Clinical trial results:
A Phase 2a/2b Double-Blind, Randomized, Placebo-Controlled Study Assessing Efficacy, Safety, and Dose-Response of Vatelizumab in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS)

Summary

EudraCT number	2014-001643-20
Trial protocol	DE PL SE
Global end of trial date	06 April 2016

Results information

Result version number	v1 (current)
This version publication date	22 July 2017
First version publication date	22 July 2017

Trial information

Trial identification

Sponsor protocol code	DRI13839

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02222948
WHO universal trial number (UTN)	U1111-1153-3840
Other trial identifiers	Study name: EMPIRE

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
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	27 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

-To assess the efficacy of vatelizumab compared to placebo as measured by a reduction in new contrast-enhancing lesions (CELs) in Relapsing-Remitting Multiple Sclerosis (RRMS) subjects; and
-To evaluate mutiple doses of vatelizumab for a dose-response.

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	23 September 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	23 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	Russian Federation: 54
Country: Number of subjects enrolled	United States: 17
Country: Number of subjects enrolled	Canada: 2
Worldwide total number of subjects	112
EEA total number of subjects	39

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	112
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 21 sites in 4 countries from 23 September 2014 to 06 April 2016. A total of 183 subjects were screened, of whom, 112 randomized in the study. Based on the results of an interim analysis, a decision was made to discontinue study treatment as per Sponsor’s decision, which was notified to all investigators in October 2015.

Pre-assignment

Screening details:

First 48 subjects were randomized in 1:1 ratio to placebo or vatelizumab 1600 mg. After randomization of 48th subject, additional 120 subjects were to be randomized which was not completed based on results of an interim analysis and only 64 additional subjects randomized to vatelizumab 1600 mg,1200 mg,800 mg,400 mg or placebo in 1:1:1:1:1 ratio.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo (for vatelizumab) intravenous (IV) infusion at Week 0, 2, 4, and 8.

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

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Arm title	Vatelizumab 1600 mg

Arm description:

Vatelizumab 1600 mg IV infusion at Week 0, 2, 4, and 8.

Arm type	Experimental
Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Arm title	Vatelizumab 1200 mg

Arm description:

Vatelizumab 1200 mg IV infusion at Week 0, 2, 4, and 8.

Arm type	Experimental

Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Arm title	Vatelizumab 800 mg

Arm description:

Vatelizumab 800 mg IV infusion at Week 0, 2, 4, and 8.

Arm type	Experimental
Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Arm title	Vatelizumab 400 mg

Arm description:

Vatelizumab 400 mg IV infusion at Week 0, 2, 4, and 8.

Arm type	Experimental
Investigational medicinal product name	Vatelizumab
Investigational medicinal product code	SAR339658
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion over a 60 minutes period.

Number of subjects in period 1	Placebo	Vatelizumab 1600 mg	Vatelizumab 1200 mg
Started	38	36	13
Completed	27	30	6
Not completed	11	6	7
Consent withdrawn by subject	3	5	3
Study terminated by sponsor	7	1	4
Other than specified	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Vatelizumab 800 mg	Vatelizumab 400 mg
Started	12	13
Completed	6	6
Not completed	6	7
Consent withdrawn by subject	3	5
Study terminated by sponsor	2	2

Other than specified	1	-
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo (for vatelizumab) intravenous (IV) infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 1600 mg
Reporting group description:	
Vatelizumab 1600 mg IV infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 1200 mg
Reporting group description:	
Vatelizumab 1200 mg IV infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 800 mg
Reporting group description:	
Vatelizumab 800 mg IV infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 400 mg
Reporting group description:	
Vatelizumab 400 mg IV infusion at Week 0, 2, 4, and 8.	

Reporting group values	Placebo	Vatelizumab 1600 mg	Vatelizumab 1200 mg
Number of subjects	38	36	13
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	37.4	33.6	32.4
standard deviation	± 9.08	± 10.02	± 6.38
Gender categorical Units: Subjects			
Female	27	23	8
Male	11	13	5

Reporting group values	Vatelizumab 800 mg	Vatelizumab 400 mg	Total
Number of subjects	12	13	112
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	34.5	34.2	
standard deviation	± 8.04	± 9.42	-
Gender categorical Units: Subjects			
Female	5	9	72
Male	7	4	40

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo (for vatelizumab) intravenous (IV) infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 1600 mg
Reporting group description: Vatelizumab 1600 mg IV infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 1200 mg
Reporting group description: Vatelizumab 1200 mg IV infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 800 mg
Reporting group description: Vatelizumab 800 mg IV infusion at Week 0, 2, 4, and 8.	
Reporting group title	Vatelizumab 400 mg
Reporting group description: Vatelizumab 400 mg IV infusion at Week 0, 2, 4, and 8.	

Primary: Brain Magnetic Resonance Imaging (MRI) Assessment: Cumulative Number of New T1 Gadolinium (Gd) Contrast-Enhancing Lesions (CELs) Per MRI Scan

End point title	Brain Magnetic Resonance Imaging (MRI) Assessment: Cumulative Number of New T1 Gadolinium (Gd) Contrast-Enhancing Lesions (CELs) Per MRI Scan[1]

End point description:

Cumulative number of Gd-enhancing T1-lesions per MRI scan is the total number of Gd-enhancing T1-lesions that occurred during the treatment period divided by the total number of scans performed during the treatment period. Analysis was performed on safety population defined as randomized population who actually received at least 1 dose or part of a dose of study drug analyzed according to the treatment actually received. Here, 'n' signifies number of subjects with available data for specified timepoints.

End point type	Primary

End point timeframe:

Week 4, Week 8 and Week 12 (End of Treatment [EOT]) (maximum exposure: 62 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Placebo	Vatelizumab 1600 mg	Vatelizumab 1200 mg	Vatelizumab 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	36	13	12
Units: lesions per scan				
arithmetic mean (standard deviation)				
Week 4 (n= 33, 34, 11, 10, 11)	2.8 (± 5.41)	2 (± 2.65)	5.3 (± 8.7)	3.2 (± 3.43)
Week 8 (n= 30, 32, 8, 8, 8)	4.8 (± 8.08)	3.3 (± 4.99)	14.8 (± 16.86)	3.8 (± 3.92)
Week 12 (EOT [n= 26, 30, 7, 6, 5])	8.1 (± 12.25)	5.5 (± 7.4)	21.1 (± 39.21)	6.8 (± 6.62)

End point values	Vatelizumab 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: lesions per scan				
arithmetic mean (standard deviation)				
Week 4 (n= 33, 34, 11, 10, 11)	1.8 (± 2.64)			
Week 8 (n= 30, 32, 8, 8, 8)	1.6 (± 2.77)			
Week 12 (EOT [n= 26, 30, 7, 6, 5])	1 (± 2.24)			

Statistical analyses

No statistical analyses for this end point

Primary: Brain MRI Assessment: Cumulative Number of New or Newly Enlarging T2 Lesions per MRI Scan

End point title	Brain MRI Assessment: Cumulative Number of New or Newly Enlarging T2 Lesions per MRI Scan[2]

End point description:

Number of Gd-enhancing T2-lesions per scan is the total number of Gd-enhancing T2-lesions that occurred during the treatment period divided by the total number of scans performed during the treatment period. Analysis was performed on safety population. Here, 'n' signifies number of subjects with available data for specified timepoints.

End point type	Primary

End point timeframe:

Week 4, Week 8 and Week 12 (EOT) (maximum exposure: 62 days)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Placebo	Vatelizumab 1600 mg	Vatelizumab 1200 mg	Vatelizumab 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	36	13	12
Units: lesions per scan				
arithmetic mean (standard deviation)				
Week 4 (n= 33, 34, 11, 10, 11)	3.5 (± 6.3)	2.9 (± 3.37)	6.5 (± 9.23)	4.7 (± 5.83)
Week 8 (n= 30, 32, 8, 8, 8)	6.4 (± 9.94)	6 (± 8.25)	15.8 (± 17.79)	5.4 (± 5.18)
Week 12 (EOT [n= 26, 30, 7, 6, 5])	10.2 (± 14.29)	7.9 (± 9.58)	21.4 (± 36.57)	8.7 (± 8.38)

End point values	Vatelizumab 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			

Units: lesions per scan				
arithmetic mean (standard deviation)				
Week 4 (n= 33, 34, 11, 10, 11)	2.7 (± 3.58)			
Week 8 (n= 30, 32, 8, 8, 8)	2.8 (± 4.2)			
Week 12 (EOT [n= 26, 30, 7, 6, 5])	2 (± 3.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Serum Concentration of Vatelizumab

End point title	Pharmacokinetics: Serum Concentration of Vatelizumab[3]

End point description:

Blood samples were collected for determination of serum vatelizumab concentration at Week 0, 2, 4 and 8 prior to the start of infusion and at the end of infusion. A single PK sample was collected at Week 12 (all subjects) and Week 14, 20, and 32 (subjects not participating in separate extension study). Analysis was performed on safety population. Here, 'n' signifies number of subjects with available data for specified timepoints.

End point type	Secondary

End point timeframe:

Week 0, 2, 4, 8 (pre-dose and any time after the end of infusion); Week 12, 14, 20 and Week 32 (anytime)

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: The endpoint was planned to be analyzed only for vatelizumab, and not for placebo.

End point values	Vatelizumab 1600 mg	Vatelizumab 1200 mg	Vatelizumab 800 mg	Vatelizumab 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	13	12	13
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 0:predose (n=36,13,12,13)	12.5 (± 75.13)	0.1 (± 0.34)	0 (± 0)	0 (± 0)
Week 0:after the end of infusion (n=36,13,12,13)	478.4 (± 148.33)	363 (± 123.26)	248.9 (± 46.59)	123.8 (± 24.54)
Week 2:predose (n=35,11,10,11)	121 (± 28.1)	106.7 (± 21.13)	59.3 (± 14.08)	23 (± 10.95)
Week 2:after the end of infusion (n=35,10,9,11)	595.8 (± 124.47)	440.9 (± 77.01)	284.7 (± 42.61)	137.3 (± 35.11)
Week 4:predose (n=33,10,8,9)	198.5 (± 46.12)	181.7 (± 71.9)	106.2 (± 26.65)	45.1 (± 24.34)
Week 4:after the end of infusion (n=33,10,8,9)	657.4 (± 128.34)	512.6 (± 86.56)	325.2 (± 50.14)	163.9 (± 46.13)
Week 8:predose (n=30,6,6,6)	154.1 (± 49.38)	126.5 (± 46.58)	82.2 (± 29.87)	22.9 (± 7.23)
Week 8:after the end of infusion (n=29,6,6,6)	579.9 (± 176.2)	493.4 (± 87.59)	323.6 (± 47.36)	134.7 (± 20.89)
Week 12:(n=35,13,12,12)	130.6 (± 50.52)	136.3 (± 57)	74.6 (± 22.81)	30.7 (± 20.67)
Week 14:post-treatment (n=6,7,4,4)	64.1 (± 23.57)	68.6 (± 44.62)	28.7 (± 12.38)	9.9 (± 4.02)
Week 20:post-treatment (n= 3, 4, 5, 4)	5.3 (± 6.51)	7 (± 4.59)	2 (± 1.4)	2.4 (± 3.74)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (Week 104) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (time from the first administration of study drug to the end of the safety follow-up period [Week 104]).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo (for vatelizumab) IV infusion at Week 0, 2, 4, and 8.

Reporting group title	Vatelizumab 1600 mg

Reporting group description:

Vatelizumab 1600 mg IV infusion at Week 0, 2, 4, and 8.

Reporting group title	Vatelizumab 1200 mg

Reporting group description:

Vatelizumab 1200 mg IV infusion at Week 0, 2, 4, and 8.

Reporting group title	Vatelizumab 800 mg

Reporting group description:

Vatelizumab 800 mg IV infusion at Week 0, 2, 4, and 8.

Reporting group title	Vatelizumab 400 mg

Reporting group description:

Vatelizumab 400 mg IV infusion at Week 0, 2, 4, and 8.

Serious adverse events	Placebo	Vatelizumab 1600 mg	Vatelizumab 1200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	0 / 13 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	0 / 13 (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

Serious adverse events	Vatelizumab 800 mg	Vatelizumab 400 mg	

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (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	Placebo	Vatelizumab 1600 mg	Vatelizumab 1200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 38 (34.21%)	9 / 36 (25.00%)	2 / 13 (15.38%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 38 (5.26%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 38 (2.63%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Infusion Related Reaction			
subjects affected / exposed	2 / 38 (5.26%)	1 / 36 (2.78%)	2 / 13 (15.38%)
occurrences (all)	2	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 38 (13.16%)	5 / 36 (13.89%)	1 / 13 (7.69%)
occurrences (all)	5	5	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	1 / 38 (2.63%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 38 (0.00%)	3 / 36 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Gastritis Erosive			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Endocrine disorders			
Autoimmune Thyroiditis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Oral Herpes			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 38 (5.26%)	0 / 36 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Urinary Tract Infection			
subjects affected / exposed	2 / 38 (5.26%)	1 / 36 (2.78%)	0 / 13 (0.00%)
occurrences (all)	3	1	0

Non-serious adverse events	Vatelizumab 800 mg	Vatelizumab 400 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	3 / 13 (23.08%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infusion Related Reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Gastritis Erosive			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Autoimmune Thyroiditis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			
Oral Herpes			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			

subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Urinary Tract Infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2015	Amendment 1 addresses the following changes: •Modified treatment discontinuation criteria: changed the threshold from >10 to >8 new CELs and/or new/newly enlarging T2 lesions for assessing MS disease activity on MRI scan:For subjects who developed more than 8 new CELs and/or 8 new/newly enlarging T2 lesions instead of 10 new CELs and/or 10 new/newly enlarging T2 lesions on any MRI scan after the second infusion of IMP, the Investigator was advised to review the subject's disease status and consider withdrawing the subject from study treatment and starting an approved MS therapy. The central MRI reader would notified the Investigator, study coordinator, and Sponsor when a subject had met these MRI criteria. •Correct description of collection of informed consent for optional extension study at Week 8: Informed consent to be obtained prior to enrolment in the extension study and to be detailed in that protocol only. •Updated text regarding extension study. •Provided additional information regarding acquisition of MRI scan. •Corrected and clarified typos, inconsistencies throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As per sponsor's decision, the study was discontinued in October 2015 based on planned interim analysis of the primary endpoint. Not linked to any safety concern.

Notes: