Clinical trial results:
A 6-month, Randomized, Active Comparator, Open-label, Multi-Center Study to Evaluate Patient Outcomes, Safety and Tolerability of Fingolimod (FTY720) 0.5 mg/day in Patients with Relapsing Remitting Multiple Sclerosis who are candidates for MS therapy change from Previous Disease Modifying Therapy.

Summary

EudraCT number	2010-024017-31
Trial protocol	IT
Global end of trial date	04 June 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	CFTY720DIT02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01317004
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma, AG, 41 613241111,
Scientific contact	Study Director, 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	04 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 June 2014
Global end of trial reached?	Yes
Global end of trial date	04 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the change in patient-reported treatment satisfaction after six months of treatment with fingolimod 0.5mg/day vs. DMT standard of care using the global satisfaction subscale of the Treatment Satisfaction Questionnaire for Medication (TSQM-9).

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	25 May 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: 65
Worldwide total number of subjects	65
EEA total number of subjects	65

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Actual enrollment = 61 because 65 participants were randomized to the study, but only 61 participants received at least one dose of study medication.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Multiple Sclerosis Disease Modifying Treatment (MS DMT)

Arm description:

Patients randomized in this arm received selected Standard MS DMT such as Interferon beta-1b or Interferon beta-1a or Glatiramer acetate for 6 months.

Arm type	Active comparator
Investigational medicinal product name	MS DMT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intravesical solution/solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Selected Standard MS Disease Modifying Treatment (DMT) such as Interferon beta-1b or Interferon beta-1a or Glatiramer acetate for 6 months.

Arm title	Fingolimod

Arm description:

Patients randomized in this arm received Fingolimod 0.5 mg/day oral capsule for 6 months core period.

Arm type	Experimental
Investigational medicinal product name	Fingolimod
Investigational medicinal product code	FTY720
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Fingolimod 0.5 mg/day oral capsule for 6 months.

Number of subjects in period 1[1]	Multiple Sclerosis Disease Modifying Treatment (MS DMT)	Fingolimod
Started	11	50
Completed	5	47
Not completed	6	3
Consent withdrawn by subject	1	-
Adverse event, non-fatal	3	3
Protocol deviation	2	-

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: Actual enrollment = 61 because 65 participants were randomized to the study, but only 61 participants received at least one dose of study medication.

Baseline characteristics

Reporting groups	
Reporting group title	Fingolimod
Reporting group description:	
Patients randomized in this arm received Fingolimod 0.5 mg/day oral capsule for 6 months core period.	
Reporting group title	Multiple Sclerosis Disease Modifying Treatment (MS DMT)
Reporting group description:	
Patients randomized in this arm received selected Standard MS DMT such as Interferon beta-1b or Interferon beta-1a or Glatiramer acetate for 6 months.	

Reporting group values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)	Total
Number of subjects	50	11	61
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	50	11	61
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	37.96	35.82	
standard deviation	± 8.69	± 7.22	-
Gender, Male/Female Units: Participants			
Female	32	8	40
Male	18	3	21

End points

End points reporting groups

Reporting group title	Multiple Sclerosis Disease Modifying Treatment (MS DMT)
Reporting group description:	
Patients randomized in this arm received selected Standard MS DMT such as Interferon beta-1b or Interferon beta-1a or Glatiramer acetate for 6 months.	
Reporting group title	Fingolimod
Reporting group description:	
Patients randomized in this arm received Fingolimod 0.5 mg/day oral capsule for 6 months core period.	

Primary: Change from baseline in patient-reported treatment satisfaction

End point title	Change from baseline in patient-reported treatment satisfaction
End point description:	
The Treatment Satisfaction Questionnaire for Medication (TSQM-9) is a psychometric measure of a patient's satisfaction with medication. It consists of 3 subscales: effectiveness, convenience and global satisfaction. The scores were computed by adding items for each domain, i.e. 1 to 3 for effectiveness, 4 - 6 for convenience and 7 to 9 for global satisfaction. The lowest possible score (1 for each item and 3 for all 3 subscales) was subtracted from the composite score and divided by the greatest possible score range. The greatest range was (7-1) X 3 items = 18 for the effectiveness and convenience, and (5-1) x 3 items = 12 for global satisfaction. This provided a transformed score between 0 and 1 that was then multiplied by 100. A positive change from baseline indicates improvement.	
End point type	Primary
End point timeframe:	
baseline, 6 months	

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	10		
Units: score on a scale				
arithmetic mean (standard deviation)	19.57 (± 21)	5.83 (± 16.47)		

Statistical analyses

Statistical analysis title	Change from Baseline
Comparison groups	Fingolimod v Multiple Sclerosis Disease Modifying Treatment (MS DMT)

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: Change from baseline in patient-reported Activities of Daily Living (ADL)

End point title	Change from baseline in patient-reported Activities of Daily Living (ADL)

End point description:

The PRIMUS activity measure is a 15-item assessment used to evaluate patient-reported activities of daily living. The PRIMUS activities score was calculated summing the 15 items, after recoding the responses from 1 - 3 to 0 - 2. Therefore, the total score ranged from 0 - 3-, where high scores were indicative of greater function limitation. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline, 6 months

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	11		
Units: score on a scale				
arithmetic mean (standard deviation)	0.19 (± 2.75)	0.15 (± 1.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in patient-reported fatigue

End point title	Change from baseline in patient-reported fatigue

End point description:

The fatigue Severity Scale (FSS) is a 9-item scale used to assess fatigue. The FSS score was calculated summing the 9 items of the questionnaire and dividing by the number of non-missing items (each item is based on a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree)). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

6 months

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	11		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.18 (± 1.46)	-0.32 (± 1.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in patient–reported effectiveness and convenience

End point title	Change from baseline in patient–reported effectiveness and convenience

End point description:

The Treatment Satisfaction Questionnaire for Medication (TSQM-9) is a psychometric measure of a patient's satisfaction with medication. It consists of 3 subscales: effectiveness, convenience and global satisfaction. The scores were computed by adding items for each domain, i.e. 1 to 3 for effectiveness, 4 - 6 for convenience and 7 to 9 for global satisfaction. The lowest possible score (1 for each item and 3 for all 3 subscales) was subtracted from the composite score and divided by the greatest possible score range. The greatest range was (7-1) X 3 items = 18 for the effectiveness and convenience, and (5-1) x 3 items = 12 for global satisfaction. This provided a transformed score between 0 and 1 that was then multiplied by 100. A positive change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

6 months

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	10		
Units: score on a scale				
arithmetic mean (standard deviation)				
Effectiveness	13.53 (± 28.39)	-1.67 (± 32.4)		
Convenience	24.64 (± 18.28)	12.78 (± 25.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in patient-reported depression

End point title	Change from baseline in patient-reported depression

End point description:

The Beck Depression Inventory Fast Screen (BDI-FS) is a brief, multiple choice, self reported inventory designed to evaluate depression in patients with medical illness. The BDI-FS score was calculated summing the 7 items of the questionnaire. Each item ranged from 0 (not present) to 3 (severe). The total score ranges from 0-3 (minimal depression), 4-8 (mild depression), 9-12 (moderate depression) and 13-21 (severe depression). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

6 months

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	11		
Units: score on a scale				
arithmetic mean (standard deviation)	-1.15 (± 3.59)	-0.12 (± 3.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in patient-reported health related quality of life (QOL)

End point title	Change from baseline in patient-reported health related quality of life (QOL)

End point description:

The SF-36v2 is a validated health-related quality of life instrument used in numerous disease states, including MS. It is a self-administered survey that measures 8 domains of health including: physical functioning, role limitations due to physical health, pain, general health, energy/fatigue, social functioning, role limitations due to emotional problems and emotional well-being. Additionally, two summary scale scores can be calculated: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). If half or more questions within a domain were answered, then a score was calculated for that domain. Otherwise, the patient score for that domain was set to missing. If the patient was missing any 1 of the 8 scale scores, then the physical and mental component scores were set to missing. An algorithm was used to create a score from 0 to 100 for each domain score and component score. A positive change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

6 months

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	9		
Units: score on a scale				
arithmetic mean (standard deviation)				
Physical functioning (n=41,9)	1.71 (± 23.07)	-1.11 (± 20.73)		
Role limitations due to physical health (n=42,9)	7.14 (± 37.97)	5.56 (± 27.32)		
Pain (n=45,9)	6.56 (± 24.32)	14.44 (± 15.25)		
General health (n=44,8)	4.52 (± 19.43)	6.25 (± 14.08)		
Energy/fatigue (n=43,9)	2.33 (± 18.81)	6.48 (± 33.24)		
Social functioning (n=45,9)	7.78 (± 24.9)	6.94 (± 25.85)		
Role limitations d/t emotional problems (n=45,9)	7.04 (± 41.82)	3.7 (± 38.89)		
Emotional well-being (n=43,9)	2.51 (± 16.88)	4.89 (± 28.13)		
PCS (n=40,8)	4.52 (± 18.05)	7.83 (± 15.86)		
MCS (n=40,8)	5.88 (± 18.21)	7.28 (± 24.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Physician-reported Clinical Global Impression of Improvement (CGI-I)

End point title	Physician-reported Clinical Global Impression of Improvement (CGI-I)

End point description:

The CGI-I is a rating scale allowing a physician-reported global evaluation of the subject's improvement over time. The Investigator assessed the subject's clinical change relative to the symptoms at baseline on the CGI-I, a seven-point scale, with rating as follows: 1=Very much improved, 2=Much improved, 3=Minimally improved, 4=No change, 5=Minimally worse, 6=Much worse, 7=Very much worse. A lower score and a negative change from baseline indicate improvement.

End point type	Secondary

End point timeframe:

6 months

End point values	Fingolimod	Multiple Sclerosis Disease Modifying Treatment (MS DMT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	9		
Units: Percentage of participants				
number (not applicable)				

Much improved	13.64	11.11		
Minimally improved	36.36	11.11		
No change	47.73	66.67		
Minimally worse	2.27	11.11		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Fingolimod

Reporting group description:

Fingolimod

Reporting group title	Standard MS DMT

Reporting group description:

Standard MS DMT

Serious adverse events	Fingolimod	Standard MS DMT	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 50 (8.00%)	1 / 11 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Human papilloma virus test positive			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Multiple sclerosis relapse			

subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	2 / 50 (4.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drug ineffective			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Fingolimod	Standard MS DMT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 50 (58.00%)	7 / 11 (63.64%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	2 / 50 (4.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cyst			

subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	1 / 50 (2.00%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Injection site reaction			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Testicular disorder			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 50 (4.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	4 / 50 (8.00%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Weight decreased			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Foot fracture			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Road traffic accident			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Brugada syndrome			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 50 (4.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	8 / 50 (16.00%)	0 / 11 (0.00%)	
occurrences (all)	8	0	

Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 50 (2.00%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

Rash erythematous			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Muscle contracture			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 50 (4.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 50 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Dyslipidaemia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia			

subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 11 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2013	Amendment 1: The main purpose of amendment 1 was to allow patients completing this study to be included in CFTY720DIT07, an open-label study aimed at guaranteeing therapeutic continuity to patients who had completed international or local studies of fingolimod (CFTY720D2399, CFTY720DIT01, CFTY720DIT02, CFTY720DIT03) but were not eligible for drug reimbursement from the Italian National Health Service and did not have any other valid therapeutic option. Furthermore, the study aimed to generate long-term safety and tolerability data in a population that was different from the one treated in normal clinical practice, according to the indications currently approved in Italy. Protocol CFTY720DIT07 initially called for the enrollment of roughly 200 patients. However, the number of patients that needed to continue therapy was actually only 25, a number not compatible with some of the above-mentioned objectives due to the reduced significance ofthe tolerability and safety data emerging from such a limited number of cases. This amendment also clarified Exclusion criterion related to patients with an acute relapse of MS added. Better clarification of exclusion of patients with chronic diseases of the immune system. Exclusion criteria related to cardiovascular conditions updated. Exclusion of patients taking medications that lower heart rate added. Exclusion criterion concerning prior intake of fingolimod added. Exclusion criterion related to prior participation in a clinical trial with other S1P-receptor modulators added. Appendix 4 "Guidance for observation of patients taking their first dose of fingolimod" updated to reflect final CHMP recommendations. Safety monitoring guidelines updated to reflect fingolimod prescribing information.
16 December 2013	Amendment 2: It was decided that the need to guarantee therapeutic continuity in situations as these could be met more simply and adequately through a compassionate use program, as per Ministerial Decree May 8, 2003. Therefore, Novartis continued to provide the drug on an individual basis to guarantee therapeutic continuity to patients in treatment with Gilenya who were present for their end of study visit. Amendment 2 also clarified the Protocol Synopsis section: ,Study completion and post-study treatment: information on study CFTY720DIT07 deleted. Background: information updated with cumulative data from clinical studies (cutoff date 31 August 2013). Clarification on MS Relapse Activity and Reporting: corticosteroid usage for treatment of relapse and Exclusion Criteria: inconsistency regarding the timeframe before re-screening after virus zoster vaccination corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported