



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 | v2 (current) |
| This version publication date | 14 May 2023 |
| First version publication date | 11 October 2022 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | ALXN1210-ALS-308 |
|-----------------------|------------------|

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 |
|------------------------------|-----|

| | |
|------------------|-------------------------|
| 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 |
|------------------|---------------------|

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 |
|------------------|---------------------|

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 |
|----------|--------------|

| | |
|--|-----------------------|
| 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 | 5 |
| 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 |
|-----------------------|-------------------------|

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 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 |
|----------------------------|-------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

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 |
|----------------------------|---------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

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 |
|-----------------------|-------------------------|

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 |
|----------------------------|-------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

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 |
|----------------------------|---------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

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] |
|-----------------|---|

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 |
|----------------|---------|

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 |
|-----------------|---|

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 |
|----------------|-----------|

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 Percent Predicted Slow Vital Capacity

| | |
|-----------------|---|
| End point title | Change From Baseline In Percent Predicted Slow Vital Capacity |
|-----------------|---|

End point description:

Slow vital capacity measures slow and gradual expulsion of air from the lungs using a spirometer. 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: percentage of predicted volume | | | | |
| arithmetic mean (standard deviation) | -20.9 (± 19.74) | -21.3 (± 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 Week 156

| 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 |
| 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. Force of measurement is reported in megascoring (lower, upper, total). The total megascoring is defined as the average of the non-missing ratios over baseline for all the muscles involved. The megascoring at baseline is always 100. The range of a potential megascoring can not be determined in advance. A megascoring >100 indicates more strength compared to baseline. 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 | 26 | 13 | | |
| Units: % (as the unit of megascoring) | | | | |
| 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 |
| 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 |
| 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 (\pm 40.40) | 73.1 (\pm 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 |
| 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 |
| 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 (\pm 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 |
| 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. There were no participants with evaluable C5 data in the Placebo arm at Week 50. | |

| | |
|------------------------------|-----------|
| 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 (± 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 |
|-----------------|---|

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. There were no participants with evaluable C5 data in the Placebo arm 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 Week 156

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 |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Randomized Controlled Period: 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 q8w up to Week 42 (inclusive).

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Open Label Extension Period: Placebo |
|-----------------------|--------------------------------------|

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 |
|-----------------------|--|

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 |
|-----------------------|---------------------------------------|

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 | | | |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| Psychiatric disorders | | | |
| 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 |
| 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 |
| 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 |
| Investigations | | | |
| 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 |
| 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 |
| Injury, poisoning and procedural complications | | | |
| 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 |
| 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 |
| 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 |

| | | | |
|---|-----------------|---------------|----------------|
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 | | | |
| 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 |
| 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 |

| | | | |
|---|-----------------|---------------|----------------|
| 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 |
| 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 |
| 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 |
| 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 |
| Gastrointestinal disorders | | | |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| Hepatobiliary disorders | | | |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 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 |
| 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 |
| 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 |
| 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 |

| 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 | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 127 (1.57%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| 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 | | |
| 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 | | |
| 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 | | |
| Investigations | | | |
| 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 | | |
| 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 | | |

| | | | |
|---|-----------------|--|--|
| Injury, poisoning and procedural complications | | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |

| | | | |
|---|-----------------|--|--|
| 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 | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| Headache | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| 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 | | |
| Gastrointestinal disorders | | | |
| 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 | | |
| 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 | | |
| 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 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| 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 | | |
| Pancreatitis | | | |
| 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 | | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |

| | | | |
|---|-----------------|--|--|
| 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 | | |
| 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 | | |
| 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 | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| 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 | | |
| Pyelonephritis | | | |
| 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 | | |
| 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 aspiration | | | |
| subjects affected / exposed | 2 / 127 (1.57%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| 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 | | |
| Malnutrition | | | |
| 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 | | |

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 |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 5 (20.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Contusion | | | |

| | | | |
|---|---|--|---|
| subjects affected / exposed occurrences (all) | 11 / 255 (4.31%) 13 | 0 / 5 (0.00%) 0 | 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 | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 8 / 127 (6.30%) | | |
| occurrences (all) | 13 | | |
| 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.

Notes: