Clinical trial results:
A Phase 2b Dose-finding Study for SAR442168, a Bruton's Tyrosine Kinase Inhibitor, in Participants With Relapsing Multiple Sclerosis

Summary

EudraCT number	2018-003927-12
Trial protocol	SE ES NL SK EE
Global end of trial date	02 January 2020

Results information

Result version number	v1 (current)
This version publication date	31 December 2020
First version publication date	31 December 2020

Trial information

Trial identification

Sponsor protocol code	DRI15928

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03889639
WHO universal trial number (UTN)	U1111-1220-0572

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	16 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the dose-response relationship for SAR442168 to reduce the number of new active brain lesions.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 31
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Estonia: 8
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Russian Federation: 28
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Ukraine: 26
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	130
EEA total number of subjects	50

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)	130
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 44 active centers in 10 countries. A total of 168 subjects were screened from 29-March-2019 to 29-August-2019, of which 38 subjects were screen failures. Screen failures were mainly due to selection criteria not met.

Pre-assignment

Screening details:

A total of 130 subjects were randomised and treated in this study. Subjects were centrally assigned to 1 of 8 arms (4 dose groups at an equal ratio to start with SAR442168 [all considered as Cohort 1] or placebo [all considered as Cohort 2]).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: SAR442168 5 mg Then Placebo

Arm description:

Subjects received SAR442168 5 milligrams (mg), orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 5 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 1: SAR442168 15 mg Then Placebo

Arm description:

Subjects received SAR442168 15 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental

Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 15 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 1: SAR442168 30 mg Then Placebo

Arm description:

Subjects received SAR442168 30 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 30 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 1: SAR442168 60 mg Then Placebo

Arm description:

Subjects received SAR442168 60 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 60 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 2: Placebo Then SAR442168 5 mg

Arm description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 5 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 5 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 2: Placebo Then SAR442168 15 mg

Arm description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 15 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 15 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 2: Placebo Then SAR442168 30 mg

Arm description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 30 mg orally once daily for 12 weeks during the 16 weeks treatment period.

To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 30 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Arm title	Cohort 2: Placebo Then SAR442168 60 mg

Arm description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 60 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Arm type	Experimental
Investigational medicinal product name	SAR442168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received SAR442168 60 mg once daily, with or without food.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to SAR442168 (up to 4 tablets) once daily, with or without food.

Number of subjects in period 1	Cohort 1: SAR442168 5 mg Then Placebo	Cohort 1: SAR442168 15 mg Then Placebo	Cohort 1: SAR442168 30 mg Then Placebo
Started	16	16	16
Completed	16	16	16
Not completed	0	0	0
Withdrawal by subject	-	-	-

Number of subjects in period 1	Cohort 1: SAR442168 60 mg Then Placebo	Cohort 2: Placebo Then SAR442168 5 mg	Cohort 2: Placebo Then SAR442168 15 mg
Started	16	17	16
Completed	16	17	16
Not completed	0	0	0
Withdrawal by subject	-	-	-

Number of subjects in period 1	Cohort 2: Placebo Then SAR442168 30 mg	Cohort 2: Placebo Then SAR442168 60 mg
Started	17	16
Completed	17	15
Not completed	0	1
Withdrawal by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: SAR442168 5 mg Then Placebo
Reporting group description:	
Subjects received SAR442168 5 milligrams (mg), orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 1: SAR442168 15 mg Then Placebo
Reporting group description:	
Subjects received SAR442168 15 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 1: SAR442168 30 mg Then Placebo
Reporting group description:	
Subjects received SAR442168 30 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 1: SAR442168 60 mg Then Placebo
Reporting group description:	
Subjects received SAR442168 60 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 2: Placebo Then SAR442168 5 mg
Reporting group description:	
Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 5 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 2: Placebo Then SAR442168 15 mg
Reporting group description:	
Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 15 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 2: Placebo Then SAR442168 30 mg
Reporting group description:	
Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 30 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	
Reporting group title	Cohort 2: Placebo Then SAR442168 60 mg
Reporting group description:	
Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 60 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.	

Reporting group values	Cohort 1: SAR442168 5 mg Then Placebo	Cohort 1: SAR442168 15 mg Then Placebo	Cohort 1: SAR442168 30 mg Then Placebo
Number of subjects	16	16	16

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	37.4	35.1	40.8
standard deviation	± 11.1	± 7.9	± 8.7
Gender categorical Units: Subjects			
Female	9	10	11
Male	7	6	5
Race Units: Subjects			
White	15	15	13
Black or African American	1	0	2
Asian	0	0	0
Multiple	0	0	0
Not Reported	0	1	1

Reporting group values	Cohort 1: SAR442168 60 mg Then Placebo	Cohort 2: Placebo Then SAR442168 5 mg	Cohort 2: Placebo Then SAR442168 15 mg
Number of subjects	16	17	16
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	38.1	34.8	36.7
standard deviation	± 9.1	± 8.6	± 10.7
Gender categorical Units: Subjects			
Female	15	16	11
Male	1	1	5
Race Units: Subjects			
White	15	17	14
Black or African American	1	0	1
Asian	0	0	0
Multiple	0	0	1
Not Reported	0	0	0

Reporting group values	Cohort 2: Placebo Then SAR442168 30 mg	Cohort 2: Placebo Then SAR442168 60 mg	Total
Number of subjects	17	16	130
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	37.5	36.1	
standard deviation	± 11.6	± 8.7	-

Gender categorical Units: Subjects			
Female	10	9	91
Male	7	7	39
Race Units: Subjects			
White	16	14	119
Black or African American	0	1	6
Asian	0	1	1
Multiple	0	0	1
Not Reported	1	0	3

End points

End points reporting groups

Reporting group title	Cohort 1: SAR442168 5 mg Then Placebo

Reporting group description:

Subjects received SAR442168 5 milligrams (mg), orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 1: SAR442168 15 mg Then Placebo

Reporting group description:

Subjects received SAR442168 15 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 1: SAR442168 30 mg Then Placebo

Reporting group description:

Subjects received SAR442168 30 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 1: SAR442168 60 mg Then Placebo

Reporting group description:

Subjects received SAR442168 60 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 5 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 5 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 15 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 15 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 30 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 30 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 60 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 60 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Subject analysis set title	Cohort 2: Pooled Placebo
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received placebo matching to SAR442168 orally once daily for first 4 weeks during the 16 weeks treatment period.

Subject analysis set title	Cohorts 1 and 2: SAR442168 5 mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received SAR442168 5 mg orally once daily for 12 weeks (either in Cohort 1 or 2) during the 16 weeks treatment period.

Subject analysis set title	Cohorts 1 and 2: SAR442168 15 mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received SAR442168 15 mg orally once daily for 12 weeks (either in Cohort 1 or 2) during the 16 weeks treatment period.

Subject analysis set title	Cohorts 1 and 2: SAR442168 30 mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received SAR442168 30 mg orally once daily for 12 weeks (either in Cohort 1 or 2) during the 16 weeks treatment period.

Subject analysis set title	Cohorts 1 and 2: SAR442168 60 mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received SAR442168 60 mg orally once daily for 12 weeks (either in Cohort 1 or 2) during the 16 weeks treatment period.

Subject analysis set title	Cohort 1: SAR442168 5 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received SAR442168 5 mg orally once daily in Cohort 1.

Subject analysis set title	Cohort 1: SAR442168 15 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received SAR442168 15 mg orally once daily in Cohort 1.

Subject analysis set title	Cohort 1: SAR442168 30 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received SAR442168 30 mg orally once daily in Cohort 1.

Subject analysis set title	Cohort 1: SAR442168 60 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received SAR442168 60 mg orally once daily in Cohort 1.

Primary: Brain Magnetic Resonance Imaging (MRI) Assessment: Number of New Gadolinium (Gd) Enhancing T1-hyperintense Lesions

End point title	Brain Magnetic Resonance Imaging (MRI) Assessment: Number of New Gadolinium (Gd) Enhancing T1-hyperintense Lesions

End point description:

Number of new Gd-enhancing T1-hyperintense lesions was detected by brain MRI at the end of 12 weeks of SAR442168 treatment (i.e., at Week 12 for Cohort 1 subjects and Week 16 for Cohort 2 subjects). Analysis was performed on modified intent-to-treat (mITT) population that included all randomly assigned subjects exposed to the study drug, analysed according to the treatment assigned by randomisation. Data was planned to be collected and analysed on pooled population of subjects at each dose level of SAR442168 (either in Cohort 1 and 2) and pooled population of subjects receiving Placebo in Cohort 2 and was not planned to collected during placebo administration in Cohort 1 (Weeks 12 to 16). Here, "number of subjects analysed" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

After 12 weeks of SAR442168 treatment for SAR442168 reporting arms (i.e., at Week 12 for Cohort 1 subjects, at Week 16 for Cohort 2 subjects) and at Week 4 for Cohort 2 placebo

End point values	Cohort 2: Pooled Placebo	Cohorts 1 and 2: SAR442168 5 mg	Cohorts 1 and 2: SAR442168 15 mg	Cohorts 1 and 2: SAR442168 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	31	31	33
Units: lesions				
arithmetic mean (standard deviation)	1.03 (± 2.50)	1.39 (± 3.20)	0.77 (± 1.48)	0.76 (± 3.31)

End point values	Cohorts 1 and 2: SAR442168 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: lesions				
arithmetic mean (standard deviation)	0.13 (± 0.43)			

Statistical analyses

Statistical analysis title	SAR442168 5 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 5 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95 percentage (%) confidence interval (CI) were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 5 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1673 [1]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	-56.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-193.99
upper limit	17.05

Notes:

[1] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 15 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 15 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 15 mg v Cohort 2: Pooled Placebo

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.354 [2]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	-62.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-356.24
upper limit	41.91

Notes:

[2] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 30 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 30 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 30 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7674 [3]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	13.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-126.05
upper limit	66.89

Notes:

[3] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 60 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 60 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 60 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0178 [4]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	85.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	28.02
upper limit	96.88

Notes:

[4] - Threshold for significance for p value was 0.05.

Secondary: Number of New or Enlarging T2 Lesions

End point title	Number of New or Enlarging T2 Lesions

End point description:

Number of new and enlarging T2 lesions was detected by brain MRI at the end of 12 weeks of SAR442168 treatment (i.e. at Week 12 for Cohort 1 subjects and Week 16 for Cohort 2 subjects). Analysis was performed on mITT population. Data was planned to be collected and analysed on pooled population of subjects at each dose level of SAR442168 (either in Cohort 1 and 2) and pooled population of subjects receiving Placebo in Cohort 2 and was not planned to collected during placebo administration in Cohort 1 (Week 12 to 16). Here, "number of subjects analysed" signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

After 12 weeks of SAR442168 treatment for SAR442168 reporting arms (i.e. at Week 12 for Cohort 1 subjects, at Week 16 for Cohort 2 subjects), and at Week 4 for Cohort 2 placebo

End point values	Cohort 2: Pooled Placebo	Cohorts 1 and 2: SAR442168 5 mg	Cohorts 1 and 2: SAR442168 15 mg	Cohorts 1 and 2: SAR442168 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	31	31	33
Units: lesions				
arithmetic mean (standard deviation)	2.12 (± 5.16)	1.90 (± 3.97)	1.32 (± 1.83)	1.30 (± 4.90)

End point values	Cohorts 1 and 2: SAR442168 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: lesions				
arithmetic mean (standard deviation)	0.23 (± 0.62)			

Statistical analyses

Statistical analysis title	SAR442168 5 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 5 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model without adjusting for baseline T2 lesion activity as all subjects had at least one T2 lesion at baseline.

Comparison groups	Cohorts 1 and 2: SAR442168 5 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7736 [5]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	10.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-86.49
upper limit	56.73

Notes:

[5] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 15 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 15 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model without adjusting for baseline T2 lesion activity as all subjects had at least one T2 lesion at baseline.

Comparison groups	Cohorts 1 and 2: SAR442168 15 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.248 [6]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	37.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.08
upper limit	71.32

Notes:

[6] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 30 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 30 mg (Cohort 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model without adjusting for baseline T2 lesion activity as all subjects had at least one T2 lesion at baseline.

Comparison groups	Cohorts 1 and 2: SAR442168 30 mg v Cohort 2: Pooled Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3081 [7]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	38.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.61
upper limit	75.85

Notes:

[7] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 60 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 60 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model without adjusting for baseline T2 lesion activity as all subjects had at least one T2 lesion at baseline.

Comparison groups	Cohorts 1 and 2: SAR442168 60 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [8]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	89.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	68.39
upper limit	96.41

Notes:

[8] - Threshold for significance for p value was 0.05.

Secondary: Total Number of Gd-enhancing T1-hyperintense Lesions

End point title	Total Number of Gd-enhancing T1-hyperintense Lesions

End point description:

Total number of Gd-enhancing T1-hyperintense lesions was detected by brain MRI at the end of 12 weeks of SAR442168 treatment (i.e., at Week 12 for Cohort 1 subjects and Week 16 for Cohort 2 subjects). Analysis was performed on mITT population. Data was planned to be collected and analysed on pooled population of subjects at each dose level of SAR442168 (either in Cohort 1 and 2) and pooled population of subjects receiving Placebo in Cohort 2 and was not planned to collected during placebo administration in Cohort 1 (Weeks 12 to 16) . Here, "number of subjects analysed" signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

After 12 weeks of SAR442168 treatment for SAR442168 reporting arms (i.e. at Week 12 for Cohort 1 subjects, at Week 16 for Cohort 2 subjects), and at Week 4 for Cohort 2 placebo

End point values	Cohort 2: Pooled Placebo	Cohorts 1 and 2: SAR442168 5 mg	Cohorts 1 and 2: SAR442168 15 mg	Cohorts 1 and 2: SAR442168 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	31	31	33
Units: lesions				
arithmetic mean (standard deviation)	1.36 (± 3.52)	1.77 (± 4.10)	0.87 (± 1.59)	1.18 (± 4.87)

End point values	Cohorts 1 and 2: SAR442168 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: lesions				
arithmetic mean (standard deviation)	0.29 (± 0.86)			

Statistical analyses

Statistical analysis title	SAR442168 5 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 5 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 5 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1525 [9]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	-62.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-214.44
upper limit	16.38

Notes:

[9] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 15 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 15 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 15 mg v Cohort 2: Pooled

	Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4606 [10]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	-47.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-312.91
upper limit	47.4

Notes:

[10] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 30 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 30 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 30 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.949 [11]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-138.96
upper limit	60.54

Notes:

[11] - Threshold for significance for p value was 0.05.

Statistical analysis title	SAR442168 60 mg/Placebo

Statistical analysis description:

Relative reduction in lesions in SAR442168 60 mg (Cohorts 1 and 2) when compared with placebo (Cohort 2) with 95% CI were reported. Analysis was performed using a negative binomial regression model adjusted for baseline gadolinium-enhancing T1-hyperintense lesion activity (presence/absence).

Comparison groups	Cohorts 1 and 2: SAR442168 60 mg v Cohort 2: Pooled Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2324 [12]
Method	Negative binomial regression model
Parameter estimate	Relative reduction in lesions
Point estimate	65.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-96.21
upper limit	93.77

Notes:

[12] - Threshold for significance for p value was 0.05.

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs): Weeks 1-4 Period

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs): Weeks 1-4 Period

End point description:

Adverse event (AE):any unfavorable and unintended sign, symptom, or disease temporally associated with use of study drug. Serious AE (SAE):any untoward medical occurrence that, at any dose resulted in death, life-threatening, inpatient hospitalisation or prolongation of existing hospitalisation, disability/incapacity, congenital anomaly/birth defect, or medical event. TEAEs:AEs that developed, worsened, or became serious during on-treatment period(for this endpoint- "Weeks 1 to 4 period": time from 1st administration of study drug to Week4). Cohorts 1 and 2 received SAR442168 and placebo for 1st 4weeks, respectively. Safety population:all subjects from randomised population who had received at least 1 dose or part of dose of study drug. Data was planned to be collected and analysed on subjects at each dose level of SAR442168 in Cohort 1 and pooled population of subjects receiving Placebo in Cohort2 and not planned to be collected during Cohort1 Placebo administration (Weeks 12 to 16).

End point type	Secondary

End point timeframe:

From Baseline up to Week 4

End point values	Cohort 2: Pooled Placebo	Cohort 1: SAR442168 5 mg	Cohort 1: SAR442168 15 mg	Cohort 1: SAR442168 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	66	16	16	16
Units: subjects				
TEAE	23	5	3	2
TESAE	0	0	0	0

End point values	Cohort 1: SAR442168 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: subjects				
TEAE	5			
TESAE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events and Treatment-emergent Serious Adverse Events: SAR442168 Treatment Period

End point title	Number of Subjects With Treatment-emergent Adverse Events and Treatment-emergent Serious Adverse Events: SAR442168 Treatment Period

End point description:

AE: any unfavorable and unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with use of study drug. SAE: any untoward medical occurrence that, at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, persistent disability/incapacity, congenital anomaly/birth defect, or medical event. TEAEs: AEs that developed, worsened, or became serious during on-treatment period (for this endpoint defined as "SAR442168 treatment period" which was considered as Weeks 1 to 12 for Cohort 1 and Weeks 4 to 16 for Cohort 2). Data was planned to be collected and analysed on pooled subjects at each dose level of SAR442168 (either in Cohort 1 or 2), and was not planned to be collected during placebo administration in either Cohort 1 or 2. Analysis was performed on safety population. Here, "number of subjects analysed" signifies number of subjects evaluable for this treatment period.

End point type	Secondary

End point timeframe:

Weeks 1 to 12 for Cohort 1 subjects and Weeks 4 to 16 for Cohort 2 subjects

End point values	Cohorts 1 and 2: SAR442168 5 mg	Cohorts 1 and 2: SAR442168 15 mg	Cohorts 1 and 2: SAR442168 30 mg	Cohorts 1 and 2: SAR442168 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	32	33	32
Units: subjects				
TEAE	19	17	18	16
TESAE	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Individual Clinically Relevant Abnormalities in Laboratory Tests (Haematology, Chemistry, Urinalysis), Vital Signs, and Electrocardiograms (ECG)

End point title	Number of Subjects With Individual Clinically Relevant Abnormalities in Laboratory Tests (Haematology, Chemistry, Urinalysis), Vital Signs, and Electrocardiograms (ECG)

End point description:

Individual clinically relevant abnormalities: Potentially clinically significant abnormalities (PCSA) considered as SAEs or TEAEs leading to study treatment discontinuation or study discontinuation during the on-treatment period (time from first study drug administration until Week 16), considering all evaluations performed during the on-treatment period that included unscheduled or repeated evaluations. Analysis was performed on safety population. Data was planned to be collected and analysed on pooled population of subjects at each dose level of SAR442168 (either in Cohort 1 or 2), and pooled population of subjects receiving Placebo in Cohort 2 and was not planned to be collected during placebo administration in Cohort 1 (Weeks 12 to 16).

End point type	Secondary

End point timeframe:

Baseline up to Week 12 for Cohort 1 subjects; Baseline up to Week 4 for Cohort 2 Placebo and from Week 4 to 16 for Cohort 2 SAR442168 receiving subjects

End point values	Cohort 2: Pooled Placebo	Cohorts 1 and 2: SAR442168 5 mg	Cohorts 1 and 2: SAR442168 15 mg	Cohorts 1 and 2: SAR442168 30 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	66	33	32	33
Units: subjects				
Haematology	0	0	0	0
Chemistry	0	0	0	0
Urinalysis	0	0	0	0
Vital Signs	0	0	0	0
ECGs	0	0	0	0

End point values	Cohorts 1 and 2: SAR442168 60 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: subjects				
Haematology	0			
Chemistry	0			
Urinalysis	0			
Vital Signs	0			
ECGs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from the signature of the informed consent form until the end of the study (Week 16) regardless of seriousness or relationship to study drug.

Adverse event reporting additional description:

Reported AEs and deaths are TEAEs that developed, worsened, or became serious during the treatment-emergent period (time from the first dose of study treatment up to 30 days after last dose of study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Cohort 1: SAR442168 5 mg Then Placebo

Reporting group description:

Subjects received SAR442168 5 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, eachsubject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 1: SAR442168 15 mg Then Placebo

Reporting group description:

Subjects received SAR442168 15 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 1: SAR442168 30 mg Then Placebo

Reporting group description:

Subjects received SAR442168 30 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 1: SAR442168 60 mg Then Placebo

Reporting group description:

Subjects received SAR442168 60 mg, orally once daily for first 12 weeks then crossed over to matching placebo orally once daily for 4 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 5 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 5 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo then SAR442168 15 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 15 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 and placebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 30 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 30 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 andplacebo, to achieve the specified daily dose of SAR442168.

Reporting group title	Cohort 2: Placebo Then SAR442168 60 mg

Reporting group description:

Subjects received placebo matching to SAR442168 tablets, orally once daily for first 4 weeks then crossed over to SAR442168 60 mg orally once daily for 12 weeks during the 16 weeks treatment period. To maintain the blinding, each subject was given a total of 4 tablets daily, either of SAR442168 or SAR442168 andplacebo, to achieve the specified daily dose of SAR442168.

Serious adverse events	Cohort 1: SAR442168 5 mg Then Placebo	Cohort 1: SAR442168 15 mg Then Placebo	Cohort 1: SAR442168 30 mg Then Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (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	Cohort 1: SAR442168 60 mg Then Placebo	Cohort 2: Placebo Then SAR442168 5 mg	Cohort 2: Placebo then SAR442168 15 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2: Placebo Then SAR442168 30 mg	Cohort 2: Placebo Then SAR442168 60 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Multiple Sclerosis Relapse			

subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: SAR442168 5 mg Then Placebo	Cohort 1: SAR442168 15 mg Then Placebo	Cohort 1: SAR442168 30 mg Then Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	8 / 16 (50.00%)	8 / 16 (50.00%)
Vascular disorders			
Hot Flush			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chronic Fatigue Syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injection Site Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oedema Peripheral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy To Animal			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Cervix Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Premenstrual Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Uterine Polyp			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sinus Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Grief Reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood Glucose Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood Immunoglobulin M Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Red Blood Cell Count Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reticulocyte Count Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Weight Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Accidental Overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Animal Bite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Arthropod Sting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rib Fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Cystic Lymphangioma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Sinus Bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Supraventricular Extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	3	1	0
Hypersomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Migraine			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Migraine Without Aura			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle Spasticity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Restless Legs Syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Tension Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry Eye			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Eye Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Chronic Gastritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Constipation			

subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Dental Caries			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Stomatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Petechiae			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal Colic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary Incontinence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Back Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle Spasms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscle Twitching			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Herpes Zoster			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oral Herpes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Tonsillitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Urinary Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Vulvovaginal Candidiasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1: SAR442168 60 mg Then Placebo	Cohort 2: Placebo Then SAR442168 5 mg	Cohort 2: Placebo then SAR442168 15 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)	13 / 17 (76.47%)	12 / 16 (75.00%)
Vascular disorders			
Hot Flush			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chronic Fatigue Syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Injection Site Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oedema Peripheral			

subjects affected / exposed	2 / 16 (12.50%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Immune system disorders			
Allergy To Animal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Cervix Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dysmenorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Premenstrual Headache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Uterine Polyp			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sinus Pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract			

Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Grief Reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood Glucose Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood Immunoglobulin M Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Red Blood Cell Count Decreased			

subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reticulocyte Count Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Weight Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Animal Bite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Arthropod Sting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rib Fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Cystic Lymphangioma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sinus Bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Supraventricular Extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 16 (12.50%)	2 / 17 (11.76%)	4 / 16 (25.00%)
occurrences (all)	2	2	4
Hypersomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Migraine Without Aura			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Muscle Spasticity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Restless Legs Syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tension Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Dry Eye			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Chronic Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dental Caries			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Renal Colic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary Incontinence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Back Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Bursitis			

subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscle Spasms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle Twitching			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Herpes Zoster			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Oral Herpes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Respiratory Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Urinary Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal Candidiasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Cohort 2: Placebo Then SAR442168 30 mg	Cohort 2: Placebo Then SAR442168 60 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 17 (64.71%)	11 / 16 (68.75%)	
Vascular disorders			
Hot Flush			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
General disorders and administration			

site conditions			
Chronic Fatigue Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Injection Site Erythema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Oedema Peripheral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Allergy To Animal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Cervix Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dysmenorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Premenstrual Headache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Uterine Polyp			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	

Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal Pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Sinus Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Upper Respiratory Tract Inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Grief Reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Irritability			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Aspartate Aminotransferase Increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Blood Glucose Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Blood Immunoglobulin M Decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Red Blood Cell Count Decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Reticulocyte Count Decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Weight Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 17 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	4	
Animal Bite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Arthropod Sting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Rib Fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			

Cystic Lymphangioma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Sinus Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Supraventricular Extrasystoles			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 17 (5.88%)	2 / 16 (12.50%)	
occurrences (all)	1	5	
Hypersomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Migraine Without Aura			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Muscle Spasticity			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Restless Legs Syndrome			

subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Tension Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Eye disorders			
Dry Eye			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Eye Pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Chronic Gastritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Dental Caries			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nausea			

subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Petechiae			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Renal Colic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Urinary Incontinence			

subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Urinary Tract Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Back Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Bursitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Muscle Spasms			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Muscle Twitching			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pain In Extremity			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Herpes Zoster			

subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	3	
Oral Herpes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory Tract Infection			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Urinary Tract Infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Viral Upper Respiratory Tract			

Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal Candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2019	1. Addition of Weeks 2 and 6 hematology tests in response to the request by Health Canada. 2. Modification of the inclusion criteria to extend the time (i.e., up to 2 months after the last study dose) that a female subject had to use a double contraception method including a highly effective method of birth control, in response to the request by Health Canada. 3. Increase of maximum amount of blood collected per subject over the duration of the study from 60 to 70 millilitres (mL), and from 105 to 115 mL for subjects in the biomarker sub-study. 4. Addition of creatine phosphokinase to protocol-required safety laboratory assessments in response to the request by the United States Food and Drug Administration (FDA).
09 April 2019	1. Addition of clinical site visit (for hematology) in the schedule of activities at Weeks 2 and 6, and physical examination at Week 4. 2. Addition of "OR" in the inclusion criterion to clarify that subject had to have at least 1 documented relapse within the previous year OR greater than or equal to (>=) 2 documented relapses within the previous 2 years OR >=1 active Gd-enhancing brain lesion on an MRI scan in the past 6 months and prior to screening. 3. Update of exclusion criterion to delete "if more than 81 milligram (mg)/day" as aspirin use was prohibited in the study. 4. Addition of short course of non-acetylsalicylic acid nonsteroidal anti-inflammatory drug (NSAIDs) to permitted co-medications to specify that only short courses of NSAIDs could be used; also prolonged use might increase the risk of bleeding. 5. Addition of text regarding use of avoidance of use of proton pump inhibitors and timing of concomitant use of antacids and H2-receptor antagonists. 6. Addition of the sentence: "Female subjects of childbearing potential were eligible to participate if they agreed to use double methods of contraception, including 1 highly effective method consistently and correctly.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported