Clinical trial results:
A Phase 2, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of pegcetacoplan in subjects with amyotrophic lateral sclerosis (ALS)

Summary

EudraCT number	2019-003797-10
Trial protocol	IE FR BE DE CZ NL IT
Global end of trial date	13 July 2023

Results information

Result version number	v1 (current)
This version publication date	27 February 2025
First version publication date	27 February 2025

Trial information

Trial identification

Sponsor protocol code	APL2-ALS-206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04579666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Apellis Pharmaceuticals Inc.
Sponsor organisation address	100 5th Avenue, Waltham, Massachusetts, United States, 02451
Public contact	Apellis Clinical Trial Information Line, Apellis Pharmaceuticals Inc., +1 833-284-6361, clinicaltrials@apellis.com
Scientific contact	Apellis Clinical Trial Information Line, Apellis Pharmaceuticals Inc., +1 833-284-6361, clinicaltrials@apellis.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	13 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of twice per week subcutaneous (SC) doses of pegcetacoplan 1080 milligram (mg) compared to placebo in subjects with sporadic amyotrophic lateral sclerosis (ALS) as measured by the Combined Assessment of Function and Survival (CAFS) rank score (joint-rank score)

Protection of trial subjects:

This research was carried out in accordance with the protocol, applicable regulations, the ethical principles set forth in the Declaration of Helsinki, and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Harmonised Guideline for Good Clinical Practice E6 Revision 2. An external, independent data monitoring committee assessed the safety, tolerability and efficacy data of the study periodically.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2020
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	Argentina: 24
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Italy: 29
Country: Number of subjects enrolled	Japan: 20
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	Ukraine: 13
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	249
EEA total number of subjects	154

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)	171
From 65 to 84 years	77
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This Phase 2, placebo-controlled study was conducted in subjects diagnosed with ALS. A total of 249 subjects were randomized in a 2:1 ratio to either receive pegcetacoplan or placebo.

Pre-assignment

Screening details:

Study consists of 5 periods: 6-week screening period, 52-week randomized treatment period (RTP), 52-week open-label treatment period (OLP), 52-week long-term extension treatment period and a 6-week off-treatment follow-up period. Study was terminated early during OLP due to lack of efficacy as determined by the Week 52 data and no safety concerns.

Period 1

Period 1 title	RTP (Up to Week 52)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	RTP: Pegcetacoplan

Arm description:

Subjects received pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegcetacoplan
Investigational medicinal product code	APL-2
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegcetacoplan 1080 mg was administered as an SC injection/infusion twice per week for 52 weeks in the RTP.

Arm title	RTP: Placebo

Arm description:

Subjects received placebo matching pegcetacoplan as SC injection/infusion twice per week for 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo matching pegcetacoplan was administered as SC injection/infusion twice per week for 52 weeks in the RTP.

Number of subjects in period 1	RTP: Pegcetacoplan	RTP: Placebo
Started	169	80
Completed	99	51
Not completed	70	29
Physician decision	4	1
Consent withdrawn by subject	25	11
Adverse event, non-fatal	4	3
Death	24	9
Site terminated by sponsor	7	5
Study terminated by sponsor	2	-
Unspecified	2	-
Lost to follow-up	1	-
Progressive disease	1	-

Period 2

Period 2 title	OLP (From Week 52 up to Week 104)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLP: Pegcetacoplan/Pegcetacoplan

Arm description:

Eligible subjects who had received pegcetacoplan in RTP entered OLP and continued to receive pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegcetacoplan
Investigational medicinal product code	APL-2
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegcetacoplan 1080 mg was administered as an SC injection/infusion twice per week for 52 weeks in the OLP.

Arm title	OLP: Placebo/Pegcetacoplan

Arm description:

Eligible subjects who had received placebo matching pegcetacoplan in RTP entered OLP to receive pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.

Arm type	Experimental

Investigational medicinal product name	Pegcetacoplan
Investigational medicinal product code	APL-2
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegcetacoplan 1080 mg was administered as an SC injection/infusion twice per week for 52 weeks in the OLP.

Number of subjects in period 2[1]	OLP: Pegcetacoplan/Pegcetacoplan	OLP: Placebo/Pegcetacoplan
Started	97	50
Completed	0	0
Not completed	97	50
Consent withdrawn by subject	19	12
Physician decision	3	1
Adverse event, non-fatal	2	-
Death	10	6
Sponsor request	63	31

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: 2 subjects in RTP: Pegcetacoplan arm and 1 subject in RTP: Placebo arm withdrew after completing the RTP and before entering the OLP period.

Baseline characteristics

Reporting groups	
Reporting group title	RTP: Pegcetacoplan
Reporting group description:	
Subjects received pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.	
Reporting group title	RTP: Placebo
Reporting group description:	
Subjects received placebo matching pegcetacoplan as SC injection/infusion twice per week for 52 weeks.	

Reporting group values	RTP: Pegcetacoplan	RTP: Placebo	Total
Number of subjects	169	80	249
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	57.0	57.7	
standard deviation	± 12.47	± 11.02	-
Gender categorical Units: Subjects			
Female	64	25	89
Male	105	55	160
Race Units: Subjects			
Caucasian	130	67	197
Black or African American	0	0	0
North East Asian	14	6	20
South East Asian	0	0	0
Other	13	5	18
Unknown	12	2	14
Ethnicity Units: Subjects			
Hispanic or Latino	27	15	42
Not Hispanic or Latino	124	62	186
Unknown or Not Reported	18	3	21

End points

End points reporting groups

Reporting group title	RTP: Pegcetacoplan
Reporting group description:	
Subjects received pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.	
Reporting group title	RTP: Placebo
Reporting group description:	
Subjects received placebo matching pegcetacoplan as SC injection/infusion twice per week for 52 weeks.	
Reporting group title	OLP: Pegcetacoplan/Pegcetacoplan
Reporting group description:	
Eligible subjects who had received pegcetacoplan in RTP entered OLP and continued to receive pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.	
Reporting group title	OLP: Placebo/Pegcetacoplan
Reporting group description:	
Eligible subjects who had received placebo matching pegcetacoplan in RTP entered OLP to receive pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.	

Primary: RTP: Combined Assessment of Function and Survival (CAFS) Rank Score (Joint-Rank Score) at Week 52

End point title	RTP: Combined Assessment of Function and Survival (CAFS) Rank Score (Joint-Rank Score) at Week 52
End point description:	
CAFS scale is combined endpoint ranking subjects' clinical outcomes based on ALS Functional Rating Scale-Revised (ALSFRS-R) and survival time.For ALSFRS-R,12 functions were rated on 5-point ordinal rating scales (0 to 4);total score 0-48 (sum of all 12 items);higher score indicated better functioning.For survival time, longer the subject survives indicated better outcome.Each subject's outcome was compared to every other subject outcome in trial in series of pairwise comparisons,summed scores (sum of comparisons [+1 {better}, 0 {tie}, -1 {worse}]) were ranked and ranged from 001-247 (number of subjects in modified [m]ITT population).Reported values:mean rank scores in each group for composite endpoint.Higher rank indicated better outcome. mITT set:all randomized subjects who received at least 1 dose of randomized treatment (pegcetacoplan or placebo) and who died or had postbaseline assessment of endpoint that was used in CAFS.Only subjects with data collected at Week 52 are reported.	
End point type	Primary
End point timeframe:	
Week 52	

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	79		
Units: score on a scale				
least squares mean (standard error)	123.0 (± 4.17)	126.0 (± 6.89)		

Statistical analyses

Statistical analysis title	Difference in LS means for CAFS

Statistical analysis description:

Analysis of covariance (ANCOVA) was used to analyze the ranks of the CAFS score with treatment as a fixed effect, adjusted for baseline ALSFRS-R total score, time from symptom onset, baseline Log neurofilament light chain (NfL), and the randomization stratification factors (location of first muscle weakness and use of riluzole and edaravone).

Comparison groups	RTP: Pegcetacoplan v RTP: Placebo
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7205
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.5
upper limit	13.5

Primary: RTP: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	RTP: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)[1]

End point description:

An AE was any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug related. An SAE was any AE or suspected adverse reaction that, in the view of the investigator, resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or was a congenital anomaly or birth defect. TEAEs were AEs that started on or after first dose of study drug or started before first dose of study drug but increased in severity on or after the first dose of study drug up to 56 days post last dose of study drug. The safety set for RTP included all subjects who received at least 1 dose of study drug: pegcetacoplan or placebo.

End point type	Primary

End point timeframe:

From first dose of study drug (Day 1) up to 56 days post last dose of study drug, approximately 60 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, statistical analysis is not provided.

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	80		
Units: subjects				
TEAEs	137	61		
TESAEs	57	27		

Statistical analyses

No statistical analyses for this end point

Primary: OLP: Number of Subjects With Treatment-emergent Adverse Events and Treatment-emergent Serious Adverse Events

End point title	OLP: Number of Subjects With Treatment-emergent Adverse Events and Treatment-emergent Serious Adverse Events[2]

End point description:

An AE was any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug related. An SAE was any AE or suspected adverse reaction that, in the view of the investigator, resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or was a congenital anomaly or birth defect. TEAEs were AEs that started on or after first dose of study drug or started before first dose of study drug but increased in severity on or after the first dose of study drug up to 56 days post last dose of study drug. The safety set for the OLP included only those subjects who received at least 1 dose of the open-label treatment.

End point type	Primary

End point timeframe:

From first dose of study drug (Week 52) up to 56 days post last dose of study drug, approximately 60 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, statistical analysis is not provided.

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	50		
Units: subjects				
TEAEs	54	33		
TESAEs	24	14		

Statistical analyses

No statistical analyses for this end point

Primary: RTP: Number of Subjects With Positive Response to Columbia-Suicide Severity Rating Scale (C-SSRS) up to Week 52

End point title	RTP: Number of Subjects With Positive Response to Columbia-Suicide Severity Rating Scale (C-SSRS) up to Week 52[3]

End point description:

C-SSRS is a measure used to identify and assess individuals at risk for suicide and included "yes" or "no" responses for assessment of SI and SB. SI items classified on 5-item scale:1 (wish to be dead),2 (non-specific active suicidal thoughts),3 (active SI with any methods without intent to act),4 (active SI

with some intent to act, without specific plan) and 5 (active SI with a specific plan and intent).SB items classified on 5-item scale:0 (preparatory acts or behavior),1 (aborted attempt),2 (interrupted attempt),3 (actual attempt [non-fatal]) and 4 (completed suicide).Numeric ratings provided for SI: total score 0 to 25, for SB: total score 0 to 16; higher scores for both indicate more severity. Baseline was defined as last available, non-missing observation prior to first study drug administration. The safety set for RTP included all subjects who received at least 1 dose of study drug: pegcetacoplan or placebo.

End point type	Primary

End point timeframe:

Baseline (Day 1) up to Week 52

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, statistical analysis is not provided.

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	80		
Units: subjects				
SI only	16	6		
SB only	0	0		
SI and SB	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: OLP: Number of Subjects With Positive Response to Columbia-Suicide Severity Rating Scale up to Week 104

End point title	OLP: Number of Subjects With Positive Response to Columbia-Suicide Severity Rating Scale up to Week 104[4]

End point description:

C-SSRS is a measure used to identify and assess individuals at risk for suicide and included "yes" or "no" responses for assessment of suicidal ideation (SI) and suicidal behavior (SB).SI items classified on 5-item scale:1 (wish to be dead),2 (non-specific active suicidal thoughts),3 (active SI with any methods without intent to act),4 (active SI with some intent to act, without specific plan) and 5 (active SI with a specific plan and intent).SB items classified on 5-item scale:0 (preparatory acts or behavior),1 (aborted attempt),2 (interrupted attempt),3 (actual attempt [non-fatal]) and 4 (completed suicide).Numeric ratings provided for SI: total score 0 to 25, for SB: total score 0 to 16; higher scores for both indicate more severity. Baseline was defined as last available, non-missing observation prior to first study drug administration. The safety set for the OLP included only those subjects who received at least 1 dose of the open-label treatment.

End point type	Primary

End point timeframe:

From Baseline (Week 52) up to Week 104

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, statistical analysis is not provided.

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	50		
Units: subjects				
SI only	11	3		
SB only	0	0		
SI and SB	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: RTP: Change From Baseline in the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) Score at Week 52

End point title	RTP: Change From Baseline in the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) Score at Week 52

End point description:

The ALSFRS-R included 12 items for assessment of functional status: speech, salivation, swallowing, handwriting, cutting food and handling utensils, dressing and hygiene, turning in bed and adjusting bed clothes, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency. Each item ranged from 0 (no ability) to 4 (normal ability). Individual item scores were summed to produce a total score between 0 (worst) and 48 (best) with higher scores meaning better outcome. Least squares mean is presented here. Baseline was defined as the last available, non-missing observation prior to first study drug administration. The ITT set for RTP included all randomized subjects who received at least 1 dose of randomized treatment (pegcetacoplan or placebo). Only those subjects with data collected at Baseline and Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	79		
Units: score on a scale				
least squares mean (standard error)	-16.5 (± 0.81)	-15.8 (± 1.20)		

Statistical analyses

Statistical analysis title	Difference in LS means for ALSFRS-R at Week 52

Statistical analysis description:

The mixed-effect model for repeated measures (MMRM) included fixed categorical effects for treatment, week, and the week-by-treatment interaction, as well as the continuous, fixed covariate of the baseline value of the endpoint, and the week-by-baseline interaction, baseline log NfL, time from symptoms onset to the first dose of study drug, and randomization stratification factors location of first muscle weakness and use of riluzole and/or edaravone).

Comparison groups	RTP: Pegcetacoplan v RTP: Placebo
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6447
Method	MMRM
Parameter estimate	Difference in LS mean
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	2.2

Secondary: RTP: Change From Baseline in Percent Predicted Slow Vital Capacity (%SVC) at Week 52

End point title	RTP: Change From Baseline in Percent Predicted Slow Vital Capacity (%SVC) at Week 52

End point description:

SVC is a pulmonary function test and predictor of functional loss in ALS. It was conducted at clinic visits with the clinic spirometer which reflected the maximum amount of air that could be exhaled slowly. %SVC is the actual volume exhaled in the first 1 second, divided by the normal value for that actual value for a person of that age, gender, height and weight. Baseline was defined as the last available, non-missing observation prior to first study drug administration. Analysis was performed on the ITT population. Only those subjects with data collected at baseline and Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	75		
Units: percentage of predicted SVC				
least squares mean (standard error)	-39.2 (± 2.30)	-32.6 (± 3.17)		

Statistical analyses

Statistical analysis title	Difference in LS means for %SVC at Week 52

Statistical analysis description:

The MMRM included fixed categorical effects for treatment, week, and the week-by-treatment interaction, as well as the continuous, fixed covariate of the baseline value of the endpoint, and the week-by-baseline interaction, baseline log NfL, time from symptoms onset to the first dose of study drug, and randomization stratification factors (location of first muscle weakness and use of riluzole and/or edaravone).

Comparison groups	RTP: Pegcetacoplan v RTP: Placebo

Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0949
Method	MMRM
Parameter estimate	Difference in LS mean
Point estimate	-6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.3
upper limit	1.2

Secondary: RTP: Change From Baseline in Muscle Strength at Week 52

End point title	RTP: Change From Baseline in Muscle Strength at Week 52

End point description:

Muscle strength was measured using handheld dynamometry (HHD) and assessed the following muscles: first dorsal interosseous, wrist extension, elbow extension, elbow flexion, shoulder flexion, knee extension, knee flexion, and ankle dorsiflexion, on both sides of the body. Baseline was defined as the last available, non-missing observation prior to first study drug administration. Analysis was performed on the ITT population. Only those subjects with data collected at baseline and Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	75		
Units: pounds				
least squares mean (standard error)	-0.78 (± 0.06)	-0.59 (± 0.10)		

Statistical analyses

Statistical analysis title	Difference in LS means for muscle strength-Week 52

Statistical analysis description:

The MMRM included fixed categorical effects for treatment, week, and the week-by-treatment interaction, as well as the continuous, fixed covariate of the baseline value of the endpoint, and the week-by-baseline interaction, baseline log NfL, time from symptoms onset to the first dose of study drug, and randomization stratification factors (location of first muscle weakness and use of riluzole and/or edaravone).

Comparison groups	RTP: Pegcetacoplan v RTP: Placebo

Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0935
Method	MMRM
Parameter estimate	Difference in LS mean
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.03

Secondary: RTP: Number of Subjects With an Event of Death or Permanent Tracheostomy or Permanent Assisted Ventilation at Week 52

End point title	RTP: Number of Subjects With an Event of Death or Permanent Tracheostomy or Permanent Assisted Ventilation at Week 52

End point description:

Subjects with an event (that is, either death or permanent tracheostomy or permanent assisted ventilation) in RTP are reported. Analysis was performed on the ITT population.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to Week 52

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	80		
Units: subjects	42	27		

Statistical analyses

No statistical analyses for this end point

Secondary: RTP: Change From Baseline in ALS Assessment Questionnaire (ALSAQ)-40 at Week 52

End point title	RTP: Change From Baseline in ALS Assessment Questionnaire (ALSAQ)- 40 at Week 52

End point description:

The ALSAQ-40 was a 40-item validated questionnaire designed to assess health related quality of life (QoL) over the previous 2 weeks in subjects with ALS. It represented 5 dimensions of health status; each scored from 0 (never, or best) to 4 (always, or worst). 5 dimensions evaluated were: physical mobility (10 items: 1-10; possible score of 0-40); activities of daily living/independence (10 items: 11-20; possible score of 0-40); eating and drinking (3 items: 21-23; possible score of 0-12); communication (7 items: 24-30; possible score: 0-28) and emotional functioning (10 items: 31-40; possible score: 0-40). The total score 0 (no impairment) to 160 (severe impairment) was calculated by adding the 5 dimension scores; least squares mean is presented here. Higher scores indicated worse

QoL. Analysis was performed on the ITT population. Only those subjects with data collected at baseline and Week 52 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	RTP: Pegcetacoplan	RTP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	79		
Units: score on a scale				
least squares mean (standard error)	31.3 (± 1.35)	24.8 (± 1.94)		

Statistical analyses

Statistical analysis title	Difference in LS means for ALSAQ-40 at Week 52

Statistical analysis description:

The MMRM included fixed categorical effects for treatment, week, and the week-by-treatment interaction, as well as the continuous, fixed covariate of the baseline value of the endpoint, and the week-by-baseline interaction, baseline log NfL, time from symptoms onset to the first dose of study drug, and randomization stratification factors (location of first muscle weakness and use of riluzole and/or edaravone).

Comparison groups	RTP: Pegcetacoplan v RTP: Placebo
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0069
Method	MMRM
Parameter estimate	Difference in LS mean
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	11.1

Secondary: OLP: Change From Baseline in the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised Score at Week 104

End point title	OLP: Change From Baseline in the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised Score at Week 104

End point description:

The ALSFRS-R included 12 items for assessment of functional status: speech, salivation, swallowing, handwriting, cutting food and handling utensils, dressing and hygiene, turning in bed and adjusting bed clothes, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency. Each item ranged from 0 (no ability) to 4 (normal ability). Individual item scores were summed to produce a total score between 0 (worst) and 48 (best) with higher scores meaning better outcome. Mean is presented here. Baseline was defined as the last observed value for the efficacy assessment prior to taking the first dose of study drug in OLP. The ITT set for OLP included all randomized subjects who received at least 1 dose

of open label treatment. Only those subjects with data collected at specified timepoints are reported. Here, 99999=Standard deviation cannot be calculated when only 1 subject analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 52) and Week 104

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	1		
Units: score on a scale				
arithmetic mean (standard deviation)	-19.0 (± 10.82)	-28.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLP: Change From Baseline in Percent Predicted Slow Vital Capacity at Week 104

End point title	OLP: Change From Baseline in Percent Predicted Slow Vital Capacity at Week 104

End point description:

SVC is a pulmonary function test and predictor of functional loss in ALS. It was planned to be conducted at clinic visits with the clinic spirometer which reflected the maximum amount of air that could be exhaled slowly. %SVC is the actual volume exhaled in the first 1 second, divided by the normal value for that actual value for a person of that age, gender, height and weight. Baseline was defined as the last available, non-missing observation prior to first study drug administration. Analysis was planned to be performed on the ITT population. Data was not collected as the study was terminated early.

End point type	Secondary

End point timeframe:

Baseline (Week 52) and Week 104

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: percentage of predicted normal				
least squares mean (standard error)	()	()		

Notes:

[5] - Data was not collected as the study was terminated early.

[6] - Data was not collected as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: OLP: Change From Baseline in Muscle Strength at Week 104

End point title	OLP: Change From Baseline in Muscle Strength at Week 104

End point description:

Muscle strength was planned to be measured using HHD and assessed the following muscles: first dorsal interosseous, wrist extension, elbow extension, elbow flexion, shoulder flexion, knee extension, knee flexion, and ankle dorsiflexion, on both sides of the body. Baseline was defined as the last available, non-missing observation prior to first study drug administration. Analysis was planned to be performed on the ITT population. Data was not collected as the study was terminated early.

End point type	Secondary

End point timeframe:

Baseline (Week 52) and Week 104

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	0[8]		
Units: pounds				
least squares mean (standard error)	()	()		

Notes:

[7] - Data was not collected as the study was terminated early.

[8] - Data was not collected as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: OLP: Number of Subjects With an Event of Death or Permanent Tracheostomy or Permanent Assisted Ventilation at Week 104

End point title	OLP: Number of Subjects With an Event of Death or Permanent Tracheostomy or Permanent Assisted Ventilation at Week 104

End point description:

Subjects with an event of death are reported. Subjects were planned to be assessed for permanent tracheostomy or permanent assisted ventilation) in OLP; however, that data was not collected as study was terminated early. Analysis was performed on the ITT population.

End point type	Secondary

End point timeframe:

Baseline (Week 52) and Week 104

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	50		
Units: subjects	10	6		

Statistical analyses

No statistical analyses for this end point

Secondary: OLP: Change From Baseline in ALS Assessment Questionnaire-40 at Week 104

End point title	OLP: Change From Baseline in ALS Assessment Questionnaire-40 at Week 104

End point description:

The ALSAQ-40 was a 40-item validated questionnaire designed to assess health related QoL over the previous 2 weeks in subjects with ALS. It represented 5 dimensions of health status; each scored from 0 (never, or best) to 4 (always, or worst). 5 dimensions evaluated were: physical mobility (10 items: 1-10; possible score of 0-40); activities of daily living/independence (10 items: 11-20; possible score of 0-40); eating and drinking (3 items: 21-23; possible score of 0-12); communication (7 items: 24-30; possible score: 0-28) and emotional functioning (10 items: 31-40; possible score: 0-40). The total score 0 (no impairment) to 160 (severe impairment) was planned to be calculated by adding the 5 dimension scores. Higher scores would have indicated worse QoL. Analysis was planned to be performed on the ITT population. Data was not collected as the study was terminated early.

End point type	Secondary

End point timeframe:

Baseline (Week 52) and Week 104

End point values	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: score on a scale				
least squares mean (standard error)	()	()		

Notes:

[9] - Data was not collected as the study was terminated early.

[10] - Data was not collected as the study was terminated early.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with an Event of Death During the Study

End point title	Number of Subjects with an Event of Death During the Study

End point description:

Total number of subjects who died in the study are reported. Analysis was performed on the ITT population.

End point type	Secondary

End point timeframe:

RTP: Baseline (Day 1) up to Week 52; OLP: Baseline (Week 52) up to Week 104

End point values	RTP: Pegcetacoplan	RTP: Placebo	OLP: Pegcetacoplan/ Pegcetacoplan	OLP: Placebo/Pegcetacoplan
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	169	80	97	50
Units: subjects	26	11	10	6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs, TESAEs and deaths were collected from first dose of study drug (RTP: Day 1/OLP: Week 52) up to 56 days post last dose of study drug, approximately 60 weeks each for RTP and OLP.

Adverse event reporting additional description:

RTP: Safety set included all subjects who received at least 1 dose of study treatment, pegcetacoplan or placebo. OLP: Safety set included only subjects who received at least 1 dose of the open-label treatment. RTP reporting groups: MedDRA 23.0.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	RTP: Pegcetacoplan

Reporting group description:

Subjects received pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.

Reporting group title	RTP: Placebo

Reporting group description:

Subjects received placebo matching pegcetacoplan as SC injection/infusion twice per week for 52 weeks.

Reporting group title	OLP: Pegcetacoplan/Pegcetacoplan

Reporting group description:

Eligible subjects who had received pegcetacoplan in RTP entered OLP and continued to receive pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.

Reporting group title	OLP: Placebo/Pegcetacoplan

Reporting group description:

Eligible subjects who had received placebo matching pegcetacoplan in RTP entered OLP to receive pegcetacoplan 1080 mg SC injection/infusion twice per week for 52 weeks.

Serious adverse events	RTP: Pegcetacoplan	RTP: Placebo	OLP: Pegcetacoplan/Pegcetacoplan
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 169 (33.73%)	27 / 80 (33.75%)	24 / 97 (24.74%)
number of deaths (all causes)	26	11	10
number of deaths resulting from adverse events	26	11	9
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic cancer			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Metastatic uterine cancer			

subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 169 (0.00%)	2 / 80 (2.50%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Gastrostomy			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory Failure			
subjects affected / exposed	13 / 169 (7.69%)	7 / 80 (8.75%)	4 / 97 (4.12%)
occurrences causally related to treatment / all	0 / 13	1 / 7	0 / 5
deaths causally related to treatment / all	0 / 9	0 / 4	0 / 1
Pneumonia aspiration			
subjects affected / exposed	7 / 169 (4.14%)	2 / 80 (2.50%)	4 / 97 (4.12%)
occurrences causally related to treatment / all	1 / 7	1 / 2	0 / 4
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 2
Dyspnoea			
subjects affected / exposed	5 / 169 (2.96%)	2 / 80 (2.50%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 169 (0.59%)	1 / 80 (1.25%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory disorder			
subjects affected / exposed	1 / 169 (0.59%)	1 / 80 (1.25%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute Respiratory Failure			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Hypoxia			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Obstructive airways disorder			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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 distress			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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 Symptom			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (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
Bronchial secretion retention			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Acute Stress Disorder			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (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
Confusional state			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			

Device dislocation			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight Decreased			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Humerus Fracture			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Head Injury			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (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
Ankle Fracture			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Cardiac disorders			
Pericarditis			

subjects affected / exposed	1 / 169 (0.59%)	1 / 80 (1.25%)	0 / 97 (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
Angina Pectoris			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Atrial Fibrillation			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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 Failure Acute			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardio-Respiratory Arrest			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Amyotrophic Lateral Sclerosis			
subjects affected / exposed	6 / 169 (3.55%)	3 / 80 (3.75%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 6	0 / 3	0 / 0
Headache			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Bulbar Palsy			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (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
Syncope			

subjects affected / exposed	0 / 169 (0.00%)	2 / 80 (2.50%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Optic Atrophy			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	3 / 169 (1.78%)	3 / 80 (3.75%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 169 (1.18%)	0 / 80 (0.00%)	0 / 97 (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
Diarrhoea			
subjects affected / exposed	2 / 169 (1.18%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Abdominal Pain			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Hepatitis			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Ischaemic skin ulcer			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	2 / 169 (1.18%)	0 / 80 (0.00%)	0 / 97 (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
Haematuria			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Renal Colic			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (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
Renal Failure			
subjects affected / exposed	0 / 169 (0.00%)	1 / 80 (1.25%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			

subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 169 (4.14%)	2 / 80 (2.50%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 169 (1.18%)	2 / 80 (2.50%)	2 / 97 (2.06%)
occurrences causally related to treatment / all	2 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
COVID-19 pneumonia			
subjects affected / exposed	2 / 169 (1.18%)	0 / 80 (0.00%)	0 / 97 (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
Urinary Tract Infection			
subjects affected / exposed	1 / 169 (0.59%)	1 / 80 (1.25%)	0 / 97 (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
Febrile infection			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Pneumonia moraxella			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			

subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Sepsis			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	3 / 97 (3.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Stoma site infection			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
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 bacterial			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Urosepsis			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Nasopharyngitis			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Viral Rash			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	1 / 169 (0.59%)	0 / 80 (0.00%)	0 / 97 (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
Food refusal			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	0 / 97 (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
Dehydration			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLP: Placebo/Pegcetacoplan		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 50 (28.00%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	6		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic cancer			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastatic uterine cancer			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrostomy			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory Failure			

subjects affected / exposed	3 / 50 (6.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Pneumonia aspiration				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Dyspnoea				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory disorder				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute Respiratory Failure				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive airways disorder				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				

subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sleep Apnoea Syndrome				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Symptom				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial secretion retention				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Acute Stress Disorder				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device dislocation				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				

Weight Decreased			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus Fracture			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head Injury			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle Fracture			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Craniocerebral injury			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina Pectoris			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Atrial Fibrillation				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac Failure Acute				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-Respiratory Arrest				
subjects affected / exposed	0 / 50 (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	2 / 50 (4.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Headache				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bulbar Palsy				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Optic Atrophy				
subjects affected / exposed	0 / 50 (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 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal Pain			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders			
Ischaemic skin ulcer			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Colic			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Failure			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia moraxella				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 50 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stoma site infection			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral Rash			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food refusal			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dehydration			

subjects affected / exposed	0 / 50 (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	RTP: Pegcetacoplan	RTP: Placebo	OLP: Pegcetacoplan/Pegcetacoplan
Total subjects affected by non-serious adverse events			
subjects affected / exposed	124 / 169 (73.37%)	55 / 80 (68.75%)	31 / 97 (31.96%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	37 / 169 (21.89%)	14 / 80 (17.50%)	6 / 97 (6.19%)
occurrences (all)	57	23	10
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 169 (1.78%)	5 / 80 (6.25%)	1 / 97 (1.03%)
occurrences (all)	3	5	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	12 / 169 (7.10%)	7 / 80 (8.75%)	5 / 97 (5.15%)
occurrences (all)	12	7	5
Diarrhoea			
subjects affected / exposed	10 / 169 (5.92%)	5 / 80 (6.25%)	0 / 97 (0.00%)
occurrences (all)	10	5	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 169 (4.14%)	5 / 80 (6.25%)	0 / 97 (0.00%)
occurrences (all)	7	5	0
Pneumonia aspiration			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	2 / 97 (2.06%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 169 (4.73%)	5 / 80 (6.25%)	0 / 97 (0.00%)
occurrences (all)	8	5	0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	28 / 169 (16.57%)	13 / 80 (16.25%)	6 / 97 (6.19%)
occurrences (all)	28	14	6
Nasopharyngitis			
subjects affected / exposed	10 / 169 (5.92%)	4 / 80 (5.00%)	0 / 97 (0.00%)
occurrences (all)	12	4	0
Upper respiratory tract infection			
subjects affected / exposed	10 / 169 (5.92%)	4 / 80 (5.00%)	5 / 97 (5.15%)
occurrences (all)	13	4	5
Urinary tract infection			
subjects affected / exposed	6 / 169 (3.55%)	5 / 80 (6.25%)	1 / 97 (1.03%)
occurrences (all)	7	5	1
Pneumonia			
subjects affected / exposed	0 / 169 (0.00%)	0 / 80 (0.00%)	4 / 97 (4.12%)
occurrences (all)	0	0	4

Non-serious adverse events	OLP: Placebo/Pegcetacoplan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 50 (40.00%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		

Diarrhoea			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Pneumonia aspiration			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	4		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Pneumonia			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2020	Added an exploratory endpoint and associated language. Updated the exclusion criteria and language in the immunogenicity section. Added benefit/risk information and Coronavirus Disease 2019 (COVID-19) risk mitigation measures. Removed interim analysis and analysis information related to population pharmacokinetic and exposure-response modeling.
25 June 2020	Updated information related to serious adverse events and pregnancy. Added a new section to describe drug abuse, misuse, overdose, and medication error.
27 July 2020	The language regarding use of riluzole and edaravone was updated to allow for dose alterations or discontinuation should the investigator have any safety concerns. Added a new section for COVID-19 testing. Updated the information regarding adverse events, disease progression and pregnancy.
05 April 2021	Clarified the language regarding subject transition to the open-label portion of the study. Updated exclusion criteria. Language updated for: time period for resting prior to ECG and pregnancy testing, the definitions of AEs and SAEs for clarity, the relationships to study drug and to reflect that the mITT set will be used for the primary efficacy analysis of CAFS. Added a new section for Severity of Event. Additional details added regarding the ethical conduct of the study to incorporate national laws and regulation.
09 February 2022	Modified secondary and exploratory endpoints. Language was added to provide guidance in the event that direct-to-subject shipment is required during the course of the study, where approved. The at-home assessment of SVC was changed to an exploratory endpoint.
04 January 2023	Added an open-label long-term extension period. Updated a few exploratory endpoints. Clarified that long-term extension was no longer planned, it will be Part 4 of the study. Updated the exclusion criteria, blinding description and statistical methodology for the secondary efficacy endpoints. Added the newly approved medication (Relyvrio) for the treatment of ALS. Updated the language regarding vaccinations to provide further clarity and regarding anti-pegcetacoplan peptide antibody and anti-polyethylene glycol antibody collection.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early, during the OLP, due to lack of efficacy as determined by the Week 52 data and no safety concerns.

Notes: