Clinical trial results:
A Randomized, Blinded, Parallel-Group, Phase 2 Study Exploring the Safety, Tolerability, and Efficacy of Multiple Regimens of Natalizumab in Adult Subjects With Relapsing Multiple Sclerosis

Summary

EudraCT number	2010-024000-10
Trial protocol	BE DE ES IT
Global end of trial date	03 October 2014

Results information

Result version number	v1 (current)
This version publication date	04 February 2016
First version publication date	15 July 2015

Trial information

Trial identification

Sponsor protocol code	101MS206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01405820
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 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	03 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to explore the effects of multiple regimens of natalizumab on disease activity and safety in participants with relapsing-remitting Multiple Sclerosis (RRMS).

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 participant 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. Participants 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	01 August 2011
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	Germany: 71
Country: Number of subjects enrolled	France: 57
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Italy: 109
Worldwide total number of subjects	290
EEA total number of subjects	290

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)	290
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 4 weeks prior to study entry.

Period 1

Period 1 title	Randomized Treatment 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	Natalizumab 300 mg IV every 4 weeks

Arm description:

Natalizumab 300 mg intravenous (IV) every 4 weeks for 60 weeks.

Arm type	Active comparator
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Arm title	Natalizumab 300 mg SC every 4 weeks

Arm description:

Natalizumab 300 mg subcutaneous (SC) every 4 weeks for 60 weeks.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for SC Injection
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Arm title	Natalizumab 300 mg IV every 12 weeks

Arm description:

Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

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

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Arm title	Natalizumab 300 mg SC every 12 weeks

Arm description:

Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.

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

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Investigational medicinal product name	Natalizumab for SC Injection
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Arm title	Natalizumab 150 mg IV every 12 weeks

Arm description:

Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

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

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Arm title	Natalizumab 150 mg SC every 12 weeks

Arm description:

Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for SC Injection
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

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

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Number of subjects in period 1	Natalizumab 300 mg IV every 4 weeks	Natalizumab 300 mg SC every 4 weeks	Natalizumab 300 mg IV every 12 weeks
Started	54	45	52
Completed	43	35	9
Not completed	11	10	43
Withdrew prior to dosing	-	-	-
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	6	2	2
Physician decision	-	2	1
Adverse event, non-fatal	3	3	3
Incorrect study treatment	-	-	3
Not Specified	2	2	1
Treatment arm closed	-	-	20
Rescue	-	1	13

Number of subjects in period 1	Natalizumab 300 mg SC every 12 weeks	Natalizumab 150 mg IV every 12 weeks	Natalizumab 150 mg SC every 12 weeks
Started	54	47	38
Completed	3	2	1
Not completed	51	45	37
Withdrew prior to dosing	1	-	-
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	2	-	-

Physician decision	-	-	-
Adverse event, non-fatal	-	2	1
Incorrect study treatment	-	2	-
Not Specified	1	-	-
Treatment arm closed	36	33	28
Rescue	10	8	8

Period 2

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

Arms

Are arms mutually exclusive?	No
Arm title	Natalizumab 300 mg IV every 4 weeks

Arm description:

Natalizumab 300 mg IV every 4 weeks for 60 weeks. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks.

Arm title	Natalizumab 300 mg SC every 4 weeks

Arm description:

Natalizumab 300 mg SC every 4 weeks for 60 weeks. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks.

Arm title	Natalizumab 300 mg IV every 12 weeks

Arm description:

Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Arm type	Experimental

Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks.

Arm title	Natalizumab 300 mg SC every 12 weeks

Arm description:

Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks.

Arm title	Natalizumab 150 mg IV every 12 weeks

Arm description:

Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All subjects received study treatment every 4 weeks.

Arm title	Natalizumab 150 mg SC every 12 weeks

Arm description:

Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Arm type	Experimental
Investigational medicinal product name	Natalizumab for Subcutaneous Injection
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

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

Dosage and administration details:

All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Number of subjects in period 2	Natalizumab 300 mg IV every 4 weeks	Natalizumab 300 mg SC every 4 weeks	Natalizumab 300 mg IV every 12 weeks
Started	44	35	42
Completed	40	33	39
Not completed	4	2	3
Consent withdrawn by subject	3	1	1
Physician decision	-	-	1
Adverse event, non-fatal	-	-	-
Not Specified	1	1	1

Number of subjects in period 2	Natalizumab 300 mg SC every 12 weeks	Natalizumab 150 mg IV every 12 weeks	Natalizumab 150 mg SC every 12 weeks
Started	42	42	32
Completed	37	40	30
Not completed	5	2	2
Consent withdrawn by subject	1	-	1
Physician decision	2	1	-
Adverse event, non-fatal	1	-	-
Not Specified	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Natalizumab 300 mg IV every 4 weeks
Reporting group description:	
Natalizumab 300 mg intravenous (IV) every 4 weeks for 60 weeks.	
Reporting group title	Natalizumab 300 mg SC every 4 weeks
Reporting group description:	
Natalizumab 300 mg subcutaneous (SC) every 4 weeks for 60 weeks.	
Reporting group title	Natalizumab 300 mg IV every 12 weeks
Reporting group description:	
Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.	
Reporting group title	Natalizumab 300 mg SC every 12 weeks
Reporting group description:	
Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.	
Reporting group title	Natalizumab 150 mg IV every 12 weeks
Reporting group description:	
Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.	
Reporting group title	Natalizumab 150 mg SC every 12 weeks
Reporting group description:	
Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.	

Reporting group values	Natalizumab 300 mg IV every 4 weeks	Natalizumab 300 mg SC every 4 weeks	Natalizumab 300 mg IV every 12 weeks
Number of subjects	54	45	52
Age, Customized Units: participants			
18 to 19 years	0	1	0
20 to 29 years	7	11	7
30 to 39 years	22	15	21
40 to 49 years	20	16	17
50 to 56 years	5	2	7
Age Continuous Units: years			
arithmetic mean	38.4	36.3	38.7
standard deviation	± 7.84	± 8.92	± 8.43
Gender, Male/Female Units: participants			
Female	39	29	37
Male	15	16	15

Reporting group values	Natalizumab 300 mg SC every 12 weeks	Natalizumab 150 mg IV every 12 weeks	Natalizumab 150 mg SC every 12 weeks
Number of subjects	54	47	38

Age, Customized Units: participants			
18 to 19 years	0	0	0
20 to 29 years	7	5	11
30 to 39 years	24	21	14
40 to 49 years	17	16	9
50 to 56 years	6	5	4
Age Continuous Units: years			
arithmetic mean	38.7	38.7	36
standard deviation	± 7.85	± 8.61	± 9.03
Gender, Male/Female Units: participants			
Female	41	34	24
Male	13	13	14

Reporting group values	Total		
Number of subjects	290		
Age, Customized Units: participants			
18 to 19 years	1		
20 to 29 years	48		
30 to 39 years	117		
40 to 49 years	95		
50 to 56 years	29		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: participants			
Female	204		
Male	86		

End points

End points reporting groups

Reporting group title	Natalizumab 300 mg IV every 4 weeks
Reporting group description:	
Natalizumab 300 mg intravenous (IV) every 4 weeks for 60 weeks.	
Reporting group title	Natalizumab 300 mg SC every 4 weeks
Reporting group description:	
Natalizumab 300 mg subcutaneous (SC) every 4 weeks for 60 weeks.	
Reporting group title	Natalizumab 300 mg IV every 12 weeks
Reporting group description:	
Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.	
Reporting group title	Natalizumab 300 mg SC every 12 weeks
Reporting group description:	
Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.	
Reporting group title	Natalizumab 150 mg IV every 12 weeks
Reporting group description:	
Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.	

Reporting group title	Natalizumab 150 mg SC every 12 weeks
Reporting group description:	
Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.	

Reporting group title	Natalizumab 300 mg IV every 4 weeks
Reporting group description:	
Natalizumab 300 mg IV every 4 weeks for 60 weeks. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.	
Reporting group title	Natalizumab 300 mg SC every 4 weeks
Reporting group description:	
Natalizumab 300 mg SC every 4 weeks for 60 weeks. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.	
Reporting group title	Natalizumab 300 mg IV every 12 weeks
Reporting group description:	
Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.	
Reporting group title	Natalizumab 300 mg SC every 12 weeks
Reporting group description:	
Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.	
Reporting group title	Natalizumab 150 mg IV every 12 weeks
Reporting group description:	
Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.	
Reporting group title	Natalizumab 150 mg SC every 12 weeks
Reporting group description:	
Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.	

Primary: Cumulative Number of Combined Unique Active Lesions

End point title	Cumulative Number of Combined Unique Active Lesions[1]

End point description:

Cumulative number of combined unique active lesions (sum of the number of new gadolinium (Gd)-enhancing lesions and new or newly enlarging T2 hyperintense lesions not associated with Gd-enhancement on T1 weighted scans) based on brain magnetic resonance imaging (MRI) scans up to Week 60. Modified intent-to-treat (mITT) population: all randomized subjects who received at least 1 dose of study drug, had at least 1 efficacy assessment, and had no statistical protocol deviations.

End point type	Primary

End point timeframe:

Up to Week 60

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: Descriptive statistics were planned for this endpoint, and are presented here.

End point values	Natalizumab 300 mg IV every 4 weeks	Natalizumab 300 mg SC every 4 weeks	Natalizumab 300 mg IV every 12 weeks	Natalizumab 300 mg SC every 12 weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	44	45	50
Units: lesions				
arithmetic mean (standard deviation)	0.23 (± 1.262)	0.02 (± 0.151)	3.84 (± 8.054)	3.08 (± 8.216)

End point values	Natalizumab 150 mg IV every 12 weeks	Natalizumab 150 mg SC every 12 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: lesions				
arithmetic mean (standard deviation)	6.09 (± 15.424)	6.44 (± 11.285)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were analyzed during the randomized and open-label periods separately. Randomized period: AEs, after 1st randomized dose on Day 0 and prior to open-label infusion of natalizumab at Week 60 (±5 days); SAEs also between Screening and dosing on Day 0.

Adverse event reporting additional description:

Open-label period: on or after open-label infusion of natalizumab at Week 60 through to Week 72 (±2 weeks). If participant did not receive natalizumab infusions during the open-label period (Week 60 to Week 72), all events with an onset date after Day 0 were considered as occurring during the randomized treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Randomized Period: Natalizumab 300 mg IV every 4 weeks

Reporting group description:

Natalizumab 300 mg IV every 4 weeks for 60 weeks.

Reporting group title	Randomized Period: Natalizumab 300 mg SC every 4 weeks

Reporting group description:

Natalizumab 300 mg SC every 4 weeks for 60 weeks.

Reporting group title	Randomized Period: Natalizumab 300 mg IV every 12 weeks

Reporting group description:

Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.

Reporting group title	Randomized Period: Natalizumab 300 mg SC every 12 weeks

Reporting group description:

Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.

Reporting group title	Randomized Period: Natalizumab 150 mg IV every 12 weeks

Reporting group description:

Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods.

Reporting group title	Randomized Period: Natalizumab 150 mg SC every 12 weeks

Reporting group description:

Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods.

Reporting group title	Open-label Period: Natalizumab 300 mg IV every 4 weeks

Reporting group description:

Natalizumab 300 mg IV every 4 weeks for 60 weeks. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Reporting group title	Open-label Period: Natalizumab 300 mg SC every 4 weeks

Reporting group description:

Natalizumab 300 mg SC every 4 weeks for 60 weeks. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Reporting group title	Open-label Period: Natalizumab 300 mg IV every 12 weeks

Reporting group description:

Natalizumab 300 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Reporting group title	Open-label Period: Natalizumab 300 mg SC every 12 weeks

Reporting group description:

Natalizumab 300 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during

the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Reporting group title	Open-label Period: Natalizumab 150 mg IV every 12 weeks

Reporting group description:

Natalizumab 150 mg IV every 12 weeks for 60 weeks with matching IV placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Reporting group title	Open-label Period: Natalizumab 150 mg SC every 12 weeks

Reporting group description:

Natalizumab 150 mg SC every 12 weeks for 60 weeks with matching SC placebo administered during the intervening 4-week periods. Open-label natalizumab treatment 300 mg IV at Weeks 60, 64, and 68.

Serious adverse events	Randomized Period: Natalizumab 300 mg IV every 4 weeks	Randomized Period: Natalizumab 300 mg SC every 4 weeks	Randomized Period: Natalizumab 300 mg IV every 12 weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 54 (12.96%)	4 / 45 (8.89%)	4 / 52 (7.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma In Situ			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Adenocarcinoma Metastatic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			

subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	1 / 54 (1.85%)	2 / 45 (4.44%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (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
Cerebrovascular Insufficiency			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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
Coma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 45 (2.22%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (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
Abdominal Pain			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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
Psychiatric disorders			

Bipolar I Disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (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
Pathological Gambling			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (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
Renal and urinary disorders			
Automatic Bladder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Retention			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (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
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 45 (2.22%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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
Meningitis Enteroviral			

subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Progressive Multifocal Leukoencephalopathy			
subjects affected / exposed	1 / 54 (1.85%)	0 / 45 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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
Bronchitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (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	Randomized Period: Natalizumab 300 mg SC every 12 weeks	Randomized Period: Natalizumab 150 mg IV every 12 weeks	Randomized Period: Natalizumab 150 mg SC every 12 weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 53 (5.66%)	4 / 47 (8.51%)	1 / 38 (2.63%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma In Situ			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Lung Adenocarcinoma Metastatic			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	0 / 38 (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
Radius Fracture			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	0 / 38 (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
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	0 / 38 (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
Cerebrovascular Insufficiency			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	0 / 38 (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
Coma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Polyneuropathy			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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

Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Abdominal Pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Psychiatric disorders			
Bipolar I Disorder			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Pathological Gambling			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Renal and urinary disorders			
Automatic Bladder			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Urinary Retention			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	0 / 38 (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
Meningitis Enteroviral			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Progressive Multifocal Leukoencephalopathy			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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
Urosepsis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (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	Open-label Period: Natalizumab 300 mg IV every 4 weeks	Open-label Period: Natalizumab 300 mg SC every 4 weeks	Open-label Period: Natalizumab 300 mg IV every 12 weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)	1 / 35 (2.86%)	0 / 42 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma In Situ			

subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Lung Adenocarcinoma Metastatic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Epilepsy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Cerebrovascular Insufficiency			

subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Coma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Polyneuropathy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Abdominal Pain			
subjects affected / exposed	0 / 44 (0.00%)	1 / 35 (2.86%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar I Disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Pathological Gambling			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Renal and urinary disorders			
Automatic Bladder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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

Urinary Retention			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Meningitis Enteroviral			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Progressive Multifocal Leukoencephalopathy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Urosepsis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (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
Bronchitis			

subjects affected / exposed	0 / 44 (0.00%)	1 / 35 (2.86%)	0 / 42 (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	Open-label Period: Natalizumab 300 mg SC every 12 weeks	Open-label Period: Natalizumab 150 mg IV every 12 weeks	Open-label Period: Natalizumab 150 mg SC every 12 weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 42 (2.38%)	1 / 42 (2.38%)	2 / 32 (6.25%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma In Situ			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Lung Adenocarcinoma Metastatic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Nervous system disorders			

Multiple Sclerosis Relapse			
subjects affected / exposed	1 / 42 (2.38%)	1 / 42 (2.38%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Cerebrovascular Insufficiency			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Coma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Polyneuropathy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Abdominal Pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Psychiatric disorders			
Bipolar I Disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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

Pathological Gambling			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Renal and urinary disorders			
Automatic Bladder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Urinary Retention			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Meningitis Enteroviral			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Progressive Multifocal Leukoencephalopathy			

subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Urosepsis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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
Bronchitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (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

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

Non-serious adverse events	Randomized Period: Natalizumab 300 mg IV every 4 weeks	Randomized Period: Natalizumab 300 mg SC every 4 weeks	Randomized Period: Natalizumab 300 mg IV every 12 weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 54 (74.07%)	31 / 45 (68.89%)	31 / 52 (59.62%)
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	0 / 54 (0.00%)	0 / 45 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 54 (0.00%)	1 / 45 (2.22%)	3 / 52 (5.77%)
occurrences (all)	0	1	3
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	8 / 54 (14.81%)	6 / 45 (13.33%)	13 / 52 (25.00%)
occurrences (all)	9	6	14
Headache			
subjects affected / exposed	4 / 54 (7.41%)	9 / 45 (20.00%)	7 / 52 (13.46%)
occurrences (all)	7	12	18
Paraesthesia			

subjects affected / exposed	2 / 54 (3.70%)	1 / 45 (2.22%)	2 / 52 (3.85%)
occurrences (all)	3	2	2
Sciatica			
subjects affected / exposed	1 / 54 (1.85%)	1 / 45 (2.22%)	3 / 52 (5.77%)
occurrences (all)	1	2	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 54 (11.11%)	6 / 45 (13.33%)	4 / 52 (7.69%)
occurrences (all)	6	6	4
Injection Site Pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 45 (2.22%)	0 / 52 (0.00%)
occurrences (all)	0	4	0
Pyrexia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 45 (2.22%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Pain			
subjects affected / exposed	0 / 54 (0.00%)	3 / 45 (6.67%)	0 / 52 (0.00%)
occurrences (all)	0	4	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 54 (7.41%)	4 / 45 (8.89%)	2 / 52 (3.85%)
occurrences (all)	4	5	2
Nausea			
subjects affected / exposed	3 / 54 (5.56%)	4 / 45 (8.89%)	2 / 52 (3.85%)
occurrences (all)	3	4	2
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	4 / 45 (8.89%)	0 / 52 (0.00%)
occurrences (all)	1	4	0
Constipation			
subjects affected / exposed	2 / 54 (3.70%)	1 / 45 (2.22%)	0 / 52 (0.00%)
occurrences (all)	2	1	0
Abdominal Pain			
subjects affected / exposed	1 / 54 (1.85%)	4 / 45 (8.89%)	0 / 52 (0.00%)
occurrences (all)	1	4	0
Toothache			

subjects affected / exposed	4 / 54 (7.41%)	0 / 45 (0.00%)	0 / 52 (0.00%)
occurrences (all)	7	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	2 / 54 (3.70%)	1 / 45 (2.22%)	1 / 52 (1.92%)
occurrences (all)	2	1	1
Cough			
subjects affected / exposed	3 / 54 (5.56%)	0 / 45 (0.00%)	0 / 52 (0.00%)
occurrences (all)	4	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 54 (1.85%)	3 / 45 (6.67%)	2 / 52 (3.85%)
occurrences (all)	1	3	2
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	3 / 54 (5.56%)	2 / 45 (4.44%)	3 / 52 (5.77%)
occurrences (all)	4	2	3
Pain in Extremity			
subjects affected / exposed	2 / 54 (3.70%)	3 / 45 (6.67%)	2 / 52 (3.85%)
occurrences (all)	2	3	2
Arthralgia			
subjects affected / exposed	3 / 54 (5.56%)	4 / 45 (8.89%)	0 / 52 (0.00%)
occurrences (all)	3	4	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 54 (24.07%)	8 / 45 (17.78%)	8 / 52 (15.38%)
occurrences (all)	19	8	14
Urinary Tract Infection			
subjects affected / exposed	8 / 54 (14.81%)	5 / 45 (11.11%)	3 / 52 (5.77%)
occurrences (all)	10	7	4
Influenza			
subjects affected / exposed	4 / 54 (7.41%)	2 / 45 (4.44%)	1 / 52 (1.92%)
occurrences (all)	4	3	1
Pharyngitis			
subjects affected / exposed	3 / 54 (5.56%)	1 / 45 (2.22%)	1 / 52 (1.92%)
occurrences (all)	3	1	1

Bronchitis			
subjects affected / exposed	2 / 54 (3.70%)	3 / 45 (6.67%)	0 / 52 (0.00%)
occurrences (all)	2	5	0
Gastroenteritis			
subjects affected / exposed	1 / 54 (1.85%)	3 / 45 (6.67%)	2 / 52 (3.85%)
occurrences (all)	1	6	2
Sinusitis			
subjects affected / exposed	2 / 54 (3.70%)	0 / 45 (0.00%)	3 / 52 (5.77%)
occurrences (all)	3	0	4
Oral Herpes			
subjects affected / exposed	4 / 54 (7.41%)	1 / 45 (2.22%)	0 / 52 (0.00%)
occurrences (all)	6	1	0

Non-serious adverse events	Randomized Period: Natalizumab 300 mg SC every 12 weeks	Randomized Period: Natalizumab 150 mg IV every 12 weeks	Randomized Period: Natalizumab 150 mg SC every 12 weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 53 (64.15%)	31 / 47 (65.96%)	17 / 38 (44.74%)
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	2 / 38 (5.26%)
occurrences (all)	1	0	2
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	17 / 53 (32.08%)	12 / 47 (25.53%)	5 / 38 (13.16%)
occurrences (all)	18	15	5
Headache			
subjects affected / exposed	5 / 53 (9.43%)	3 / 47 (6.38%)	4 / 38 (10.53%)
occurrences (all)	6	4	5
Paraesthesia			
subjects affected / exposed	3 / 53 (5.66%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	4	0	0
Sciatica			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 53 (1.89%)	2 / 47 (4.26%)	1 / 38 (2.63%)
occurrences (all)	1	2	1
Injection Site Pain			
subjects affected / exposed	3 / 53 (5.66%)	0 / 47 (0.00%)	3 / 38 (7.89%)
occurrences (all)	7	0	7
Pyrexia			
subjects affected / exposed	1 / 53 (1.89%)	3 / 47 (6.38%)	1 / 38 (2.63%)
occurrences (all)	1	3	1
Pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 53 (1.89%)	4 / 47 (8.51%)	0 / 38 (0.00%)
occurrences (all)	1	4	0
Nausea			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	2 / 53 (3.77%)	1 / 47 (2.13%)	0 / 38 (0.00%)
occurrences (all)	2	1	0
Constipation			
subjects affected / exposed	1 / 53 (1.89%)	3 / 47 (6.38%)	0 / 38 (0.00%)
occurrences (all)	1	3	0
Abdominal Pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal Pain			
subjects affected / exposed	4 / 53 (7.55%)	0 / 47 (0.00%)	1 / 38 (2.63%)
occurrences (all)	4	0	1
Cough			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 53 (1.89%)	2 / 47 (4.26%)	1 / 38 (2.63%)
occurrences (all)	1	2	1
Pain in Extremity			
subjects affected / exposed	2 / 53 (3.77%)	2 / 47 (4.26%)	1 / 38 (2.63%)
occurrences (all)	3	2	1
Arthralgia			
subjects affected / exposed	1 / 53 (1.89%)	3 / 47 (6.38%)	0 / 38 (0.00%)
occurrences (all)	1	3	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 53 (16.98%)	8 / 47 (17.02%)	4 / 38 (10.53%)
occurrences (all)	16	8	4
Urinary Tract Infection			
subjects affected / exposed	4 / 53 (7.55%)	4 / 47 (8.51%)	1 / 38 (2.63%)
occurrences (all)	5	6	4
Influenza			
subjects affected / exposed	2 / 53 (3.77%)	8 / 47 (17.02%)	0 / 38 (0.00%)
occurrences (all)	2	9	0
Pharyngitis			
subjects affected / exposed	1 / 53 (1.89%)	4 / 47 (8.51%)	1 / 38 (2.63%)
occurrences (all)	1	4	1
Bronchitis			
subjects affected / exposed	4 / 53 (7.55%)	0 / 47 (0.00%)	1 / 38 (2.63%)
occurrences (all)	4	0	1

Gastroenteritis			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	1 / 38 (2.63%)
occurrences (all)	2	0	1
Sinusitis			
subjects affected / exposed	2 / 53 (3.77%)	2 / 47 (4.26%)	0 / 38 (0.00%)
occurrences (all)	2	2	0
Oral Herpes			
subjects affected / exposed	1 / 53 (1.89%)	1 / 47 (2.13%)	0 / 38 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	Open-label Period: Natalizumab 300 mg IV every 4 weeks	Open-label Period: Natalizumab 300 mg SC every 4 weeks	Open-label Period: Natalizumab 300 mg IV every 12 weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 44 (4.55%)	4 / 35 (11.43%)	2 / 42 (4.76%)
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Injection Site Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pain in Extremity			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 44 (4.55%)	1 / 35 (2.86%)	1 / 42 (2.38%)
occurrences (all)	2	1	1
Urinary Tract Infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 44 (0.00%)	1 / 35 (2.86%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 35 (5.71%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Sinusitis			

subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Oral Herpes			
subjects affected / exposed	0 / 44 (0.00%)	0 / 35 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Open-label Period: Natalizumab 300 mg SC every 12 weeks	Open-label Period: Natalizumab 150 mg IV every 12 weeks	Open-label Period: Natalizumab 150 mg SC every 12 weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	4 / 42 (9.52%)	6 / 32 (18.75%)
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	0 / 42 (0.00%)	3 / 42 (7.14%)	2 / 32 (6.25%)
occurrences (all)	0	3	2
Headache			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Injection Site Pain			

subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pain in Extremity			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Urinary Tract Infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 42 (0.00%)	1 / 42 (2.38%)	3 / 32 (9.38%)
occurrences (all)	0	1	3
Pharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Oral Herpes			

subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 42 (0.00%) 0	0 / 32 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2011	The primary reason for this amendment was the addition of optional exploratory pharmacogenomic analysis using DNA samples derived from whole blood collected at Baseline. The purpose of the analysis was to explore identification of genetic variation associated with study treatment response and to explore host genetic mutations that may increase individual subjects' susceptibility or resistance to developing PML.
28 February 2012	The primary reason for this amendment was to align the safety information in the protocol related to the risk factors for the development of PML with the established risk factors described in the Patient Information Sheet and the ICF.
16 November 2012	The primary reason for this amendment was to revise the frequency of anti-JCV antibody testing in subjects who were anti-JCV antibody negative to align with the current safety recommendations for Tysabri.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported