Clinical trial results:
A PHASE 2 STUDY OF THE SAFETY, EFFICACY, AND PHARMACODYNAMICS OF RTA 408 IN THE TREATMENT OF MITOCHONDRIAL MYOPATHY

Summary

EudraCT number	2014-003501-15
Trial protocol	DK
Global end of trial date	30 November 2017

Results information

Result version number	v1 (current)
This version publication date	11 July 2021
First version publication date	11 July 2021

Trial information

Trial identification

Sponsor protocol code	408-C-1403

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02255422
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Reata Pharmaceuticals, Inc.
Sponsor organisation address	5320 Legacy Drive, Plano, United States, 75024
Public contact	Clinical Operations, Reata Pharmaceuticals, 1 9728652219, 408C1403DNK@reatapharma.com
Scientific contact	Clinical Operations, Reata Pharmaceuticals, 1 9728652219, 408C1403DNK@reatapharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2017
Global end of trial reached?	Yes
Global end of trial date	30 November 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary:
- To evaluate the change in peak work during maximal exercise testing
- To evaluate the safety and tolerability of RTA 408

Protection of trial subjects:

The DSMB consisted of external clinical experts supported by an independent statistical group who reviewed unblinded safety data throughout the study and made recommendations as appropriate regarding the opening of cohorts and subsequent parts of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	53
EEA total number of subjects	15

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)	50
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with Mitochondrial myopathy as evidenced by a history of exercise intolerance with/without weakness and/or progressive exercise intolerance and have a known primary mitochondrial DNA mutation or nuclear DNA defect associated with reduced activity of at least 1 mitochondrially encoded respiratory chain complex were recruited per protocol.

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?	No
Arm title	Placebo capsules

Arm description:

Placebo capsules administered orally once daily for 12 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo Capsules
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo capsules administered orally once daily for 12 weeks

Arm title	Omaveloxolone Capsules 2.5 and 5 mg

Arm description:

Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5mg administered orally once daily for 10 weeks

Arm type	Experimental
Investigational medicinal product name	Omaveloxolone Capsules 2.5 and 5 mg
Investigational medicinal product code	RTA 408
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5mg administered orally once daily for 10 weeks

Arm title	Omaveloxolone Capsules 10 mg

Arm description:

Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks

Arm type	Experimental

Investigational medicinal product name	Omaveloxolone Capsules 10 mg
Investigational medicinal product code	RTA 408
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks

Arm title	Omaveloxolone Capsules 20 mg

Arm description:

Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Omaveloxolone Capsules 20 mg
Investigational medicinal product code	RTA 408
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 weeks

Arm title	Omaveloxolone Capsules 40 mg

Arm description:

Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Omaveloxolone Capsules 40 mg
Investigational medicinal product code	RTA 408
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks

Arm title	Omaveloxolone Capsules 80 mg

Arm description:

Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Omaveloxolone Capsules 80 mg
Investigational medicinal product code	RTA 408
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks

Arm title	Omaveloxolone Capsules 160 mg

Arm description:

Omaveloxolone (RTA 408) 160 mg capsules administered orally once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Omaveloxolone Capsules 160 mg
Investigational medicinal product code	RTA 408
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Omaveloxolone (RTA 408) 160 mg capsules administered orally once daily for 12 weeks

Number of subjects in period 1	Placebo capsules	Omaveloxolone Capsules 2.5 and 5 mg	Omaveloxolone Capsules 10 mg
Started	13	6	6
Completed	13	6	5
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Lost to follow-up	-	-	1

Number of subjects in period 1	Omaveloxolone Capsules 20 mg	Omaveloxolone Capsules 40 mg	Omaveloxolone Capsules 80 mg
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Omaveloxolone Capsules 160 mg
Started	10
Completed	8
Not completed	2
Consent withdrawn by subject	2
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo capsules
Reporting group description:	
Placebo capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 2.5 and 5 mg
Reporting group description:	
Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5mg administered orally once daily for 10 weeks	
Reporting group title	Omaveloxolone Capsules 10 mg
Reporting group description:	
Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 20 mg
Reporting group description:	
Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 40 mg
Reporting group description:	
Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 80 mg
Reporting group description:	
Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 160 mg
Reporting group description:	
Omaveloxolone (RTA 408) 160 mg capsules administered orally once daily for 12 weeks	

Reporting group values	Placebo capsules	Omaveloxolone Capsules 2.5 and 5 mg	Omaveloxolone Capsules 10 mg
Number of subjects	13	6	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	41.1	52.3	49.8
standard deviation	± 11.86	± 9.61	± 14.05
Gender categorical Units: Subjects			
Female	9	1	3
Male	4	5	3

Ethnicity Units: Subjects			
Hispanic or Latino	2	0	1
Not Hispanic or Latino	11	6	5
Unknown or Not Reported	0	0	0

Reporting group values	Omaveloxolone Capsules 20 mg	Omaveloxolone Capsules 40 mg	Omaveloxolone Capsules 80 mg
Number of subjects	6	6	6
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	45.5	45.2	30.7
standard deviation	± 14.08	± 4.71	± 10.25
Gender categorical Units: Subjects			
Female	4	5	4
Male	2	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	6	6
Unknown or Not Reported	0	0	0

Reporting group values	Omaveloxolone Capsules 160 mg	Total	
Number of subjects	10	53	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous Units: years			
arithmetic mean	39.8		
standard deviation	± 15.27	-	
Gender categorical Units: Subjects			
Female	6	32	
Male	4	21	
Ethnicity Units: Subjects			
Hispanic or Latino	3	6	
Not Hispanic or Latino	7	47	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Placebo capsules
Reporting group description:	
Placebo capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 2.5 and 5 mg
Reporting group description:	
Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5mg administered orally once daily for 10 weeks	
Reporting group title	Omaveloxolone Capsules 10 mg
Reporting group description:	
Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 20 mg
Reporting group description:	
Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 40 mg
Reporting group description:	
Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 80 mg
Reporting group description:	
Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks	
Reporting group title	Omaveloxolone Capsules 160 mg
Reporting group description:	
Omaveloxolone (RTA 408) 160 mg capsules administered orally once daily for 12 weeks	

Primary: Change of Peak Workload (in Watts/kg) During Exercise Testing

End point title	Change of Peak Workload (in Watts/kg) During Exercise Testing
End point description:	
Cycle ergometry using a stationary recumbent bike was used to conduct maximal exercise testing. Peak work is defined as the workload at which patients reach maximal volition (defined as an inability to continue to exercise due to exhaustion). Change of peak workload during exercise testing was measured at baseline, Week 4, and Week 12. Change from baseline at Week 12 reported	
End point type	Primary
End point timeframe:	
12 Weeks	

End point values	Placebo capsules	Omaveloxolone Capsules 2.5 and 5 mg	Omaveloxolone Capsules 10 mg	Omaveloxolone Capsules 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13[1]	6[2]	6[3]	6[4]
Units: Watts/kg				
least squares mean (standard error)	0.0090 (± 0.0388)	0.020 (± 0.0544)	-0.0300 (± 0.0544)	0.1050 (± 0.0596)

Notes:

[1] - Placebo capsules administered orally once daily for 12 weeks

[2] - Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5 mg adminis

[3] - Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks

[4] - Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 week

End point values	Omaveloxolone Capsules 40 mg	Omaveloxolone Capsules 80 mg	Omaveloxolone Capsules 160 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6[5]	6[6]	9[7]	
Units: Watts/kg				
least squares mean (standard error)	-0.0520 (± 0.0544)	-0.0660 (± 0.0544)	0.0020 (± 0.0465)	

Notes:

[5] - Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks

[6] - Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks

[7] - Omaveloxolone (RTA 408) 160 mg capsules administered once daily for 12 weeks

Statistical analyses

Statistical analysis title	Primary Objective

Statistical analysis description:

Primary Objective: To evaluate the change in peak work during maximal exercise testing in the following comparison groups: Placebo, Omaveloxolone Capsules 2.5 and 5 mg, Omaveloxolone Capsules 10 mg, Omaveloxolone Capsules 20 mg, Omaveloxolone Capsules 40 mg, Omaveloxolone Capsules 80 mg, Omaveloxolone Capsules 160 mg

Comparison groups	Placebo capsules v Omaveloxolone Capsules 2.5 and 5 mg v Omaveloxolone Capsules 10 mg v Omaveloxolone Capsules 20 mg v Omaveloxolone Capsules 40 mg v Omaveloxolone Capsules 80 mg v Omaveloxolone Capsules 160 mg
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7321 [8]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1051
upper limit	0.0743
Variability estimate	Standard error of the mean
Dispersion value	0.0446

Notes:

[8] - P-Value relates to difference in change in peak work from baseline relative to placebo for all doses pooled. Statistical significance was defined as $p<0.05$

Secondary: Change in 6-minute Walk Test (6MWT) Distance

End point title	Change in 6-minute Walk Test (6MWT) Distance

End point description:

Patients were instructed to walk as far as they could along a marked path for 6 minutes. Distance walked was measured. If patients used a cane or walking assist device at Screening, the same walking assist device was to be used for all 6MWT assessments.

End point type	Secondary

End point timeframe:

6MWT was assessed at Week 4, Week 8, and Week 12 and compared to baseline

End point values	Placebo capsules	Omaveloxolone Capsules 2.5 and 5 mg	Omaveloxolone Capsules 10 mg	Omaveloxolone Capsules 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13[9]	6[10]	6[11]	6[12]
Units: Meters				
least squares mean (standard error)				
Week 4	40.462 (± 10.0539)	19.333 (± 14.9658)	18.2500 (± 14.9658)	-9.2000 (± 16.3942)
Week 8	24.923 (± 9.9381)	12.865 (± 15.7374)	33.9170 (± 15.1418)	13.8000 (± 16.5870)
Week 12	29.846 (± 12.9276)	17.167 (± 19.6519)	17.7500 (± 19.6519)	28.2000 (± 21.5275)

Notes:

[9] - Placebo capsules administered orally once daily for 12 weeks

[10] - Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5 mg adminis

[11] - Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks

[12] - Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 weeks

End point values	Omaveloxolone Capsules 40 mg	Omaveloxolone Capsules 80 mg	Omaveloxolone Capsules 160 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6[13]	6[14]	9[15]	
Units: Meters				
least squares mean (standard error)				
Week 4	-11.6670 (± 14.9658)	9.9170 (± 14.9658)	10.8330 (± 12.2195)	
Week 8	11.0000 (± 15.1418)	17.5830 (± 15.1418)	28.9440 (± 12.3633)	
Week 12	-7.833 (± 19.6519)	6.2500 (± 19.6519)	8.5710 (± 16.4721)	

Notes:

[13] - Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks

[14] - Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks

[15] - Omaveloxolone (RTA 408) 160 mg capsules administered once daily for 12 weeks

Statistical analyses

Statistical analysis title	Secondary Objective: Wk 4 change in 6MWT

Statistical analysis description:

Secondary Objective: To evaluate the change in 6-minute walk test (6MWT) distance at Week 4

Comparison groups	Placebo capsules v Omaveloxolone Capsules 2.5 and 5 mg v Omaveloxolone Capsules 10 mg v Omaveloxolone Capsules 20 mg v Omaveloxolone Capsules 40 mg v Omaveloxolone Capsules 80 mg v Omaveloxolone Capsules 160 mg

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [16]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-33.448
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.855
upper limit	-10.042
Variability estimate	Standard error of the mean
Dispersion value	11.6473

Notes:

[16] - P-value comparison is for difference in change in six minute walk distance from baseline within each dosage group relative to placebo. Statistical significance defined as p<0.05.

Statistical analysis title	Secondary Objective: Wk 8 change in 6MWT

Statistical analysis description:

Secondary Objective: To evaluate the change in 6-minute walk test (6MWT) distance at Week 8

Comparison groups	Placebo capsules v Omaveloxolone Capsules 2.5 and 5 mg v Omaveloxolone Capsules 10 mg v Omaveloxolone Capsules 20 mg v Omaveloxolone Capsules 40 mg v Omaveloxolone Capsules 80 mg v Omaveloxolone Capsules 160 mg
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7325 [17]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.963
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.133
upper limit	19.207
Variability estimate	Standard error of the mean
Dispersion value	11.53

Notes:

[17] - Statistical significance was defined as p<0.05. The p-value comparison is for the difference in change in 6MWD from baseline within each dosage group relative to placebo.

Statistical analysis title	Secondary Objective: Wk 12 change in 6MWT

Statistical analysis description:

Secondary Objective: To evaluate the change in 6-minute walk test (6MWT) distance at Week 12

Comparison groups	Placebo capsules v Omaveloxolone Capsules 2.5 and 5 mg v Omaveloxolone Capsules 10 mg v Omaveloxolone Capsules 20 mg v Omaveloxolone Capsules 40 mg v Omaveloxolone Capsules 80 mg v Omaveloxolone Capsules 160 mg

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221 [18]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-18.594
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.739
upper limit	11.55
Variability estimate	Standard error of the mean
Dispersion value	15.0004

Notes:

[18] - Statistical significance was defined as $p<0.05$. The p-value comparison is for the difference in change in 6MWD from baseline within each dosage group relative to placebo.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

16 weeks

Adverse event reporting additional description:

Significant adverse events are collected from the time of the first dose of study drug until the final visit or 30 days following final study dose for patients who terminated early. Both investigator assessment/questioning (systematic) and patient self reporting (non-systematic) are used in this study but were reported by the investigators as a con

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Placebo capsules

Reporting group description:

Placebo capsules administered orally once daily for 12 weeks

Reporting group title	Omaveloxolone Capsules 2.5 and 5 mg

Reporting group description:

Omaveloxolone (RTA 408) 2.5 mg capsules administered orally once daily for 2 weeks then 5mg administered orally once daily for 10 weeks

Reporting group title	Omaveloxolone Capsules 10 mg

Reporting group description:

Omaveloxolone (RTA 408) 10 mg capsules administered orally once daily for 12 weeks

Reporting group title	Omaveloxolone Capsules 20 mg

Reporting group description:

Omaveloxolone (RTA 408) 20 mg capsules administered orally once daily for 12 weeks

Reporting group title	Omaveloxolone Capsules 40 mg

Reporting group description:

Omaveloxolone (RTA 408) 40 mg capsules administered orally once daily for 12 weeks

Reporting group title	Omaveloxolone Capsules 80 mg

Reporting group description:

Omaveloxolone (RTA 408) 80 mg capsules administered orally once daily for 12 weeks

Reporting group title	Omaveloxolone Capsules 160 mg

Reporting group description:

Omaveloxolone (RTA 408) 160 mg capsules administered orally once daily for 12 weeks

Serious adverse events	Placebo capsules	Omaveloxolone Capsules 2.5 and 5 mg	Omaveloxolone Capsules 10 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrioventricular dissociation			

subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tonic convulsion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (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
Hemiparesis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic neuritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Omaveloxolone Capsules 20 mg	Omaveloxolone Capsules 40 mg	Omaveloxolone Capsules 80 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrioventricular dissociation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tonic convulsion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Optic neuritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Omaveloxolone Capsules 160 mg		

Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrioventricular dissociation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Tonic convulsion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Optic neuritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo capsules	Omaveloxolone Capsules 2.5 and 5 mg	Omaveloxolone Capsules 10 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)	4 / 6 (66.67%)	6 / 6 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Eyelid operation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 13 (30.77%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	4	0	3
Feeling abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Energy increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Nasopharyngitis			

subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Localised infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Menorrhagia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Cough			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			

subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dysphemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachyphrenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram PR prologation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Ankle fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Penis injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Migraine			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Restless leg syndrome			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Head titubation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Myoclonus			

subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Photophobia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 13 (23.08%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	3	1	1
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nausea			

subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Blister			

subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pruritus generalized			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary hesitation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 13 (7.69%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	3 / 13 (23.08%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Flank pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	4
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Laryngitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sialoadenitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Sinusitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blister infected			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			
subjects affected / exposed	1 / 13 (7.69%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abnormal loss of weight			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Omaveloxolone Capsules 20 mg	Omaveloxolone Capsules 40 mg	Omaveloxolone Capsules 80 mg

Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 6 (83.33%)	3 / 6 (50.00%)	2 / 6 (33.33%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Surgical and medical procedures Eyelid operation subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 2
Feeling abnormal subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Energy increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Malaise subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 2	0 / 6 (0.00%) 0
Immune system disorders Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Localised infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Reproductive system and breast disorders Pelvic pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachyphrenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prologation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ankle fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Concussion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Penis injury			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Restless leg syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Head titubation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	5	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus generalized			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle twitching			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Laryngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sialoadenitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blister infected			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abnormal loss of weight			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypoglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Omaveloxolone Capsules 160 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			

Eyelid operation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Feeling abnormal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Energy increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Immune system disorders			
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Localised infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Menorrhagia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	5		
Menstruation irregular			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Nasal congestion subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Sinus congestion subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Dysphemia subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Tachyphrenia	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1		

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Electrocardiogram PR prologation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Brain natriuretic peptide increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Liver function test abnormal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Serum ferritin decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Weight increased			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ankle fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Concussion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Muscle strain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Penis injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cardiac disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Restless leg syndrome			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Head titubation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Myoclonus			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear discomfort			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dry mouth			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Retching			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pruritus generalized			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

Proteinuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary hesitation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle twitching			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Rhinitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				
subjects affected / exposed	3 / 10 (30.00%)			
occurrences (all)	3			
Laryngitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Fungal infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pharyngitis streptococcal				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Sialoadenitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blister infected				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tooth infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Urinary tract infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all) Iron deficiency subjects affected / exposed occurrences (all) Abnormal loss of weight subjects affected / exposed occurrences (all) Hypoglycaemia subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 September 2014	Version 2.0 (No patients were enrolled under Protocol v1 or v2 of the protocol.): Modified to reflect study centers in the European Union; Updated estimated timeline based on revised study design and Changed to peak work (specified in watts/kg) instead of peak workload (specified in watts)
13 October 2014	Version 3.0: PK characterization added as an objective of the study, per FDA recommendation; Additional samples collected for PK analysis purposes; Added moderate or strong inhibitors or inducers of cytochrome P450 3A4 as excluded medications, per FDA recommendation: exclude patients with clinically significant liver disease, per FDA recommendation; Clarifications made throughout
23 June 2015	Version 4.0: Enrollment of up to 2 additional cohorts in Part 1 may require more sites; Assigned new study manager; Modify Part 1 of the study to allow for up to 2 additional cohorts of patients; Modify Part 2 to allow the 2 doses of RTA 408 to be selected from doses cleared by the DSMB in Part 1; Allow approximately 16 additional patients (2 cohorts of approximately 8 patients each); Clarifications given changes to study design; added guidance to maintain assessment order across visits to limit impact on functional assessments; screening window widened to accommodate operational complexities including patient travel and genetic testing confirmation if needed; clarification regarding maximal exercise assessments; clarification regarding timing for PK collections for Cohort 3 and Cohort 4; added ethics committee references for ex-US sites; minor clarification throughout.
29 October 2015	Version 5.0: Change in clinical manager; Added serious adverse event report hotline phone number for Europe; Update study duration due to additional cohorts included in Part 1 of the study; Modify Part 1 of the study to allow for up to 8 cohorts of patients; condensed the description of each dosing cohort within Part 1 of the study; Modified the description of each dosing cohort and specified that the maximum RTA 408 dose will be 160 mg; Number of patients increased with the addition of more cohorts in Part 1; Clarification that cohorts 2 through 8 will be a randomized to a cohort-specific dose or placebo; Clarification that two dose levels of RTA 408 and placebo will be used in Part 2; Updated dose levels in Part 1 and clarification regarding dose selection in Part 2; Clarification of randomization in Part 1 for additional cohorts; Explicit exclusion that patients who are pregnant or breastfeeding may not participate in the study; Clarification of randomization in Part 1 for additional cohorts; Updated to allow for use of 50-mg capsule; Clarification for sites outside of the US regarding expiry information being provided on treatment kits intended for use in the EU; Updated Safety CRO international reporting information; Clarifications made throughout.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31896620