Clinical trial results:
A Phase 2a, Randomized, Placebo-Controlled Clinical Trial to Evaluate the Efficacy, Safety and Tolerability of MK-7264 on Acute Cough in Participants with Induced Viral Upper Respiratory Tract Infection

Summary

EudraCT number	2017-000472-28
Trial protocol	GB
Global end of trial date	19 November 2018

Results information

Result version number	v1
This version publication date	27 November 2019
First version publication date	27 November 2019

Trial information

Trial identification

Sponsor protocol code	MK-7264-013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03569033
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)	No
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	19 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to evaluate the efficacy, safety, and tolerability of gefapixant (MK-7264) in adult participants with induced viral upper respiratory tract infections (URTI).

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	04 July 2018
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	United Kingdom: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	0
Adults (18-64 years)	46
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were in good general health and susceptible to human rhinovirus type 16 (HRV-16). Additional inclusion criteria applied.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Gefapixant 45 mg BID

Arm description:

Participants received a gefapixant 45 mg tablet twice daily (BID) for 7 days.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	MK-7264
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 45 mg gefapixant tablet BID for 7 days

Arm title	Placebo BID

Arm description:

Participants received a matching placebo tablet BID for 7 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One matching placebo tablet BID for 7 days

Number of subjects in period 1	Gefapixant 45 mg BID	Placebo BID
Started	23	23
Completed	23	23

Baseline characteristics

Reporting groups	
Reporting group title	Gefapixant 45 mg BID
Reporting group description:	
Participants received a gefapixant 45 mg tablet twice daily (BID) for 7 days.	
Reporting group title	Placebo BID
Reporting group description:	
Participants received a matching placebo tablet BID for 7 days.	

Reporting group values	Gefapixant 45 mg BID	Placebo BID	Total
Number of subjects	23	23	46
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	24.9	24.3	
standard deviation	± 7.4	± 5.6	-
Sex: Female, Male Units: Subjects			
Female	4	4	8
Male	19	19	38
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	21	21	42
More than one race	1	0	1
Unknown or Not Reported	0	0	0

End points

End points reporting groups	
Reporting group title	Gefapixant 45 mg BID
Reporting group description:	
Participants received a gefapixant 45 mg tablet twice daily (BID) for 7 days.	
Reporting group title	Placebo BID
Reporting group description:	
Participants received a matching placebo tablet BID for 7 days.	

Primary: Awake Coughs per Hour on Day 3	
End point title	Awake Coughs per Hour on Day 3
End point description:	
Awake cough frequency (coughs per hour) was assessed by an objective digital cough-counting device (VitaloJAK™ cough monitor) on Day 3. The analysis population for this end point included all randomized participants who received at least 1 dose of trial intervention and had confirmation of viral shedding at 72 hours post inoculation with human rhinovirus type 16 (HRV-16).	
End point type	Primary
End point timeframe:	
Day 3	

End point values	Gefapixant 45 mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: Coughs per hour				
least squares mean (confidence interval 95%)	2.38 (1.01 to 3.75)	2.70 (1.21 to 4.19)		

Statistical analyses

Statistical analysis title	Awake Coughs per Hour on Day 3
Comparison groups	Gefapixant 45 mg BID v Placebo BID
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.748
Method	Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.29
upper limit	1.66

Secondary: Change From Baseline in the Cough Severity Visual Analog Scale (VAS) Score on Day 3

End point title	Change From Baseline in the Cough Severity Visual Analog Scale (VAS) Score on Day 3

End point description:

The Cough Severity VAS was scored from 0 to 100 using a 100 mm visual analogue scale. Participants were asked to mark on a 100 mm scale between 0 (no cough) and 100 (the worst cough severity). Cough VAS was evaluated at Baseline (BL) and on Day 3. The analysis population for this end point included all randomized participants who received at least 1 dose of trial intervention and had confirmation of viral shedding at 72 hours post inoculation with HRV-16.

End point type	Secondary

End point timeframe:

Baseline and Day 3

End point values	Gefapixant 45 mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: Percent change				
least squares mean (confidence interval 95%)	6.07 (1.79 to 10.35)	5.08 (0.39 to 9.78)		

Statistical analyses

Statistical analysis title	Chg from BL in Cough Severity VAS Score on Day 3
Comparison groups	Gefapixant 45 mg BID v Placebo BID
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.754
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.33
upper limit	7.3

Secondary: Change From Baseline in the Cough Severity Diary (CSD) Score on Day 3

End point title	Change From Baseline in the Cough Severity Diary (CSD) Score on Day 3

End point description:

The CSD is a 7-item, disease-specific, patient-reported outcome measure with a recall period of "today" (the current day). The measure evaluates frequency of cough (3 items); intensity of cough (2 items); and disruption due to cough (2 items). Each item is rated on an 11-point scale, ranging from 0 to 10, with higher scores indicating greater severity. A CSD total score was calculated at Baseline (BL) and on Day 3. The analysis population for this end point included all randomized participants who received at least 1 dose of trial intervention and had confirmation of viral shedding at 72 hours post inoculation with HRV-16.

End point type	Secondary

End point timeframe:

Baseline and Day 3

End point values	Gefapixant 45 mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: Percent change				
least squares mean (confidence interval 95%)	2.71 (0.46 to 4.97)	1.91 (-0.55 to 4.38)		

Statistical analyses

Statistical analysis title	Chg from BL in CSD Score on Day 3
Comparison groups	Gefapixant 45 mg BID v Placebo BID
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.627
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	4.1

Secondary: Change From Baseline in the Leicester Cough Questionnaire (LCQ)-Acute Score on Day 3

End point title	Change From Baseline in the Leicester Cough Questionnaire (LCQ)-Acute Score on Day 3

End point description:

The LCQ-Acute is a 19-item health-related quality-of-life (HRQoL) questionnaire specific for acute cough which contains three domains (i.e., physical, psychological, and social). It is calculated as a mean score for each domain ranging from 1 to 7, and total score ranging from 3 to 21. Each item on the LCQ-acute assesses symptoms or the impact of symptoms on HRQoL in the last 24 hours using a 7-point Likert scale ranging from 1 to 7. Higher scores indicate better HRQoL. Participants' perception of their cough severity was assessed, based on the LCQ-Acute score, at Baseline (BL) and on Day 3. The analysis

population for this end point included all randomized participants who received at least 1 dose of trial intervention and had confirmation of viral shedding at 72 hours post inoculation with HRV-16.

End point type	Secondary

End point timeframe:

Baseline and Day 3

End point values	Gefapixant 45 mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: Percent change				
least squares mean (confidence interval 95%)	-0.26 (-0.51 to -0.01)	-0.35 (-0.62 to -0.08)		

Statistical analyses

Statistical analysis title	Chg from BL in LCQ-Acute Score on Day 3
Comparison groups	Gefapixant 45 mg BID v Placebo BID
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.631
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.45

Secondary: Percentage of Participants Who Experienced One or More Adverse Events (AEs)

End point title	Percentage of Participants Who Experienced One or More Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this end point included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to 21 days

End point values	Gefapixant 45 mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: Percentage of participants				
number (not applicable)	100	95.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Discontinued Treatment Due to an Adverse Event (AE)

End point title	Percentage of Participants Who Discontinued Treatment Due to an Adverse Event (AE)

End point description:

An AE is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this end point included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Day 7

End point values	Gefapixant 45 mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: Percentage of participants				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 21 days	
Adverse event reporting additional description:	
All randomized participants who received at least 1 dose of study treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	MK-7264 45 mg BID
Reporting group description:	
Participants received a gefapixant 45 mg tablet BID for 7 days.	
Reporting group title	Placebo
Reporting group description:	
Participants received a matching placebo tablet BID for 7 days.	

Serious adverse events	MK-7264 45 mg BID	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 23 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	MK-7264 45 mg BID	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)	22 / 23 (95.65%)	
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	10	0	
Hypogeusia			

subjects affected / exposed	3 / 23 (13.04%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
General disorders and administration site conditions			
Medical device site erythema			
subjects affected / exposed	16 / 23 (69.57%)	17 / 23 (73.91%)	
occurrences (all)	16	17	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	3 / 23 (13.04%)	0 / 23 (0.00%)	
occurrences (all)	4	0	
Salivary hypersecretion			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	20 / 23 (86.96%)	21 / 23 (91.30%)	
occurrences (all)	20	22	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 23 (8.70%)	1 / 23 (4.35%)	
occurrences (all)	2	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? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated because the data did not support study endpoints for acute cough, based on an interim efficacy analysis; not due to safety concerns.

Notes: