Clinical trial results:
An Open-Label Study to Assess the Safety and Tolerability of Zenhale® (a Fixed-Dose Combination of Mometasone Furoate/Formoterol Fumarate Delivered by Metered Dose Inhaler) in 40 Subjects with Persistent Asthma (Protocol No. 206-00 [P08212])

Summary

EudraCT number	2014-004583-38
Trial protocol	Outside EU/EEA
Global end of trial date	27 September 2012

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	24 July 2015

Trial information

Trial identification

Sponsor protocol code	P08212

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01566149
WHO universal trial number (UTN)	-
Other trial identifiers	Merck: MK-0887A-206

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 September 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 September 2012
Global end of trial reached?	Yes
Global end of trial date	27 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety, tolerability, and effectiveness of 2 strengths of Mometasone Furoate/Formoterol Fumarate (MF/F) Metered Dose Inhaler (MDI) in the treatment of persistent asthma in adults and adolescents.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Asthma

Evidence for comparator: -

Actual start date of recruitment	15 March 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	Vietnam: 49
Worldwide total number of subjects	49
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	44
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from one study site in Vietnam between March 2012 and September 2012.

Pre-assignment

Screening details:

Participants who were previously on medium-dose asthma medication were assigned to Mometasone Furoate/Formoterol Fumarate (MF/F) 200/10 mcg Metered Dose Inhaler (MDI) twice daily (BID) and participants who were previously on high-dose asthma medication were assigned to MF/F 400/10 mcg MDI BID.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MF/F 400/10 mcg MDI BID

Arm description:

Participants receiving MF/F 400/10 mcg MDI BID for 12 weeks

Arm type	Active comparator
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate (MF/F) Metered Dose Inhaler (MDI)
Investigational medicinal product code	
Other name	SCH 418131, MK-0887A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

MF/F MDI, with Mometasone Furoate at doses of 200 mcg or 400 mcg, and Formoterol Fumarate at a dose of 10 mcg

Arm title	MF/F 200/10 mcg MDI BID

Arm description:

Participants receiving MF/F 200/10 mcg MDI BID for 12 weeks

Arm type	Active comparator
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate (MF/F) Metered Dose Inhaler (MDI)
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Routes of administration	Inhalation use

Dosage and administration details:

MF/F MDI, with Mometasone Furoate at doses of 200 mcg or 400 mcg, and Formoterol Fumarate at a dose of 10 mcg

Number of subjects in period 1	MF/F 400/10 mcg MDI BID	MF/F 200/10 mcg MDI BID
Started	25	24
Completed	23	21
Not completed	2	3
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-
Non-compliance with study medication	-	2
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	MF/F 200/10 mcg MDI BID
Reporting group description:	
Participants receiving MF/F 200/10 mcg MDI BID for 12 weeks	
Reporting group title	MF/F 400/10 mcg MDI BID
Reporting group description:	
Participants receiving MF/F 400/10 mcg MDI BID for 12 weeks	

Reporting group values	MF/F 200/10 mcg MDI BID	MF/F 400/10 mcg MDI BID	Total
Number of subjects	24	25	49
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)	0	0	0
Adolescents (12-17 years)	4	0	4
Adults (18-64 years)	20	24	44
From 65-84 years	0	1	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	35.4	41.2	
standard deviation	± 14.48	± 14.91	-
Gender, Male/Female Units: participants			
Female	14	12	26
Male	10	13	23

End points

End points reporting groups

Reporting group title	MF/F 400/10 mcg MDI BID
Reporting group description:	
Participants receiving MF/F 400/10 mcg MDI BID for 12 weeks	
Reporting group title	MF/F 200/10 mcg MDI BID
Reporting group description:	
Participants receiving MF/F 200/10 mcg MDI BID for 12 weeks	

Primary: Number of Participants with At Least One Adverse Event (AE)

End point title	Number of Participants with At Least One Adverse Event (AE)[1]
End point description:	
An AE was defined as any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product. This endpoint was based on the Full Analysis Set (FAS) population, which consisted of all participants assigned treatment who received at least one dose of study medication.	
End point type	Primary
End point timeframe:	
Up to Week 14	

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: No statistical analysis was performed for the end point Number of Participants with At Least One Adverse Event (AE).

End point values	MF/F 200/10 mcg MDI BID	MF/F 400/10 mcg MDI BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: participants				
number (not applicable)	5	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with At Least One Drug-Related AE

End point title	Number of Participants with At Least One Drug-Related AE[2]
End point description:	
A drug-related AE was defined as any AE for which there is reasonable possibility of drug relationship as assessed by the Investigator. This endpoint was based on the FAS population, which consisted of all participants assigned treatment who received at least one dose of study medication.	
End point type	Primary
End point timeframe:	
Up to Week 14	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for the end point Number of Participants with At Least One Drug-Related AE.

End point values	MF/F 200/10 mcg MDI BID	MF/F 400/10 mcg MDI BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with At Least One Serious AE

End point title	Number of Participants with At Least One Serious AE[3]

End point description:

A serious AE was defined as any untoward medical occurrence or effect that at any dose: results in death; is life-threatening; requires hospitalization or prolongation of existing hospitalization; results in persistent or significant disability or incapacity; is a congenital anomaly or birth defect; and/or cancer. This endpoint was based on the FAS population, which consisted of all participants assigned treatment who received at least one dose of study medication.

End point type	Primary

End point timeframe:

Up to Week 14

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for the end point Number of Participants with At Least One Serious AE.

End point values	MF/F 200/10 mcg MDI BID	MF/F 400/10 mcg MDI BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued from the Study Due to an AE

End point title	Number of Participants Who Discontinued from the Study Due to an AE[4]

End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product. This endpoint was based on the FAS population, which consisted of all participants assigned treatment who received at least one dose of study medication.

End point type	Primary

End point timeframe:

Up to Week 12

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for the end point Number of Participants Who Discontinued from the Study Due to an AE.

End point values	MF/F 200/10 mcg MDI BID	MF/F 400/10 mcg MDI BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: participants				
number (not applicable)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Week 12

End point title	Mean Change from Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Week 12

End point description:

Baseline was defined as the highest FEV1 value of three assessments prior to first dose of study drug. If two (or all three) spirometry efforts had identical FEV1, the FEV1 from the effort with the highest Forced Vital Capacity (FVC) was to be recorded. Week 12 FEV1 was assessed as the morning FEV1 at the end of the dosing interval (trough FEV1). For participants who discontinued prior to Week 12, the FEV1 measurement from the discontinuation visit was to be be carried forward to Week 12 if (and only if) the participant's study medication compliance rate prior to discontinuation was at least 85%. This endpoint was based on the FAS population, which consisted of all participants assigned treatment who received at least one dose of study medication.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MF/F 200/10 mcg MDI BID	MF/F 400/10 mcg MDI BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: liters				
arithmetic mean (standard deviation)				
Baseline FEV1	2.397 (± 0.6824)	2.215 (± 0.6206)		

Week 12 FEV1	2.503 (± 0.7418)	2.27 (± 0.6041)		
Change from Baseline in FEV1 at Week 12	0.106 (± 0.2892)	0.054 (± 0.2055)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 14	
Adverse event reporting additional description:	
The FAS population consisted of all participants assigned treatment who received at least one dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups	
Reporting group title	MF/F 400/10 mcg MDI BID
Reporting group description:	
Participants receiving MF/F 400/10 mcg MDI BID for 12 weeks	
Reporting group title	MF/F 200/10 mcg MDI BID
Reporting group description:	
Participants receiving MF/F 200/10 mcg MDI BID for 12 weeks	

Serious adverse events	MF/F 400/10 mcg MDI BID	MF/F 200/10 mcg MDI BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	MF/F 400/10 mcg MDI BID	MF/F 200/10 mcg MDI BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 25 (32.00%)	5 / 24 (20.83%)	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	2 / 25 (8.00%)	1 / 24 (4.17%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	2 / 25 (8.00%)	1 / 24 (4.17%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	2 / 25 (8.00%)	0 / 24 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 25 (8.00%)	3 / 24 (12.50%)	
occurrences (all)	2	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported