Clinical trial results:
A Multi-centre and Prospective Trial to Evaluate the Effects on Multiple Sclerosis Related Fatigue During Treatment With Tysabri® in Patients With Relapsing Remitting Multiple Sclerosis Over the Course of 12 Months

Summary

EudraCT number	2008-008065-35
Trial protocol	SE
Global end of trial date	30 June 2011

Results information

Result version number	v1 (current)
This version publication date	08 February 2019
First version publication date	08 February 2019

Trial information

Trial identification

Sponsor protocol code	TYNERGY

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00884481
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 Binney Street, Cambridge, Massachusetts, United States, 02142
Public contact	Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	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	30 June 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the multiple sclerosis (MS) related fatigue during treatment with natalizumab as measured by changes on the fatigue scale for motor and cognitive functions (FSMC) over the course of 12 months.

Protection of trial subjects:

Subjects were treated according to clinical practice; protection of subjects was ensured by health care professional (HCP) as per clinical practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 2009
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	Denmark: 23
Country: Number of subjects enrolled	Sweden: 83
Country: Number of subjects enrolled	Austria: 29
Country: Number of subjects enrolled	Norway: 60
Worldwide total number of subjects	195
EEA total number of subjects	195

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)	195
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 4 countries- Sweden, Denmark, Norway and Austria.

Pre-assignment

Screening details:

A total of 205 subjects were screened, 10 subjects were considered screening failures. Total 195 subjects were enrolled in the study and started treatment of Natalizumab.

Period 1

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

Arms

Arm title	Natalizumab

Arm description:

Subjects with MS-related fatigue received Natalizumab infusion as per the summary of product characteristics (SmPC).

Arm type	Experimental
Investigational medicinal product name	Natalizumab
Investigational medicinal product code	
Other name	Tysabri®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Natalizumab infusion as per the SmPC.

Number of subjects in period 1	Natalizumab
Started	195
Completed	164
Not completed	31
Moved/Long Travel Distance	6
Informed Consent Withdrawn	3
Other	8
Non-fulfillment of in/exclusion criteria	1
Antibodies Against Tysabri	3
Due to Adverse Event	8
Pregnancy/pregnancy wish	2

Baseline characteristics

Reporting groups	
Reporting group title	Natalizumab
Reporting group description:	
Subjects with MS-related fatigue received Natalizumab infusion as per the summary of product characteristics (SmPC).	

Reporting group values	Natalizumab	Total	
Number of subjects	195	195	
Age Categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	39.7		
standard deviation	± 9.2	-	
Gender Categorical			
Units: Subjects			
Female	139	139	
Male	56	56	

End points

End points reporting groups

Reporting group title	Natalizumab

Reporting group description:

Subjects with MS-related fatigue received Natalizumab infusion as per the summary of product characteristics (SmPC).

Primary: Change From Baseline in Total Fatigue Scale for Motor and Cognitive Functions (FSMC) Score at Month 12

End point title	Change From Baseline in Total Fatigue Scale for Motor and Cognitive Functions (FSMC) Score at Month 12[1]

End point description:

FSMC is a 20-item questionnaire (Ten questions relate to motor fatigue and ten to cognitive fatigue) and produces a score between 1 and 5 for each scored question (ranging from "does not apply at all" to "applies completely"). Items are summed to generate a total score and transformed to a scale with a range of 20 to 100, where higher scores indicate higher levels of fatigue. A negative change from baseline indicates improvement. Intention to treat (ITT) population included all subjects who were enrolled and treated with Natalizumab.

End point type	Primary

End point timeframe:

Baseline, Month 12

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 statistics were planned to be reported for this endpoint.

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	162[2]			
Units: score on a scale				
least squares mean (standard error)	-9.00 (± 1.10)			

Notes:

[2] - Number of subjects analysed signifies those subjects who were evaluable for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total FSMC Fatigue Score at Month 3, 6, and 9

End point title	Change From Baseline in Total FSMC Fatigue Score at Month 3, 6, and 9

End point description:

FSMC is a 20-item questionnaire (Ten questions relate to motor fatigue and ten to cognitive fatigue) and produces a score between 1 and 5 for each scored question (ranging from "does not apply at all" to "applies completely"). Items are summed to generate a total score and transformed to a scale with a range of 20 to 100, where higher scores indicate higher levels of fatigue. A negative change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here ‘n’ signifies the number of subjects who were evaluated at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Month 3, 6, and 9

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: score on a scale				
least squares mean (standard error)				
Baseline (n =195)	-0.21 (± 0.06)			
Change at Month 3 (n =180)	-5.09 (± 0.81)			
Change at Month 6 (n =173)	-7.03 (± 0.94)			
Change at Month 9 (n =161)	-8.58 (± 1.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FSMC Motor Score at Month 3, 6 and 9

End point title	Change From Baseline in FSMC Motor Score at Month 3, 6 and 9

End point description:

FSMC is a 20-item questionnaire that includes 10 questions related to motor fatigue and produces a score between 1 and 5 for each scored question (ranging from "does not apply at all" to "applies completely"). Items are summed to generate a total score and transformed to a scale with a range of 10 to 50, where higher scores indicate higher levels of motor fatigue. A negative change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 3, 6 and 9

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: score on a Scale				
least squares mean (standard error)				
Baseline (n =195)	-0.25 (± 0.06)			
Change at Month 3 (n =180)	-2.80 (± 0.44)			
Change at Month 6 (n =172)	-3.74 (± 0.50)			
Change at Month 9 (n =161)	-4.71 (± 0.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FSMC Cognitive Scores at Month 3, 6 and 9

End point title	Change From Baseline in FSMC Cognitive Scores at Month 3, 6 and 9

End point description:

FSMC is a 20-item questionnaire that includes 10 questions relate to cognitive fatigue and produces a score between 1 and 5 for each scored question (ranging from "does not apply at all" to "applies completely"). Items are summed to generate a total score and transformed to a scale with a range of 10 to 50, where higher scores indicate higher levels of cognitive fatigue. A negative change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 3, 6 and 9

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: score on a scale				
least squares mean (standard error)				
Baseline (n =195)	-0.20 (± 0.05)			
Change at Month 3 (n =180)	-2.29 (± 0.42)			
Change at Month 6 (n =173)	-3.29 (± 0.50)			
Change at Month 9 (n =161)	-3.89 (± 0.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Capacity for Work Questionnaire (CWQ) Score at Month 6 and 12

End point title	Change From Baseline in Capacity for Work Questionnaire (CWQ) Score at Month 6 and 12

End point description:

The CWQ contained several different questions to measure subjects' Capacity for Work. Only one question – Question 1 – could be analysed across countries. CWQ Question 1 was used to analyse whether the subjects increased their number of weekly working hours. The question 'How many hours per week are you working?' was divided into 6 categories 0, 1- 10, 11-20, 21-30, 31-40 and 'Other'. Subjects with more working hours showed improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, measure type 'number' indicates odds ratio for Question 1. An odds ratio larger than 1 means improvement from baseline to month 6 and 12, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	119[3]			
Units: odds ratio				
number (confidence interval 95%)				
Change at Month 6	0.91 (0.57 to 1.44)			
Change at Month 12	0.90 (0.57 to 1.42)			

Notes:

[3] - Number of subjects evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health-Related Quality of Life (HRQoL) Short Form Questionnaire (SF-12) Score at Month 6 and 12

End point title	Change From Baseline in Health-Related Quality of Life (HRQoL) Short Form Questionnaire (SF-12) Score at Month 6 and 12

End point description:

HRQoL SF-12 is a multipurpose short form survey with 12 questions. The questions were combined, scored, and weighted to create two scales that provide glimpses into mental and physical functioning and overall health-related-quality of life. Both components were computed using the scores of 12 questions and range from 0 to 100, where a 0 score indicates the lowest level of health and 100 indicates the highest level of health. A positive change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	172[4]			
Units: score on a scale				
least squares mean (standard error)				
Physical; Baseline (n =172)	-0.37 (± 0.056)			
Physical; Change at Month 6 (n =143)	3.84 (± 0.574)			
Physical; Change at Month 12 (n =137)	3.89 (± 0.582)			
Mental; Baseline (n =172)	-0.57 (± 0.058)			
Mental; Change at Month 6 (n =143)	4.20 (± 0.724)			
Mental; Change at Month 12 (n =137)	4.17 (± 0.737)			

Notes:

[4] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Epworth Sleepiness Scale (ESS) Score at Month 6 and 12

End point title	Change From Baseline in Epworth Sleepiness Scale (ESS) Score at Month 6 and 12

End point description:

The ESS was consisted of very short questionnaire to measure daytime sleepiness. The questionnaire asked the subjects to rate his or her probability of falling asleep on a scale of increasing probability from 0 to 3 for eight different situations that most people engage in during their daily lives, though not necessarily every day. The scores for the eight questions were added together to obtain a single number. A number in the 0–9 range was considered to be normal while a number in the 10–24 range indicated that expert medical advice was required. The total ESS score is the sum of 8 item-scores and can range between 0 and 24, where higher scores indicate higher levels of a person's level of daytime sleepiness. A negative change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	172[5]			
Units: score on a scale				
least squares mean (standard error)				
Baseline (n =172)	-0.38 (± 0.054)			
Change at Month 6 (n =155)	-1.05 (± 0.271)			
Change at Month 12 (n =143)	-1.33 (± 0.278)			

Notes:

[5] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Center for Epidemiologic Studies Depression Scale (CES-D) Score at Month 6 and 12

End point title	Change From Baseline in Center for Epidemiologic Studies Depression Scale (CES-D) Score at Month 6 and 12

End point description:

CES-D was used to assess depressive symptoms. It is based on a 20 items questionnaire with each score ranging from 0 to 3. If more than 4 items are missing the sum score will be set to missing as well. A score of 16 or greater is considered depressed. A negative change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	172[6]			
Units: score on a scale				
least squares mean (standard error)				
Baseline (n =172)	-0.46 (± 0.053)			
Change at Month 6 (n =153)	-3.73 (± 0.667)			
Change at Month 12 (n =143)	-3.91 (± 0.685)			

Notes:

[6] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Paced Auditory Serial Addition Test (PASAT) Score at Month 6 and 12

End point title	Change From Baseline in Paced Auditory Serial Addition Test (PASAT) Score at Month 6 and 12

End point description:

The PASAT is a measure of cognitive function that specifically assesses auditory information processing speed and flexibility, as well as calculation ability. Stimulus presentation rates were adapted for use with MS subjects. The PASAT is presented on audio compact disk to control the rate of stimulus presentation. Single digits are presented either every 3 seconds (PASAT 1) or every 2 seconds (PASAT 2), and the subject must add each new digit to the one immediately prior to it. The test score is the sum of the total number of correct sums given (out of 60 possible) in each trial. An increase in score indicates an improvement in condition. A positive change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	172[7]			
Units: score on a scale				
least squares mean (standard error)				
Baseline (n =172)	-0.33 (± 0.05)			
Change at Month 6 (n =143)	3.82 (± 0.66)			
Change at Month 12 (n =130)	4.84 (± 0.68)			

Notes:

[7] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Symbol Digit Modalities Test (SDMT) Score at Baseline, Month 6, 12

End point title	Symbol Digit Modalities Test (SDMT) Score at Baseline, Month 6, 12

End point description:

SDMT is a screening test for cognitive impairment. Subjects are given 90 seconds in which to pair specific numbers with given geometric figures using a key. The score is the number of correctly coded items from 0-110 in 90 seconds. The total score provides a measure of the speed and accuracy of symbol-digit substitution. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	172[8]			
Units: score on a scale				
least squares mean (standard error)				
Before 6MWT; Baseline (n =171)	47.9 (± 0.99)			
Before 6MWT; Month 6 (n =156)	51.0 (± 1.04)			
Before 6MWT; Month 12 (n =143)	52.3 (± 1.07)			
After 6MWT; Baseline (n =169)	51.0 (± 1.11)			
After 6MWT; Month 6 (n =151)	55.1 (± 1.19)			
After 6MWT; Month 12 (n =138)	56.8 (± 1.23)			

Notes:

[8] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Six-Minute Walk Test (6MWT) Score at Month 6 and 12

End point title	Change From Baseline in Six-Minute Walk Test (6MWT) Score at Month 6 and 12

End point description:

The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. A positive change from baseline indicates improvement. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	172[9]			
Units: score on a scale				
least squares mean (standard error)				
Baseline (n =172)	-0.14 (± 0.043)			
Change at Month 6 (n =149)	23.6 (± 6.2)			
Change at Month 12 (n =135)	20.6 (± 6.5)			

Notes:

[9] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Expanded Disability Status Scale (EDSS) Score at Month 6 and 12

End point title	Change From Baseline in Expanded Disability Status Scale (EDSS) Score at Month 6 and 12

End point description:

The EDSS measures disability status is a derived score based on functional system score and ambulation (actual distance walked). EDSS on a scale ranges from 0 to 10, with higher scores indicating more disability. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: score on a scale				
least squares mean (confidence interval 95%)				
Change at Month 6 (n =176)	-0.50 (-0.750 to -0.250)			
Change at Month 12 (n =163)	-0.75 (-0.750 to -0.500)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Daily Number of Steps

End point title	Average Daily Number of Steps

End point description:

Step counter is a device for measuring the number of steps a person has taken when actively walking.

to calculate amount of Walking. ITT population included all subjects who were enrolled and treated with Natalizumab. Here, 'n' signifies those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	161[10]			
Units: number of steps				
least squares mean (standard error)				
Baseline (n =161)	4808 (± 383)			
Month 6 (n =145)	4866 (± 405)			
Month 12 (n =128)	4962 (± 429)			

Notes:

[10] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Fatigue Medication at Baseline, Month 3, 6, 9 and 12

End point title	Number of Subjects With Fatigue Medication at Baseline, Month 3, 6, 9 and 12

End point description:

ITT population included all subjects who were enrolled and treated with Natalizumab.

End point type	Secondary

End point timeframe:

Baseline, Month 3, 6, 9 and 12

End point values	Natalizumab			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: subjects				
No fatigue medication at all at Baseline	182			
More than zero times but less at Baseline	2			
Five days per month or more but less at Baseline	0			
Every other day or more but less at Baseline	2			
Every day at Baseline	9			
No fatigue medication at all at Month 3	172			
More than zero times but less at Month 3	3			

Five days per month or more but less at Month 3	3			
Every other day or more but less at Month 3	1			
Every day at Month 3	6			
No fatigue medication at all at Month 6	164			
More than zero times but less at Month 6	5			
Five days per month or more but less at Month 6	0			
Every other day or more but less at Month 6	3			
Every day at Month 6	7			
No fatigue medication at all at Month 9	154			
More than zero times but less at Month 9	2			
Five days per month or more but less at Month 9	0			
Every other day or more but less at Month 9	0			
Every day at Month 9	10			
No fatigue medication at all at Month 12	151			
More than zero times but less at Month 12	2			
Five days per month or more but less at Month 12	0			
Every other day or more but less at Month 12	1			
Every day at Month 12	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Month 12

Adverse event reporting additional description:

Adverse events were only recorded and collected for the subjects recruited in Sweden (83 subjects). ITT population, here equivalent to the safety population. Due to non-availability of MedDRA version, we have reported version as 0.0.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	0.0

Reporting groups

Reporting group title	Natalizumab

Reporting group description:

Subjects with MS-related fatigue received Natalizumab infusion as per the summary of product characteristics (SmPC).

Serious adverse events	Natalizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 83 (7.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pain			

subjects affected / exposed	1 / 83 (1.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pilonidal cyst			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Natalizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 83 (87.95%)		
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 83 (24.10%)		
occurrences (all)	22		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	5 / 83 (6.02%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 83 (6.02%)		
occurrences (all)	5		

Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 36 / 83 (43.37%) 48 7 / 83 (8.43%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported