Carotid IMT (Intima Media Thickening) Study (0524A-041)(TERMINATED) (ACHIEVE)

This study has been terminated.

Sponsor:
Merck Sharp & Dohme Corp.

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

ClinicalTrials.gov Identifier:
NCT00384293

First received: October 3, 2006
Last updated: September 28, 2015
Last verified: September 2015
History of Changes

Purpose

This is a 105-week clinical study in patients with heterozygous familial hypercholesterolemia on intensive Low Density Lipoprotein-cholesterol (LDL-C) lowering therapy intended to assess the affects of MK0524A on carotid intima media thickening using ultrasound compared to patients taking placebo. There will be 12 scheduled clinic visits involving review of medical history, physical exam, vital signs, laboratory testing, ultrasound imaging, and electrocardiograms.

Condition	Intervention	Phase
Hypercholesterolemia, Familial	Drug: Comparator: niacin (+) laropiprant (MK0524A) Drug: Comparator: placebo	Phase 3

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 Worldwide, Double-Blind, Randomized, Placebo-Controlled Study of MK0524A 2g Coadministered With Intensive LDL-C Lowering Therapy Compared to Intensive LDL-C Lowering Therapy Alone on Carotid Artery Intima Media Thickening (cIMT) in Patients With Heterozygous Familial Hypercholesterolemia (heFH)

Resource links provided by NLM:

Genetics Home Reference related topics: Chanarin-Dorfman syndrome cholesteryl ester storage disease hypercholesterolemia

MedlinePlus related topics: Cholesterol

Drug Information available for: Niacin

Genetic and Rare Diseases Information Center resources: Hyperlipoproteinemia Type 2

U.S. FDA Resources

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

Primary Outcome Measures:

- Change in Mean Carotid Intima Media Thickness [Time Frame: after 96 weeks of postrandomization treatment] [Designated as safety issue: No]

  change in mean carotid intima media thickness defined as a composite measure of the left and right common, bulb, and internal carotid artery.

Secondary Outcome Measures:

- Change in Lipid Profile [Time Frame: after 96 weeks of postrandomization treatment] [Designated as safety issue: No]

Enrollment:	937
Study Start Date:	September 2006
Study Completion Date:	August 2008
Primary Completion Date:	August 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: 1 MK0524A	Drug: Comparator: niacin (+) laropiprant (MK0524A) niacin (+) laropiprant (2 g) po qd. Other Name: MK0524A
Placebo Comparator: 2 placebo	Drug: Comparator: placebo niacin (+) laropiprant (2 g) placebo po qd.

Eligibility

Ages Eligible for Study:	18 Years to 70 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	Yes

Criteria

Inclusion Criteria:

- Patients who are 18 to 70 years of age with Heterozygous Familial Hypercholesterolemia and a LDL-C greater than or equal to 100mg/dL and triglycerides less than or equal to 400mg/dL at Visit 1 while on a stable dose of intensive LDL-C lowering therapy

Exclusion Criteria:

- A condition which, in the opinion of the investigator, might pose a risk to the patient or interfere with participating in the study
- Patients with less than 80% drug study compliance
- Patients with chronic medical conditions known to influence serum lipids or lipoproteins or significantly affect the ultrasound acoustic window
- Patients with unstable dose of medications
- Pregnant or lactating women, or women intending to become pregnant are excluded
- Patient with diabetes mellitus that is poorly controlled, or is taking new or recently adjusted antidiabetic pharmacotherapy (with the exception of +/- 10 units of insulin)
- Patients with the following conditions: high grade stenosis (greater than 75%) of the carotid artery, chronic heart failure, uncontrolled/unstable cardiac arrhythmias, unstable hypertension, active or chronic hepatobiliary or hepatic disease, HIV positive, episode of gout (within 1 year)

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: NCT00384293

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:	NCT00384293 History of Changes
Other Study ID Numbers:	0524A-041 2006_506
Study First Received:	October 3, 2006
Results First Received:	July 23, 2009
Last Updated:	September 28, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Hypercholesterolemia	Hyperlipoproteinemias
Hyperlipoproteinemia Type II	Lipid Metabolism Disorders
Dyslipidemias	Lipid Metabolism, Inborn Errors
Genetic Diseases, Inborn	Metabolic Diseases
Hyperlipidemias	Metabolism, Inborn Errors

ClinicalTrials.gov processed this record on April 13, 2016

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Results First Received: July 23, 2009

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:	Hypercholesterolemia, Familial
Interventions:	Drug: Comparator: niacin (+) laropiprant (MK0524A) 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
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
There was an MK0524A active run-in period prior to randomization. Per protocol, patients were scheduled to receive MK0524A 1g orally once daily for 4 weeks. The MK0524A dose was then increased to 2g (2x 1g tablets), once daily, for an additional 4 weeks prior to randomization.

Reporting Groups

	Description
MK0524A Active Run-In Period	Patients who received MK0524A during active run-in (Visit 2). Per protocol, patients were scheduled to receive MK0524A 1g orally once daily for 4 weeks. The MK0524A dose was then increased to 2g (2x 1g tablets), once daily, at Visit 3 for an additional 4 weeks prior to randomization.
MK0524A, 2 g (Postrandomization Period)	Patients who were randomized to MK0524A, 2 g (oral administration) once daily.
Placebo (Postrandomization Period)	Patients who were randomized to placebo

Participant Flow for 2 periods

Period 1: MK0524A Active Run-In, Pre-randomization

	MK0524A Active Run-In Period	MK0524A, 2 g (Postrandomization Period)	Placebo (Postrandomization Period)
STARTED	**937**	**0**	**0**
Entered Active run-in, MK0524A 1 g	**937** [1]	**0**	**0**
MK0524A Dose Increased to 2 g	**813** [2]	**0**	**0**
COMPLETED	**433**	**0**	**0**
NOT COMPLETED	**504**	**0**	**0**
Adverse Event	**120**	**0**	**0**
Lost to Follow-up	**1**	**0**	**0**
Withdrawal by Subject	**24**	**0**	**0**
Not cIMT eligible at Visit 3	**340**	**0**	**0**
Trial Termination	**16**	**0**	**0**
Certified Sonographer Not Available	**2**	**0**	**0**
Patient Unable to Complete cIMT Scan	**1**	**0**	**0**

[1] Entered active run-in period and received MK0524A 1 g
[2] MK0524A dose increased to 2 g in active run-in period

Period 2: Post-randomization Period

	MK0524A Active Run-In Period	MK0524A, 2 g (Postrandomization Period)	Placebo (Postrandomization Period)
STARTED	**0**	**214**	**219**
Received ≥1 Dose of MK0524A Study Drug	**0**	**214** [1]	**218**
COMPLETED	**0**	**0**	**0**
NOT COMPLETED	**0**	**214**	**219**
Adverse Event	**0**	**23**	**7**
Lost to Follow-up	**0**	**2**	**1**
Protocol Violation	**0**	**1**	**0**
Withdrawal by Subject	**0**	**8**	**6**
Trial Termination	**0**	**180**	**204**

Patient Randomized in Error	**0**	**0**	**1**

[1] Received at least one dose of randomized study drug (All Patients as Treated Population)

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
MK0524A, 2 g (Postrandomization Period)	Patients who were randomized to MK0524A, 2 g (oral administration) once daily.
Placebo (Postrandomization Period)	Patients who were randomized to placebo
Total	Total of all reporting groups

Baseline Measures

	MK0524A, 2 g (Postrandomization Period)	**Placebo (Postrandomization Period)**	**Total**
Number of Participants [units: participants]	**214**	**218**	**432**
Age [units: years] Mean (Standard Deviation)	**53.1 (8.94)**	**54.5 (8.22)**	**53.8 (8.60)**
Gender [units: participants]			
Female	**76**	**82**	**158**
Male	**138**	**136**	**274**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change in Mean Carotid Intima Media Thickness [Time Frame: after 96 weeks of postrandomization treatment]

Measure Type	Primary
Measure Title	Change in Mean Carotid Intima Media Thickness
Measure Description	change in mean carotid intima media thickness defined as a composite measure of the left and right common, bulb, and internal carotid artery.
Time Frame	after 96 weeks of postrandomization treatment
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.
study prematurely terminated, no efficacy analyses were performed

Reporting Groups

	Description
MK0524A Active Run-In Period	Patients who received MK0524A during active run-in (Visit 2). Per protocol, patients were scheduled to receive MK0524A 1g orally once daily for 4 weeks. The MK0524A dose was then increased to 2g (2x 1g tablets), once daily, at Visit 3 for an additional 4 weeks prior to randomization.
MK0524A, 2 g (Postrandomization Period)	Patients who were randomized to MK0524A, 2 g (oral administration) once daily.
Placebo (Postrandomization Period)	Patients who were randomized to placebo

Measured Values

	MK0524A Active Run-In Period	MK0524A, 2 g (Postrandomization Period)	Placebo (Postrandomization Period)
Number of Participants Analyzed [units: participants]	**0**	**0**	**0**
Change in Mean Carotid Intima Media Thickness			

No statistical analysis provided for Change in Mean Carotid Intima Media Thickness

2. Secondary: Change in Lipid Profile [Time Frame: after 96 weeks of postrandomization treatment]

Measure Type	Secondary
Measure Title	Change in Lipid Profile
Measure Description	No text entered.
Time Frame	after 96 weeks of postrandomization treatment
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.
study prematurely terminated, no efficacy analyses were performed

Reporting Groups

	Description
MK0524A Active Run-In Period	Patients who received MK0524A during active run-in (Visit 2). Per protocol, patients were scheduled to receive MK0524A 1g orally once daily for 4 weeks. The MK0524A dose was then increased to 2g (2x 1g tablets), once daily, at Visit 3 for an additional 4 weeks prior to randomization.
MK0524A, 2 g (Postrandomization Period)	Patients who were randomized to MK0524A, 2 g (oral administration) once daily.
Placebo (Postrandomization Period)	Patients who were randomized to placebo

Measured Values

	MK0524A Active Run-In Period	MK0524A, 2 g (Postrandomization Period)	Placebo (Postrandomization Period)
Number of Participants Analyzed [units: participants]	0	0	0
Change in Lipid Profile			

No statistical analysis provided for Change in Lipid Profile

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
MK0524A Active Run-In Period	Patients who received MK0524A during active run-in (Visit 2). Per protocol, patients were scheduled to receive MK0524A 1g orally once daily for 4 weeks. The MK0524A dose was then increased to 2g (2x 1g tablets), once daily, at Visit 3 for an additional 4 weeks prior to randomization.
MK0524A, 2 g (Postrandomization Period)	Patients who were randomized to MK0524A, 2 g (oral administration) once daily.
Placebo (Postrandomization Period)	Patients who were randomized to placebo

Serious Adverse Events

	MK0524A Active Run-In Period	MK0524A, 2 g (Postrandomization Period)	Placebo (Postrandomization Period)
Total, serious adverse events			
# participants affected	10	5	8
Cardiac disorders			
Acute coronary syndrome * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Acute myocardial infarction * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Acute pectoris * 1			
# participants affected / at risk	0/937 (0.00%)	1/214 (0.47%)	0/218 (0.00%)
Angina unstable * 1			
# participants affected / at risk	1/937 (0.11%)	1/214 (0.47%)	1/218 (0.46%)
Atrial fibrillation * 1			

# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Myocardial infarction * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Gastrointestinal disorders			
Pancreatitis * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Constipation * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
General disorders			
Pyrexia * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Hepatobiliary disorders			
Hepatitis * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Immune system disorders			
Anaphylactic shock * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Infections and infestations			
Diverticulitis * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Staphylococcal sepsis * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Injury, poisoning and procedural complications			
Limb injury * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Metabolism and nutrition disorders			
Hypoglycaemia * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome * 1			
# participants affected / at risk	0/937 (0.00%)	2/214 (0.93%)	0/218 (0.00%)
Intervertebral disc protrusion * 1			
# participants affected / at risk	0/937 (0.00%)	1/214 (0.47%)	1/218 (0.46%)
Osteoarthritis * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Toe deformity * 1			
# participants affected / at risk	0/937 (0.00%)	0/214 (0.00%)	1/218 (0.46%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer metastatic * 1			
# participants affected / at risk	1/937 (0.11%)	0/214 (0.00%)	0/218 (0.00%)

Papillary thyroid cancer * 1			
# participants affected / at risk	**1/937 (0.11%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Pregnancy, puerperium and perinatal conditions			
Pregnancy * 1			
# participants affected / at risk	**0/937 (0.00%)**	**0/214 (0.00%)**	**1/218 (0.46%)**
Renal and urinary disorders			
Renal failure acute * 1			
# participants affected / at risk	**1/937 (0.11%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Reproductive system and breast disorders			
Ovarian cyst * 1			
# participants affected / at risk	**0/937 (0.00%)**	**1/214 (0.47%)**	**0/218 (0.00%)**
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism * 1			
# participants affected / at risk	**0/937 (0.00%)**	**0/214 (0.00%)**	**1/218 (0.46%)**
Vascular disorders			
Arterial stenosis * 1			
# participants affected / at risk	**1/937 (0.11%)**	**0/214 (0.00%)**	**0/218 (0.00%)**

* Events were collected by non-systematic assessment

1 Term from vocabulary, MedDRA 10.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	2%

Reporting Groups

	Description
MK0524A Active Run-In Period	Patients who received MK0524A during active run-in (Visit 2). Per protocol, patients were scheduled to receive MK0524A 1g orally once daily for 4 weeks. The MK0524A dose was then increased to 2g (2x 1g tablets), once daily, at Visit 3 for an additional 4 weeks prior to randomization.
MK0524A, 2 g (Postrandomization Period)	Patients who were randomized to MK0524A, 2 g (oral administration) once daily.
Placebo (Postrandomization Period)	Patients who were randomized to placebo

Other Adverse Events

	MK0524A Active Run-In Period	**MK0524A, 2 g (Postrandomization Period)**	**Placebo (Postrandomization Period)**

Total, other (not including serious) adverse events			
# participants affected	**395**	**74**	**54**
Gastrointestinal disorders			
Diarrhoea [*1]			
# participants affected / at risk	**20/937 (2.13%)**	**8/214 (3.74%)**	**4/218 (1.83%)**
Nausea [*1]			
# participants affected / at risk	**24/937 (2.56%)**	**5/214 (2.34%)**	**0/218 (0.00%)**
Vomiting [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**5/214 (2.34%)**	**0/218 (0.00%)**
General disorders			
Fatigue [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**6/214 (2.80%)**	**5/218 (2.29%)**
Infections and infestations			
Influenza [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**14/214 (6.54%)**	**18/218 (8.26%)**
Nasopharyngitis [*1]			
# participants affected / at risk	**23/937 (2.45%)**	**14/214 (6.54%)**	**13/218 (5.96%)**
Upper respiratory tract infection [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**4/214 (1.87%)**	**6/218 (2.75%)**
Musculoskeletal and connective tissue disorders			
Arthralgia [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**8/214 (3.74%)**	**3/218 (1.38%)**
Back pain [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**8/214 (3.74%)**	**6/218 (2.75%)**
Myalgia [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**6/214 (2.80%)**	**8/218 (3.67%)**
Pain in extremity [*1]			
# participants affected / at risk	**0/937 (0.00%)**	**2/214 (0.93%)**	**7/218 (3.21%)**
Nervous system disorders			
Headache [*1]			
# participants affected / at risk	**52/937 (5.55%)**	**10/214 (4.67%)**	**5/218 (2.29%)**
Paraesthesia [*1]			
# participants affected / at risk	**47/937 (5.02%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Burning Sensation [*1]			
# participants affected / at risk	**25/937 (2.67%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Dizziness [*1]			
# participants affected / at risk	**21/937 (2.24%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Skin and subcutaneous tissue disorders			

Pruritus [*1]			
# participants affected / at risk	**78/937 (8.32%)**	**10/214 (4.67%)**	**2/218 (0.92%)**
Erythema [*1]			
# participants affected / at risk	**23/937 (2.45%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Rash [*1]			
# participants affected / at risk	**22/937 (2.35%)**	**0/214 (0.00%)**	**0/218 (0.00%)**
Vascular disorders			
Flushing [*1]			
# participants affected / at risk	**184/937 (19.64%)**	**5/214 (2.34%)**	**0/218 (0.00%)**
Hot flush [*1]			
# participants affected / at risk	**37/937 (3.95%)**	**0/214 (0.00%)**	**0/218 (0.00%)**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 10.0

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

After a detailed review of pooled carotid IMT data from contemporary studies, the Steering Committee recommended that Merck prematurely stop the study; as designed, the study was significantly underpowered. Efficacy analyses were not performed.

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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ClinicalTrials.gov Identifier:	NCT00384293 History of Changes
Other Study ID Numbers:	0524A-041 2006_506
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