Clinical trial results:
A Phase III, Open-Label, Extension Trial of ECU-NMO-301 To Evaluate The Safety And Efficacy of Eculizumab in Patients With Relapsing Neuromyelitis Optica (NMO)

Summary

EudraCT number	2013-001151-12
Trial protocol	DE IT GB ES AT CZ DK FR HR
Global end of trial date	12 July 2021

Results information

Result version number	v1 (current)
This version publication date	30 June 2022
First version publication date	30 June 2022

Trial information

Trial identification

Sponsor protocol code	ECU-NMO-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02003144
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	06 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2021
Global end of trial reached?	Yes
Global end of trial date	12 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine whether eculizumab long-term use is safe and effective in participants with relapsing NMO.

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	12 January 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Croatia: 3
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Japan: 12
Country: Number of subjects enrolled	Korea, Republic of: 10
Country: Number of subjects enrolled	Malaysia: 4
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	Thailand: 7
Country: Number of subjects enrolled	Turkey: 10
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United States: 28

Worldwide total number of subjects	119
EEA total number of subjects	21

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)	108
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who completed ECU-NMO-301 (NCT01892345) were eligible to participate in ECU-NMO-302. This is an open-label study in which all participants were administered intravenous eculizumab. However, to maintain the blind of ECU-NMO-301, all participants underwent a 4-week Blind Induction Phase before entering the Open-label Maintenance Phase.

Period 1

Period 1 title	Blind Induction Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Eculizumab

Arm description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-NMO-301 were administered eculizumab (900 milligrams [mg]) plus matching placebo via intravenous (IV) infusion on Day 1 and Weeks 1 through 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

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

Dosage and administration details:

Participants received placebo matched to eculizumab at prespecified dose and timepoints.

Arm title	Eculizumab/Eculizumab

Arm description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-NMO-301 were administered eculizumab (1200 mg) via IV infusion on Day 1 and Week 2 and placebo at Weeks 1 and 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

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

Dosage and administration details:

Participants received eculizumab at prespecified dose and timepoints.

Number of subjects in period 1	Placebo/Eculizumab	Eculizumab/Eculizumab
Started	41	78
Received at Least 1 Dose of Study Drug	41	78
Completed	41	78

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Eculizumab

Arm description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-NMO-301 were administered eculizumab (900 milligrams [mg]) plus matching placebo via intravenous (IV) infusion on Day 1 and Weeks 1 through 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

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

Dosage and administration details:

Participants received eculizumab at prespecified dose and timepoints.

Arm title	Eculizumab/Eculizumab

Arm description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-NMO-301 were administered eculizumab (1200 mg) via IV infusion on Day 1 and Week 2 and placebo at Weeks 1 and 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

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

Dosage and administration details:

Participants received eculizumab at prespecified dose and timepoints.

Number of subjects in period 2	Placebo/Eculizumab	Eculizumab/Eculizumab
Started	41	78
Received at least 1 dose of study drug	41	78
Completed	32	64
Not completed	9	14
Consent withdrawn by subject	4	5
Physician decision	1	1
Adverse event, non-fatal	2	1
Pregnancy	-	2
Other than specified	2	4
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo/Eculizumab
Reporting group description:	
Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-NMO-301 were administered eculizumab (900 milligrams [mg]) plus matching placebo via intravenous (IV) infusion on Day 1 and Weeks 1 through 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.	
Reporting group title	Eculizumab/Eculizumab
Reporting group description:	
Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-NMO-301 were administered eculizumab (1200 mg) via IV infusion on Day 1 and Week 2 and placebo at Weeks 1 and 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.	

Reporting group values	Placebo/Eculizumab	Eculizumab/Eculizumab	Total
Number of subjects	41	78	119
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	37	71	108
From 65-84 years	4	7	11
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	46.0	46.6	
standard deviation	± 13.82	± 13.77	-
Sex: Female, Male Units: participants			
Female	36	74	110
Male	5	4	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	11	13
Not Hispanic or Latino	37	63	100
Unknown or Not Reported	2	4	6
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	13	32	45
Black or African American	7	3	10
White	21	40	61

Other	0	1	1
Unknown or Not Reported	0	1	1

End points

End points reporting groups

Reporting group title	Placebo/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-NMO-301 were administered eculizumab (900 milligrams [mg]) plus matching placebo via intravenous (IV) infusion on Day 1 and Weeks 1 through 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Reporting group title	Eculizumab/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-NMO-301 were administered eculizumab (1200 mg) via IV infusion on Day 1 and Week 2 and placebo at Weeks 1 and 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Reporting group title	Placebo/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-NMO-301 were administered eculizumab (900 milligrams [mg]) plus matching placebo via intravenous (IV) infusion on Day 1 and Weeks 1 through 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Reporting group title	Eculizumab/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-NMO-301 were administered eculizumab (1200 mg) via IV infusion on Day 1 and Week 2 and placebo at Weeks 1 and 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. TEAEs were defined as an AE with onset on or after the first study drug dose in Study ECU-NMO-302. A SAE was defined as an untoward medical occurrence that at any dose either results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event. A summary of serious and all other non-serious adverse events, regardless of causality, is located in the Reported Adverse Events module. The Extension Safety Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302.

End point type	Primary

End point timeframe:

Baseline up to end of study (up to 6.5 years)

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	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: participants				
TEAEs	41	70		
SAEs	14	26		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With At Least 1 Post Baseline C-SSRS Assessment (Suicide-Related Thoughts or Behaviours) Abnormality

End point title	Percentage of Participants With At Least 1 Post Baseline C-SSRS Assessment (Suicide-Related Thoughts or Behaviours) Abnormality[2]

End point description:

The C-SSRS is a validated questionnaire to capture occurrence, severity, and frequency of suicide-related thoughts and behaviours, and has a binary response (yes/no). Suicidal Ideation: a "yes" answer to any one of 5 suicidal ideation questions: Wish to be Dead; Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods (Not Planned) without Intent to Act; Active Suicidal Ideation with Some Intent to Act, without Specific Plan; and Active Suicidal Ideation with Specific Plan and Intent. Suicidal Behaviour: a "yes" answer to any of 5 suicidal behaviour questions: Preparatory Acts or Behaviour, Aborted Attempt, Interrupted Attempt, Actual Attempt (non-fatal), and Completed Suicide. Suicidal Ideation or Behaviour: a "yes" answer to the following question: Self-injurious behaviour without suicidal intent. The Extension Safety Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302.

End point type	Primary

End point timeframe:

Baseline up to end of study (up to 6.5 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned to be reported for this endpoint.

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: percentage of participants				
number (not applicable)				
Suicidal Ideation	9.8	6.4		
Suicidal Behavior	0.0	1.3		
Suicidal Ideation or Behavior	9.8	6.4		

Statistical analyses

No statistical analyses for this end point

Primary: On-Trial Annualized Relapse Rate (ARR) as Determined by the Treating

Physician

End point title	On-Trial Annualized Relapse Rate (ARR) as Determined by the Treating Physician[3]

End point description:

The On-trial ARR was computed as the total number of relapses divided by the total number of participant years in the study period. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment.

End point type	Primary

End point timeframe:

Baseline up to end of study (up to 6.5 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned to be reported for this endpoint.

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: relapses/years on study				
arithmetic mean (standard deviation)	0.128 (± 0.4576)	0.061 (± 0.2186)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With An On-trial Relapse as Determined by the Treating Physician

End point title	Number of Participants With An On-trial Relapse as Determined by the Treating Physician[4]

End point description:

An On-trial Relapse was defined as a new onset of neurologic symptoms or worsening of existing neurologic symptoms with an objective change (clinical sign) on neurologic examination that persisted for more than 24 hours as confirmed by the treating physician. An adjudicated On-trial Relapse was defined as an On-trial Relapse that was positively adjudicated by the relapse adjudication committee. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment.

End point type	Primary

End point timeframe:

Baseline up to end of study (up to 6.5 years)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned to be reported for this endpoint.

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: participants	5	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Expanded Disability Status Scale (EDSS) score

End point title	Change From Baseline in Expanded Disability Status Scale (EDSS) score

End point description:

Disease-related disability was measured by the EDSS. The EDSS quantifies disability in 8 Functional Systems (FS) and allows neurologists to assign a Functional System Score (FSS) in each of these. The Functional Systems are pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, and other. The EDSS is an ordinal clinical rating scale that ranges from 0 (normal neurologic examination) to 10 (death) in half-point increments. A decrease in score indicates improvement. Baseline was defined as the last available assessment prior to the first study drug infusion in Study ECU-NMO-302. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment. Here, Number Analyzed signifies those participants who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 52, 104 and 156

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 78)	4.34 (± 1.879)	3.97 (± 1.736)		
Change from Baseline at Week 52 (n=35, 73)	-0.24 (± 0.721)	0.01 (± 0.571)		
Change from Baseline at Week 104 (n=22, 36)	-0.39 (± 0.830)	-0.11 (± 0.536)		
Change from Baseline at Week 156 (n=13, 16)	-0.38 (± 1.003)	-0.38 (± 1.057)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Modified Rankin Scale (mRS) Score

End point title	Change From Baseline in Modified Rankin Scale (mRS) Score

End point description:

Disease-related disability was measured by the mRS score. The mRS is a commonly used scale for measuring the degree of disability or dependence in the daily activities of people who have suffered

from a neurological disability. The scale ranges from 0 (no symptoms at all) to 6 (death) in whole-point increments. A decrease in score indicates improvement. Baseline was defined as the last available assessment prior to the first study drug infusion in Study ECU-NMO-302. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment. Here, Number Analyzed signifies those participants who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 52, 104 and 156

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 78)	2.39 (± 1.358)	1.88 (± 1.269)		
Change from Baseline at Week 52 (n=37, 72)	-0.27 (± 0.932)	-0.04 (± 0.458)		
Change from Baseline at Week 104 (n=22, 36)	-0.41 (± 1.182)	-0.14 (± 0.543)		
Change from Baseline at Week 156 (n=13, 16)	-0.62 (± 1.446)	-0.31 (± 0.602)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hauser Ambulation Index (HAI) in Participants With Abnormal Baseline Ambulatory Function

End point title	Change from Baseline in Hauser Ambulation Index (HAI) in Participants With Abnormal Baseline Ambulatory Function

End point description:

The HAI evaluates gait and was used to assess the time and effort used by the participant to walk 25 feet (8 meters). The scale ranges from 0 to 9, with 0 being the best score (asymptomatic; fully active) and 9 being the worst (restricted to wheelchair; unable to transfer self independently). A decrease in score indicates improvement. Baseline is defined as the last available assessment prior to the first study drug infusion in Study ECU-NMO-302. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure and Number Analyzed signifies those participants who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 52, 104 and 156

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	66		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=40, 66)	2.83 (± 2.123)	2.35 (± 2.257)		
Change from Baseline at Week 52 (n=36, 59)	-0.44 (± 1.132)	0.08 (± 0.816)		
Change from Baseline at Week 104 (n=21, 29)	-0.57 (± 1.777)	0.07 (± 1.033)		
Change from Baseline at Week 156 (n=13, 14)	-1.08 (± 1.706)	0.07 (± 1.269)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life (EuroQoL) 5-Dimension Questionnaire (EQ-5D) Health Status Score

End point title	Change From Baseline in European Quality of Life (EuroQoL) 5-Dimension Questionnaire (EQ-5D) Health Status Score

End point description:

The EuroQoL EQ-5D is a generic, standardized, self-administered instrument that provides a simple, descriptive profile and a single index value for health status. The EQ-5D comprises 5 dimensions of health: mobility, pain/discomfort, anxiety/depression, and overall health (each dimension consists of 3 levels ranging from no problems to extreme problems) and self-care (ranging of 6 levels ranging from no problems to extreme problems). From these scores, a summary index score is derived ranging from less than 0 to 1, with higher scores representing a better health status. Baseline is defined as the last available assessment prior to the first study drug infusion in Study ECU-NMO-302. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment. Here, Number Analyzed signifies those participants who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 52, 104 and 156

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	78		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 78)	62.00 (± 22.012)	72.27 (± 20.941)		
Change from Baseline at Week 52 (n=37, 73)	2.22 (± 13.294)	-0.78 (± 12.388)		
Change from Baseline at Week 104 (n=22, 36)	0.05 (± 18.867)	1.28 (± 11.295)		
Change from Baseline at Week 156 (n=13, 16)	11.00 (± 19.374)	-4.13 (± 18.421)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Kurtzke Visual Functional System Scores (FSS) in Participants With Abnormal Baseline Visual Function

End point title	Change From Baseline in Kurtzke Visual Functional System Scores (FSS) in Participants With Abnormal Baseline Visual Function

End point description:

The EDSS assesses multiple Kurtzke functional systems in the context of a standard neurological exam, including visual function. The visual score ranges from 0 to 6. A score of 0 implies the participant has normal visual function. Higher scores represent worse disability. Baseline is defined as the last available assessment prior to the first study drug infusion in Study EC-NMO-302. The Extension Full Analysis Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302 and had a post-IP-infusion efficacy assessment. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure and Number Analyzed signifies those participants who were evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 52, 104 and 156

End point values	Placebo/Eculizumab	Eculizumab/Eculizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	67		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=28, 67)	3.75 (± 2.030)	3.60 (± 2.031)		
Change from Baseline at Week 52 (n=26, 62)	-0.08 (± 0.392)	-0.06 (± 0.569)		
Change from Baseline at Week 104 (n=15, 31)	-0.13 (± 0.352)	-0.10 (± 0.651)		
Change from Baseline at Week 156 (n=11, 14)	0.00 (± 0.000)	-0.29 (± 0.994)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to end of study (up to 6.5 years)

Adverse event reporting additional description:

The Extension Safety Set consisted of all participants who had received at least 1 dose of eculizumab in Study ECU-NMO-302.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-NMO-301 were administered eculizumab (900 mg) plus matching placebo via IV infusion on Day 1 and Weeks 1 through 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Reporting group title	Eculizumab (Combined Total)

Reporting group description:

All participants who received at least 1 dose of eculizumab in the extension study. Participants received open-label eculizumab (1200 mg) every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Reporting group title	Eculizumab/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-NMO-301 were administered eculizumab (1200 mg) via IV infusion on Day 1 and Week 2 and placebo at Weeks 1 and 3. Open-Label Maintenance Phase: Participants received open-label eculizumab (1200 mg) via IV infusion every 2 weeks starting at Week 4 and continued for up to 6.5 years.

Serious adverse events	Placebo/Eculizumab	Eculizumab (Combined Total)	Eculizumab/Eculizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 41 (34.15%)	40 / 119 (33.61%)	26 / 78 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesteatoma			

subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Anembryonic gestation			
subjects affected / exposed[1]	0 / 36 (0.00%)	1 / 110 (0.91%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometriosis	Additional description: The N for this adverse event has been adjusted to the number of females in the study as it is a sex-specific event.		
subjects affected / exposed[2]	0 / 36 (0.00%)	1 / 110 (0.91%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Bronchiectasis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal septum deviation			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Catatonia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	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 / 41 (2.44%)	2 / 119 (1.68%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	2 / 41 (4.88%)	5 / 119 (4.20%)	3 / 78 (3.85%)
occurrences causally related to treatment / all	1 / 4	2 / 8	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic neuritis			
subjects affected / exposed	1 / 41 (2.44%)	3 / 119 (2.52%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	1 / 1	2 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aphasia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparaesthesia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental impairment			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasticity			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromuscular blockade			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyelitis optica pseudo relapse			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Irritable bowel syndrome			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	2 / 41 (4.88%)	3 / 119 (2.52%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 41 (0.00%)	2 / 119 (1.68%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 41 (2.44%)	2 / 119 (1.68%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			

subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	5 / 119 (4.20%)	3 / 78 (3.85%)
occurrences causally related to treatment / all	1 / 2	1 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 119 (1.68%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 41 (0.00%)	2 / 119 (1.68%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 41 (0.00%)	2 / 119 (1.68%)	2 / 78 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			

subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia pyelonephritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gonorrhoea			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective tenosynovitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			

subjects affected / exposed	1 / 41 (2.44%)	1 / 119 (0.84%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 119 (0.84%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The number of subjects exposed for this adverse event has been adjusted to the number of females in the study as it is a sex-specific event.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The number of subjects exposed for this adverse event has been adjusted to the number of females in the study as it is a sex-specific event.

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

Non-serious adverse events	Placebo/Eculizumab	Eculizumab (Combined Total)	Eculizumab/Eculizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 41 (97.56%)	110 / 119 (92.44%)	70 / 78 (89.74%)
Investigations			
Blood pressure increased			
subjects affected / exposed	3 / 41 (7.32%)	3 / 119 (2.52%)	0 / 78 (0.00%)
occurrences (all)	3	3	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	6 / 41 (14.63%)	10 / 119 (8.40%)	4 / 78 (5.13%)
occurrences (all)	10	16	6
Fall			
subjects affected / exposed	3 / 41 (7.32%)	3 / 119 (2.52%)	0 / 78 (0.00%)
occurrences (all)	14	14	0
Thermal burn			
subjects affected / exposed	3 / 41 (7.32%)	6 / 119 (5.04%)	3 / 78 (3.85%)
occurrences (all)	8	11	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 41 (7.32%)	8 / 119 (6.72%)	5 / 78 (6.41%)
occurrences (all)	3	10	7

Headache			
subjects affected / exposed	12 / 41 (29.27%)	27 / 119 (22.69%)	15 / 78 (19.23%)
occurrences (all)	34	174	140
Hypoaesthesia			
subjects affected / exposed	2 / 41 (4.88%)	7 / 119 (5.88%)	5 / 78 (6.41%)
occurrences (all)	3	9	6
Paraesthesia			
subjects affected / exposed	3 / 41 (7.32%)	6 / 119 (5.04%)	3 / 78 (3.85%)
occurrences (all)	3	7	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 41 (7.32%)	9 / 119 (7.56%)	6 / 78 (7.69%)
occurrences (all)	3	10	7
Iron deficiency anaemia			
subjects affected / exposed	2 / 41 (4.88%)	7 / 119 (5.88%)	5 / 78 (6.41%)
occurrences (all)	2	7	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 41 (14.63%)	18 / 119 (15.13%)	12 / 78 (15.38%)
occurrences (all)	8	27	19
Fatigue			
subjects affected / exposed	4 / 41 (9.76%)	11 / 119 (9.24%)	7 / 78 (8.97%)
occurrences (all)	13	20	7
Oedema peripheral			
subjects affected / exposed	1 / 41 (2.44%)	5 / 119 (4.20%)	4 / 78 (5.13%)
occurrences (all)	1	5	4
Peripheral swelling			
subjects affected / exposed	3 / 41 (7.32%)	5 / 119 (4.20%)	2 / 78 (2.56%)
occurrences (all)	4	6	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 41 (19.51%)	14 / 119 (11.76%)	6 / 78 (7.69%)
occurrences (all)	17	28	11
Dyspepsia			
subjects affected / exposed	4 / 41 (9.76%)	6 / 119 (5.04%)	2 / 78 (2.56%)
occurrences (all)	5	14	9

Constipation			
subjects affected / exposed	4 / 41 (9.76%)	10 / 119 (8.40%)	6 / 78 (7.69%)
occurrences (all)	5	12	7
Nausea			
subjects affected / exposed	7 / 41 (17.07%)	10 / 119 (8.40%)	3 / 78 (3.85%)
occurrences (all)	17	21	4
Toothache			
subjects affected / exposed	5 / 41 (12.20%)	6 / 119 (5.04%)	1 / 78 (1.28%)
occurrences (all)	7	8	1
Dental caries			
subjects affected / exposed	1 / 41 (2.44%)	5 / 119 (4.20%)	4 / 78 (5.13%)
occurrences (all)	1	6	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 41 (17.07%)	12 / 119 (10.08%)	5 / 78 (6.41%)
occurrences (all)	10	19	9
Oropharyngeal pain			
subjects affected / exposed	4 / 41 (9.76%)	9 / 119 (7.56%)	5 / 78 (6.41%)
occurrences (all)	4	13	9
Asthma			
subjects affected / exposed	3 / 41 (7.32%)	5 / 119 (4.20%)	2 / 78 (2.56%)
occurrences (all)	5	7	2
Rhinorrhoea			
subjects affected / exposed	2 / 41 (4.88%)	6 / 119 (5.04%)	4 / 78 (5.13%)
occurrences (all)	2	7	5
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 41 (4.88%)	6 / 119 (5.04%)	4 / 78 (5.13%)
occurrences (all)	3	8	5
Dermatitis			
subjects affected / exposed	3 / 41 (7.32%)	3 / 119 (2.52%)	0 / 78 (0.00%)
occurrences (all)	3	3	0
Skin lesion			
subjects affected / exposed	3 / 41 (7.32%)	3 / 119 (2.52%)	0 / 78 (0.00%)
occurrences (all)	4	4	0
Renal and urinary disorders			

Urinary incontinence			
subjects affected / exposed	3 / 41 (7.32%)	4 / 119 (3.36%)	1 / 78 (1.28%)
occurrences (all)	3	4	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 41 (7.32%)	6 / 119 (5.04%)	3 / 78 (3.85%)
occurrences (all)	4	8	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 41 (19.51%)	23 / 119 (19.33%)	15 / 78 (19.23%)
occurrences (all)	13	38	25
Back pain			
subjects affected / exposed	5 / 41 (12.20%)	16 / 119 (13.45%)	11 / 78 (14.10%)
occurrences (all)	9	33	24
Pain in extremity			
subjects affected / exposed	5 / 41 (12.20%)	12 / 119 (10.08%)	7 / 78 (8.97%)
occurrences (all)	13	35	22
Muscular weakness			
subjects affected / exposed	1 / 41 (2.44%)	5 / 119 (4.20%)	4 / 78 (5.13%)
occurrences (all)	1	5	4
Muscle spasms			
subjects affected / exposed	5 / 41 (12.20%)	10 / 119 (8.40%)	5 / 78 (6.41%)
occurrences (all)	7	13	6
Musculoskeletal pain			
subjects affected / exposed	0 / 41 (0.00%)	5 / 119 (4.20%)	5 / 78 (6.41%)
occurrences (all)	0	5	5
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	11 / 41 (26.83%)	28 / 119 (23.53%)	17 / 78 (21.79%)
occurrences (all)	24	51	27
Nasopharyngitis			
subjects affected / exposed	16 / 41 (39.02%)	29 / 119 (24.37%)	13 / 78 (16.67%)
occurrences (all)	35	67	32
Influenza			
subjects affected / exposed	9 / 41 (21.95%)	19 / 119 (15.97%)	10 / 78 (12.82%)
occurrences (all)	14	25	11

Urinary tract infection			
subjects affected / exposed	11 / 41 (26.83%)	24 / 119 (20.17%)	13 / 78 (16.67%)
occurrences (all)	29	59	30
Cystitis			
subjects affected / exposed	4 / 41 (9.76%)	9 / 119 (7.56%)	5 / 78 (6.41%)
occurrences (all)	6	12	6
Oral herpes			
subjects affected / exposed	4 / 41 (9.76%)	8 / 119 (6.72%)	4 / 78 (5.13%)
occurrences (all)	17	21	4
Bronchitis			
subjects affected / exposed	3 / 41 (7.32%)	7 / 119 (5.88%)	4 / 78 (5.13%)
occurrences (all)	6	12	6
Herpes zoster			
subjects affected / exposed	3 / 41 (7.32%)	5 / 119 (4.20%)	2 / 78 (2.56%)
occurrences (all)	3	5	2
Pneumonia			
subjects affected / exposed	3 / 41 (7.32%)	4 / 119 (3.36%)	1 / 78 (1.28%)
occurrences (all)	4	6	2
Periodontitis			
subjects affected / exposed	0 / 41 (0.00%)	4 / 119 (3.36%)	4 / 78 (5.13%)
occurrences (all)	0	5	5
Pharyngitis			
subjects affected / exposed	4 / 41 (9.76%)	5 / 119 (4.20%)	1 / 78 (1.28%)
occurrences (all)	4	5	1
Sinusitis			
subjects affected / exposed	3 / 41 (7.32%)	4 / 119 (3.36%)	1 / 78 (1.28%)
occurrences (all)	4	8	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2013	Incorporated changes in the amended protocol for Study ECU-NMO-301 version 4.0 dated 16 Oct 2013, which addressed issues/concerns from the Investigators as well as recommended changes from Institutional Review Board, Independent Ethics Committee, and Competent Authorities.
01 June 2015	• Aligned with amended protocol for Study ECU-NMO-301 version 5.0 dated 25 Feb 2015: Allowed qualified non-physician healthcare professionals to conduct the EDSS rating Expanded the number of investigational sites Extended the estimated date of first participant enrolled from 2014 to 2015 and estimated date of last participant completed from 2018 to 2019 Provided flexibility for the supplemental investigational product dose administration time from "within 60 minutes" to "preferably within 1-2 hours" after each plasma exchange cycle Changed the definition of the Per Protocol population from participants who have "no major protocol deviations or inclusion/exclusion criteria deviations" to "no major protocol deviations or key inclusion/exclusion criteria deviations" Allowed the Treating Physician's designee to perform the mRS assessment • Detailed instructions for supplemental dosing after PE that take into account the possibility of PE during the Blind Induction Phase.
03 August 2016	• Established an Adjudication Committee to perform independent blinded reviews of all On-trial Relapses as determined by the Treating Physician • Added a sensitivity analysis for the change in ARR between the baseline ARR and Adjudicated On-trial ARR including all relapses when on eculizumab treatment in Study ECU-NMO-302 using a Wilcoxon signed rank test.
22 March 2018	• Extended the study duration from 4 years to 5.5 years • Reduced the number of visits at which pharmacokinetics/pharmacodynamics (PK/PD) samples were to be collected • Added an appendix to describe the procedures for collection of post-study follow-up information from participants who withdrew from the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported