Clinical trial results:
Long-term follow-up at 10-years of patients enrolled in the fingolimod Phase 2 program in relapsing multiple sclerosis

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results

Summary

EudraCT number	2013-002660-17
Trial protocol	IT PT DK
Global end of trial date	02 December 2015

Results information

Result version number	v1 (current)
This version publication date	11 July 2018
First version publication date	11 July 2018

Trial information

Trial identification

Sponsor protocol code	CFTY720D2201E2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02307838
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
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 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to investigate whether continuous use of fingolimod over 10 years reduced the progression of disability, as measured by the mean Expanded Disability Status Scale (EDSS) score, compared to shorter treatment duration.

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	10 June 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 47
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Portugal: 20
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	Switzerland: 13
Worldwide total number of subjects	175
EEA total number of subjects	115

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)	175
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This extension study was a multicenter follow-up study of participants who enrolled in FTY720D2201 (NCT02307838). Although participants in this study did not receive study treatment, the participant flow is based on the treatments receive in FTY720D2201.

Pre-assignment

Screening details:

A total of 177 participants were enrolled into the study. However, 2 participants were erroneously enrolled into the study because they did not meet the inclusion criteria. Therefore, they were not included in any analyses, and as such, the participant flow is based on 175 participants.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	FTY720 5.0 mg

Arm description:

In FTY720D2201, participants received FTY720 5.0 mg every day (q.d.) oral dose for 6 months.

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:

In FTY720D2201, participants received FTY720 5.0 mg every day (q.d.) oral dose for 6 months.

Arm title	FTY720 1.25 mg

Arm description:

In FTY720D2201, participants received FTY720 1.25 mg q.d. oral dose for 6 months.

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:

In FTY720D2201, participants received FTY720 1.25 mg q.d. oral dose for 6 months

Arm title	Placebo

Arm description:

In FTY720D2201, participants received matching placebo to FTY720 q.d. for 6 months.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

In FTY720D2201, participants received matching placebo to FTY720 q.d. for 6 months.

Number of subjects in period 1	FTY720 5.0 mg	FTY720 1.25 mg	Placebo
Started	56	64	55
Completed	56	64	55

Baseline characteristics

Reporting groups	
Reporting group title	FTY720 5.0 mg
Reporting group description:	
In FTY720D2201, participants received FTY720 5.0 mg every day (q.d.) oral dose for 6 months.	
Reporting group title	FTY720 1.25 mg
Reporting group description:	
In FTY720D2201, participants received FTY720 1.25 mg q.d. oral dose for 6 months.	
Reporting group title	Placebo
Reporting group description:	
In FTY720D2201, participants received matching placebo to FTY720 q.d. for 6 months.	

Reporting group values	FTY720 5.0 mg	FTY720 1.25 mg	Placebo
Number of subjects	56	64	55
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)	56	64	55
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	36.9	37.4	37.9
standard deviation	± 10.25	± 8.66	± 9.28
Gender, Male/Female Units: Subjects			
Female	38	43	36
Male	18	21	19

Reporting group values	Total		
Number of subjects	175		
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)	175		

From 65-84 years	0		
85 years and over	0		

Age Continuous Units: Years arithmetic mean standard deviation	- -		
Gender, Male/Female Units: Subjects			
Female	117		
Male	58		

Subject analysis sets

Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Non-continuous: Other DMTs
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for less than 8 years. Also, participants were exposed to high-efficacy DMTs for less than 2 years. This group may have included participants who did not report any DMTs at all.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Non-continuous: High efficacy DMTs
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for less than 8 years. Also, participants were exposed to high efficacy disease modifying therapies (DMTs) for at least 2 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description: Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Continuous

Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	

Reporting group values	Continuous	Non-continuous	Non-continuous: Other DMTs
Number of subjects	104	16	55
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years)			

Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	 37.4 ± 8.47	 31.9 ± 9.05	 38.9 ± 10.49
Gender, Male/Female Units: Subjects Female Male	 63 41	 13 3	 41 14

Reporting group values	Non-continuous	Non-continuous: High efficacy DMTs	Continuous
Number of subjects	71	16	103
Age categorical Units: Subjects In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	 ±	 ±	 ±
Gender, Male/Female Units: Subjects Female Male	 	 	

Reporting group values	Non-continuous	Non-continuous	Continuous
Number of subjects	69	70	98
Age categorical Units: Subjects In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			

Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Gender, Male/Female Units: Subjects			
Female Male			

Reporting group values	Non-continuous	Continuous	Non-continuous
Number of subjects	54	96	53
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Gender, Male/Female Units: Subjects			
Female Male			

Reporting group values	Continuous	Non-continuous	Continuous
Number of subjects	97	56	95
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±

Gender, Male/Female Units: Subjects			
Female Male			

Reporting group values	Non-continuous	Continuous	Non-continuous
Number of subjects	55	85	48
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Gender, Male/Female Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	FTY720 5.0 mg
Reporting group description:	
In FTY720D2201, participants received FTY720 5.0 mg every day (q.d.) oral dose for 6 months.	
Reporting group title	FTY720 1.25 mg
Reporting group description:	
In FTY720D2201, participants received FTY720 1.25 mg q.d. oral dose for 6 months.	
Reporting group title	Placebo
Reporting group description:	
In FTY720D2201, participants received matching placebo to FTY720 q.d. for 6 months.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Non-continuous: Other DMTs
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years. Also, participants were exposed to high-efficacy DMTs for less than 2 years. This group may have included participants who did not report any DMTs at all.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Non-continuous: High efficacy DMTs
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years. Also, participants were exposed to high efficacy disease modifying therapies (DMTs) for at least 2 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.	
Subject analysis set title	Continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.

Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.

Subject analysis set title	Continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.

Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.

Subject analysis set title	Continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.

Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.

Subject analysis set title	Continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.

Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.

Subject analysis set title	Continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.

Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.

Subject analysis set title	Continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for at least 8 years.

Subject analysis set title	Non-continuous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had exposure to FTY720 (study drug or commercially) for less than 8 years.

Primary: Change from baseline (BL) in Expanded Disability Status Scale (EDSS)

End point title	Change from baseline (BL) in Expanded Disability Status Scale (EDSS)

End point description:

EDSS is a scale for assessing neurologic impairment in MS. It consists of eight functional systems (FS) which are used to derive the EDSS steps (score) ranging from 0 (normal) to 10 (death due to MS). The functional systems are Visual, Brain Stem, Pyramidal, Cerebellar, Sensory, Bowel and Bladder, Cerebral and Other functions. Based on the assessment of each FS, the participant's score is determined between 0 to 10. A negative change from baseline indicates improvement.

End point type	Primary

End point timeframe:

baseline from core study (CFTY720D2201 (NCT00333138)), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	71		
Units: score on a scale				
least squares mean (standard error)	0.58 (± 0.154)	1.17 (± 0.185)		

Statistical analyses

Statistical analysis title	Change from BL in EDSS
Comparison groups	Continuous v Non-continuous
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0155
Method	ANCOVA
Parameter estimate	Difference in LS Means
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	-0.11

Secondary: Number of participants with disability progression

End point title	Number of participants with disability progression

End point description:

Disability progression is defined as: 1.5-point increase from baseline in participants with baseline EDSS score = 0.0; OR 1-point increase in EDSS from baseline in participants with baseline EDSS score of 1.0 to 5.0 inclusive; OR 0.5-point increase in EDSS from baseline in participants with baseline EDSS score >5.0.

End point type	Secondary

End point timeframe:

10 Years

End point values	Continuous	Non-continuous: Other DMTs	Non-continuous: High efficacy DMTs	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	55	16	
Units: Participants	35	29	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with EDSS <4 or <6

End point title	Number of participants with EDSS <4 or <6

End point description:

EDSS is a scale for assessing neurologic impairment in MS. It consists of eight functional systems (FS) which are used to derive the EDSS steps (score) ranging from 0 (normal) to 10 (death due to MS). The functional systems are Visual, Brain Stem, Pyramidal, Cerebellar, Sensory, Bowel and Bladder, Cerebral and Other functions. Based on the assessment of each FS, the participant's score is determined between 0 to 10. A positive change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous: Other DMTs	Non-continuous: High efficacy DMTs	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	55	16	
Units: Participants				
EDSS <4	78	31	10	
EDSS <6	90	41	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants not using a wheelchair or being bedridden

End point title	Number of participants not using a wheelchair or being bedridden

End point description:

The number of participants not using a wheelchair or being bedridden was assessed.

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous: Other DMTs	Non-continuous: High efficacy DMTs	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	55	16	
Units: Participants	99	46	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants classified as secondary progressive MS (SPMS)

End point title	Number of participants classified as secondary progressive MS (SPMS)

End point description:

Participants who were classified as SPMS were assessed.

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous: Other DMTs	Non-continuous: High efficacy DMTs	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	55	16	
Units: Participants	10	14	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with first use of an ambulatory device

End point title	Percentage of participants with first use of an ambulatory device

End point description:

First use of an ambulatory device was considered from EDSS 6.0 for participants having started FTY720D2201 (NCT00333138) with an EDSS score below 6.0.

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	103	69		
Units: Percentage of participants				
number (not applicable)	12.4	17.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier estimate of time to first use of a wheelchair

End point title	Kaplan Meier estimate of time to first use of a wheelchair

End point description:

First use of a wheelchair was considered from EDSS 7.0 for participants having started FTY720D2201 (NCT00333138) with an EDSS score below 7.0.

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	71		
Units: KM estimate				
number (not applicable)	4.9	16.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Multiple Sclerosis Fuctional Composite (MSFC) component: nine hole peg test (9-HPT)

End point title	Change from baseline in Multiple Sclerosis Fuctional Composite (MSFC) component: nine hole peg test (9-HPT)

End point description:

The 9-HPT is a quantitative measure of upper extremity (arm and hand) function. Both the dominant and non-dominant hands are tested twice (two consecutive trials of the dominant hand, followed immediately by two consecutive trials of the non-dominant hand). The time limit per trial is 300 seconds. The right and left hand scores were the time in seconds it took to insert and remove 9 pegs ((the average scores from the four trials on the 9-HPT (the two trials for each hand are averaged, converted to the reciprocals of the mean times for each hand and then the two reciprocals are averaged)). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline from core study, CFTY720D2201 (NCT00333138), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	71		
Units: seconds				
arithmetic mean (standard deviation)	2.29 (± 5.772)	5.06 (± 14.523)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in MSFC component: paced auditory serial addition test (PASAT) score

End point title	Change from baseline in MSFC component: paced auditory serial addition test (PASAT) score

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. The PASAT is the last measure administered at each visit. It is presented on audio compact disc (CD) to control the rate of stimulus presentation. Single digits are presented every 3 seconds and the patient must add each new digit to the one immediately prior to it. The test result is the number of correct sums given (out of 60 possible). A positive change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline from core study (CFTY720D2201 (NCT00333138)), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	70		
Units: score on a scale				
arithmetic mean (standard deviation)	0.54 (± 8.273)	-5.39 (± 12.428)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in MSFC component: timed 25-foot walk test score

End point title	Change from baseline in MSFC component: timed 25-foot walk test score

End point description:

The Timed 25-Foot Walk is a quantitative measure of lower extremity function. The patient is directed to one end of a clearly marked 25-foot (7.62 m) course and is instructed to walk 25 feet (7.62 meter) as quickly as possible, but safely. The task is immediately administered again by having the patient walk back the same distance. Patients may use assistive devices when doing this task. The test scores were the time in seconds it took to walk the 25 feet. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline from core study (CFTY720D2201 (NCT00333138)), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	70		
Units: score on a scale				
arithmetic mean (standard deviation)	1.32 (± 11.632)	3.89 (± 16.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Multiple Sclerosis Functional Composite (MSFC) Z score

End point title	Change from baseline in Multiple Sclerosis Functional Composite (MSFC) Z score

End point description:

MSFC is a composite measure encompassing information from the nine-hole peg test (arm dimension), timed 25 foot walk (leg dimension) and PASAT. The MSFC composite score was calculated as follows: (1) the average scores from the four trials on the 9-HPT (the two trials for each hand were averaged, converted to the reciprocals of the mean times for each hand and then the two reciprocals were averaged); (2) the average scores of two 25-Foot Timed Walk trials; (3) the number correct from the PASAT-3. The MSFC is based on the concept that scores for these three dimensions—arm, leg, and cognitive function are combined to create a single score (the MSFC) that can be used to detect change over time in a group of multiple sclerosis patients. This was done by creating Z-scores for each component of the MSFC, and averaging them to create an overall composite score. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline from core study (CFTY720D2201 (NCT00333138)), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	69		
Units: Z score				
arithmetic mean (standard deviation)	-0.11 (± 0.536)	-0.6 (± 1.297)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total volume in T2 lesion

End point title	Total volume in T2 lesion

End point description:

Total volume in T2 lesion was assessed by magnetic resonance imaging (MRI).

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	54		
Units: mm^3				
arithmetic mean (standard deviation)	8685.4 (± 7743.05)	11279 (± 12570.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total volume of T2 lesion

End point title	Change from baseline in total volume of T2 lesion

End point description:

Total volume in T2 lesion was assessed by magnetic resonance imaging (MRI). A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline from core study (CFTY720D2201 (NCT00333138)), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	53		
Units: mm^3				
arithmetic mean (standard deviation)	1031.7 (± 3725.8)	3636.7 (± 5259.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Third ventricle diameter

End point title	Third ventricle diameter
End point description: Third ventricle diameter was assessed by MRI.	
End point type	Secondary
End point timeframe: 10 years	

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	56		
Units: mm				
arithmetic mean (standard deviation)	5.28 (± 2.047)	5.57 (± 2.648)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in third ventricle diameter

End point title	Change from baseline in third ventricle diameter
End point description: Third ventricle diameter was assessed by MRI. A negative change from baseline indicates improvement.	
End point type	Secondary
End point timeframe: baseline from core study (CFTY720D2201 (NCT00333138)), 10 years	

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	95	55		
Units: mm				
arithmetic mean (standard deviation)	0.8 (± 0.848)	0.92 (± 0.784)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage brain volume change (PBVC)

End point title	Percentage brain volume change (PBVC)

End point description:

PVBC was assessed by MRI. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

baseline from core study (CFTY720D2201 (NCT00333138)), 10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	48		
Units: Percent change				
arithmetic mean (standard deviation)	-9.28 (± 4.412)	-9.87 (± 2.909)		

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation coeffcients between FTY treatment duration and disability progression parameters

End point title	Correlation coeffcients between FTY treatment duration and disability progression parameters

End point description:

The correlation between FTY treatment duration and disability progression outcomes was assessed. The number presented in the table is the Pearson correlation coefficient, r.

End point type	Secondary

End point timeframe:

10 years

End point values	Continuous	Non-continuous		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	71		
Units: Pearson correlation coeffcient				
number (not applicable)				
EDSS score at year 10 (n=101,71)	-0.12	-0.09		
Time to 1st use of a cane/crutch/walker (n=13,15)	0.35	0.11		
Time to first documenting EDSS of >= 6.0 (n=12,11)	0.27	0		
Time to first use of a wheelchair (n=5,12)	0.57	0.33		
Time to first becoming bedridden (n=0,0)	9999	9999		
Time to first SPMS classification (n=10,16)	0.38	0.32		
Year 10 PASAT-3 score (n=93,56)	-0.14	0.28		
Year 10 PASAT-3 score change from BL (n=93,56)	0.01	0.39		

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.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Non-Continuous other DMTs

Reporting group description:

Non-Continuous other DMTs

Serious adverse events	Non-Continuous other DMTs		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Non-Continuous other DMTs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)		
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results

Notes: