Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Safety and Efficacy of Ravulizumab in Complement-Inhibitor-Naïve Adult Patients With Generalized Myasthenia Gravis

Summary

EudraCT number	2018-003243-39
Trial protocol	DE AT NL DK ES FR CZ GB PT IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	03 June 2022
First version publication date	03 June 2022

Trial information

Trial identification

Sponsor protocol code	ALXN1210-MG-306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03920293
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Inc.
Sponsor organisation address	100 College Street, New Haven, CT, United States, 06510
Public contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals Inc., +33 7 87148158, clinicaltrials.eu@alexion.com
Scientific contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals Inc., +33 7 87148158, clinicaltrials.eu@alexion.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	30 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this study is to evaluate the safety and efficacy of ravulizumab for the treatment of participants with generalized myasthenia gravis (gMG).

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:
• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
• Applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines
• Applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Czechia: 8
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United States: 74
Worldwide total number of subjects	175
EEA total number of subjects	60

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)	115
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized 1:1 to either the ravulizumab or placebo group during the Randomized-Controlled Period. Following the placebo-controlled part of the study, participants were transitioned to the ongoing Open-Label Extension Period to receive treatment with ravulizumab.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomized-Controlled Period: Ravulizumab

Arm description:

Participants received a weight-based single loading dose (2400 to 3000 milligrams [mg]) of ravulizumab intravenously (IV) on Day 1, followed by regular maintenance IV weight-based doses (3000 to 3600 mg) of ravulizumab beginning on Day 15 once every 8 weeks (q8w), during the 26-week Randomized-Controlled Period of the study.

Arm type	Experimental
Investigational medicinal product name	Ravulizumab
Investigational medicinal product code	
Other name	ALXN1210 Ultomiris
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received ravulizumab at prespecified dose and timepoints.

Arm title	Randomized-Controlled Period: Placebo

Arm description:

Participants received a weight-based single loading dose of placebo IV on Day 1, followed by regular maintenance IV weight-based doses of placebo beginning on Day 15 q8w, during the 26-week Randomized-Controlled Period of the study.

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

Dosage and administration details:

Participants received placebo at prespecified dose and timepoints.

Number of subjects in period 1	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo
Started	86	89
Received at Least 1 Dose of Study Drug	86	89
Completed	79	83
Not completed	7	6
Adverse event, serious fatal	2	-
Consent withdrawn by subject	2	1
Physician decision	1	2
Adverse event, non-fatal	-	2
Sponsor Decision	-	1
Protocol deviation	1	-
Noncompliance	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Randomized-Controlled Period: Ravulizumab
Reporting group description:	
Participants received a weight-based single loading dose (2400 to 3000 milligrams [mg]) of ravulizumab intravenously (IV) on Day 1, followed by regular maintenance IV weight-based doses (3000 to 3600 mg) of ravulizumab beginning on Day 15 once every 8 weeks (q8w), during the 26-week Randomized-Controlled Period of the study.	
Reporting group title	Randomized-Controlled Period: Placebo
Reporting group description:	
Participants received a weight-based single loading dose of placebo IV on Day 1, followed by regular maintenance IV weight-based doses of placebo beginning on Day 15 q8w, during the 26-week Randomized-Controlled Period of the study.	

Reporting group values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo	Total
Number of subjects	86	89	175
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	58.0	53.3	
standard deviation	± 13.82	± 16.05	-
Sex: Female, Male Units: participants			
Female	44	45	89
Male	42	44	86
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	5	7
Not Hispanic or Latino	79	78	157
Unknown or Not Reported	5	6	11
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	15	16	31
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	4	6

White	67	61	128
Other	0	1	1
Unknown or Not Reported	2	6	8

End points

End points reporting groups

Reporting group title	Randomized-Controlled Period: Ravulizumab
Reporting group description:	
Participants received a weight-based single loading dose (2400 to 3000 milligrams [mg]) of ravulizumab intravenously (IV) on Day 1, followed by regular maintenance IV weight-based doses (3000 to 3600 mg) of ravulizumab beginning on Day 15 once every 8 weeks (q8w), during the 26-week Randomized-Controlled Period of the study.	
Reporting group title	Randomized-Controlled Period: Placebo
Reporting group description:	
Participants received a weight-based single loading dose of placebo IV on Day 1, followed by regular maintenance IV weight-based doses of placebo beginning on Day 15 q8w, during the 26-week Randomized-Controlled Period of the study.	

Primary: Change From Baseline In Myasthenia Gravis-Activities Of Daily Living (MG-ADL) Total Score At Week 26

End point title	Change From Baseline In Myasthenia Gravis-Activities Of Daily Living (MG-ADL) Total Score At Week 26
End point description:	
MG-ADL: 8-point questionnaire focusing on relevant symptoms/functional performance of activities of daily living in participants with MG. The 8 items of MGADL questionnaire derived from symptom-based components of original 13-item QMG scale to assess disability secondary to ocular (2 items), bulbar (3 items), respiratory (1 item), and gross motor or limb (2 items) impairment related to effects from MG. In this functional status instrument, each response was graded 0 (normal)-3 (most severe). Range of total MG-ADL score: 0-24. Decrease in score indicated improvement. Estimates based on MMRM that included treatment group, stratification factor region, and MG-ADL total score at baseline, study visit, and study visit by treatment group interaction. Full Analysis Set: All randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline, Week 26	

End point values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	89		
Units: units on a scale				
least squares mean (standard error)	-3.1 (± 0.38)	-1.4 (± 0.37)		

Statistical analyses

Statistical analysis title	Ravulizumab versus Placebo
Comparison groups	Randomized-Controlled Period: Ravulizumab v Randomized-Controlled Period: Placebo

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0009 [1]
Method	MMRM
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[1] - Statistical significance was tested at α=0.05.

Secondary: Change From Baseline In The Quantitative Myasthenia Gravis (QMG) Total Score At Week 26

End point title	Change From Baseline In The Quantitative Myasthenia Gravis (QMG) Total Score At Week 26

End point description:

The QMG scoring system consisted of 13 items: ocular (2 items), facial (1 item), bulbar (2 items), gross motor (6 items), axial (1 item), and respiratory (1 item); each graded 0 to 3, with 3 being the most severe. The range of total QMG score is 0 to 39. The QMG scoring system was considered to be an objective evaluation of therapy for MG and was based on quantitative testing of sentinel muscle groups. A decrease in score indicated improvement. Estimates were based on MMRM that included treatment group, stratification factor region, and QMG total score at baseline, study visit, and study visit by treatment group interaction. Full Analysis Set: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	89		
Units: units on a scale				
least squares mean (standard error)	-2.8 (± 0.46)	-0.8 (± 0.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Quantitative Myasthenia Gravis (QMG) Total Score Reduction of at Least 5 Points At Week 26

End point title	Percentage of Participants With a Quantitative Myasthenia Gravis (QMG) Total Score Reduction of at Least 5 Points At Week 26

End point description:

The QMG scoring system consisted of 13 items: ocular (2 items), facial (1 item), bulbar (2 items), gross motor (6 items), axial (1 item), and respiratory (1 item); each graded 0 to 3, with 3 being the most severe. The range of total QMG score is 0 to 39. A decrease in score indicated improvement. Percentage of participants with a ≥5-point reduction in the QMG total score are reported. Estimates were based on a generalized linear mixed model (GLMM) that included treatment group, stratification factor region and QMG total score at baseline, study visit and study visit by treatment group interaction. Full Analysis Set: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

End point values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	89		
Units: percentage of participants				
number (confidence interval 95%)	30.0 (19.2 to 43.5)	11.3 (5.6 to 21.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In the Revised 15 Component Myasthenia Gravis Quality of Life (MG-QOL15r) At Week 26

End point title	Change From Baseline In the Revised 15 Component Myasthenia Gravis Quality of Life (MG-QOL15r) At Week 26

End point description:

The revised Myasthenia Gravis Qualify of Life 15-item scale (MG-QOL15r) is a health-related QoL evaluative instrument specific to participants with MG. MG-QOL15r was designed to provide information about participants' perception of impairment and disability, determine the degree to which disease manifestations are tolerated, and to be administered and interpreted easily. Each item was graded on a scale of 0 to 2, with 2 being the most severe. The range of MG-QOL15r score is 0 to 30. Higher scores indicated greater extent of and dissatisfaction with MG-related dysfunction. Estimates are based on MMRM that included treatment group, stratification factor region and MG-QOL15r score at baseline, study visit and study visit by treatment group interaction. Full Analysis Set: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	89		
Units: score on a scale				
least squares mean (standard error)	-3.3 (± 0.71)	-1.6 (± 0.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Neurological Quality of Life (Neuro-QoL) Fatigue Score at Week 26

End point title	Change from Baseline in Neurological Quality of Life (Neuro-QoL) Fatigue Score at Week 26

End point description:

The Neuro-QOL Fatigue is a reliable and validated brief 19-item survey of fatigue, completed by the participant. Each items was rated on a scale of 1 to 5, with 5 being the most severe. The range of total score is 19 to 95. Higher scores indicated greater fatigue and greater impact of MG on activities. Estimates were based on MMRM that included treatment group, stratification factor region and Neuro-QoL Fatigue score at baseline, study visit, and study visit by treatment group interaction. Full Analysis Set: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	89		
Units: units on a scale				
least squares mean (standard error)	-7.0 (± 1.92)	-4.8 (± 1.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Myasthenia Gravis Activities of Daily Living (MG-ADL) Total Score Reduction of at Least 3 Points At Week 26

End point title	Percentage of Participants with a Myasthenia Gravis Activities of Daily Living (MG-ADL) Total Score Reduction of at Least 3 Points At Week 26

End point description:

MG-ADL is an 8-point questionnaire that focused on relevant symptoms and functional performance of

activities of daily living in participants with MG. The 8 items of the MGADL questionnaire derived from symptom-based components of the original 13-item QMG scale to assess disability secondary to ocular (2 items), bulbar (3 items), respiratory (1 item), and gross motor or limb (2 items) impairment related to effects from MG. In this functional status instrument, each response was graded 0 (normal)-3 (most severe). Range of total MG-ADL score was 0-24. A decrease in score indicated improvement. Percentage of participants with a ≥3-point reduction in the MG-ADL total score are reported. Estimates based on a GLMM that included treatment group, stratification factor region and MG-ADL total score at baseline, study visit and study visit by treatment group interaction. Full Analysis Set: All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

End point values	Randomized-Controlled Period: Ravulizumab	Randomized-Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	89		
Units: percentage of participants				
number (confidence interval 95%)	56.7 (44.3 to 68.3)	34.1 (23.8 to 46.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (after dosing) through Week 26

Adverse event reporting additional description:

Treatment-emergent adverse events reported during the 26-week randomized-controlled period of the study are presented. The Open-Label Extension Period is ongoing, and results will be presented when the study is completed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Randomized-Controlled Period: Placebo

Reporting group description:

Participants received a weight-based single loading dose of placebo IV on Day 1, followed by regular maintenance IV weight-based doses of placebo beginning on Day 15 q8w, during the 26-week Randomized-Controlled Period of the study.

Following the placebo-controlled part of the study, participants were transitioned to the ongoing Open-Label Extension Period to receive treatment with ravulizumab.

Reporting group title	Randomized-Controlled Period: Ravulizumab

Reporting group description:

Participants received a weight-based single loading dose (2400 to 3000 mg) of ravulizumab IV on Day 1, followed by regular maintenance IV weight-based doses (3000 to 3600 mg) of ravulizumab beginning on Day 15 q8w during the 26-week Randomized-Controlled Period of the study.

Following the placebo-controlled part of the study, participants were transitioned to the ongoing Open-Label Extension Period to receive treatment with ravulizumab.

Serious adverse events	Randomized-Controlled Period: Placebo	Randomized-Controlled Period: Ravulizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 89 (15.73%)	20 / 86 (23.26%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral neoplasm			

subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			

subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion-related reaction			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Congestive cardiomyopathy			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 89 (0.00%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myasthenia gravis crisis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Facial paresis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	3 / 89 (3.37%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Granuloma skin			

subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal osteoarthritis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 89 (0.00%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	

Arthritis bacterial			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 89 (2.25%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Steroid diabetes			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Randomized-Controlled Period: Placebo	Randomized-Controlled Period: Ravulizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 89 (84.27%)	77 / 86 (89.53%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 89 (3.37%)	8 / 86 (9.30%)	
occurrences (all)	3	9	
Headache			
subjects affected / exposed	23 / 89 (25.84%)	16 / 86 (18.60%)	
occurrences (all)	27	19	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 89 (5.62%)	1 / 86 (1.16%)	
occurrences (all)	6	1	
Fatigue			

subjects affected / exposed	6 / 89 (6.74%)	6 / 86 (6.98%)	
occurrences (all)	6	7	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 89 (12.36%)	13 / 86 (15.12%)	
occurrences (all)	15	14	
Abdominal pain			
subjects affected / exposed	0 / 89 (0.00%)	5 / 86 (5.81%)	
occurrences (all)	0	6	
Nausea			
subjects affected / exposed	9 / 89 (10.11%)	9 / 86 (10.47%)	
occurrences (all)	10	12	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 89 (5.62%)	7 / 86 (8.14%)	
occurrences (all)	5	7	
Arthralgia			
subjects affected / exposed	7 / 89 (7.87%)	6 / 86 (6.98%)	
occurrences (all)	8	8	
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 89 (3.37%)	5 / 86 (5.81%)	
occurrences (all)	3	5	
Urinary tract infection			
subjects affected / exposed	4 / 89 (4.49%)	5 / 86 (5.81%)	
occurrences (all)	5	7	
Nasopharyngitis			
subjects affected / exposed	5 / 89 (5.62%)	3 / 86 (3.49%)	
occurrences (all)	7	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2018	The purpose of this amendment was to change duration of safety follow-up after last dose; add additional details on assessments, align pregnancy and clinical laboratory testing frequency with infusions; change supplemental dosing recommendations and sample collection when rescue therapy is provided; and update adverse event and pregnancy/contraception language.
25 October 2019	The purpose of this amendment was to revise secondary and exploratory endpoints, to decrease burden to participants by reduction in assessment and visit frequency, to provide additional guidance for supplemental dosing, and to clarify minor operational aspects of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported