Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Assess Safety, Tolerability, and Single-Dose Pharmacokinetics of MK-0462 in Migraineurs Aged 6 to 17 Years

Summary

EudraCT number	2011-002348-28
Trial protocol	Outside EU/EEA
Global end of trial date	17 September 2010

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	05 July 2015

Trial information

Trial identification

Sponsor protocol code	0462-083

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00604812
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000084-PIP02-10
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	17 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 September 2010
Global end of trial reached?	Yes
Global end of trial date	17 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A study to assess the safety, tolerability, and single dose pharmacokinetics of a marketed drug in pediatric participants with migraines. After completion of a portion of the study (Panels A and B), a regulatory agency issued an amended request that the 12-17 year old age group studied should include a similar number of male and female participants. Therefore, the study was amended to add an additional panel of participants (Panel C) to ensure gender balance specifically in this age group.

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	17 December 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: 31
Worldwide total number of subjects	31
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)	13
Adolescents (12-17 years)	18
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 31 subjects were enrolled in the study.

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	Panel A Rizatriptan

Arm description:

Participants allocated to Panel A and randomized to receive a single dose of rizatriptan 5 mg orally disintegrating tablet (ODT) on Day 1. Participants weighing 20-39 kg were allocated to Panel A.

Arm type	Experimental
Investigational medicinal product name	rizatriptan benzoate (5 mg)
Investigational medicinal product code	
Other name	MAXALT®, MK-0462
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 5 mg administered on Day 1.

Arm title	Panel A Placebo

Arm description:

Participants allocated to Panel A and randomized to receive a single dose of rizatriptan 5 mg ODT placebo on Day 1. Participants weighing 20-39 kg were allocated to Panel A.

Arm type	Placebo
Investigational medicinal product name	Rizatriptan 5 mg Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 5 mg placebo administered on Day 1.

Arm title	Panel B Rizatriptan

Arm description:

Participants allocated to Panel B and randomized to receive a single dose of rizatriptan 10 mg ODT on Day 1. Participants weighing 40 kg and above were allocated to Panel B.

Arm type	Experimental

Investigational medicinal product name	rizatriptan benzoate (10 mg)
Investigational medicinal product code	
Other name	MAXALT®, MK-0462
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 10 mg administered on Day 1.

Arm title	Panel B Placebo

Arm description:

Participants allocated to Panel B and randomized to receive a single dose of rizatriptan 10 mg ODT placebo on Day 1. Participants weighing 40 kg and above were allocated to Panel B.

Arm type	Placebo
Investigational medicinal product name	Rizatriptan 10 mg Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 10 mg placebo administered on Day 1.

Arm title	Panel C Rizatriptan

Arm description:

Participants allocated to Panel C and randomized to receive a single dose of rizatriptan ODT on Day 1. Participants in Panel C weighing 20-39 kg received a 5 mg dose and participants weighing 40 kg and above received a 10 mg dose. Panel C was added to the study by amendment to increase the number of male participants in the 12-17 year old age group.

Arm type	Experimental
Investigational medicinal product name	rizatriptan benzoate (5 mg)
Investigational medicinal product code	
Other name	MAXALT®, MK-0462
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 5 mg administered on Day 1.

Investigational medicinal product name	rizatriptan benzoate (10 mg)
Investigational medicinal product code	
Other name	MAXALT®, MK-0462
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 10 mg administered on Day 1.

Arm title	Panel C Placebo

Arm description:

Participants allocated to Panel C and randomized to receive a single dose of rizatriptan ODT placebo on Day 1. Participants in Panel C weighing 20-39 kg received a 5 mg placebo dose and participants weighing 40 kg and above received a 10 mg placebo dose. Panel C was added to the study by amendment to increase the number of male participants in the 12-17 year old age group.

Arm type	Placebo
Investigational medicinal product name	Rizatriptan 5 mg Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: A single dose of rizatriptan 5 mg placebo administered on Day 1.	
Investigational medicinal product name	Rizatriptan 10 mg Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single dose of rizatriptan 10 mg placebo administered on Day 1.

Number of subjects in period 1	Panel A Rizatriptan	Panel A Placebo	Panel B Rizatriptan
Started	9	3	10
Completed	9	3	10

Number of subjects in period 1	Panel B Placebo	Panel C Rizatriptan	Panel C Placebo
Started	3	5	1
Completed	3	5	1

Baseline characteristics

Reporting groups	
Reporting group title	Panel A Rizatriptan
Reporting group description:	
Participants allocated to Panel A and randomized to receive a single dose of rizatriptan 5 mg orally disintegrating tablet (ODT) on Day 1. Participants weighing 20-39 kg were allocated to Panel A.	
Reporting group title	Panel A Placebo
Reporting group description:	
Participants allocated to Panel A and randomized to receive a single dose of rizatriptan 5 mg ODT placebo on Day 1. Participants weighing 20-39 kg were allocated to Panel A.	
Reporting group title	Panel B Rizatriptan
Reporting group description:	
Participants allocated to Panel B and randomized to receive a single dose of rizatriptan 10 mg ODT on Day 1. Participants weighing 40 kg and above were allocated to Panel B.	
Reporting group title	Panel B Placebo
Reporting group description:	
Participants allocated to Panel B and randomized to receive a single dose of rizatriptan 10 mg ODT placebo on Day 1. Participants weighing 40 kg and above were allocated to Panel B.	
Reporting group title	Panel C Rizatriptan
Reporting group description:	
Participants allocated to Panel C and randomized to receive a single dose of rizatriptan ODT on Day 1. Participants in Panel C weighing 20-39 kg received a 5 mg dose and participants weighing 40 kg and above received a 10 mg dose. Panel C was added to the study by amendment to increase the number of male participants in the 12-17 year old age group.	
Reporting group title	Panel C Placebo
Reporting group description:	
Participants allocated to Panel C and randomized to receive a single dose of rizatriptan ODT placebo on Day 1. Participants in Panel C weighing 20-39 kg received a 5 mg placebo dose and participants weighing 40 kg and above received a 10 mg placebo dose. Panel C was added to the study by amendment to increase the number of male participants in the 12-17 year old age group.	

Reporting group values	Panel A Rizatriptan	Panel A Placebo	Panel B Rizatriptan
Number of subjects	9	3	10
Age categorical Units: Subjects			
Ages 6 to <12	8	3	2
Ages 12 to 17	1	0	8
Gender categorical Units: Subjects			
Female	3	2	5
Male	6	1	5
Weight Units: Subjects			
20-39 kg	9	3	0
≥40 kg	0	0	10

Reporting group values	Panel B Placebo	Panel C Rizatriptan	Panel C Placebo
Number of subjects	3	5	1

Age categorical Units: Subjects			
Ages 6 to <12	0	0	0
Ages 12 to 17	3	5	1
Gender categorical Units: Subjects			
Female	3	0	0
Male	0	5	1
Weight Units: Subjects			
20-39 kg	0	1	0
≥40 kg	3	4	1

Reporting group values	Total		
Number of subjects	31		
Age categorical Units: Subjects			
Ages 6 to <12	13		
Ages 12 to 17	18		
Gender categorical Units: Subjects			
Female	13		
Male	18		
Weight Units: Subjects			
20-39 kg	13		
≥40 kg	18		

Subject analysis sets	
Subject analysis set title	Panel A
Subject analysis set type	Full analysis
Subject analysis set description: Includes the participants from the 5 mg rizatriptan group (n=9) and the matching placebo group (n=3).	
Subject analysis set title	Panel B
Subject analysis set type	Full analysis
Subject analysis set description: Includes the participants from the 10 mg rizatriptan group (n=10) and the matching placebo group (n=3).	
Subject analysis set title	Panel C
Subject analysis set type	Full analysis
Subject analysis set description: Includes the participants who received 5 mg rizatriptan (n=1), 10 mg rizatriptan (n=4), and the matching placebo (n=1)	
Subject analysis set title	Rizatriptan 5 mg
Subject analysis set type	Full analysis
Subject analysis set description: Combined participants from Panel A and Panel C randomized to receive a single dose of rizatriptan 5 mg ODT on Day 1.	
Subject analysis set title	Rizatriptan 10 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Combined participants from Panel B and Panel C randomized to receive a single dose of rizatriptan 10 mg ODT on Day 1.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Combined Placebo groups from panels A, B, and C.

Reporting group values	Panel A	Panel B	Panel C
Number of subjects	12	13	6
Age categorical Units: Subjects			
Ages 6 to <12	11	2	0
Ages 12 to 17	1	11	6
Gender categorical Units: Subjects			
Female	5	8	0
Male	7	5	6
Weight Units: Subjects			
20-39 kg	12	0	1
≥40 kg	0	13	5

Reporting group values	Rizatriptan 5 mg	Rizatriptan 10 mg	Placebo
Number of subjects	10	14	7
Age categorical Units: Subjects			
Ages 6 to <12	8	2	3
Ages 12 to 17	2	12	4
Gender categorical Units: Subjects			
Female	3	5	5
Male	7	9	2
Weight Units: Subjects			
20-39 kg	10	0	3
≥40 kg	0	14	4

End points

End points reporting groups

Reporting group title	Panel A Rizatriptan
Reporting group description:	
Participants allocated to Panel A and randomized to receive a single dose of rizatriptan 5 mg orally disintegrating tablet (ODT) on Day 1. Participants weighing 20-39 kg were allocated to Panel A.	
Reporting group title	Panel A Placebo
Reporting group description:	
Participants allocated to Panel A and randomized to receive a single dose of rizatriptan 5 mg ODT placebo on Day 1. Participants weighing 20-39 kg were allocated to Panel A.	
Reporting group title	Panel B Rizatriptan
Reporting group description:	
Participants allocated to Panel B and randomized to receive a single dose of rizatriptan 10 mg ODT on Day 1. Participants weighing 40 kg and above were allocated to Panel B.	
Reporting group title	Panel B Placebo
Reporting group description:	
Participants allocated to Panel B and randomized to receive a single dose of rizatriptan 10 mg ODT placebo on Day 1. Participants weighing 40 kg and above were allocated to Panel B.	
Reporting group title	Panel C Rizatriptan
Reporting group description:	
Participants allocated to Panel C and randomized to receive a single dose of rizatriptan ODT on Day 1. Participants in Panel C weighing 20-39 kg received a 5 mg dose and participants weighing 40 kg and above received a 10 mg dose. Panel C was added to the study by amendment to increase the number of male participants in the 12-17 year old age group.	
Reporting group title	Panel C Placebo
Reporting group description:	
Participants allocated to Panel C and randomized to receive a single dose of rizatriptan ODT placebo on Day 1. Participants in Panel C weighing 20-39 kg received a 5 mg placebo dose and participants weighing 40 kg and above received a 10 mg placebo dose. Panel C was added to the study by amendment to increase the number of male participants in the 12-17 year old age group.	
Subject analysis set title	Panel A
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes the participants from the 5 mg rizatriptan group (n=9) and the matching placebo group (n=3).	
Subject analysis set title	Panel B
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes the participants from the 10 mg rizatriptan group (n=10) and the matching placebo group (n=3).	
Subject analysis set title	Panel C
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes the participants who received 5 mg rizatriptan (n=1), 10 mg rizatriptan (n=4), and the matching placebo (n=1)	
Subject analysis set title	Rizatriptan 5 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Combined participants from Panel A and Panel C randomized to receive a single dose of rizatriptan 5 mg ODT on Day 1.	
Subject analysis set title	Rizatriptan 10 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Combined participants from Panel B and Panel C randomized to receive a single dose of rizatriptan 10 mg ODT on Day 1.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Combined Placebo groups from panels A, B, and C.

Primary: Number of Participants with Serious and Non-Serious Adverse Events During Study

End point title	Number of Participants with Serious and Non-Serious Adverse Events During Study[1]

End point description:

All adverse events spontaneously reported by participant and/or observed by investigator. Analysis was performed on data obtained from the All Participants as Treated population, which is all participants who received at least one dose of the investigational drug.

End point type	Primary

End point timeframe:

24 Hours

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: No statistical comparison of the presented study groups was performed for this measure.

End point values	Rizatriptan 5 mg	Rizatriptan 10 mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	14	7	
Units: participants				
Serious Adverse Events	0	0	0	
Non-Serious Adverse Events	3	7	3	
No Adverse Events Reported	7	7	4	

Statistical analyses

No statistical analyses for this end point

Primary: Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan - Area Under the Curve (AUC(0-∞))

End point title	Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan - Area Under the Curve (AUC(0-∞))[2][3]

End point description:

Preliminary pharmacokinetics data; AUC(0-∞); i.e., area under the concentration-time plot. Analysis was performed on data obtained from the Per Protocol population, which is the subset of participants who comply with the protocol sufficiently to ensure that these data will be likely to exhibit the effects of treatment, according to the underlying scientific model. Compliance covers exposure to treatment, availability of measurements and absence of major protocol violations.

End point type	Primary

End point timeframe:

24 Hours

Notes:

[2] - 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: No statistical comparison of the presented study groups was performed for this measure.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Summary rizatriptan pharmacokinetic data is not provided for study arms that received only placebo (i.e, did not receive rizatriptan).

End point values	Panel A Rizatriptan	Panel B Rizatriptan	Panel C Rizatriptan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	5	
Units: ng*hr/mL				
arithmetic mean (standard deviation)	59.4 (± 11.5)	84 (± 19.8)	67.93 (± 25.17)	

Statistical analyses

No statistical analyses for this end point

Primary: Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan – Maximum Concentration (Cmax)

End point title	Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan – Maximum Concentration (Cmax)[4][5]

End point description:

Preliminary pharmacokinetics data; Cmax; i.e, highest concentration of drug achieved. Analysis was performed on data obtained from the Per Protocol population, which is the subset of participants who comply with the protocol sufficiently to ensure that these data will be likely to exhibit the effects of treatment, according to the underlying scientific model. Compliance covers exposure to treatment, availability of measurements and absence of major protocol violation

End point type	Primary

End point timeframe:

24 Hours

Notes:

[4] - 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: No statistical comparison of the presented study groups was performed for this measure.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Summary rizatriptan pharmacokinetic data is not provided for study arms that received only placebo (i.e, did not receive rizatriptan).

End point values	Panel A Rizatriptan	Panel B Rizatriptan	Panel C Rizatriptan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	5	
Units: ng/mL				
arithmetic mean (standard deviation)	24.6 (± 7.2)	25 (± 8.1)	18.4 (± 5.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan – Time to Maximum Concentration (Tmax)

End point title	Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan – Time to Maximum Concentration (Tmax)[6]

End point description:

Preliminary pharmacokinetics data; Tmax; i.e., amount of time required to reach maximum concentration. Analysis was performed on data obtained from the Per Protocol population, which is the subset of participants who comply with the protocol sufficiently to ensure that these data will be likely to exhibit the effects of treatment, according to the underlying scientific model. Compliance covers exposure to treatment, availability of measurements and absence of major protocol violation.

End point type	Secondary

End point timeframe:

24 Hours

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Summary rizatriptan pharmacokinetic data is not provided for study arms that received only placebo (i.e, did not receive rizatriptan).

End point values	Panel A Rizatriptan	Panel B Rizatriptan	Panel C Rizatriptan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	5	
Units: hours				
median (full range (min-max))	1 (0.3 to 2)	1.5 (0.3 to 3)	1.3 (0.7 to 1.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan – Apparent half-life (Apparent t½)

End point title	Preliminary Pharmacokinetic Data Following Single Dose Administration of Rizatriptan – Apparent half-life (Apparent t½)[7]

End point description:

Preliminary pharmacokinetics data; Apparent t½. Analysis was performed on data obtained from the Per Protocol population, which is the subset of participants who comply with the protocol sufficiently to ensure that these data will be likely to exhibit the effects of treatment, according to the underlying scientific model. Compliance covers exposure to treatment, availability of measurements and absence of major protocol violation.

End point type	Secondary

End point timeframe:

24 Hours

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Summary rizatriptan pharmacokinetic data is not provided for study arms that received only placebo (i.e, did not receive rizatriptan).

End point values	Panel A Rizatriptan	Panel B Rizatriptan	Panel C Rizatriptan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9[8]	10[9]	5[10]	
Units: hours				
arithmetic mean (standard deviation)	1.3 (± 0.1)	1.6 (± 0.2)	1.6 (± 0.4)	

Notes:

[8] - Summary statistics presented are the harmonic mean and pseudo-standard deviation

[9] - Summary statistics presented are the harmonic mean and pseudo-standard deviation

[10] - Summary statistics presented are the harmonic mean and pseudo-standard deviation

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
24 Hours	
Adverse event reporting additional description:	
Analysis was performed on data obtained from the All Participants as Treated population, which is all participants who received at least one dose of the investigational drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	Rizatriptan 5 mg
Reporting group description:	
Combined participants from Panel A and Panel C randomized to receive a single dose of rizatriptan 5 mg ODT on Day 1.	
Reporting group title	Rizatriptan 10 mg
Reporting group description:	
Combined participants from Panel B and Panel C randomized to receive a single dose of rizatriptan 10 mg ODT on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Combined Placebo groups from panels A, B, and C.	

Serious adverse events	Rizatriptan 5 mg	Rizatriptan 10 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 14 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Rizatriptan 5 mg	Rizatriptan 10 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	7 / 14 (50.00%)	3 / 7 (42.86%)
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	1 / 10 (10.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Scratch			
subjects affected / exposed	0 / 10 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 10 (10.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Hypersomnia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 10 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

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