Clinical trial results:
A Randomized, Double blind, Placebo Controlled Phase II Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of ARGX 113 in Patients with Myasthenia Gravis who have Generalized Muscle Weakness

Summary

EudraCT number	2016-002938-73
Trial protocol	BE SE ES NL IT
Global end of trial date	20 October 2017

Results information

Result version number	v1 (current)
This version publication date	03 November 2018
First version publication date	03 November 2018

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1602

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02965573
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	argenx
Sponsor organisation address	Industriepark 7, Zwijnaarde, Belgium, 9052
Public contact	Regulatory, argenx BVBA, +32 9310 3400, regulatory@argenx.com
Scientific contact	Regulatory, argenx BVBA, +32 9310 3400, regulatory@argenx.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of ARGX 113.

Protection of trial subjects:

Safety assessments consisted of monitoring and recording all AEs, including SAEs, and pregnancies; suicidality assessment; safety laboratory testing, measurement of vital signs, ECGs, physical examinations; and other tests that were deemed critical to the safety evaluation of the study in all subjects who received at least 1 dose of the IMP.

Background therapy:

In this study, standard of care (SoC) for a patient was the stable dose and administration of their MG treatment prior to enrollment. Permitted SoC for MG treatment under this protocol included azathioprine (AZA), other non steroidal immunosuppressant drugs (NSIDs: e.g., methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil, and cyclophosphamide), steroids, as well as cholinesterase inhibitors. Patients had to be on a stable dose and frequency of SoC prior to enrollment as detailed in the protocol and for the duration of the study.

Evidence for comparator: -

Actual start date of recruitment	30 December 2016
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	Canada: 1
Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Italy: 4
Worldwide total number of subjects	24
EEA total number of subjects	19

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)	0
Adults (18-64 years)	18
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted by 15 Investigators at 15 study centers (i.e., study centers that consented at least 1 patient) in 8 countries (Belgium, Canada, Italy, the Netherlands, Poland, Spain, Sweden, and United States). A total of 24 subjects were randomized in the study.

Pre-assignment

Screening details:

The study included a maximum Screening period of 15 days to evaluate patients' eligibility. Evaluations at screening and confirmation at visit 1 were used to determine the eligibility of each subject for randomization in the study. Subjects who failed to meet the eligibility criteria were considered screen failures.

Period 1

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

Blinding implementation details:

The IMPs (ARGX-113 and placebo) were identical in physical appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	ARGX-113

Arm description: -

Arm type	Experimental
Investigational medicinal product name	efgartigimod
Investigational medicinal product code	ARGX-113
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ARGX-113 was administered weekly for 4 weeks by intravenous infusion.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was administered weekly for 4 weeks by intravenous use.

Number of subjects in period 1	ARGX-113	Placebo
Started	12	12
Completed	11	12
Not completed	1	0
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	ARGX-113
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	ARGX-113	Placebo	Total
Number of subjects	12	12	24
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	10	18
From 65-84 years	4	2	6
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	7	8	15
Male	5	4	9

End points

End points reporting groups

Reporting group title	ARGX-113
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: 1. Adverse events

End point title	1. Adverse events[1]
End point description:	
End point type	Primary
End point timeframe:	
The entire duration of the study.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint is analysed by means of descriptive statistics.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Number of events/ Number of patients				
Number of events	60	44		
Patients with at least 1 TEAE	10	10		
Patients with at least 1 nonTEAE	2	4		
Patients with at least 1 serious TEAE	0	0		
Patients withdrawn with at least 1 serious TEAE	0	0		
Patients with at least 1 related serious TEAE	0	0		
Patients who discontinued due to a TEAE	0	0		
Patients with at least 1 TEAE CTCAE >=3	0	0		
Patients with at least 1 related TEAE	8	3		
Number of deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: 2. MG-ADL Score Change from Baseline

End point title	2. MG-ADL Score Change from Baseline
End point description:	

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Score change				
median (full range (min-max))				
Day 1 (Baseline)	7.5 (5 to 15)	8.0 (5 to 13)		
Day 8	-1.0 (-10 to 0)	-0.5 (-4 to 2)		
Day 15	-2.0 (-9 to 0)	-2.0 (-7 to 0)		
Day 22	-3.5 (-8 to 0)	-2.0 (-7 to 1)		
Day 29	-4.0 (-8 to 0)	-1.0 (-7 to 0)		
Day 36	-3.5 (-10 to 1)	-1.5 (-6 to 1)		
Day 43	-4.0 (-8 to 1)	-1.0 (-8 to 1)		
Day 50	-3 (-11 to -1)	-1.0 (-9 to 0)		
Day 64	-2.5 (-9 to 1)	-1.0 (-8 to 5)		
Day 78	-3.0 (-10 to 1)	-1.0 (-9 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3. QMG score change from baseline

End point title	3. QMG score change from baseline

End point description:

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Score change from baseline				
median (full range (min-max))				
Day 1 (Baseline)	14.0 (6 to 30)	12.5 (3 to 24)		
Day 8	-2.0 (-10 to 0)	0 (-3 to 4)		
Day 15	-3.0 (-12 to 1)	-1.5 (-8 to 2)		
Day 22	-3.0 (-14 to 3)	-2.0 (-8 to 4)		
Day 29	-4.5 (-16 to 1)	-1.0 (-8 to 4)		
Day 36	-3.5 (-16 to 2)	-0.5 (-10 to 1)		

Day 43	-3.5 (-15 to 3)	-2.0 (-10 to 6)		
Day 50	-5.0 (-16 to 2)	-1.0 (-10 to 3)		
Day 64	-2.0 (-15 to 2)	-1.0 (-13 to 3)		
Day 78	-2.0 (-18 to 3)	-1.5 (-11 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. MGC score change from baseline

End point title	4. MGC score change from baseline

End point description:

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Score change from baseline				
median (full range (min-max))				
Day 1 (baseline)	14.0 (6 to 37)	14.0 (8 to 25)		
Day 8	-4.0 (-17 to 4)	-0.5 (-6 to 3)		
Day 15	-5.5 (-16 to 4)	-3.5 (-14 to 1)		
Day 22	-5.5 (-19 to 2)	-3.5 (-11 to 0)		
Day 29	-8.0 (-19 to 5)	-4.0 (-12 to 4)		
Day 36	-7.5 (-21 to 7)	-4.0 (-12 to 4)		
Day 43	-10.5 (-20 to 7)	-5.0 (-12 to 8)		
Day 50	-5.0 (-23 to 1)	-2.5 (-13 to 4)		
Day 64	-6.0 (-21 to 4)	-3.0 (-15 to 7)		
Day 78	-8.0 (-23 to 6)	-3.5 (-14 to 5)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. MGQoL15r score change from baseline

End point title	5. MGQoL15r score change from baseline

End point description:

Myasthenia Gravis Quality of Life-15 (revised version)

End point type	Secondary

End point timeframe:
From Day 1 (Baseline) until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Score change from baseline				
median (full range (min-max))				
Day 1 (Baseline)	21.0 (10 to 28)	12.5 (5 to 25)		
Day 8	0 (-20 to 2)	0 (-5 to 2)		
Day 15	-2.5 (-16 to 0)	0 (-6 to 3)		
Day 22	-3.0 (-17 to 0)	0 (-8 to 2)		
Day 29	-3.0 (-18 to 2)	0 (-8 to 2)		
Day 36	-6.0 (-19 to 2)	-1.0 (-11 to 3)		
Day 43	-4.5 (-19 to 2)	0 (-10 to 3)		
Day 50	-4.0 (-12 to 2)	-1.0 (-10 to 3)		
Day 64	-3.0 (-15 to 2)	0 (-10 to 3)		
Day 78	-3.0 (-15 to 5)	-0.5 (-10 to 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Maximum reduction from Baseline across visit days for the various scores

End point title	6. Maximum reduction from Baseline across visit days for the various scores

End point description:

End point type	Secondary

End point timeframe:
From Day 1 (Baseline) until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Maximum reduction				
median (full range (min-max))				
Myasthenia Gravis Activities of Daily Living	-4.5 (-11 to 0)	-2.0 (-9 to 0)		
Quantitative Myasthenia Gravis	-4.5 (-18 to -2)	-4.0 (-13 to 1)		
Myasthenia Gravis Composite	-10.5 (-23 to -1)	-6.5 (-15 to -2)		

Myasthenia Gravis Quality of Life-15 (revised v.)	-6.0 (-20 to -1)	-3.0 (-11 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Pharmacokinetics: Cmax

End point title	7. Pharmacokinetics: Cmax

End point description:

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) until Day 22.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12[2]	0[3]		
Units: µg/mL				
median (full range (min-max))				
Day 1	173.5 (114 to 276)	(to)		
Day 8	173.0 (117 to 219)	(to)		
Day 15	156.0 (110 to 209)	(to)		
Day 22	156.0 (113 to 253)	(to)		

Notes:

[2] - As of Day 8, values for n=11

[3] - No pharmacokinetic analysis was performed for placebo-treated subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Pharmacokinetics: Tmax

End point title	8. Pharmacokinetics: Tmax

End point description:

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) until Day 22.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	0[4]		
Units: Hours				
median (full range (min-max))				
Day 1	2.44 (2.08 to 2.58)	(to)		
Day 8	2.50 (2.08 to 2.50)	(to)		
Day 15	2.50 (2.07 to 2.50)	(to)		
Day 22	2.46 (2.08 to 2.67)	(to)		

Notes:

[4] - No pharmacokinetic analysis was performed for placebo-treated subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Evaluation of total IgG

End point title	9. Evaluation of total IgG

End point description:

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: µg/mL				
median (full range (min-max))				
Day 1 (Baseline)	8825 (4340 to 19800)	6855 (4670 to 14700)		
Day 8	5400 (2610 to 13800)	7220 (4050 to 13900)		
Day 15	3825 (1620 to 9120)	7840 (4480 to 14300)		
Day 22	2475 (1680 to 4790)	6800 (4800 to 12900)		
Day 29	2540 (1370 to 7600)	6460 (4330 to 13200)		
Day 36	4590 (1410 to 8430)	6745 (5180 to 9940)		
Day 43	3870 (2240 to 12300)	7210 (3880 to 10600)		
Day 50	5310 (2410 to 14300)	7435 (4530 to 11100)		
Day 57	6070 (3080 to 16400)	7610 (4890 to 13300)		

Day 64	6220 (3940 to 13100)	7225 (4480 to 14400)		
Day 71	6080 (2750 to 21700)	7585 (4180 to 14700)		
Day 78	7095 (1890 to 24200)	7420 (5000 to 14200)		

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Evaluation of anti-AChR antibodies

End point title	10. Evaluation of anti-AChR antibodies

End point description:

End point type	Secondary

End point timeframe:

From Day 1 until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: nmol/L				
median (full range (min-max))				
Day 1	7.030 (0.265 to 106.000)	11.115 (0.398 to 186.000)		
Day 8	5.035 (0.265 to 51.700)	10.715 (0.401 to 223.000)		
Day 15	4.185 (0.265 to 38.100)	11.845 (0.379 to 179.000)		
Day 22	2.160 (0.265 to 34.900)	11.545 (0.366 to 169.000)		
Day 29	3.755 (0.265 to 32.100)	6.185 (0.265 to 173.000)		
Day 36	4.280 (0.265 to 40.100)	12.200 (0.380 to 188.000)		
Day 43	5.590 (0.265 to 46.300)	3.310 (0.361 to 168.000)		
Day 50	5.390 (0.265 to 52.400)	6.805 (0.379 to 162.000)		
Day 57	6.330 (0.265 to 73.600)	7.390 (0.370 to 213.000)		
Day 64	6.470 (0.265 to 73.700)	7.375 (0.366 to 169.000)		
Day 71	7.790 (0.265 to 73.100)	13.050 (0.367 to 181.000)		
Day 78	7.165 (0.265 to 88.900)	7.425 (0.356 to 165.000)		

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Evaluation of the incidence of anti-drug antibodies

End point title	11. Evaluation of the incidence of anti-drug antibodies

End point description:

End point type	Secondary

End point timeframe:

From Day 1 until Day 78.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects				
Subjects with pre-dose ADA titers	4	2		
Subjects with post-dose ADA titers	4	3		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 12. Percentage of patients with sustained clinically relevant improvement (drop in MG-ADL score ≥ 2)

End point title	12. Percentage of patients with sustained clinically relevant improvement (drop in MG-ADL score ≥ 2)

End point description:

Sustained clinically relevant improvement is defined in this case as starting the latest 1 week after last infusion of IMP and lasting for ≥ 4 consecutive weeks.

End point type	Post-hoc

End point timeframe:

For the duration of the study

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage				
number (not applicable)	75.0	33.3		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 13. Percentage of patients with sustained clinically relevant improvement (drop in MG-ADL ≥ 2)

End point title	13. Percentage of patients with sustained clinically relevant improvement (drop in MG-ADL ≥ 2)

End point description:

Sustained clinically relevant improvement is defined as starting at the latest 1 week after last infusion of IMP and lasting for ≥ 6 weeks.

End point type	Post-hoc

End point timeframe:

For the duration of the study.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage				
number (not applicable)	75	25		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 14. Percentage of patients showing at least x points reduction in total MG-ADL score at Day 29

End point title	14. Percentage of patients showing at least x points reduction in total MG-ADL score at Day 29

End point description:

End point type	Post-hoc

End point timeframe:

At Day 29

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage				
number (not applicable)				
Change from baseline: -2	83	42		
Change from baseline: -3	75	33		
Change from baseline: -4	58	33		
Change from baseline: -5	42	25		
Change from baseline: -6	25	17		
Change from baseline: -7	25	8		
Change from baseline: -8	17	0		
Change from baseline: -9	0	0		
Change from baseline: -10	0	0		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 15. Percentage of patients showing at least x points reduction in total MG-ADL score at Day 36

End point title	15. Percentage of patients showing at least x points reduction in total MG-ADL score at Day 36

End point description:

End point type	Post-hoc

End point timeframe:

Day 36

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage				
number (not applicable)				
Change from baseline: -2	75	50		
Change from baseline: -3	67	33		
Change from baseline: -4	50	25		
Change from baseline: -5	42	25		
Change from baseline: -6	33	17		
Change from baseline: -7	33	0		
Change from baseline: -8	17	0		
Change from baseline: -9	8	0		
Change from baseline: -10	8	0		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 16. Percentage of patients with sustained clinically relevant improvement (drop in QMG score ≥ 3)

End point title	16. Percentage of patients with sustained clinically relevant improvement (drop in QMG score ≥ 3)

End point description:

Sustained response is defined as starting at the latest 1 week after last infusion of IMP and lasting for ≥ 4 consecutive weeks.

End point type	Post-hoc

End point timeframe:

For the duration of the study.

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage				
number (not applicable)	58.3	16.7		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 17. Percentage of patients showing at least x points reduction in total QMG score at Day 29

End point title	17. Percentage of patients showing at least x points reduction in total QMG score at Day 29

End point description:

End point type	Post-hoc

End point timeframe:

Day 29

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11[5]		
Units: Percentage				
number (not applicable)				
Change from baseline: -3	58	27		
Change from baseline: -4	58	27		
Change from baseline: -5	50	18		
Change from baseline: -6	42	18		

Change from baseline: -7	25	18		
Change from baseline: -8	25	9		
Change from baseline: -9	25	0		
Change from baseline: -10	17	0		
Change from baseline: -11	8	0		
Change from baseline: -12	8	0		

Notes:

[5] - missing value in 1 patient

Statistical analyses

No statistical analyses for this end point

Post-hoc: 18. Percentage of patients showing at least x points reduction in total QMG score at Day 36

End point title	18. Percentage of patients showing at least x points reduction in total QMG score at Day 36

End point description:

End point type	Post-hoc

End point timeframe:

Day 36

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Percentage				
number (not applicable)				
Change from baseline: -3	58	33		
Change from baseline: -4	50	25		
Change from baseline: -5	42	17		
Change from baseline: -6	33	17		
Change from baseline: -7	33	8		
Change from baseline: -8	33	8		
Change from baseline: -9	25	8		
Change from baseline: -10	25	8		
Change from baseline: -11	25	0		
Change from baseline: -12	25	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For each subject, adverse events were recorded from the time of signing the informed consent form until last visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	ARGX-113
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	ARGX-113	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	ARGX-113	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)	10 / 12 (83.33%)	
Investigations			
B-lymphocyte count decreased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Lymphocyte count decreased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	4	0	
Monocyte count decreased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	4	0	
Neutrophil count increased			

subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 12 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	9	5	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	
occurrences (all)	1	3	
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			

Tooth abscess subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 12 (16.67%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported