



Clinical trial results:

A Phase 3, Double-Blind, Randomized, Placebo-Controlled, Parallel Group, Multicenter Study With an Open-Label Extension to Evaluate the Efficacy and Safety of Ravulizumab in Patients With Amyotrophic Lateral Sclerosis (ALS)

Summary

EudraCT number	2019-004619-30
Trial protocol	IE SE GB DE DK ES NL BE FR IT
Global end of trial date	17 October 2021

Results information

Result version number	v1
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	ALXN1210-ALS-308
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04248465
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 787148158, clinicaltrials.eu@alexion.com
Scientific contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals Inc., +33 787148158, clinicaltrials.eu@alexion.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2021
Global end of trial reached?	Yes
Global end of trial date	17 October 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of ravulizumab compared with placebo on amyotrophic lateral sclerosis functional rating scale-revised (ALSFRS-R) score in adult participants with amyotrophic lateral sclerosis (ALS)

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 March 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 22
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 51
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	Sweden: 17
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Japan: 26
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 70
Worldwide total number of subjects	382
EEA total number of subjects	221

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)	267
From 65 to 84 years	114
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted from 30 Mar 2020 to 17 Oct 2021.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	Ravulizumab/Ravulizumab
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Arm description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then once every 8 weeks (q8w) up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 milligrams (mg) dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

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

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

Arm title	Placebo/Ravulizumab
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Arm description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

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 matched to ravulizumab at prespecified dose and timepoints.

Number of subjects in period 1	Ravulizumab/Ravulizumab	Placebo/Ravulizumab
Started	255	127
Received at least 1 dose of study drug	255	127
Completed	15	5
Not completed	240	122
Adverse event, serious fatal	12	5
Consent withdrawn by subject	30	17
Physician decision	1	1
Adverse event, non-fatal	2	-
Study Terminated by Sponsor	194	99
Lost to follow-up	1	-

Period 2

Period 2 title	Open-label Extension Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ravulizumab/Ravulizumab

Arm description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then once every 8 weeks (q8w) up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 milligrams (mg) dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

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

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

Arm title	Placebo/Ravulizumab
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Arm description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

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

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

Number of subjects in period 2 ^[1]	Ravulizumab/Ravulizumab	Placebo/Ravulizumab
	Started	14
Received at Least 1 Dose of Study Drug	14	5
Completed	0	0
Not completed	14	5
Consent withdrawn by subject	-	1
Study Terminated by Sponsor	14	4

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 Subject discontinued the study from Ravulizumab arm prior to entering the Open Label Extension Period.

Baseline characteristics

Reporting groups

Reporting group title	Ravulizumab/Ravulizumab
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Reporting group description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then once every 8 weeks (q8w) up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 milligrams (mg) dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group title	Placebo/Ravulizumab
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Reporting group description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group values	Ravulizumab/Ravulizumab	Placebo/Ravulizumab	Total
Number of subjects	255	127	382
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	58.6 ± 10.57	58.0 ± 11.03	-
Sex: Female, Male Units: participants			
Female	94	58	152
Male	161	69	230

Subject analysis sets

Subject analysis set title	Ravulizumab
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then, during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 mg dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Subject analysis set title	Placebo
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group values	Ravulizumab	Placebo	
Number of subjects	255	127	
Age categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	58.6 ± 10.57	58.0 ± 11.03	
Sex: Female, Male Units: participants			
Female	94	58	
Male	161	69	

End points

End points reporting groups

Reporting group title	Ravulizumab/Ravulizumab
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Reporting group description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then once every 8 weeks (q8w) up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 milligrams (mg) dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group title	Placebo/Ravulizumab
-----------------------	---------------------

Reporting group description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group title	Ravulizumab/Ravulizumab
-----------------------	-------------------------

Reporting group description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then once every 8 weeks (q8w) up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 milligrams (mg) dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group title	Placebo/Ravulizumab
-----------------------	---------------------

Reporting group description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Subject analysis set title	Ravulizumab
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then, during the Open Label Extension Period, participants received ravulizumab, with a blinded 900 mg dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Subject analysis set title	Placebo
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Subject analysis set type	Full analysis
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Subject analysis set description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive) during the Randomized Controlled Period. Then during the Open Label Extension Period, participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Primary: Change From Baseline In Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) Total Score

End point title	Change From Baseline In Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) Total Score ^[1]
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End point description:

The ALSFRS-Revised is a validated instrument for evaluating the levels of the functional status of participants with amyotrophic lateral sclerosis (ALS) in 4 areas, including bulbar, gross motor activity, fine motor activity, and respiratory functions. The scale included 12 functional items and each item is rated on a 0 to 4 scale, with a maximum total score of 48. A higher score indicated greater retention of function. Baseline was defined as last non-missing value on or before first study drug administration. Full analysis set (FAS) included all randomized participants who received at least 1 dose of study drug

grouped by randomized treatment group. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure.

End point type	Primary
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End point timeframe:

Baseline, Week 50

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned to be reported for this endpoint.

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	14		
Units: units on a scale				
arithmetic mean (standard deviation)	-11.9 (± 7.30)	-10.6 (± 6.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Ventilator Assistance-free Survival

End point title	Time To Ventilator Assistance-free Survival
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End point description:

Ventilation Assistance-Free Survival (VAFS) is a composite endpoint of survival and severe and irreversible respiratory decline. The use of VAFS allowed for the collection of survival data that was not impacted by survival prolongation from noninvasive or permanent ventilatory interventions which could prolong life without impacting underlying disease progression. FAS included all randomized participants who received at least 1 dose of study drug grouped by randomized treatment group.

End point type	Secondary
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End point timeframe:

Up to Week 50

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	255	127		
Units: months				
median (full range (min-max))	6.05 (0.79 to 11.10)	7.69 (4.83 to 9.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Slow Vital Capacity

End point title	Change From Baseline In Slow Vital Capacity
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End point description:

Slow vital capacity is a spirometry technique that utilizes slow and gradual expulsion of air from the lungs. The full volume of expired air was measured as a proportion of the expected vital capacity of the participant based on biometric features such as age, height, and sex. FAS included all randomized participants who received at least 1 dose of study drug grouped by randomized treatment group. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure.

End point type Secondary

End point timeframe:

Baseline, Week 50

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	9		
Units: units on a scale				
arithmetic mean (standard deviation)	-20.9 (\pm 19.74)	-21.3 (\pm 13.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Events, and TEAEs Leading To Study Drug Discontinuation

End point title Number of Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Events, and TEAEs Leading To Study Drug Discontinuation

End point description:

An adverse event (AE) was defined as any unfavorable and unintended sign (for example, including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or procedure, whether or not considered related to the medicinal product or procedure, which occurred during the course of the clinical study. TEAEs were defined as AEs that occurred on or after the date and time of study drug administration, or those that first occurred before dosing but worsened in frequency or severity after study drug administration. A summary of all Serious Adverse Events and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety Set included all participants who received at least 1 dose of study drug grouped by treatment actually received (for reporting exposure and safety data).

End point type Secondary

End point timeframe:

Baseline up to Day 351

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	255	127		
Units: participants				
TEAEs	204	108		
Treatment Emergent Serious AEs	41	24		
TEAE Leading to Study Drug Discontinuation	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Muscle Strength As Assessed By Handheld Dynamometry

End point title	Change From Baseline In Muscle Strength As Assessed By Handheld Dynamometry
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End point description:

Handheld dynamometry (HHD) is a procedure for quantitative strength testing. Muscle strength testing was performed on prespecified muscles in the upper and lower extremities bilaterally and the force measurements were recorded. FAS included all randomized participants who received at least 1 dose of study drug grouped by randomized treatment group. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 50

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	13		
Units: units on a scale				
arithmetic mean (standard deviation)	-46.5 (± 27.57)	-53.4 (± 20.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Serum Neurofilament Light Chain

End point title	Change From Baseline In Serum Neurofilament Light Chain
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End point description:

FAS included all randomized participants who received at least 1 dose of study drug grouped by randomized treatment group. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 50

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	7		
Units: units on a scale				
arithmetic mean (standard deviation)	91.5 (± 40.40)	73.1 (± 27.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Ravulizumab Concentration Over the Study Duration

End point title	Change From Baseline in Serum Ravulizumab Concentration Over the Study Duration
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End point description:

Pharmacokinetic Analysis Set (PKAS) included all participants who received at least 1 dose of the study drug and had at least 1 postdose pharmacokinetic (PK) sample. This endpoint was planned to be reported for Ravulizumab arm only.

End point type	Secondary
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End point timeframe:

Baseline, Predose at Week 50

End point values	Ravulizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: micrograms per milliliter				
geometric mean (geometric coefficient of variation)	634 (± 29.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Free Complement Component 5 (C5) Concentration Over the Study Duration

End point title	Change From Baseline in Serum Free Complement Component 5 (C5) Concentration Over the Study Duration
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End point description:

Pharmacodynamic analysis set (PDAS) included all participants who received at least 1 dose of the study drug and had at least 1 postdose pharmacodynamics (PD) sample. Here, Number of Participants

analyzed signifies those participants who were evaluable for this outcome measure.

End point type	Secondary
End point timeframe:	
Baseline, Predose at Week 50	

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	0 ^[2]		
Units: micrograms/milliliter				
arithmetic mean (standard deviation)	-155.2 (\pm 24.42)	()		

Notes:

[2] - As per the planned analysis, number of participants in this group were 0 for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Antidrug Antibodies (ADAs) to ALXN1210

End point title	Number of Participants With Positive Antidrug Antibodies (ADAs) to ALXN1210
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End point description:

Blood samples were collected to evaluate antibody response through development of ADAs. PDAS included all participants who received at least 1 dose of the study drug and had at least 1 postdose PD sample. Here, Number of Participants analyzed signifies those participants who were evaluable at Week 50.

End point type	Secondary
End point timeframe:	
Week 50	

End point values	Ravulizumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	0 ^[3]		
Units: participants	0			

Notes:

[3] - As per the planned analysis, number of participants in this group were 0 for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 351

Adverse event reporting additional description:

Safety Set included all participants who received at least 1 dose of study drug grouped by treatment actually received (for reporting exposure and safety data). "All-Cause Mortality" reports all deaths that occurred during the study, including the deaths that led to Study Discontinuation.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Randomized Controlled Period: Ravulizumab
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Reporting group description:

Participants received a weight-based loading dose of ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive).

Reporting group title	Open Label Extension Period: Placebo
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Reporting group description:

Participants received ravulizumab, with a blinded loading dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group title	Open Label Extension Period: Ravulizumab
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Reporting group description:

Participants received ravulizumab, with a blinded 900 mg dose at Week 50, followed by an open-label ravulizumab maintenance dose at Week 52, then q8w for up to 106 weeks of treatment.

Reporting group title	Randomized Controlled Period: Placebo
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Reporting group description:

Participants received a weight-based loading dose of placebo matched to ravulizumab on Day 1, followed by a weight-based maintenance dose on Day 15, then q8w up to Week 42 (inclusive).

Serious adverse events	Randomized Controlled Period: Ravulizumab	Open Label Extension Period: Placebo	Open Label Extension Period: Ravulizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 255 (16.08%)	0 / 5 (0.00%)	2 / 14 (14.29%)
number of deaths (all causes)	15	0	0
number of deaths resulting from adverse events			
Surgical and medical procedures			
Euthanasia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			

subjects affected / exposed	2 / 255 (0.78%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Pyrexia			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Immune system disorders			
Infusion related hypersensitivity reaction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
Social circumstances			
Feeding tube user			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	8 / 255 (3.14%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 255 (1.18%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			

subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Pneumonitis aspiration			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Pulmonary embolism			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory disorder			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Aspiration			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
Cough			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	2 / 255 (0.78%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Assisted suicide			

subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Investigations			
Myocardial necrosis marker increased			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Weight decreased			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Femur fracture			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrostomy failure			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrostomy tube site complication			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Hip fracture			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Rib fracture			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Skin laceration			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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

Subarachnoid haemorrhage			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
Syncope			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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			
Abdominal pain			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Colitis ulcerative			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Dysphagia			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Pancreatitis			

subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Pancreatitis relapsing			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Constipation			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Cholecystitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 255 (1.18%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	2 / 255 (0.78%)	0 / 5 (0.00%)	0 / 14 (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
Bronchitis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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 bacterial			

subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Pyelonephritis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Appendicitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (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
COVID-19			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Euglycaemic diabetic ketoacidosis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (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
Malnutrition			

subjects affected / exposed	1 / 255 (0.39%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Randomized Controlled Period: Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 127 (18.90%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Surgical and medical procedures			
Euthanasia			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Complication associated with device			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Infusion related hypersensitivity reaction			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Feeding tube user			

subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	4 / 127 (3.15%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 2		
Dyspnoea			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis aspiration			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	4 / 127 (3.15%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 1		
Respiratory disorder			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspiration			

subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Assisted suicide			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrostomy failure			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrostomy tube site complication			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin laceration			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 127 (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 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis relapsing			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			

subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 127 (3.94%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 1		
Pneumonia aspiration			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Euglycaemic diabetic ketoacidosis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	0 / 127 (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	Open Label Extension Period: Ravulizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	196 / 255 (76.86%)	1 / 5 (20.00%)	3 / 14 (21.43%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	54 / 255 (21.18%)	1 / 5 (20.00%)	1 / 14 (7.14%)
occurrences (all)	81	1	1
Contusion			
subjects affected / exposed	11 / 255 (4.31%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	13	0	0
Ankle fracture			

subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	1 / 5 (20.00%) 1	0 / 14 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	42 / 255 (16.47%) 62	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	22 / 255 (8.63%) 40	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	26 / 255 (10.20%) 29 23 / 255 (9.02%) 28 4 / 255 (1.57%) 6	0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0	0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	13 / 255 (5.10%) 14	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all) Arthralgia	21 / 255 (8.24%) 31	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0

subjects affected / exposed occurrences (all)	18 / 255 (7.06%) 23	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	12 / 255 (4.71%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	12	0	0
Hordeolum			
subjects affected / exposed	0 / 255 (0.00%)	1 / 5 (20.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Randomized Controlled Period: Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 127 (83.46%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	36 / 127 (28.35%)		
occurrences (all)	65		
Contusion			
subjects affected / exposed	8 / 127 (6.30%)		
occurrences (all)	13		
Ankle fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 127 (17.32%)		
occurrences (all)	29		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 127 (8.66%)		
occurrences (all)	11		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 127 (3.94%)		
occurrences (all)	5		
Nausea			

subjects affected / exposed occurrences (all)	10 / 127 (7.87%) 10		
Diarrhoea subjects affected / exposed occurrences (all)	9 / 127 (7.09%) 10		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	8 / 127 (6.30%) 8		
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all)	5 / 127 (3.94%) 7		
Arthralgia subjects affected / exposed occurrences (all)	4 / 127 (3.15%) 5		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	11 / 127 (8.66%) 12		
Hordeolum subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2020	The main purpose of this amendment is to update study procedures: ventilator utilization at all visits, timing of PK and ADA sampling, allowance of home or alternative healthcare facility visits and home SVC assessment, and deletion of selected Short-Form Health Survey (SF-36) assessments, deoxyribonucleic acid/ribonucleic acid sample collections, and HHD assessments. Updates also include addition of a second methodology for the primary analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The IDMC recommended the study be discontinued due to lack of efficacy with ravulizumab.
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Notes: