A Study to Evaluate MK1903 in Patients With Dyslipidemia (MK1903-004)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

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

ClinicalTrials.gov Identifier:
NCT00847197

First received: February 18, 2009
Last updated: November 19, 2015
Last verified: November 2015
History of Changes

Purpose

This study will evaluate the lipid-modifying effect and tolerability of MK1903 when compared to placebo in patients with dyslipidemia who are not on a statin or other lipid-modifying therapy.

Condition	Intervention	Phase
Dyslipidemia	Drug: MK1903 Drug: Comparator: Placebo	Phase 2

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

Official Title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Lipid-Modifying Effect and Tolerability of MK1903 in Patients With Dyslipidemia

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

Primary Outcome Measures:

- Percent Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) (mg/dL) [Time Frame: Baseline and Week 4] [Designated as safety issue: No]
- Percent Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) (mg/dL) [Time Frame: Baseline and Week 4] [Designated as safety issue: No]

Secondary Outcome Measures:

- Percent Change From Baseline in Triglycerides (mg/dL) [Time Frame: Baseline and 4 Weeks] [Designated as safety issue: No]

Enrollment:	191
Study Start Date:	June 2008
Study Completion Date:	September 2009
Primary Completion Date:	September 2009 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: 1 MK1903	Drug: MK1903 Three 50 mg capsules MK1903 by mouth every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
Placebo Comparator: 2 Placebo to MK1903	Drug: Comparator: Placebo Three 50 mg capsules placebo to MK1903 every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.

Eligibility

Ages Eligible for Study:	18 Years to 70 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Participant is not on a statin or other lipid-modifying therapy
- Low or moderate risk participant
- Male participants, and female participants not of reproductive potential

Exclusion Criteria:

- Female participant of reproductive potential
- Participant is pregnant, breastfeeding, or expecting to conceive during the study
- Participant has history of cancer within 5 years of study (except certain types of skin and cervical cancer)
- Participant is a user of recreational or illicit drugs or has a recent history of drug and/or alcohol abuse
- Participant has donated or received blood within 8 weeks of study start or intends to give/receive blood during the study
- Participant consumes more than 3 alcoholic drinks per day or more than 14 alcoholic drinks per week
- Participant is currently experiencing menopausal hot flashes
- Participant currently engages in vigorous exercise or an aggressive diet regimen
- Participant is at high risk for heart conditions
- Participant has Type 1 or Type 2 diabetes mellitus
- Participant has poorly controlled cardiac arrhythmias
- Participant has a history of stroke or other hemorrhage
- Participant has poorly controlled high blood pressure
- Participant has a thyroid condition or other endocrine/metabolic disease that would affect serum lipids
- Participant has a disease of the kidney or liver
- Participant has an ulcer within 3 months of screening
- Participant is Human Immunodeficiency Virus (HIV) positive
- Participant is taking cyclical hormonal contraceptives or non-continuous hormone replacement therapy
- Participant is taking or has taken an Organic Anion Transporter (OAT1/3) inhibitor/substrate within 3 days of screening
- Participant has taken an anti-obesity medication within 3 months of screening
- Participant is taking coumarins
- Participant is taking Non-steroidal Anti-inflammatory Drugs (NSAIDs) (acetaminophen and Cyclooxygenase-2 (COX-2) inhibitors are allowed)
- Participant is taking more than 100 mg aspirin per day
- Participant is being treated with oral, intravenous, or injected corticosteroids or anabolic agents

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: NCT00847197

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Monitor Merck Sharp & Dohme Corp.

More Information

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00847197 History of Changes
Other Study ID Numbers:	1903-004 2009_542
Study First Received:	February 18, 2009
Results First Received:	August 27, 2010
Last Updated:	November 19, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:
Dyslipidemias
Lipid Metabolism Disorders
Metabolic Diseases

ClinicalTrials.gov processed this record on May 08, 2016

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Results First Received: August 27, 2010

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Dyslipidemia
Interventions:	Drug: MK1903 Drug: Comparator: Placebo

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
Participants were recruited at 26 sites in 8 different countries from February 2009 to August 2009.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Participants had a 2-week placebo run-in period prior to randomization. 402 participants were screened of which 211 participants were excluded (194 participants did not meet inclusion criteria, 15 participants withdrew, 1 participant was lost to follow-up and 1 participant had an adverse event).

Reporting Groups

	Description
MK1903	Three 50 mg capsules MK1903 by mouth every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
Placebo	Three 50 mg capsules placebo to MK1903 every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.

Participant Flow: Overall Study

	MK1903	Placebo
STARTED	**116**	**75**
COMPLETED	**92**	**70**
NOT COMPLETED	**24**	**5**
Adverse Event	**21**	**3**
Protocol Violation	**0**	**1**
Withdrawal by Subject	**3**	**1**

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
MK1903	Three 50 mg capsules MK1903 by mouth every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
Placebo	Three 50 mg capsules placebo to MK1903 every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
Total	Total of all reporting groups

Baseline Measures

	MK1903	Placebo	Total
Number of Participants [units: participants]	**116**	**75**	**191**
Age [units: years] Mean (Standard Deviation)	**52.6 (10.4)**	**50.9 (11.1)**	**51.9 (10.7)**
Gender [units: participants]			
Female	**45**	**28**	**73**
Male	**71**	**47**	**118**

Region [1] [units: participants]			
United States	**56**	**38**	**94**
Ex-United States	**60**	**37**	**97**
Body Mass Index (BMI) Category [units: participants]			
< 25	**20**	**14**	**34**
25 - 30	**65**	**42**	**107**
31 - 39	**28**	**17**	**45**
=> 40	**3**	**2**	**5**
Coronary Heart Disease (CHD) Risk Category [units: Participants]			
Low Risk	**90**	**59**	**149**
Multiple Risk	**26**	**16**	**42**
Prior Niacin History [units: Participants]			
Yes	**10**	**11**	**21**
No	**106**	**64**	**170**
Glycemic Status [units: Participants]			
Normal (< 100 mg/dL)	**79**	**53**	**132**
Impaired Fasting Glucose (≥ 100 & ≤ 125 mg/dL)	**36**	**21**	**57**
Others (> 125 mg/dL)	**1**	**1**	**2**
Weight [units: Kilogram] Mean (Standard Deviation)	**81.9 (17.9)**	**81.6 (17.5)**	**81.7 (17.7)**
Height [units: Centimeter] Mean (Standard Deviation)	**168.3 (10.5)**	**167.9 (10.2)**	**168.2 (10.3)**
Body Mass Index [units: kg/m^2] Mean (Standard Deviation)	**28.7 (5.0)**	**28.7 (4.5)**	**28.7 (4.8)**
Systolic Blood Pressure [units: mm Hg] Mean (Standard Deviation)	**122.9 (13.6)**	**122.3 (13.5)**	**122.7 (13.5)**
Diastolic Blood Pressure [units: mm Hg] Mean (Standard Deviation)	**77.9 (8.9)**	**77.1 (9.0)**	**77.6 (8.9)**
Pulse [units: beats/minute] Mean (Standard Deviation)	**67.8 (8.8)**	**68.5 (8.9)**	**68.1 (8.8)**

[1] Ex-United States: Malaysia, Canada, Peru, Philipines, Colombia, Sweden, Finland

Outcome Measures

Hide All Outcome Measures

1. Primary: Percent Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) (mg/dL) [Time Frame: Baseline and Week 4]

Measure Type	Primary
Measure Title	Percent Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) (mg/dL)
Measure Description	No text entered.
Time Frame	Baseline and Week 4
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.
The Full Analysis Set (FAS) population served as the primary population for the analysis of efficacy data. FAS is a subset of all randomized participants with following reasons for exclusion: 1. failure to receive at least 1 dose of study treatment 2. lack of any post-randomization endpoint data subsequent to at least 1 dose of study treatment.

Reporting Groups

	Description
MK1903	Three 50 mg capsules MK1903 by mouth every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
Placebo	Three 50 mg capsules placebo to MK1903 every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.

Measured Values

	MK1903	**Placebo**
Number of Participants Analyzed [units: participants]	**112**	**75**
Percent Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) (mg/dL) [units: Percent Change] Mean (Standard Deviation)	**-0.3 (16.3)**	**-1.5 (12.9)**

Statistical Analysis 1 for Percent Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) (mg/dL)

Groups [1]	All groups
Method [2]	Mixed Models Analysis
P Value [3]	0.926
Mean Difference (Final Values) [4]	0.2
Standard Error of the mean	(2.1)
95% Confidence Interval	-3.9 to 4.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For the analysis of percent change from baseline in LDL-C at study endpoint, a Longitudinal Analysis of Covariance (ANCOVA) method was used. The repeated measures model included terms for treatment, time (Day 15, 29), and the interaction of time-by-

	treatment. The analysis model also adjusted for baseline, baseline-by-time interaction, region and gender.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	The test for the treatment difference in terms of percentage change from baseline to a given time point was done using the contrast statement.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The significance test was 2-tailed with α=0.05.
[4]	Other relevant estimation information:
	No text entered.

2. Primary: Percent Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) (mg/dL) [Time Frame: Baseline and Week 4]

Measure Type	Primary
Measure Title	Percent Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) (mg/dL)
Measure Description	No text entered.
Time Frame	Baseline and Week 4
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.
The Full Analysis Set (FAS) population served as the primary population for the analysis of efficacy data. FAS is a subset of all randomized participants with following reasons for exclusion: 1. failure to receive at least 1 dose of study treatment 2. lack of any post-randomization endpoint data subsequent to at least 1 dose of study treatment.

Reporting Groups

	Description
MK1903	Three 50 mg capsules MK1903 by mouth every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
Placebo	Three 50 mg capsules placebo to MK1903 every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.

Measured Values

	MK1903	**Placebo**
Number of Participants Analyzed [units: participants]	**112**	**75**
Percent Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) (mg/dL) [units: Percent Change] Mean (Standard Deviation)	**6.0 (13.0)**	**0.7 (11.7)**

Statistical Analysis 1 for Percent Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) (mg/dL)

Groups [1]	All groups
[2]	Mixed Models Analysis

Method	
P Value [3]	0.013
Mean Difference (Final Values) [4]	4.6
Standard Error of the mean	(1.8)
95% Confidence Interval	1.0 to 8.1

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For the analysis of percent change from baseline in LDL-C at study endpoint, a Longitudinal Analysis of Covariance (ANCOVA) method was used. The repeated measures model included terms for treatment, time (Day 15, 29), and the interaction of time-by-treatment. The analysis model also adjusted for baseline, baseline-by-time interaction, region and gender.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	The test for the treatment difference in terms of percentage change from baseline to a given time point was done using the contrast statement.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The significance test was 2-tailed with α=0.05.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: Percent Change From Baseline in Triglycerides (mg/dL) [Time Frame: Baseline and 4 Weeks]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Triglycerides (mg/dL)
Measure Description	No text entered.
Time Frame	Baseline and 4 Weeks
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.
The Full Analysis Set (FAS) population served as the primary population for the analysis of efficacy data. FAS is a subset of all randomized participants with following reasons for exclusion: 1. failure to receive at least 1 dose of study treatment 2. lack of any post-randomization endpoint data subsequent to at least 1 dose of study treatment.

Reporting Groups

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Measured Values

	MK1903	**Placebo**
Number of Participants Analyzed		

[units: participants]	**112**	**75**
Percent Change From Baseline in Triglycerides (mg/dL) **[units: Percent Change]** **Mean (Standard Deviation)**	**-13.2 (32.7)**	**-2.0 (39.5)**

Statistical Analysis 1 for Percent Change From Baseline in Triglycerides (mg/dL)

Groups [1]	All groups
Method [2]	Wilcoxon's Rank Sum Test
P Value [3]	0.02
Median Difference (Final Values) [4]	-10.3
Standard Error of the mean	(8.6)
95% Confidence Interval	-18.9 to -1.9

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Triglycerides was analyzed by non-parametric methods with terms for treatment, gender and region. Specifically, the analysis of variance (ANOVA) model was applied to the Tukey's normal scores of the percent change from baseline. The estimate of the difference in medians between MK1903 and the placebo groups utilizing the Hodges-Lehmann estimate and a distribution-free 95% CI for the difference based on Wilcoxon's rank sum test was provided.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	The significance test was 2-tailed with α=0.05.
[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	Reported Adverse Event (AE) data were collected from 6-Feb-09 to 5-Oct-09.
Additional Description	AE information was collected by continuous monitoring of participant's labs and clinical symptoms during the course of the study. AEs were usually reported during routine clinic visits and the 14-day telephone contact conducted after the participant's last visit and the expected date of Visit 4 for discontinued participants.

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	Description
MK1903	Three 50 mg capsules MK1903 by mouth every 8 hours for 4 weeks. All participants will receive placebo for a 2 week run-in period.
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Serious Adverse Events

	MK1903	Placebo
Total, serious adverse events		
# participants affected / at risk	**0/116 (0.00%)**	**0/75 (0.00%)**

Other Adverse Events

Hide Other Adverse Events

Time Frame	Reported Adverse Event (AE) data were collected from 6-Feb-09 to 5-Oct-09.
Additional Description	AE information was collected by continuous monitoring of participant's labs and clinical symptoms during the course of the study. AEs were usually reported during routine clinic visits and the 14-day telephone contact conducted after the participant's last visit and the expected date of Visit 4 for discontinued participants.

Frequency Threshold

Threshold above which other adverse events are reported	2%

Reporting Groups

	Description
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Other Adverse Events

	MK1903	Placebo
Total, other (not including serious) adverse events		
# participants affected / at risk	**76/116 (65.52%)**	**26/75 (34.67%)**
Eye disorders		
Eye disorders † 1		
# participants affected / at risk	**1/116 (0.86%)**	**2/75 (2.67%)**
Gastrointestinal disorders		
Gastrointestinal disorders † 1		
# participants affected / at risk	**3/116 (2.59%)**	**3/75 (4.00%)**
General disorders		
General disorders and administration site conditions † 1		
# participants affected / at risk	**0/116 (0.00%)**	**4/75 (5.33%)**
Infections and infestations		
Infections and infestations † 1		
# participants affected / at risk	**5/116 (4.31%)**	**4/75 (5.33%)**
Injury, poisoning and procedural complications		

Injury, poisoning and procedural complications † 1		
# participants affected / at risk	**5/116 (4.31%)**	**3/75 (4.00%)**
Investigations		
Investigations † 1		
# participants affected / at risk	**3/116 (2.59%)**	**1/75 (1.33%)**
Musculoskeletal and connective tissue disorders		
Musculoskeletal and connective tissue disorders † 1		
# participants affected / at risk	**4/116 (3.45%)**	**4/75 (5.33%)**
Nervous system disorders		
Nervous system disorders † 1		
# participants affected / at risk	**18/116 (15.52%)**	**5/75 (6.67%)**
Respiratory, thoracic and mediastinal disorders		
Respiratory, thoracic and mediastinal disorders † 1		
# participants affected / at risk	**5/116 (4.31%)**	**0/75 (0.00%)**
Skin and subcutaneous tissue disorders		
Skin and subcutaneous tissue disorders † 1		
# participants affected / at risk	**32/116 (27.59%)**	**2/75 (2.67%)**
Vascular disorders		
Vascular disorders † 1		
# participants affected / at risk	**42/116 (36.21%)**	**8/75 (10.67%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (12.0)

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:** Merck agreements may vary with individual investigators, but will not prohibit any investigator from publishing. Merck supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

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