Clinical trial results:
Efficacy and Safety of 200mcg BID Mometasone Furoate Nasal Spray (MFNS) versus Placebo as Adjunctive Treatment to Antibiotics in Relief of Symptoms of Acute Bacterial Sinusitis

Summary

EudraCT number	2014-004925-42
Trial protocol	Outside EU/EEA
Global end of trial date	23 July 2008

Results information

Result version number	v1 (current)
This version publication date	15 March 2016
First version publication date	19 July 2015

Trial information

Trial identification

Sponsor protocol code	P04824

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00423176
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Registration Number: MK-0887-122

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	12 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 June 2008
Global end of trial reached?	Yes
Global end of trial date	23 July 2008
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of Nasonex® (mometasone furoate nasal spray), when used together with an antibiotic, for the relief of symptoms associated with acute bacterial sinusitis. Efficacy was based on both subjective (assessment of symptom severity by the patient) and objective measurements (computed tomography [CT] imaging of the sinuses).

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	21 December 2006
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: 237
Worldwide total number of subjects	237
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)	11
Adults (18-64 years)	213
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 237 subjects at 65 centers were enrolled, received randomized treatment assignment, and received at least one dose of study medication (MFNS = 114, Placebo = 123).

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	Placebo

Arm description:

Matching placebo nasal spray twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID or amoxicillin 1 gm/clavulanic acid 62.5 mg BID, depending on age).

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

Dosage and administration details:

Placebo, 2 sprays in each nostril BID for 29 days

Investigational medicinal product name	amoxicillin/clavulanic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants 12 to 15 years of age: one tablet of amoxicillin 875 mg/clavulanic acid 125 mg BID for 10 days
Participants 16 years of age and older: two tablets of amoxicillin 1 gm/clavulanic acid 62.5 mg BID for 10 days

Arm title	Mometasone furoate nasal spray (MFNS)

Arm description:

MFNS twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID for participants 12 to 15 years of age or amoxicillin 1 gm/clavulanic acid 62.5mg BID for participants 16 years of age or older).

Arm type	Experimental
Investigational medicinal product name	MFNS
Investigational medicinal product code	
Other name	MK-0887, SCH 032088, mometasone furoate monohydrate, Nasonex®
Pharmaceutical forms	Nasal spray

Routes of administration	Intranasal use
Dosage and administration details: MFNS 50 mcg/spray, 2 sprays in each nostril BID for 29 days	
Investigational medicinal product name	amoxicillin/clavulanic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Participants 12 to 15 years of age: one tablet of amoxicillin 875 mg/clavulanic acid 125 mg BID for 10 days Participants 16 years of age and older: two tablets of amoxicillin 1 gm/clavulanic acid 62.5 mg BID for 10 days	

Number of subjects in period 1	Placebo	Mometasone furoate nasal spray (MFNS)
Started	123	114
Completed	94	98
Not completed	29	16
Did not meet protocol eligibility	4	2
Consent withdrawn by subject	3	4
Adverse event, non-fatal	6	4
Treatment Failure	6	1
Lost to follow-up	7	4
Protocol deviation	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Mometasone furoate nasal spray (MFNS)
Reporting group description:	
MFNS twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID for participants 12 to 15 years of age or amoxicillin 1 gm/clavulanic acid 62.5mg BID for participants 16 years of age or older).	
Reporting group title	Placebo
Reporting group description:	
Matching placebo nasal spray twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID or amoxicillin 1 gm/clavulanic acid 62.5 mg BID, depending on age).	

Reporting group values	Mometasone furoate nasal spray (MFNS)	Placebo	Total
Number of subjects	114	123	237
Age Categorical Units: participants			
<=18 years	5	6	11
Between 18 and 65 years	106	107	213
>=65 years	3	10	13
Age Continuous Units: years			
arithmetic mean	39.3	39	
standard deviation	± 13.2	± 14.9	-
Gender, Male/Female Units: participants			
Female	80	72	152
Male	34	51	85

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Matching placebo nasal spray twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID or amoxicillin 1 gm/clavulanic acid 62.5 mg BID, depending on age).	
Reporting group title	Mometasone furoate nasal spray (MFNS)
Reporting group description:	
MFNS twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID for participants 12 to 15 years of age or amoxicillin 1 gm/clavulanic acid 62.5mg BID for participants 16 years of age or older).	

Primary: Baseline change in AM/PM PRIOR Major Symptoms Score (MSS) minus sinus headache averaged over Days 1 to 29

End point title	Baseline change in AM/PM PRIOR Major Symptoms Score (MSS) minus sinus headache averaged over Days 1 to 29
End point description:	
The least squares mean decrease from Baseline in AM/PM PRIOR MSS, excluding sinus headache, averaged over Days 1 to 29. PRIOR is the participant's status over the previous 12 hours (reflective). The MSS was defined as the sum of the following participant-evaluated symptoms: facial pain/pressure/tenderness, sinus headache (excluded), purulent rhinorrhea, post-nasal drip, and nasal stuffiness/congestion. MSS scores are as follows: 0=none, 1=mild, 2=moderate, 3=severe for each individual symptom, range is 0 to 12. All randomized participants with both Baseline and postbaseline values were analyzed.	
End point type	Primary
End point timeframe:	
29-day Treatment Period and 2-week no-treatment Follow-up Period (f/u)	

End point values	Mometasone furoate nasal spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105[1]	116[2]		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	8.57 (± 1.78)	8.78 (± 2.03)		
Days 1-29	-4.9 (± 2.69)	-4.46 (± 2.54)		
Days 30-43 (follow-up)	-6.59 (± 2.81)	-5.77 (± 2.98)		

Notes:

[1] - Days 1-29, n=105
Days 30-43 (f/u), n=96
[2] - Days 1-29, n=116
Days 30-43 (f/u), n=97

Statistical analyses

Statistical analysis title	Change from BL in MSS: Days 1-29 average
Statistical analysis description:	
ANCOVA was not performed as prespecified in the protocol due to early termination of the study. Means,	

standard deviations (SD) and 95% confidence intervals (CI) were based on summaries without adjusting for model covariates.

Comparison groups	Mometasone furoate nasal spray (MFNS) v Placebo
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	0.25

Statistical analysis title	Change from BL in MSS: Days 30-43 average

Statistical analysis description:

ANCOVA was not performed as prespecified in the protocol due to early termination of the study. Means, standard deviations (SD) and 95% confidence intervals (CI) were based on summaries without adjusting for model covariates.

Comparison groups	Mometasone furoate nasal spray (MFNS) v Placebo
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	0

Primary: Change from Baseline to Endpoint in percent of opacification of the maxillary sinus that had the maximum opacification score at Baseline

End point title	Change from Baseline to Endpoint in percent of opacification of the maxillary sinus that had the maximum opacification score at Baseline

End point description:

A coronal computerized tomography was obtained to visualize all nasal sinuses and the ostiomeatal complex. Opacification was measured as a percentage of the area of the sinus that was occupied by either fluid or mucosal thickening. The change in percentage of opacification of one maxillary sinus (the one with the highest percentage of opacification) as compared to antibiotic treatment alone. The percentage of opacification was measured and the change from baseline for that percentage was reported. All randomized participants with both Baseline and postbaseline values were analyzed. Endpoint was defined as the last treatment visit.

End point type	Primary

End point timeframe:

29-day Treatment Period and 2-week no-treatment Follow-up Period

End point values	Mometasone furoate nasal spray (MFNS)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	103		
Units: Percentage of opacification				
arithmetic mean (standard deviation)				
Baseline	50.7 (± 30.4)	56.8 (± 31.7)		
Change from Baseline at Endpoint	-23.7 (± 35.2)	-32.5 (± 32)		

Statistical analyses

Statistical analysis title	Change from BL in % of Opacification of MS

Statistical analysis description:

ANCOVA was not performed as prespecified in the protocol due to early termination of the study. Means, standard deviations (SD) and 95% confidence intervals (CI) were based on summaries without adjusting for model covariates.

Comparison groups	Mometasone furoate nasal spray (MFNS) v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	18.2

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 up to Day 43	
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	11.1

Reporting groups	
Reporting group title	Mometasone Furoate Nasal Spray (MFNS)
Reporting group description:	
MFNS twice daily (BID) for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID for participants 12 to 15 years of age or amoxicillin 1 gm/clavulanic acid 62.5mg BID for participants 16 years of age or older).	
Reporting group title	Placebo
Reporting group description:	
Matching placebo nasal spray BID for 29 days, plus antibiotic for the first 10 days (amoxicillin 875 mg/clavulanic acid 125 mg BID or amoxicillin 1 gm/clavulanic acid 62.5mg BID, depending on age).	

Serious adverse events	Mometasone Furoate Nasal Spray (MFNS)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 114 (0.00%)	1 / 123 (0.81%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Musculoskeletal and connective tissue disorders			
Neck Pain			
subjects affected / exposed	0 / 114 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Mometasone Furoate Nasal Spray (MFNS)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 114 (19.30%)	17 / 123 (13.82%)	
Nervous system disorders			

Headache			
subjects affected / exposed	6 / 114 (5.26%)	1 / 123 (0.81%)	
occurrences (all)	7	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 114 (14.91%)	14 / 123 (11.38%)	
occurrences (all)	19	14	
Infections and infestations			
Fungal Infection			
subjects affected / exposed	6 / 114 (5.26%)	3 / 123 (2.44%)	
occurrences (all)	6	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2006	Amendment 1 (AM1) increased the treatment period from 15 to 29 days, added a co-primary endpoint of change in percent of opacification of the maxillary sinus and revised the primary objective accordingly, revised the secondary endpoints, revised eligibility criteria, and revised the statistical sections to reflect the new co-primary endpoint.
08 March 2007	AM2 added ~20 additional study centers, added a new treatment assessment scale (Overall Treatment Effect Scale), revised eligibility criteria, clarified some study procedures, and added a subanalysis.
02 November 2007	AM3 increased the number of study centers to 120 and revised a screening/eligibility criterion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 July 2008	The study was terminated by the sponsor before the planned enrollment of 600 subjects was completed; total enrollment was 237 participants. The decision to terminate the study early was based on business priorities and slower than anticipated enrollment of participants. Study termination was not related to any safety issue and took place before any data were unblinded or analyzed.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early due to a very high screening failure rate (mainly caused by the necessity to demonstrate CT changes at baseline indicative of acute sinusitis), which limits any conclusions.

Notes: