Clinical trial results:
An 8 Week Study to Evaluate the Effectiveness of Adding Montelukast to Inhaled Corticosteroid (ICS) to the ICS/Long-Acting Beta 2-Agonist Therapy in Adult Subjects With Asthma and Allergic Rhinitis

Summary

EudraCT number	2014-004775-23
Trial protocol	Outside EU/EEA
Global end of trial date	30 January 2008

Results information

Result version number	v1 (current)
This version publication date	01 March 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	0476-383

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00545844
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 January 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2008
Global end of trial reached?	Yes
Global end of trial date	30 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Effectiveness of adding montelukast to inhaled corticosteroids in adult participants with both uncontrolled asthma and allergic rhinitis.

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	02 April 2007
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	Canada: 313
Worldwide total number of subjects	313
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)	13
Adults (18-64 years)	252
From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first 25 asthmatic participants seen consecutively at each site were invited to participate.

Treatment phase: From the Survey population, blocks of 8 were allowed to participate. All participants took 1 tablet of montelukast 10 mg once a day at bedtime.

First participant in: 02-APR-2007 Last participant out: 25-JAN-2008

Pre-assignment

Screening details:

The anticipated Enrollment was 440, with an expected dropout rate of 20% over the 8-week period, thus 369 patients should complete the study.

Period 1

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

Blinding implementation details:

This was an open-label study.

Arms

Are arms mutually exclusive?	No
Arm title	All Patients

Arm description:

Participants took montelukast sodium, 10 mg, one tablet once a day for 8 weeks as add on therapy to usual current asthma controller treatment.

Participants with comorbid allergic rhinitis and uncontrolled asthma were invited to participate in the treatment phase of the study. Of the 1004 participants who completed the survey phase, there were 319 eligible participants who advanced and participated in the treatment phase. Of the 319 eligible participants who advanced to the treatment phase 6 did not meet inclusion criteria leaving 313 patients.

Arm type	Experimental
Investigational medicinal product name	Montelukast sodium
Investigational medicinal product code	
Other name	SINGULAIR®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast sodium 10 mg tablet taken by mouth at bedtime.

Arm title	Treatment Phase (All Patients) Week 8

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Montelukast sodium
Investigational medicinal product code	
Other name	SINGULAIR®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast sodium 10 mg tablet taken by mouth at bedtime.

Arm title	Treatment Phase (All Patients) Week 0

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Montelukast sodium
Investigational medicinal product code	
Other name	SINGULAIR®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Montelukast sodium 10 mg tablet taken by mouth at bedtime.

Number of subjects in period 1	All Patients	Treatment Phase (All Patients) Week 8	Treatment Phase (All Patients) Week 0
Started	313	301	313
Completed	301	301	301
Not completed	12	0	12
Consent withdrawn by subject	2	-	2
Lost to follow-up	9	-	9
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	All Patients

Reporting group description:

Participants took montelukast sodium, 10 mg, one tablet once a day for 8 weeks as add on therapy to usual current asthma controller treatment.

Participants with comorbid allergic rhinitis and uncontrolled asthma were invited to participate in the treatment phase of the study. Of the 1004 participants who completed the survey phase, there were 319 eligible participants who advanced and participated in the treatment phase. Of the 319 eligible participants who advanced to the treatment phase 6 did not meet inclusion criteria leaving 313 patients.

Reporting group values	All Patients	Total	
Number of subjects	313	313	
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)	13	13	
Adults (18-64 years)	252	252	
From 65-84 years	48	48	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	46.1		
standard deviation	± 17.2	-	
Gender, Male/Female Units: Participants			
Female	199	199	
Male	114	114	
Inhaled Corticosteroids or Inhaled Corticosteroids / Long-Acting Beta 2-Agonist Use Units: Subjects			
Inhaled Corticosteroids Only	154	154	
Inhaled Corticosteroids/Long-Acting Beta 2-Agonist	153	153	
Missing	6	6	
Allergic Rhinitis Diagnosis Duration Units: Months			
arithmetic mean	131.4		
standard deviation	± 135.4	-	
Asthma Diagnosis Duration Units: Months			
arithmetic mean	147.6		
standard deviation	± 139	-	

End points

End points reporting groups

Reporting group title	All Patients
Reporting group description:	
Participants took montelukast sodium, 10 mg, one tablet once a day for 8 weeks as add on therapy to usual current asthma controller treatment. Participants with comorbid allergic rhinitis and uncontrolled asthma were invited to participate in the treatment phase of the study. Of the 1004 participants who completed the survey phase, there were 319 eligible participants who advanced and participated in the treatment phase. Of the 319 eligible participants who advanced to the treatment phase 6 did not meet inclusion criteria leaving 313 patients.	
Reporting group title	Treatment Phase (All Patients) Week 8
Reporting group description: -	
Reporting group title	Treatment Phase (All Patients) Week 0
Reporting group description: -	
Subject analysis set title	Treatment Phase (All Patients) Week 0
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants at Week 0.	
Subject analysis set title	Treatment Phase (All Patients) Week 8
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants at Week 8.	
Subject analysis set title	Treatment Phase (All Patients) Week 8
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants at Week 8.	
Subject analysis set title	Treatment Phase (All Patients) Week 8
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants at Week 8.	

Primary: Asthma Control

End point title	Asthma Control[1]
End point description:	
Asthma control was assessed by the Canadian Asthma Consensus Guidelines at week 0 and week 8. Participants were considered uncontrolled if they answered “yes” to at least 2 of the 8 asthma control parameters.	
End point type	Primary
End point timeframe:	
8 weeks (from Week 0 to Week 8)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were to be provided.

End point values	Treatment Phase (All Patients) Week 0	Treatment Phase (All Patients) Week 8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	313	301[2]		
Units: Participants				
number (not applicable)				
Uncontrolled	312	72		
Controlled	0	229		
Missing	1	0		

Notes:

[2] - Results are based on 301 participants in the Intent-to-Treat (ITT) population with results at Week 8

Statistical analyses

No statistical analyses for this end point

Secondary: The mean change in Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) overall score

End point title	The mean change in Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) overall score

End point description:

Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) consists of 14 questions to assess participant's overall quality of life related to allergic rhinitis on a scale of 0 (least impairment) to 6 (greatest impairment). The score is the mean of the 14 questions, ranging from 0 to 6. Change is computed as Week 8 score – Week 0 score.

End point type	Secondary

End point timeframe:

8 weeks (from Week 0 to Week 8)

End point values	Treatment Phase (All Patients) Week 0	Treatment Phase (All Patients) Week 8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	313[3]	286[4]		
Units: Units on a Scale				
arithmetic mean (standard deviation)	0 (± 0)	-1.45 (± 1.35)		

Notes:

[3] - Baseline is set to zero for the purpose of this analysis.

[4] - Result based on 286 participants in the ITT population with MiniRQLQ data at Week 8.

Statistical analyses

Statistical analysis title	Mean Change in Mini Rhinoconjunctivitis Quality

Statistical analysis description:

Change from baseline at Week 8

Comparison groups	Treatment Phase (All Patients) Week 8 v Treatment Phase (All Patients) Week 0

Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.001
Method	t-test, 2-sided

Notes:

[5] - A total of 286 participants were included in the Week 8 analysis.

Secondary: Effectiveness of Montelukast Therapy Used in Combination With Inhaled Corticosteroids or Inhaled Corticosteroids / Long-Acting Beta 2-Agonist in Improving the Symptoms of Asthma Using the Asthma Control Questionnaire (ACQ)

End point title	Effectiveness of Montelukast Therapy Used in Combination With Inhaled Corticosteroids or Inhaled Corticosteroids / Long-Acting Beta 2-Agonist in Improving the Symptoms of Asthma Using the Asthma Control Questionnaire (ACQ)

End point description:

The Asthma Control Questionnaire consists of 7 specific questions that were used to assess participant's asthma control at Week 0 and Week 8. The mean score per question is used to determine the level of control, with a final score ranging from 0 (well-controlled) to 6 (extremely poorly-controlled) units on a scale.

End point type	Secondary

End point timeframe:

8 weeks (from Week 0 to Week 8)

End point values	Treatment Phase (All Patients) Week 0	Treatment Phase (All Patients) Week 8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	313	300[6]		
Units: Units on a Scale				
arithmetic mean (standard deviation)	2.03 (± 0.8)	0.92 (± 0.8)		

Notes:

[6] - 300 participants in the ITT population completed the ACQ at Week 8.

Statistical analyses

Statistical analysis title	Change from baseline in ACQ

Statistical analysis description:

Change from baseline at Week 8

Comparison groups	Treatment Phase (All Patients) Week 0 v Treatment Phase (All Patients) Week 8
Number of subjects included in analysis	613
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	< 0.001
Method	t-test, 2-sided

Notes:

[7] - 300 participants were included in the Week 8 analysis.

Other pre-specified: Patient Global Satisfaction

End point title	Patient Global Satisfaction

End point description:

At week 0 and week 8, patients were asked to complete a single question describing how satisfied they were regarding their asthma controller medication.

End point type	Other pre-specified

End point timeframe:

8 weeks (from Week 0 to Week 8)

End point values	Treatment Phase (All Patients) Week 0	Treatment Phase (All Patients) Week 8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	313	301[8]		
Units: Participants				
number (not applicable)				
Very satisfied	24	136		
Satisfied	77	110		
Neither satisfied or dissatisfied	104	36		
Dissatisfied	97	16		
Very dissatisfied	11	1		
Missing	0	2		

Notes:

[8] - Results are based on 301 participants in the ITT population that completed Week 8.

Statistical analyses

Statistical analysis title	Change in patient satisfaction

Statistical analysis description:

McNemar-Bowker test is McNemar chi-squared statistic for binary matched pairs, with Bowker chi-squared fit test of symmetry model (tests all rows of data) (cf. Agresti, 2007)

Comparison groups	Treatment Phase (All Patients) Week 0 v Treatment Phase (All Patients) Week 8
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	< 0.001
Method	McNemar-Bowker

Notes:

[9] - 301 participants were included in the Week 8 analysis.

Other pre-specified: Physician Global Satisfaction

End point title	Physician Global Satisfaction

End point description:

At week 0 and week 8, physicians were asked to complete a single question describing how satisfied they were regarding their patient’s asthma controller medication.

End point type	Other pre-specified

End point timeframe:

8 weeks (from Week 0 to Week 8)

End point values	Treatment Phase (All Patients) Week 0	Treatment Phase (All Patients) Week 8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	313	301[10]		
Units: Participants				
number (not applicable)				
Very satisfied	7	135		
Satisfied	54	110		
Neither satisfied or dissatisfied	104	30		
Dissatisfied	142	25		
Very dissatisfied	4	1		
Missing	2	0		

Notes:

[10] - Results are based on the 301 participants in the ITT population that completed Week 8.

Statistical analyses

Statistical analysis title	Change in Physician Global Satisfaction

Statistical analysis description:

McNemar-Bowker test is McNemar chi-squared statistic for binary matched pairs, with Bowker chi-squared fit test of symmetry model (tests all rows of data) (cf. Agresti, 2007)

Comparison groups	Treatment Phase (All Patients) Week 0 v Treatment Phase (All Patients) Week 8
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	< 0.001
Method	McNemar-Bowker

Notes:

[11] - 301 participants were included in the Week 8 analysis.

Other pre-specified: Patient Global Allergic Rhinitis Symptoms Assessment

End point title	Patient Global Allergic Rhinitis Symptoms Assessment

End point description:

At week 0 and week 8, patients were asked to complete one question describing their perception of their allergic rhinitis symptoms.

End point type	Other pre-specified

End point timeframe:

8 weeks (from Week 0 to Week 8)

End point values	Treatment Phase (All Patients) Week 0	Treatment Phase (All Patients) Week 8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	313	301[12]		
Units: Participants				
number (not applicable)				
A non-issue as I do not have these symptoms	11	41		
Not really bothersome	35	129		
Bothersome a little of the time	73	77		
Bothersome some of the time	91	40		
Bothersome a good bit of the time	94	13		
Missing	9	1		

Notes:

[12] - Results are based on 301 participants in the ITT population that completed Week 8.

Statistical analyses

Statistical analysis title	Change in Patient Global Allergic Rhinitis

Statistical analysis description:

McNemar-Bowker test is McNemar chi-squared statistic for binary matched pairs, with Bowker chi-squared fit test of symmetry model (tests all rows of data) (cf. Agresti, 2007)

Comparison groups	Treatment Phase (All Patients) Week 0 v Treatment Phase (All Patients) Week 8
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	< 0.001
Method	McNemar-Bowker

Notes:

[13] - 301 participants were included in the Week 8 analysis.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 10 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0
Reporting groups	
Reporting group title	All Patients

Reporting group description: -

Serious adverse events	All Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 313 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0.3 %

Non-serious adverse events	All Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 313 (3.51%)		
Cardiac disorders			
Palpitations			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 313 (0.32%)		
occurrences (all)	1		
Immune system disorders			
Allergic reaction Not Otherwise Specified			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 313 (0.32%)		
occurrences (all)	1		
Gastrointestinal disorders			

Diarrhea alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Nausea alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Swollen tongue alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Upset stomach alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Respiratory, thoracic and mediastinal disorders Asthma exacerbation alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Nasal congestion alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Wheezing alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Asthma aggravated alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Skin and subcutaneous tissue disorders			

Rash alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Psychiatric disorders Insomnia alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 1		
Musculoskeletal and connective tissue disorders Muscular pain alternative dictionary used: MedDRA 10.0 subjects affected / exposed occurrences (all)	 1 / 313 (0.32%) 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

None reported