Clinical trial results:
A Multicenter, Open-label Immunogenicity and Safety Study of Subcutaneous Natalizumab 300 mg Administered to Subjects With Relapsing Multiple Sclerosis

Summary

EudraCT number	2014-000917-30
Trial protocol	DE IT DK BE
Global end of trial date	04 June 2015

Results information

Result version number	v1 (current)
This version publication date	14 May 2016
First version publication date	14 May 2016

Trial information

Trial identification

Sponsor protocol code	101MS207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02142192
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, Massachusetts , United States, 02142
Public contact	Biogen Study Medical Director, Biogen , clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen , clinicaltrials@biogen.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	04 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 June 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the immunogenicity of natalizumab 300 mg subcutaneous (SC) administered to subjects with relapsing multiple sclerosis (RMS). The secondary objectives are to evaluate the safety of natalizumab SC injections and to evaluate the efficacy of natalizumab SC injections on relapses and on new magnetic resonance imaging (MRI) lesions.

Protection of trial subjects:

Written informed consent was obtained from each subject prior to evaluations being performed for eligibility. Subjects were given adequate time to review the information in the informed consent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study. Through the informed consent process each subject was made aware of the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken. Any side effects or other health issues occurring during the study were followed up by the study doctor. Subjects were able to stop taking part in the study at any time without giving any reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subject eligibility for the study was determined within approximately 6 weeks prior to study entry. The screening period was extended if there were unforeseen delays in receiving laboratory results necessary for assessing eligibility.

Period 1

Period 1 title	Natalizumab (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Natalizumab

Arm description:

Natalizumab 300 mg SC every 4 weeks for up to 44 weeks

Arm type	Experimental
Investigational medicinal product name	natalizumab
Investigational medicinal product code	
Other name	Tysabri
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to be treated with open-label natalizumab (300 mg SC) at Day 1 and Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, and 44

Number of subjects in period 1	Natalizumab
Started	2
Completed	0
Not completed	2
Sponsor decision to terminate trial	2

Baseline characteristics

Reporting groups	
Reporting group title	Natalizumab
Reporting group description:	
Natalizumab 300 mg SC every 4 weeks for up to 44 weeks	

Reporting group values	Natalizumab	Total	
Number of subjects	2	2	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	1	1	

End points

End points reporting groups

Reporting group title	Natalizumab

Reporting group description:

Natalizumab 300 mg SC every 4 weeks for up to 44 weeks

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population was defined as all subjects who received at least 1 dose of study treatment and had at least 1 post-baseline assessment of the parameter being analyzed.

Primary: Number of Subjects With Persistent Anti-natalizumab Antibodies Over 48 Weeks

End point title	Number of Subjects With Persistent Anti-natalizumab Antibodies Over 48 Weeks[1]

End point description:

Persistent anti-natalizumab antibodies are defined as 2 positive anti-natalizumab test results separated by at least 6 weeks, with at least 1 positive test result occurring at or after the Week 24 Visit. Due to early termination, assessments were completed at screening, post-baseline Week 12, and at Safety Follow-up (12 weeks after last dose administered).

End point type	Primary

End point timeframe:

Screening, Post-Baseline Week 12, Safety Follow-up (12 weeks after last dose administered [up to 172 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: No statistical analyses of the data were performed, since only 2 subjects were enrolled prior to study termination. Data were listed only.

End point values	Safety population			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: Subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Post-injection Adverse Events (AEs)

End point title	Number of Subjects with Post-injection Adverse Events (AEs)

End point description:

The number of subjects with post-injection AEs including hypersensitivity reactions, anaphylactic reactions and other AEs occurring within 1 hour after SC natalizumab dosing.

End point type	Secondary

End point timeframe:

Day 1 to Safety Follow-up (12 weeks after last dose administered [up to 172 days])

End point values	Safety population			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: Subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Relapse or With New or Enlarging T2 Lesions

End point title	Number of Subjects With Clinical Relapse or With New or Enlarging T2 Lesions

End point description:

The number of subjects with clinical relapse, or with new or enlarging T2 lesion(s), as determined by a central MRI reading center, over 48 weeks. Clinical relapse is defined as new or recurrent neurologic symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurologic findings upon examination by the Neurologist. The subject must have had objective signs on the neurologist's examination that confirm the event.

End point type	Secondary

End point timeframe:

Up to Safety Follow-up (12 weeks after last dose administered [up to 172 days])

End point values	Safety population			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: Subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Gadolinium (Gd)-enhancing Lesions

End point title	Number of Subjects With Gadolinium (Gd)-enhancing Lesions

End point description:

Brain MRI scans were planned to occur during screening and then again at the Week 48 Visit and were to include T2 as well as T1 sequences with and without gadolinium (Gd). The data from all of the scheduled MRI scans were evaluated at a central MRI reading center to determine the level of disease activity. Due to early termination of the study, scans were performed at screening only.

End point type	Secondary

End point timeframe:

Screening

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Subjects				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With AEs and Serious AEs (SAEs)

End point title	Number of Subjects With AEs and Serious AEs (SAEs)

End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An SAE is any untoward medical occurrence that at any dose (i) results in death, (ii) places the subject at immediate risk of death, (iii) requires inpatient hospitalization or prolongation of existing hospitalization, (iv) results in persistent or significant disability/incapacity or (v) results in a congenital anomaly/birth defect.

End point type	Secondary

End point timeframe:

AEs: Day 1 to Safety Follow-up (12 weeks after last dose administered [up to 172 days]); SAEs: Informed Consent to Safety Follow-up (12 weeks after last dose administered [up to 172 days])

End point values	Safety population			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: Subjects				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs: Day 1 to Safety Follow-up (12 weeks after last dose administered [up to 172 days]); SAEs: Informed Consent to Safety Follow-up (12 weeks after last dose administered [up to 172 days])	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	Safety Population
Reporting group description: All subjects who received at least 1 dose of study treatment and had at least 1 post-baseline assessment.	

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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.

This study was terminated early by Biogen. This decision was independent of any safety, efficacy, or regulatory concerns related to natalizumab.

Notes: