Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Satralizumab (SA237) as Monotherapy in Patients With Neuromyelitis Optica (NMO) and Neuromyelitis Optica Spectrum Disorder (NMOSD)

Summary

EudraCT number	2015-005431-41
Trial protocol	PL RO HR
Global end of trial date	31 January 2022

Results information

Result version number	v2 (current)
This version publication date	20 February 2023
First version publication date	27 September 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BN40900

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02073279
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	31 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2022
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 evaluate the efficacy of satralizumab monotherapy compared with placebo in participants with NMO and NMOSD. In addition, safety, pharmacodynamics (PD), pharmacokinetics (PK), and immunogenicity of satralizumab were evaluated.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 August 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Georgia: 1
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Malaysia: 1
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Ukraine: 10
Country: Number of subjects enrolled	United States: 47
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Romania: 1
Worldwide total number of subjects	95
EEA total number of subjects	15

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)	94
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The Double-blind (DB) period lasted up to the primary clinical cut-off date (CCOD: 12 Oct 2018) when the study reached 1.5 years since the date of randomization of the last participant enrolled.
The Open Label Period lasted up to clinical cut-off date (31-Jan-2022).

Pre-assignment

Screening details:

Participants with neuromyelitis optica (NMO) or NMO spectrum disorder (NMOSD) were randomized 2:1 to receive either satralizumab 120 mg or matching placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo, then Satralizumab

Arm description:

Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period up to protocol-defined relapse. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD). At the CCOD, participants who had not experienced a relapse during the DB period were invited to initiate satralizumab 120 mg SC injection (at Weeks 0, 2 and 4, and Q4W thereafter) after 4 weeks from their last study treatment dose in the DB period.

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

Dosage and administration details:

Placebo was administered subcutaneously (SC) at Weeks 0, 2, and 4, and thereafter once every 4 weeks.

Arm title	Satralizumab, then Satralizumab

Arm description:

Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period. All OLE participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter.

Arm type	Experimental
Investigational medicinal product name	Satralizumab
Investigational medicinal product code	
Other name	SA237
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Satralizumab was administered SC at Weeks 0, 2, and 4, and thereafter once every 4 weeks.

Number of subjects in period 1	Placebo, then Satralizumab	Satralizumab, then Satralizumab
Started	32	63
Completed	28	56
Not completed	4	7
Consent withdrawn by subject	2	2
Adverse event, non-fatal	1	1
Ongoing in study	1	2
Switched to another treatment	-	1
Protocol deviation	-	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo, then Satralizumab

Arm description:

Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period up to protocol-defined relapse. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD). At the CCOD, participants who had not experienced a relapse during the DB period were invited to initiate satralizumab 120 mg SC injection (at Weeks 0, 2 and 4, and Q4W thereafter) after 4 weeks from their last study treatment dose in the DB period.

Arm type	Placebo
Investigational medicinal product name	Satralizumab
Investigational medicinal product code	
Other name	SA237
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Satralizumab was administered SC at Weeks 0, 2, and 4, and thereafter once every 4 weeks.

Arm title	Satralizumab, then Satralizumab

Arm description:

Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period. All OLE participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter.

Arm type	Experimental

Investigational medicinal product name	Satralizumab
Investigational medicinal product code	
Other name	SA237
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Satralizumab was administered SC at Weeks 0, 2, and 4, and thereafter once every 4 weeks.

Number of subjects in period 2	Placebo, then Satralizumab	Satralizumab, then Satralizumab
Started	28	56
Completed	21	41
Not completed	7	15
Consent withdrawn by subject	4	5
Adverse event, non-fatal	1	-
Switched to another treatment	1	4
Lost to follow-up	-	4
Refused Treatment/Did Not Cooperate	-	1
Lack of efficacy	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo, then Satralizumab
Reporting group description:	
Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period up to protocol-defined relapse. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD). At the CCOD, participants who had not experienced a relapse during the DB period were invited to initiate satralizumab 120 mg SC injection (at Weeks 0, 2 and 4, and Q4W thereafter) after 4 weeks from their last study treatment dose in the DB period.	
Reporting group title	Satralizumab, then Satralizumab
Reporting group description:	
Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period. All OLE participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter.	

Reporting group values	Placebo, then Satralizumab	Satralizumab, then Satralizumab	Total
Number of subjects	32	63	95
Age categorical Units: Subjects			
Adults (18-64 years)	32	62	94
From 65-84 years	0	1	1
Age Continuous Units: Years			
arithmetic mean	40.5	45.3	
standard deviation	± 10.5	± 12.0	-
Sex: Female, Male Units: Participants			
Male	1	17	18
Female	31	46	77

End points

End points reporting groups

Reporting group title	Placebo, then Satralizumab

Reporting group description:

Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period up to protocol-defined relapse. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD). At the CCOD, participants who had not experienced a relapse during the DB period were invited to initiate satralizumab 120 mg SC injection (at Weeks 0, 2 and 4, and Q4W thereafter) after 4 weeks from their last study treatment dose in the DB period.

Reporting group title	Satralizumab, then Satralizumab

Reporting group description:

Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period. All OLE participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter.

Reporting group title	Placebo, then Satralizumab

Reporting group description:

Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period up to protocol-defined relapse. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD). At the CCOD, participants who had not experienced a relapse during the DB period were invited to initiate satralizumab 120 mg SC injection (at Weeks 0, 2 and 4, and Q4W thereafter) after 4 weeks from their last study treatment dose in the DB period.

Reporting group title	Satralizumab, then Satralizumab

Reporting group description:

Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period. All OLE participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter.

Primary: Time to First Protocol-Defined Relapse (TFR) in the Double-Blind (DB) Period

End point title	Time to First Protocol-Defined Relapse (TFR) in the Double-Blind (DB) Period

End point description:

TFR is time from randomization to first occurrence of relapse in the DB period. Protocol-defined relapse was occurrence of new/worsening neurological symptoms attributable to NMO/NMOSD. Symptoms persisted for >24 hours and not attributable to confounding clinical factors (e.g., fever, infection, injury, change in mood, adverse reactions to medications). New/worsening neurological symptoms that occurred < 31 days following onset of a protocol-defined relapse were considered part of same relapse (2 relapses with onset days in 30 days of one another was counted as 1 relapse), onset date used in analysis was the date of first relapse. Intent-to-treat (ITT) population: all randomized participants. 999999=upper limit of CI was not reached due to low number of participants with events. 99999=median was not reached due to low number of participants with events.

End point type	Primary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: weeks				
median (confidence interval 95%)	128.3 (29.9 to 999999)	99999 (135.7 to 999999)		

Statistical analyses

Statistical analysis title	Satralizumab versus Placebo
Statistical analysis description:	
Stratified by prior therapy (B-cell depleting therapy or immunosuppressants/others) and most recent attack (first attack or relapse).	
Comparison groups	Placebo, then Satralizumab v Satralizumab, then Satralizumab
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0184
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.89

Secondary: Change in Visual Analogue Scale (VAS) for Pain from Baseline to Week 24

End point title	Change in Visual Analogue Scale (VAS) for Pain from Baseline to Week 24
End point description:	
The VAS is a subjective measure of pain consisting of a 100 mm line with two endpoints representing 0 = "no pain" and 100 = "pain as bad as it could be". Participants rated their pain by placing a mark on the line corresponding to their current level of pain. The distance along the line from the "no pain" marker was measured with a ruler giving a pain score out of 100. A higher score indicated more pain and lower scores reflected a better health state. A negative change from baseline indicates an improvement. ANCOVA was used for analysis to report the adjusted mean and standard error (SE). ITT population included all participants randomized to the treatment groups. Missing data were imputed by BOCF method.	
End point type	Secondary
End point timeframe:	
Baseline, Week 24	

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard error)				
Baseline (n=32, 62)	27.563 (± 5.438)	31.661 (± 3.665)		
Change from Baseline to Week 24 (n=32, 62)	-5.949 (± 4.832)	-2.735 (± 4.260)		

Statistical analyses

Statistical analysis title	Satralizumab versus Placebo
Comparison groups	Placebo, then Satralizumab v Satralizumab, then Satralizumab
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4436 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.215
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.086
upper limit	11.515
Variability estimate	Standard error of the mean
Dispersion value	4.178

Notes:

[1] - ANCOVA model: treatment group as fixed effect and baseline measurements, prior therapy, most recent attack (first attack/relapse) as covariates.

Secondary: Change in Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale from Baseline to Week 24

End point title	Change in Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale from Baseline to Week 24

End point description:

The FACIT Fatigue scale is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days. As each of the 13 items of the scale ranges from 0-4, the range of possible scores was computed using FACIT scoring algorithm as 0-52, where 0 is the worst possible score and 52 the best which indicated less fatigue. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. Missing data were imputed by BOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard error)				
Baseline (n=32, 62)	29.656 (± 2.280)	30.590 (± 1.492)		
Change from Baseline to Week 24 (n=32, 62)	3.602 (± 1.820)	5.709 (± 1.610)		

Statistical analyses

Statistical analysis title	Satralizumab versus Placebo
Comparison groups	Placebo, then Satralizumab v Satralizumab, then Satralizumab
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1824 [2]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.107
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.008
upper limit	5.221
Variability estimate	Standard error of the mean
Dispersion value	1.567

Notes:

[2] - ANCOVA model: treatment group as fixed effect and baseline measurements, prior therapy, most recent attack (first attack/relapse) as covariates.

Secondary: Relapse-Free Rate During the DB Period

End point title	Relapse-Free Rate During the DB Period

End point description:

Protocol-defined relapse was occurrence of new or worsening neurological symptoms attributable to neurological neuromyelitis optica (NMO) or neuromyelitis optica spectrum disorder (NMOSD). Symptoms had to persist for >24 hours and not be attributable to confounding clinical factors (e.g., fever, infection, injury, change in mood, adverse reactions to medications). New or worsening neurological symptoms that occurred < 31 days following onset of a protocol-defined relapse were considered part of same relapse (i.e., if 2 relapses had onset days that were 30 days of one another, they were counted only as 1 relapse), and onset date used in analysis was the date of first relapse. ITT population included all participants randomized to the treatment groups. 6666= 0 participants.

End point type	Secondary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	56		
Units: percentage				
number (not applicable)				
Week 12 (n=23, 56)	74.87	88.89		
Week 24 (n=22, 54)	71.61	85.71		
Week 36 (n=19, 49)	61.85	79.37		
Week 48 (n=19, 46)	61.85	76.13		
Week 72 (n=13, 43)	51.21	74.40		
Week 96 (n=9, 30)	51.21	72.14		
Week 120 (n=3, 16)	51.21	72.14		
Week 144 (n=2, 12)	34.14	62.80		
Week 168 (n=1, 10)	34.14	62.80		
Week 192 (n=1, 3)	34.14	62.80		
Week 216 (n=1, 0)	34.14	6666		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Relapse Rate (ARR) During the DB Period

End point title	Annualized Relapse Rate (ARR) During the DB Period

End point description:

The ARR is calculated as the total number participants with relapses experienced divided by the patient-years at risk. Protocol-defined relapse was occurrence of new/worsening neurological symptoms attributable to neurological NMO/NMOSD. Symptoms persisted for >24 hours and not attributable to confounding clinical factors (e.g., fever, infection, injury, change in mood, adverse reactions to medications). New/worsening neurological symptoms that occurred < 31 days following onset of a protocol-defined relapse were considered part of same relapse (2 relapses with onset days in 30 days of one another was counted as 1 relapse), onset date used in analysis was the date of first relapse. ITT population included all participants randomized to the treatment groups.

End point type	Secondary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: patients w relapse/patient-years at risk				
number (confidence interval 95%)	0.41 (0.24 to	0.17 (0.10 to		

0.67)	0.26)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Short Form Generic Health Survey (SF-36) Bodily Pain Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Short Form Generic Health Survey (SF-36) Bodily Pain Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	42.86 (± 11.28)	43.20 (± 11.08)		
Change from Baseline at Week 24 (n=20, 54)	-0.89 (± 8.35)	-0.13 (± 8.09)		
Change from Baseline at Week 48 (n=18, 46)	1.75 (± 5.42)	1.36 (± 8.89)		
Change from Baseline at Week 72 (n=13, 43)	3.19 (± 8.04)	0.91 (± 9.23)		
Change from Baseline at Week 96 (n=8, 31)	3.43 (± 5.60)	2.38 (± 7.82)		
Change from Baseline at Week 120 (n=3, 16)	0.00 (± 8.07)	0.53 (± 6.21)		
Change from Baseline at Week 144 (n=2, 12)	-2.22 (± 8.84)	2.59 (± 6.66)		
Change from Baseline at Week 168 (n=1, 10)	0.80 (± 9999)	4.19 (± 7.01)		
Change from Baseline at Week 192 (n=1, 2)	-8.47 (± 9999)	0 (± 0)		
Change from Baseline at Week 216 (n=1, 0)	-12.50 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 General Health Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 General Health Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants analyzed for the time point.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	39.43 (± 9.50)	39.72 (± 10.41)		
Change from Baseline at Week 24 (n=20, 54)	-0.52 (± 9.96)	0.49 (± 6.46)		
Change from Baseline at Week 48 (n=18, 46)	1.85 (± 9.72)	1.01 (± 7.61)		
Change from Baseline at Week 72 (n=13, 43)	4.83 (± 12.41)	3.21 (± 6.57)		
Change from Baseline at Week 96 (n=8, 31)	6.60 (± 9.10)	3.45 (± 6.42)		
Change from Baseline at Week 120 (n=3, 16)	8.72 (± 13.55)	3.60 (± 7.02)		
Change from Baseline at Week 144 (n=2, 12)	5.23 (± 14.11)	2.82 (± 8.00)		
Change from Baseline at Week 168 (n=1, 10)	-7.13 (± 9999)	5.04 (± 9.45)		
Change from Baseline at Week 192 (n=1, 2)	-4.75 (± 9999)	8.32 (± 11.77)		
Change from Baseline at Week 216 (n=1, 0)	-4.75 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Mental Health Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Mental Health Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	42.86 (± 12.69)	46.78 (± 10.10)		
Change from Baseline at Week 24 (n=20, 54)	0.79 (± 9.02)	1.84 (± 7.05)		
Change from Baseline at Week 48 (n=18, 46)	-0.58 (± 7.32)	2.67 (± 7.89)		
Change from Baseline at Week 72 (n=13, 43)	2.62 (± 6.32)	1.95 (± 7.85)		
Change from Baseline at Week 96 (n=8, 31)	-3.60 (± 6.08)	2.36 (± 7.38)		
Change from Baseline at Week 120 (n=3, 16)	-2.62 (± 6.92)	0.82 (± 10.32)		
Change from Baseline at Week 144 (n=2, 12)	1.31 (± 1.85)	2.83 (± 9.43)		
Change from Baseline at Week 168 (n=1, 10)	5.23 (± 9999)	2.62 (± 8.89)		
Change from Baseline at Week 192 (n=1, 2)	-13.08 (± 9999)	-3.93 (± 12.95)		
Change from Baseline at Week 216 (n=1, 0)	-2.62 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Physical Functioning Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Physical Functioning Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	38.70 (± 12.24)	39.48 (± 10.99)		
Change from Baseline at Week 24 (n=20, 54)	2.20 (± 4.62)	1.96 (± 6.12)		
Change from Baseline at Week 48 (n=18, 46)	2.34 (± 6.90)	3.33 (± 6.76)		
Change from Baseline at Week 72 (n=13, 43)	6.62 (± 9.71)	2.99 (± 6.94)		
Change from Baseline at Week 96 (n=8, 31)	5.50 (± 9.62)	3.59 (± 7.49)		
Change from Baseline at Week 120 (n=3, 16)	7.01 (± 8.63)	1.94 (± 8.05)		
Change from Baseline at Week 144 (n=2, 12)	4.79 (± 9.48)	3.19 (± 10.87)		
Change from Baseline at Week 168 (n=1, 10)	1.91 (± 9999)	-0.96 (± 8.62)		
Change from Baseline at Week 192 (n=1, 2)	-1.92 (± 9999)	4.78 (± 4.06)		
Change from Baseline at Week 216 (n=1, 0)	-3.83 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Role-Emotional Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Role-Emotional Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	42.24 (± 13.09)	42.07 (± 13.62)		
Change from Baseline at Week 24 (n=20, 54)	-1.57 (± 15.67)	3.87 (± 11.27)		
Change from Baseline at Week 48 (n=18, 46)	0.78 (± 8.57)	2.73 (± 10.30)		
Change from Baseline at Week 72 (n=13, 43)	4.55 (± 7.96)	3.89 (± 9.22)		
Change from Baseline at Week 96 (n=8, 31)	3.05 (± 11.98)	1.12 (± 11.87)		
Change from Baseline at Week 120 (n=3, 16)	-12.77 (± 14.07)	1.31 (± 14.04)		
Change from Baseline at Week 144 (n=2, 12)	-12.19 (± 17.23)	1.74 (± 13.40)		
Change from Baseline at Week 168 (n=1, 10)	0.00 (± 9999)	-0.35 (± 11.89)		
Change from Baseline at Week 192 (n=1, 2)	-13.93 (± 9999)	-3.49 (± 4.93)		
Change from Baseline at Week 216 (n=1, 0)	-10.45 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Role-Physical Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Role-Physical Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	37.86 (± 11.28)	37.43 (± 11.55)		
Change from Baseline at Week 24 (n=20, 54)	3.14 (± 9.92)	3.52 (± 8.38)		
Change from Baseline at Week 48 (n=18, 46)	4.12 (± 7.24)	5.01 (± 8.25)		
Change from Baseline at Week 72 (n=13, 43)	5.70 (± 7.65)	4.59 (± 8.56)		
Change from Baseline at Week 96 (n=8, 31)	5.62 (± 6.35)	4.83 (± 8.31)		
Change from Baseline at Week 120 (n=3, 16)	2.25 (± 8.99)	3.18 (± 9.46)		
Change from Baseline at Week 144 (n=2, 12)	-3.37 (± 11.12)	2.43 (± 8.80)		
Change from Baseline at Week 168 (n=1, 10)	0.00 (± 9999)	0.00 (± 9.10)		
Change from Baseline at Week 192 (n=1, 2)	-6.74 (± 9999)	4.49 (± 6.35)		
Change from Baseline at Week 216 (n=1, 0)	-17.97 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Social Role Functioning Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Social Role Functioning Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	42.93 (± 13.22)	41.01 (± 11.66)		
Change from Baseline at Week 24 (n=20, 54)	1.76 (± 12.42)	2.42 (± 9.63)		
Change from Baseline at Week 48 (n=18, 46)	0.56 (± 10.59)	2.62 (± 8.17)		
Change from Baseline at Week 72 (n=13, 43)	0.39 (± 11.66)	3.96 (± 7.93)		
Change from Baseline at Week 96 (n=8, 31)	0.63 (± 1.77)	3.56 (± 7.89)		
Change from Baseline at Week 120 (n=3, 16)	-5.01 (± 13.26)	0.31 (± 8.48)		
Change from Baseline at Week 144 (n=2, 12)	7.52 (± 10.63)	3.76 (± 14.68)		
Change from Baseline at Week 168 (n=1, 10)	-5.01 (± 9999)	-1.50 (± 7.86)		
Change from Baseline at Week 192 (n=1, 2)	-5.01 (± 9999)	-2.51 (± 3.54)		
Change from Baseline at Week 216 (n=1, 0)	0.00 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Vitality Domain Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Vitality Domain Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health component summary measures and a preference-based health utility index. The domain scores were transformed to a 0-100 scale, where higher scores indicate better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	40.72 (± 11.86)	46.02 (± 10.58)		
Change from Baseline at Week 24 (n=20, 54)	1.49 (± 10.22)	2.33 (± 8.29)		
Change from Baseline at Week 48 (n=18, 46)	4.79 (± 9.07)	4.15 (± 7.49)		
Change from Baseline at Week 72 (n=13, 43)	3.43 (± 9.38)	3.68 (± 6.43)		
Change from Baseline at Week 96 (n=8, 31)	0.00 (± 7.94)	4.34 (± 9.39)		
Change from Baseline at Week 120 (n=3, 16)	-1.98 (± 11.24)	3.96 (± 9.94)		
Change from Baseline at Week 144 (n=2, 12)	-9.41 (± 7.70)	4.95 (± 7.95)		
Change from Baseline at Week 168 (n=1, 10)	-5.94 (± 9999)	5.05 (± 6.58)		
Change from Baseline at Week 192 (n=1, 2)	-11.88 (± 9999)	0.00 (± 8.40)		
Change from Baseline at Week 216 (n=1, 0)	-11.88 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Mental Component Summary Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Mental Component Summary Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health summary measures and a preference-based health utility index. The component scores were transformed to a 0-100 scale, where higher score indicates better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	44.03 (± 13.93)	46.43 (± 11.55)		
Change from Baseline at Week 24 (n=20, 54)	-0.28 (± 11.19)	2.89 (± 8.96)		
Change from Baseline at Week 48 (n=18, 46)	0.09 (± 8.96)	2.63 (± 8.04)		
Change from Baseline at Week 72 (n=13, 43)	1.54 (± 8.18)	3.17 (± 7.70)		
Change from Baseline at Week 96 (n=8, 31)	-2.65 (± 6.05)	1.91 (± 9.32)		
Change from Baseline at Week 120 (n=3, 16)	-10.65 (± 11.99)	1.03 (± 12.92)		
Change from Baseline at Week 144 (n=2, 12)	-5.40 (± 8.41)	2.98 (± 12.99)		
Change from Baseline at Week 168 (n=1, 10)	-0.61 (± 9999)	1.63 (± 11.86)		
Change from Baseline at Week 192 (n=1, 2)	-14.38 (± 9999)	-5.88 (± 7.54)		
Change from Baseline at Week 216 (n=1, 0)	-4.22 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Physical Component Summary Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in SF-36 Physical Component Summary Scores at 24 Week Intervals During the DB Period

End point description:

The SF-36v2 is a multi-purpose, short form health survey with 36 questions. It has 8 domains (vitality, physical functioning, bodily pain, general health, role-physical, role emotional, social role functioning and mental health) of functional health and well-being scores as well as psychometrically based physical and mental health summary measures and a preference-based health utility index. The component scores were transformed to a 0-100 scale, where higher score indicates better quality of life. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	38.89 (± 11.20)	38.59 (± 9.68)		
Change from Baseline at Week 24 (n=20, 54)	1.78 (± 4.99)	1.05 (± 6.14)		
Change from Baseline at Week 48 (n=18, 46)	3.57 (± 4.94)	2.85 (± 4.90)		
Change from Baseline at Week 72 (n=13, 43)	5.68 (± 7.32)	2.87 (± 6.80)		
Change from Baseline at Week 96 (n=8, 31)	7.25 (± 7.08)	4.20 (± 5.90)		
Change from Baseline at Week 120 (n=3, 16)	8.95 (± 8.51)	2.68 (± 8.72)		
Change from Baseline at Week 144 (n=2, 12)	3.18 (± 10.67)	2.89 (± 7.11)		
Change from Baseline at Week 168 (n=1, 10)	-2.00 (± 9999)	1.83 (± 10.96)		
Change from Baseline at Week 192 (n=1, 2)	-1.79 (± 9999)	7.24 (± 3.35)		
Change from Baseline at Week 216 (n=1, 0)	-10.84 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EuroQoL-5 Dimensions (EQ-5D) Index Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in EuroQoL-5 Dimensions (EQ-5D) Index Scores at 24 Week Intervals During the DB Period

End point description:

The EQ-5D is a participant-answered questionnaire measuring 5 dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression with 3 possible response categories: 1) no problems; 2) some problems; 3) severe problems. The scores from 5 dimensions are used as input to generate EQ-5D index score using scoring algorithm. The EQ-5D index score is scored on a scale of -0.2 to 1. A higher score reflects a better health state. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	0.7153 (± 0.2253)	0.6881 (± 0.2040)		
Change from Baseline at Week 24 (n=20, 53)	0.0031 (± 0.1602)	0.0188 (± 0.1812)		
Change from Baseline at Week 48 (n=18, 45)	0.0016 (± 0.1176)	0.0244 (± 0.1571)		
Change from Baseline at Week 72 (n=12, 42)	0.0582 (± 0.1498)	0.0238 (± 0.1323)		
Change from Baseline at Week 96 (n=8, 30)	0.0447 (± 0.1508)	0.0460 (± 0.1067)		
Change from Baseline at Week 120 (n=3, 16)	-0.0288 (± 0.1908)	0.0099 (± 0.1636)		
Change from Baseline at Week 144 (n=2, 12)	-0.1001 (± 0.1416)	0.0063 (± 0.2299)		
Change from Baseline at Week 168 (n=1, 10)	0.0000 (± 9999)	-0.0261 (± 0.2532)		
Change from Baseline at Week 192 (n=1, 2)	-0.2002 (± 9999)	0.0299 (± 0.0423)		
Change from Baseline at Week 216 (n=1, 0)	-0.2002 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Speed of Timed 25-Foot Walk (T25W) at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Speed of Timed 25-Foot Walk (T25W) at 24 Week Intervals During the DB Period

End point description:

The T25W is an assessment of walking ability. The time (in seconds) that the participant took to walk 25 feet was measured. Speed is calculated as 1/Timed 25-Foot Walk where time is measured in seconds. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	63		
Units: 1/seconds				
arithmetic mean (standard deviation)				
Baseline (n=29, 63)	0.1442 (± 0.0793)	0.1355 (± 0.0561)		
Change from Baseline at Week 24 (n=19, 53)	0.0030 (± 0.0374)	0.0040 (± 0.0225)		
Change from Baseline at Week 48 (n=16, 45)	0.0142 (± 0.0493)	0.0115 (± 0.0306)		
Change from Baseline at Week 72 (n=11, 43)	0.0205 (± 0.0531)	0.0071 (± 0.0257)		
Change from Baseline at Week 96 (n=6, 31)	-0.0031 (± 0.0251)	0.0081 (± 0.0253)		
Change from Baseline at Week 120 (n=3, 16)	0.0489 (± 0.0301)	0.0063 (± 0.0386)		
Change from Baseline at Week 144 (n=2, 12)	0.0388 (± 0.0572)	0.0003 (± 0.0443)		
Change from Baseline at Week 168 (n=1, 9)	-0.0656 (± 9999)	-0.0155 (± 0.0379)		
Change from Baseline at Week 192 (n=1, 2)	-0.0812 (± 9999)	-0.0304 (± 0.0360)		
Change from Baseline at Week 216 (n=1, 0)	-0.0917 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Modified Rankin Scale (mRS) Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Modified Rankin Scale (mRS) Scores at 24 Week Intervals During the DB Period

End point description:

The mRS is a 7-point disability scale that assesses the degree of disability in participants with neurological impairment. Possible scores range from 0 (no symptoms at all) up to 6 (death). Higher scores reflect increased disability. A negative change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 63)	1.66 (± 1.00)	1.97 (± 0.98)		
Change from Baseline at Week 24 (n=19, 54)	-0.05 (± 0.40)	-0.04 (± 0.64)		
Change from Baseline at Week 48 (n=17, 46)	0.00 (± 0.94)	-0.13 (± 0.78)		
Change from Baseline at Week 72 (n=13, 43)	-0.08 (± 1.04)	-0.12 (± 0.63)		
Change from Baseline at Week 96 (n=8, 31)	-0.38 (± 0.74)	-0.42 (± 0.99)		
Change from Baseline at Week 120 (n=3, 16)	-1.00 (± 0.00)	-0.13 (± 0.81)		
Change from Baseline at Week 144 (n=2, 11)	-1.00 (± 1.41)	-0.09 (± 0.54)		
Change from Baseline at Week 168 (n=0, 10)	6666 (± 6666)	0.00 (± 0.67)		
Change from Baseline at Week 192 (n=1, 2)	-1.00 (± 9999)	-0.50 (± 2.12)		
Change from Baseline at Week 216 (n=1, 0)	-1.00 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Zarit Burden Interview (ZBI) Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Zarit Burden Interview (ZBI) Scores at 24 Week Intervals During the DB Period

End point description:

The ZBI is the measurement to assess caregiver burden. The 22 items ask for the strain caregivers perceive. Responses range from 0 (never) to 4 (nearly always). The overall ZBI score ranges from 0 to 88. The higher the total score, the heavier the perceived burden. A negative change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 120

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=7, 8)	19.43 (± 12.19)	11.32 (± 7.20)		
Change from Baseline at Week 24 (n=6, 4)	0.00 (± 6.20)	1.50 (± 9.68)		
Change from Baseline at Week 48 (n=6, 2)	-2.83 (± 6.11)	-3.00 (± 9.90)		
Change from Baseline at Week 72 (n=3, 1)	-5.00 (± 3.00)	-13.00 (± 9999)		
Change from Baseline at Week 96 (n=2, 0)	-1.00 (± 7.07)	6666 (± 6666)		
Change from Baseline at Week 120 (n=1, 0)	4.00 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Expanded Disability Status Scale (EDSS) Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Expanded Disability Status Scale (EDSS) Scores at 24 Week Intervals During the DB Period

End point description:

The EDSS is an ordinal scale with values from 0 points (normal neurological examination) to 10 points (death) increasing in half-point increments once an EDSS of 1.0 has been reached. Higher scores represent increased disability. A negative change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline (n=32, 63)	3.66 (± 1.61)	3.92 (± 1.50)		
Change from Baseline at Week 24 (n=20, 53)	-0.03 (± 0.38)	-0.24 (± 0.71)		
Change from Baseline at Week 48 (n=18, 46)	-0.06 (± 0.42)	-0.32 (± 0.65)		
Change from Baseline at Week 72 (n=12, 42)	0.21 (± 0.58)	-0.29 (± 0.76)		
Change from Baseline at Week 96 (n=8, 29)	-0.50 (± 0.76)	-0.03 (± 0.48)		
Change from Baseline at Week 120 (n=3, 16)	-0.50 (± 0.87)	-0.22 (± 0.91)		
Change from Baseline at Week 144 (n=2, 11)	-1.00 (± 0.71)	0.18 (± 0.68)		
Change from Baseline at Week 168 (n=1, 10)	-0.50 (± 9999)	-0.15 (± 1.13)		
Change from Baseline at Week 192 (n=1, 2)	0.00 (± 9999)	0.25 (± 1.06)		
Change from Baseline at Week 216 (n=1, 0)	-0.50 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Visual Acuity (Snellen Chart) at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Visual Acuity (Snellen Chart) at 24 Week Intervals During the DB Period

End point description:

Visual acuity was measured using Snellen 20-foot wall chart and then converted to logMAR visual acuity scoring. Lower values indicate better visual acuity. Data are reported for right eye (OD) and left eye (OS). A negative change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline: OD (n=32, 63)	0.560 (± 0.903)	0.449 (± 0.712)		
Baseline: OS (n=32, 63)	0.456 (± 0.811)	0.545 (± 0.836)		
Change from Baseline at Week 24: OD (n=20, 53)	-0.058 (± 0.512)	0.039 (± 0.434)		
Change from Baseline at Week 24: OS (n=20, 53)	0.046 (± 0.242)	-0.001 (± 0.500)		
Change from Baseline at Week 48: OD (n=18, 46)	-0.027 (± 0.097)	0.053 (± 0.434)		
Change from Baseline at Week 48: OS (n=18, 46)	0.050 (± 0.252)	-0.006 (± 0.591)		
Change from Baseline at Week 72: OD (n=12, 42)	-0.050 (± 0.140)	-0.056 (± 0.260)		
Change from Baseline at Week 72: OS (n=12, 42)	-0.083 (± 0.595)	-0.101 (± 0.492)		
Change from Baseline at Week 96: OD (n=8, 29)	-0.045 (± 0.099)	-0.081 (± 0.580)		
Change from Baseline at Week 96: OS (n=8, 29)	-0.260 (± 0.707)	-0.121 (± 0.571)		
Change from Baseline at Week 120: OD (n=3, 16)	-0.027 (± 0.142)	-0.039 (± 0.637)		
Change from Baseline at Week 120: OS (n=3, 15)	0.000 (± 0.000)	-0.229 (± 0.754)		
Change from Baseline at Week 144: OD (n=2, 11)	0.010 (± 0.127)	0.149 (± 0.618)		
Change from Baseline at Week 144: OS (n=2, 11)	0.000 (± 0.000)	-0.280 (± 0.846)		
Change from Baseline at Week 168: OD (n=1, 10)	-0.080 (± 9999)	0.134 (± 0.663)		
Change from Baseline at Week 168: OS (n=1, 10)	-0.100 (± 9999)	-0.320 (± 0.910)		
Change from Baseline at Week 192: OD (n=1, 2)	-0.180 (± 9999)	-0.110 (± 0.156)		
Change from Baseline at Week 192: OS (n=1, 2)	0.080 (± 9999)	-0.050 (± 0.071)		
Change from Baseline at Week 216: OD (n=1, 0)	-0.180 (± 9999)	6666 (± 6666)		
Change from Baseline at Week 216: OS (n=1, 0)	-0.100 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Visual Function (Low-Contrast Sloan Letter Chart [LCSLC]) Scores at 24 Week Intervals During the DB Period

End point title	Change from Baseline in Visual Function (Low-Contrast Sloan Letter Chart [LCSLC]) Scores at 24 Week Intervals During the DB Period

End point description:

The LCSLC evaluates the visual function and captures the minimum size at which individuals can perceive letters of a particular contrast level. The change in binocular visual acuity, as assessed by the number of letters read correctly from a distance of 2 meters on 100%, 2.5% and 1.25% contrast level Sloan letter charts, was analyzed. The LCSLC is scored on a scale of 0-60. Higher scores indicate better visual function. A positive change from baseline indicates an improvement. ITT population included all participants randomized to the treatment groups. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	60		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline: 100% CHART (n=29, 60)	44.3 (± 16.1)	44.4 (± 16.3)		
Baseline: 2.5% CHART (n=29, 60)	24.6 (± 16.2)	22.6 (± 15.6)		
Baseline: 1.25% CHART (n=29, 60)	17.5 (± 15.7)	14.9 (± 14.8)		
Change at Week 24: 100% CHART (n=19, 49)	0.5 (± 7.1)	2.0 (± 5.3)		
Change at Week 24: 2.5% CHART (n=19, 49)	-2.8 (± 9.1)	1.7 (± 7.1)		
Change at Week 24: 1.25% CHART (n=19, 49)	-4.2 (± 11.9)	0.1 (± 7.5)		
Change at Week 48: 100% CHART (n=16, 43)	-3.4 (± 8.7)	1.3 (± 6.1)		
Change at Week 48: 2.5% CHART (n=15, 43)	1.5 (± 6.1)	4.0 (± 9.2)		
Change at Week 48: 1.25% CHART (n=15, 43)	1.7 (± 11.3)	4.1 (± 9.3)		
Change at Week 72: 100% CHART (n=11, 41)	0.3 (± 5.9)	2.8 (± 7.3)		
Change at Week 72: 2.5% CHART (n=11, 41)	-0.6 (± 8.6)	2.6 (± 7.5)		
Change at Week 72: 1.25% CHART (n=11, 41)	-2.4 (± 8.3)	0.4 (± 10.6)		
Change at Week 96: 100% CHART (n=7, 28)	3.3 (± 13.2)	2.1 (± 12.4)		
Change at Week 96: 2.5% CHART (n=7, 28)	2.6 (± 20.1)	2.3 (± 10.8)		
Change at Week 96: 1.25% CHART (n=7, 28)	-3.4 (± 11.3)	-0.5 (± 11.3)		
Change at Week 120: 100% CHART (n=3, 14)	-1.0 (± 1.0)	1.5 (± 10.6)		
Change at Week 120: 2.5% CHART (n=3, 14)	3.7 (± 4.6)	2.1 (± 7.3)		
Change at Week 120: 1.25% CHART (n=3, 14)	-2.0 (± 5.0)	1.6 (± 9.1)		
Change at Week 144: 100% CHART (n=2, 10)	-3.5 (± 2.1)	0.4 (± 7.7)		
Change at Week 144: 2.5% CHART (n=2, 10)	17.5 (± 17.7)	1.6 (± 12.0)		

Change at Week 144: 1.25% CHART (n=2, 10)	-7.0 (± 7.1)	1.4 (± 12.2)		
Change at Week 168: 100% CHART (n=0, 10)	6666 (± 6666)	2.1 (± 6.7)		
Change at Week 168: 2.5% CHART (n=0, 10)	6666 (± 6666)	6.2 (± 8.2)		
Change at Week 168: 1.25% CHART (n=0, 10)	6666 (± 6666)	0.3 (± 12.2)		
Change at Week 192: 100% CHART (n=1, 2)	1.0 (± 9999)	-2.5 (± 3.5)		
Change at Week 192: 2.5% CHART (n=1, 2)	-1.0 (± 9999)	-1.0 (± 4.2)		
Change at Week 192: 1.25% CHART (n=1, 2)	-8.0 (± 9999)	-4.0 (± 7.1)		
Change at Week 216: 100% CHART (n=1, 0)	0.0 (± 9999)	6666 (± 6666)		
Change at Week 216: 2.5% CHART (n=1, 0)	-1.0 (± 9999)	6666 (± 6666)		
Change at Week 216: 1.25% CHART (n=1, 0)	-8.0 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least One Adverse Event in the Double-Blind Period

End point title	Number of Participants with at Least One Adverse Event in the Double-Blind Period

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Pre-existing conditions which worsen during a study are also considered as adverse events. The Safety Analysis Population (SAF) included all randomized participants who had received at least 1 dose of satralizumab or placebo.

End point type	Secondary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: participants	24	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least One Serious Adverse Event in the Double-Blind Period

End point title	Number of Participants with at Least One Serious Adverse Event in the Double-Blind Period

End point description:

A serious adverse event is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is medically significant or requires intervention to prevent one or other of the outcomes listed above. The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo.

End point type	Secondary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: participants	5	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Non-Serious Adverse Events of Special Interest in the Double-Blind Period

End point title	Number of Participants with Non-Serious Adverse Events of Special Interest in the Double-Blind Period

End point description:

Non-serious adverse events of special interest for this study included: 1) cases of an elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) in combination with either an elevated bilirubin or clinical jaundice, 2) suspected transmission of an infectious agent by the study treatment. The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo.

End point type	Secondary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Selected Adverse Events in the Double-Blind Period

End point title	Number of Participants with Selected Adverse Events in the Double-Blind Period

End point description:

Selected adverse events for this study included: 1) all infections, 2) serious infections, 3) potential opportunistic infections, 4) injection-related reactions (IRRs; an AE which occured within 24 hours after study treatment injection except where the event was not considered an allergic reaction), 5) psychiatric disorders and 6) anaphylaxis (an acute allergic/hypersensitivity reaction). The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo.

End point type	Secondary

End point timeframe:

Up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: participants				
All Infections	14	34		
Serious Infections	3	6		
Potential Opportunistic Infections	5	3		
Injection-related Reactions	5	8		
Psychiatric Disorders	4	13		
Anaphylaxis	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Suicidal Behaviors and Ideations Collected by Columbia-Suicide Severity Rating Scale in the Double-Blind Period

End point title	Number of Participants With Suicidal Behaviors and Ideations Collected by Columbia-Suicide Severity Rating Scale in the Double-Blind Period

End point description:

The Columbia-Suicide Severity Rating Scale (C-SSRS) is an assessment tool to evaluate suicidal ideation and behavior. Categories have binary responses (yes/no) and include: Wish to be Dead; Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act; Active Suicidal Ideation with Some Intent to Act, without Specific Plan; Active Suicidal Ideation with Specific Plan and Intent, Preparatory Acts and Behavior; Aborted Attempt; Interrupted Attempt; Actual Attempt (non-fatal); Completed Suicide. Suicidal ideation or behavior is indicated by a "yes" answer to any of the listed categories. A score of 0 is assigned if no suicide risk is present. A score of 1 or higher indicates suicidal ideation or behavior. The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo.

End point type	Secondary

End point timeframe:

Baseline and Post-Baseline (up to Week 216)

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: participants				
Baseline	0	9		
Post-Baseline	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Satralizumab Concentration During the DB Period

End point title	Serum Satralizumab Concentration During the DB Period[3]

End point description:

The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo. Participants from SAF who received satralizumab were evaluated for this endpoint. 9999=SD was not calculable for 1 participant.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 5, 6, 8, and every 4 weeks thereafter up to Week 204

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: Reported here is the percentage of participants with at least one positive anti-drug antibody measurement during the DB period. The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo. Participants from SAF who received satralizumab were evaluated for this endpoint. Data was summarized together for this endpoint.

End point values	Satralizumab, then Satralizumab			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: ng/mL				
arithmetic mean (standard deviation)				

Baseline (n= 62)	145.13 (± 274.87)			
Week 2 (n= 61)	8099.70 (± 4541.66)			
Week 4 (n= 56)	14602.50 (± 8931.85)			
Week 5 (n= 44)	22564.32 (± 12306.09)			
Week 6 (n= 42)	20991.43 (± 12515.82)			
Week 8 (n= 60)	14864.35 (± 9955.41)			
Week 12 (n= 55)	14760.33 (± 10695.11)			
Week 16 (n= 53)	14613.11 (± 11276.95)			
Week 20 (n= 55)	14136.62 (± 12489.83)			
Week 24 (n= 55)	15634.18 (± 13310.22)			
Week 28 (n= 53)	15538.38 (± 13406.73)			
Week 32 (n= 52)	15111.94 (± 13827.06)			
Week 36 (n= 50)	16068.58 (± 14643.61)			
Week 40 (n= 46)	15428.04 (± 16059.35)			
Week 44 (n= 46)	16110.00 (± 15363.29)			
Week 48 (n= 44)	16701.16 (± 16790.77)			
Week 52 (n= 44)	15300.57 (± 14701.05)			
Week 56 (n= 45)	16390.82 (± 16130.69)			
Week 60 (n= 43)	16050.81 (± 14779.35)			
Week 64 (n= 42)	14385.10 (± 14084.24)			
Week 68 (n= 41)	14010.46 (± 13614.03)			
Week 72 (n= 42)	12895.69 (± 13849.12)			
Week 76 (n= 42)	14139.31 (± 14549.71)			
Week 80 (n= 42)	12709.79 (± 14098.26)			
Week 84 (n= 40)	11725.05 (± 13654.04)			
Week 88 (n= 35)	13733.17 (± 13438.07)			
Week 92 (n= 32)	12928.13 (± 13302.53)			
Week 96 (n= 31)	14036.58 (± 12644.16)			
Week 100 (n= 20)	14186.50 (± 12888.23)			
Week 104 (n= 22)	16647.00 (± 15568.61)			
Week 108 (n= 22)	15970.00 (± 13525.53)			

Week 112 (n= 19)	18657.37 (± 17426.82)			
Week 116 (n= 15)	17677.33 (± 16892.59)			
Week 120 (n= 14)	16615.00 (± 16751.13)			
Week 124 (n= 15)	13734.00 (± 12687.75)			
Week 128 (n= 15)	13738.00 (± 16005.33)			
Week 132 (n= 15)	13311.73 (± 15401.04)			
Week 136 (n= 13)	14208.54 (± 15266.48)			
Week 140 (n= 13)	13404.62 (± 12392.48)			
Week 144 (n= 11)	16138.18 (± 13782.26)			
Week 148 (n= 12)	14044.33 (± 12082.37)			
Week 152 (n= 12)	14644.42 (± 13123.67)			
Week 156 (n= 11)	18856.36 (± 20378.31)			
Week 160 (n= 11)	15238.18 (± 11360.62)			
Week 164 (n= 11)	14760.00 (± 11479.99)			
Week 168 (n= 10)	14199.60 (± 9911.22)			
Week 172 (n= 7)	17971.43 (± 16962.78)			
Week 176 (n= 7)	17922.86 (± 12815.57)			
Week 180 (n= 7)	15981.43 (± 9640.78)			
Week 184 (n= 6)	17911.67 (± 15142.19)			
Week 188 (n= 4)	16442.50 (± 13180.44)			
Week 192 (n= 2)	28750.00 (± 22415.28)			
Week 196 (n= 2)	26850.00 (± 20152.54)			
Week 200 (n= 1)	45000.00 (± 9999)			
Week 204 (n= 1)	34500.00 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Interleukin-6 (IL-6) Concentration During the DB Period

End point title	Serum Interleukin-6 (IL-6) Concentration During the DB Period

End point description:

The SAF included all randomized participants who had received at least 1 dose of satralizumab or

placebo. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, and every 4 weeks thereafter up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	62		
Units: pg/mL				
arithmetic mean (standard deviation)				
Baseline (n=29, 62)	3.66 (± 6.49)	3.49 (± 5.14)		
Week 2 (n=30, 60)	5.90 (± 16.31)	30.14 (± 26.07)		
Week 4 (n=28, 61)	5.41 (± 10.02)	51.53 (± 126.49)		
Week 8 (n=26, 61)	3.30 (± 4.59)	30.88 (± 25.57)		
Week 12 (n=25, 53)	3.40 (± 4.21)	32.02 (± 24.91)		
Week 16 (n=23, 53)	3.72 (± 4.54)	28.59 (± 23.27)		
Week 20 (n=22, 55)	2.99 (± 2.88)	24.06 (± 19.59)		
Week 24 (n=20, 55)	3.68 (± 4.02)	26.27 (± 23.19)		
Week 28 (n=20, 53)	3.88 (± 4.24)	26.89 (± 24.01)		
Week 32 (n=22, 52)	3.43 (± 3.20)	33.29 (± 37.93)		
Week 36 (n=20, 50)	3.78 (± 3.65)	26.03 (± 21.75)		
Week 40 (n=19, 46)	4.82 (± 6.45)	24.16 (± 19.93)		
Week 44 (n=18, 46)	3.47 (± 3.65)	26.16 (± 20.39)		
Week 48 (n=17, 43)	4.58 (± 4.21)	29.61 (± 27.37)		
Week 52 (n=18, 44)	3.52 (± 3.36)	26.94 (± 22.26)		
Week 56 (n=15, 45)	4.13 (± 5.26)	33.15 (± 40.66)		
Week 60 (n=12, 43)	3.28 (± 3.65)	31.34 (± 25.38)		
Week 64 (n=14, 41)	4.08 (± 4.48)	30.60 (± 24.55)		
Week 68 (n=14, 41)	2.75 (± 3.35)	30.56 (± 44.67)		
Week 72 (n=12, 41)	2.95 (± 4.80)	23.16 (± 17.54)		
Week 76 (n=12, 42)	2.44 (± 3.04)	24.08 (± 16.78)		
Week 80 (n=11, 41)	1.57 (± 0.00)	24.86 (± 17.89)		
Week 84 (n=12, 40)	2.27 (± 1.84)	27.61 (± 23.04)		

Week 88 (n=9, 35)	1.57 (± 0.00)	26.51 (± 20.07)		
Week 92 (n=10, 31)	3.38 (± 4.80)	25.48 (± 17.24)		
Week 96 (n=7, 31)	1.57 (± 0.00)	24.57 (± 15.25)		
Week 100 (n=5, 18)	1.57 (± 0.00)	26.31 (± 18.74)		
Week 104 (n=7, 22)	1.57 (± 0.00)	26.30 (± 19.96)		
Week 108 (n=6, 21)	1.57 (± 0.00)	27.64 (± 23.97)		
Week 112 (n=3, 19)	1.57 (± 0.00)	27.39 (± 22.72)		
Week 116 (n=4, 15)	1.57 (± 0.00)	31.73 (± 23.27)		
Week 120 (n=3, 13)	1.57 (± 0.00)	55.92 (± 68.46)		
Week 124 (n=3, 15)	1.57 (± 0.00)	29.46 (± 19.49)		
Week 128 (n=2, 14)	1.57 (± 0.00)	31.20 (± 21.29)		
Week 132 (n=2, 15)	1.57 (± 0.00)	33.84 (± 34.36)		
Week 136 (n=2, 13)	1.57 (± 0.00)	51.83 (± 73.68)		
Week 140 (n=1, 12)	1.57 (± 9999)	41.00 (± 45.44)		
Week 144 (n=2, 11)	1.57 (± 0.00)	28.26 (± 25.64)		
Week 148 (n=2, 12)	1.57 (± 0.00)	28.76 (± 21.52)		
Week 152 (n=1, 12)	1.57 (± 9999)	28.07 (± 23.66)		
Week 156 (n=1, 11)	1.57 (± 9999)	27.25 (± 19.19)		
Week 160 (n=1, 11)	1.57 (± 9999)	29.60 (± 20.30)		
Week 164 (n=1, 11)	1.57 (± 9999)	34.00 (± 24.13)		
Week 168 (n=1, 10)	1.57 (± 9999)	26.29 (± 20.85)		
Week 172 (n=1, 7)	1.57 (± 9999)	23.57 (± 6.59)		
Week 176 (n=1, 7)	1.57 (± 9999)	27.73 (± 11.10)		
Week 180 (n=1, 7)	1.57 (± 9999)	24.09 (± 9.21)		
Week 184 (n=1, 6)	3.63 (± 9999)	17.34 (± 8.47)		
Week 188 (n=1, 4)	5.21 (± 9999)	17.78 (± 7.22)		
Week 192 (n=1, 2)	1.57 (± 9999)	16.55 (± 3.89)		
Week 196 (n=1, 2)	1.57 (± 9999)	14.45 (± 2.76)		
Week 200 (n=1, 1)	1.57 (± 9999)	36.90 (± 9999)		
Week 204 (n=1, 1)	1.57 (± 9999)	12.30 (± 9999)		
Week 208 (n=1, 0)	1.57 (± 9999)	6666 (± 6666)		
Week 212 (n=1, 0)	1.57 (± 9999)	6666 (± 6666)		
Week 216 (n=1, 0)	1.57 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Soluble IL-6 Receptor (sIL-6R) Concentration During the DB Period

End point title	Serum Soluble IL-6 Receptor (sIL-6R) Concentration During the DB Period

End point description:

The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, and every 4 weeks thereafter up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	62		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (n=32, 62)	31.88 (± 7.50)	33.18 (± 7.72)		
Week 2 (n=30, 61)	32.72 (± 8.09)	396.49 (± 80.09)		
Week 4 (n=29, 61)	44.79 (± 64.73)	509.21 (± 121.99)		
Week 8 (n=27, 61)	33.23 (± 7.21)	560.63 (± 164.11)		
Week 12 (n=26, 55)	33.02 (± 7.65)	582.36 (± 169.71)		
Week 16 (n=24, 53)	31.60 (± 8.18)	582.22 (± 204.20)		
Week 20 (n=22, 55)	32.99 (± 8.14)	555.64 (± 210.76)		
Week 24 (n=20, 55)	32.47 (± 8.69)	573.01 (± 217.93)		
Week 28 (n=20, 53)	31.83 (± 9.71)	565.29 (± 219.88)		
Week 32 (n=22, 52)	33.33 (± 9.97)	564.13 (± 215.59)		
Week 36 (n=20, 50)	34.03 (± 7.79)	572.31 (± 207.35)		
Week 40 (n=19, 46)	33.64 (± 9.44)	554.90 (± 241.34)		
Week 44 (n=18, 46)	33.97 (± 9.05)	585.62 (± 219.45)		
Week 48 (n=17, 44)	33.72 (± 8.18)	591.06 (± 213.04)		
Week 52 (n=18, 44)	33.47 (± 7.58)	575.56 (± 210.84)		
Week 56 (n=15, 45)	30.34 (± 5.21)	585.40 (± 233.38)		
Week 60 (n=13, 43)	30.58 (± 6.81)	586.40 (± 226.21)		

Week 64 (n=14, 42)	32.27 (± 7.63)	602.72 (± 239.25)		
Week 68 (n=14, 41)	31.19 (± 7.23)	617.80 (± 244.63)		
Week 72 (n=13, 42)	31.12 (± 7.76)	543.95 (± 224.00)		
Week 76 (n=12, 42)	30.56 (± 7.06)	558.67 (± 234.41)		
Week 80 (n=11, 41)	33.36 (± 9.91)	558.73 (± 235.60)		
Week 84 (n=12, 40)	30.95 (± 8.96)	552.37 (± 226.76)		
Week 88 (n=10, 35)	32.05 (± 7.23)	547.93 (± 211.74)		
Week 92 (n=10, 32)	28.93 (± 5.72)	580.64 (± 201.78)		
Week 96 (n=,8 31)	32.88 (± 5.62)	561.64 (± 205.00)		
Week 100 (n=7, 19)	31.84 (± 7.62)	559.18 (± 194.43)		
Week 104 (n=7, 22)	31.70 (± 8.81)	598.05 (± 192.99)		
Week 108 (n=6, 21)	30.55 (± 6.94)	592.06 (± 193.20)		
Week 112 (n=4, 19)	29.93 (± 8.47)	603.31 (± 227.68)		
Week 116 (n=4, 15)	34.30 (± 13.37)	609.37 (± 198.61)		
Week 120 (n=3, 13)	38.20 (± 10.96)	625.15 (± 229.67)		
Week 124 (n=3, 15)	37.87 (± 13.59)	580.07 (± 240.15)		
Week 128 (n=2, 15)	44.50 (± 2.40)	574.54 (± 214.94)		
Week 132 (n=2, 15)	29.80 (± 8.63)	575.40 (± 213.45)		
Week 136 (n=2, 13)	29.45 (± 11.53)	593.92 (± 209.84)		
Week 140 (n=1, 13)	37.20 (± 9999)	627.32 (± 232.08)		
Week 144 (n=2, 11)	31.10 (± 10.18)	693.82 (± 239.70)		
Week 148 (n=2, 12)	28.55 (± 13.08)	690.83 (± 142.94)		
Week 152 (n=1, 12)	33.60 (± 9999)	626.41 (± 229.59)		
Week 156 (n=1, 11)	39.90 (± 9999)	682.82 (± 156.88)		
Week 160 (n=1, 11)	45.00 (± 9999)	694.18 (± 127.92)		
Week 164 (n=1, 11)	43.00 (± 9999)	696.18 (± 106.76)		
Week 168 (n=1, 10)	40.60 (± 9999)	681.00 (± 122.60)		
Week 172 (n=1, 7)	49.70 (± 9999)	672.71 (± 107.83)		
Week 176 (n=1, 7)	45.50 (± 9999)	700.71 (± 90.64)		
Week 180 (n=1, 7)	55.60 (± 9999)	702.00 (± 75.60)		
Week 184 (n=1, 6)	41.60 (± 9999)	678.33 (± 78.20)		

Week 188 (n=1, 4)	40.00 (± 9999)	688.75 (± 143.82)		
Week 192 (n=1, 2)	43.40 (± 9999)	668.00 (± 192.33)		
Week 196 (n=1, 2)	38.00 (± 9999)	630.00 (± 141.42)		
Week 200 (n=1, 1)	35.80 (± 9999)	815.00 (± 9999)		
Week 204 (n=1, 1)	33.70 (± 9999)	783.00 (± 9999)		
Week 208 (n=1, 0)	35.60 (± 9999)	6666 (± 6666)		
Week 212 (n=1, 0)	30.50 (± 9999)	6666 (± 6666)		
Week 216 (n=1, 0)	37.60 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum High Sensitivity C-Reactive Protein (hsCRP) Concentration During the DB Period

End point title	Serum High Sensitivity C-Reactive Protein (hsCRP) Concentration During the DB Period

End point description:

The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo. 9999=SD was not calculable for 1 participant. 6666=0 participants.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, and every 4 weeks thereafter up to Week 216

End point values	Placebo, then Satralizumab	Satralizumab, then Satralizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	63		
Units: mg/L				
arithmetic mean (standard deviation)				
Baseline (n=32, 63)	3.08 (± 3.77)	4.95 (± 8.67)		
Week 2 (n=30, 62)	3.51 (± 4.55)	0.93 (± 2.35)		
Week 4 (n=29, 60)	3.45 (± 6.24)	0.82 (± 1.64)		
Week 8 (n=27, 61)	4.56 (± 8.97)	0.83 (± 1.99)		
Week 12 (n=26, 55)	4.23 (± 7.23)	1.23 (± 3.19)		
Week 16 (n=24, 53)	5.30 (± 9.17)	1.56 (± 4.53)		
Week 20 (n=22, 55)	4.07 (± 5.20)	1.78 (± 3.72)		
Week 24 (n=19, 55)	3.53 (± 4.08)	1.72 (± 4.05)		
Week 28 (n=20, 53)	5.85 (± 9.99)	2.35 (± 5.61)		
Week 32 (n=22, 52)	3.97 (± 5.20)	2.06 (± 4.28)		
Week 36 (n=20, 50)	3.77 (± 4.40)	1.56 (± 3.36)		
Week 40 (n=18, 45)	6.77 (± 10.92)	2.55 (± 5.53)		
Week 44 (n=18, 46)	5.44 (± 8.72)	3.31 (± 11.31)		

Week 48 (n=17, 44)	4.70 (± 5.43)	1.79 (± 3.24)		
Week 52 (n=18, 42)	3.82 (± 4.75)	1.90 (± 3.69)		
Week 56 (n=15, 45)	5.33 (± 8.87)	2.32 (± 5.44)		
Week 60 (n=13, 43)	4.54 (± 5.60)	3.20 (± 11.86)		
Week 64 (n=14, 43)	3.76 (± 4.62)	1.92 (± 3.55)		
Week 68 (n=14, 42)	3.30 (± 5.11)	3.65 (± 8.52)		
Week 72 (n=13, 42)	5.07 (± 11.87)	3.33 (± 7.30)		
Week 76 (n=12, 42)	1.98 (± 2.12)	2.79 (± 6.54)		
Week 80 (n=11, 41)	1.10 (± 0.72)	2.83 (± 7.09)		
Week 84 (n=12, 40)	2.31 (± 4.66)	3.81 (± 10.18)		
Week 88 (n=10, 35)	1.94 (± 3.38)	2.64 (± 6.56)		
Week 92 (n=10, 32)	4.49 (± 10.18)	1.94 (± 4.11)		
Week 96 (n=8, 31)	1.76 (± 2.47)	1.64 (± 3.37)		
Week 100 (n=7, 20)	0.90 (± 0.87)	1.87 (± 4.28)		
Week 104 (n=7, 22)	1.13 (± 1.01)	1.93 (± 4.43)		
Week 108 (n=6, 21)	2.20 (± 3.16)	2.56 (± 7.40)		
Week 112 (n=4, 19)	2.25 (± 2.68)	1.53 (± 2.86)		
Week 116 (n=4, 15)	2.28 (± 3.41)	1.19 (± 1.93)		
Week 120 (n=2, 14)	1.55 (± 1.63)	6.05 (± 14.33)		
Week 124 (n=3, 15)	1.50 (± 1.04)	3.24 (± 8.32)		
Week 128 (n=2, 15)	0.65 (± 0.64)	3.09 (± 7.52)		
Week 132 (n=2, 15)	2.55 (± 1.77)	2.66 (± 5.04)		
Week 136 (n=2, 15)	2.70 (± 1.27)	2.85 (± 7.29)		
Week 140 (n=1, 13)	2.50 (± 9999)	4.54 (± 9.57)		
Week 144 (n=2, 11)	2.65 (± 2.19)	0.96 (± 1.75)		
Week 148 (n=2, 12)	4.80 (± 0.99)	0.87 (± 1.44)		
Week 152 (n=1, 12)	1.20 (± 9999)	0.79 (± 0.79)		
Week 156 (n=1, 11)	1.80 (± 9999)	0.71 (± 1.17)		
Week 160 (n=1, 11)	1.20 (± 9999)	0.82 (± 1.36)		
Week 164 (n=1, 11)	1.30 (± 9999)	0.54 (± 0.50)		
Week 168 (n=1, 10)	1.30 (± 9999)	0.37 (± 0.22)		
Week 172 (n=1, 7)	1.30 (± 9999)	0.19 (± 0.09)		
Week 176 (n=1, 7)	1.30 (± 9999)	0.25 (± 0.17)		
Week 180 (n=1, 7)	1.20 (± 9999)	0.27 (± 0.16)		
Week 184 (n=1, 6)	1.10 (± 9999)	0.22 (± 0.11)		
Week 188 (n=1, 4)	2.40 (± 9999)	0.21 (± 0.13)		
Week 192 (n=1, 2)	1.10 (± 9999)	0.33 (± 0.25)		
Week 196 (n=1, 2)	2.00 (± 9999)	0.15 (± 0.00)		
Week 200 (n=1, 1)	1.10 (± 9999)	0.50 (± 9999)		
Week 204 (n=0, 1)	6666 (± 6666)	0.15 (± 9999)		
Week 208 (n=1, 0)	1.00 (± 9999)	6666 (± 6666)		
Week 212 (n=1, 0)	1.60 (± 9999)	6666 (± 6666)		
Week 216 (n=1, 0)	1.10 (± 9999)	6666 (± 6666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Drug Antibodies to Satralizumab in

the DB Period

End point title	Percentage of Participants with Anti-Drug Antibodies to Satralizumab in the DB Period[4]

End point description:

Reported here is the percentage of participants with at least one positive anti-drug antibody measurement during the DB period. The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo. Participants from SAF who received satralizumab were evaluated for this endpoint. Data was summarized together for this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 216

Notes:

[4] - 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: Reported here is the percentage of participants with at least one positive anti-drug antibody measurement during the DB period. The SAF included all randomized participants who had received at least 1 dose of satralizumab or placebo. Participants from SAF who received satralizumab were evaluated for this endpoint. Data was summarized together for this endpoint.

End point values	Satralizumab, then Satralizumab			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percentage of participants				
number (not applicable)	71.4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Double Blind Period:
Up to primary clinical cut-off date, 12 Oct 2018 (up to approximately 217 weeks)
Open Label Period:
Up to primary clinical cut-off date, 31-Jan-2022 (up to approximately 336 weeks)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo Double Blind Period

Reporting group description:

Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period.

Reporting group title	SA237 Double Blind Period

Reporting group description:

Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Participants who experienced a protocol defined relapse could continue in the Open Label Extension (OLE) period 31 days after relapse. Participants who completed the DB period without relapse could participate in the OLE period 4 weeks after receiving their last dose in the DB period.

Reporting group title	Placebo Open Label Period

Reporting group description:

Participants received matching placebo, subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD).

Reporting group title	SA237 Open Label Period

Reporting group description:

Participants received satralizumab 120 mg subcutaneous (SC) injection at Weeks 0, 2 and 4, and every 4 weeks (Q4W) thereafter throughout the double-blind (DB) period. Following the DB period, all participants received satralizumab 120 mg SC injection at Weeks 0, 2 and 4, and Q4W thereafter up to the clinical cut-off date (CCOD).

Serious adverse events	Placebo Double Blind Period	SA237 Double Blind Period	Placebo Open Label Period
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 32 (15.63%)	12 / 63 (19.05%)	3 / 28 (10.71%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian adenoma			

subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian germ cell teratoma benign			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	1 / 32 (3.13%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyelitis optica pseudo relapse			
subjects affected / exposed	1 / 32 (3.13%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Apnoea			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 32 (0.00%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 32 (0.00%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SA237 Open Label Period		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 56 (12.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian adenoma			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian germ cell teratoma benign			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			

subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural complication			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fractured sacrum			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple injuries			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Bradycardia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial aneurysm			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuromyelitis optica pseudo relapse			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo Double Blind Period	SA237 Double Blind Period	Placebo Open Label Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 32 (71.88%)	57 / 63 (90.48%)	23 / 28 (82.14%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 32 (6.25%)	7 / 63 (11.11%)	1 / 28 (3.57%)
occurrences (all)	3	9	1
Influenza like illness			
subjects affected / exposed	1 / 32 (3.13%)	2 / 63 (3.17%)	1 / 28 (3.57%)
occurrences (all)	3	5	1
Injection site erythema			
subjects affected / exposed	2 / 32 (6.25%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			
subjects affected / exposed	0 / 32 (0.00%)	3 / 63 (4.76%)	2 / 28 (7.14%)
occurrences (all)	0	3	2
Pain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences (all)	1	2	0
Immune system disorders			

Seasonal allergy			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	3 / 28 (10.71%)
occurrences (all)	0	1	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 32 (3.13%)	2 / 63 (3.17%)	3 / 28 (10.71%)
occurrences (all)	1	3	3
Oropharyngeal pain			
subjects affected / exposed	3 / 32 (9.38%)	3 / 63 (4.76%)	1 / 28 (3.57%)
occurrences (all)	3	3	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 32 (6.25%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences (all)	2	2	0
Depression			
subjects affected / exposed	0 / 32 (0.00%)	6 / 63 (9.52%)	1 / 28 (3.57%)
occurrences (all)	0	10	1
Insomnia			
subjects affected / exposed	1 / 32 (3.13%)	6 / 63 (9.52%)	3 / 28 (10.71%)
occurrences (all)	1	6	4
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	4 / 63 (6.35%)	1 / 28 (3.57%)
occurrences (all)	0	4	2
Blood cholesterol increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	3 / 28 (10.71%)
occurrences (all)	0	2	5
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 32 (3.13%)	4 / 63 (6.35%)	0 / 28 (0.00%)
occurrences (all)	1	5	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 32 (3.13%)	2 / 63 (3.17%)	2 / 28 (7.14%)
occurrences (all)	1	4	6
Neutrophil count decreased			
subjects affected / exposed	2 / 32 (6.25%)	1 / 63 (1.59%)	1 / 28 (3.57%)
occurrences (all)	2	1	6

White blood cell count decreased			
subjects affected / exposed	0 / 32 (0.00%)	5 / 63 (7.94%)	1 / 28 (3.57%)
occurrences (all)	0	9	1
Blood fibrinogen decreased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	3 / 28 (10.71%)
occurrences (all)	0	4	4
Blood potassium increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	3
Complement factor decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	2
International normalised ratio increased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 63 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Low density lipoprotein increased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 63 (1.59%)	2 / 28 (7.14%)
occurrences (all)	1	1	6
Complement factor C4 decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	3
Prothrombin time prolonged			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 32 (3.13%)	3 / 63 (4.76%)	2 / 28 (7.14%)
occurrences (all)	1	3	2
Fall			
subjects affected / exposed	2 / 32 (6.25%)	4 / 63 (6.35%)	0 / 28 (0.00%)
occurrences (all)	2	4	0
Skin abrasion			
subjects affected / exposed	2 / 32 (6.25%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			

Balance disorder			
subjects affected / exposed	2 / 32 (6.25%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences (all)	2	2	0
Dizziness			
subjects affected / exposed	2 / 32 (6.25%)	3 / 63 (4.76%)	2 / 28 (7.14%)
occurrences (all)	3	3	3
Headache			
subjects affected / exposed	4 / 32 (12.50%)	10 / 63 (15.87%)	4 / 28 (14.29%)
occurrences (all)	5	13	4
Hypoaesthesia			
subjects affected / exposed	0 / 32 (0.00%)	5 / 63 (7.94%)	2 / 28 (7.14%)
occurrences (all)	0	6	2
Paraesthesia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 32 (3.13%)	4 / 63 (6.35%)	2 / 28 (7.14%)
occurrences (all)	10	5	3
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 63 (1.59%)	1 / 28 (3.57%)
occurrences (all)	1	1	1
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 32 (6.25%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 32 (6.25%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences (all)	3	1	0
Constipation			
subjects affected / exposed	2 / 32 (6.25%)	3 / 63 (4.76%)	3 / 28 (10.71%)
occurrences (all)	2	3	3
Diarrhoea			
subjects affected / exposed	0 / 32 (0.00%)	5 / 63 (7.94%)	1 / 28 (3.57%)
occurrences (all)	0	19	1

Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 32 (6.25%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences (all)	2	2	0
Nausea			
subjects affected / exposed	2 / 32 (6.25%)	11 / 63 (17.46%)	1 / 28 (3.57%)
occurrences (all)	6	15	1
Toothache			
subjects affected / exposed	0 / 32 (0.00%)	2 / 63 (3.17%)	2 / 28 (7.14%)
occurrences (all)	0	2	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 32 (0.00%)	7 / 63 (11.11%)	1 / 28 (3.57%)
occurrences (all)	0	9	2
Rash			
subjects affected / exposed	1 / 32 (3.13%)	10 / 63 (15.87%)	3 / 28 (10.71%)
occurrences (all)	2	16	3
Dermatitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 63 (3.17%)	2 / 28 (7.14%)
occurrences (all)	0	3	2
Dermatitis contact			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 32 (6.25%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 32 (9.38%)	14 / 63 (22.22%)	3 / 28 (10.71%)
occurrences (all)	3	14	3
Back pain			
subjects affected / exposed	3 / 32 (9.38%)	4 / 63 (6.35%)	3 / 28 (10.71%)
occurrences (all)	3	5	3
Muscle spasms			
subjects affected / exposed	0 / 32 (0.00%)	3 / 63 (4.76%)	0 / 28 (0.00%)
occurrences (all)	0	3	0

Musculoskeletal stiffness			
subjects affected / exposed	0 / 32 (0.00%)	4 / 63 (6.35%)	0 / 28 (0.00%)
occurrences (all)	0	4	0
Myalgia			
subjects affected / exposed	0 / 32 (0.00%)	4 / 63 (6.35%)	1 / 28 (3.57%)
occurrences (all)	0	5	1
Pain in extremity			
subjects affected / exposed	3 / 32 (9.38%)	9 / 63 (14.29%)	2 / 28 (7.14%)
occurrences (all)	3	12	2
Arthritis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 63 (3.17%)	0 / 28 (0.00%)
occurrences (all)	2	2	0
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)	4 / 63 (6.35%)	0 / 28 (0.00%)
occurrences (all)	0	5	0
Influenza			
subjects affected / exposed	2 / 32 (6.25%)	3 / 63 (4.76%)	4 / 28 (14.29%)
occurrences (all)	3	3	4
Nasopharyngitis			
subjects affected / exposed	1 / 32 (3.13%)	9 / 63 (14.29%)	5 / 28 (17.86%)
occurrences (all)	1	11	8
Oral candidiasis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 63 (0.00%)	1 / 28 (3.57%)
occurrences (all)	3	0	1
Tooth abscess			
subjects affected / exposed	2 / 32 (6.25%)	0 / 63 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 32 (18.75%)	10 / 63 (15.87%)	8 / 28 (28.57%)
occurrences (all)	14	20	19
Urinary tract infection			

subjects affected / exposed	8 / 32 (25.00%)	11 / 63 (17.46%)	5 / 28 (17.86%)
occurrences (all)	23	36	8
Cystitis			
subjects affected / exposed	0 / 32 (0.00%)	3 / 63 (4.76%)	2 / 28 (7.14%)
occurrences (all)	0	3	2
Fungal infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 63 (1.59%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Otitis media			
subjects affected / exposed	0 / 32 (0.00%)	0 / 63 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Sinusitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 63 (3.17%)	1 / 28 (3.57%)
occurrences (all)	0	3	1

Non-serious adverse events	SA237 Open Label Period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 56 (75.00%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Influenza like illness			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	13		
Injection site erythema			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Immune system disorders			

Seasonal allergy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Blood cholesterol increased			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	9		
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Lymphocyte count decreased			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Neutrophil count decreased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		

White blood cell count decreased subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 10		
Blood fibrinogen decreased subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 5		
Blood potassium increased subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Complement factor decreased subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 10		
International normalised ratio increased subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Low density lipoprotein increased subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 3		
Complement factor C4 decreased subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Prothrombin time prolonged subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Fall subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 10		
Skin abrasion subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Nervous system disorders			

Balance disorder subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Dizziness subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 6		
Headache subjects affected / exposed occurrences (all)	8 / 56 (14.29%) 12		
Hypoaesthesia subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 5		
Paraesthesia subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 14		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	6 / 56 (10.71%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 5		

Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Nausea subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 4		
Toothache subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Dermatitis subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	6 / 56 (10.71%) 6		
Back pain subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 7		
Muscle spasms subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		

Musculoskeletal stiffness subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Myalgia subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 4			
Pain in extremity subjects affected / exposed occurrences (all)	7 / 56 (12.50%) 11			
Arthritis subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3			
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 3			
Cellulitis subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 4			
Influenza subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1			
Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 56 (10.71%) 8			
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Tooth abscess subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	10 / 56 (17.86%) 32			
Urinary tract infection				

subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	23		
Cystitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2014	V2: Study design: The randomization was stratified by prior therapy for prevention of NMO/NMOSD attack (B-cell depleting therapy or immunosuppressants/others) and the most recent attack in the last one year prior to screening (first attack or relapse). Exclusion criteria: History of drug or alcohol abuse within 1 year prior to baseline; History of acute diverticulitis that, in the Investigator's opinion, may lead to increased risk of complications such as lower gastrointestinal perforation. Screening for possible relapse during the study: A Relapse Assessment Form, including the time and content of every report of a possible event was prepared. Patients were instructed to remember accurately the time and content of every symptom of a possible relapse and to contact the study site if they had such symptoms. During the double-blind period, the site contacted the patient weekly by phone calls between the scheduled site visits, to query for any change in symptoms or other signs of a potential relapse. Assessment for suicidality was added to the safety section (Columbia-Suicide Severity Rating Scale [C-SSRS]). The number of patients who are negative for anti-AQP4 antibody at screening were limited to approximately 30% of total study population.
26 May 2014	V3: Change in protocol-defined relapse: new or worsening neurologic symptoms had to meet any of the listed symptoms. Futility analysis was removed from the role of the independent data monitoring committee (IDMC). Hypersensitivity to gadolinium was removed from the exclusion criteria. Additional procedure was added for scripted questions at patient discontinuation to minimize dropout and not to miss potential relapse. Time limit for participants to report relapse event was set. Beginning time point of TFR was modified to start at randomization. Considering the clinical practice in the US, the permitted treatment for relapse was modified. For general safety patients who had a risk of Stevens-Johnson syndrome (SJS) were excluded from the study.
02 September 2014	V4: Protocol-defined relapse criteria were updated to specify the score increase required to qualify as clinically meaningful for the Expanded Disability Status Scale (EDSS) and Functional System Score (FSS) when the baseline score is zero. Instructions for tuberculosis screening and treatment were updated.
05 November 2015	V5: The right to enter the extension period was modified in that protocol-defined relapse had to be adjudicated by the Clinical Endpoint Committee (CEC) in the double-blind Period. The open-label extension period was extended until commercial availability of the drug. Statistical method for primary analysis was changed to a log-rank based permutation test. Clarification was provided to mention that participants who experienced a relapse during the extension period could continue administration of satralizumab at the discretion of the Investigator. Screening procedure for hepatitis C virus (HCV) was modified to mention that if a patient tested positive, but ribonucleic acid (RNA) was undetectable 12 weeks after HCV treatment completion, the patient could be enrolled. Assessments performed at the Withdrawal visit were provided separately for the double-blind period and extension period. Assessments after Week 48 of the extension period were included, because the open-label extension period was extended until commercial availability.
01 March 2016	V6: Recruitment was changed from North America only to include the rest of the world. Total number of participants in the study was increased to 90. The total number of relapse events was changed because the hazard ratio assumption of satralizumab over placebo was modified. The end of the double-blind period was then defined as the date of primary analysis when the total number of relapses reached 44. Procedure for triplicate ECG was clarified for participants who consented to additional pharmacokinetic (PK) sampling.

13 July 2017	V7: Satralizumab prefilled syringe (PFS) with needle safety device (NSD) was implemented in the study. The number of participants to collect blood sample for plasmablast was expanded to all participants. Clarification was included that Zarit Burden Interview (ZBI) was optional and would be performed in selected countries for caregivers who signed informed consent to caregiver burden assessment.
14 June 2018	V8: To prevent prolonged exposure to an unknown risk-benefit balance drug, the definition of the end of the double-blind period was changed to include a maximal duration completion of 1.5 years after the date of the last participant randomized, if the target number of protocol-defined relapses (PDRs) adjudicated by Clinical Endpoint Committee (CEC) had not been reached. The analysis method for primary endpoint was changed to a stratified two-sided log-rank test using strata of prior therapy for prevention of NMO/NMOSD attack (B-cell depleting therapy or immunosuppressants/others) and the most recent attack in the last one year prior to screening (first attack or relapse). Statistical methods were clarified for VAS in pain score and FACIT fatigue scale score to be ANCOVA with hot-deck imputation. It was clarified that non-linear mixed-effects modeling would be used to analyze the sparse sampling dose-concentration-time data of satralizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported