Clinical trial results:
A Randomized, Evaluator-Blind, Crossover, Single Dose Study of the Bronchodilator Effect of Formoterol Fumarate in Combination With Mometasone Furoate Metered Dose Inhaler Delivered With and Without a Spacer Versus Placebo and Foradil® Aerolizer® in Children With Persistent Asthma (Protocol No. P06476)

Summary

EudraCT number	2014-004582-24
Trial protocol	Outside EU/EEA
Global end of trial date	15 October 2011

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	P06476

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01258803
WHO universal trial number (UTN)	-
Other trial identifiers	Merck protocol number: MK-0887A-178

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	15 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 October 2011
Global end of trial reached?	Yes
Global end of trial date	15 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A study to compare the bronchodilatory effect of a single dose of Mometasone Furoate/Formoterol Fumarate (MF/F) pressurized metered dose inhaler (MDI) delivered with and without an AeroChamber Plus® with Flow-Vu® Anti-Static Valved Holding Chamber (spacer) versus Placebo MDI (combined with and without spacer) and formoterol fumarate (F) dry powder inhaler (DPI). Participants were randomly assigned to 1 of 6 treatment sequences and each participant was to receive a single dose of each of 4 treatments in each period. Each treatment period was separated by a 5 to 7 day washout period. It assumed that a single dose MF/F MDI 100/10 mcg delivered with a spacer would produce bronchodilation, defined as a significant increase in forced expiratory volume in one second (FEV1) area under the curve from 0 to 12 hours (AUC[0-12 hr]) when compared to placebo.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 92
Worldwide total number of subjects	92
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)	92

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:

Participants were recruited from 28 study sites in the United States. Primary Therapy Period: December 2010 to October 2011.

Pre-assignment

Screening details:

The study included a 4-week Run-In Period during which participants were treated with Mometasone Furoate (MF) Dry Powdered Inhaler (DPI) 100 mcg.

Period 1

Period 1 title	Treatment Period 1 (1 dose)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Period 1: Placebo Metered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometasone Furoate/Formoterol Fumarate (MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F Dry Powder Inhaler (DPI)

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 2

Arm description:

Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 3

Arm description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer

Arm type	Experimental

Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 4

Arm description:

Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 5

Arm description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu®

Arm title	Treatment Sequence 6
Arm description:	
Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI	
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Notes:	
[1] - The roles blinded appear inconsistent with a simple blinded trial.	
Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew the treatment assignment of each subject.	

Number of subjects in period 1	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	15	16	15
Completed	15	16	15

Number of subjects in period 1	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	16
Completed	15	15	16

Period 2

Period 2 title	Treatment Period 2 (1 dose)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[2]

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Period 1: Placebo MDI with spacer, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F DPI

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Arm title	Treatment Sequence 2
Arm description:	
Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer	
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Arm title	Treatment Sequence 3
Arm description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer	
Arm type	Treatment Sequence

Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 4

Arm description:

Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 5

Arm description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu®

Arm title	Treatment Sequence 6
Arm description:	
Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI	
Arm type	Treatment Sequence
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	

Notes:

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew the treatment assignment of each subject.

Number of subjects in period 2	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	15	16	15
Completed	14	14	15
Not completed	1	2	0
Consent withdrawn by subject	-	1	-
Protocol deviation	1	1	-

Number of subjects in period 2	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	16
Completed	15	15	15
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Protocol deviation	-	-	1

Period 3

Period 3 title	Treatment Period 3 (1 dose)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[3]

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Period 1: Placebo Metered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometasone Furoate/Formoterol Fumarate (MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F Dry Powder Inhaler (DPI)

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 2

Arm description:

Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu®

Arm title	Treatment Sequence 3
Arm description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer	
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Arm title	Treatment Sequence 4
Arm description:	
Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer	
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 5

Arm description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution

Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 6

Arm description:

Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Notes:

[3] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew

the treatment assignment of each subject.

Number of subjects in period 3	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	14	14	15
Completed	14	14	14
Not completed	0	0	1
Protocol deviation	-	-	1

Number of subjects in period 3	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	15
Completed	15	15	15
Not completed	0	0	0
Protocol deviation	-	-	-

Period 4	
Period 4 title	Treatment Period 4 (1 dose)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[4]

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Period 1: Placebo MDI with spacer, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F DPI

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 2

Arm description:

Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer

Arm type	Treatment Sequence
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu®

Arm title	Treatment Sequence 3
Arm description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer	
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Arm title	Treatment Sequence 4
Arm description:	
Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer	
Arm type	Treatment Sequence
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 5

Arm description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer

Arm type	Treatment Sequence
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution

Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 6

Arm description:

Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Notes:

[4] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew

the treatment assignment of each subject.

Number of subjects in period 4	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	14	14	14
Completed	14	14	14

Number of subjects in period 4	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	15
Completed	15	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1 (1 dose)
Reporting group description: All Randomized Participants	

Reporting group values	Treatment Period 1 (1 dose)	Total	
Number of subjects	92	92	
Age, Customized Units: participants			
5-7 years	17	17	
8-11 years	75	75	
Age continuous Units:			
	9.1 ± 1.7	-	
Gender, Male/Female Units: participants			
Female	35	35	
Male	57	57	

End points

End points reporting groups

Reporting group title	Treatment Sequence 1
Reporting group description:	
Treatment Period 1: Placebo Metered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometasone Furoate/Formoterol Fumarate (MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F Dry Powder Inhaler (DPI)	
Reporting group title	Treatment Sequence 2
Reporting group description:	
Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer	
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer	
Reporting group title	Treatment Sequence 4
Reporting group description:	
Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer	
Reporting group title	Treatment Sequence 5
Reporting group description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer	
Reporting group title	Treatment Sequence 6
Reporting group description:	
Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI	
Reporting group title	Treatment Sequence 1
Reporting group description:	
Treatment Period 1: Placebo MDI with spacer, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F DPI	
Reporting group title	Treatment Sequence 2
Reporting group description:	
Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer	
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer	
Reporting group title	Treatment Sequence 4
Reporting group description:	
Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer	
Reporting group title	Treatment Sequence 5
Reporting group description:	
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer	
Reporting group title	Treatment Sequence 6
Reporting group description:	
Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI	
Reporting group title	Treatment Sequence 1
Reporting group description:	
Treatment Period 1: Placebo Metered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometasone	

Furoate/Formoterol Fumarate (MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F Dry Powder Inhaler (DPI)

Reporting group title	Treatment Sequence 2

Reporting group description:

Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer

Reporting group title	Treatment Sequence 3

Reporting group description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer

Reporting group title	Treatment Sequence 4

Reporting group description:

Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer

Reporting group title	Treatment Sequence 5

Reporting group description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer

Reporting group title	Treatment Sequence 6

Reporting group description:

Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI

Reporting group title	Treatment Sequence 1

Reporting group description:

Treatment Period 1: Placebo MDI with spacer, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F DPI

Reporting group title	Treatment Sequence 2

Reporting group description:

Treatment Period 1: F DPI, Treatment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI with spacer

Reporting group title	Treatment Sequence 3

Reporting group description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer

Reporting group title	Treatment Sequence 4

Reporting group description:

Treatment Period 1: Placebo MDI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatment Period 3: F DPI, Treatment Period 4: MF/F MDI without spacer

Reporting group title	Treatment Sequence 5

Reporting group description:

Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: Placebo MDI without spacer

Reporting group title	Treatment Sequence 6

Reporting group description:

Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI

Subject analysis set title	MF/F MDI with spacer
Subject analysis set type	Full analysis

Subject analysis set description:

Participants receiving a single dose of MF/F MDI 100/10 mcg with a spacer

Subject analysis set title	MF/F MDI without spacer
Subject analysis set type	Full analysis

Subject analysis set description:

Participants receiving a single dose of MF/F MDI 100/10 mcg without a spacer

Subject analysis set title	F DPI
Subject analysis set type	Full analysis

Subject analysis set description:

Participants receiving a single dose of F DPI 20 mcg

Subject analysis set title	Placebo MDI with or without spacer
Subject analysis set type	Full analysis

Subject analysis set description:

Participants receiving a single dose of Placebo MDI with or without a spacer

Primary: Area Under the Curve From 0-12 hours (AUC[0-12h]) of the Change From baseline in Forced Expiratory Volume in 1 Second (FEV1) After a Single Dose of MF/F MDI With Spacer Compared to Placebo MDI Combined With or Without Spacer

End point title	Area Under the Curve From 0-12 hours (AUC[0-12h]) of the Change From baseline in Forced Expiratory Volume in 1 Second (FEV1) After a Single Dose of MF/F MDI With Spacer Compared to Placebo MDI Combined With or Without Spacer

End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Primary

End point timeframe:

Up to 12 hours postdose

End point values	MF/F MDI with spacer	Placebo MDI with or without spacer		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	79		
Units: Liters				
least squares mean (standard error)	0.115 (± 0.016)	-0.009 (± 0.016)		

Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI with spacer and Placebo MDI combined with or without spacer. Analysis was performed using an analysis of covariance (ANCOVA) model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI with spacer v Placebo MDI with or without spacer

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.124
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.094
upper limit	0.154

Secondary: AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose MF/F MDI Without Spacer Compared to Placebo MDI Combined With or Without Spacer

End point title	AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose MF/F MDI Without Spacer Compared to Placebo MDI Combined With or Without Spacer

End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Up to 12 hours postdose

End point values	Placebo MDI with or without spacer	MF/F MDI without spacer		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	79		
Units: Liters				
least squares mean (standard error)	-0.009 (± 0.016)	0.093 (± 0.016)		

Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI without spacer and Placebo MDI combined with or without spacer. Analysis was performed using an ANCOVA model extracting the effects due to treatment,

sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI without spacer v Placebo MDI with or without spacer
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.102
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.073
upper limit	0.131

Secondary: AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose of MF/F MDI With Spacer Compared to MF/F MDI Without Spacer

End point title	AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose of MF/F MDI With Spacer Compared to MF/F MDI Without Spacer

End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Up to 12 hours postdose

End point values	MF/F MDI with spacer	MF/F MDI without spacer		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	79		
Units: Liters				
least squares mean (standard error)	0.115 (± 0.016)	0.093 (± 0.016)		

Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI with spacer and MF/F MDI without spacer. Analysis was

performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI with spacer v MF/F MDI without spacer
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.144
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.008
upper limit	0.052

Secondary: AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of MF/F With Spacer Compared to F DPI

End point title	AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of MF/F With Spacer Compared to F DPI

End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, space and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Up to 12 hours postdose

End point values	MF/F MDI with spacer	F DPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	79		
Units: Liters				
least squares mean (standard error)	0.115 (± 0.016)	0.097 (± 0.016)		

Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI with spacer and F DPI.

Analysis was performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI with spacer v F DPI
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.229
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.018
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.012
upper limit	0.048

Secondary: AUC (0-12h) of the Change from Baseline in FEV1 After a Single Dose of MF/F Without Spacer Compared to F DPI

End point title	AUC (0-12h) of the Change from Baseline in FEV1 After a Single Dose of MF/F Without Spacer Compared to F DPI

End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, space and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Up to 12 hours postdose

End point values	MF/F MDI without spacer	F DPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	79		
Units: Liters				
least squares mean (standard error)	0.093 (± 0.016)	0.097 (± 0.016)		

Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI without spacer and F DPI.

Analysis was performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI without spacer v F DPI
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.79
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.033
upper limit	0.025

Secondary: AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of F DPI Compared to Placebo MDI Combined With or Without Spacer

End point title	AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of F DPI Compared to Placebo MDI Combined With or Without Spacer

End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, space and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Up to 12 hours postdose

End point values	Placebo MDI with or without spacer	F DPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	79		
Units: Liters				
least squares mean (standard error)	-0.009 (± 0.016)	0.097 (± 0.016)		

Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of F DPI and Placebo MDI combined with or without spacer. Analysis was performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	F DPI v Placebo MDI with or without spacer
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.106
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.077
upper limit	0.135

Secondary: Change from Baseline in Forced Vital Capacity (FVC) After a Single Dose of MF/F MDI With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours Postdose

End point title	Change from Baseline in Forced Vital Capacity (FVC) After a Single Dose of MF/F MDI With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours Postdose

End point description:

Baseline was defined as the average of 2 predose FVC measurements (taken 30 minutes and immediately before dosing). The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Baseline and 5 and 30 minutes, 1, 2, 4, 8 and 12 hours postdose

End point values	MF/F MDI with spacer	Placebo MDI with or without spacer	MF/F MDI without spacer	F DPI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Liters				
least squares mean (standard error)				
Baseline (n=79,79,79,79)	1.914 (± 0.061)	1.913 (± 0.061)	1.931 (± 0.061)	1.928 (± 0.061)
5 minutes postdose (n=79,79,79,79)	0.028 (± 0.012)	0.018 (± 0.012)	0.005 (± 0.012)	0.032 (± 0.012)

30 minutes postdose (n=79,79,79,79)	0.037 (± 0.013)	0.009 (± 0.013)	0.02 (± 0.013)	0.017 (± 0.013)
1 hour postdose (n=79,79,79,79)	0.048 (± 0.015)	-0.003 (± 0.014)	0.027 (± 0.014)	0.022 (± 0.014)
2 hours postdose (n=79,79,79,79)	0.023 (± 0.015)	0.015 (± 0.015)	0.026 (± 0.015)	0.047 (± 0.015)
4 hours postdose (n=79,79,79,79)	0.031 (± 0.015)	-0.006 (± 0.015)	0.018 (± 0.015)	0.008 (± 0.015)
8 hours postdose (n=79,79,79,79)	-0.001 (± 0.016)	-0.006 (± 0.015)	0.007 (± 0.015)	-0.013 (± 0.015)
12 hours postdose (n=78,79,78,79)	-0.001 (± 0.017)	-0.012 (± 0.016)	-0.022 (± 0.016)	-0.014 (± 0.016)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FEV1 After a Single Dose of MF/F MDI With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours Postdose

End point title	Change from Baseline in FEV1 After a Single Dose of MF/F MDI With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours Postdose

End point description:

Baseline was defined as the average of 2 predose measurements (taken 30 minutes and immediately before dosing). The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary

End point timeframe:

Baseline and 5 and 30 minutes, 1, 2, 4, 8 and 12 hours postdose

End point values	MF/F MDI with spacer	Placebo MDI with or without spacer	MF/F MDI without spacer	F DPI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Liters				
least squares mean (standard error)				
Baseline (n=79,79,79,79)	1.554 (± 0.049)	1.547 (± 0.049)	1.563 (± 0.049)	1.57 (± 0.049)
5 minutes postdose (n=79,79,79,79)	0.111 (± 0.014)	-0.001 (± 0.014)	0.068 (± 0.013)	0.105 (± 0.013)
30 minutes postdose (n=79,79,79,79)	0.131 (± 0.017)	0.006 (± 0.016)	0.099 (± 0.016)	0.117 (± 0.016)
1 hour postdose (n=79,79,79,79)	0.159 (± 0.017)	0.007 (± 0.016)	0.131 (± 0.016)	0.136 (± 0.016)
2 hours postdose (n=79,79,79,79)	0.136 (± 0.018)	0.019 (± 0.018)	0.126 (± 0.018)	0.135 (± 0.018)

4 hours postdose (n=79,79,79,79)	0.136 (± 0.018)	0.005 (± 0.018)	0.115 (± 0.018)	0.118 (± 0.018)
8 hours postdose (n=79,79,79,79)	0.108 (± 0.018)	-0.012 (± 0.018)	0.093 (± 0.018)	0.087 (± 0.017)
12 hours postdose (n=78,79,78,79)	0.092 (± 0.019)	-0.033 (± 0.019)	0.046 (± 0.018)	0.059 (± 0.018)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Adverse event data were collected for up to 30 days after last dose of study drug (up to a total of 90 days)	
Adverse event reporting additional description:	
The Safety Population consisted of all randomized participants who received at least one dose of the study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	MF/F MDI with spacer
Reporting group description:	
Participants receiving a single dose of MF/F MDI 100/10 mcg with a spacer	
Reporting group title	F DPI
Reporting group description:	
Participants receiving a single dose of F DPI 20 mcg	
Reporting group title	Placebo MDI with or without spacer
Reporting group description:	
Participants receiving a single dose of Placebo MDI with or without a spacer	
Reporting group title	MF/F MDI without spacer
Reporting group description:	
Participants receiving a single dose of MF/F MDI 100/10 mcg without a spacer	

Serious adverse events	MF/F MDI with spacer	F DPI	Placebo MDI with or without spacer
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 90 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	MF/F MDI without spacer		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 91 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	MF/F MDI with spacer	F DPI	Placebo MDI with or without spacer
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 90 (0.00%)

Non-serious adverse events	MF/F MDI without spacer		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 91 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: In this study, no non-serious adverse events reached the 5% frequency threshold for reporting.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2010	Amendment 1: Changes to Inclusion Criterion 14: text added to be consistent with other references in protocol: Subject must be able to demonstrate his/her ability to perform reproducible expiratory maneuvers (including PEF), following the principles of the ATS/ERS guidelines. Text also modified in following procedures: 7.Review of prior medications, including washout times, with subject. Record of prior medication taken by subject within 30 days, or longer, if applicable as per washout requirements, before starting trial to be obtained; 14.Venous blood and urine samples specified in Table 8 (protocol) to be analyzed and reported by central laboratory using standard procedures. Urine pregnancy test for female subjects of childbearing potential to be taken at Screening Visit and Visit 5 or Discontinuation Visit; must be negative for subject to be considered for eligibility. If subject is menstruating at time of urine collection, it should be noted in the source and eCRF comment module. Female subjects who begin menses after Screening Visit will have urine pregnancy test at next scheduled visit. Subjects with positive test will be discontinued; 16.Subjects to refrain from using SABA for 6 hours prior to start of spirometry unless FEV1 falls below stability limit. Spirometry to be performed following principles of ATS/ERS guidelines; should be performed with subject sitting, using a chair with arms and without wheels; if necessary, undertake testing with subject standing or in another position and note on spirometry report; position should be consistent throughout study. Use of nose clips required; 17.Reversibility should be demonstrated within 30 minutes of bronchodilator administration. If subject does not meet reversibility at Visit 1, three repeat assessments can be performed during Run-in Period, prior to Baseline Visit; 18.e-Diary/PEF meter will collect and save relevant expiratory flow-volume parameters, use of rescue medication, and dosing information.
17 December 2010	Amendment 2: The only change the protocol was reinserting missing pages in Appendix 8.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported