	-5.51 (-8.75 to -2.15)	-2.63 (-7.23 to 2.21)	-3.35 (-6.66 to 0.08)

Statistical Analysis 1 for Percent Change From Baseline in Triglycerides

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.316
Least Squares Mean Difference [4]	-2.88
95% Confidence Interval	-8.53 to 2.77

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in Triglycerides

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.356
Least Squares Mean Difference [4]	-2.16
95% Confidence Interval	-6.75 to 2.43

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

[4]	Other relevant estimation information:
	No text entered.

10. Secondary: Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C) [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C)
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C) [units: percent change] Least Squares Mean (95% Confidence Interval)	**1.47 (-0.27 to 3.21)**	**1.00 (-1.43 to 3.43)**	**1.99 (0.26 to 3.73)**

Statistical Analysis 1 for Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.756
Least Squares Mean Difference [4]	0.47
95% Confidence Interval	-2.50 to 3.45

[1]	

	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.675
Least Sqares Mean Difference [4]	-0.52
95% Confidence Interval	-2.96 to 1.92

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

11. Secondary: Percent Change From Baseline in Non-high-density Lipoprotein Cholesterol (Non-HDL-C) [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Non-high-density Lipoprotein Cholesterol (Non-HDL-C)
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	Doubling Statin Dose	Rosuvastatin
Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Percent Change From Baseline in Non-high-density Lipoprotein Cholesterol (Non-HDL-C) [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-18.39 (-20.90 to -15.88)**	**-6.77 (-10.29 to -3.25)**	**-15.14 (-17.72 to -12.70)**

Statistical Analysis 1 for Percent Change From Baseline in Non-high-density Lipoprotein Cholesterol (Non-HDL-C)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Least Squares Mean Difference [4]	-11.62
95% Confidence Interval	-15.93 to -7.31

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in Non-high-density Lipoprotein Cholesterol (Non-HDL-C)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.078
Least Squares Mean Difference [4]	-3.18

95% Confidence Interval	-6.71 to 0.35

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

12. Secondary: Percent Change From Baseline in LDL-C/HDL-C Ratio [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in LDL-C/HDL-C Ratio
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Percent Change From Baseline in LDL-C/HDL-C Ratio [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-21.55 (-25.09 to -18.01)**	**-7.39 (-12.34 to -2.43)**	**-18.99 (-22.52 to -15.46)**

Statistical Analysis 1 for Percent Change From Baseline in LDL-C/HDL-C Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Least Squares Mean Difference [4]	-14.16
95% Confidence Interval	-20.23 to -8.10

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in LDL-C/HDL-C Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.313
Least Sqares Mean Difference [4]	-2.56
95% Confidence Interval	-7.53 to 2.41

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

13. Secondary: Percent Change From Baseline in TC/HDL-C Ratio [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in TC/HDL-C Ratio
Measure Description	No text entered.

Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Percent Change From Baseline in TC/HDL-C Ratio [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-12.52 (-14.83 to -10.22)**	**-4.36 (-7.58 to -1.14)**	**-10.70 (-12.99 to -8.40)**

Statistical Analysis 1 for Percent Change From Baseline in TC/HDL-C Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Least Squares Mean Difference [4]	-8.17
95% Confidence Interval	-12.10 to -4.23

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in TC/HDL-C Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.266
Least Squares Mean Difference [4]	-1.83
95% Confidence Interval	-5.05 to 1.40

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

14. Secondary: Percent Change From Baseline in Non-HDL-C/HDL-C Ratio [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Non-HDL-C/HDL-C Ratio
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**

Number of Participants Analyzed [units: participants]	**314**	**159**	**315**
Percent Change From Baseline in Non-HDL-C/HDL-C Ratio [units: percent change] Least Squares Mean (95% Confidence Interval)	**-16.77 (-20.09 to -13.45)**	**-5.32 (-9.98 to -0.66)**	**-14.64 (-17.95 to -11.32)**

Statistical Analysis 1 for Percent Change From Baseline in Non-HDL-C/HDL-C Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Least Squares Mean Difference [4]	-11.45
95% Confidence Interval	-17.16 to -5.75

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in Non-HDL-C/HDL-C Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.371
Least Squares Mean Difference [4]	-2.13
95% Confidence Interval	-6.81 to 2.54

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

15. Secondary: Percent Change From Baseline in Apolipoprotein B (Apo B) [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Apolipoprotein B (Apo B)
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**313**	**159**	**313**
Percent Change From Baseline in Apolipoprotein B (Apo B) [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-14.98 (-16.99 to -12.97)**	**-6.97 (-9.78 to -4.15)**	**-12.03 (-14.05 to -10.02)**

Statistical Analysis 1 for Percent Change From Baseline in Apolipoprotein B (Apo B)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	<0.001
Least Squares Mean Difference [4]	-8.01
95% Confidence Interval	-11.46 to -4.56

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:

	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in Apolipoprotein B (Apo B)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.041
Least Squares Mean Difference [4]	-2.95
95% Confidence Interval	-5.78 to -0.12

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

16. Secondary: Percent Change From Baseline Apolipoprotein A-I (Apo A-I) [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline Apolipoprotein A-I (Apo A-I)
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description

Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	Doubling Statin Dose	Rosuvastatin
Number of Participants Analyzed [units: participants]	**313**	**159**	**313**
Percent Change From Baseline Apolipoprotein A-I (Apo A-I) [units: Percent change] Least Squares Mean (95% Confidence Interval)	**0.64 (-0.84 to 2.11)**	**-0.93 (-2.99 to 1.12)**	**0.86 (-0.62 to 2.34)**

Statistical Analysis 1 for Percent Change From Baseline Apolipoprotein A-I (Apo A-I)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.218
Least Squares Mean Difference [4]	1.57
95% Confidence Interval	-0.93 to 4.06

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline Apolipoprotein A-I (Apo A-I)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.832
Least Squares Mean Difference [4]	-0.22
95% Confidence Interval	-2.27 to 1.83

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.

[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

17. Secondary: Percent Change From Baseline in Apo B/Apo A-I Ratio [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Apo B/Apo A-I Ratio
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**313**	**159**	**313**
Percent Change From Baseline in Apo B/Apo A-I Ratio [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-13.67 (-16.27 to -11.06)**	**-4.75 (-8.39 to -1.11)**	**-11.14 (-13.75 to -8.54)**

Statistical Analysis 1 for Percent Change From Baseline in Apo B/Apo A-I Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)

P Value [3]	<0.001
Least Squares Mean Difference [4]	-8.91
95% Confidence Interval	-13.36 to -4.47

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in Apo B/Apo A-I Ratio

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.175
Least Squares Mean Difference [4]	-2.52
95% Confidence Interval	-6.17 to 1.13

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

18. Secondary: Percent Change From Baseline in High-sensitivity C-reactive Protein (Hs-CRP) [Time Frame: Baseline and Week 6]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in High-sensitivity C-reactive Protein (Hs-CRP)
Measure Description	No text entered.
Time Frame	Baseline and Week 6
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy data were analyzed using the full analysis set (FAS) population defined as all randomized participants who received at least one dose of blinded study treatment and had baseline data.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Measured Values

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Number of Participants Analyzed [units: participants]	**313**	**159**	**315**
Percent Change From Baseline in High-sensitivity C-reactive Protein (Hs-CRP) [units: Percent change] Least Squares Mean (95% Confidence Interval)	**-4.42 (-13.94 to 6.15)**	**-1.64 (-14.93 to 13.74)**	**-9.11 (-18.13 to 0.92)**

Statistical Analysis 1 for Percent Change From Baseline in High-sensitivity C-reactive Protein (Hs-CRP)

Groups [1]	Ezetimibe/Simvastatin vs. Doubling Statin Dose
Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.749
Least Squares Mean Difference [4]	-2.78
95% Confidence Interval	-19.88 to 14.32

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change From Baseline in High-sensitivity C-reactive Protein (Hs-CRP)

Groups [1]	Ezetimibe/Simvastatin vs. Rosuvastatin

Method [2]	Longitudinal data analysis (LDA)
P Value [3]	0.494
Least Squares Mean Difference [4]	4.69
95% Confidence Interval	-8.73 to 18.10

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	All Patients as Treated (APaT) population was used for the analysis of safety data. The APaT population consisted of all randomized patients who received at least one dose of study treatment.

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Serious Adverse Events

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Total, serious adverse events			
# participants affected / at risk	**2/321 (0.62%)**	**1/162 (0.62%)**	**2/323 (0.62%)**
Cardiac disorders			
Angina pectoris †			
# participants affected / at risk	**1/321 (0.31%)**	**0/162 (0.00%)**	**0/323 (0.00%)**
# events	**1**	**0**	**0**

Angina unstable †			
# participants affected / at risk	**0/321 (0.00%)**	**0/162 (0.00%)**	**1/323 (0.31%)**
# events	**0**	**0**	**1**
Coronary artery disease †			
# participants affected / at risk	**1/321 (0.31%)**	**0/162 (0.00%)**	**0/323 (0.00%)**
# events	**1**	**0**	**0**
Myocardial infarction †			
# participants affected / at risk	**0/321 (0.00%)**	**1/162 (0.62%)**	**0/323 (0.00%)**
# events	**0**	**1**	**0**
Vascular disorders			
Arterial thrombosis limb †			
# participants affected / at risk	**0/321 (0.00%)**	**0/162 (0.00%)**	**1/323 (0.31%)**
# events	**0**	**0**	**1**

† Events were collected by systematic assessment

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	All Patients as Treated (APaT) population was used for the analysis of safety data. The APaT population consisted of all randomized patients who received at least one dose of study treatment.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Ezetimibe/Simvastatin	Ezetimibe/simvastatin 10/20 mg tablets, taken once daily for six weeks
Doubling Statin Dose	simvastatin 40 mg or atorvastatin 20 mg tablets, taken once daily for six weeks.
Rosuvastatin	Rosuvastatin 10 mg tablets, taken once daily for six weeks.

Other Adverse Events

	Ezetimibe/Simvastatin	**Doubling Statin Dose**	**Rosuvastatin**
Total, other (not including serious) adverse events			
# participants affected / at risk	**0/321 (0.00%)**	**0/162 (0.00%)**	**0/323 (0.00%)**

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** An investigator and/or his/her colleagues may publish the results for their study site independently after the multicenter publication, or 24 months after completion of the study, whichever comes first. The Sponsor must have the opportunity to review all proposed abstracts, manuscripts, or presentations regarding this study 60 days prior to submission for publication/presentation. Any information identified by the sponsor as confidential must be deleted prior to submission.

Results Point of Contact:

Name/Title: Senior Vice President,Global Clinical Development
Organization: Merck Sharp & Dohme Corp
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e-mail: ClinicalTrialsDisclosure@merck.com

No publications provided by Merck Sharp & Dohme Corp.

Publications automatically indexed to this study:

Le NA, Tomassini JE, Tershakovec AM, Neff DR, Wilson PW. Effect of Switching From Statin Monotherapy to Ezetimibe/Simvastatin Combination Therapy Compared With Other Intensified Lipid-Lowering Strategies on Lipoprotein Subclasses in Diabetic Patients With Symptomatic Cardiovascular Disease. J Am Heart Assoc. 2015 Oct 20;4(10):e001675. doi: 10.1161/JAHA.114.001675.

Rosen JB, Jimenez JG, Pirags V, Vides H, Massaad R, Hanson ME, Brudi P, Triscari J. Consistency of effect of ezetimibe/simvastatin compared with intensified lipid-lowering treatment strategies in obese and non-obese diabetic subjects. Lipids Health Dis. 2013 Jul 16;12:103. doi: 10.1186/1476-511X-12-103.

Rosen JB, Jimenez JG, Pirags V, Vides H, Hanson ME, Massaad R, McPeters G, Brudi P, Triscari J. A comparison of efficacy and safety of an ezetimibe/simvastatin combination compared with other intensified lipid-lowering treatment strategies in diabetic patients with symptomatic cardiovascular disease. Diab Vasc Dis Res. 2013 May;10(3):277-86. doi: 10.1177/1479164112465212. Epub 2013 Jan 3.

Jimenez JG, Rosen JB, Pirags V, Massaad R, Hanson ME, Brudi P, Triscari J. The efficacy and safety of ezetimibe/simvastatin combination compared with intensified lipid-lowering treatment strategies in diabetic subjects with and without metabolic syndrome. Diabetes Obes Metab. 2013

Jun;15(6):513-22. doi: 10.1111/dom.12059. Epub 2013 Jan 25.

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Health Authority:	United States: Food and Drug Administration

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