Clinical trial results:
A Phase 2, Multi-Center, Double-Blind, Randomized, Dose-Ranging, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of CK-2127107 In Patients with Amyotrophic Lateral Sclerosis (ALS)

Summary

EudraCT number	2018-000586-37
Trial protocol	IE ES NL
Global end of trial date	07 March 2019

Results information

Result version number	v1 (current)
This version publication date	14 May 2020
First version publication date	14 May 2020

Trial information

Trial identification

Sponsor protocol code	CY 5022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03160898
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cytokinetics, Inc.
Sponsor organisation address	280 East Grand Avenue, South San Francisco, California, United States, 94080
Public contact	Medical Affairs, Cytokinetics, Inc., +1 650 6242929, medicalaffairs@cytokinetics.com
Scientific contact	Medical Affairs, Cytokinetics, Inc., +1 650 6242929, medicalaffairs@cytokinetics.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	07 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 March 2019
Global end of trial reached?	Yes
Global end of trial date	07 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of CK-2127107 (hereafter referred to as reldesemtiv) versus placebo on respiratory function in patients with ALS.

Protection of trial subjects:

The study was conducted in accordance with the United States (US) Code of Federal Regulations (CFR) governing protection of human subjects (21 CFR 50), financial disclosure by clinical investigators (21 CFR 54), institutional review boards (IRBs; 21 CFR 56), investigational new drug applications (21 CFR 312), and applications for the US Food and Drug Administration approval to market a new drug (21 CFR 314), as appropriate. The study was also conducted in accordance with applicable International Council on Harmonisation (ICH) guidelines. Both the US regulations along with the ICH guidelines are commonly known as good clinical practices (GCPs).

An independent Data Monitoring Committee (DMC) assessed patient safety in an unblinded manner periodically during the study. The DMC was chartered to make recommendations to the sponsor, as appropriate, regarding modification in study design or conduct to ensure patient safety and the integrity of the study.

Background therapy:

Concomitant use of riluzole and/or edaravone was allowed during the study if patients had been taking riluzole for at least 30 days prior to screening and if patients had completed 2 cycles of edaravone by screening. Neither drug was allowed if they had not been used for at least 30 days prior to screening.

Evidence for comparator: -

Actual start date of recruitment	16 August 2017
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	Netherlands: 11
Country: Number of subjects enrolled	Spain: 38
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 100
Country: Number of subjects enrolled	United States: 284
Worldwide total number of subjects	457
EEA total number of subjects	53

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)	308
From 65 to 84 years	149
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with familial or sporadic ALS were enrolled at 65 sites in Australia, Canada, Ireland, Netherlands, Spain, and the United States. The first patient was screened on 16 August 2017 and the last patient completed on 07 March 2019.

Pre-assignment

Screening details:

Eligible patients were male or female, ≥18 to ≤80 years of age, with familial or sporadic ALS ≤24 months prior to screening. At screening, patients were to have an upright slow vial capacity (SVC) ≥60% of predicted; must have been able to swallow tablets and perform pulmonary function tests; had normal lab tests; and had a caregiver (if needed).

Period 1

Period 1 title	Overall Trial
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients in this group received placebo (to match reldesemtiv) twice daily for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo for reldesemtiv
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were randomized 1:1:1:1 to receive reldesemtiv 150 mg, 300 mg, 450 mg, or placebo, twice daily for 12 weeks. Doses were to be taken approximately 12 hours (± 2 hours) apart and within 2 hours following a meal.

Arm title	Reldesemtiv 150 mg

Arm description:

Patients in this group received 150 mg reldesemtiv twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Reldesemtiv
Investigational medicinal product code	CK-2127107
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were randomized 1:1:1:1 to receive reldesemtiv 150 mg, 300 mg, 450 mg, or placebo, twice daily for 12 weeks. Doses were to be taken approximately 12 hours (± 2 hours) apart and within 2 hours following a meal.

Arm title	Reldesemtiv 300 mg

Arm description:

Patients in this group received 300 mg reldesemtiv twice daily for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	Reldesemtiv 300 mg
Investigational medicinal product code	CK-2127107
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were randomized 1:1:1:1 to receive reldesemtiv 150 mg, 300 mg, 450 mg, or placebo, twice daily for 12 weeks. Doses were to be taken approximately 12 hours (± 2 hours) apart and within 2 hours following a meal.

Arm title	Reldesemtiv 450 mg

Arm description:

Patients in this group received 450 mg reldesemtiv twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Reldesemtiv
Investigational medicinal product code	CK-2127107
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

Patients were randomized 1:1:1:1 to receive reldesemtiv 150 mg, 300 mg, 450 mg, or placebo, twice daily for 12 weeks. Doses were to be taken approximately 12 hours (± 2 hours) apart and within 2 hours following a meal.

Number of subjects in period 1	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg
Started	115	112	113
Completed	95	100	97
Not completed	20	12	16
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	1	2	2
Physician decision	1	-	-
Adverse event, non-fatal	4	8	7
Unspecified	2	-	2
Progressive disease	4	1	2
Lost to follow-up	1	1	1
Sponsor decision	2	-	-
Difficulty traveling to clinic visits	3	-	-
Protocol deviation	1	-	2

Number of subjects in period 1	Reldesemtiv 450 mg
Started	117
Completed	98
Not completed	19
Adverse event, serious fatal	1
Consent withdrawn by subject	1

Physician decision	1
Adverse event, non-fatal	10
Unspecified	2
Progressive disease	1
Lost to follow-up	2
Sponsor decision	-
Difficulty traveling to clinic visits	1
Protocol deviation	-

Period 2

Period 2 title	Efficacy Analyses
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Reldesemtiv 300 mg & 450 mg (pooled)

Arm description:

Patients from the reldesemtiv 300 mg and 450 mg groups were pooled for analysis purposes only.

Arm type	Pooled for analysis purposes only
Investigational medicinal product name	Reldesemtiv
Investigational medicinal product code	CK-2127107
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For analysis purposes only, patients from the reldesemtiv 300 mg and 450 mg groups were pooled to evaluate the efficacy responses of the pooled group compared with those of the placebo group.

Number of subjects in period 2[1]	Reldesemtiv 300 mg & 450 mg (pooled)
Started	230
Completed	195
Not completed	35
Adverse event, serious fatal	1
Physician decision	1
Consent withdrawn by subject	3
Adverse event, non-fatal	17
Unspecified	4
Progressive disease	3

Lost to follow-up	3
Difficulty traveling to clinic visits	1
Protocol deviation	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The Reldesemtiv 300 mg & 450 mg (pooled) arm was added for efficacy analysis purposes only. A prespecified efficacy analysis was to compare this pooled group to placebo for each efficacy endpoint. All data from this arm (disposition and efficacy) derives from both the reldesemtiv 300 mg arm and the reldesemtiv 450 mg arm.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients in this group received placebo (to match reldesemtiv) twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 150 mg
Reporting group description:	
Patients in this group received 150 mg reldesemtiv twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 300 mg
Reporting group description:	
Patients in this group received 300 mg reldesemtiv twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 450 mg
Reporting group description:	
Patients in this group received 450 mg reldesemtiv twice daily for 12 weeks.	

