Clinical trial results:
A Multicenter, Double-blind, Randomized, Placebo-controlled, 4-Armed Parallel Group Study to Evaluate the Efficacy of Zolmitriptan 0.5-, 2.5- and 5-mg Nasal Spray in the Treatment of Acute Migraine Headache in Adolescents

Summary

EudraCT number	2010-019203-31
Trial protocol	SK EE LV HU PL FI DE BG
Global end of trial date	24 April 2014

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	D1220C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01211145
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	Heather Wray, Medical Science Director, AstraZeneca, 46 0 31 706 4082, heather.wray@astrazeneca.com
Scientific contact	Heather Wray, Medical Science Director, AstraZeneca, 46 0 31 706 4082, heather.wray@astrazeneca.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	24 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2013
Global end of trial reached?	Yes
Global end of trial date	24 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of ZOMIG nasal spray 0.5, 2.5, and 5 mg with placebo in the acute treatment of migraine headache in adolescents (aged 12 to 17 years), as measured by the primary outcome variable of pain-free status at 2 hours post-treatment.

Protection of trial subjects:

An Ethics Committee (EC)/Institutional Review Board (IRB) approved the final study protocol, including the final version of the informed consent form and assent form, and any other written information provided to the patients. Substantial changes to the study protocol were documented in study protocol amendments, which were also approved by each EC/IRB. The investigator ensured the distribution of these documents to the applicable EC/IRB and to the study site staff.

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonization (ICH)/Good Clinical Practice (GCP) and applicable regulatory requirements and the AstraZeneca policy on Bioethics.

The principal investigator (PI) at each center ensured that the patient and their parent/guardian/legal representative were given full and adequate oral and written information about the nature, purpose, possible risk, and benefit of the study. Patients were notified that they were free to discontinue from the study at any time.

The patient's parent/guardian/legal representative's signed and dated informed consent, and the patient's signed and dated assent, were obtained before conducting any procedure specific for the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 363
Country: Number of subjects enrolled	Hungary: 219
Country: Number of subjects enrolled	Slovakia: 77
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Serbia: 36
Country: Number of subjects enrolled	Latvia: 20
Country: Number of subjects enrolled	Finland: 19
Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	Estonia: 7

Country: Number of subjects enrolled	Bulgaria: 1
Worldwide total number of subjects	798
EEA total number of subjects	388

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)	798
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter study was conducted between 7 October 2010 and 31 October 2013.

Pre-assignment

Screening details:

The study had a 30 day run-in period and up to a 10-week double-blind treatment period. Patients were randomized to receive ZOMIG nasal spray 0.5, 2.5, 5.0 mg, or matching placebo spray to treat a migraine headache. 1653 patients were enrolled, 798 were randomized.

Pre-assignment period milestones

Number of subjects started	1653[1]
Number of subjects completed	798

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Unknown: 109
Reason: Number of subjects	Exclusion Criteria: 107
Reason: Number of subjects	Pregnancy: 1
Reason: Number of subjects	Physician decision: 13
Reason: Number of subjects	Inclusion Criteria: 300
Reason: Number of subjects	Placebo responder: 325

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: In the country by country count which I entered, I included patients who were randomized while the form apparently is trying to align it with the number enrolled. I feel the number randomized in each country is the more appropriate count since these are the patients who contributed to the corresponding analyses.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo to ZOMIG nasal spray

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:

one spray

Arm title	ZOMIG 0.5 mg

Arm description: ZOMIG nasal spray	
Arm type	Experimental
Investigational medicinal product name	zolmitriptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use
Dosage and administration details: one spray	
Arm title	ZOMIG 2.5 mg
Arm description: ZOMIG nasal spray	
Arm type	Experimental
Investigational medicinal product name	zolmitriptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use
Dosage and administration details: one spray	
Arm title	ZOMIG 5 mg
Arm description: ZOMIG nasal spray	
Arm type	Experimental
Investigational medicinal product name	zolmitriptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use
Dosage and administration details: one spray	

Number of subjects in period 1	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg
Started	296	115	99
Completed	270	98	86
Not completed	26	17	13
Eligibility criteria not fulfilled	16	12	10
Patient decision	2	1	-
Severe noncompliance to protocol	1	-	-
Study-specific withdrawal criteria	1	-	-
Reason not specified	3	2	2
Lost to follow-up	3	2	1

Number of subjects in period 1	ZOMIG 5 mg

Started	288
Completed	268
Not completed	20
Eligibility criteria not fulfilled	15
Patient decision	2
Severe noncompliance to protocol	-
Study-specific withdrawal criteria	-
Reason not specified	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo to ZOMIG nasal spray	
Reporting group title	ZOMIG 0.5 mg
Reporting group description:	
ZOMIG nasal spray	
Reporting group title	ZOMIG 2.5 mg
Reporting group description:	
ZOMIG nasal spray	
Reporting group title	ZOMIG 5 mg
Reporting group description:	
ZOMIG nasal spray	

Reporting group values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg
Number of subjects	296	115	99
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	296	115	99
Age Continuous |			
Units: Years			
arithmetic mean	14.3	14.5	14.6
standard deviation	± 1.67	± 1.72	± 1.77
Gender, Male/Female			
All randomized patients			
Units: Participants			
Female	188	71	62
Male	108	44	37
Race			
Race			
Units: Subjects			
White	275	106	91
Black or African-American	14	8	7
Asian	2	0	0
American Indian or Alaska Native	1	0	0
Other	4	1	1

Reporting group values	ZOMIG 5 mg	Total	
Number of subjects	288	798	
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	288	798	
Age Continuous |			
Units: Years			
arithmetic mean	14.5		
standard deviation	± 1.67	-	

Gender, Male/Female			
All randomized patients			
Units: Participants			
Female	172	493	
Male	116	305	
Race			
Race			
Units: Subjects			
White	271	743	
Black or African-American	15	44	
Asian	0	2	
American Indian or Alaska Native	0	1	
Other	2	8	

Subject analysis sets

Subject analysis set title	All Patients Randomized
Subject analysis set type	Intention-to-treat

Subject analysis set description:
All Patients Randomized

Reporting group values	All Patients Randomized		
Number of subjects	798		
Age categorical Units: Subjects			
Adolescents (12-17 years)	798		
Age Continuous | Units: Years			
arithmetic mean	14.4		
standard deviation	± 1.69		
Gender, Male/Female			
All randomized patients			
Units: Participants			
Female	493		
Male	305		
Race			
Race			
Units: Subjects			
White	743		
Black or African-American	44		
Asian	2		
American Indian or Alaska Native	1		
Other	8		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo to ZOMIG nasal spray	
Reporting group title	ZOMIG 0.5 mg
Reporting group description: ZOMIG nasal spray	
Reporting group title	ZOMIG 2.5 mg
Reporting group description: ZOMIG nasal spray	
Reporting group title	ZOMIG 5 mg
Reporting group description: ZOMIG nasal spray	
Subject analysis set title	All Patients Randomized
Subject analysis set type	Intention-to-treat
Subject analysis set description: All Patients Randomized	

Primary: Pain-free status at 2 hours post-treatment

End point title	Pain-free status at 2 hours post-treatment
End point description:	
End point type	Primary
End point timeframe: 2 hours post-treatment.	

End point values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg	ZOMIG 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	253	91	81	229
Units: Participants				
Yes	42	20	20	68
No	211	71	61	161

Statistical analyses

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 0.5 mg

Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.312 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.5

Notes:

[1] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 2.5 mg
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.071 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	3.26

Notes:

[2] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 5 mg
Number of subjects included in analysis	482
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	3.39

Notes:

[3] - Unadjusted

Secondary: Pain-free status at 24 hours post-treatment

End point title	Pain-free status at 24 hours post-treatment

End point description:

End point type	Secondary

End point timeframe:

24 hours post-treatment

End point values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg	ZOMIG 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	251	91	80	227
Units: Participants				
Yes	155	59	60	155
No	96	32	20	72

Statistical analyses

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 0.5 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.575 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.91

Notes:

[4] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 2.5 mg
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.032 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	3.31

Notes:

[5] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 5 mg
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.137 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.95

Notes:

[6] - Unadjusted

Secondary: Headache response at 2 hours post-treatment

End point title	Headache response at 2 hours post-treatment

End point description:

Headache response is a binary response variable derived from the headache intensities recorded in the patient diary. Headache response is defined as a reduction in headache pain intensity from severe or moderate to mild or none with no use of rescue medication prior to the assessment.

End point type	Secondary

End point timeframe:

2 hours post-treatment

End point values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg	ZOMIG 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	253	91	81	229
Units: Participants				
Yes	99	40	43	116
No	154	51	38	113

Statistical analyses

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 0.5 mg
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.458 [7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.96

Notes:

[7] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 2.5 mg
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.021 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	3.03

Notes:

[8] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 5 mg
Number of subjects included in analysis	482
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	2.32

Notes:
[9] - Unadjusted

Secondary: Headache response at 24 hours post-treatment

End point title	Headache response at 24 hours post-treatment

End point description:

Headache response is a binary response variable derived from the headache intensities recorded in the patient diary. Headache response is defined as a reduction in headache pain intensity from severe or moderate to mild or none with no use of rescue medication prior to the assessment.

End point type	Secondary

End point timeframe:

24 hours post-treatment

End point values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg	ZOMIG 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	251	91	80	227
Units: Participants				
Yes	170	63	61	168
No	81	28	19	59

Statistical analyses

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 0.5 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.753 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.84

Notes:
[10] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 2.5 mg

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.145 [11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	2.79

Notes:

[11] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 5 mg
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.127 [12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	2.04

Notes:

[12] - Unadjusted

Secondary: Sustained headache response at 2 hours

End point title	Sustained headache response at 2 hours

End point description:

Sustained headache response at 2 hours is a binary response variable derived from the headache intensities recorded in the patient diary. Sustained headache response is defined as a reduction in migraine headache pain intensity from severe or moderate to mild or none a 1 hr. which is then maintained (without a return to moderate or severe pain) at 2 hrs. with no use of rescue medication prior to the 2 hr. assessment.

End point type	Secondary

End point timeframe:

Up to 2 hours post-treatment

End point values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg	ZOMIG 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	251	91	81	224
Units: Participants				
Yes	59	27	27	66
No	192	64	54	158

Statistical analyses

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 0.5 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.274 [13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.32

Notes:

[13] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 5 mg
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.127 [14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	2.08

Notes:

[14] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 2.5 mg

Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.067 [15]
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	2.91

Notes:

[15] - Unadjusted

Secondary: Use of rescue medication during the first 24 hours after treatment

End point title	Use of rescue medication during the first 24 hours after treatment

End point description:

End point type	Secondary

End point timeframe:

24 hours post-treatment.

End point values	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg	ZOMIG 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	253	91	81	231
Units: Participants				
Yes	80	22	18	47
No	173	69	63	184

Statistical analyses

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 0.5 mg
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.153 [16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.16

Notes:

[16] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 2.5 mg
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.087 [17]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.08

Notes:

[17] - Unadjusted

Statistical analysis title	Odds ratio comparison
Comparison groups	Placebo v ZOMIG 5 mg
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004 [18]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.83

Notes:

[18] - Unadjusted

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During double-blind treatment	
Adverse event reporting additional description:	
Safety Analysis Set (Number of Patients at Risk: Placebo=253; ZOMIG 0.5 mg=92; ZOMIG 2.5 mg=81; ZOMIG 5 mg=231)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo to ZOMIG nasal spray	
Reporting group title	ZOMIG 0.5 mg
Reporting group description:	
ZOMIG nasal spray	
Reporting group title	ZOMIG 2.5 mg
Reporting group description:	
ZOMIG nasal spray	
Reporting group title	ZOMIG 5 mg
Reporting group description:	
ZOMIG nasal spray	

Serious adverse events	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	ZOMIG 5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 231 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	ZOMIG 0.5 mg	ZOMIG 2.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 253 (9.88%)	14 / 92 (15.22%)	9 / 81 (11.11%)
Injury, poisoning and procedural complications			
Administration related reaction			
subjects affected / exposed	0 / 253 (0.00%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dysgeusia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 253 (1.19%)	6 / 92 (6.52%)	5 / 81 (6.17%)
occurrences (all)	3	6	5
Dizziness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 253 (0.79%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	2	1	0
Paraesthesia			
subjects affected / exposed	1 / 253 (0.40%)	1 / 92 (1.09%)	1 / 81 (1.23%)
occurrences (all)	1	1	1
Hypoaesthesia			
subjects affected / exposed	1 / 253 (0.40%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	1	1	0
Somnolence			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Bradykinesia			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 253 (0.00%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Feeling cold			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 253 (0.00%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 253 (0.40%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	3 / 253 (1.19%)	0 / 92 (0.00%)	1 / 81 (1.23%)
occurrences (all)	3	0	1
Abdominal pain upper			
subjects affected / exposed	3 / 253 (1.19%)	0 / 92 (0.00%)	1 / 81 (1.23%)
occurrences (all)	3	0	1
Vomiting			
subjects affected / exposed	3 / 253 (1.19%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	3	0	0
Oral discomfort			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Oral pruritus			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal discomfort			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 253 (1.58%)	1 / 92 (1.09%)	2 / 81 (2.47%)
occurrences (all)	4	1	2
Oropharyngeal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 253 (1.58%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	4	1	0
Throat irritation			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Pharyngeal oedema			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Rhinalgia			
subjects affected / exposed	2 / 253 (0.79%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	2	0	0

Rhinorrhoea			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	2 / 253 (0.79%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Hiccups			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Throat tightness			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0

Muscular weakness			
subjects affected / exposed	1 / 253 (0.40%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 253 (0.00%)	0 / 92 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 253 (0.00%)	1 / 92 (1.09%)	0 / 81 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	ZOMIG 5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 231 (25.54%)		
Injury, poisoning and procedural complications			
Administration related reaction			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	29 / 231 (12.55%)		
occurrences (all)	29		
Dizziness			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	6 / 231 (2.60%)		
occurrences (all)	6		
Paraesthesia			
subjects affected / exposed	2 / 231 (0.87%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	3 / 231 (1.30%)		
occurrences (all)	3		
Bradykinesia			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Burning sensation			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Head discomfort			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 231 (1.30%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Facial pain			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Feeling cold			

subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye irritation			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Photopsia			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 231 (2.16%)		
occurrences (all)	5		
Abdominal pain upper			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Oral discomfort			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Oral pain			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		

Oral pruritus			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Nasal discomfort			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 231 (3.03%)		
occurrences (all)	7		
Oropharyngeal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 231 (3.03%)		
occurrences (all)	7		
Throat irritation			
subjects affected / exposed	3 / 231 (1.30%)		
occurrences (all)	3		
Pharyngeal oedema			
subjects affected / exposed	2 / 231 (0.87%)		
occurrences (all)	2		
Rhinalgia			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Hiccups			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Nasal congestion			

subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Throat tightness			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Psychiatric disorders			
Disorientation			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 231 (0.87%)		
occurrences (all)	2		
Joint stiffness			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	0 / 231 (0.00%)		
occurrences (all)	0		
Musculoskeletal discomfort			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 231 (0.43%)		
occurrences (all)	1		
Neck pain			

subjects affected / exposed occurrences (all) Pain in jaw subjects affected / exposed occurrences (all)	1 / 231 (0.43%) 1 1 / 231 (0.43%) 1		
Infections and infestations Influenza subjects affected / exposed occurrences (all)	 0 / 231 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2010	1) Increased number of study sites and added Europe, deleted South Africa;
10 January 2012	2) Changed inclusion criteria; changed randomization from strictly sequential assignment to blocked randomization schedule
06 September 2012	3) Changed international coordinating investigator; changed details of interim analyses; changed inclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to futility at the interim analysis, fewer subjects were randomized to the 0.5- and 2.5-mg groups. This precluded a full evaluation of these treatment arms at the end of the study.

Notes: