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	v2 (current)
This version publication date	12 May 2024
First version publication date	03 June 2022
Version creation reason	

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	Randomized-Controlled Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

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	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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

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	Ravulizumab	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	-

Period 2

Period 2 title	Open- Label Extension Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ravulizumab to 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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

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	Placebo to Ravulizumab

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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

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 2[1]	Ravulizumab to Ravulizumab	Placebo to Ravulizumab
Started	78	83
Completed	60	63
Not completed	18	20
Consent withdrawn by subject	7	9
Physician decision	5	3
Subjects transitioned to other t/t by Investigator	3	5
Death	3	3

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: 1 participant in the Ravulizumab group withdrew from the study and did not enter the open label extension period.

Baseline characteristics

Reporting groups	
Reporting group title	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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.	
Reporting group title	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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.	

Reporting group values	Ravulizumab	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	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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

Reporting group title	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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

Reporting group title	Ravulizumab to 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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

Reporting group title	Placebo to Ravulizumab

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. After the randomized-controlled part of the study, participants were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

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	Ravulizumab	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	Ravulizumab v 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	Ravulizumab	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	Ravulizumab	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	Ravulizumab	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	Ravulizumab	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	Ravulizumab	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) up to 2 years

Adverse event reporting additional description:

Treatment-emergent adverse events were reported for 26-week randomized-controlled period and open-label extension period separately.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

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.

Reporting group title	Open-Label Extension Period: Placebo to Ravulizumab

Reporting group description:

After the randomized-controlled part of the study, participants in the placebo group were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

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	Open-Label Extension Period: Ravulizumab to Ravulizumab

Reporting group description:

After the randomized-controlled part of the study, participants in the ravulizumab group were transitioned to the ongoing open-label extension period to receive treatment with ravulizumab IV for up to 2 years.

Serious adverse events	Randomized-Controlled Period: Ravulizumab	Open-Label Extension Period: Placebo to Ravulizumab	Randomized-Controlled Period: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 86 (23.26%)	32 / 83 (38.55%)	14 / 89 (15.73%)
number of deaths (all causes)	2	3	0
number of deaths resulting from adverse events	2	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ureteral neoplasm			

subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Malignant melanoma			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Breast cancer			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pancreatic cystadenoma			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Vascular disorders			
Vein rupture			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Hypotension			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Deep vein thrombosis			

subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
General physical health deterioration			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Fatigue			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Death			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Chest pain			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pyrexia			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			

Uterine prolapse			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Lung infiltration			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Dyspnoea exertional			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pleural effusion			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pulmonary embolism			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Psychiatric disorders			
Suicide attempt			

subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Anxiety			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Acute psychosis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Depression			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Panic attack			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Infusion-related reaction			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fall			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Spinal compression fracture			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Head injury			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Post procedural complication			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Toxicity to various agents			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic fracture			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Cardiac disorders			

Congestive cardiomyopathy			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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 failure congestive			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Angina pectoris			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Myocardial infarction			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Mitral valve stenosis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Coronary artery disease			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Angina unstable			

subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Prinzmetal angina			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Myasthenia gravis crisis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Transient ischaemic attack			
subjects affected / exposed	2 / 86 (2.33%)	0 / 83 (0.00%)	0 / 89 (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
Syncope			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Trigeminal neuralgia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	3 / 89 (3.37%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			

subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Dysarthria			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Headache			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Intercostal neuralgia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Cataract			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Enteritis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 86 (1.16%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Pancreatitis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Gastric polyps			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Abdominal pain			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Small intestinal obstruction			

subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pancreatitis acute			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Skin and subcutaneous tissue disorders			
Granuloma skin			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
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 failure			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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

Acute kidney injury			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 86 (1.16%)	1 / 83 (1.20%)	0 / 89 (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
Spinal stenosis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendonitis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Nodal osteoarthritis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Muscular weakness			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Neck pain			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Neuropathic arthropathy			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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

Osteoarthritis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Synovitis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Arthralgia			
subjects affected / exposed	0 / 86 (0.00%)	9 / 83 (10.84%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 15	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Myalgia			
subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 86 (0.00%)	10 / 83 (12.05%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasms			

subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Gangrene			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
COVID-19 pneumonia			
subjects affected / exposed	2 / 86 (2.33%)	2 / 83 (2.41%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Diverticulitis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
COVID-19			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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 respiratory syncytial viral			

subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Infected skin ulcer			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Cellulitis			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	2 / 89 (2.25%)
occurrences causally related to treatment / all	0 / 0	1 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Anal abscess			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			

subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Neisseria infection			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Infection			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Gonococcal infection			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pneumonia viral			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Pyelonephritis			

subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Sepsis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Suspected COVID-19			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Influenza			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Metabolism and nutrition disorders			
Steroid diabetes			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (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
Diabetic ketoacidosis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (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
Electrolyte imbalance			

subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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
Hypercalcaemia			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (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

Serious adverse events	Open-Label Extension Period: Ravulizumab to Ravulizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 78 (30.77%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ureteral neoplasm			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic cystadenoma				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Vein rupture				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Fatigue				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Chest pain				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Uterine prolapse				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infiltration				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Suicide attempt				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute psychosis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Panic attack				

subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion-related reaction			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Lumbar vertebral fracture				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural complication				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic fracture				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Congestive cardiomyopathy				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mitral valve stenosis				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery occlusion				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prinzmetal angina				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Myasthenia gravis crisis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Trigeminal neuralgia				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myasthenia gravis				
subjects affected / exposed	4 / 78 (5.13%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Facial paresis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysarthria				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intercostal neuralgia				

subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pancreatitis			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestinal obstruction			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric polyps			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Granuloma skin			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Urticaria				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Nephrotic syndrome				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal stenosis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendonitis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Nodal osteoarthritis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuropathic arthropathy				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	11 / 78 (14.10%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 0			
Tenosynovitis				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	4 / 78 (5.13%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	6 / 78 (7.69%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	6 / 78 (7.69%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Muscle spasms				
subjects affected / exposed	2 / 78 (2.56%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Gastroenteritis viral				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	0 / 78 (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 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	4 / 78 (5.13%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected skin ulcer				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neisseria infection				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gonococcal infection				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suspected COVID-19				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Steroid diabetes				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus inadequate control				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrolyte imbalance				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 78 (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	Randomized-Controlled Period: Ravulizumab	Open-Label Extension Period: Placebo to Ravulizumab	Randomized-Controlled Period: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 86 (89.53%)	79 / 83 (95.18%)	75 / 89 (84.27%)
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 86 (0.00%)	10 / 83 (12.05%)	0 / 89 (0.00%)
occurrences (all)	0	11	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences (all)	0	7	0
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 86 (18.60%)	17 / 83 (20.48%)	23 / 89 (25.84%)
occurrences (all)	19	21	27
Dizziness			
subjects affected / exposed	8 / 86 (9.30%)	6 / 83 (7.23%)	3 / 89 (3.37%)
occurrences (all)	9	10	3
Myasthenia gravis			
subjects affected / exposed	0 / 86 (0.00%)	3 / 83 (3.61%)	0 / 89 (0.00%)
occurrences (all)	0	3	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 86 (6.98%)	1 / 83 (1.20%)	6 / 89 (6.74%)
occurrences (all)	7	1	6
Pyrexia			
subjects affected / exposed	1 / 86 (1.16%)	2 / 83 (2.41%)	5 / 89 (5.62%)
occurrences (all)	1	2	6
General physical health deterioration			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 86 (1.16%)	0 / 83 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Death			

subjects affected / exposed	0 / 86 (0.00%)	0 / 83 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 86 (10.47%)	9 / 83 (10.84%)	9 / 89 (10.11%)
occurrences (all)	12	18	10
Abdominal pain			
subjects affected / exposed	5 / 86 (5.81%)	4 / 83 (4.82%)	0 / 89 (0.00%)
occurrences (all)	6	5	0
Diarrhoea			
subjects affected / exposed	13 / 86 (15.12%)	10 / 83 (12.05%)	11 / 89 (12.36%)
occurrences (all)	14	12	15
Vomiting			
subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences (all)	0	5	0
Abdominal pain upper			
subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences (all)	0	5	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 86 (0.00%)	6 / 83 (7.23%)	0 / 89 (0.00%)
occurrences (all)	0	6	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 86 (0.00%)	1 / 83 (1.20%)	0 / 89 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 86 (0.00%)	7 / 83 (8.43%)	0 / 89 (0.00%)
occurrences (all)	0	8	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 86 (6.98%)	9 / 83 (10.84%)	7 / 89 (7.87%)
occurrences (all)	8	15	8
Back pain			

subjects affected / exposed	7 / 86 (8.14%)	10 / 83 (12.05%)	5 / 89 (5.62%)
occurrences (all)	7	10	5
Myalgia			
subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences (all)	0	5	0
Pain in extremity			
subjects affected / exposed	0 / 86 (0.00%)	2 / 83 (2.41%)	0 / 89 (0.00%)
occurrences (all)	0	2	0
Muscle spasms			
subjects affected / exposed	0 / 86 (0.00%)	5 / 83 (6.02%)	0 / 89 (0.00%)
occurrences (all)	0	5	0
Infections and infestations			
COVID-19			
subjects affected / exposed	5 / 86 (5.81%)	26 / 83 (31.33%)	3 / 89 (3.37%)
occurrences (all)	5	28	3
Urinary tract infection			
subjects affected / exposed	5 / 86 (5.81%)	8 / 83 (9.64%)	4 / 89 (4.49%)
occurrences (all)	7	13	5
Nasopharyngitis			
subjects affected / exposed	3 / 86 (3.49%)	11 / 83 (13.25%)	5 / 89 (5.62%)
occurrences (all)	3	18	7
Bronchitis			
subjects affected / exposed	0 / 86 (0.00%)	4 / 83 (4.82%)	0 / 89 (0.00%)
occurrences (all)	0	4	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 86 (0.00%)	9 / 83 (10.84%)	0 / 89 (0.00%)
occurrences (all)	0	9	0

Non-serious adverse events	Open-Label Extension Period: Ravulizumab to Ravulizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 78 (98.72%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	3		

Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 3 / 78 (3.85%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Myasthenia gravis subjects affected / exposed occurrences (all)	 12 / 78 (15.38%) 19 4 / 78 (5.13%) 5 4 / 78 (5.13%) 6		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) General physical health deterioration subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Non-cardiac chest pain subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Death subjects affected / exposed occurrences (all)	 0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 1 / 78 (1.28%) 1 1 / 78 (1.28%) 1		

Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all)	 7 / 78 (8.97%) 8 4 / 78 (5.13%) 4 6 / 78 (7.69%) 6 1 / 78 (1.28%) 2 0 / 78 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 4 / 78 (5.13%) 4		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 4 / 78 (5.13%) 7		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	 4 / 78 (5.13%) 4		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Myalgia	 11 / 78 (14.10%) 14 6 / 78 (7.69%) 6		

subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
Infections and infestations			
COVID-19			
subjects affected / exposed	30 / 78 (38.46%)		
occurrences (all)	32		
Urinary tract infection			
subjects affected / exposed	7 / 78 (8.97%)		
occurrences (all)	9		
Nasopharyngitis			
subjects affected / exposed	8 / 78 (10.26%)		
occurrences (all)	10		
Bronchitis			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
Upper respiratory tract infection			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	4		

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