EU Clinical Trials Register

Clinical trial results:
A Double-Blind, Randomized, Placebo-Controlled, Multicenter, Parallel-Group, Adaptive-Design, Dose-Ranging Study of MK-1029 in Adult Subjects with Persistent Asthma.

Summary

EudraCT number	2012-000643-27
Trial protocol	DE IT GB
Global end of trial date	08 July 2014

Results information

Result version number	v1 (current)
This version publication date	08 March 2016
First version publication date	24 June 2015

Trial information

Trial identification

Sponsor protocol code	1029-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01656395
WHO universal trial number (UTN)	-
Other trial identifiers	MK-1029-012: 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2014
Global end of trial reached?	Yes
Global end of trial date	08 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This adaptive design, dose-ranging study of MK-1029 will assess the dose-related efficacy and safety of MK-1029 compared with placebo using measures of lung function (forced expiratory volume in 1 second [FEV1]). The primary objectives are (1) To demonstrate that MK-1029, compared with placebo, results in dose-related improvements in FEV1 over the last 6 weeks of the 12-week active-treatment period; and (2) To determine the dose-related safety and tolerability of MK-1029 as monotherapy and as concomitant dosing with montelukast over 12 weeks. The primary hypothesis is: MK-1029 is superior to placebo in a dose-related fashion in the average change from baseline in FEV1 over the last 6 weeks of the 12-week active-treatment period.

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.

The following additional measure defined for this individual study was in place for the protection of trial subjects:
Participants were provided with a short-acting ß-agonist (SABA, albuterol/salbutamol) to use as rescue medication throughout the study.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	23 August 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 132
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Canada: 22
Country: Number of subjects enrolled	Chile: 5
Country: Number of subjects enrolled	Colombia: 20
Country: Number of subjects enrolled	Guatemala: 50
Country: Number of subjects enrolled	Japan: 74
Country: Number of subjects enrolled	Peru: 60
Country: Number of subjects enrolled	Puerto Rico: 5
Country: Number of subjects enrolled	South Africa: 26

Country: Number of subjects enrolled	United States: 131
Worldwide total number of subjects	576
EEA total number of subjects	183

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	563
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants aged 18 to 65 (changed from "aged 18 to 75" in Protocol Amendment 02) with a consistent clinical history, for at least one year, of symptoms of persistent asthma that may include, but are not limited to, dyspnea, wheezing, chest tightness, cough, and/or sputum production were screened for this study.

Period 1

Period 1 title	Treatment Period - 12 weeks (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Study drug was administered in a double-blind, double-dummy fashion.

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-1029 10 mg

Arm description:

Parts I-II: Participants receive MK-1029 10 mg tablets once daily (QD) for 12 weeks

Arm type	Experimental
Investigational medicinal product name	MK-1029
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-1029 10 mg, 30 mg or 150 mg oral tablets taken QD at bedtime

Arm title	MK-1029 30 mg

Arm description:

Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks

Arm type	Experimental
Investigational medicinal product name	MK-1029
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-1029 10 mg, 30 mg or 150 mg oral tablets taken QD at bedtime

Arm title	MK-1029 60 mg

Arm description:

Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks

Arm type	Experimental

Investigational medicinal product name	MK-1029
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-1029 10 mg, 30 mg or 150 mg oral tablets taken QD at bedtime

Arm title	MK-1029 150 mg

Arm description:

Parts I-II: Participants receive MK-1029 150 mg tablets QD for 12 weeks

Arm type	Experimental
Investigational medicinal product name	MK-1029
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-1029 10 mg, 30 mg or 150 mg oral tablets taken QD at bedtime

Arm title	Montelukast

Arm description:

Parts I-II: Participants receive montelukast 10 mg tablets QD for 12 weeks

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

Dosage and administration details:

Montelukast 10 mg oral tablet taken QD at bedtime

Arm title	Placebo

Arm description:

Parts I-II: Participants receive placebo tablets QD for 12 weeks

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

Dosage and administration details:

Placebo oral tablets taken QD at bedtime

Number of subjects in period 1	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg
Started	60	127	142
Completed	43	93	106
Not completed	17	34	36
Consent withdrawn by subject	3	1	4
Physician decision	2	3	3
Adverse event, non-fatal	1	14	5
Other, unspecified	-	-	1
Pregnancy	-	-	1
Non-compliance with study drug	1	1	-
Screen failure	2	1	7
Lost to follow-up	1	-	-
Progressive disease	-	-	-
Lack of efficacy	1	8	6
Protocol deviation	6	6	9

Number of subjects in period 1	MK-1029 150 mg	Montelukast	Placebo
Started	53	60	134
Completed	41	46	94
Not completed	12	14	40
Consent withdrawn by subject	2	-	3
Physician decision	2	3	3
Adverse event, non-fatal	4	5	7
Other, unspecified	-	-	1
Pregnancy	-	-	-
Non-compliance with study drug	-	1	1
Screen failure	1	-	8
Lost to follow-up	-	-	-
Progressive disease	-	-	1
Lack of efficacy	1	1	6
Protocol deviation	2	4	10

Baseline characteristics

Reporting groups

Reporting group title	MK-1029 10 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 10 mg tablets once daily (QD) for 12 weeks	
Reporting group title	MK-1029 30 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 60 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 150 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 150 mg tablets QD for 12 weeks	
Reporting group title	Montelukast
Reporting group description:	
Parts I-II: Participants receive montelukast 10 mg tablets QD for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Parts I-II: Participants receive placebo tablets QD for 12 weeks	

Reporting group values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg
Number of subjects	60	127	142
Age categorical Units: Subjects			
Adults (18-64 years)	60	123	138
From 65-84 years	0	4	4
Gender categorical Units: Subjects			
Female	33	78	77
Male	27	49	65

Reporting group values	MK-1029 150 mg	Montelukast	Placebo
Number of subjects	53	60	134
Age categorical Units: Subjects			
Adults (18-64 years)	52	58	132
From 65-84 years	1	2	2
Gender categorical Units: Subjects			
Female	31	32	87
Male	22	28	47

Reporting group values	Total		
Number of subjects	576		

Age categorical Units: Subjects			
Adults (18-64 years)	563		
From 65-84 years	13		
Gender categorical Units: Subjects			
Female	338		
Male	238		

End points

End points reporting groups

Reporting group title	MK-1029 10 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 10 mg tablets once daily (QD) for 12 weeks	
Reporting group title	MK-1029 30 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 60 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 150 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 150 mg tablets QD for 12 weeks	
Reporting group title	Montelukast
Reporting group description:	
Parts I-II: Participants receive montelukast 10 mg tablets QD for 12 weeks	

Reporting group title	Placebo
Reporting group description:	
Parts I-II: Participants receive placebo tablets QD for 12 weeks	

Primary: Average Change from Baseline in Forced Expiratory Volume in 1 Second (FEV1)

End point title	Average Change from Baseline in Forced Expiratory Volume in 1 Second (FEV1)
End point description:	
FEV1 is the amount of air (in liters) forcibly exhaled in one second. The Full Analysis Set included participants who were considered T helper cell type 2 (TH2)-High participants. TH2-High participants had EITHER a peripheral blood absolute eosinophil count ≥0.30 X 10^9/L OR a peripheral blood absolute eosinophil count ≥0.14 X 10^9/L and serum total Immunoglobulin E (IgE) ≥100 IU/mL at Visit 1. TH2-Low asthmatics were operationally defined as meeting neither of these criteria. Baseline was the average FEV1 during the placebo run-in period. The ending value was the average FEV1 over the last 6 weeks of a 12-week treatment period.	
End point type	Primary
End point timeframe:	
Baseline and last 6 weeks of treatment	

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57[1]	50[2]	47[3]	52[4]
Units: Liters				
least squares mean (confidence interval 95%)	0.065 (-0.009 to 0.139)	0.004 (-0.075 to 0.083)	0.063 (-0.019 to 0.144)	0.036 (-0.04 to 0.112)

Notes:

[1] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[2] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[3] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[4] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[5]	58[6]		
Units: Liters				
least squares mean (confidence interval 95%)	0.039 (-0.033 to 0.111)	0.043 (-0.032 to 0.119)		

Notes:

[5] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[6] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in FEV1: MK-1029 10 mg vs. Placebo

Statistical analysis description:

Difference in least squares (LS) means for average change from Baseline over Week 6 to Week 12 in FEV1: MK-1029 10 mg vs. Placebo. Constrained longitudinal data analysis (cLDA) model includes terms for visit as categorical variable, prior inhaled corticosteroid (ICS) use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.685
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.084
upper limit	0.127

Statistical analysis title	Change in FEV1: MK-1029 30 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in FEV1: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.477
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.149
upper limit	0.07

Statistical analysis title	Change in FEV1: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in FEV1: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.733
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.019
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.092
upper limit	0.13

Statistical analysis title	Change in FEV1: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in FEV1: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.89
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.008

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.115
upper limit	0.1

Statistical analysis title	Change in FEV1: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in FEV1: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.935
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.109
upper limit	0.1

Primary: Percentage of Participants Who Experience Adverse Events (AEs)

End point title	Percentage of Participants Who Experience Adverse Events (AEs)[7]

End point description:

An AE 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 study drug. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition which is temporally associated with the use of the study drug, is also an AE.

End point type	Primary

End point timeframe:

Up to 14 weeks

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this end point.

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[8]	126[9]	135[10]	52[11]
Units: Percentage of participants				
number (not applicable)	44.8	48.4	47.4	53.8

Notes:

[8] - All randomized participants who received ≥1 dose of study drug.

[9] - All randomized participants who received ≥1 dose of study drug.

[10] - All randomized participants who received ≥1 dose of study drug.

[11] - All randomized participants who received ≥1 dose of study drug.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[12]	126[13]		
Units: Percentage of participants				
number (not applicable)	56.7	57.9		

Notes:

[12] - All randomized participants who received ≥1 dose of study drug.

[13] - All randomized participants who received ≥1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinue Study Drug Due to AEs

End point title	Percentage of Participants Who Discontinue Study Drug Due to AEs[14]

End point description:

An AE 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 study drug. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition which is temporally associated with the use of the study drug, is also an AE.

End point type	Primary

End point timeframe:

Up to 12 weeks

Notes:

[14] - 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 analyses were planned for this end point.

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[15]	126[16]	135[17]	52[18]
Units: Percentage of participants				
number (not applicable)	1.7	10.3	3.7	7.7

Notes:

[15] - All randomized participants who received ≥1 dose of study drug.

[16] - All randomized participants who received ≥1 dose of study drug.

[17] - All randomized participants who received ≥1 dose of study drug.

[18] - All randomized participants who received ≥1 dose of study drug.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[19]	126[20]		
Units: Percentage of participants				
number (not applicable)	8.3	5.6		

Notes:

[19] - All randomized participants who received ≥1 dose of study drug.

[20] - All randomized participants who received ≥1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Days with Asthma Exacerbations

End point title	Percentage of Days with Asthma Exacerbations

End point description:

An asthma exacerbation day was defined as a day with ANY of the following: a decrease from Baseline in morning (AM) Peak Expiratory Flow (PEF) of more than 20%, an AM PEF of less than 180 L/min, an increase in SABA use of more than 70% (and a minimum increase of at least 2 puffs), an increase from Baseline in Daytime Asthma Symptom Score of more than 50%, an overnight asthma symptom of: Awake "all night", or an asthma attack. The percentage of asthma exacerbation days was calculated. The ending value was calculated as the percentage of days with asthma exacerbations over the last 6 weeks of a 12-week treatment period.

End point type	Secondary

End point timeframe:

Last 6 weeks of treatment

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44[21]	39[22]	37[23]	46[24]
Units: Percent of asthma exacerbation days				
least squares mean (confidence interval 95%)	17.704 (10.657 to 24.75)	15.812 (8.334 to 23.29)	15.435 (7.752 to 23.118)	20.238 (13.353 to 27.124)

Notes:

[21] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[22] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[23] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[24] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47[25]	39[26]		
Units: Percent of asthma exacerbation days				
least squares mean (confidence interval 95%)	19.657 (12.845 to 26.47)	24.904 (17.424 to 32.384)		

Notes:

[25] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[26] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Asthma Exacerbation Days: MK-1029 10 mg

Statistical analysis description:

Difference in LS means for percent of asthma exacerbation day over Week 6 through Week 12: MK-1029 10 mg vs. Placebo. Analysis of covariance (ANCOVA) model with the covariate for treatment groups and prior ICS use (Yes/No). Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.169
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.48
upper limit	3.08

Statistical analysis title	Asthma Exacerbation Days: MK-1029 30 mg

Statistical analysis description:

Difference in LS means for percent of asthma exacerbation days over Week 6 through Week 12: MK-1029 30 mg vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.092
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.092
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.67
upper limit	1.485

Statistical analysis title	Asthma Exacerbation Days: MK-1029 60 mg

Statistical analysis description:

Difference in LS means for percent of asthma exacerbation days over Week 6 through Week 12: MK-1029 60 mg vs. Placebo. ANOVA model included terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.083
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.469
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.19
upper limit	1.25

Statistical analysis title	Asthma Exacerbation Days: MK-1029 150 mg

Statistical analysis description:

Difference in LS means for percent of asthma exacerbation day over Week 6 through Week 12: MK-1029 150 mg vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.666
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.83
upper limit	5.501

Statistical analysis title	Asthma Exacerbation Days: Montelukast

Statistical analysis description:

Difference in LS means for percent of asthma exacerbation days over Week 6 through Week 12: Montelukast vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.308
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.247
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.36
upper limit	4.871

Secondary: Average Change from Baseline in Daytime Symptom Score (DSS)

End point title	Average Change from Baseline in Daytime Symptom Score (DSS)

End point description:

In the evening just before going to bed, participants scored their asthma symptoms for the period since arising by answering the following 4 questions in eDiaries: 1) How often did you experience asthma symptoms today?, 2) How much did your asthma symptoms bother you?, 3) How much activity could you do today? and 4) How often did your asthma affect your activities today? The 4 questions were scored on a 7-point scale (0=best to 6=worst). Baseline was the average DSS score during the placebo run-in period. The ending value was the average DSS Score over the last 6 weeks of a 12-week treatment period.

End point type	Secondary

End point timeframe:

Baseline and last 6 weeks of treatment

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45[27]	41[28]	40[29]	49[30]
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.398 (-0.612 to -0.184)	-0.134 (-0.358 to 0.091)	-0.364 (-0.591 to -0.137)	-0.12 (-0.325 to 0.086)

Notes:

[27] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[28] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[29] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[30] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[31]	43[32]		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.411 (-0.617 to -0.206)	-0.276 (-0.495 to -0.056)		

Notes:

[31] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[32] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in DSS: MK-1029 10 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline to Week 12 in DSS: MK-1029 10 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.429
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.122
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.427
upper limit	0.182

Statistical analysis title	Change in DSS: MK-1029 30 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline to Week 12 in DSS: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.142
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.169
upper limit	0.454

Statistical analysis title	Change in DSS: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline to Week 12 in DSS: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.579
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.089
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.402
upper limit	0.225

Statistical analysis title	Change in DSS: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline to Week 12 in DSS: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.305
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.156
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.142
upper limit	0.454

Statistical analysis title	Change in DSS: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline to Week 12 in DSS: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.372
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.136
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.434
upper limit	0.163

Secondary: Average Change from Baseline in Use of SABA

End point title	Average Change from Baseline in Use of SABA

End point description:

Twice daily (upon arising and before going to sleep), participants recorded the total number of puff (actuations) of SABA used for asthma symptoms in their eDiaries. This end point was defined as the number of SABA puffs used in one day and was calculated based on eDiary entries as the sum of daytime and nighttime number of puffs of SABA. Baseline was the average number of SABA puffs used in one day during the placebo run-in period. The ending value was calculated as the average number of SABA puffs used in one day over the last 6 weeks of a 12-week treatment period.

End point type	Secondary

End point timeframe:

Baseline and last 6 weeks of treatment

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[33]	41[34]	40[35]	49[36]
Units: Puffs				
least squares mean (confidence interval 95%)	-1.373 (-1.847 to -0.899)	-0.902 (-1.42 to -0.421)	-0.955 (-1.461 to -0.45)	-0.571 (-1.031 to -0.111)

Notes:

[33] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[34] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[35] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[36] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[37]	43[38]		
Units: Puffs				
least squares mean (confidence interval 95%)	-1.234 (-1.694 to -0.774)	-0.845 (-1.334 to -0.356)		

Notes:

[37] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[38] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in SABA Use: MK-1029 10 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in SABA use: MK-1029 10 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.114
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.528
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.184
upper limit	0.128

Statistical analysis title	Change in SABA Use: MK-1029 30 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in SABA use: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Placebo v MK-1029 30 mg
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.827
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.075
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.6

Statistical analysis title	Change in SABA Use: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in SABA use: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.789
upper limit	0.569

Statistical analysis title	Change in SABA Use: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in SABA use: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Placebo v MK-1029 150 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.403
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.275
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.371
upper limit	0.921

Statistical analysis title	Change in SABA Use: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in SABA use: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.237
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.389
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.035
upper limit	0.257

Secondary: Average Change from Baseline in Number of Nocturnal Awakenings

End point title	Average Change from Baseline in Number of Nocturnal Awakenings

End point description:

This end point was defined as the number of nights per week (between consecutive visits) that a participant awakened with asthma. The end point was based on eDiariy entries and was calculated by dividing the number of nights a participant awakened with asthma (positive responses of once, more than once, awake "all night") by the total number of nights (all responses) and then multiplying by 7 (standardized to a 7-day period). Baseline was the average number of nocturnal awakenings during the placebo run-in period. The ending value was calculated as the average number of nocturnal awakenings over the last 6 weeks of a 12-week treatment period.

End point type	Secondary

End point timeframe:

Baseline and last 6 weeks of treatment

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[39]	41[40]	40[41]	49[42]
Units: Numer of awakenings				
least squares mean (confidence interval 95%)	-1.277 (-1.861 to -0.692)	-0.9 (-1.518 to -0.282)	-1.286 (-1.912 to -0.661)	-1.277 (-1.844 to -0.71)

Notes:

[39] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[40] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[41] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[42] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[43]	43[44]		
Units: Numer of awakenings				
least squares mean (confidence interval 95%)	-1.107 (-1.674 to -0.54)	-1.036 (-1.639 to -0.432)		

Notes:

[43] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[44] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in Nocturnal Awakenings: MK-1029 10 mg
Statistical analysis description:	

Difference in LS means for average change from Baseline over Week 6 to Week 12 in nocturnal awakenings: MK-1029 10 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.565
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.241
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.066
upper limit	0.583

Statistical analysis title	Change in Nocturnal Awakenings: MK-1029 30 mg
Statistical analysis description:	

Difference in LS means for average change from Baseline over Week 6 to Week 12 in nocturnal awakenings: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.754
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.135
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.713
upper limit	0.983

Statistical analysis title	Change in Nocturnal Awakenings: MK-1029 60 mg

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in nocturnal awakenings: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.563
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.251
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.104
upper limit	0.603

Statistical analysis title	Change in Nocturnal Awakenings: MK-1029 150 mg

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in nocturnal awakenings: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.559
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.241
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.053
upper limit	0.571

Statistical analysis title	Change in Nocturnal Awakenings: Montelukast

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in nocturnal awakenings: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.863
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.071
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.883
upper limit	0.741

Secondary: Average Change from Baseline in Morning (AM) and Evening (PM) Peak Expiratory Flow (PEF)

End point title	Average Change from Baseline in Morning (AM) and Evening (PM) Peak Expiratory Flow (PEF)

End point description:

PEF is a measure in liters, of the maximum flow during an exhalation. The average change from Baseline in AM/PM PEF over the last 6 weeks of a 12-week treatment period was calculated. Baseline was the average AM/PM PEF value during the placebo run-in period.

End point type	Secondary

End point timeframe:

Baseline and last 6 weeks of treatment

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[45]	41[46]	40[47]	49[48]
Units: Liters				
least squares mean (confidence interval 95%)	-1.857 (-16.13 to 12.413)	3.85 (-11.26 to 18.96)	7.174 (-8.124 to 22.472)	2.713 (-11.12 to 16.543)

Notes:

[45] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[46] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[47] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[48] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[49]	43[50]		
Units: Liters				
least squares mean (confidence interval 95%)	-4.005 (-17.83 to 9.825)	-2.401 (-17.16 to 12.357)		

Notes:

[49] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[50] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in AM/PM PEF: MK-1029 10 mg vs. Placebo
Statistical analysis description:	

Difference in LS means for average change from Baseline over Week 6 to Week 12 in AM/PM PEF: MK-1029 10 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.958
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.544
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.92
upper limit	21.007

Statistical analysis title	Change in AM/PM PEF: MK-1029 30 mg vs. Placebo
Statistical analysis description:	

Difference in LS means for average change from Baseline over Week 6 to Week 12 in AM/PM PEF: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.559
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	6.251
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.81
upper limit	27.307

Statistical analysis title	Change in AM/PM PEF: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in AM/PM PEF: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.374
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	9.575
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.62
upper limit	30.766

Statistical analysis title	Change in AM/PM PEF: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in AM/PM PEF: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.618
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	5.114
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.04
upper limit	25.272

Statistical analysis title	Change in AM/PM PEF: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for average change from Baseline over Week 6 to Week 12 in AM/PM PEF: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.876
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-1.604
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.76
upper limit	18.554

Secondary: Change from Baseline in Asthma Quality of Life Questionnaire with Standardised Activities [AQLQ(S)] Overall and Domain Scores

End point title	Change from Baseline in Asthma Quality of Life Questionnaire with Standardised Activities [AQLQ(S)] Overall and Domain Scores

End point description:

The AQLQ(S) is a 32-item questionnaire with questions on 4 domains (asthma symptoms, activity limitation, emotional function and environmental stimuli) over the previous 2 weeks. Responses were scored on a 7-point scale (1=worst to 7=best). Each domain score is defined as the average score of all answered questions in that domain. The AQLQ(S) Overall Score is defined as the average of all available item scores. The changes from baseline are presented for the overall scores and the individual domain scores. Baseline was the last measurement taken prior to the first double-blind study drug. The ending values were calculated as the average AQLQ(S) Overall Score and domain scores at Week 12 of a 12-week treatment period. Statistical analyses are provided for the AQLQ(S) Overall Scores only.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[51]	47[52]	42[53]	47[54]
Units: Score on a scale				
arithmetic mean (standard deviation)				
Overall Score	0.53 (± 1.01)	0.26 (± 1)	0.7 (± 1.04)	1 (± 1.25)
Activity Domain	0.46 (± 1.05)	0.27 (± 0.98)	0.62 (± 1.08)	0.96 (± 1.32)
Symptoms Domain	0.59 (± 1.2)	0.34 (± 1.24)	0.8 (± 1.12)	1.02 (± 1.25)
Emotional Function Domain	0.55 (± 1.35)	0.06 (± 1.17)	0.75 (± 1.26)	1.12 (± 1.62)
Environmental Stimuli Domain	0.53 (± 1.19)	0.21 (± 0.9)	0.54 (± 1.2)	0.89 (± 1.47)

Notes:

[51] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[52] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[53] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[54] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[55]	54[56]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Overall Score	0.74 (± 1.03)	0.46 (± 1.18)		
Activity Domain	0.66 (± 1.03)	0.44 (± 1.18)		
Symptoms Domain	0.83 (± 1.11)	0.47 (± 1.29)		
Emotional Function Domain	0.7 (± 1.2)	0.45 (± 1.37)		
Environmental Stimuli Domain	0.7 (± 1.18)	0.49 (± 1.43)		

Notes:

[55] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[56] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in AQLQ(S) Overall Score: MK-1029 10 mg
Statistical analysis description:	

Difference in LS means for change from Baseline to Week 12 in AQLQ(S) Overall Score: MK-1029 10 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.682
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.288
upper limit	0.44

Statistical analysis title	Change in AQLQ(S) Overall Score: MK-1029 30 mg
Statistical analysis description:	

Difference in LS means for change from Baseline to Week 12 in AQLQ(S) Overall Score: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.807
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.047

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.422
upper limit	0.329

Statistical analysis title	Change in AQLQ(S) Overall Score: MK-1029 60 mg

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in AQLQ(S) Overall Score: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.403
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.165
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.222
upper limit	0.552

Statistical analysis title	Change in AQLQ(S) Overall Score: MK-1029 150 mg

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in AQLQ(S) Overall Score: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.375
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.001
upper limit	0.751

Statistical analysis title	Change in AQLQ(S) Overall Score: Montelukast

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in AQLQ(S) Overall Score: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Positive differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.086
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	0.319
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.683

Secondary: Percentage of Participants with a ≥0.5 Increase in AQLQ(S) Overall and Domain Scores from Baseline

End point title	Percentage of Participants with a ≥0.5 Increase in AQLQ(S) Overall and Domain Scores from Baseline

End point description:

The percentage of participants who experienced a ≥0.5 increase in AQLQ(S) Overall and Domain Scores at Week 12 compared to Baseline was calculated. Statistical analyses are provide for the AQLQ(S) Overall Score response rate only.

End point type	Secondary

End point timeframe:

Week 12

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[57]	47[58]	42[59]	45[60]
Units: Percentage of participants				
number (not applicable)				
Overall Score	48.99	40.49	57.22	64.48
Activity Domain	47.19	40.46	50	60.07
Symptoms Domain	52.59	42.63	59.66	57.76
Emotional Function Domain	56.19	31.95	62.1	57.76
Environmental Stimuli Domain	41.79	42.6	59.66	59.97

Notes:

[57] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[58] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[59] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[60] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52[61]	53[62]		
Units: Percentage of participants				
number (not applicable)				
Overall Score	64.08	46.14		
Activity Domain	52.36	42.61		
Symptoms Domain	64.08	48.13		
Emotional Function Domain	53.91	49.9		
Environmental Stimuli Domain	53.16	48.13		

Notes:

[61] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[62] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	AQLQ(S) Response: MK-1029 10 mg vs. Placebo
Statistical analysis description:	
Difference in LS means for AQLQ(S) Response Rate: MK-1029 10 mg vs. Placebo. P-values, estimates and 95% confidence intervals (CIs) are based on the Miettinen and Nurminen (MN) method stratified by prior ICS use (Yes/No).	
Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7687
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	21.3

Statistical analysis title	AQLQ(S) Response: MK-1029 30 mg vs. Placebo
Statistical analysis description:	
Difference in LS means for AQLQ(S) Response Rate: MK-1029 30 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).	
Comparison groups	MK-1029 30 mg v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4943
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	-6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.9
upper limit	12.2

Statistical analysis title	AQLQ(S) Response: MK-1029 60 mg vs. Placebo
Statistical analysis description:	
Difference in LS means for AQLQ(S) Response Rate: MK-1029 60 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).	
Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3003
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	29.6

Statistical analysis title	AQLQ(S) Response: MK-1029 150 mg vs. Placebo
Statistical analysis description:	
Difference in LS means for AQLQ(S) Response Rate: MK-1029 150 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).	
Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0774
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	17.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	35.7

Statistical analysis title	AQLQ(S) Response: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for AQLQ(S) Response Rate: Montelukast vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).

Comparison groups	Montelukast v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0555
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	18.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	35.5

Secondary: Change from Baseline in Asthma Control Questionnaire (ACQ) Score

End point title	Change from Baseline in Asthma Control Questionnaire (ACQ) Score

End point description:

Participants were asked to evaluate their asthma over the previous week by answering these 6 questions: How often were you woken by your asthma during the night? How bad were your asthma symptoms when you woke up in the morning? How limited were you in your activities because of your asthma? How much shortness of breath did you experience because of your asthma? How much of the time did you wheeze? How many puffs/inhalations of short-acting bronchodilator (e.g. Ventolin/Bricanyl) have you used each day? Each response to a question was scored on a 7-point scale (0=best to 6=worst). The ACQ score is the average of the 6-items scores. The Baseline value was the last measurement taken prior to the first double-blind study drug. The ending value was calculated as the average ACQ Score at Week 12 of a 12-week treatment period.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[63]	47[64]	42[65]	47[66]
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.807 (-1.088 to -0.527)	-0.736 (-1.033 to -0.438)	-0.855 (-1.17 to -0.541)	-1.066 (-1.364 to -0.768)

Notes:

[63] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[64] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[65] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[66] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52[67]	54[68]		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.931 (-1.215 to -0.648)	-0.704 (-0.982 to -0.426)		

Notes:

[67] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[68] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Change in ACQ Score: MK-1029 10 mg vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ Score: MK-1029 10 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.603
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.104
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.495
upper limit	0.288

Statistical analysis title	Change in ACQ Score: MK-1029 30 mg vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ Score: MK-1029 30 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.875
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.032
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.436
upper limit	0.372

Statistical analysis title	Change in ACQ Score: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ Score: MK-1029 60 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.476
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.151
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.568
upper limit	0.265

Statistical analysis title	Change in ACQ Score: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ Score: MK-1029 150 mg vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.079
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.362

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.767
upper limit	0.042

Statistical analysis title	Change in ACQ Score: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ Score: Montelukast vs. Placebo. cLDA model includes terms for visit as categorical variable, prior ICS use (Yes/No) and treatment by visit. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.257
Method	cLDA model
Parameter estimate	Mean difference (final values)
Point estimate	-0.227
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.621
upper limit	0.166

Secondary: Percentage of Participants with a ≥0.5 Decrease in ACQ Score from Baseline

End point title	Percentage of Participants with a ≥0.5 Decrease in ACQ Score from Baseline

End point description:

The percentage of participants who experienced a ≥0.5 decrease in ACQ Score at Week 12 compared to Baseline was calculated.

End point type	Secondary

End point timeframe:

Week 12

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[69]	47[70]	42[71]	45[72]
Units: Percentage of participants				
number (not applicable)	65.51	59.57	66.6	71.11

Notes:

[69] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[70] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[71] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[72] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51[73]	54[74]		
Units: Percentage of participants				
number (not applicable)	64.72	62.43		

Notes:

[73] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[74] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	ACQ Response: MK-1029 10 mg vs. Placebo
Statistical analysis description:	

Difference in LS means for change from Baseline to Week 12 in ACQ response rate: MK-1029 10 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.742
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.1
upper limit	21.1

Statistical analysis title	ACQ Response: MK-1029 30 mg vs. Placebo
Statistical analysis description:	

Difference in LS means for change from Baseline to Week 12 in ACQ response rate: MK-1029 30 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7248
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	-3.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.1
upper limit	15.4

Statistical analysis title	ACQ Response: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ response rate: MK-1029 60 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6991
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.6
upper limit	22.6

Statistical analysis title	ACQ Response: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ response rate: MK-1029 150 mg vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).

Comparison groups	Placebo v MK-1029 150 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3934
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	26.2

Statistical analysis title	ACQ Response: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for change from Baseline to Week 12 in ACQ response rate: Montelukast vs. Placebo. P-values, estimates and 95% CIs are based on the MN method stratified by prior ICS use (Yes/No).

Comparison groups	Montelukast v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8032
Method	MN method
Parameter estimate	Mean difference (final values)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	20.5

Secondary: Percentage of Participants with Asthma Attacks

End point title	Percentage of Participants with Asthma Attacks

End point description:

An asthma attack was defined as asthma symptoms during the previous 24 hours requiring one or more of the following: Corticosteroid use (systemic), Unscheduled visit to the doctor or urgent care clinic, Unscheduled visit to the emergency department or Hospitalization. The ending value was calculated as the average percentage of participants who experienced asthma attacks over Week 6 to Week 12 of a 12-week treatment period.

End point type	Secondary

End point timeframe:

Over Week 6 to Week 12

End point values	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg	MK-1029 150 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43[75]	39[76]	37[77]	45[78]
Units: Percentage of participants				
least squares mean (confidence interval 95%)	0.482 (-0.159 to 1.122)	0.182 (-0.49 to 0.854)	0.017 (-0.673 to 0.708)	0.637 (0.011 to 1.262)

Notes:

[75] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[76] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[77] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[78] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

End point values	Montelukast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47[79]	39[80]		
Units: Percentage of participants				
least squares mean (confidence interval 95%)	0.248 (-0.364 to 0.86)	0.557 (-0.115 to 1.23)		

Notes:

[79] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

[80] - TH2-High participants who received ≥1 study drug dose & were evaluable for this end point.

Statistical analyses

Statistical analysis title	Asthma Attack Days: MK-1029 10 mg vs. Placebo

Statistical analysis description:

Difference in LS means for percent of asthma attack days over Week 6 to Week 12 of a 12-week treatment period: MK-1209 10 mg vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 10 mg v Placebo
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.873
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.075
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.004
upper limit	0.853

Statistical analysis title	Asthma Attack Days: MK-1029 30 mg vs. Placebo

Statistical analysis description:

Difference in LS means for percent of asthma attack days over Week 6 to Week 12 of a 12-week treatment period: MK-1209 30 mg vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 30 mg v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.376
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.326
upper limit	0.575

Statistical analysis title	Asthma Attack Days: MK-1029 60 mg vs. Placebo

Statistical analysis description:

Difference in LS means for percent of asthma attack days over Week 6 to Week 12 of a 12-week treatment period: MK-1209 60 mg vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 60 mg v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.504
upper limit	0.423

Statistical analysis title	Asthma Attack Days: MK-1029 150 mg vs. Placebo

Statistical analysis description:

Difference in LS means for percent of asthma attack days over Week 6 to Week 12 of a 12-week treatment period: MK-1209 150 mg vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	MK-1029 150 mg v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.865
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.079
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.839
upper limit	0.997

Statistical analysis title	Asthma Attack Days: Montelukast vs. Placebo

Statistical analysis description:

Difference in LS means for percent of asthma attack days over Week 6 to Week 12 of a 12-week treatment period: Montelukast vs. Placebo. ANOVA model includes terms for prior ICS use (Yes/No) and treatment. Negative differences are in favor of the first treatment group in the comparison (MK-1029 or Montelukast).

Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.503
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.309
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.219
upper limit	0.6

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Up to 14 weeks (Up to 2 weeks after last dose of study drug)	
Adverse event reporting additional description:	
The safety population consisted of all randomized participants who received ≥1 dose of study drug.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	MK-1029 10 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 10 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 30 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 60 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 30 mg tablets QD for 12 weeks	
Reporting group title	MK-1029 150 mg
Reporting group description:	
Parts I-II: Participants receive MK-1029 150 mg tablets QD for 12 weeks	
Reporting group title	Montelukast
Reporting group description:	
Parts I-II: Participants receive montelukast 10 mg tablets QD for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Parts I-II: Participants receive placebo tablets QD for 12 weeks	

Serious adverse events	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 58 (0.00%)	2 / 126 (1.59%)	2 / 135 (1.48%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 58 (0.00%)	1 / 126 (0.79%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

	MK-1029 150 mg	Montelukast	Placebo
Cardiac failure congestive			
subjects affected / exposed	0 / 58 (0.00%)	0 / 126 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tension headache			
subjects affected / exposed	0 / 58 (0.00%)	0 / 126 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 58 (0.00%)	1 / 126 (0.79%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 58 (0.00%)	0 / 126 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Kaposi's varicelliform eruption			
subjects affected / exposed	0 / 58 (0.00%)	1 / 126 (0.79%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 126 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 126 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MK-1029 150 mg	Montelukast	Placebo
Total subjects affected by serious adverse events			

subjects affected / exposed	1 / 52 (1.92%)	0 / 60 (0.00%)	1 / 126 (0.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)

Uterine leiomyoma

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders

Cardiac failure congestive

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders

Tension headache

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders

Asthma

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory failure

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations

Kaposi's varicelliform eruption

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia

subjects affected / exposed	0 / 52 (0.00%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 60 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MK-1029 10 mg	MK-1029 30 mg	MK-1029 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 58 (25.86%)	24 / 126 (19.05%)	27 / 135 (20.00%)
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	4 / 58 (6.90%)	2 / 126 (1.59%)	7 / 135 (5.19%)
occurrences (all)	4	2	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 58 (0.00%)	4 / 126 (3.17%)	2 / 135 (1.48%)
occurrences (all)	0	4	2
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 58 (6.90%)	15 / 126 (11.90%)	5 / 135 (3.70%)
occurrences (all)	5	19	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 58 (1.72%)	2 / 126 (1.59%)	2 / 135 (1.48%)
occurrences (all)	1	2	2
Cystitis			
subjects affected / exposed	0 / 58 (0.00%)	1 / 126 (0.79%)	2 / 135 (1.48%)
occurrences (all)	0	1	2
Gastroenteritis			

subjects affected / exposed	3 / 58 (5.17%)	0 / 126 (0.00%)	1 / 135 (0.74%)
occurrences (all)	3	0	1
Nasopharyngitis			
subjects affected / exposed	4 / 58 (6.90%)	6 / 126 (4.76%)	10 / 135 (7.41%)
occurrences (all)	4	6	10

Non-serious adverse events	MK-1029 150 mg	Montelukast	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 52 (36.54%)	19 / 60 (31.67%)	42 / 126 (33.33%)
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 52 (1.92%)	2 / 60 (3.33%)	6 / 126 (4.76%)
occurrences (all)	1	3	6
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 52 (5.77%)	0 / 60 (0.00%)	3 / 126 (2.38%)
occurrences (all)	3	0	3
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	8 / 52 (15.38%)	11 / 60 (18.33%)	17 / 126 (13.49%)
occurrences (all)	8	12	19
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 52 (5.77%)	1 / 60 (1.67%)	3 / 126 (2.38%)
occurrences (all)	3	1	3
Cystitis			
subjects affected / exposed	3 / 52 (5.77%)	0 / 60 (0.00%)	2 / 126 (1.59%)
occurrences (all)	3	0	2
Gastroenteritis			
subjects affected / exposed	2 / 52 (3.85%)	0 / 60 (0.00%)	2 / 126 (1.59%)
occurrences (all)	2	0	2
Nasopharyngitis			
subjects affected / exposed	7 / 52 (13.46%)	5 / 60 (8.33%)	12 / 126 (9.52%)
occurrences (all)	7	5	14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2012	Amendment 01: The major reasons for this amendment are to: 1) Specify that the list of excluded medications includes strong inhibitors, or substrates, of organic anion transporting polypeptide 1B1 (OATP1B1) and OATP1B3, to modify the list, and to indicate that the list provided is not exclusive; 2) Insert flexible language allowing investigators to administer between 2 and 4 puffs of albuterol/salbutamol for reversibility testing; and 3) Add additional exploratory analyses for the relationship between efficacy of MK-1029 and peripheral-blood eosinophil counts and/or serum total IgE concentrations in the Statistical Analysis Plan.
03 January 2013	Amendment 02: The primary reasons for this amendment are to 1) Conform with requests by regulatory authorities (e.g., clarify which visits apply to pharmacokinetic measurements in Japan and better define "abstinence" in Subject Inclusion Criterion 3; 2) Indicate changes to the inclusion criteria related to age range, FEV1 predicted values for participants on controllers, and participant treatment categories; and 3) Revise the definition of TH2-High participants on controllers.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 July 2014	This study was terminated due to futility based on Interim Analysis #2.	-

Notes:

Limitations and caveats

 None reported