Clinical trial results:
A Double-masked, Placebo-controlled Study with Open-label Period to Evaluate the Efficacy and Safety of MEDI-551 in Adult Subjects with Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorders

Summary

EudraCT number	2014-000253-36
Trial protocol	CZ DE EE BG PL ES HU GR NL
Global end of trial date	06 November 2020

Results information

Result version number	v1 (current)
This version publication date	19 November 2021
First version publication date	19 November 2021

Trial information

Trial identification

Sponsor protocol code	CD-IA-MEDI-551-1155

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02200770
WHO universal trial number (UTN)	U1111-1159-8686

Notes:

Sponsors

Sponsor organisation name	MedImmune LLC
Sponsor organisation address	OneMedImmune Way, Gaithersburg, United States, MD 20878
Public contact	MedImmune LLC, Global ClinicalLead, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	MedImmune LLC, Global ClinicalLead, +1 877-240-9479, information.center@astrazeneca.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	09 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the efficacy of inebilizumab versus placebo in reducing the risk of an neuromyelitis optica spectrum disorders (NMOSD) attack in participants with NMOSD.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Colombia: 15
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Moldova, Republic of: 1
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Peru: 15
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	Serbia: 10
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Taiwan: 3

Country: Number of subjects enrolled	Thailand: 11
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	United States: 41
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Poland: 21
Country: Number of subjects enrolled	Czechia: 8
Worldwide total number of subjects	231
EEA total number of subjects	56

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)	221
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 231 participants were randomised at 81 participating sites in 24 countries. Out of 231 participants, 1 participant was randomised but not treated due to an NMOSD attack on the day of randomisation prior to dosing.

Period 1

Period 1 title	Randomized-controlled Period (RCP)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Inebilizumab

Arm description:

Aquaporin-4-antibody (AQP4-IgG) sero positive and sero negative participants received intravenous (IV) dose of placebo matched to inebilizumab on Day 1 and Day 15 of the randomized-controlled period (RCP). The participants who entered open-label period (OLP) received IV inebilizumab 300 mg on both Day 1 and Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the Safety Follow up Period (SFP) at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Arm type	Experimental
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:

Intravenous dose of placebo matched to inebilizumab was administered on Day 1 and Day 15 of the RCP.

Arm title	Inebilizumab/Inebilizumab

Arm description:

AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab (MEDI551) 300 mg on Day 1 and Day 15 of RCP. The participants who entered OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Inebilizumab
Investigational medicinal product code	MEDI-551
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received IV dose of inebilizumab 300 mg on Day 1 and Day 15 of the RCP.

Number of subjects in period 1[1]	Placebo/Inebilizumab	Inebilizumab/Inebilizumab
Started	56	174
Completed	54	169
Not completed	2	5
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	2
Not specified	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Total 231 participants were randomized in the study, out of which one participant did not receive any treatment due to an NMOSD attack on the day of randomisation prior to dosing. Baseline characteristics are reported only for treated (230) participants.

Period 2

Period 2 title	Open-label Period (OLP)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Inebilizumab

Arm description:

Aquaporin-4-antibody (AQP4-IgG) sero positive and sero negative participants received intravenous (IV) dose of placebo matched to inebilizumab on Day 1 and Day 15 of the randomized-controlled period (RCP). The participants who entered open-label period (OLP) received IV inebilizumab 300 mg on both Day 1 and Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Inebilizumab
Investigational medicinal product code	
Other name	MEDI-551
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants who received placebo in RCP and entered in OLP received IV inebilizumab 300 mg on both Day 1 and Day 15 followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP.

Arm title	Inebilizumab/Inebilizumab

Arm description:

AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab (MEDI551) 300 mg on Day 1 and Day 15 of RCP. The participants who entered OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last

dose of study drug.

Arm type	Experimental
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 who received inebilizumab in RCP and entered in OLP received IV placebo matched to inebilizumab on Day 15.

Investigational medicinal product name	Inebilizumab
Investigational medicinal product code	
Other name	MEDI-551
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants who received inebilizumab in RCP and entered in OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP.

Number of subjects in period 2[2]	Placebo/Inebilizumab	Inebilizumab/Inebilizumab
Started	51	165
Completed	43	131
Not completed	8	34
Adverse event, serious fatal	1	2
Consent withdrawn by subject	-	14
Adverse event, non-fatal	1	2
Not specified	6	15
Lost to follow-up	-	1

Notes:

[2] - 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: Three participants in Placebo/Inebilizumab arm and 4 participants in Inebilizumab/Inebilizumab arm, did not roll over to open-label period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo/Inebilizumab
Reporting group description:	
Aquaporin-4-antibody (AQP4-IgG) sero positive and sero negative participants received intravenous (IV) dose of placebo matched to inebilizumab on Day 1 and Day 15 of the randomized-controlled period (RCP). The participants who entered open-label period (OLP) received IV inebilizumab 300 mg on both Day 1 and Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the Safety Follow up Period (SFP) at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.	
Reporting group title	Inebilizumab/Inebilizumab
Reporting group description:	
AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab (MEDI551) 300 mg on Day 1 and Day 15 of RCP. The participants who entered OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.	

Reporting group values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab	Total
Number of subjects	56	174	230
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)	52	168	220
From 65-84 years	4	6	10
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	42.6	43.0	
standard deviation	± 13.9	± 11.6	-
Sex: Female, Male Units: Participants			
Female	50	159	209
Male	6	15	21
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	14	19
Asian	8	39	47
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	15	20

White	28	92	120
More than one race	0	1	1
Unknown or Not Reported	10	13	23
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	15	28	43
Not Hispanic or Latino	41	146	187
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Placebo/Inebilizumab

Reporting group description:

Aquaporin-4-antibody (AQP4-IgG) sero positive and sero negative participants received intravenous (IV) dose of placebo matched to inebilizumab on Day 1 and Day 15 of the randomized-controlled period (RCP). The participants who entered open-label period (OLP) received IV inebilizumab 300 mg on both Day 1 and Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the Safety Follow up Period (SFP) at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Reporting group title	Inebilizumab/Inebilizumab

Reporting group description:

AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab (MEDI551) 300 mg on Day 1 and Day 15 of RCP. The participants who entered OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Reporting group title	Placebo/Inebilizumab

Reporting group description:

Aquaporin-4-antibody (AQP4-IgG) sero positive and sero negative participants received intravenous (IV) dose of placebo matched to inebilizumab on Day 1 and Day 15 of the randomized-controlled period (RCP). The participants who entered open-label period (OLP) received IV inebilizumab 300 mg on both Day 1 and Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Reporting group title	Inebilizumab/Inebilizumab

Reporting group description:

AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab (MEDI551) 300 mg on Day 1 and Day 15 of RCP. The participants who entered OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.

Subject analysis set title	Any Inebilizumab
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab 300 mg on Day 1 and Day 15 in RCP or IV inebilizumab 300 mg on both Day 1 and Day 15 in OLP; followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP.

Primary: Time to Adjudication Committee (AC)-Determined NMOSD Attack During RCP

End point title	Time to Adjudication Committee (AC)-Determined NMOSD Attack During RCP

End point description:

The NMOSD attack is defined as the presence of new or worsening symptom(s) related to NMOSD that meet at least one of the 18 protocol-defined attack criteria. These criteria were developed in conjunction with a panel of disease experts and with Food and Drug Administration input, and were intended to be clinically meaningful, objective, quantifiable, and able to be used worldwide. Only attacks positively adjudicated by the AC were used for the primary analysis. The arbitrary numbers 0.99999, 99999.0, and 9999.9 signified the data for lower limit of Confidence Interval (CI), upper limit of CI, and median, respectively, were not calculated because there were insufficient NMOSD attacks to determine the data

for the specified arm. The Intent-to-treat (ITT) population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment.

End point type	Primary

End point timeframe:

Day 1 (Baseline) through Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	174		
Units: Days				
median (confidence interval 95%)	9999.9 (142.0 to 99999.0)	9999.9 (0.99999 to 99999.0)		

Statistical analyses

Statistical analysis title	Total Placebo Vs Total Inebilizumab
Comparison groups	Inebilizumab/Inebilizumab v Placebo/Inebilizumab
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.272
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1496
upper limit	0.4961

Secondary: Percentage of Participants With Worsening in Expanded Disability Severity Scale (EDSS) Score From Baseline to the Last Visit of RCP

End point title	Percentage of Participants With Worsening in Expanded Disability Severity Scale (EDSS) Score From Baseline to the Last Visit of RCP

End point description:

EDSS and its associated functional system (FS) score provide a system for quantifying disability and monitoring changes in the level of disability over time. EDSS is a scale for assessing neurologic impairment in multiple sclerosis (MS). It consists of 7 FS (visual FS, brainstem FS, pyramidal FS, cerebellar FS, sensory FS, bowel and bladder FS, and cerebral FS) which are used to derive EDSS score ranging from 0 (normal neurological exam) to 10 (death from MS). A negative change from baseline indicates improvement. A participant was considered to have a worsening in overall EDSS score of at least 2 if baseline EDSS score was 0, or at least 1 point if baseline EDSS score is 1 to 5, or at least 0.5 point if baseline EDSS score is 5.5 or more. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) through Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	174		
Units: Percentage of Participants				
number (not applicable)	33.9	14.9		

Statistical analyses

Statistical analysis title	Total Placebo Vs Total Inebilizumab
Comparison groups	Placebo/Inebilizumab v Inebilizumab/Inebilizumab
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0033
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.352
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1755
upper limit	0.7059

Secondary: Change From Baseline in Low-Contrast Visual Acuity Binocular Score to the Last Visit of RCP

End point title	Change From Baseline in Low-Contrast Visual Acuity Binocular Score to the Last Visit of RCP

End point description:

Low-contrast visual acuity test is used to determine the number of letters that can be read on a standardized low-contrast Landolt C Broken Rings Chart held at a distance of 3 meters. Binocular score is the number of letters read correctly on an eye chart using both eyes simultaneously. The total score ranges from 0-70. Higher score indicates better vision. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Participants with low contrast visual acuity binocular score were analysed for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) through Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	171		
Units: Score on scale				
least squares mean (standard error)	1.442 (± 1.217)	1.576 (± 0.935)		

Statistical analyses

Statistical analysis title	Total Placebo Vs Total Inebilizumab
Comparison groups	Placebo/Inebilizumab v Inebilizumab/Inebilizumab
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9026
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.134
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.0254
upper limit	2.2941
Variability estimate	Standard error of the mean
Dispersion value	1.096

Secondary: Cumulative Number of Active Magnetic Resonance Imaging (MRI) Lesions During RCP

End point title	Cumulative Number of Active Magnetic Resonance Imaging (MRI) Lesions During RCP

End point description:

The number of new gadolinium-enhancing lesions and new or enlarging T2 lesions were measured by MRI of the brain, optic nerve, and spinal cord. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Participants with observed MRI lesions were analysed for this endpoint.

End point type	Secondary

End point timeframe:

From Screening (Day -28) to Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	79		
Units: Number of lesions				
arithmetic mean (standard deviation)	2.3 (± 1.3)	1.6 (± 1.0)		

Statistical analyses

Statistical analysis title	Total Placebo Vs Total Inebilizumab
Comparison groups	Placebo/Inebilizumab v Inebilizumab/Inebilizumab
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0034
Method	Negative Binomial Regression
Parameter estimate	Rate Ratio
Point estimate	0.566
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3866
upper limit	0.8279

Secondary: Number of NMOSD-related in-patient Hospitalizations During RCP

End point title	Number of NMOSD-related in-patient Hospitalizations During RCP

End point description:

Participants with relapsing NMOSD have recurrent attacks that can be severe and result in blindness, paralysis, and even death and consequently, such attacks frequently result in in-patient hospitalizations. In-patient hospitalization is defined as a stay in hospital that goes beyond midnight of the first day of admission. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Participants with in-patient hospitalisation were analysed for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) through Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	11		
Units: Number of In-patient Hospitalizations				
arithmetic mean (standard deviation)	1.4 (± 0.7)	1.0 (± 0)		

Statistical analyses

Statistical analysis title	Total Placebo Vs Total Inebilizumab
Comparison groups	Placebo/Inebilizumab v Inebilizumab/Inebilizumab
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0146
Method	Negative Binomial Regression
Parameter estimate	Rate Ratio
Point estimate	0.317
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1257
upper limit	0.7972

Secondary: Annualized AC-determined NMOSD Attack Rate During any Exposure to Inebilizumab

End point title	Annualized AC-determined NMOSD Attack Rate During any Exposure to Inebilizumab

End point description:

Annualized attack rate is defined as total number of AC-determined attacks divided by total person years. Total person-years is calculated as the sum of the person-years for individual participant. Person-year for individual participant = (Date of last day before safety follow-up period - first inebilizumab dose date +1)/365.25. Annualized AC-determined NMOSD attack rate during any exposure to inebilizumab (in RCP and OLP) is reported. Any inebilizumab population was analysed which included all participants who received at least one dose of inebilizumab either in the RCP or OLP.

End point type	Secondary

End point timeframe:

For participants randomised to inebilizumab: Day 1 of RCP through end of OLP (approximately 3.5 years); and for participants randomised to placebo: Day 1 of OLP through the end of OLP (approximately 3 years)

End point values	Any Inebilizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	225			
Units: Annualized attack rate				
number (not applicable)	0.086			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) During RCP

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) During RCP

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event is any AE that resulted in death, life threatening, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, is a congenital anomaly/birth defect in offspring of a study participant, is an important medical event that may jeopardize the participant or may require medical intervention. TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug during the RCP. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment received.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) through Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	174		
Units: Participants				
TEAEs	41	127		
TESAEs	6	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs and TESAEs During OLP

End point title	Number of Participants With TEAEs and TESAEs During OLP

End point description:

An AE is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event is any AE that resulted in death, life threatening, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, is a congenital anomaly/birth defect in offspring of a study participant, is an important medical event that may jeopardize the participant or may require medical intervention. TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug during the OLP. Open-label

population was analysed which included all participants who received at least one dose of inebilizumab during OLP.

End point type	Secondary

End point timeframe:

Day 198 through end of OLP period (maximum of 3 years after the last participant entered, until regulatory approval or study discontinuation, whichever occurs first) (approximately 3 years)

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	165		
Units: Participants				
TEAEs	45	144		
TESAEs	19	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs and TESAEs During SFP (Open-label Population)

End point title	Number of Participants With TEAEs and TESAEs During SFP (Open-label Population)

End point description:

An AE is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event is any AE that resulted in death, life threatening, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, is a congenital anomaly/birth defect in offspring of a study participant, is an important medical event that may jeopardize the participant or may require medical intervention. TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug during the OLP. Participant who prematurely discontinued from the RCP or OLP entered in the SFP. Open-label population was analysed which included all participants who received at least one dose of inebilizumab during OLP.

End point type	Secondary

End point timeframe:

Every 3 months for a total of 1 year after the last dose of study drug (approximately 3 years)

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	165		
Units: Participants				
TEAEs	3	5		
TESAEs	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs and TESAEs During SFP (Non-OLP Population)

End point title	Number of Participants With TEAEs and TESAEs During SFP (Non-OLP Population)

End point description:

An AE is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event is any AE that resulted in death, life threatening, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, is a congenital anomaly/birth defect in offspring of a study participant, is an important medical event that may jeopardize the participant or may require medical intervention. TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug during the OLP. Participant who prematurely discontinued from the RCP or OLP entered in the SFP. Non-OLP population was analysed which included all participants who received any dose of study drug, analysed according to the treatment received in RCP, but did not roll over to OLP.

End point type	Secondary

End point timeframe:

Every 3 months for a total of 1 year after the last dose of study drug (approximately 3 years)

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Participants				
TEAEs	2	3		
TESAEs	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least a 2-Grade Shift From Baseline to Worst Toxicity Grade in Hematology and Chemistry During RCP

End point title	Number of Participants With at Least a 2-Grade Shift From Baseline to Worst Toxicity Grade in Hematology and Chemistry During RCP

End point description:

Number of participants with at least a 2-grade shift from baseline to worst toxicity grade in hematology and chemistry during RCP is reported. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment received.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) through Day 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	173		
Units: Participants				
Hemoglobin (decreased)	0	2		
Leukocytes (decreased)	1	11		
Lymphocytes (decreased)	5	35		
Lymphocytes (increased)	4	1		
Neutrophils (decreased)	0	10		
Alanine Aminotransferase (increased)	1	4		
Aspartate Aminotransferase (increased)	2	1		
Bilirubin (increased)	2	1		
Cholesterol (increased)	2	5		
Creatinine (increased)	1	5		
Gamma glutamyl transferase (increased)	1	6		
Glucose (decreased)	1	1		
Glucose (increased)	5	1		
Potassium (decreased)	0	1		
Sodium (decreased)	1	2		
Triglycerides (increased)	2	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least a 2-Grade Shift From Baseline to Worst Toxicity Grade in Hematology and Chemistry During OLP

End point title	Number of Participants With at Least a 2-Grade Shift From Baseline to Worst Toxicity Grade in Hematology and Chemistry During OLP

End point description:

Number of participants with at least a 2-grade shift from baseline to worst toxicity grade in hematology and chemistry during OLP is reported. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment received.

End point type	Secondary

End point timeframe:

Day 198 through end of OLP (maximum of 3 years after the last participant enters, until regulatory approval or study discontinuation, whichever occurs first) (approximately 3 years)

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	165		
Units: Participants				
Hemoglobin (decreased)	2	6		
Leukocytes (decreased)	1	12		
Lymphocytes (decreased)	9	21		

Lymphocytes (increased)	1	4		
Neutrophils (decreased)	1	16		
Alanine aminotransferase (increased)	45	2		
Albumin (decreased)	0	3		
Alkaline phosphatase (increased)	1	1		
Aspartate aminotransferase (increased)	2	3		
Cholesterol (increased)	1	5		
Creatinine (increased)	3	7		
Gamma glutamyl transferase (increased)	1	10		
Glucose (decreased)	0	3		
Glucose (increased)	5	5		
Potassium (decreased)	0	1		
Potassium (increased)	1	2		
Sodium (decreased)	2	1		
Triglycerides (increased)	4	6		
Urate (increased)	1	1		
Hemoglobin (increased)	0	1		
Bilirubin	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Serum Concentration (Tmax) of Inebilizumab (During RCP)

End point title	Time to Maximum Serum Concentration (Tmax) of Inebilizumab (During RCP)[1]

End point description:

Time to maximum serum concentration of inebilizumab during RCP is reported. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Here, 'n' denotes the number of participants who had adequate pharmacokinetic sample of inebilizumab per the specified dose levels (Dose 1 and Dose 2).

End point type	Secondary

End point timeframe:

Dose 1 (Pre and post dose on Day 1 and Day 8); and Dose 2 (pre and post dose on Day 15; and Days 29, 57, 85, 113, 155, and 197)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic analysis was not planned for Placebo/Inebilizumab arm but only for Inebilizumab/Inebilizumab arm.

End point values	Inebilizumab/Inebilizumab			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: Days				
median (full range (min-max))				
Dose 1 (n = 173)	0.07 (0.07 to 7.00)			
Dose 2 (n = 168)	0.07 (0.07 to 14.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Inebilizumab (During RCP)

End point title	Maximum Observed Serum Concentration (Cmax) of Inebilizumab (During RCP)[2]

End point description:

Maximum observed serum concentration of inebilizumab during RCP is reported. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Here, 'n' denotes the number of participants who had adequate pharmacokinetic sample of inebilizumab per the specified dose levels (Dose 1 and Dose 2).

End point type	Secondary

End point timeframe:

Dose 1 (Pre and post dose on Day 1 and Day 8); and Dose 2 (pre and post dose on Day 15; and Days 29, 57, 85, 113, 155, and 197)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic analysis was not planned for Placebo/Inebilizumab arm but only for Inebilizumab/Inebilizumab arm.

End point values	Inebilizumab/Inebilizumab			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Dose 1 (n = 173)	97.7 (± 37.4)			
Dose 2 (n = 168)	108 (± 45.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration Time Curve of the Dosing Interval (AUC0-14d) of Inebilizumab (During RCP)

End point title	Area Under the Serum Concentration Time Curve of the Dosing Interval (AUC0-14d) of Inebilizumab (During RCP)[3]

End point description:

Area under the serum concentration time curve of the dosing interval (AUC0-14d) of inebilizumab during RCP is reported. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Here, 'n' denotes the number of participants who had adequate pharmacokinetic sample of inebilizumab per the specified dose levels (Dose 1 and Dose 2).

End point type	Secondary

End point timeframe:

Dose 1 (Pre and post dose on Day 1 and Day 8); and Dose 2 (pre and post dose on Day 15; and Days 29, 57, 85, 113, 155, and 197)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic analysis was not planned for Placebo/Inebilizumab arm but only for Inebilizumab/Inebilizumab arm.

End point values	Inebilizumab/Inebilizumab			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: µg*d/mL				
geometric mean (geometric coefficient of variation)				
Dose 1 (n = 167)	667 (± 31.3)			
Dose 2 (n = 164)	967 (± 39.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Drug Antibodies (ADA) Titer to Inebilizumab (During RCP)

End point title	Number of Participants With Positive Anti-Drug Antibodies (ADA) Titer to Inebilizumab (During RCP)

End point description:

Number of participants with positive ADA titer to inebilizumab during RCP is reported. The ITT population was analysed which included all participants who were randomised, received any study drug, and grouped according to their randomised treatment. Here, 'n' denotes the number of participants who had adequate ADA samples. Baseline (BL) was predose on Day 1.

End point type	Secondary

End point timeframe:

Pre and post dose on Day 1; and on Days 29, 85, and 197

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	174		
Units: Participants				
ADA +ve anytime including BL (n = 56, 174)	8	17		
ADA +ve at BL; not detected post-BL (n = 56, 171)	0	5		
ADA +ve post-BL; positive at BL (n = 56, 171)	4	7		
ADA +ve post-BL; not detected at BL (n = 56, 171)	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Drug Antibodies (ADA) Titer to Inebilizumab (During OLP)

End point title	Number of Participants With Positive Anti-Drug Antibodies (ADA) Titer to Inebilizumab (During OLP)

End point description:

Number of participants with positive ADA titer to inebilizumab in OLP is reported. Open-label population was analysed which included all participants who received at least one dose of inebilizumab during OLP. Here, 'n' denotes the number of participants who had adequate ADA samples. The BL was predose on Day 1.

End point type	Secondary

End point timeframe:

Pre and post dose on Day 1; and on Days 92, 183, 274, and then every 6 months (maximum of 3 years after the last participant enters, until regulatory approval or study discontinuation, whichever occurs first) (approximately 3 years)

End point values	Placebo/Inebilizumab	Inebilizumab/Inebilizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	165		
Units: Participants				
ADA +ve anytime including BL (n = 51, 165)	9	22		
ADA +ve at BL; not detected post-BL (n = 51, 162)	0	5		
ADA +ve post-BL and positive at BL (n = 51, 162)	4	7		
ADA +ve post-BL; not detected at BL (n = 51, 162)	5	10		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until last study visit (approximately 5 years 10 months)	
Adverse event reporting additional description:	
Adverse events are reported for all 3 study periods combined (RCP, OLP, and SFP).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Total Inebilizumab
Reporting group description:	
AQP4-IgG sero positive and sero negative participants received IV dose of inebilizumab 300 mg on Day 1 and Day 15 of RCP. The participants who entered OLP received IV inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.	
Reporting group title	Total Placebo
Reporting group description:	
AQP4-IgG sero positive and sero negative participants received IV dose of placebo matched to inebilizumab on Day 1 and Day 15 of the RCP. The participants who entered open-label period (OLP) received IV inebilizumab 300 mg on both Day 1 and Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant enters the OLP. Participants had choice to enter in the SFP at any point during RCP or OLP and were free to pursue other treatment options otherwise prohibited during the RCP and OLP. Participants continued in the SFP for 12 months from last dose of study drug.	

Serious adverse events	Total Inebilizumab	Total Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 174 (16.09%)	24 / 56 (42.86%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer female			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
Shock			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 174 (0.57%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pickwickian syndrome			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 174 (0.57%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
International normalised ratio increased			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Burns third degree			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			

subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis transverse			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	3 / 174 (1.72%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Optic neuritis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral nerve palsy			

subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post cardiac arrest syndrome			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unresponsive to stimuli			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic encephalopathy			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Deafness			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness unilateral			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Constipation			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis acute			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 174 (0.57%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 174 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Steroid withdrawal syndrome			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 174 (1.15%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 174 (0.57%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Connective tissue disorder			

subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 174 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 174 (1.72%)	3 / 56 (5.36%)	
occurrences causally related to treatment / all	1 / 5	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	3 / 174 (1.72%)	7 / 56 (12.50%)	
occurrences causally related to treatment / all	0 / 3	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chorioretinitis			

subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroborreliosis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 174 (0.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	0 / 174 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Total Inebilizumab	Total Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	164 / 174 (94.25%)	50 / 56 (89.29%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 174 (1.72%)	3 / 56 (5.36%)	
occurrences (all)	9	4	
Hypotension			
subjects affected / exposed	1 / 174 (0.57%)	3 / 56 (5.36%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 174 (6.90%)	3 / 56 (5.36%)	
occurrences (all)	16	3	
Influenza like illness			
subjects affected / exposed	3 / 174 (1.72%)	4 / 56 (7.14%)	
occurrences (all)	6	6	
Pyrexia			
subjects affected / exposed	7 / 174 (4.02%)	5 / 56 (8.93%)	
occurrences (all)	10	12	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 174 (8.62%)	6 / 56 (10.71%)	
occurrences (all)	18	15	
Psychiatric disorders			
Depression			
subjects affected / exposed	8 / 174 (4.60%)	6 / 56 (10.71%)	
occurrences (all)	8	6	
Insomnia			

subjects affected / exposed	10 / 174 (5.75%)	6 / 56 (10.71%)	
occurrences (all)	10	6	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	11 / 174 (6.32%)	3 / 56 (5.36%)	
occurrences (all)	18	3	
Infusion related reaction			
subjects affected / exposed	22 / 174 (12.64%)	9 / 56 (16.07%)	
occurrences (all)	44	16	
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 174 (3.45%)	3 / 56 (5.36%)	
occurrences (all)	6	3	
Headache			
subjects affected / exposed	27 / 174 (15.52%)	11 / 56 (19.64%)	
occurrences (all)	76	13	
Hypoaesthesia			
subjects affected / exposed	12 / 174 (6.90%)	2 / 56 (3.57%)	
occurrences (all)	24	3	
Paraesthesia			
subjects affected / exposed	12 / 174 (6.90%)	2 / 56 (3.57%)	
occurrences (all)	15	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 174 (6.32%)	4 / 56 (7.14%)	
occurrences (all)	12	4	
Eye disorders			
Dry eye			
subjects affected / exposed	4 / 174 (2.30%)	6 / 56 (10.71%)	
occurrences (all)	4	6	
Eye pain			
subjects affected / exposed	8 / 174 (4.60%)	5 / 56 (8.93%)	
occurrences (all)	27	5	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	3 / 174 (1.72%)	4 / 56 (7.14%)	
occurrences (all)	3	4	
Constipation			
subjects affected / exposed	9 / 174 (5.17%)	7 / 56 (12.50%)	
occurrences (all)	13	7	
Diarrhoea			
subjects affected / exposed	15 / 174 (8.62%)	8 / 56 (14.29%)	
occurrences (all)	19	10	
Gastritis			
subjects affected / exposed	3 / 174 (1.72%)	3 / 56 (5.36%)	
occurrences (all)	3	3	
Nausea			
subjects affected / exposed	11 / 174 (6.32%)	8 / 56 (14.29%)	
occurrences (all)	16	8	
Vomiting			
subjects affected / exposed	9 / 174 (5.17%)	5 / 56 (8.93%)	
occurrences (all)	11	7	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 174 (2.87%)	3 / 56 (5.36%)	
occurrences (all)	5	3	
Eczema			
subjects affected / exposed	4 / 174 (2.30%)	4 / 56 (7.14%)	
occurrences (all)	5	4	
Pruritus			
subjects affected / exposed	7 / 174 (4.02%)	6 / 56 (10.71%)	
occurrences (all)	7	6	
Rash			
subjects affected / exposed	6 / 174 (3.45%)	3 / 56 (5.36%)	
occurrences (all)	10	3	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	2 / 174 (1.15%)	3 / 56 (5.36%)	
occurrences (all)	2	3	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	28 / 174 (16.09%)	12 / 56 (21.43%)	
occurrences (all)	37	14	
Back pain			
subjects affected / exposed	24 / 174 (13.79%)	8 / 56 (14.29%)	
occurrences (all)	38	8	
Muscle spasms			
subjects affected / exposed	5 / 174 (2.87%)	4 / 56 (7.14%)	
occurrences (all)	8	6	
Muscular weakness			
subjects affected / exposed	4 / 174 (2.30%)	4 / 56 (7.14%)	
occurrences (all)	9	4	
Myalgia			
subjects affected / exposed	4 / 174 (2.30%)	3 / 56 (5.36%)	
occurrences (all)	4	5	
Pain in extremity			
subjects affected / exposed	11 / 174 (6.32%)	8 / 56 (14.29%)	
occurrences (all)	20	13	
Infections and infestations			
Bronchitis			
subjects affected / exposed	12 / 174 (6.90%)	5 / 56 (8.93%)	
occurrences (all)	13	6	
Conjunctivitis			
subjects affected / exposed	5 / 174 (2.87%)	3 / 56 (5.36%)	
occurrences (all)	6	5	
Influenza			
subjects affected / exposed	17 / 174 (9.77%)	4 / 56 (7.14%)	
occurrences (all)	20	10	
Nasopharyngitis			
subjects affected / exposed	38 / 174 (21.84%)	11 / 56 (19.64%)	
occurrences (all)	69	17	
Oral herpes			
subjects affected / exposed	5 / 174 (2.87%)	4 / 56 (7.14%)	
occurrences (all)	6	8	
Rhinitis			

subjects affected / exposed	9 / 174 (5.17%)	2 / 56 (3.57%)	
occurrences (all)	10	3	
Upper respiratory tract infection			
subjects affected / exposed	28 / 174 (16.09%)	10 / 56 (17.86%)	
occurrences (all)	51	15	
Urinary tract infection			
subjects affected / exposed	40 / 174 (22.99%)	20 / 56 (35.71%)	
occurrences (all)	77	54	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 174 (0.57%)	4 / 56 (7.14%)	
occurrences (all)	1	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2014	Changes were made to update Section 2.1.1 (Primary Objective) and Section 1.6.1 (Primary Hypothesis) as: revised participant population for the primary analysis to include both AQP4-IgG seropositive and seronegative participants; Section 2.2.1 (Primary Endpoint) as: revised the timeframe of the primary endpoint definition from Days 183 to 197 to coincide with increased length of RCP, extended by 2 weeks to account for 2-week oral corticosteroid use between Days 1 and 14; removed restriction that primary analysis will be based on AQP4-IgG seropositive participants. The changes were also made to Section 3.1.1 (Overview), Section 3.2.4.1 (Primary Endpoint), Section 4.1.2 (Inclusion Criteria), Section 4.2.1 (Enrollment/Screening Period), Section 4.2.2.1 (Randomized-controlled Treatment Period), and Section 4.2.2.2 (OLP)
10 December 2015	The majority of changes were to clarify text and tables. Some updates were made in response to scientific advice from the European Medicines Agency and others in response to updates to the Investigator's Brochure. Text in multiple sections was amended to clarify: • The eligibility of AQP4- IgG seronegative participants will be determined by an independent Ethics Committee to reflect actual practice. • Participants may exit the OLP at any time for any reason, including seeking alternative treatment options. • The study is event driven and enrollment of participants will stop when a total of 67 AC determined NMOSD attacks occur. • The study population may be increased up to 252 participants if the ratio of the cumulative number of AC-determined NMOSD attacks to participant ratio is approximately 27% or less. Also, changes are made to Protocol Synopsis, Section 3.1.1.1 (RCP), Section 4.1.2 (Inclusion Criteria), Section 4.1.3 (Exclusion Criteria), Section 4.2.4. (Managing Subjects With Worsening Attacks), Section 4.2.5 (Study Procedures for Attack Follow-up Visit), Section 4.8.2 (Sample Size and Power Calculations), and Section 5.2 (Definition of SAEs).
18 October 2016	This protocol amendment included text revisions to provide additional clarification for the following sections of the Protocol: Section 4.8.3.1 (Primary Analyses) and Section 4.8.3.2 (Additional Analyses of the Primary Endpoint): Based on feedback from FDA to allow a wider window for the statistical analysis of the primary endpoint to prevent valid attacks from being excluded from analysis; Section 4.8.10.2 (Futility Assessment) and Appendix 10 (Details of Futility Analysis): Text was clarified to provide further information on how the futility assessment will be performed.
08 March 2017	The primary reasons for changes included removal of the sample size reassessment (as agreed with the FDA) and the inclusion of clear guidance that stopping enrollment is event driven and based on the occurrence of 67 AC-determined NMOSD attacks or when 252 participants have been enrolled, whichever occurs first. In addition, the updates were included in Section 1.4 (Summary of Clinical Experience), Section 5.3 (Definition of adverse event of special interest), and Section 5.6.3 (progressive multifocal leukoencephalopathy).
16 July 2018	This amendment incorporates updates in definitions, processes for safety reporting, numerous administrative and personnel changes, and corrects existing errors. Changes are made in Synopsis, Section 3.1.1 (Overview), Section 3.1.1.1 (Screening Period), Section 4.1.1 (Number of Subjects), Section 4.2.1 (Enrollment/Screening Period), Section 4.8.2 (Sample Size and Power Calculations), Section 4.1.3 (Exclusion Criteria), Section 4.2.2.1 (RCP), Table 6 (Schedule of RCP Study Procedures), Section 4.2.2.2 (OLP), Table 7 (Schedule of OLP Study Procedures), Section 4.5.1.2 (Treatment Administration), Section 4.3.1.2 (Neuroaxis MRI Scan), Section 4.7.2 (Prohibited Concomitant Medications), and Section 5.6.2 (Hepatic Function Abnormality).

11 October 2018	The primary purpose of this amendment was to make changes to the protocol based on the recommendations from the Independent Data Monitoring Committee, based on evidence of efficacy and safety, to stop study enrollment and allow participants in the RCP at that time the option to enter the OLP. In addition, minor copy-editing and formatting issues were corrected throughout the document. Changes to the protocol reflecting the change above were made throughout the protocol (Synopsis, Sections 3.1, 4.2, 4.4, 4.5, 4.8, and 6.3, and Table 2).

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.

No participant from 'Inebilizumab /Inebilizumab' and 1 participant from 'Placebo/Inebilizumab' rolled over to SFP. A study period with 0 participants started in any arm is not acceptable (EudraCT limitation); so, not included SFP in 'Disposition.

Notes: