Clinical trial results:
A Phase Ib Randomized, Placebo-Controlled Clinical Trial to Study the Safety and Bronchodilatory Effect of MK-0476 in Patients with Chronic Asthma

Summary

EudraCT number	2014-004776-27
Trial protocol	Outside EU/EEA
Global end of trial date	29 December 2008

Results information

Result version number	v1 (current)
This version publication date	22 February 2016
First version publication date	19 July 2015

Trial information

Trial identification

Sponsor protocol code	0476-388

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00739297
WHO universal trial number (UTN)	-
Other trial identifiers	MK-0476-388: 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	29 December 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2008
Global end of trial reached?	Yes
Global end of trial date	29 December 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study tested the safety and effectiveness of a range of doses of MK-0476 (montelukast) compared to placebo on improved lung function based on forced expiratory volume in 1 second (FEV1) in participants aged 15 to 65 years with chronic asthma. This study was a 4-period crossover study during which participants were randomized to receive 3 out of the 5 possible dose strengths of montelukast and 1 dose strength of placebo over the 4 treatment periods using adaptive randomization.

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	26 June 2008
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 States: 68
Worldwide total number of subjects	68
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)	0
Adolescents (12-17 years)	2
Adults (18-64 years)	65
From 65 to 84 years	1

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 6 centers in the United States between July and December 2008.

Pre-assignment

Screening details:

117 participants were screened; 49 were excluded. Randomized participants met the following criteria during the prestudy period: FEV1 50-85% predicted while withholding short-acting beta agonist (SABA) and reversibility of airway obstruction >12% following SABA at Visits 1 and 2.

Period 1

Period 1 title	First Intervention (Visit 3 to Visit 4)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	Total Population
Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to montelukast 25 mcg or 250 mcg inhalation powder via dry powder inhaler (DPI), administered as a single dose

Investigational medicinal product name	Albuterol sulfate
Investigational medicinal product code	
Other name	ProAir® HFA
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol sulfate 90 mcg/actuation, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded short-acting beta-agonist (SABA), administered as 2 puffs from a metered dose inhaler (MDI)

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered to provide 25 mcg, 100 mcg, 250 mcg, 500 mcg or 1000 mcg montelukast as a single dose

Investigational medicinal product name	Placebo for albuterol sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to albuterol sulfate, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded placebo to albuterol, administered as 2 puffs from a MDI

Number of subjects in period 1	Total Population
Started	68
Completed	68

Period 2

Period 2 title	First Washout Period of 4-7 Days
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No treatment was administered during the washout period.

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Total Population
Started	68
Completed	66
Not completed	2
Adverse event, non-fatal	2

Period 3

Period 3 title	Second Intervention (Visit 5 to Visit 6)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	Total Population
Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered as a single dose

Investigational medicinal product name	Albuterol sulfate
Investigational medicinal product code	
Other name	ProAir® HFA
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol sulfate 90 mcg/actuation, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded short-acting beta-agonist (SABA), administered as 2 puffs from a metered dose inhaler (MDI)

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered to provide 25 mcg, 100 mcg, 250 mcg, 500 mcg or 1000 mcg montelukast as a single dose

Investigational medicinal product name	Placebo for albuterol sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to albuterol sulfate, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded placebo to albuterol, administered as 2 puffs from a MDI

Number of subjects in period 3	Total Population
Started	66
Completed	66

Period 4	
Period 4 title	Second Washout Period of 4-7 Days
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No treatment was administered during the washout period.

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Total Population
Started	66
Completed	66

Period 5

Period 5 title	Third Intervention (Visit 7 to Visit 8)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	Total Population
Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered as a single dose

Investigational medicinal product name	Albuterol sulfate
Investigational medicinal product code	
Other name	ProAir® HFA
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol sulfate 90 mcg/actuation, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded short-acting beta-agonist (SABA), administered as 2 puffs from a metered dose inhaler (MDI)

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered to provide 25 mcg, 100 mcg, 250 mcg, 500 mcg or 1000 mcg montelukast as a single dose

Investigational medicinal product name	Placebo for albuterol sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to albuterol sulfate, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded placebo to albuterol, administered as 2 puffs from a MDI

Number of subjects in period 5	Total Population
Started	66
Completed	66

Period 6

Period 6 title	Third Washout Period of 4-7 Days
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No treatment was administered during the washout period.

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 6	Total Population
Started	66
Completed	66

Period 7

Period 7 title	Fourth Intervention(Visit 9 to Visit 10)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Total Population

Arm description:

Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Arm type	Total Population
Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered as a single dose

Investigational medicinal product name	Albuterol sulfate
Investigational medicinal product code	
Other name	ProAir® HFA
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol sulfate 90 mcg/actuation, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded short-acting beta-agonist (SABA), administered as 2 puffs from a metered dose inhaler (MDI)

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	MK-0476
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Montelukast 25 mcg or 250 mcg inhalation powder via DPI, administered to provide 25 mcg, 100 mcg, 250 mcg, 500 mcg or 1000 mcg montelukast as a single dose

Investigational medicinal product name	Placebo for albuterol sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to albuterol sulfate, 4 hours after receiving blinded study medication (montelukast or placebo), participants received a single witnessed dose of blinded placebo to albuterol, administered as 2 puffs from a MDI

Number of subjects in period 7	Total Population
Started	66
Completed	65
Not completed	1
Participant unable to attend last visit	1

Baseline characteristics

Reporting groups	
Reporting group title	First Intervention (Visit 3 to Visit 4)
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group values	First Intervention (Visit 3 to Visit 4)	Total	
Number of subjects	68	68	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	65	65	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	39.1		
standard deviation	± 12.6	-	
Gender categorical Units: Subjects			
Female	32	32	
Male	36	36	
FEV1 (Forced Expiratory Volume in One Second)			
FEV1 is the amount of air, in liters, forcibly expired in one second.			
Units: liters			
arithmetic mean	2.44		
standard deviation	± 0.63	-	

End points

End points reporting groups

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Reporting group title	Total Population
Reporting group description:	
Participants were randomized to receive 1 of 3 dose strengths of montelukast or 1 dose strength of placebo at either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after the intervention. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).	

Subject analysis set title	Montelukast+Albuterol
Subject analysis set type	Full analysis

Subject analysis set description:

Montelukast (data for each participant are pooled across all 3 of the active doses received by that participant) + Albuterol (data for each participant are pooled across all 3 administrations of active albuterol, as added to active montelukast)

Subject analysis set title	Montelukast+Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Montelukast (data for each participant are pooled across all 3 of the active doses received by that participant) + Placebo for albuterol (data for each participant are pooled across all 3 administrations of placebo for albuterol, as added to active montelukast)

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive placebo for montelukast on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after placebo for montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Subject analysis set title	25 mcg Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive montelukast 25 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Subject analysis set title	100 mcg Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive montelukast 100 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Subject analysis set title	250 mcg Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive montelukast 250 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Subject analysis set title	500 mcg Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive montelukast 500 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Subject analysis set title	1000 mcg Montelukast
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive montelukast 1000 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Primary: Change from baseline in FEV1 over 4 hours

End point title	Change from baseline in FEV1 over 4 hours

End point description:

FEV1 measurements taken at 0 (=baseline), 10, 20, 30, 45, 60, 120, 180 and 240 minutes contributed to the average change from baseline over 4 hours. The number of minutes between consecutive measurements was used as weighting factor. The time-weighted average change was standardized by dividing by the time associated with the last measurement.

End point type	Primary

End point timeframe:

0 (=baseline) to 4 hours after treatment with montelukast

End point values	Placebo	25 mcg Montelukast	100 mcg Montelukast	250 mcg Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67[1]	42[2]	30[3]	66[4]
Units: liters				
least squares mean (confidence interval 95%)	0.03 (-0.03 to 0.1)	0.07 (0 to 0.14)	0.13 (0.06 to 0.2)	0.1 (0.04 to 0.16)

Notes:

[1] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[2] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[3] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[4] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

End point values	500 mcg Montelukast	1000 mcg Montelukast		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[5]	36[6]		
Units: liters				
least squares mean (confidence interval 95%)	0.09 (0.01 to 0.16)	0.12 (0.05 to 0.19)		

Notes:

[5] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[6] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

Statistical analyses

Statistical analysis title	Montelukast 25 mcg vs. Placebo

Statistical analysis description:

Difference in least squares (LS) means of time-weighted average change from baseline in FEV1 over 4 hours - Montelukast 25 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	25 mcg Montelukast v Placebo

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.096
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.08

Statistical analysis title	Montelukast 100 mcg vs. Placebo

Statistical analysis description:

Difference in LS means of time-weighted average change from baseline in FEV1 over 4 hours - Montelukast 100 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	100 mcg Montelukast v Placebo
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.15

Statistical analysis title	Montelukast 250 mcg vs. Placebo

Statistical analysis description:

Difference in LS means of time-weighted average change from baseline in FEV1 over 4 hours - Montelukast 250 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	250 mcg Montelukast v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.11

Statistical analysis title	Montelukast 500 mcg vs. Placebo

Statistical analysis description:

Difference in LS means of time-weighted average change from baseline in FEV1 over 4 hours - Montelukast 500 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	500 mcg Montelukast v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.081
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.11

Statistical analysis title	Montelukast 1000 mcg vs. Placebo

Statistical analysis description:

Difference in LS means of time-weighted average change from baseline in FEV1 over 4 hours - Montelukast 1000 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	1000 mcg Montelukast v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.13

Secondary: Change from baseline in FEV1 over 90 minutes after albuterol/placebo

administration	
End point title	Change from baseline in FEV1 over 90 minutes after albuterol/placebo administration

End point description:

FEV1 measurements taken at 0 (=baseline), 15, 30, 60, and 90 minutes after albuterol/placebo administration contributed to the average change from baseline over 90 minutes. The number of minutes between consecutive measurements was used as weighting factor. The time-weighted average change was standardized by dividing by the time associated with the last measurement.

End point type	Secondary

End point timeframe:

4 hours (equals time point at which albuterol or albuterol placebo is administered) to 5.5 hours after treatment with montelukast

End point values	Montelukast+Albuterol	Montelukast+Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26[7]	41[8]		
Units: liters				
least squares mean (confidence interval 95%)	0.34 (0.22 to 0.45)	0.15 (0.06 to 0.24)		

Notes:

[7] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[8] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

Statistical analyses

Statistical analysis title	Difference in LS means

Statistical analysis description:

Difference in LS means of time-weighted average change from baseline in FEV1 over 90 minutes after anbuterol/placebo administration - Montelukast+Albuterol vs. Montelukast+Placebo. Based on a repeated measures model with terms for treatment (albuterol/placebo), dose, treatment-by-dose interaction and baseline FEV1.

Comparison groups	Montelukast+Placebo v Montelukast+Albuterol
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Repeated measures model
Parameter estimate	Mean difference in least squares
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.34

Other pre-specified: Change from baseline in FEV1 at 8 hours after treatment with montelukast

End point title	Change from baseline in FEV1 at 8 hours after treatment with montelukast

End point description:

Average change from baseline in FEV1 at 8 hours after single dose montelukast administration.

End point type	Other pre-specified

End point timeframe:

0 (baseline) and 8 hours after treatment with montelukast

End point values	Placebo	25 mcg Montelukast	100 mcg Montelukast	250 mcg Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67[9]	42[10]	30[11]	66[12]
Units: liters				
least squares mean (confidence interval 95%)	0.06 (-0.02 to 0.14)	0.11 (0.03 to 0.2)	0.13 (0.04 to 0.23)	0.11 (0.03 to 0.19)

Notes:

[9] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[10] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[11] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[12] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

End point values	500 mcg Montelukast	1000 mcg Montelukast		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[13]	35[14]		
Units: liters				
least squares mean (confidence interval 95%)	0.12 (0.02 to 0.22)	0.14 (0.05 to 0.23)		

Notes:

[13] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.
[14] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

Statistical analyses

Statistical analysis title	Montelukast 25 mcg vs. Placebo

Statistical analysis description:

Difference in LS means for change from baseline in FEV1 at 8 hours after montelukast administration - Montelukast 25 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	25 mcg Montelukast v Placebo
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.12

Statistical analysis title	Montelukast 100 mcg vs. Placebo

Statistical analysis description:

Difference in LS means for change from baseline in FEV1 at 8 hours after montelukast administration - Montelukast 100 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	100 mcg Montelukast v Placebo
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.15

Statistical analysis title	Montelukast 250 mcg vs. Placebo

Statistical analysis description:

Difference in LS means for change from baseline in FEV1 at 8 hours after montelukast administration - Montelukast 250 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	250 mcg Montelukast v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.097
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.11

Statistical analysis title	Montelukast 500 mcg vs. Placebo

Statistical analysis description:

Difference in LS means for change from baseline in FEV1 at 8 hours after montelukast administration - Montelukast 500 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	500 mcg Montelukast v Placebo
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.175
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.14

Statistical analysis title	Montelukast 1000 mcg vs. Placebo

Statistical analysis description:

Difference in LS means for change from baseline in FEV1 at 8 hours after montelukast administration - Montelukast 1000 mcg vs. Placebo. Based on a mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	1000 mcg Montelukast v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.15

Other pre-specified: Change from baseline in FEV1 at 24 hours after treatment with montelukast

End point title	Change from baseline in FEV1 at 24 hours after treatment with montelukast

End point description:

Average change from baseline in FEV1 at 24 hours after single dose montelukast administration.

End point type	Other pre-specified

End point timeframe:

0 (baseline) and 24 hours after treatment with montelukast

End point values	Placebo	25 mcg Montelukast	100 mcg Montelukast	250 mcg Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67[15]	42[16]	29[17]	66[18]
Units: liters				
least squares mean (confidence interval 95%)	0.02 (-0.06 to 0.09)	0.05 (-0.03 to 0.13)	0.1 (0.01 to 0.19)	0.06 (-0.01 to 0.13)

Notes:

[15] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

[16] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

[17] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

[18] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

End point values	500 mcg Montelukast	1000 mcg Montelukast		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[19]	36[20]		
Units: liters				
least squares mean (confidence interval 95%)	0.08 (-0.01 to 0.18)	0.09 (0.01 to 0.18)		

Notes:

[19] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

[20] - All randomized participants who received ≥1 study drug dose & had baseline & post-treatment data.

Statistical analyses

Statistical analysis title	Montelukast 25 mcg vs. Placebo

Statistical analysis description:

Difference in LS means in change from baseline in FEV1 at 24 hours after montelukast administration - Montelukast 25 mcg vs. Placebo. Based on mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	25 mcg Montelukast v Placebo
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.1

Statistical analysis title	Montelukast 100 mcg vs. Placebo
Statistical analysis description:	
Difference in LS means in change from baseline in FEV1 at 24 hours after montelukast administration - Montelukast 100 mcg vs. Placebo. Based on mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.	
Comparison groups	100 mcg Montelukast v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.17

Statistical analysis title	Montelukast 250 mcg vs. Placebo
Statistical analysis description:	
Difference in LS means in change from baseline in FEV1 at 24 hours after montelukast administration - Montelukast 250 mcg vs. Placebo. Based on mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.	
Comparison groups	250 mcg Montelukast v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.117
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.1

Statistical analysis title	Montelukast 500 mcg vs. Placebo
Statistical analysis description:	
Difference in LS means in change from baseline in FEV1 at 24 hours after montelukast administration - Montelukast 500 mcg vs. Placebo. Based on mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.	
Comparison groups	500 mcg Montelukast v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.111
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.15

Statistical analysis title	Montelukast 1000 mcg vs. Placebo

Statistical analysis description:

Difference in LS means in change from baseline in FEV1 at 24 hours after montelukast administration - Montelukast 1000 mcg vs. Placebo. Based on mixed-effects model with terms for treatment (including dose of montelukast), period and baseline FEV1.

Comparison groups	1000 mcg Montelukast v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	Mixed models analysis
Parameter estimate	Mean difference in least squares
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.15

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 4 weeks (Up to 1 day after last dose of study drug)

Adverse event reporting additional description:

The safety population consisted of all randomized participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive placebo for montelukast on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions, either albuterol or placebo for albuterol was administered 4 hours after placebo for montelukast. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Reporting group title	25 mcg Montelukast

Reporting group description:

Participants were randomized to receive montelukast 25 mcg (microgram) on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast 25 mcg. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Reporting group title	100 mcg Montelukast

Reporting group description:

Participants were randomized to receive montelukast 100 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast 100 mcg. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Reporting group title	250 mcg Montelukast

Reporting group description:

Participants were randomized to receive montelukast 250 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast 250 mcg. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Reporting group title	500 mcg Montelukast

Reporting group description:

Participants were randomized to receive montelukast 500 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast 500 mcg. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Reporting group title	1000 mcg Montelukast

Reporting group description:

Participants were randomized to receive montelukast 1000 mcg on either Intervention I (Visit 3), Intervention II (Visit 5), Intervention III (Visit 7) or Intervention IV (Visit 9). At all interventions either albuterol or placebo for albuterol was administered 4 hours after montelukast 1000 mcg. During the washout periods separating the intervention periods, participants received no study treatment (i.e., participants did not receive montelukast or placebo treatment).

Serious adverse events	Placebo	25 mcg Montelukast	100 mcg Montelukast
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	250 mcg Montelukast	500 mcg Montelukast	1000 mcg Montelukast
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 66 (0.00%)	0 / 25 (0.00%)	0 / 36 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	25 mcg Montelukast	100 mcg Montelukast
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 67 (5.97%)	1 / 41 (2.44%)	0 / 30 (0.00%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 67 (1.49%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Sinus congestion			
subjects affected / exposed	0 / 67 (0.00%)	1 / 41 (2.44%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 67 (1.49%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 41 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	250 mcg Montelukast	500 mcg Montelukast	1000 mcg Montelukast
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 66 (4.55%)	3 / 25 (12.00%)	0 / 36 (0.00%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Excoriation			

subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 66 (0.00%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 66 (0.00%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 66 (0.00%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	0 / 66 (0.00%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 66 (0.00%)	0 / 25 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

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

None reported