Clinical trial results:
Placebo-Controlled Study of Mometasone Furoate Nasal Spray (MFNS) 200 mcg QD in the Treatment of Seasonal Allergic Rhinitis

Summary

EudraCT number	2014-004875-21
Trial protocol	Outside EU/EEA
Global end of trial date	19 June 2007

Results information

Result version number	v1 (current)
This version publication date	01 March 2016
First version publication date	15 July 2015

Trial information

Trial identification

Sponsor protocol code	P05067

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00453063
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 June 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2007
Global end of trial reached?	Yes
Global end of trial date	19 June 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is designed to assess the efficacy of mometasone furoate nasal spay (MFNS) once daily (QD) compared with placebo in subjects with seasonal allergic rhinitis (SAR) in reducing the total nasal symptom score (TNSS) and the total ocular symptom score (TOSS).

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	16 March 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 426
Worldwide total number of subjects	426
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)	48
Adults (18-64 years)	369
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 426 participants were randomized at 24 study centers in the US to the following treatments: MFNS 200 mcg QD (n=211) and placebo (n=215).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Mometasone Furoate Nasal Spray (MFNS)

Arm description:

MFNS 200 mcg (two sprays in each nostril) once daily (QD) in the morning. Each spray is equal to 50 mcg.

Arm type	Experimental
Investigational medicinal product name	mometasone furoate
Investigational medicinal product code	
Other name	Nasonex, SCH 032088
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

50 mcg/spray, two sprays in each nostril once daily (ie, 200 mcg QD) in the morning

Arm title	Placebo

Arm description:

Two sprays in each nostril once daily

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Two sprays in each nostril once daily in the morning

Number of subjects in period 1	Mometasone Furoate Nasal Spray (MFNS)	Placebo
Started	211	215
Completed	208	212
Not completed	3	3
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	2
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Mometasone Furoate Nasal Spray (MFNS)
Reporting group description:	
MFNS 200 mcg (two sprays in each nostril) once daily (QD) in the morning. Each spray is equal to 50 mcg.	
Reporting group title	Placebo
Reporting group description:	
Two sprays in each nostril once daily	

Reporting group values	Mometasone Furoate Nasal Spray (MFNS)	Placebo	Total
Number of subjects	211	215	426
Age categorical Units: Subjects			
≤18 years	18	30	48
Between 18 and 65 years	188	181	369
≥65 years	5	4	9
Gender categorical Units: Subjects			
Female	140	130	270
Male	71	85	156

End points

End points reporting groups

Reporting group title	Mometasone Furoate Nasal Spray (MFNS)
Reporting group description:	
MFNS 200 mcg (two sprays in each nostril) once daily (QD) in the morning. Each spray is equal to 50 mcg.	
Reporting group title	Placebo
Reporting group description:	
Two sprays in each nostril once daily	

Primary: Change from Baseline in the Average AM Instantaneous (NOW) Total Nasal Symptom Score (TNSS) Averaged Over Days 2 to 15

End point title	Change from Baseline in the Average AM Instantaneous (NOW) Total Nasal Symptom Score (TNSS) Averaged Over Days 2 to 15

End point description:

TNSS was defined as the sum of the following four nasal symptoms: rhinorrhea, nasal congestion/stuffiness, nasal itching, sneezing; each symptom scored on a scale of 0 = none, 1 = mild, 2 = moderate, and 3 = severe. The best possible score on this scale is 0 and the worst possible score on this scale is 12.

Participants with a missing evaluation at a given visit or time point were not included in the analysis for that evaluation. This included participants without a baseline score for a given change-from-baseline evaluation.

End point type	Primary

End point timeframe:

Baseline to Day 15

End point values	Mometasone Furoate Nasal Spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209[1]	213[2]		
Units: units on a scale				
least squares mean (standard deviation)				
Baseline TNSS	9.83 (± 1.56)	9.69 (± 1.56)		
Change from Baseline in TNSS	-2.36 (± 2.07)	-1.71 (± 2.07)		

Notes:

[1] - All randomized participants were to be included in the analysis (intent-to-treat principle).

[2] - All randomized participants were to be included in the analysis (intent-to-treat principle).

Statistical analyses

Statistical analysis title	Change from BL in AM NOW TNSS: Day 2-15 average

Statistical analysis description:

The co-primary statistical comparison of the effects of MFNS in the reduction of TNSS was based on the comparison of MFNS versus placebo in the average AM change from Baseline (BL) in the instantaneous (NOW) scores over Days 2 to 15 at the two-sided alpha = 0.05. Least Squares (LS) means, pooled standard deviation, and 95% Confidence Intervals were obtained from an ANCOVA model with treatment and site effect with baseline TNSS as a covariate.

Comparison groups	Mometasone Furoate Nasal Spray (MFNS) v Placebo
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Confidence interval	
level	95 %

Primary: Change from Baseline in the Average AM Instantaneous (NOW) Total Ocular Symptom Score (TOSS) Averaged Over Days 2 to 15

End point title	Change from Baseline in the Average AM Instantaneous (NOW) Total Ocular Symptom Score (TOSS) Averaged Over Days 2 to 15

End point description:

TOSS was defined as the sum of the following three ocular symptoms: redness of eyes, itching/burning eyes, and tearing/watering eyes; each symptom scored on a scale of 0 = none, 1 = mild, 2 = moderate, and 3 = severe. The best possible score on this scale is 0 and the worst possible score on this scale is 9.

Participants with a missing evaluation at a given visit or time point were not included in the analysis for that evaluation. This included participants without a baseline score for a given change-from-baseline evaluation.

End point type	Primary

End point timeframe:

Baseline to Day 15

End point values	Mometasone Furoate Nasal Spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209[3]	213[4]		
Units: units on a scale				
least squares mean (standard deviation)				
Baseline TOSS	7.07 (± 1.54)	7.01 (± 1.54)		
Change from Baseline in TOSS	-1.52 (± 1.59)	-1.36 (± 1.59)		

Notes:

[3] - All randomized participants were to be included in the analysis (intent-to-treat principle).

[4] - All randomized participants were to be included in the analysis (intent-to-treat principle).

Statistical analyses

Statistical analysis title	Change from BL in AM NOW TOSS: Day 2-15 average

Statistical analysis description:

The co-primary statistical comparison of the effects of MFNS in the reduction of TOSS was based on the comparison of MFNS versus placebo in the average AM change from BL in the instantaneous (NOW) scores over Days 2 to 15 at the two-sided alpha = 0.05. LS means, pooled standard deviation, and 95% Confidence Intervals were obtained from an ANCOVA model with treatment and site effect with baseline TOSS as a covariate.

Comparison groups	Mometasone Furoate Nasal Spray (MFNS) v Placebo

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.304
Method	ANCOVA
Confidence interval	
level	95 %

Secondary: Change from Baseline in AM NOW Nasal Congestion Score (NCS) Averaged Over Days 2 to 15

End point title	Change from Baseline in AM NOW Nasal Congestion Score (NCS) Averaged Over Days 2 to 15

End point description:

Nasal congestion was one of the symptoms measured in the TNSS and was scored on a scale of 0 = none, 1 = mild, 2 = moderate, and 3 = severe. The best possible score on this scale is 0 and the worst possible score on this scale is 3.

Participants with a missing evaluation at a given visit or time point were not included in the analysis for that evaluation. This included participants without a baseline score for a given change-from-baseline evaluation.

End point type	Secondary

End point timeframe:

Baseline to Day 15

End point values	Mometasone Furoate Nasal Spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209[5]	213[6]		
Units: units on a scale				
least squares mean (standard deviation)				
Baseline Nasal Congestion Score	2.66 (± 0.4)	2.64 (± 0.4)		
Change from Baseline in Nasal Congestion Score	-0.54 (± 0.54)	-0.39 (± 0.54)		

Notes:

[5] - All randomized participants were to be included in the analysis (intent-to-treat principle).

[6] - All randomized participants were to be included in the analysis (intent-to-treat principle).

Statistical analyses

Statistical analysis title	Change from BL in AM NOW NCS: Day 2-15 average

Statistical analysis description:

LS means, pooled standard deviation, and 95% Confidence Intervals were obtained from an ANCOVA model with treatment and site effect with baseline Nasal Congestion Score as a covariate.

Comparison groups	Mometasone Furoate Nasal Spray (MFNS) v Placebo

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA
Confidence interval	
level	95 %

Secondary: Change from Baseline in Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) Total Score at Endpoint (last post baseline evaluation carried forward)

End point title	Change from Baseline in Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) Total Score at Endpoint (last post baseline evaluation carried forward)

End point description:

The RQLQ consisted of 28 items that fell into the following seven domains: activities, sleep, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional. Each of the items was scored from 0 = not troubled to 6 = extremely troubled, and the total of the seven domains was the primary focus of this quality of life evaluation. The best possible score on this scale is 0 and the worst possible score on this scale is 42. The Endpoint was the last post baseline evaluation carried forward and was Day 15 for the majority of the participants.

End point type	Secondary

End point timeframe:

Baseline to Day 15

End point values	Mometasone Furoate Nasal Spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189[7]	182[8]		
Units: units on a scale				
least squares mean (standard deviation)				
Baseline RQLQ Total Score	4.19 (± 0.97)	4.42 (± 0.97)		
Change from Baseline in RQLQ Total Score	-1.63 (± 1.37)	-1.36 (± 1.37)		

Notes:

[7] - RQLQ tool only validated in participants ≥18 years of age, so only administered to this age group.

[8] - RQLQ tool only validated in participants ≥18 years of age, so only administered to this age group.

Statistical analyses

Statistical analysis title	Change from BL in RQLQ at Endpoint

Statistical analysis description:

LS means, pooled standard deviation, and 95% Confidence Intervals were obtained from an ANCOVA model with treatment and site effect with baseline RQLQ as a covariate.

Comparison groups	Mometasone Furoate Nasal Spray (MFNS) v Placebo

Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063
Method	ANCOVA
Confidence interval	
level	95 %

Secondary: Change from Baseline in AM Peak Nasal Inspiratory Flow (PNIF) Averaged Over Days 2 to 15

End point title	Change from Baseline in AM Peak Nasal Inspiratory Flow (PNIF) Averaged Over Days 2 to 15

End point description:

Participants were to measure nasal airflow twice daily (in the morning prior to study drug dosing and in the evening) using their PNIF meter. The highest of 3 assessments was to be recorded in the electronic diary. The PNIF meter limits were between 30 and 370 liters/minute. Normal values range between 100 and 150 liters/minute. A positive change from Baseline correlates with improved nasal air flow.

Participants with a missing evaluation at a given visit or time point were not included in the analysis for that evaluation. This included participants without a baseline score for a given change-from-baseline evaluation.

End point type	Secondary

End point timeframe:

Baseline to Day 15

End point values	Mometasone Furoate Nasal Spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209[9]	213[10]		
Units: liters/minute				
least squares mean (standard deviation)				
Baseline PNIF	89.11 (± 37.2)	88.85 (± 37.2)		
Change from Baseline in PNIF	10.15 (± 21.1)	8.24 (± 21.1)		

Notes:

[9] - All randomized participants were to be included in the analysis (intent-to-treat principle).

[10] - All randomized participants were to be included in the analysis (intent-to-treat principle).

Statistical analyses

Statistical analysis title	Change from BL in PNIF: Day 2-15 average

Statistical analysis description:

LS means, pooled standard deviation, and 95% Confidence Intervals were obtained from an ANCOVA model with treatment and site effect with baseline PNIF as a covariate.

Comparison groups	Mometasone Furoate Nasal Spray (MFNS) v Placebo

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.356
Method	ANCOVA
Confidence interval	
level	95 %

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From Day 1 up to 30 days after study completion/discontinuation (up to 45 days total)

Adverse event reporting additional description:

All randomized participants were to be included in the analysis (intent-to-treat principle).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Placebo

Reporting group description:

Two sprays in each nostril once daily

Reporting group title	Mometasone Furoate Nasal Spray (MFNS)

Reporting group description:

MFNS 200 mcg (two sprays in each nostril) once daily (QD) in the morning. Each spray is equal to 50 mcg.

Serious adverse events	Placebo	Mometasone Furoate Nasal Spray (MFNS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 215 (0.00%)	0 / 211 (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	Placebo	Mometasone Furoate Nasal Spray (MFNS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 215 (0.00%)	0 / 211 (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: No adverse events were reported which exceeded the threshold of 5%.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2007	The primary purpose of Amendment 1 (AM1) was to add TOSS as a co-primary endpoint and add change from baseline in AM PNIF (averaged over Days 2-15) as a key secondary endpoint. AM1 also reduced the planned total enrollment from 500 to 460, designated the Baseline Visit for investigator evaluation, revised inclusion criteria, specified an intent-to treat principle for efficacy analyses, and revised the statistical testing method of the co-primary endpoints.
28 May 2007	The primary purpose of AM2 was to add secondary objectives and endpoints for RQLQ and AM NOW nasal congestion, and to clarify AEs and vital signs as Safety endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported