Clinical trial results:
A Phase III, Randomized, Active-Controlled, Parallel-Group Clinical Trial to Study the Efficacy and Long-Term Safety of Mometasone Furoate / Formoterol Fumarate (MF/F, MK- 0887A [SCH418131]), Compared with Mometasone Furoate (MF, MK-0887 [SCH032088]), in Children with Persistent Asthma

Summary

EudraCT number	2009-010110-30
Trial protocol	LV HU DK Outside EU/EEA
Global end of trial date	04 December 2017

Results information

Result version number	v2 (current)
This version publication date	04 October 2019
First version publication date	07 April 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	MK-0887A-087

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02741271
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., ClinicalTrialsDiclosure@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	04 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2017
Global end of trial reached?	Yes
Global end of trial date	04 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of mometasone furoate/formoterol (MF/F) 100/10 mcg twice daily (BID), compared with mometasone furoate (MF) 100 mcg BID, by evaluating lung function during the first 12 weeks of double-blind treatment in children ages 5–11 years with persistent asthma.

Protection of trial subjects:

This study was conducted in conformance with the ethical principles originating from the Declaration of Helsinki, Good Clinical Practice (GCP) requirements and applicable country and/or local statutes and regulations regarding Independent Ethics Committee (IEC) review, informed consent/assent, and the protection of human participants in biomedical research as stated in the Sponsor's Code of Conduct for Interventional Clinical Trials. The Code of Conduct includes a description of how the study was monitored to ensure compliance with GCP.

Background therapy: -

Evidence for comparator:

To assess the efficacy of MF/F combination therapy, mometasone furoate (MF) monotherapy is the comparator chosen, allowing the trial to demonstrate the contribution of the formoterol (F) component to the clinical benefits of the fixed-dose combination of MF/F in children. The safety and effectiveness of MF monotherapy and F monotherapy has already been established from controlled clinical trials in adults and adolescents, and most recently has been evaluated in children 5-11 years of age (P086 and P178, respectively). The MF comparator product has the same formulation as the MF/F combination product, with the exception that the drug substance F has been removed.

Actual start date of recruitment	11 May 2016
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	Colombia: 11
Country: Number of subjects enrolled	Guatemala: 35
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Latvia: 9
Country: Number of subjects enrolled	Mexico: 28
Country: Number of subjects enrolled	Romania: 14
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	South Africa: 13
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	181
EEA total number of subjects	41

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)	181
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible participants had been adequately controlled on a stable dose of an inhaled corticosteroid (ICS)/LABA for at least 4 weeks prior to Visit 1. There were 182 randomized participants, of whom 181 received at least one dose of blinded study medication as reflected in the enrollment data.

Period 1

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

Blinding implementation details:

A double-blind/masking technique was used during the double-blind treatment Period. MF/F 50/5 mcg and MF 50 mcg, both given by metered-dose inhaler (MDI), were packaged identically so that blind/masking was maintained. The randomized dosages of MF/F 100/10 mcg or MF 100 mcg were obtained after inhalation of two puffs of MF/F 50/5 mcg or MF 50 mcg, respectively. The Run-in Period was open-label MF monotherapy, taken as 2 puffs of MF 50 mcg BID.

Arms

Are arms mutually exclusive?	Yes
Arm title	MF/F MDI 100/10 mcg BID

Arm description:

Eligible participants were assigned randomly to receive double-blinded mometasone furoate/formoterol fumarate (MF/F; MK-0887A) administered as 2 puffs of MF/F 50/5 mcg BID for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	mometasone furoate/formoterol
Investigational medicinal product code	
Other name	MK-0887A SCH418131
Pharmaceutical forms	Pressurised inhalation, suspension
Routes of administration	Inhalation use

Dosage and administration details:

Administered BID via MDI

Arm title	MF MDI 100 mcg BID

Arm description:

Eligible participants were assigned randomly to receive double-blinded mometasone furoate (MF; MK-0887) administered as 2 puffs of MF 50 mcg BID for 24 weeks.

Arm type	Active comparator
Investigational medicinal product name	mometasone furoate
Investigational medicinal product code	
Other name	MK-0887 SCH032088
Pharmaceutical forms	Pressurised inhalation, suspension
Routes of administration	Inhalation use

Dosage and administration details:

Administered BID via MDI

Number of subjects in period 1	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID
Started	91	90
Completed	89	88
Not completed	2	2
Lost to follow-up	2	-
Withdrawal by parent/guardian	-	2

Baseline characteristics

Reporting groups	
Reporting group title	MF/F MDI 100/10 mcg BID
Reporting group description:	
Eligible participants were assigned randomly to receive double-blinded mometasone furoate/formoterol fumarate (MF/F; MK-0887A) administered as 2 puffs of MF/F 50/5 mcg BID for 24 weeks.	
Reporting group title	MF MDI 100 mcg BID
Reporting group description:	
Eligible participants were assigned randomly to receive double-blinded mometasone furoate (MF; MK-0887) administered as 2 puffs of MF 50 mcg BID for 24 weeks.	

Reporting group values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID	Total
Number of subjects	91	90	181
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	91	90	181
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
This study included children (5 to 11 years of age) with persistent asthma.			
Units: years			
arithmetic mean	9.1	9.1	
standard deviation	± 1.7	± 1.7	-
Gender Categorical Units: Subjects			
Female	46	43	89
Male	45	47	92
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	2	7
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	10	10	20
White	43	41	84
More than one race	33	37	70
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	40	38	78
Not Hispanic or Latino	51	52	103

Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	MF/F MDI 100/10 mcg BID
Reporting group description:	
Eligible participants were assigned randomly to receive double-blinded mometasone furoate/formoterol fumarate (MF/F; MK-0887A) administered as 2 puffs of MF/F 50/5 mcg BID for 24 weeks.	
Reporting group title	MF MDI 100 mcg BID
Reporting group description:	
Eligible participants were assigned randomly to receive double-blinded mometasone furoate (MF; MK-0887) administered as 2 puffs of MF 50 mcg BID for 24 weeks.	
Subject analysis set title	Total
Subject analysis set type	Safety analysis
Subject analysis set description:	
All treated participants	
Subject analysis set title	Pooled MF/F 100/10 mcg and MF 100 mcg (PK Sub-trial)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
MF/F 100/10 mcg and MF 100 mcg	

Primary: Change from Baseline in Morning (AM) Post-Dose % Predicted Forced Expiratory Volume in One Second (FEV1) in the Area Under the Curve (AUC)0-60

End point title	Change from Baseline in Morning (AM) Post-Dose % Predicted Forced Expiratory Volume in One Second (FEV1) in the Area Under the Curve (AUC)0-60
End point description:	
This endpoint reflects changes in lung function data (forced expiratory volume in 1 second) measured across 0 to 60 minutes post-dose (at 0, 5, 15, 30 and 60 minutes) and averaged across study visits in the Treatment Period (Day 1, Week 1, Week 4, Week 8 and Week 12) compared to Baseline. Baseline was the average of % predicted FEV1 values at 30 min and 0 min pre-dose. At each visit, the area under the curve is calculated over the postdose timepoints. Units are standardized to percent predicted FEV1 by dividing the AUC calculation by the duration of the observed AUC. The analysed population included participants who received at least one dose of randomised trial medication with at least one primary efficacy evaluation.	
End point type	Primary
End point timeframe:	
Baseline, and average of Day 1, Weeks 1, 4, 8, and 12	

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Percent predicted FEV1				
arithmetic mean (standard deviation)				
Baseline	79.21 (± 11.44)	78.48 (± 12.79)		
Change from Baseline	8.99 (± 8.29)	3.96 (± 5.92)		

Statistical analyses

Statistical analysis title	MF/F 100/10 mcg MDI BID vs MF 100 mcg MDI BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 as measured across 0 to 60 minutes post-dose

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	5.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.21
upper limit	7.2

Primary: Participants Experiencing At Least One Adverse Event (AE)

End point title	Participants Experiencing At Least One Adverse Event (AE)[1]

End point description:

An Adverse Event (AE) is defined as any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition temporally associated with the use of the Sponsor's product, is also an AE. Safety summaries, including the number and percentage of participants, were provided for AEs, serious AEs (SAEs), and drug-related AEs. The analysed population was all randomised participants who received at least one dose of trial medication.

End point type	Primary

End point timeframe:

Up to 26 weeks

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: Safety summaries were provided for AEs in accordance with the statistical analysis plan

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID	Total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	91	90	181	
Units: Participants				
Participants with at least 1 AE	37	52	89	
Participants with SAEs	1	2	3	
Participants with Drug-Related Nonserious AEs	1	4	5	
Participants with Drug-Related SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Participants Discontinuing From Study Medication Due to an AE

End point title	Participants Discontinuing From Study Medication Due to an

End point description:

An Adverse Event (AE) is defined as any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition temporally associated with the use of the Sponsor's product, is also an AE. The analysed population was all randomised participants who received at least one dose of trial medication.

End point type	Primary

End point timeframe:

Up to 24 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety summaries were provided for AEs in accordance with the statistical analysis plan

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID	Total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	91	90	181	
Units: Participants				
Participants Who Discontinued Treatment Due to AE	0	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline AM Post-Dose Percent Predicted FEV1 on Day 1 of Treatment

End point title	Change from Baseline AM Post-Dose Percent Predicted FEV1 on Day 1 of Treatment

End point description:

The key secondary objective was to determine the onset of action for the efficacy of MF/F MDI 100/10 mcg BID, compared with MF MDI 100 mcg BID. The post-dose AM % predicted FEV1 was averaged sequentially, and the change from baseline on Day 1 was assessed. This key secondary endpoint was controlled for multiplicity in a step-down fashion, based on trial success defined as a statistically significant improvement in the primary endpoint for MF/F vs MF. Missing data were imputed using control-based multiple imputations with the cLDA model. The analysed population was all participants who received at least one dose of randomised trial medication with at least one efficacy evaluation.

End point type	Secondary

End point timeframe:

Baseline and Day 1, assessed at 4 h, 2 h and 60, 30, 15 and 5 min post-dose time points

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Percent predicted FEV1				
arithmetic mean (standard deviation)				
Baseline	79.21 (± 11.44)	78.48 (± 12.79)		
Change from Baseline (5 min post-dose on Day 1)	5.20 (± 6.93)	0.95 (± 4.33)		
Change from Baseline (15 min post-dose on Day 1)	8.00 (± 7.12)	1.38 (± 4.42)		
Change from Baseline (30 min post-dose on Day 1)	9.56 (± 7.02)	3.05 (± 4.99)		
Change from Baseline (60 min post-dose on Day 1)	11.05 (± 8.51)	4.92 (± 6.06)		
Change from Baseline (2 hr post-dose on Day 1)	12.71 (± 9.53)	5.87 (± 6.52)		
Change from Baseline (4 hr post-dose on Day 1)	11.61 (± 10.31)	5.68 (± 7.38)		

Statistical analyses

Statistical analysis title	MF/F 100/10 MDI BID vs MF 100 mcg MDI BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at 5 minutes post-dose on Day 1. This endpoint was multiplicity controlled.

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	5.91

Statistical analysis title	MF/F 100/10 mcg MDI BID vs MF 100 mcg MDI BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at 15 minutes post-dose on Day 1. This endpoint was multiplicity controlled.

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	6.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.89
upper limit	8.39

Statistical analysis title	MF/F 100/10 mcg MDI BID vs MF 100 mcg MDI BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at 30 minutes post-dose on Day 1. This endpoint was multiplicity controlled.

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	6.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.1
upper limit	8.67

Statistical analysis title	MF/F 100/10 mcg MDI BID vs MF 100 mcg MDI BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at 60 minutes post-dose on Day 1. This endpoint was multiplicity controlled.

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	6.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.09
upper limit	8.28

Statistical analysis title	MF/F 100/10 mcg MDI BID vs MF 100 mcg MDI BID
Statistical analysis description:	
Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at 2 hours post-dose on Day 1. This endpoint was multiplicity controlled.	
Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	7.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.74
upper limit	9.35

Statistical analysis title	MF/F 100/10 mcg MDI BID vs MF 100 mch MDI BID
Statistical analysis description:	
Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at 4 hours post-dose on Day 1. This endpoint was multiplicity controlled.	
Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA with multiple imputation
Parameter estimate	LSM Difference
Point estimate	6.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.53
upper limit	8.56

Secondary: Change from Baseline AM Post-Dose % Predicted FEV1 AUC 0-4 Hours on Day 1 and Week 12 of Treatment

End point title	Change from Baseline AM Post-Dose % Predicted FEV1 AUC 0-4

	Hours on Day 1 and Week 12 of Treatment

End point description:

This endpoint reflects changes in lung function data (forced expiratory volume in 1 second) measured across 0 to 4 hours post-dose on Day 1 and Week 12 compared to Baseline. Baseline was the average of 30 and 0 minutes pre-dose % predicted FEV1 values. The AUC was calculated over the scheduled timepoints of 0 min, 5 min, 15 min, 30 min, 60 min, 2 hr and 4 hr postdose. Units are standardized to percent predicted FEV1 by dividing the AUC calculation by the duration of the observed AUC. The analysed population was all participants who received at least one dose of randomised trial medication with at least one efficacy evaluation.

End point type	Secondary

End point timeframe:

Baseline, Day 1 and Week 12

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	89		
Units: Percent predicted FEV1				
arithmetic mean (standard deviation)				
Baseline	79.21 (± 11.44)	78.48 (± 12.79)		
Change from Baseline at 4 hr Post-dose on Day 1	7.13 (± 5.35)	2.70 (± 3.09)		
Change from Baseline at 4 hr Post-dose at Week 12	7.56 (± 11.20)	4.87 (± 7.72)		

Statistical analyses

Statistical analysis title	MF/F 100/10 mcg BID vs. MF 100 mcg BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 on Day 1

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA without multiple imputation
Parameter estimate	LSM Difference (4 hr post-dose)
Point estimate	6.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.36
upper limit	8.27

Statistical analysis title	MF/F 100/10 mcg BID vs. MF 100 mcg BID

Statistical analysis description:	
Comparative analysis of MF/F vs MF for the change from baseline in % predicted FEV1 at Week 12	
Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	cLDA without multiple imputation
Parameter estimate	LSM Difference (4 hr post-dose)
Point estimate	3.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	6.26

Secondary: Change from Baseline in AM Pre-Dose % Predicted FEV1 with MF/F MDI 100/10 mcg BID or MF MDI 100 mcg BID Over the First 12 Weeks of Treatment

End point title	Change from Baseline in AM Pre-Dose % Predicted FEV1 with MF/F MDI 100/10 mcg BID or MF MDI 100 mcg BID Over the First 12 Weeks of Treatment

End point description:

The change from baseline in AM pre-dose % predicted FEV1 with MF/F MDI 100/10 mcg BID vs MF MDI 100 mcg BID averaged over 12 weeks treatment was assessed. This secondary analysis of the change from baseline used the cLDA method without multiple imputation. A model-based MAR approach was used for missing data. The analysed population was all participants who received at least one dose of randomised trial medication with at least one efficacy evaluation across the treatment period.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, and 12 (Averaged)

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Percent predicted FEV1				
arithmetic mean (standard deviation)				
Baseline	79.21 (± 11.44)	78.22 (± 12.93)		
Change from Baseline (Weeks 4, 8, and 12)	1.51 (± 7.15)	0.44 (± 5.49)		

Statistical analyses

Statistical analysis title	MF/F 100/10 MDI BID vs MF 100 mcg MDI BID

Statistical analysis description:

Comparative analysis of MF/F vs MF for the change from baseline in AM pre-dose % predicted FEV1 averaged across Weeks 4, 8, and 12

Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.197
Method	cLDA without multiple imputation
Parameter estimate	LSM Difference
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	4.11

Secondary: Mean Change from Baseline in Total Daily Use of Short-Acting Beta-Agonist (SABA) Rescue Medication with MF/F MDI 100/10 mcg BID or MF MDI 100 mcg BID Over the First 12 Weeks of Treatment

End point title	Mean Change from Baseline in Total Daily Use of Short-Acting Beta-Agonist (SABA) Rescue Medication with MF/F MDI 100/10 mcg BID or MF MDI 100 mcg BID Over the First 12 Weeks of Treatment

End point description:

To evaluate the efficacy of MF/F MDI 100/10 mcg BID compared with MF MDI 100 mcg BID, the change from baseline in total daily short-acting beta agonist (SABA) use (puffs per day) was averaged and assessed. All participants received SABA MDIs (albuterol 90 mcg or salbutamol 100 mcg) for as needed relief of asthma symptoms. This secondary analysis of the change from baseline used the cLDA method without multiple imputation. A model-based MAR approach was used for missing data. The analysed population included all participants who received at least one dose of randomised trial medication with at least one efficacy evaluation.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12 (Averaged)

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Puffs per day				
arithmetic mean (standard deviation)				
Baseline	0.25 (± 0.66)	0.13 (± 0.50)		
Change from Baseline Over Weeks 1-12 (Average)	-0.12 (± 0.58)	-0.02 (± 0.52)		

Statistical analyses

Statistical analysis title	MF/F 100/10 MDI BID vs MF 100 mcg MDI BID
Statistical analysis description:	
Comparative analysis of MF/F vs MF for the change from baseline in SABA use over 12 weeks	
Comparison groups	MF/F MDI 100/10 mcg BID v MF MDI 100 mcg BID
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.968
Method	cLDA without multiple imputation
Parameter estimate	LSM Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.07

Secondary: Participants Using SABA Rescue Medication Across Weeks 1-12 of the Treatment Period

End point title	Participants Using SABA Rescue Medication Across Weeks 1-12 of the Treatment Period
End point description:	
To evaluate the efficacy of MF/F MDI 100/10 mcg BID compared with MF MDI 100 mcg BID, the number of participants using SABA rescue medication in Weeks 1-12 (individually) of the double-blind treatment period was assessed. All participants received SABA MDIs (albuterol 90 mcg or salbutamol 100 mcg) for as-needed relief of asthma symptoms. Data were provided for all participants who received at least one dose of randomized trial medication and had at least one efficacy evaluation.	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 1-12 (Averaged)	

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Participants				
Baseline	23	17		
Weeks 1-12	41	45		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants Whose SABA Rescue Medication Use Increased Across Weeks 1-12 of the Treatment Period

End point title	Participants Whose SABA Rescue Medication Use Increased Across Weeks 1-12 of the Treatment Period

End point description:

To evaluate the efficacy of MF/F MDI 100/10 mcg BID compared with MF MDI 100 mcg BID, the number of participants whose use of SABA rescue medication increased in Weeks 1-12 (individually) of the double-blind treatment period was assessed. All participants received SABA MDIs (albuterol 90 mcg or salbutamol 100 mcg) for relief of asthma symptoms. The analysed population included all participants who received at least one dose of randomised trial medication with at least one efficacy evaluation.

End point type	Secondary

End point timeframe:

Weeks 1-12 (Averaged)

End point values	MF/F MDI 100/10 mcg BID	MF MDI 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Participants	24	34		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve of Mometasone Furoate from Time 0 to 12 hours (AUC0-12)

End point title	Area Under the Plasma Concentration-Time Curve of Mometasone Furoate from Time 0 to 12 hours (AUC0-12)

End point description:

Blood samples were collected predose, and 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12 in a subset of participants who consented to take part in a PK sub-trial. Per protocol, descriptive MF pharmacokinetics were summarized without regard to treatment assignment. The analysis population was participants who consented to take part in the PK sub-trial and had evaluable data for AUC(0-12).

End point type	Secondary

End point timeframe:

Predose, 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12

End point values	Pooled MF/F 100/10 mcg and MF 100 mcg (PK Sub-trial)			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*pg/mL				
geometric mean (geometric coefficient of variation)	109 (± 55.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve of Mometasone Furoate From Time 0 to Time of Last Measurable Concentration (AUC0-last)

End point title	Area Under the Plasma Concentration-Time Curve of Mometasone Furoate From Time 0 to Time of Last Measurable Concentration (AUC0-last)

End point description:

Blood samples were collected predose, and 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12 in a subset of participants who consented to take part in a PK sub-trial. Per protocol, descriptive MF pharmacokinetics were summarized without regard to treatment assignment. The analysis population was participants who consented to take part in the PK sub-trial and had evaluable data for AUC(0-last).

End point type	Secondary

End point timeframe:

Predose, 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12

End point values	Pooled MF/F 100/10 mcg and MF 100 mcg (PK Sub-trial)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr*pg/mL				
geometric mean (geometric coefficient of variation)	106 (± 53.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Mometsone Furoate

End point title	Maximum Plasma Concentration (Cmax) of Mometsone Furoate

End point description:

Blood samples were collected predose, and 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12 in a subset of participants who consented to take part in a PK sub-trial. Per protocol, descriptive MF pharmacokinetics were summarized without regard to treatment assignment. The analysis population was participants who consented to take part in the PK sub-trial and had evaluable data for Cmax.

End point type	Secondary

End point timeframe:

Predose, 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12

End point values	Pooled MF/F 100/10 mcg and MF 100 mcg (PK Sub-trial)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: pg/mL				
geometric mean (geometric coefficient of variation)	16 (± 68.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of Mometsone Furoate

End point title	Time to Maximum Plasma Concentration (Tmax) of Mometsone Furoate

End point description:

Blood samples were collected predose, and 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12 in a subset of
participants who consented to take part in a PK sub-trial. Per protocol, descriptive MF pharmacokinetics were
summarized without regard to treatment assignment. The analysis population was participants who consented to take part in the PK sub-trial and had evaluable data for Tmax.

End point type	Secondary

End point timeframe:

Predose, 0.75, 1.5, 3, 8, and 12 hours postdose at Week 12

End point values	Pooled MF/F 100/10 mcg and MF 100 mcg (PK Sub-trial)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr				
median (full range (min-max))	1.47 (0.50 to 12.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 26 weeks	
Adverse event reporting additional description:	
All participants who received double-blind treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	MF MDI 100 mcg
Reporting group description: -	
Reporting group title	MF/F MDI 100/10 mcg
Reporting group description: -	

Serious adverse events	MF MDI 100 mcg	MF/F MDI 100/10 mcg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 90 (2.22%)	1 / 91 (1.10%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 90 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 90 (1.11%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 90 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Epididymitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MF MDI 100 mcg	MF/F MDI 100/10 mcg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 90 (35.56%)	22 / 91 (24.18%)	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	14 / 90 (15.56%)	10 / 91 (10.99%)	
occurrences (all)	19	13	
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 90 (3.33%)	5 / 91 (5.49%)	
occurrences (all)	4	5	
Nasopharyngitis			
subjects affected / exposed	8 / 90 (8.89%)	2 / 91 (2.20%)	
occurrences (all)	9	3	
Pharyngitis			
subjects affected / exposed	6 / 90 (6.67%)	1 / 91 (1.10%)	
occurrences (all)	6	1	
Rhinitis			
subjects affected / exposed	5 / 90 (5.56%)	0 / 91 (0.00%)	
occurrences (all)	5	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 90 (3.33%)	9 / 91 (9.89%)	
occurrences (all)	3	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2016	The control-based imputation of missing %-predicted FEV1 data was amended to become part of the primary analysis (it was originally proposed as a sensitivity analysis). The original, primary method of imputation based on the Missing-At-Random assumption, was moved to one of the supportive analyses. Note that the primary endpoint, %-predicted FEV1, remains the same.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported