



## Clinical trial results:

### A Phase III, Double-Blind, Randomized, Placebo-Controlled Cross-Over Clinical Trial to Study the Efficacy and Safety of MK-0476 in Japanese Pediatric Subjects with Seasonal Allergic Rhinitis

#### Summary

EudraCT number	2014-004774-42
Trial protocol	Outside EU/EEA
Global end of trial date	01 September 2013

#### Results information

Result version number	v1
This version publication date	01 March 2016
First version publication date	09 July 2015

#### Trial information

##### Trial identification

Sponsor protocol code	0476-519
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01857063
WHO universal trial number (UTN)	-
Other trial identifiers	MK-0476-519: Merck protocol number

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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2013
Global end of trial reached?	Yes
Global end of trial date	01 September 2013
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

This study will evaluate the efficacy and safety of montelukast (MK-0476) in the treatment of Japanese pediatric participants with seasonal allergic rhinitis (SAR). The primary hypothesis of this study is that montelukast is superior to placebo in the treatment of nasal symptoms in SAR.

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	10 June 2013
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	Japan: 220
Worldwide total number of subjects	220
EEA total number of subjects	0

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)	68
Adolescents (12-17 years)	152
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Japanese participants aged 10 to 15 years who had allergic rhinitis symptoms (Japanese Cedar [JC] pollinosis) were screened for this study.

### Period 1

Period 1 title	Treatment Period 1 (7 days)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Montelukast/Placebo

Arm description:

Participants receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 1 and receive placebo chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Arm type	Experimental
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast 5 mg chewable tablets orally once daily for 7 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo chewable tablets orally once daily for 7 days

<b>Arm title</b>	Placebo/Montelukast
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Arm description:

Participants receive placebo chewable tablets for 7 days during Treatment Period 1 and receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

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

Dosage and administration details:

Placebo chewable tablets orally once daily for 7 days

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast 5 mg chewable tablets orally once daily for 7 days

<b>Number of subjects in period 1</b>	Montelukast/Placebo	Placebo/Montelukast
Started	110	110
Completed	108	106
Not completed	2	4
Consent withdrawn by subject	1	3
Physician decision	1	-
Adverse event, non-fatal	-	1

## Period 2

Period 2 title	Treatment Period 2 (7 days)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo/Montelukast

Arm description:

Participants receive placebo chewable tablets for 7 days during Treatment Period 1 and receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

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

Dosage and administration details:

Placebo chewable tablets orally once daily for 7 days

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast 5 mg chewable tablets orally once daily for 7 days

<b>Arm title</b>	Montelukast/Placebo
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Arm description:

Participants receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 1 and receive placebo chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Arm type	Experimental
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast 5 mg chewable tablets orally once daily for 7 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo chewable tablets orally once daily for 7 days

<b>Number of subjects in period 2</b>	Placebo/Montelukast	Montelukast/Placebo
Started	106	108
Completed	104	104
Not completed	2	4
Physician decision	1	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	2

## Baseline characteristics

### Reporting groups

Reporting group title	Montelukast/Placebo
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Reporting group description:

Participants receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 1 and receive placebo chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Reporting group title	Placebo/Montelukast
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Reporting group description:

Participants receive placebo chewable tablets for 7 days during Treatment Period 1 and receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Reporting group values	Montelukast/Placebo	Placebo/Montelukast	Total
Number of subjects	110	110	220
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	31	37	68
Adolescents (12-17 years)	79	73	152
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	12.6	12.4	
standard deviation	± 1.5	± 1.6	-
Gender, Male/Female Units: participants			
Female	55	51	106
Male	55	59	114

## End points

### End points reporting groups

Reporting group title	Montelukast/Placebo
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Reporting group description:

Participants receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 1 and receive placebo chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Reporting group title	Placebo/Montelukast
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Reporting group description:

Participants receive placebo chewable tablets for 7 days during Treatment Period 1 and receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Reporting group title	Placebo/Montelukast
-----------------------	---------------------

Reporting group description:

Participants receive placebo chewable tablets for 7 days during Treatment Period 1 and receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Reporting group title	Montelukast/Placebo
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Reporting group description:

Participants receive montelukast 5 mg chewable tablets for 7 days during Treatment Period 1 and receive placebo chewable tablets for 7 days during Treatment Period 2. There is a 7-day washout period between Treatment Periods 1 and 2.

Subject analysis set title	Montelukast - Efficacy
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants receive montelukast 5 mg for 7 days, regardless of sequence. Efficacy analysis set includes all randomized participants who took at least one dose of study drug (montelukast), and had a baseline assessment and at least one post-baseline assessment in a treatment period.

Subject analysis set title	Montelukast - Safety
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Participants receive montelukast 5 mg for 7 days, regardless of sequence. Safety analysis set includes all randomized participants who received at least one dose of study drug (montelukast). Adverse events (AEs) are reported by study drug (montelukast) taken at time of the event.

Subject analysis set title	Placebo - Safety
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Participants receive placebo for 7 days, regardless of sequence. Safety analysis set includes all randomized participants who received at least one dose of study drug (placebo for montelukast). Adverse events (AEs) are reported by study drug (placebo for montelukast) taken at time of the event.

Subject analysis set title	Placebo - Efficacy
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants receive placebo for 7 days, regardless of sequence. Efficacy analysis set includes all randomized participants who took at least one dose of study drug (placebo for montelukast), and had a baseline assessment and at least one post-baseline assessment in a treatment period.

### Primary: Change from Baseline in Total Nasal Symptom Score (TNSS) Averaged During 3 Hours of Exposure

End point title	Change from Baseline in Total Nasal Symptom Score (TNSS) Averaged During 3 Hours of Exposure
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End point description:

The TNSS is the sum of the three nasal symptom scores for nasal congestion, nasal discharge and sneezing. Participants completed a questionnaire about their nasal symptoms. Scores ranged from 0 to 4 for each of the three nasal symptoms, with a total possible score ranging from 0 to 12 and a higher

score indicating more severe nasal symptoms. The Baseline TNSS was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline TNSS was assessed on Day 7 of a treatment period during 3 hours of exposure to JC pollen in the chamber room, as an average of measurements at 30, 60, 90, 120, 150 and 180 minutes. Analysis was done by study drug as taken.

End point type	Primary
End point timeframe:	
Baseline and after 3 hours of pollen exposure on Day 7 of each treatment period	

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)	1.17 (1.03 to 1.31)	1.18 (1.04 to 1.32)		

## Statistical analyses

<b>Statistical analysis title</b>	Difference in least squares (LS) means
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Statistical analysis description:

Difference in LS means of change from Baseline in TNSS averaged during 3 hours of exposure - Montelukast vs. Placebo. Based on longitudinal data analysis (LDA) model with Baseline TNSS as a covariate, sequence, treatment and period as fixed effects and participants as a random effect.

Comparison groups	Montelukast - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.913 <sup>[1]</sup>
Method	Longitudinal Data Analysis (LDA)
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.1

Notes:

[1] - LDA model with baseline TNSS as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

## Primary: Percentage of Participants Who Experience at Least One Adverse Event

End point title	Percentage of Participants Who Experience at Least One Adverse Event <sup>[2]</sup>
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End point description:

An adverse event is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Participants were monitored for occurrence adverse events for up to 14 days after last dose of study drug. Analysis was done by study drug as taken.

End point type	Primary
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End point timeframe:

Up to 5 weeks

Notes:

[2] - 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: No statistical analysis was planned for this end point.

<b>End point values</b>	Montelukast - Safety	Placebo - Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	216	218		
Units: percentage of participants				
number (not applicable)	22	36		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Weighted TNSS Averaged During 3 Hours of Exposure

End point title	Change from Baseline in Weighted TNSS Averaged During 3 Hours of Exposure
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End point description:

TNSS was weighted as 2:1:1 for nasal congestion, nasal discharge and sneezing. The Weighted TNSS ranged from 0 to 16, with a higher score indicating more severe weighted total nasal symptoms. The Baseline Weighted TNSS was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline TNSS was assessed on Day 7 of a treatment period during 3 hours of exposure to JC pollen in the chamber room, as an average of measurements at 30, 60, 90, 120, 150 and 180 minutes. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and after 3 hours of pollen exposure on Day 7 of each treatment period

<b>End point values</b>	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)	1.85 (1.63 to 2.07)	1.86 (1.63 to 2.08)		

### Statistical analyses

<b>Statistical analysis title</b>	Difference in LS means
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Statistical analysis description:

Difference in LS means for change from Baseline in weighted TNSS averaged during 3 hours of exposure - Montelukast vs. Placebo. Based on LDA model with Baseline weighted TNSS as a covariate, sequence, treatment and period as fixed effects and participants as a random effect.

Comparison groups	Montelukast - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.953 <sup>[3]</sup>
Method	LDA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.16

Notes:

[3] - LDA model with baseline Weighted TNSS as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

### Secondary: Change from Baseline in Nasal Congestion Score Averaged During 3 Hours of Exposure

End point title	Change from Baseline in Nasal Congestion Score Averaged During 3 Hours of Exposure
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End point description:

The Nasal Congestion Score was assessed as 0 = No symptoms of nasal congestion to 4 = Completely obstructed all day, with a possible Nasal Congestion Score ranging from 0 to 4 and a higher score indicating more severe nasal congestion. The Baseline Nasal Congestion Score was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline Nasal Congestion Score was assessed on Day 7 of a treatment period during 3 hours of exposure to JC pollen in the chamber room, as an average of measurements at 30, 60, 90, 120, 150 and 180 minutes. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and after 3 hours of pollen exposure on Day 7 of each treatment period

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)	0.68 (0.59 to 0.76)	0.68 (0.59 to 0.76)		

### Statistical analyses

Statistical analysis title	Difference in LS means
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Statistical analysis description:

Difference in LS means of change from Baseline in Nasal Congestion Score averaged during 3 hours of exposures - Montelukast vs. Placebo. Based on LDA model with Baseline Nasal Congestion Score as a covariate, sequence, treatment and period as fixed effects and participants as a random effect.

Comparison groups	Montelukast - Efficacy v Placebo - Efficacy
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Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.974 [4]
Method	LDA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.07

Notes:

[4] - LDA model with baseline nasal congestion score as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

### Secondary: Change from Baseline in Nasal Discharge Score Averaged During 3 Hours of Exposure

End point title	Change from Baseline in Nasal Discharge Score Averaged During 3 Hours of Exposure
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End point description:

The Nasal Discharge Score was assessed as 0 = 0 times participant blew his/her nose to 4 = 21 or more times participant blew his/her nose, with a possible Nasal Discharge Score ranging from 0 to 4 and a higher score indicating more severe nasal discharge. The Baseline Nasal Discharge Score was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline Nasal Discharge Score was assessed on Day 7 of a treatment period during 3 hours of exposure to JC pollen in the chamber room, as an average of measurements at 30, 60, 90, 120, 150 and 180 minutes. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and after 3 hours of pollen exposure on Day 7 of each treatment period

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)	0.29 (0.25 to 0.34)	0.32 (0.27 to 0.37)		

### Statistical analyses

Statistical analysis title	Difference in LS means
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Statistical analysis description:

Difference in LS means for change from Baseline in Nasal Discharge Score averaged during 3 hours of exposure - Montelukast vs. Placebo. Based on LDA model with Baseline Nasal Discharge Score as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

Comparison groups	Montelukast - Efficacy v Placebo - Efficacy
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Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182 <sup>[5]</sup>
Method	LDA
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.01

Notes:

[5] - LDA model with baseline nasal discharge score as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

### Secondary: Change from Baseline in Sneezing Score Averaged During 3 Hours of Exposure

End point title	Change from Baseline in Sneezing Score Averaged During 3 Hours of Exposure
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End point description:

The Sneezing Score was assessed as 0 = 0 times participant sneezed to 4 = 21 or more times participant sneezed, with a possible Sneezing Score ranging from 0 to 4 and a higher score indicating more severe sneezing. The Baseline Sneezing Score was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline Sneezing Score was assessed on Day 7 of a treatment period during 3 hours of exposure to JC pollen in the chamber room, as an average of measurements at 30, 60, 90, 120, 150 and 180 minutes. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and after 3 hours of pollen exposure on Day 7 of each treatment period

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)	0.2 (0.16 to 0.24)	0.18 (0.14 to 0.22)		

### Statistical analyses

Statistical analysis title	Difference in LS means
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Statistical analysis description:

Difference in LS means for change from Baseline in Sneezing Score averaged during 3 hours of exposure - Montelukast vs. Placebo. Based on LDA model with Baseline Sneezing Score as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

Comparison groups	Montelukast - Efficacy v Placebo - Efficacy
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Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.161 <sup>[6]</sup>
Method	LDA
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.05

Notes:

[6] - LDA model with baseline sneezing score as a covariate, sequence, treatment and period as fixed effects and participant as a random effect.

### Secondary: Change from Baseline in TNSS at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room

End point title	Change from Baseline in TNSS at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room
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End point description:

The TNSS is the sum of the three nasal symptom scores for nasal congestion, nasal discharge and sneezing. The possible TNSS ranged from 0 to 12, with a higher score indicating more severe total nasal symptoms. The Baseline TNSS was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline TNSS was assessed on Day 7 of a treatment period at 30, 60, 90, 120, 150 and 180 minutes after entering the chamber room. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and at 30, 60, 90, 120, 150 and 180 minutes after entering chamber room on Day 7 of a treatment period

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)				
30 minutes after entering chamber room	0.54 (0.42 to 0.67)	0.59 (0.46 to 0.71)		
60 minutes after entering chamber room	1 (0.84 to 1.16)	1.07 (0.91 to 1.23)		
90 minutes after entering chamber room	1.36 (1.18 to 1.55)	1.31 (1.12 to 1.49)		
120 minutes after entering chamber room	1.38 (1.18 to 1.57)	1.35 (1.16 to 1.54)		
150 minutes after entering chamber room	1.38 (1.19 to 1.57)	1.35 (1.16 to 1.54)		
180 minutes after entering chamber room	1.39 (1.19 to 1.59)	1.4 (1.21 to 1.6)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Weighted TNSS at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room

End point title	Change from Baseline in Weighted TNSS at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room
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End point description:

TNSS was weighted as 2:1:1 for nasal congestion, nasal discharge and sneezing. The possible Weighted TNSS ranged from 0 to 16, with a higher score indicating more severe total nasal symptoms. The Baseline TNSS was assessed on Day 7 of a treatment period prior to entering the chamber room. The post-Baseline Weighted TNSS was assessed on Day 7 of a treatment period at 30, 60, 90, 120, 150 and 180 minutes after entering the chamber room. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and at 30, 60, 90, 120, 150 and 180 minutes after entering chamber room on Day 7 of a treatment period

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)				
30 minutes after entering chamber room	0.86 (0.67 to 1.05)	0.91 (0.72 to 1.11)		
60 minutes after entering chamber room	1.55 (1.31 to 1.79)	1.63 (1.4 to 1.87)		
90 minutes after entering chamber room	2.11 (1.83 to 2.38)	2.04 (1.76 to 2.32)		
120 minutes after entering chamber room	2.17 (1.87 to 2.47)	2.17 (1.87 to 2.47)		
150 minutes after entering chamber room	2.21 (1.92 to 2.51)	2.16 (1.86 to 2.46)		
180 minutes after entering chamber room	2.22 (1.91 to 2.53)	2.21 (1.9 to 2.52)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Nasal Congestion Score at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room

End point title	Change from Baseline in Nasal Congestion Score at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room
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End point description:

The Nasal Congestion Score was assessed as 0 = No symptoms of nasal congestion to 4 = Completely obstructed all day. The possible Nasal Congestion Score ranged from 0 to 4, with a higher score indicating more severe nasal congestion. The Nasal Congestion Score was assessed on Day 7 prior to entering the chamber room and at 30, 60, 90, 120, 150 and 180 minutes after entering the chamber room. Analysis was done by study drug as taken.

End point type	Secondary
End point timeframe:	
Baseline and at 30, 60, 90, 120, 150 and 180 minutes after entering chamber room on Day 7 of a treatment period	

End point values	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)				
30 minutes after entering chamber room	0.32 (0.24 to 0.39)	0.33 (0.25 to 0.4)		
60 minutes after entering chamber room	0.55 (0.46 to 0.63)	0.56 (0.48 to 0.65)		
90 minutes after entering chamber room	0.74 (0.64 to 0.85)	0.73 (0.63 to 0.83)		
120 minutes after entering chamber room	0.8 (0.68 to 0.91)	0.82 (0.7 to 0.94)		
150 minutes after entering chamber room	0.83 (0.72 to 0.95)	0.81 (0.7 to 0.93)		
180 minutes after entering chamber room	0.83 (0.7 to 0.95)	0.81 (0.69 to 0.93)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Nasal Discharge Score at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room

End point title	Change from Baseline in Nasal Discharge Score at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room
End point description:	
The Nasal Discharge Score was assessed as 0 = 0 times participant blew his/her nose to 4 = 21 or more times participant blew his/her nose. The possible Nasal Discharge Score ranged from 0 to 4, with a higher score indicating more severe nasal discharge. The Nasal Discharge Score was assessed on Day 7 prior to entering the chamber room and at 30, 60, 90, 120, 150 and 180 minutes after entering the chamber room. Analysis was done by study drug as taken.	
End point type	Secondary
End point timeframe:	
Baseline and at 30, 60, 90, 120, 150 and 180 minutes after entering chamber room on Day 7 of a treatment period	

<b>End point values</b>	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)				
30 minutes after entering chamber room	0.13 (0.08 to 0.18)	0.17 (0.12 to 0.22)		
60 minutes after entering chamber room	0.27 (0.21 to 0.34)	0.33 (0.27 to 0.4)		
90 minutes after entering chamber room	0.39 (0.32 to 0.46)	0.38 (0.31 to 0.45)		
120 minutes after entering chamber room	0.34 (0.27 to 0.4)	0.36 (0.29 to 0.42)		
150 minutes after entering chamber room	0.31 (0.24 to 0.37)	0.32 (0.25 to 0.39)		
180 minutes after entering chamber room	0.33 (0.26 to 0.4)	0.37 (0.3 to 0.44)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Sneezing Score at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room

End point title	Change from Baseline in Sneezing Score at 30, 60, 90, 120, 150 and 180 Minutes After Entering Chamber Room
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End point description:

The Sneezing Score was assessed as 0 = 0 times participant sneezed to 4 = 21 or more times participant sneezed. The possible Sneezing Score ranged from 0 to 4, with a higher score indicating more severe sneezing. The Sneezing Score was assessed on Day 7 prior to entering the chamber room and at 30, 60, 90, 120, 150 and 180 minutes after entering the chamber room. Analysis was done by study drug as taken.

End point type	Secondary
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End point timeframe:

Baseline and at 30, 60, 90, 120, 150 and 180 minutes after entering chamber room on Day 7 of a treatment period

<b>End point values</b>	Montelukast - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	213	211		
Units: score on a scale				
least squares mean (confidence interval 95%)				
30 minutes after entering chamber room	0.09 (0.05 to 0.14)	0.09 (0.05 to 0.14)		
60 minutes after entering chamber room	0.18 (0.12 to 0.23)	0.18 (0.12 to 0.23)		
90 minutes after entering chamber room	0.23 (0.16 to 0.29)	0.2 (0.13 to 0.26)		

120 minutes after entering chamber room	0.25 (0.19 to 0.31)	0.17 (0.11 to 0.23)		
150 minutes after entering chamber room	0.24 (0.18 to 0.3)	0.21 (0.15 to 0.27)		
180 minutes after entering chamber room	0.23 (0.17 to 0.3)	0.23 (0.16 to 0.29)		

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 14 days after last dose of study drug (Up to 5 weeks)

Adverse event reporting additional description:

The All Participants as Treated (APaT) population consisted of all randomized participants who received at least one dose of study drug. AEs are reported by dose taken at time of the AE and not by randomly assigned sequence.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants receive placebo for 7 days, regardless of sequence.

Reporting group title	Montelukast
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Reporting group description:

Participants receive montelukast 5 mg for 7 days, regardless of sequence.

<b>Serious adverse events</b>	Placebo	Montelukast	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 218 (0.00%)	0 / 216 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

<b>Non-serious adverse events</b>	Placebo	Montelukast	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 218 (7.80%)	10 / 216 (4.63%)	
Investigations			
Protein urine present			
subjects affected / exposed	17 / 218 (7.80%)	10 / 216 (4.63%)	
occurrences (all)	17	10	

## **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? No

### **Limitations and caveats**

None reported