Reporting group values	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg
Number of subjects	115	112	113
Age categorical Units: Subjects			
Adults (18-64 years)	74	81	80
From 65-84 years	41	31	33
Gender categorical Units: Subjects			
Female	47	41	42
Male	68	71	71

Reporting group values	Reldesemtiv 450 mg	Total	
Number of subjects	117	457	
Age categorical Units: Subjects			
Adults (18-64 years)	73	308	
From 65-84 years	44	149	
Gender categorical Units: Subjects			
Female	50	180	
Male	67	277	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Patients in this group received placebo (to match reldesemtiv) twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 150 mg
Reporting group description:	
Patients in this group received 150 mg reldesemtiv twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 300 mg
Reporting group description:	
Patients in this group received 300 mg reldesemtiv twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 450 mg
Reporting group description:	
Patients in this group received 450 mg reldesemtiv twice daily for 12 weeks.	
Reporting group title	Reldesemtiv 300 mg & 450 mg (pooled)
Reporting group description:	
Patients from the reldesemtiv 300 mg and 450 mg groups were pooled for analysis purposes only.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set consisted of all randomized patients who received any amount of study drug and had a baseline and at least 1 postbaseline efficacy assessment.	

Primary: Change from Baseline to Week 12 in Percent Predicted Slow Vital Capacity

End point title	Change from Baseline to Week 12 in Percent Predicted Slow Vital Capacity
End point description:	
Slow vital capacity was measured using a spirometer (in units of liters). Following 3 to 5 breaths at rest, patients were instructed to take as deep an inspiration as possible followed by a maximum exhalation (blowing out all the air in their lungs). Values obtained were converted to percent predicted values (ie, the test result as a percent of predicted values for the patients of similar demographic and baseline characteristics [eg, height, age, sex]).	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

End point values	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg	Reldesemtiv 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	112	113	117
Units: percent				
least squares mean (standard error)	-6.46 (± 0.964)	-4.97 (± 0.952)	-4.62 (± 0.963)	-4.58 (± 0.927)

End point values	Reldesemtiv 300 mg & 450 mg (pooled)			

Subject group type	Reporting group			
Number of subjects analysed	230			
Units: percent				
least squares mean (standard error)	-4.60 (± 0.701)			

Statistical analyses

Statistical analysis title	Reldesemtiv 150 mg - placebo comparison of change
Statistical analysis description:	
Difference in LS mean changes from baseline: reldesemtiv 150 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 150 mg
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2501
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	4.03
Variability estimate	Standard error of the mean
Dispersion value	1.291

Statistical analysis title	Reldesemtiv 300 mg - placebo comparison of change
Statistical analysis description:	
Difference in LS mean changes from baseline: reldesemtiv 300 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 300 mg
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1549
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	4.38
Variability estimate	Standard error of the mean
Dispersion value	1.29

Statistical analysis title	Reldesemtiv 450 mg - placebo comparison of change
Statistical analysis description:	
Difference in LS mean changes from baseline: reldesemtiv 450 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 450 mg
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1417
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	4.38
Variability estimate	Standard error of the mean
Dispersion value	1.274

Statistical analysis title	Reldesemtiv 300&450 mg (pooled)-placebo comparison
Statistical analysis description:	
Difference in LS mean changes from baseline: reldesemtiv 300 mg & 450 mg (pooled) minus placebo	
Comparison groups	Placebo v Reldesemtiv 300 mg & 450 mg (pooled)
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0964
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	4.05
Variability estimate	Standard error of the mean
Dispersion value	1.115

Secondary: Slope from Baseline to Week 12 in Muscle Strength Mega-Score

End point title	Slope from Baseline to Week 12 in Muscle Strength Mega-Score

End point description:

Muscle strength of 6 muscle groups (elbow flexion, wrist extension, first dorsal interosseous, hip flexion, knee extension, and ankle dorsiflexion) and hand grip strength were measured bilaterally using a hand-

held dynamometer. Muscle strength was measure twice for each body location; if the variability between the first 2 measures was > 15%, a third measure was obtained.

The muscle strength of each measured body location as a percent of change from baseline was determined using the equation: ([postbaseline value – baseline value] / baseline value) × 100.

The mega-score was a composite score that averaged strength across muscle groups. It was calculated as the mean of the muscle strength scores among the 6 muscle groups and hand grip strength, each measured bilaterally (totaling 14 body locations).

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg	Reldesemtiv 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	112	113	117
Units: change/day				
least squares mean (standard error)	-0.1444 (± 0.02492)	-0.1198 (± 0.02463)	-0.1299 (± 0.02474)	-0.0956 (± 0.02421)

End point values	Reldesemtiv 300 mg & 450 mg (pooled)			
Subject group type	Reporting group			
Number of subjects analysed	230			
Units: change/day				
least squares mean (standard error)	-0.1127 (± 0.01731)			

Statistical analyses

Statistical analysis title	Reldesemtiv 150 mg - placebo comparison of change

Statistical analysis description:

Difference in LS mean changes from baseline: reldesemtiv 150 mg minus placebo

Comparison groups	Reldesemtiv 150 mg v Placebo
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4824
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.0246
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0442
upper limit	0.0935

Statistical analysis title	Reldesemtiv 300 mg - placebo comparison of change
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 300 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 300 mg
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6787
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.0146
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0544
upper limit	0.0835

Statistical analysis title	Reldesemtiv 450 mg - placebo comparison of change
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 450 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 450 mg
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1604
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.0488
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0194
upper limit	0.1171

Statistical analysis title	Reldesemtiv 300&450 mg (pooled)-placebo comparison
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 300 mg & 450 mg (pooled) minus placebo	
Comparison groups	Placebo v Reldesemtiv 300 mg & 450 mg (pooled)

Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2966
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.0317
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0279
upper limit	0.0913

Secondary: Change from Baseline to Week 12 in ALS Functional Rating Scale - Revised (ALSFRS-R) Total Score

End point title	Change from Baseline to Week 12 in ALS Functional Rating Scale - Revised (ALSFRS-R) Total Score

End point description:

The ALSFRS-R is used to measure the progression and severity of disability in patients with ALS. The ALSFRS-R consists of 12 questions, assessing a patient's capability and independence in functional activities relevant to ALS, categorized in the following 4 domains: gross motor tasks, fine motor tasks, bulbar functions, and respiratory function. Each question is scored from 0 (indicating incapable or dependent) to 4 (normal). The total score ranges from 0 to 48. Higher scores reflect more normal function and lower scores reflect more impaired
function.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg	Reldesemtiv 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	112	113	117
Units: ALSFRS-R Total Score				
least squares mean (standard error)	-3.53 (± 0.313)	-2.40 (± 0.311)	-2.62 (± 0.317)	-2.94 (± 0.307)

End point values	Reldesemtiv 300 mg & 450 mg (pooled)			
Subject group type	Reporting group			
Number of subjects analysed	230			
Units: ALSFRS-R Total Score				
least squares mean (standard error)	-2.78 (± 0.228)			

Statistical analyses

Statistical analysis title	Reldesemtiv 150 mg - placebo comparison of change
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 150 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 150 mg
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0087
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.97
Variability estimate	Standard error of the mean
Dispersion value	0.427

Statistical analysis title	Reldesemtiv 300 mg - placebo comparison of change
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 300 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 300 mg
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0351
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	1.75
Variability estimate	Standard error of the mean
Dispersion value	0.43

Statistical analysis title	Reldesemtiv 450 mg - placebo comparison of change
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 450 mg minus placebo	
Comparison groups	Placebo v Reldesemtiv 450 mg
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1642
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	1.43
Variability estimate	Standard error of the mean
Dispersion value	0.425

Statistical analysis title	Reldesemtiv 300&450 mg (pooled)-placebo comparison
Statistical analysis description: Difference in LS mean changes from baseline: reldesemtiv 300 mg & 450 mg (pooled) minus placebo	
Comparison groups	Placebo v Reldesemtiv 300 mg & 450 mg (pooled)
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0435
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	1.48
Variability estimate	Standard error of the mean
Dispersion value	0.371

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from administration of the first dose of study drug through 4 weeks after the last dose of study drug

Adverse event reporting additional description:

An AE was treatment-emergent if it started or worsened (eg, increased in severity) during or after the first dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Patients in this group received placebo (to match reldesemtiv) twice daily for 12 weeks.

Reporting group title	Reldesemtiv 150 mg

Reporting group description:

Patients in this group received 150 mg reldesemtiv twice daily for 12 weeks.

Reporting group title	Reldesemtiv 300 mg

Reporting group description:

Patients in this group received 300 mg reldesemtiv twice daily for 12 weeks.

Reporting group title	Reldesemtiv 450 mg

Reporting group description:

Patients in this group received 450 mg reldesemtiv twice daily for 12 weeks.

Serious adverse events	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 115 (8.70%)	8 / 112 (7.14%)	8 / 113 (7.08%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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
Blood creatine phosphokinase			

increased			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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
Weight decreased			
subjects affected / exposed	1 / 115 (0.87%)	1 / 112 (0.89%)	0 / 113 (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
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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
Joint dislocation			
subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	0 / 113 (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
Traumatic fracture			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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
Subclavian vein thrombosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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

Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle contractions involuntary			
subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	0 / 113 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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			
Pain			

subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	0 / 113 (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
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 115 (0.00%)	2 / 112 (1.79%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	0 / 113 (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
Rectal prolapse			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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			
Prostatomegaly			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	0 / 113 (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
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			

subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	2 / 115 (1.74%)	0 / 112 (0.00%)	0 / 113 (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
Pulmonary embolism			
subjects affected / exposed	2 / 115 (1.74%)	0 / 112 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
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			
Urinary tract infection			
subjects affected / exposed	1 / 115 (0.87%)	1 / 112 (0.89%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	0 / 113 (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
Device related sepsis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Parainfluenzae virus infection			
subjects affected / exposed	0 / 115 (0.00%)	0 / 112 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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
Urosepsis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 112 (0.00%)	0 / 113 (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

Serious adverse events	Reldesemtiv 450 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 117 (6.84%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Glomerular filtration rate decreased			

subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Traumatic fracture			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subclavian vein thrombosis			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Palpitations			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dizziness			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscle contractions involuntary			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			

subjects affected / exposed	0 / 117 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 117 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal prolapse				
subjects affected / exposed	0 / 117 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Prostatomegaly				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic ovarian cyst				
subjects affected / exposed	0 / 117 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 117 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 117 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pulmonary embolism			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related sepsis			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parainfluenzae virus infection			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 117 (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: 5 %

Non-serious adverse events	Placebo	Reldesemtiv 150 mg	Reldesemtiv 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 115 (82.61%)	99 / 112 (88.39%)	97 / 113 (85.84%)
Investigations			
Cystatin C increased			
subjects affected / exposed	2 / 115 (1.74%)	7 / 112 (6.25%)	9 / 113 (7.96%)
occurrences (all)	2	7	9
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 115 (0.87%)	6 / 112 (5.36%)	6 / 113 (5.31%)
occurrences (all)	1	6	6
Alanine aminotransferase increased			
subjects affected / exposed	1 / 115 (0.87%)	2 / 112 (1.79%)	5 / 113 (4.42%)
occurrences (all)	1	2	6
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 115 (0.87%)	2 / 112 (1.79%)	3 / 113 (2.65%)
occurrences (all)	1	2	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	15 / 115 (13.04%)	8 / 112 (7.14%)	14 / 113 (12.39%)
occurrences (all)	28	15	15
Post-traumatic pain			
subjects affected / exposed	2 / 115 (1.74%)	6 / 112 (5.36%)	8 / 113 (7.08%)
occurrences (all)	2	8	11
Skin abrasion			

subjects affected / exposed	5 / 115 (4.35%)	8 / 112 (7.14%)	3 / 113 (2.65%)
occurrences (all)	7	10	4
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 115 (13.04%)	16 / 112 (14.29%)	16 / 113 (14.16%)
occurrences (all)	18	18	19
Dizziness			
subjects affected / exposed	11 / 115 (9.57%)	8 / 112 (7.14%)	11 / 113 (9.73%)
occurrences (all)	13	12	13
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 115 (10.43%)	14 / 112 (12.50%)	19 / 113 (16.81%)
occurrences (all)	14	14	20
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	14 / 115 (12.17%)	10 / 112 (8.93%)	13 / 113 (11.50%)
occurrences (all)	16	13	14
Constipation			
subjects affected / exposed	5 / 115 (4.35%)	7 / 112 (6.25%)	13 / 113 (11.50%)
occurrences (all)	5	8	15
Diarrhoea			
subjects affected / exposed	8 / 115 (6.96%)	12 / 112 (10.71%)	6 / 113 (5.31%)
occurrences (all)	8	15	6
Dry mouth			
subjects affected / exposed	2 / 115 (1.74%)	2 / 112 (1.79%)	6 / 113 (5.31%)
occurrences (all)	2	2	6
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 115 (1.74%)	1 / 112 (0.89%)	2 / 113 (1.77%)
occurrences (all)	4	1	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 115 (1.74%)	8 / 112 (7.14%)	4 / 113 (3.54%)
occurrences (all)	2	9	5
Pain in extremity			

subjects affected / exposed	5 / 115 (4.35%)	1 / 112 (0.89%)	3 / 113 (2.65%)
occurrences (all)	6	1	3
Muscle spasms			
subjects affected / exposed	1 / 115 (0.87%)	6 / 112 (5.36%)	2 / 113 (1.77%)
occurrences (all)	1	7	2
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	9 / 115 (7.83%)	6 / 112 (5.36%)	10 / 113 (8.85%)
occurrences (all)	9	6	10
Urinary tract infection			
subjects affected / exposed	8 / 115 (6.96%)	3 / 112 (2.68%)	5 / 113 (4.42%)
occurrences (all)	9	5	5
Upper respiratory tract infection			
subjects affected / exposed	3 / 115 (2.61%)	7 / 112 (6.25%)	1 / 113 (0.88%)
occurrences (all)	4	7	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 115 (3.48%)	3 / 112 (2.68%)	7 / 113 (6.19%)
occurrences (all)	4	3	7
Dehydration			
subjects affected / exposed	0 / 115 (0.00%)	1 / 112 (0.89%)	6 / 113 (5.31%)
occurrences (all)	0	1	6

Non-serious adverse events	Reldesemtiv 450 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 117 (91.45%)		
Investigations			
Cystatin C increased			
subjects affected / exposed	20 / 117 (17.09%)		
occurrences (all)	22		
Glomerular filtration rate decreased			
subjects affected / exposed	10 / 117 (8.55%)		
occurrences (all)	11		
Alanine aminotransferase increased			
subjects affected / exposed	11 / 117 (9.40%)		
occurrences (all)	14		
Aspartate aminotransferase increased			

subjects affected / exposed	9 / 117 (7.69%)		
occurrences (all)	11		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	17 / 117 (14.53%)		
occurrences (all)	26		
Post-traumatic pain			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	6		
Skin abrasion			
subjects affected / exposed	5 / 117 (4.27%)		
occurrences (all)	7		
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 117 (10.26%)		
occurrences (all)	13		
Dizziness			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	7		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	20 / 117 (17.09%)		
occurrences (all)	24		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	22 / 117 (18.80%)		
occurrences (all)	23		
Constipation			
subjects affected / exposed	10 / 117 (8.55%)		
occurrences (all)	10		
Diarrhoea			
subjects affected / exposed	4 / 117 (3.42%)		
occurrences (all)	4		
Dry mouth			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences (all)	1		

Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 6 / 117 (5.13%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	 8 / 117 (6.84%) 10 6 / 117 (5.13%) 7 1 / 117 (0.85%) 1		
Infections and infestations Viral upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 9 / 117 (7.69%) 9 5 / 117 (4.27%) 7 1 / 117 (0.85%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all)	 7 / 117 (5.98%) 8 6 / 117 (5.13%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported