EU Clinical Trials Register

Clinical trial results:
Randomized Controlled Trial of Lasmiditan Over Four Migraine Attacks
Summary

EudraCT number	2018-001661-17
Trial protocol	GB NL DE DK CZ ES AT HU IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	28 June 2021
First version publication date	28 June 2021

Trial information

Trial identification

Sponsor protocol code	H8H-MC-LAIJ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03670810
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17131

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	Interim
Date of interim/final analysis	12 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 June 2020
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of lasmiditan 200 mg and 100 mg on migraine headache pain freedom compared to placebo.
- To evaluate the consistency of response to lasmiditan 200 mg and 100 mg compared to placebo.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 2019
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	China: 136
Country: Number of subjects enrolled	India: 39
Country: Number of subjects enrolled	Mexico: 95
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	United States: 82
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 28
Country: Number of subjects enrolled	Denmark: 30
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Germany: 275
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Spain: 61
Country: Number of subjects enrolled	Switzerland: 19
Country: Number of subjects enrolled	Czechia: 96
Country: Number of subjects enrolled	United Kingdom: 490
Worldwide total number of subjects	1471
EEA total number of subjects	572

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)	1431
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were considered study completers after treating 4 migraine attacks or after completing 4 months of study duration regardless of number of treated attacks.

Pre-assignment

Screening details:

An ITT evaluable attack is defined as a treated attack of least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.
Results for maximum extended enrollment will be posted after the study completion.

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	100 mg Lasmiditan

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lamiditan
Investigational medicinal product code	LY573144
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one 100 mg Lasmiditan tablet administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one 50 mg Lasmiditan matching placebo tablet and one 100-mg Lasmiditan matching placebo tablet to maintain blind administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks..

Arm title	200 mg Lasmiditan

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lasmiditan
Investigational medicinal product code	LY573144
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received two 100 mg Lasmiditan tablets administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one 50 mg Lasmiditan matching placebo tablet to maintain blind. Tablets were administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Arm title	Control 1 Sequence

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lasmiditan
Investigational medicinal product code	LY573144
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one 50 mg Lasmiditan tablet administered orally to treat migraine attack 3. Tablets were administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received two 100 mg Lasmiditan matching placebo tablet to maintain blind for migraine attacks 1, 2 and 4. Tablets were administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Arm title	Control 2 Sequence

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lasmiditan
Investigational medicinal product code	LY573144
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one 50 mg Lasmiditan tablet administer orally to treat migraine attack 4. Tablets were administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received two 100 mg Lasmiditan matching placebo tablet to maintain blind for migraine attacks 1, 2, and 3. Tablets were administered orally within 4 hours of onset of a single migraine attack, up to 4 migraine attacks.

Number of subjects in period 1	100 mg Lasmiditan	200 mg Lasmiditan	Control 1 Sequence
Started	485	486	249
Treated at Least One Migraine Attack	485	486	249
Completed	381	369	208
Not completed	104	117	41
Consent withdrawn by subject	20	20	8
Physician decision	3	-	1
Adverse event, non-fatal	36	38	2
Pregnancy	1	1	-
Non-compliance with study drug	-	2	3
Lost to follow-up	6	6	4
Continuing Study	27	29	12
Missing	1	1	-
Lack of efficacy	8	8	3
Protocol deviation	2	12	8

Number of subjects in period 1	Control 2 Sequence
Started	251
Treated at Least One Migraine Attack	251
Completed	213
Not completed	38
Consent withdrawn by subject	9
Physician decision	-
Adverse event, non-fatal	4
Pregnancy	-
Non-compliance with study drug	-
Lost to follow-up	6
Continuing Study	10
Missing	1
Lack of efficacy	4
Protocol deviation	4

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	1471	1471	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41.40		
standard deviation	± 12.40	-	
Gender categorical Units: Subjects			
Female	1237	1237	
Male	234	234	
Ethnicity Units: Subjects			
Hispanic or Latino	135	135	
Not Hispanic or Latino	1184	1184	
Unknown or Not Reported	152	152	
Race Units: Subjects			
American Indian or Alasks Native	80	80	
Asian	221	221	
Black or African American	27	27	
Native Hawaiian or Other Pacific Islander	1	1	
White	1117	1117	
Multiple	3	3	
Missing	22	22	
Region of Enrollment Units: Subjects			
Austria	11	11	
Belgium	28	28	
China	136	136	
Denmark	30	30	
France	22	22	
Germany	275	275	
Hungary	17	17	
India	39	39	
Italy	22	22	
Mexico	95	95	
Netherlands	10	10	
Russian Federation	38	38	
Spain	61	61	

Switzerland	19	19	
United Kingdom	490	490	
United States	82	82	
Czechia	96	96	

End points

End points reporting groups

Reporting group title	100 mg Lasmiditan
Reporting group description: -	
Reporting group title	200 mg Lasmiditan
Reporting group description: -	
Reporting group title	Control 1 Sequence
Reporting group description: -	
Reporting group title	Control 2 Sequence
Reporting group description: -	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who received 50 mg Lasmiditan matching placebo to treat migraine attacks 1, 2 and 4 in Control 1 Sequence or attacks 1, 2, and 3 in Control 2 Sequence.

Subject analysis set title	Control
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who received 50 mg Lasmiditan to treat migraine attack 3 in Control 1 Sequence and migraine attack 4 in Control 2 Sequence.

Primary: Percentage of Participants That Are Pain Free 2 Hours Postdose During the First Attack

End point title	Percentage of Participants That Are Pain Free 2 Hours Postdose During the First Attack[1]

End point description:

Pain-free is defined as mild, moderate, or severe headache pain becoming none at 2 hours postdose during the first attack.

Analysis Population Description (ADP): All randomized participants who used at least 1 dose of study drug for an Intent-to-Treat (ITT) evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Primary

End point timeframe:

2 Hours Postdose

Notes:

[1] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: percentage of participants				
number (not applicable)	25.8	29.3	8.4	

Statistical analyses

Statistical analysis title	Pain Free 2 Hours Postdose First Attack 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.56
upper limit	8.73

Statistical analysis title	Pain Free 2 Hours Postdose First Attack 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.07
upper limit	6.77

Primary: Percentage of Participants That Are Pain Free at 2 Hours Postdose in at Least 2 Out of 3 Attacks

End point title	Percentage of Participants That Are Pain Free at 2 Hours Postdose in at Least 2 Out of 3 Attacks[2]

End point description:

To evaluate the 2 out of 3 primary consistency endpoint, the results of ITT evaluable attacks in the lasmiditan 100-mg and 200-mg groups will be assessed, and the ITT-evaluable attacks treated with placebo in the control group will be used for comparison. For participants with more than 3 ITT evaluable attacks, only the first 3 will be considered. Pain-free was defined as mild, moderate, or severe headache pain becoming none at the indicated assessment time.

APD: All randomized participants who experienced at least 2 successes or 2 failures during their first 2 or 3 ITT evaluable attacks.

End point type	Primary

End point timeframe:

2 Hours Postdose

Notes:

[2] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	340	336	373	
Units: percentage of participants				
number (not applicable)	14.4	24.4	4.3	

Statistical analyses

Statistical analysis title	Pain Free in at Least 2 Out of 3 Attacks 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	713
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.01
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	6.76

Statistical analysis title	Pain Free in at Least 2 Out of 3 Attacks 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	709
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.01
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.13
upper limit	12.67

Secondary: Percentage of Participants That Are Pain Free 2 Hours Postdose During the First Attack in Triptan Insufficient Responders.

End point title	Percentage of Participants That Are Pain Free 2 Hours Postdose During the First Attack in Triptan Insufficient Responders.[3]

End point description:

Pain-free is defined as mild, moderate, or severe headache pain becoming none at 2 hours postdose during the first attack. A triptan insufficient responder is defined as: 1) Scoring ≤5 on 4 questions from the Migraine Treatment Optimization Questionnaire (mTOQ-6) that defines participants with poor or very poor response to their current regimen; 2) Indicated they obtained pain freedom at 2 hours in 0 out of 3, or 1 out of 3 attacks when treated with the most recent triptan, or 3)Are not currently taking triptan and discontinued their most recent triptan due to lack of efficacy, tolerability issue, or contradictions to a past triptan.

APD: All randomized participants who were triptan insufficient responders and used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	183	203	193	
Units: percentage of participants				
number (not applicable)	24.0	25.6	8.8	

Statistical analyses

Statistical analysis title	Triptan Insufficient Responder 1st Attack 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	6.02

Statistical analysis title	Triptan Insufficient Responder 1st Attack 200 mg
Comparison groups	200 mg Lasmiditan v Placebo

Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.97
upper limit	6.42

Secondary: Percentage of Participants That Are Pain Free at 2 Hours Postdose in at Least 2 Out of 3 Attacks in Triptan Insufficient Responders

End point title	Percentage of Participants That Are Pain Free at 2 Hours Postdose in at Least 2 Out of 3 Attacks in Triptan Insufficient Responders[4]

End point description:

Headache pain-free is defined as a reduction in pain severity from mild, moderate, or severe at baseline to none at the indicated assessment time. A subject is not counted as being pain-free at a specific time point if she or he used rescue or recurrence medication at or before the specific time point.

APD: All randomized participants who were triptan insufficient responders and experienced a sufficient number of successes or failures, (2 successes or 2 failures) during their first 2 or 3 ITT-evaluable attacks.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[4] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	17	31	7	
Units: percentage of participants				
number (not applicable)	11.0	20.1	4.3	

Statistical analyses

Statistical analysis title	TIR 2 out 3 Attacks 100 mg
Comparison groups	100 mg Lasmiditan v Placebo

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	6.78

Statistical analysis title	TIR 2 Out of 3 Attacks 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	13.25

Secondary: Percentage of Participants With no Disability as Measured by the Disability Item, at 2 Hours Postdose During the First Attack

End point title	Percentage of Participants With no Disability as Measured by the Disability Item, at 2 Hours Postdose During the First Attack[5]

End point description:

Percentage of participants with no disability as measured by the disability item, at 2 hours postdose during the first attack. Disability was measured by determining the level of interference with normal activities with 4 response options including not at all; mild interference, marked interference; and need complete bed rest.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: percentage of participants				
number (not applicable)	18.6	19.8	9.5	

Statistical analyses

Statistical analysis title	Disability Item 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	3.33

Statistical analysis title	Disability Item 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	3.67

Secondary: Percentage of Participants With 24-Hour Sustained Pain Freedom During the First Attack

End point title	Percentage of Participants With 24-Hour Sustained Pain Freedom During the First Attack[6]

End point description:

Sustained pain freedom defined as pain free at 2 and 24 hours with no rescue medication.

APD: All randomized participants who received at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: percentage of participants				
number (not applicable)	13.6	17.3	4.3	

Statistical analyses

Statistical analysis title	24 Hour Sustained Pain Freedom 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	6.02

Statistical analysis title	24 Hour Sustained Pain Freedom 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.77
upper limit	7.88

Secondary: Percentage of Participants With Pain Relief at 2 Hours Postdose in at Least 2 Out of 3 Attacks

End point title	Percentage of Participants With Pain Relief at 2 Hours Postdose in at Least 2 Out of 3 Attacks[7]

End point description:

Headache pain relief is defined as a reduction in pain severity from moderate to severe at baseline to mild or none at 2 hours postdose in at least 2 out of 3 attacks. To evaluate at least 2 out of 3 consistency endpoints, the results of ITT-evaluable attacks in the lasmiditan 100-mg and 200-mg groups will be assessed, and the ITT-evaluable attacks treated with placebo in the control group will be used for comparison. For patients with more than 3 ITT-evaluable attacks, only the first 3 with the same treatment will be considered.

APD: All randomized participants who experienced a sufficient number of successes or failures, (2 successes or 2 failures) during their first 2 or 3 ITT-evaluable attacks.

End point type	Secondary

End point timeframe:

2 Hours Postdose

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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	332	333	320	
Units: percentage of participants				
number (not applicable)	62.3	66.7	36.9	

Statistical analyses

Statistical analysis title	Pain Relief 2 out of 3 Attacks 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	652
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.11
upper limit	4.01

Statistical analysis title	Pain Relief 2 out of 3 Attacks 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	653
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.53
upper limit	4.85

Secondary: Percentage of Participants Free of Most Bothersome Symptom (MBS) Associated With Migraine at 2 Hours Postdose During the First Attack

End point title	Percentage of Participants Free of Most Bothersome Symptom (MBS) Associated With Migraine at 2 Hours Postdose During the First Attack[8]

End point description:

MBS freedom is defined as the absence of the associated symptom of migraine (nausea, phonophobia, or photophobia) at the indicated assessment time that was identified at baseline as the most bothersome symptom.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[8] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	376	395	396	
Units: percentage of participants				
number (not applicable)	40.4	39.0	28.0	

Statistical analyses

Statistical analysis title	Free of MBS 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	772
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	2.35

Statistical analysis title	Free of MBS 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	791
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.21
upper limit	2.2

Secondary: Percentage of Participants With Pain Relief at 2 Hours Post Dose During the First Attack

End point title	Percentage of Participants With Pain Relief at 2 Hours Post Dose During the First Attack[9]

End point description:

Headache pain-relief is defined as a reduction in pain severity from moderate or severe at baseline to mild or none, or a reduction in pain severity from mild at baseline to none, at the indicated assessment time.

APD: All randomized participants who use at least 1 dose of study drug for an ITT evaluable attack,

defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[9] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: percentage of participants				
number (not applicable)	65.4	65.2	41.3	

Statistical analyses

Statistical analysis title	Pain Relief 2 Hours Postdose 1st Attack 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	3.57

Statistical analysis title	Pain Relief 2 Hours Postdose 1st Attack 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.04
upper limit	3.53

Secondary: Percentage of Participants Requiring Rescue Medication for Migraine Within 24 Hours of Treatment During the First Attack

End point title	Percentage of Participants Requiring Rescue Medication for Migraine Within 24 Hours of Treatment During the First Attack[10]

End point description:

Percentage of participants requiring rescue medication for migraine within 2 to 24 hours of treatment during the first attack.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

24 Hours

Notes:

[10] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	311	307	406	
Units: percentage of participants				
number (not applicable)	19.6	19.2	29.3	

Statistical analyses

Statistical analysis title	Rescue Medication 1st Attack 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	717
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.65

Statistical analysis title	Rescue Medication 1st Attack 200 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	717
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.6

Secondary: Percentage of Participants That Are Free of Symptoms Associated With Migraine at 2 Hours Postdose During the First Attack

End point title	Percentage of Participants That Are Free of Symptoms Associated With Migraine at 2 Hours Postdose During the First Attack[11]

End point description:

Total migraine freedom is defined as no pain and no migraine associated symptoms (photophobia, phonophobia, nausea, and vomiting) at 2 hours postdose during the first attack.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[11] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: percentage of participants				
number (not applicable)	17.9	21.0	7.2	

Statistical analyses

Statistical analysis title	Free of Migraine Associated Symptoms 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.79
upper limit	4.28

Statistical analysis title	Free of Migraine Associated Symptoms 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	5.15

Secondary: Percentage of Participants With Migraine Recurrence at 24 Hours During the First Attack

End point title	Percentage of Participants With Migraine Recurrence at 24 Hours During the First Attack[12]

End point description:

Percentage of participants with migraine recurrence at 24 hours during the first attack defined as return of any headache in participants who were pain free at 2 hours.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at

or before 2 hours postdose.

End point type	Secondary

End point timeframe:

24 hours

Notes:

[12] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	108	127	37	
Units: percentage of participants				
number (not applicable)	30.6	22.0	37.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Pain Freedom, Pain Relief, Freedom From MBS, and No Disability Postdose During First Attack

End point title	Percentage of Participants With Pain Freedom, Pain Relief, Freedom From MBS, and No Disability Postdose During First Attack[13]

End point description:

Percentage of participants with pain freedom, pain relief, freedom from MBS, and no disability postdose during first attack.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

30 Minutes (Min) and 1 Hour (Hr) Postdose

Notes:

[13] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: Percentage of Participants				
number (not applicable)				
Pain Freedom (30 Min)	1.4	1.6	0.2	
Pain Freedom (1 Hr)	6.0	12.7	2.0	
Pain Relief (30 Min)	18.6	22.4	14.0	
Pain Relief (1 Hr)	48.7	47.2	29.3	

Freedom from MBS (30 Min)	12.5	14.4	11.4
Freedom from MBS (1 Hr)	23.7	28.9	22.0
No Disability Postdose During 1st Attack (30 Min)	3.1	2.3	2.3
No Disability Postdose During First Attack (1 Hr)	6.0	9.9	5.0

Statistical analyses

Statistical analysis title	Pain Freedom 30 Min Postdose 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.086
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	53.37

Statistical analysis title	Pain Freedom 30 Min. Postdose 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	59.08

Statistical analysis title	Pain Freedom 1 Hour Postdose
Comparison groups	100 mg Lasmiditan v Placebo

Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.42
upper limit	6.68

Statistical analysis title	Pain Freedom 1 Hour Postdose
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.43
upper limit	14.44

Statistical analysis title	Pain Relief 30 Min Postdose 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	2.03

Statistical analysis title	Pain Relief 30 Min Postdose 200 mg

Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	2.52

Statistical analysis title	Pain Relief 1 Hour Postdose 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.74
upper limit	3.06

Statistical analysis title	Pain Relief 1 Hour Postdose 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.64
upper limit	2.88

Statistical analysis title	Freedom from MBS 30 Min 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.651
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.71

Statistical analysis title	Freedom from MBS 30 Min 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.22
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.98

Statistical analysis title	Freedom from MBS 1 Hour 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.54

Statistical analysis title	Freedom from MBS 1 Hour 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.98

Secondary: Change from Baseline in Total Score as Measured by the Migraine Disability Assessment Test (MIDAS) Scale

End point title	Change from Baseline in Total Score as Measured by the Migraine Disability Assessment Test (MIDAS) Scale[14]

End point description:

The MIDAS is a participant-rated scale which was designed to quantify headache-related disability over a 3-month period. This instrument consists of 5 items that reflect the number of days reported as missed, or with reduced productivity at work or home and social events. Each question is answered as the number of days during the past 3 months of assessment, ranging from 0 to 90, with the total score being the summation of the 5 numeric responses. A higher value is indicative of more disability.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[14] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Control	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	447	437	451	
Units: Score on a Scale				
arithmetic mean (standard deviation)	-10.7 (± 24.36)	-12.0 (± 21.38)	-13.1 (± 21.40)	

Statistical analyses

Statistical analysis title	Change from Baseline MIDAS 100 mg
Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	898
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.092
Method	ANCOVA

Statistical analysis title	Change from Baseline MIDAS 200 mg
Comparison groups	200 mg Lasmiditan v Control
Number of subjects included in analysis	888
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.211
Method	ANCOVA

Secondary: Percentage of Participants Very much Better or Much Better as Measured by Patient Global Impression of Change (PGI-C) at 2 Hours Postdose During the First Attack

End point title	Percentage of Participants Very much Better or Much Better as Measured by Patient Global Impression of Change (PGI-C) at 2 Hours Postdose During the First Attack[15]

End point description:

The PGI-C is a one-item questionnaire that asks participants to provide their impression of change since taking the medicine. The PGI-C is measured using a 7-point Likert scale, with 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse, and 7 = very much worse. Reported are participants whose combined impression of change since taking the medicine was very much better and much better at 2 hours postdose.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[15] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: Percentage of Participants				
number (not applicable)	29.8	30.0	13.3	

Statistical analyses

Statistical analysis title	PGI-C 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	4.05

Statistical analysis title	PGI-C 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.12
upper limit	4.26

Secondary: Migraine Quality of Life Questionnaire (MQoLQ) Score at 24 Hours Post First Dose of Study During First Attack

End point title	Migraine Quality of Life Questionnaire (MQoLQ) Score at 24 Hours Post First Dose of Study During First Attack[16]

End point description:

The 24-hour Migraine Quality of Life Questionnaire (24-hr MQoLQ) has been specifically developed to measure the HRQoL of patients with migraine within a 24-hour period after having taken migraine medication A domain score is calculated by summing the responses to the 3 questions and the domain score ranges from 3 to 21, with lower scores indicating less impairment. The questionnaire will be administered 24 hours after dosing with study drug during each migraine. The analysis of variance

(ANOVA) model was used with region and treatment adjusted for the overall treatment effect.

APD: All randomized participants who used at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:
24 Hours Post First Dose

Notes:

[16] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	289	303	293	
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Social Functioning	12.4 (± 4.8)	12.1 (± 4.7)	11.7 (± 4.7)	
Migraine Symptoms	12.4 (± 4.1)	12.5 (± 4.2)	11.4 (± 4.4)	
Feeling/Concern	11.2 (± 4.5)	11.2 (± 4.5)	10.3 (± 4.2)	

Statistical analyses

Statistical analysis title	Social Functioning 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.056
Method	ANOVA

Statistical analysis title	Social Functioning 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	596
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.267
Method	ANOVA

Statistical analysis title	Migraine Symptoms 100 mg
Comparison groups	100 mg Lasmiditan v Placebo

Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANOVA

Statistical analysis title	Migraine Symptoms 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	596
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANOVA

Statistical analysis title	Feeling/Concerns 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	ANOVA

Statistical analysis title	Feelings/Concerns 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	596
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	ANOVA

Secondary: Percentage of Participants Satisfied With Their Treatment Measured by a 4-Item Questionnaire

End point title	Percentage of Participants Satisfied With Their Treatment Measured by a 4-Item Questionnaire[17]

End point description:

Treatment satisfaction was evaluated at the End of Study (EoS) visit by determining the participant's level of satisfaction (ranging from extremely dissatisfied to extremely satisfied); their willingness to take this treatment again (ranging from strongly disagree to strongly agree) and if they would they recommend this treatment to another participants (ranging from strongly disagree to strongly agree).

APD: All randomized participants who use at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[17] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Control	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	452	444	460	
Units: Percentage of Participants				
number (not applicable)				
Recommend Treatment - Agree/Strongly Agree	57.2	58.1	52.0	
Willing to Take Treatment - Agree/Strongly Agree	61.5	58.9	64.3	
Extremely/Very Satisfied/Satisfied with Medication	48.9	51.6	43.5	
Prefer This Treatment	31.2	32.7	29.1	

Statistical analyses

Statistical analysis title	Recommend Treatment - Agree/Strongly Agree 100 mg

Statistical analysis description:

   Agree and Strongly Agree

Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	912
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.62

Statistical analysis title	Recommend Treatment - Agree/Strongly Agree 200 mg

Statistical analysis description:

   Agree and Strongly Agree

Comparison groups	200 mg Lasmiditan v Control

Number of subjects included in analysis	904
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.67

Statistical analysis title	Take Treatment Again - Agree/Strongly Agree 100 mg
Statistical analysis description:	
Agree and Strongly Agree	
Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	912
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.376
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.16

Statistical analysis title	Take Treatment Again - Agree/Strongly Agree 200 mg
Statistical analysis description:	
Agree and Strongly Agree	
Comparison groups	200 mg Lasmiditan v Control
Number of subjects included in analysis	904
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.03

Statistical analysis title	Extremely/Very/ Satisfied with Medication 100 mg
Statistical analysis description:	
Extremely/Very Satisfied and Satisfied	
Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	912
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.096
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.62

Statistical analysis title	Extremely/Very/ Satisfied with Medication 200 mg
Statistical analysis description:	
Extremely/Very Satisfied and Satisfied	
Comparison groups	200 mg Lasmiditan v Control
Number of subjects included in analysis	904
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.8

Statistical analysis title	PreferThis Treatment 100 mg
Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	912
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.445
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.49

Statistical analysis title	Prefer This Treatment 200 mg
Comparison groups	200 mg Lasmiditan v Control
Number of subjects included in analysis	904
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.243
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.58

Secondary: Change From Baseline in Utility at 24 Hours Postdose as Measured by the EuroQol 5-Dimension 5-Level Scale (EQ-5D-5L) at 24 Hours Postdose During First Attack

End point title	Change From Baseline in Utility at 24 Hours Postdose as Measured by the EuroQol 5-Dimension 5-Level Scale (EQ-5D-5L) at 24 Hours Postdose During First Attack[18]

End point description:

The EQ-5D-5L questionnaire is a participant-rated scale that assesses health status, it consists of 2 parts. The first part assesses 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) that have 5 possible levels of response (no problems, slight problems, moderate problems, severe problems, extreme problems).The EQ-5D can be used to generate a health state index score, which is used to compute quality-adjusted life years for utilization in health economic analyses. The health state index score is calculated based on the responses to the 5 dimensions, providing a single value on a scale from less than 0 (where 0 is a health state equivalent to death) to 1 (perfect health), with higher scores indicating better health utility. ANCOVA was used to assess the effect of Lasmiditan over placebo or control. The model includes fixed categorical effect of treatment and geographic region and baseline as covariate.

End point type	Secondary

End point timeframe:

Baseline, 24 hr Postdose

APD: All randomized participants who use at least 1 dose of study drug for an ITT evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours pos

Notes:

[18] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: Score on a Scale				
arithmetic mean (standard deviation)	0.2499 (± 0.25788)	0.2271 (± 0.29854)	0.2122 (± 0.25729)	

Statistical analyses

Statistical analysis title	EQ-5D-5L for First Attack
Comparison groups	100 mg Lasmiditan v 200 mg Lasmiditan v Placebo
Number of subjects included in analysis	1296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.142
Method	ANCOVA

Secondary: Percentage of Participants That Are Pain Free at 2 Hours Postdose in at Least 3 Out of 4 Attacks

End point title	Percentage of Participants That Are Pain Free at 2 Hours Postdose in at Least 3 Out of 4 Attacks[19]

End point description:

Headache pain-free is defined as a reduction in pain severity from mild, moderate, or severe to none at the indicated assessment time (2 hours postdose). To evaluate 3 out of 4 consistency endpoints; all ITT-evaluable attacks will be used. For the control group, the results of all ITT-evaluable attacks treated with lasmiditan 50 mg or placebo will be included. The control group is used for comparison. The population for 3 out of 4 consistency endpoints with sufficient number of successes or failures is defined as all patients who experienced at least 3 successes or 2 failures during ITT-evaluable attacks.

APD: All randomized participants who experienced a sufficient number of successes or failures, (3 out of 4 attacks) during ITT evaluable attacks for any of the consistency analyses.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[19] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Control	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	325	306	387	
Units: Percentage of Participants				
number (not applicable)	7.4	10.8	2.6	

Statistical analyses

Statistical analysis title	Pain Free 3 out of 4 Attacks 100 mg
Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	712
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.42
upper limit	6.4

Statistical analysis title	Pain Free 3 out of 4 Attacks 200 mg
Comparison groups	200 mg Lasmiditan v Control
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.22
upper limit	9.47

Secondary: Percentage of Participants With Pain Relief at 2 Hours Postdose in at Least 3 Out of 4 Attacks

End point title	Percentage of Participants With Pain Relief at 2 Hours Postdose in at Least 3 Out of 4 Attacks[20]

End point description:

Headache pain-relief is defined as a reduction in pain severity from moderate or severe at baseline to mild or none, or a reduction in pain severity from mild at baseline to none, at the indicated assessment time (2 hours postdose). To evaluate 3 out of 4 consistency endpoints; all ITT-evaluable attacks will be used. For the control group, the results of all ITT-evaluable attacks treated with lasmiditan 50 mg or placebo will be included. The control group is used for comparison. The population for 3 out of 4 consistency endpoints with sufficient number of successes or failures is defined as all patients who experienced at least 3 successes or 2 failures during ITT-evaluable attacks.

APD: All randomized participants who experienced a sufficient number of successes or failures, (3 successes or 2 failures) during ITT-evaluable attacks for any of the consistency analyses.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[20] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Control	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	260	235	317	
Units: Percentage of Participants				
number (not applicable)	40.8	49.8	21.8	

Statistical analyses

Statistical analysis title	Pain Relief 3 Out of 4 Attacks 100 mg
Comparison groups	100 mg Lasmiditan v Control
Number of subjects included in analysis	577
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.74
upper limit	3.62

Statistical analysis title	Pain Relief 3 Out of 4 Attacks 200 mg
Comparison groups	200 mg Lasmiditan v Control
Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	5.2

Secondary: Percentage of Participants with Associated Migraines Symptoms of Nausea, Vomiting, Photophobia, and Phonophobia Present at 2 Hours Postdose for First Attack

End point title	Percentage of Participants with Associated Migraines Symptoms of Nausea, Vomiting, Photophobia, and Phonophobia Present at 2 Hours Postdose for First Attack[21]

End point description:

Presence of associated migraine symptoms at 2 hours postdose at first migraine attack, including each of the following: phonophobia, photophobia, nausea, and vomiting.

APD: All randomized participants who used at least 1 dose of study drug for an Intent-to-Treat (ITT) evaluable attack, defined as a treated attack of at least mild pain severity with any postdose pain severity assessments at or before 2 hours postdose.

End point type	Secondary

End point timeframe:

2 Hours Postdose

Notes:

[21] - 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: Subject analysis sets titled Placebo and Control were created to report results for participants who were randomized to the Control 1 and Control 2 arms.

End point values	100 mg Lasmiditan	200 mg Lasmiditan	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	419	434	443	
Units: percentage of participants				
number (not applicable)				
Nausea	29.1	29.0	29.1	
Phonophobia	26.7	23.5	40.6	
Photophobia	38.2	39.9	55.3	
Vomiting	1.2	3.0	2.7	

Statistical analyses

Statistical analysis title	Nausea 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.953
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.36

Statistical analysis title	Nausea 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.768
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.41

Statistical analysis title	Phonophobia 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.71

Statistical analysis title	Phonophobia 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.62

Statistical analysis title	Photophobia 100 mg
Comparison groups	100 mg Lasmiditan v Placebo
Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.63

Statistical analysis title	Photophobia 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.71

Statistical analysis title	Vomiting 100 mg
Comparison groups	100 mg Lasmiditan v Placebo

Number of subjects included in analysis	862
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.129
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.25

Statistical analysis title	Vomiting 200 mg
Comparison groups	200 mg Lasmiditan v Placebo
Number of subjects included in analysis	877
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.769
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	2.43

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Double Blind Phase

Adverse event reporting additional description:

H8H-MC-LAIJ

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	100 mg Lasmiditan

Reporting group description:

Participants received one 100 mg Lasmiditan tablet with one 50 mg Lasmiditan matching placebo tablet and one 100-mg Lasmiditan matching placebo tablet to maintain blind.

Reporting group title	200 mg Lasmiditan

Reporting group description:

Participants received two 100 mg Lasmiditan tablets with one 50 mg Lasmiditan matching placebo tablet to maintain blind.

Reporting group title	Control

Reporting group description:

Control 1: Participants received one 50 mg Lasmiditan matching placebo tablet and two 100 mg Lasmiditan matching placebo tablets to maintain blind for migraine attacks 1, 2, and 4 and one 50 mg Lasmiditan tablet with two 100 mg Lasmiditan matching placebo tablets to maintain blind, for migraine attack 3.
Control 2: Participants received one 50 mg Lasmiditan matching placebo tablet and two 100 mg Lasmiditan matching placebo tablets to maintain blind for migraine attacks 1, 2, and 3, and one 50 mg Lasmiditan tablet with two 100 mg Lasmiditan matching placebo tablets to maintain blind for migraine attack 4.

Serious adverse events	100 mg Lasmiditan	200 mg Lasmiditan	Control
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 485 (1.44%)	8 / 486 (1.65%)	7 / 500 (1.40%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung adenocarcinoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nasopharyngeal cancer stage iii			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications

hand fracture

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ligament rupture

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

lower limb fracture

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders

headache

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

hemiplegic migraine

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

medication overuse headache

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
migraine			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sensory loss			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
serotonin syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vestibular migraine			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
endometriosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[1]	0 / 403 (0.00%)	0 / 418 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
heavy menstrual bleeding			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed[2]	0 / 403 (0.00%)	1 / 418 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intermenstrual bleeding			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[3]	1 / 403 (0.25%)	0 / 418 (0.00%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
haemorrhoids thrombosed			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tracheal mass			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
liver disorder			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders

suicidal ideation

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations

abscess oral

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

appendicitis

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

bronchitis

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

otitis media

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	100 mg Lasmiditan	200 mg Lasmiditan	Control
Total subjects affected by non-serious adverse events			
subjects affected / exposed	328 / 485 (67.63%)	352 / 486 (72.43%)	184 / 500 (36.80%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
uterine leiomyoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[4]	0 / 403 (0.00%)	0 / 418 (0.00%)	1 / 416 (0.24%)
occurrences (all)	0	0	1
Vascular disorders			
flushing			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	4	0	0
hot flush			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	2 / 486 (0.41%)	4 / 500 (0.80%)
occurrences (all)	5	2	4
hypertension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	0	1	1
peripheral coldness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
poor peripheral circulation			

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
raynaud's phenomenon			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
antibiotic prophylaxis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
tooth repair			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	22 / 485 (4.54%)	30 / 486 (6.17%)	3 / 500 (0.60%)
occurrences (all)	30	51	4
chest discomfort			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 485 (0.62%)	4 / 486 (0.82%)	3 / 500 (0.60%)
occurrences (all)	5	7	3
chills			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 485 (1.03%)	5 / 486 (1.03%)	3 / 500 (0.60%)
occurrences (all)	6	5	4
discomfort			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	7 / 486 (1.44%)	1 / 500 (0.20%)
occurrences (all)	5	11	1
fatigue			
alternative dictionary used:			

MedDRA 24.0			
subjects affected / exposed	53 / 485 (10.93%)	72 / 486 (14.81%)	19 / 500 (3.80%)
occurrences (all)	75	106	21

feeling abnormal

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	9 / 485 (1.86%)	19 / 486 (3.91%)	2 / 500 (0.40%)
occurrences (all)	9	25	2

feeling drunk

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	6	2	0

feeling cold

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 485 (1.03%)	1 / 486 (0.21%)	2 / 500 (0.40%)
occurrences (all)	9	1	2

feeling hot

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	6 / 486 (1.23%)	2 / 500 (0.40%)
occurrences (all)	4	8	2

feeling of body temperature change

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

feeling of relaxation

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	2	0

gait disturbance

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	4 / 486 (0.82%)	0 / 500 (0.00%)
occurrences (all)	5	4	0

general physical health deterioration

alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

hunger

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

illness

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	1 / 500 (0.20%)
occurrences (all)	0	2	1

influenza like illness

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	1	2	0

malaise

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	6 / 485 (1.24%)	7 / 486 (1.44%)	2 / 500 (0.40%)
occurrences (all)	9	9	2

non-cardiac chest pain

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	2	1	1

oedema peripheral

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

pain

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	2 / 486 (0.41%)	1 / 500 (0.20%)
occurrences (all)	3	2	1

peripheral swelling

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	2 / 500 (0.40%)
occurrences (all)	0	0	2

pyrexia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	2 / 500 (0.40%)
occurrences (all)	0	3	2
sensation of blood flow			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
sensation of foreign body			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
sense of oppression			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
swelling face			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
thirst			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	3 / 486 (0.62%)	1 / 500 (0.20%)
occurrences (all)	2	3	1
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
seasonal allergy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			

dysmenorrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[5]	1 / 403 (0.25%)	0 / 418 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0
erection increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[6]	0 / 82 (0.00%)	1 / 68 (1.47%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
intermenstrual bleeding			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[7]	0 / 403 (0.00%)	0 / 418 (0.00%)	1 / 416 (0.24%)
occurrences (all)	0	0	1
menstrual disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[8]	1 / 403 (0.25%)	0 / 418 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0
menstruation irregular			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[9]	0 / 403 (0.00%)	1 / 418 (0.24%)	0 / 416 (0.00%)
occurrences (all)	0	1	0
polymenorrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[10]	0 / 403 (0.00%)	0 / 418 (0.00%)	1 / 416 (0.24%)
occurrences (all)	0	0	1
vaginal haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[11]	0 / 403 (0.00%)	1 / 418 (0.24%)	0 / 416 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	2 / 500 (0.40%)
occurrences (all)	0	2	4
dry throat			
alternative dictionary used:			

MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

dyspnoea
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	4 / 485 (0.82%)	2 / 486 (0.41%)	1 / 500 (0.20%)
occurrences (all)	4	2	1

dysphonia
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

epistaxis
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	2	0	0

nasal congestion
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

oropharyngeal pain
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	3	0	1

rhinorrhoea
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

sinonasal obstruction
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

sinus pain
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

Psychiatric disorders

abnormal dreams
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	5 / 485 (1.03%)	6 / 486 (1.23%)	1 / 500 (0.20%)
occurrences (all)	5	9	1

agitation
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	4 / 486 (0.82%)	1 / 500 (0.20%)
occurrences (all)	2	4	1

aggression
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	2	0	0

apathy
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

anxiety
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	6 / 485 (1.24%)	10 / 486 (2.06%)	4 / 500 (0.80%)
occurrences (all)	8	10	4

attention deficit hyperactivity disorder
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

confusional state
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	6 / 486 (1.23%)	0 / 500 (0.00%)
occurrences (all)	2	6	0

depressed mood
alternative dictionary used: MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	7 / 486 (1.44%)	3 / 500 (0.60%)
occurrences (all)	4	8	3

depression

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	0	1	1

depressive symptom

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

derealisation

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

disorientation

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	3	3	0

dyssomnia

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

emotional disorder

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

emotional distress

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

euphoric mood

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	3 / 486 (0.62%)	1 / 500 (0.20%)
occurrences (all)	2	4	2

fear			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
hallucination			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
hallucination, auditory			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	2	0
hallucination, visual			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	6 / 486 (1.23%)	0 / 500 (0.00%)
occurrences (all)	7	6	0
insomnia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	6 / 485 (1.24%)	11 / 486 (2.26%)	3 / 500 (0.60%)
occurrences (all)	8	20	3
irritability			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	1	2	0
mood altered			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
nervousness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	1 / 500 (0.20%)
occurrences (all)	0	2	1
nightmare			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	2 / 485 (0.41%)	4 / 486 (0.82%)	1 / 500 (0.20%)
occurrences (all)	4	5	1

poor quality sleep
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

restlessness
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	6 / 486 (1.23%)	3 / 500 (0.60%)
occurrences (all)	3	9	3

sleep disorder
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	5 / 486 (1.03%)	0 / 500 (0.00%)
occurrences (all)	1	7	0

somatic symptom disorder
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	3	0	0

suicidal ideation
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

Investigations
blood cholesterol increased
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

blood creatinine increased
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

electrocardiogram t wave abnormal
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

gamma-glutamyltransferase increased
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

heart rate increased
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	4 / 485 (0.82%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	5	1	1

heart rate decreased
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

intraocular pressure increased
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

muscle strength abnormal
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

pulse abnormal
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

total bile acids increased
  alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

Injury, poisoning and procedural complications
  epicondylitis
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

fall
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00 %)
occurrences (all)	0	1	0

joint dislocation
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

ligament sprain
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

limb injury
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	1	0	1

muscle rupture
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

rib fracture
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

Cardiac disorders
  bradycardia
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	0	1	1

cardiovascular disorder
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

palpitations

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	12 / 485 (2.47%)	7 / 486 (1.44%)	3 / 500 (0.60%)
occurrences (all)	19	9	3

supraventricular extrasystoles

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

supraventricular tachycardia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

tachycardia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	5	1	0

Nervous system disorders

allodynia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

altered state of consciousness

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	3	0

amnesia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

anosmia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

aphasia
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	1	3	0

ataxia
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	1	3	0

autonomic nervous system imbalance
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

balance disorder
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	10 / 485 (2.06%)	14 / 486 (2.88%)	2 / 500 (0.40%)
occurrences (all)	16	16	2

bradykinesia
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

burning sensation
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

cervical cord compression
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

cognitive disorder
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	1	2	0

clumsiness

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

coordination abnormal

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	2	4	0

depressed level of consciousness

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	2	0	0

disturbance in attention

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	7 / 485 (1.44%)	11 / 486 (2.26%)	1 / 500 (0.20%)
occurrences (all)	9	11	1

dizziness postural

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 485 (0.62%)	0 / 486 (0.00%)	2 / 500 (0.40%)
occurrences (all)	4	0	2

dizziness

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	154 / 485 (31.75%)	182 / 486 (37.45%)	44 / 500 (8.80%)
occurrences (all)	227	320	59

dysaesthesia

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

dyskinesia

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	0	2	0

dysgeusia

alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	1	1	1

dysarthria

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	7 / 486 (1.44%)	0 / 500 (0.00%)
occurrences (all)	1	7	0

fine motor skill dysfunction

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	0	3	0

formication

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	4	2	0

head discomfort

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	4 / 485 (0.82%)	2 / 486 (0.41%)	2 / 500 (0.40%)
occurrences (all)	4	3	2

headache

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	9 / 485 (1.86%)	9 / 486 (1.85%)	7 / 500 (1.40%)
occurrences (all)	9	10	8

hemiparesis

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

hypersomnia

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	3	4	0

hypoaesthesia

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	24 / 485 (4.95%)	16 / 486 (3.29%)	7 / 500 (1.40%)
occurrences (all)	33	24	9

hypotonia

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	1	3	0

lethargy

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	5 / 485 (1.03%)	7 / 486 (1.44%)	0 / 500 (0.00%)
occurrences (all)	6	11	0

memory impairment

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	2	0	2

mental impairment

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

migraine

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	4 / 485 (0.82%)	1 / 486 (0.21%)	2 / 500 (0.40%)
occurrences (all)	4	1	2

migraine with aura

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

muscle contractions involuntary

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

muscle spasticity

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

myoclonus

  alternative dictionary used:
  MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

paraesthesia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	70 / 485 (14.43%)	93 / 486 (19.14%)	21 / 500 (4.20%)
occurrences (all)	102	170	25

presyncope

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	2 / 486 (0.41%)	1 / 500 (0.20%)
occurrences (all)	4	2	1

psychomotor hyperactivity

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

restless legs syndrome

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	4 / 486 (0.82%)	1 / 500 (0.20%)
occurrences (all)	6	6	1

sciatica

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	0	1	1

sedation

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	3	0	0

sensory disturbance

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

serotonin syndrome

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

slow speech			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	0	2	0
somnolence			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	32 / 485 (6.60%)	54 / 486 (11.11%)	12 / 500 (2.40%)
occurrences (all)	47	82	12
speech disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	0	3	0
taste disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0
tension headache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	2	1	2
tremor			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	9 / 485 (1.86%)	12 / 486 (2.47%)	3 / 500 (0.60%)
occurrences (all)	9	19	3
Ear and labyrinth disorders			
acute vestibular syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	2	0
deafness transitory			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
ear discomfort			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	2	0	0

ear pain

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

hyperacusis

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	1	0	1

tinnitus

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	5 / 485 (1.03%)	9 / 486 (1.85%)	1 / 500 (0.20%)
occurrences (all)	5	10	1

vertigo

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	44 / 485 (9.07%)	47 / 486 (9.67%)	7 / 500 (1.40%)
occurrences (all)	66	79	7

vertigo positional

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	3	0	0

Eye disorders

abnormal sensation in eye

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

blepharospasm

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

diplopia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	0	4	0

eye pain

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

eye movement disorder

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

eye pruritus

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

eyelid ptosis

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

metamorphopsia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

mydriasis

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

ocular discomfort

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

ocular hyperaemia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

photophobia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	4 / 486 (0.82%)	1 / 500 (0.20%)
occurrences (all)	3	5	1
photopsia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	5 / 486 (1.03%)	0 / 500 (0.00%)
occurrences (all)	3	6	0
pupillary reflex impaired			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
vision blurred			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 485 (1.03%)	9 / 486 (1.85%)	0 / 500 (0.00%)
occurrences (all)	5	12	0
visual impairment			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	7 / 486 (1.44%)	0 / 500 (0.00%)
occurrences (all)	2	11	0
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
abdominal discomfort			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	3 / 486 (0.62%)	1 / 500 (0.20%)
occurrences (all)	0	4	1
abdominal pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	3 / 486 (0.62%)	1 / 500 (0.20%)
occurrences (all)	4	3	1
abdominal pain upper			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 485 (0.21%)	4 / 486 (0.82%)	11 / 500 (2.20%)
occurrences (all)	1	6	14

diarrhoea

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	6 / 485 (1.24%)	6 / 486 (1.23%)	8 / 500 (1.60%)
occurrences (all)	8	9	9

dry mouth

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	6 / 485 (1.24%)	11 / 486 (2.26%)	1 / 500 (0.20%)
occurrences (all)	9	15	3

dyspepsia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	3 / 486 (0.62%)	2 / 500 (0.40%)
occurrences (all)	3	3	2

epigastric discomfort

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

flatulence

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	1	2	1

gastritis

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	2 / 500 (0.40%)
occurrences (all)	2	0	3

gastrooesophageal reflux disease

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	1 / 500 (0.20%)
occurrences (all)	0	5	1

glossodynia

alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

hypoaesthesia oral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 485 (0.62%)	6 / 486 (1.23%)	2 / 500 (0.40%)
occurrences (all)	3	6	4
irritable bowel syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
mouth ulceration			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
nausea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	54 / 485 (11.13%)	70 / 486 (14.40%)	29 / 500 (5.80%)
occurrences (all)	65	103	34
paraesthesia oral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	3 / 486 (0.62%)	2 / 500 (0.40%)
occurrences (all)	4	3	3
toothache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	0 / 500 (0.00%)
occurrences (all)	0	2	0
vomiting			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	12 / 485 (2.47%)	18 / 486 (3.70%)	11 / 500 (2.20%)
occurrences (all)	13	22	13
Skin and subcutaneous tissue disorders			
cold sweat			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	1	3	0
erythema			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	2

hyperhidrosis
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	4 / 485 (0.82%)	3 / 486 (0.62%)	4 / 500 (0.80%)
occurrences (all)	4	4	5

night sweats
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

photosensitivity reaction
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

pruritus
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	3	0	1

rash
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

skin burning sensation
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

skin lesion
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

Renal and urinary disorders
  chromaturia
    alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

nephrolithiasis
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

pollakiuria
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

renal pain
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

Musculoskeletal and connective tissue disorders
arthralgia
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	2 / 486 (0.41%)	3 / 500 (0.60%)
occurrences (all)	0	2	3

back pain
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	2 / 485 (0.41%)	3 / 486 (0.62%)	3 / 500 (0.60%)
occurrences (all)	2	3	3

bone pain
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

bursitis
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

costochondritis
alternative dictionary used:
MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

joint stiffness

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

limb discomfort

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	8 / 485 (1.65%)	8 / 486 (1.65%)	2 / 500 (0.40%)
occurrences (all)	12	11	2

mobility decreased

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

muscle fatigue

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

muscle spasms

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	4 / 485 (0.82%)	7 / 486 (1.44%)	4 / 500 (0.80%)
occurrences (all)	5	7	4

muscle tightness

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

muscle twitching

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	3 / 485 (0.62%)	6 / 486 (1.23%)	1 / 500 (0.20%)
occurrences (all)	5	9	1

muscular weakness

alternative dictionary used: MedDRA 24.0

subjects affected / exposed	22 / 485 (4.54%)	29 / 486 (5.97%)	2 / 500 (0.40%)
occurrences (all)	32	45	3

musculoskeletal pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
musculoskeletal chest pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
musculoskeletal stiffness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	1	0	1
myalgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	2	1	0
neck pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 485 (0.41%)	3 / 486 (0.62%)	4 / 500 (0.80%)
occurrences (all)	2	3	4
osteoarthritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
pain in extremity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	1	4	0
synovial cyst			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
Infections and infestations			

bacterial vaginosis

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[12]	1 / 403 (0.25%)	1 / 418 (0.24%)	0 / 416 (0.00%)
occurrences (all)	1	1	0

bronchitis

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

conjunctivitis

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

cystitis

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1

diverticulitis

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

febrile infection

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

gastroenteritis

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	1 / 500 (0.20%)
occurrences (all)	0	1	1

gastroenteritis viral

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

influenza

alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 485 (0.00%)	3 / 486 (0.62%)	2 / 500 (0.40%)
occurrences (all)	0	3	2

laryngitis
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	2 / 500 (0.40%)
occurrences (all)	0	0	2

lower respiratory tract infection
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

nasopharyngitis
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	8 / 485 (1.65%)	8 / 486 (1.65%)	9 / 500 (1.80%)
occurrences (all)	8	8	9

oral herpes
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	3 / 500 (0.60%)
occurrences (all)	0	0	3

otitis externa
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

periodontitis
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

pharyngitis
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0

pulpitis dental
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0

rhinitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 485 (0.62%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	3	0	0
skin infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	8 / 485 (1.65%)	2 / 486 (0.41%)	4 / 500 (0.80%)
occurrences (all)	8	2	4
urinary tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	1	1	0
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 485 (0.21%)	0 / 486 (0.00%)	0 / 500 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 485 (0.82%)	3 / 486 (0.62%)	0 / 500 (0.00%)
occurrences (all)	4	4	0
food craving			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
hyperuricaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
hypoglycaemia			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 485 (0.00%)	0 / 486 (0.00%)	1 / 500 (0.20%)
occurrences (all)	0	0	1
increased appetite			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 485 (0.00%)	1 / 486 (0.21%)	0 / 500 (0.00%)
occurrences (all)	0	1	0

Notes:

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2018	Amendment (a): Changes in design of the trial (options for second dose and related secondary objectives were removed), Change of an exclusion criterion (removal of exclusion criteria #17: exclusion of patients with hepatitis/HIV), Change to duration (optional open label extension for up to one year)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported