Clinical trial results:
An Open-Label, Multi-center, Expanded Access Study With Fingolimod in Patients With Relapsing-Remitting Multiple Sclerosis for Whom no Suitable Therapy Exists

Summary

EudraCT number	2011-000770-60
Trial protocol	IT
Global end of trial date	02 April 2013

Results information

Result version number	v1 (current)
This version publication date	03 December 2020
First version publication date	03 December 2020

Trial information

Trial identification

Sponsor protocol code	CFTY720DIT03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland, 21040
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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	02 April 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 April 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To provide early access to fingolimod to subjects who have been diagnosed with relapsing-remitting multiple sclerosis and for whom no suitable therapy exists i.e. where existing therapies have failed. Anther objective was to generate additional safety and tolerability data, according to the label recommended by Committee for Medicinal Products for Human Use (CHMP), in a population resembling that of future clinical practice.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 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	Italy: 912
Worldwide total number of subjects	912
EEA total number of subjects	912

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)	912
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 77 sites in Italy. The first participant was screened on 09 June 2011. The last study visit occurred on 02 April 2013.

Pre-assignment

Screening details:

1044 potential subjects were screened. Out of which, 912 were enrolled and 906 subjects received at least one dose of the study drug.

Pre-assignment period milestones

Number of subjects started	912
Number of subjects completed	906

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 6

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	All Participants

Arm description:

Fingolimod capsules 0.5 mg, with or without food, orally, once daily at the same time for up to approximately 12 months.

Arm type	Experimental
Investigational medicinal product name	Fingolimod
Investigational medicinal product code	FTY720D
Other name	FTY720, Gilenya©
Pharmaceutical forms	Capsule, hard
Routes of administration	Oromucosal use

Dosage and administration details:

Fingolimod, single dose of 0.5 milligrams (mg) administered orally.

Number of subjects in period 1[1]	All Participants
Started	906
Completed	825
Not completed	81
Consent withdrawn by subject	12
Adverse event, non-fatal	34
Confirmation of increase in ALT>5xULN & AST>5xULN)	3

Pregnancy	3
Decrease in lymphocytes counts	3
Lost to follow-up	12
Reason not specified	13
Early study termination by the Sponsor	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 6 subjects who were enrolled but not treated are not included in the study.

Baseline characteristics

Reporting groups	
Reporting group title	All Participants
Reporting group description:	
Fingolimod capsules 0.5 mg, with or without food, orally, once daily at the same time for up to approximately 12 months.	

Reporting group values	All Participants	Total	
Number of subjects	906	906	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	39.10		
standard deviation	± 9.872	-	
Gender categorical			
Units: Subjects			
Female	579	579	
Male	327	327	

End points

End points reporting groups

Reporting group title	All Participants

Reporting group description:

Fingolimod capsules 0.5 mg, with or without food, orally, once daily at the same time for up to approximately 12 months.

Primary: Percentage of Subjects Experiencing any Serious Adverse Event

End point title	Percentage of Subjects Experiencing any Serious Adverse

End point description:

The Full Analysis Set (FAS) included all subjects who received at least one dose of fingolimod.

End point type	Primary

End point timeframe:

From first dose of study drug and up to end of the study (Up to approximately 22 months).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed.

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	906			
Units: percentage of subjects				
number (not applicable)	2.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From study start visit up to completion; up to approximately 22 months.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Female Potentially Fertile
Reporting group description: Female Potentially Fertile	
Reporting group title	Female Menopausal or surgically sterilized
Reporting group description: Female Menopausal or surgically sterilized	
Reporting group title	Male
Reporting group description: Male	

Serious adverse events	Female Potentially Fertile	Female Menopausal or surgically sterilized	Male
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 502 (3.39%)	2 / 77 (2.60%)	7 / 327 (2.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Tongue operation			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Oedema peripheral			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Troponin increased			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block			

subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dementia			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Epilepsy			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Hemiparesis			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Multiple sclerosis relapse			
subjects affected / exposed	2 / 502 (0.40%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Syncope			
subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Macular oedema			
subjects affected / exposed	2 / 502 (0.40%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis cholestatic			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Pyelonephritis			

subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	0 / 327 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 502 (0.00%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Female Potentially Fertile	Female Menopausal or surgically sterilized	Male
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 502 (25.10%)	26 / 77 (33.77%)	64 / 327 (19.57%)
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 502 (1.99%)	0 / 77 (0.00%)	3 / 327 (0.92%)
occurrences (all)	10	0	3
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 502 (1.99%)	1 / 77 (1.30%)	5 / 327 (1.53%)
occurrences (all)	10	1	5
Chest discomfort			
subjects affected / exposed	2 / 502 (0.40%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	4 / 502 (0.80%)	0 / 77 (0.00%)	5 / 327 (1.53%)
occurrences (all)	4	0	5
Influenza like illness			
subjects affected / exposed	6 / 502 (1.20%)	0 / 77 (0.00%)	0 / 327 (0.00%)
occurrences (all)	6	0	0
Irritability			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Pyrexia			

subjects affected / exposed	10 / 502 (1.99%)	1 / 77 (1.30%)	5 / 327 (1.53%)
occurrences (all)	11	1	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 502 (1.00%)	1 / 77 (1.30%)	3 / 327 (0.92%)
occurrences (all)	5	1	3
Dyspnoea			
subjects affected / exposed	7 / 502 (1.39%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	7	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	6 / 502 (1.20%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences (all)	6	0	1
Depression			
subjects affected / exposed	7 / 502 (1.39%)	2 / 77 (2.60%)	2 / 327 (0.61%)
occurrences (all)	7	2	2
Insomnia			
subjects affected / exposed	4 / 502 (0.80%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	4	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 502 (0.40%)	2 / 77 (2.60%)	5 / 327 (1.53%)
occurrences (all)	2	2	5
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 502 (0.20%)	2 / 77 (2.60%)	2 / 327 (0.61%)
occurrences (all)	1	2	2
Lymphocyte count			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	1 / 502 (0.20%)	0 / 77 (0.00%)	5 / 327 (1.53%)
occurrences (all)	1	0	6
Cardiac disorders			
Bradycardia			
subjects affected / exposed	6 / 502 (1.20%)	1 / 77 (1.30%)	8 / 327 (2.45%)
occurrences (all)	6	1	8

Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 502 (0.80%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	4	1	1
Headache			
subjects affected / exposed	24 / 502 (4.78%)	6 / 77 (7.79%)	7 / 327 (2.14%)
occurrences (all)	26	6	7
Neuralgia			
subjects affected / exposed	2 / 502 (0.40%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	2	1	1
Optic neuritis			
subjects affected / exposed	1 / 502 (0.20%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	1	1	1
Restless legs syndrome			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	11 / 502 (2.19%)	2 / 77 (2.60%)	2 / 327 (0.61%)
occurrences (all)	13	2	2
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	3 / 502 (0.60%)	1 / 77 (1.30%)	2 / 327 (0.61%)
occurrences (all)	3	1	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 502 (0.40%)	2 / 77 (2.60%)	1 / 327 (0.31%)
occurrences (all)	2	2	1

Constipation			
subjects affected / exposed	2 / 502 (0.40%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	2	1	1
Diarrhoea			
subjects affected / exposed	4 / 502 (0.80%)	1 / 77 (1.30%)	4 / 327 (1.22%)
occurrences (all)	4	1	5
Nausea			
subjects affected / exposed	13 / 502 (2.59%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences (all)	15	0	1
Vomiting			
subjects affected / exposed	4 / 502 (0.80%)	1 / 77 (1.30%)	2 / 327 (0.61%)
occurrences (all)	4	1	2
Skin and subcutaneous tissue disorders			
Actinic cheilitis			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 502 (0.20%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	1	1	0
Pruritus allergic			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 502 (0.20%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	1	1	0
Joint stiffness			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	0	2	1
Muscle rigidity			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0

Muscular weakness			
subjects affected / exposed	2 / 502 (0.40%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	2	1	1
Synovial cyst			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 502 (0.80%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	5	1	1
Cystitis			
subjects affected / exposed	6 / 502 (1.20%)	3 / 77 (3.90%)	0 / 327 (0.00%)
occurrences (all)	6	3	0
Gastroenteritis viral			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Infectious mononucleosis			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	9 / 502 (1.79%)	4 / 77 (5.19%)	6 / 327 (1.83%)
occurrences (all)	9	4	6
Nasopharyngitis			
subjects affected / exposed	9 / 502 (1.79%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences (all)	10	0	1
Oral herpes			
subjects affected / exposed	12 / 502 (2.39%)	0 / 77 (0.00%)	1 / 327 (0.31%)
occurrences (all)	15	0	2
Pharyngotonsillitis			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 502 (0.20%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	1	1	1
Urinary tract infection			

subjects affected / exposed	3 / 502 (0.60%)	1 / 77 (1.30%)	1 / 327 (0.31%)
occurrences (all)	3	1	2
Viral infection			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	0 / 327 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 502 (0.00%)	1 / 77 (1.30%)	2 / 327 (0.61%)
occurrences (all)	0	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 March 2012	The following updates were made as per Amendment 01: • Modification of the procedures to be followed in order to monitor the effect of fingolimod in case of first administration or restart of treatment after an interruption greater than 14 consecutive days.
03 September 2012	The following updates were made as per Amendment 02: • Exclusion criteria related to cardiovascular conditions • Exclusion of patients taking medications that lower heart rate • Appendix 1 "Guidance for observation of patients taking their first dose of fingolimod and for management of bradycardia" to reflect final CHMP recommendations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported