



## Clinical trial results:

### A Single Dose Study to Evaluate the Safety, Tolerability and Pharmacokinetics of ER Niacin/Laropiprant in Adolescents with Heterozygous Familial Hypercholesterolemia

#### Summary

EudraCT number	2012-001443-49
Trial protocol	GB Outside EU/EEA
Global end of trial date	13 December 2012

#### Results information

Result version number	v2 (current)
This version publication date	24 April 2016
First version publication date	13 June 2015
Version creation reason	

#### Trial information

##### Trial identification

Sponsor protocol code	0524A-158
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01583647
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000063-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	13 December 2012
Is this the analysis of the primary completion data?	No

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Global end of trial reached?	Yes
Global end of trial date	13 December 2012
Was the trial ended prematurely?	Yes

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Notes:

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**General information about the trial**

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Main objective of the trial:

To compare the pharmacokinetics of laropiprant following administration of a single dose of 1 (Panel A) and 2 (Panel B) combination tablets of MK-0524A (1000mg ER niacin/20mg laropiprant) between adolescents with heterozygous familial hypercholesterolemia and healthy adults (historical data from MK-0524A P057 and P059).

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Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

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Background therapy: -

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Evidence for comparator: -

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Actual start date of recruitment	23 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	South Africa: 3
Worldwide total number of subjects	10
EEA total number of subjects	2

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Notes:

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**Subjects enrolled per age group**

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In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	10
Adults (18-64 years)	0

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From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

MK-0524A-158 was terminated after the Phase 3 study HPS2-THRIVE (MK-0524A -042;NCT00461630) didn't meet its primary endpoint of reduction of major vascular events; there was also a significant increase in some types of non-fatal serious adverse events. MK-0524A-158 was terminated after 10 participants completed Panel A. Panel B was not conducted.

### Pre-assignment

Screening details:

The study enrolled participants 10 to 16 years of age, with a genotype-confirmed or clinical diagnosis of heterozygous hypercholesterolemia. Other inclusion and exclusion criteria applied.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

<b>Arm title</b>	MK-0524A 1 g/20 mg (Panel A)
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Arm description:

Single oral dose of 1 tablet of MK-0524A. Each tablet contained Extended Release (ER) Niacin 1g and laropirant 20 mg

Arm type	Experimental
Investigational medicinal product name	MK-0524A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose of 1 or 2 tablets of MK-0524A (1g ER niacin/20mg laropirant)

<b>Number of subjects in period 1</b>	MK-0524A 1 g/20 mg (Panel A)
Started	10
Completed	10

## Baseline characteristics

### Reporting groups

Reporting group title	MK-0524A 1 g/20 mg (Panel A)
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Reporting group description:

Single oral dose of 1 tablet of MK-0524A. Each tablet contained Extended Release (ER) Niacin 1g and laropirant 20 mg

Reporting group values	MK-0524A 1 g/20 mg (Panel A)	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	15.4		
standard deviation	± 0.8	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	5	5	

## End points

### End points reporting groups

Reporting group title	MK-0524A 1 g/20 mg (Panel A)
Reporting group description: Single oral dose of 1 tablet of MK-0524A. Each tablet contained Extended Release (ER) Niacin 1g and laropiprant 20 mg	

### Primary: Plasma Area Under the Concentration Curve from 0 to infinity (AUC<sub>0-∞</sub>) of Laropiprant

End point title	Plasma Area Under the Concentration Curve from 0 to infinity (AUC <sub>0-∞</sub> ) of Laropiprant <sup>[1]</sup>
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End point description:

The study was terminated during Panel A and the decision was made to not analyze the blood and urine pharmacokinetic samples collected during Panel A; Panel B was not conducted.

End point type	Primary
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End point timeframe:

Predose Day 1 up to 24 hours postdose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Blood and urine pharmacokinetic samples were not analyzed. No statistical analyses could be performed.

<b>End point values</b>	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[2]</sup>			
Units: h * n g /mL				
geometric mean (confidence interval 95%)	( to )			

Notes:

[2] - Blood and urine samples from Panel A were not analyzed.

### Statistical analyses

No statistical analyses for this end point

### Primary: Plasma Maximum Concentration (C<sub>max</sub>) of Laropiprant

End point title	Plasma Maximum Concentration (C <sub>max</sub> ) of Laropiprant <sup>[3]</sup>
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End point description:

The study was terminated during Panel A and the decision was made to not analyze the blood and urine pharmacokinetic samples collected during Panel A; Panel B was not conducted.

End point type	Primary
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End point timeframe:

Predose on Day 1 up to 48 hours postdose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Blood and urine pharmacokinetic samples were not analyzed. No statistical analyses could be performed.

<b>End point values</b>	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[4]</sup>			
Units: ng /mL				
geometric mean (confidence interval 95%)	( to )			

Notes:

[4] - Blood and urine pharmacokinetic samples collected during Panel A were not analyzed

## Statistical analyses

No statistical analyses for this end point

### Primary: Total urinary excretion of niacin and niacin metabolites

End point title	Total urinary excretion of niacin and niacin metabolites <sup>[5]</sup>
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End point description:

The study was terminated during Panel A and the decision was made to not analyze the blood and urine pharmacokinetic samples collected during Panel A; Panel B was not conducted.

End point type	Primary
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End point timeframe:

Predose on Day 1 up to 72 hours postdose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Blood and urine pharmacokinetic samples were not analyzed. No statistical analyses could be performed.

<b>End point values</b>	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[6]</sup>			
Units: µmol				
geometric mean (confidence interval 95%)	( to )			

Notes:

[6] - Blood and urine pharmacokinetic samples collected during Panel A were not analyzed

## Statistical analyses

No statistical analyses for this end point

### Primary: Plasma Cmax of nicotinuric acid (NUA)

End point title	Plasma Cmax of nicotinuric acid (NUA) <sup>[7]</sup>
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End point description:

The study was terminated during Panel A and the decision was made to not analyze the blood and urine pharmacokinetic samples collected during Panel A; Panel B was not conducted.

End point type	Primary
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End point timeframe:

Predose on Day 1 up to 48 hours postdose

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Blood and urine pharmacokinetic samples were not analyzed. No statistical analyses could be performed.

<b>End point values</b>	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[8]</sup>			
Units: ng /mL				
geometric mean (confidence interval 95%)	( to )			

Notes:

[8] - Blood and urine pharmacokinetic samples collected during Panel A were not analyzed

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

up to 14 days

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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### Reporting groups

Reporting group title	1 tablet of MK-0524A 1 g/20 mg
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Reporting group description:

Participants who received at least 1 dose of study drug.

Serious adverse events	1 tablet of MK-0524A 1 g/20 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	1 tablet of MK-0524A 1 g/20 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)		
Injury, poisoning and procedural complications			
Bruising of arm			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Sprain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Facial flushing			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Gastrointestinal disorders Abdominal pain lower subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Renal and urinary disorders Diuresis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Musculoskeletal and connective tissue disorders Low back pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 December 2012	MK-0524A-158 was terminated after the Phase 3 study HPS2-THRIVE (MK-0524A-042;NCT00461630) didn't meet its primary endpoint of reduction of major vascular events; there was also a significant increase in some types of non-fatal serious adverse events in the Phase 3 HPS2-THRIVE study.	-

Notes:

### Limitations and caveats

None reported