



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
-----------------------	-----------

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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 December 2012
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 December 2012
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

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).

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.

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

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

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

Arm title	MK-0524A 1 g/20 mg (Panel A)
------------------	------------------------------

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)

Number of subjects in period 1	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)
-----------------------	------------------------------

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_{0-∞}) of Laropiprant

End point title	Plasma Area Under the Concentration Curve from 0 to infinity (AUC _{0-∞}) of Laropiprant ^[1]
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
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.

End point values	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[2]			
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_{max}) of Laropiprant

End point title	Plasma Maximum Concentration (C _{max}) of Laropiprant ^[3]
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
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.

End point values	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[4]			
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 ^[5]
-----------------	---

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
----------------	---------

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.

End point values	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
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) ^[7]
-----------------	--

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
----------------	---------

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.

End point values	MK-0524A 1 g/20 mg (Panel A)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[8]			
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
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	15.1
--------------------	------

Reporting groups

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

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

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