



## Clinical trial results:

### A Prospective, Non-interventional, Multicenter, Open-label Safety and Efficacy Study of Intravenous Natalizumab Administered to Patients With Relapsing Forms of Multiple Sclerosis who Participated in STRATA Summary

EudraCT number	2014-003669-97
Trial protocol	BE
Global end of trial date	12 January 2017

#### Results information

Result version number	v1 (current)
This version publication date	22 August 2019
First version publication date	22 August 2019

#### Trial information

##### Trial identification

Sponsor protocol code	BEL-TYS-14-10675
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 Binney Street, Cambridge, 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	12 January 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 January 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective for this study was long-term safety (incidence and pattern of serious adverse events) in subjects receiving natalizumab.

Protection of trial subjects:

Written informed consent was obtained from each subject prior to evaluations 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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 December 2014
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: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	7
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited from 4 sites in Belgium.

### Pre-assignment

Screening details:

A total of 7 subjects with relapsing forms of multiple sclerosis were enrolled in the study.

### Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Natalizumab 300 milligram (mg)
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Arm description:

Subjects received single dose of natalizumab 300 mg infusion, intravenously, once every 4 weeks for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Natalizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single dose of natalizumab 300 mg infusion, intravenously, once every 4 weeks for 96 weeks

Number of subjects in period 1	Natalizumab 300 milligram (mg)
Started	7
Completed	3
Not completed	4
Consent withdrawn by subject	1
Unknown	1
Subject moved to another center	1
Treatment Stopped	1

## Baseline characteristics

### Reporting groups

Reporting group title	Overall Period
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Reporting group description:

Subjects received single dose of natalizumab 300 mg infusion, intravenously, once every 4 weeks for 96 weeks.

Reporting group values	Overall Period	Total	
Number of subjects	7	7	
Age Categorical Units: Subjects			
Age Continuous Units: years median full range (min-max)	59 18 to 61	-	
Gender Categorical Units: Subjects			
Female	6	6	
Male	1	1	

## End points

### End points reporting groups

Reporting group title	Natalizumab 300 milligram (mg)
Reporting group description: Subjects received single dose of natalizumab 300 mg infusion, intravenously, once every 4 weeks for 96 weeks.	

### Primary: Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs) <sup>[1]</sup>
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End point description:

An AE is any untoward medical occurrence in a subject 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 results in death, places the subject at immediate risk of death, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, or is a medically important event. Safety analysis set included all subjects enrolled in the study.

End point type	Primary
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End point timeframe:

up to 96 weeks

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: Only descriptive analysis was planned to be reported for this endpoint.

End point values	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: subjects				
AEs	5			
SAEs	1			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Expanded Disability Status Scale (EDSS) Score to Measure Disability Progression at Week 0, 24, 48, 72 and 96

End point title	Expanded Disability Status Scale (EDSS) Score to Measure Disability Progression at Week 0, 24, 48, 72 and 96
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End point description:

EDSS is used to measure disability progression. EDSS score ranges from 0.0 (normal neurological exam) to 10.0 (death due to multiple sclerosis {MS}). Disability progression is defined as 1.5-point increase from baseline in subjects with baseline EDSS score = 0.0; OR 1-point increase in EDSS from baseline in subjects with baseline EDSS score of 1.0 to 5.0 inclusive; OR 0.5-point increase in EDSS from baseline in subjects with baseline EDSS score >5.0. Higher scores indicates worsening of disability progression. Full analysis set (FAS) included all subjects enrolled in the study.

End point type	Secondary
End point timeframe:	
Baseline, Week 24, 48, 72 and 96	

<b>End point values</b>	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: score on a scale				
median (full range (min-max))				
Week 0	2.0 (2.0 to 2.5)			
Week 24	2.5 (2.0 to 2.5)			
Week 48	2.5 (2.0 to 2.5)			
Week 72	2.5 (2.0 to 2.5)			
Week 96	2.25 (2.0 to 2.5)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Clinical Relapses

End point title	Number of Subjects with Clinical Relapses
End point description:	
Multiple Sclerosis (MS) disease activity was assessed by the occurrence of clinical relapses over the study period. FAS included all subjects enrolled in the study.	
End point type	Secondary
End point timeframe:	
up to week 96	

<b>End point values</b>	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: subjects	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Positive Anti-JC Virus (JCV) Antibodies

End point title	Percentage of Subjects with Positive Anti-JC Virus (JCV) Antibodies
End point description: FAS included all subjects enrolled in the study. Here, '99999' signifies data was not collected at Week 96 for subjects with positive anti-JC virus.	
End point type	Secondary
End point timeframe: Baseline, Week 24, 48, 72 and 96	

<b>End point values</b>	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percentage of subjects				
Week 0	71			
Week 24	80			
Week 48	75			
Week 72	100			
Week 96	99999			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Frequent Magnetic Resonance Imaging (MRI) Monitoring at Week 24, 48, 72 and 96

End point title	Percentage of Subjects With Frequent Magnetic Resonance Imaging (MRI) Monitoring at Week 24, 48, 72 and 96
End point description: MRI monitoring in MS subjects performed as per Belgian Study Group of MS (BSGMS) guidelines. FAS included all subjects enrolled in the study.	
End point type	Secondary
End point timeframe: Week 24, 48, 72 and 96	

<b>End point values</b>	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percentage of subjects				
number (not applicable)				
Week 24	29			
Week 48	0			
Week 72	50			

Week 96	50			
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## Statistical analyses

No statistical analyses for this end point

## Secondary: EuroQol-5D (EQ-5D) Score to Assess Quality of life (QoL) at Week 0, 24, 48, 72 and 96

End point title	EuroQol-5D (EQ-5D) Score to Assess Quality of life (QoL) at Week 0, 24, 48, 72 and 96
End point description: The health-related quality of life (HRQoL) was measured using the global evaluation scale of the EuroQol-5 Dimensions (EQ-5D) questionnaire every 6 months. Subjects were asked to evaluate their health status on a scale from 0 (worst possible health status) to 10 (best possible health status). Highest scores indicates healthy quality of life. A average score for all the subjects were reported. FAS included all subjects enrolled in the study.	
End point type	Secondary
End point timeframe: Baseline, Week 24, 48, 72 and 96	

End point values	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: score on a scale				
median (full range (min-max))				
Week 0	7.00 (7.00 to 7.50)			
Week 24	7.00 (7.00 to 7.50)			
Week 48	7.50 (7.00 to 7.50)			
Week 72	7.50 (7.00 to 7.50)			
Week 96	7.00 (7.00 to 7.50)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cognitive Evaluation by Symbol Digit Modalities Test (SDMT) at Week 0, 24, 48, 72 and 96

End point title	Cognitive Evaluation by Symbol Digit Modalities Test (SDMT) at Week 0, 24, 48, 72 and 96
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End point description:

Data for this endpoint was not collected.

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End point type	Secondary
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End point timeframe:

Baseline, Week 24, 48, 72 and 96

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<b>End point values</b>	Natalizumab 300 milligram (mg)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[2]</sup>			
Units: score on a scale				
arithmetic mean (standard deviation)	( )			

Notes:

[2] - Data was not collected.

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 96 weeks

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	PI observed events
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Dictionary version	0.0
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### Reporting groups

Reporting group title	Natalizumab 300 mg
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Reporting group description:

Subjects received single dose of natalizumab 300 mg infusion, intravenously, once every 4 weeks for 96 weeks.

Serious adverse events	Natalizumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Fracture (right malleolar)			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Natalizumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)		
General disorders and administration site conditions			
Fracture (4th right finger)			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Common cold			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Diarrhea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Abdominal cramps			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Urinary infection			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Allergic reaction to spiruline			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastric reflux			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Throat infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
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**

None reported