Clinical trial results:
A 48-week, double-blind, randomized, multi-center, parallelgroup study comparing structural changes in the retina and evolution of visual function after immediate versus delayed treatment with fingolimod in patients with acute demyelinating optic neuritis

Summary

EudraCT number	2012-002968-27
Trial protocol	ES IT GB DE
Global end of trial date	07 May 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	29 July 2015

Trial information

Trial identification

Sponsor protocol code	CFTY720D2402

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01757691
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	07 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 May 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess if fingolimod will reduce the mean retinal nerve fiber layer (RNFL) thinning (measured as the OCT-determined difference between the RNFLT of the affected eye after 18 weeks of treatment and the baseline RNFLT of the fellow eye) relative to placebo in patients with suspected ADON, all of whom will receive standard steroid treatment.

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.
Patients suffering from a MS relapse during the study and agreeing to continue the study after formal re-consenting were to be treated with a standard course of intravenous corticosteroids (methylprednisolone) on an in-patient or out-patient basis as clinically warranted. Intravenous steroid treatment for a relapse should have consisted of 3 to 5 days and up to 1000 mg methylprednisolone daily. Use of any oral tapering was not permitted.
Standard-of-care procedures were to be followed during treatment of relapses as well as the instructions in the protocol for the conduct of the study MRI during relapse and steroid treatment.
Investigators were to have considered the added immunosuppressive effects of corticosteroid therapy and increased vigilance regarding infections during such treatment and in the weeks following administration.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	15 August 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	2
EEA total number of subjects	1

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)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was terminated due to low patient enrollment.

Pre-assignment

Screening details:

There was a screening period of -1 to - 14 Days during which patient was treated with standard steroid therapy. Approximately 126 were planned to be enrolled.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Arms

Arm title	Fingolimod 0.5mg/Daily

Arm description:

Oral capsule dose was given once daily for 48 weeks

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:

The study medication (fingolimod 0.5 mg or placebo) was dispensed at the randomization visit after patient eligibility was
confirmed and at each visit. The patient was instructed to take 1 capsule of study medication once daily by mouth, preferably at the same time every day, with or without food.
At the Week 18 visit, patients in the placebo treatment arm were switched over to fingolimod 0.5 mg once daily. The study treatment arm continued to be blinded to the site and patient.
Detailed guidelines for monitoring of patients taking their first dose of study drug and management of bradycardia were outlined in the protocol. The first dose of study drug at the study center was administered at a time that allowed for the required 6-hour post-dose monitoring and for additional time for extended monitoring, if necessary. The patient was discharged after specific discharge criteria were met. Dose adjustments were not allowed, but dose interruptions were based on outlined criteria.

Number of subjects in period 1	Fingolimod 0.5mg/Daily
Started	2
Completed	0
Not completed	2
Administrative problems	2

Baseline characteristics

Reporting groups	
Reporting group title	Fingolimod 0.5mg/Daily
Reporting group description: Oral capsule dose was given once daily for 48 weeks	

Reporting group values	Fingolimod 0.5mg/Daily	Total	
Number of subjects	2	2	
Age categorical Units: Subjects			
Adults (18-64 years)	2	2	
Gender categorical Units: Subjects			
Female	2	2	

End points

End points reporting groups

Reporting group title	Fingolimod 0.5mg/Daily
Reporting group description:	
Oral capsule dose was given once daily for 48 weeks	

Primary: Mean Retinal Nerve Fiber Layer (RNFL) Thinning in Patients Treated With Fingolimod 0.5mg/Day, Relative to Patients Treated With Placebo

End point title	Mean Retinal Nerve Fiber Layer (RNFL) Thinning in Patients Treated With Fingolimod 0.5mg/Day, Relative to Patients Treated With Placebo[1]
End point description:	
Due to early termination and low patient enrollment the primary outcome measure was not analyzed	
End point type	Primary
End point timeframe:	
Baseline and Week 18	

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: Due to early termination and insufficient patient enrollment the primary outcome measure was not analyzed

End point values	Fingolimod 0.5mg/Daily			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Participants				

Notes:

[2] - Due to early termination and low patient enrollment the primary outcome measure was not analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Low Contrast Visual Acuity (LCVA)

End point title	Low Contrast Visual Acuity (LCVA)
End point description:	
Due to early termination and low patient enrollment this trial was not powered for efficacy.	
End point type	Secondary
End point timeframe:	
Baseline, Week 48	

End point values	Fingolimod 0.5mg/Daily			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Participants				

Notes:

[3] - Due to early termination and low patient enrollment this trial was not powered for efficacy

Statistical analyses

No statistical analyses for this end point

Secondary: Vision Based Quality of Life (QoL) Utility Score

End point title	Vision Based Quality of Life (QoL) Utility Score

End point description:

Due to early termination and low patient enrollment this trial was not powered for efficacy.

End point type	Secondary

End point timeframe:

Baseline, Week 18, Week 48

End point values	Fingolimod 0.5mg/Daily			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Participants				

Notes:

[4] - Due to early termination and low patient enrollment this trial was not powered for efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients Converting to Either 2005 or 2010 McDonald MS or to CDMS

End point title	Proportion of Patients Converting to Either 2005 or 2010 McDonald MS or to CDMS

End point description:

Due to early termination and low patient enrollment this trial was not powered for efficacy.

End point type	Secondary

End point timeframe:

Baseline, Week 18, Week 48

End point values	Fingolimod 0.5mg/Daily			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Participants				

Notes:

[5] - Due to early termination and low patient enrollment this trial was not powered for efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Particpants With Adverse Events as a Measure of Safety and Tolerability

End point title	Number of Particpants With Adverse Events as a Measure of Safety and Tolerability

End point description:

Number of particpants with Adverse events as a measure of safety and tolerability.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8, 12, 18, 24, 36, 48, 60

End point values	Fingolimod 0.5mg/Daily			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants				
Adverse Events (AE)	1			
Death	0			
Non-Fatal Serious Adverse Event (SAE)	0			

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	17.0

Reporting groups

Reporting group title	Fingolimod 0.5 mg/day for 48 weeks (immediate treatment)

Reporting group description:

Fingolimod 0.5 mg/day for 48 weeks (immediate treatment)

Serious adverse events	Fingolimod 0.5 mg/day for 48 weeks (immediate treatment)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Fingolimod 0.5 mg/day for 48 weeks (immediate treatment)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2		

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.

In Dec-2013, Novartis reprioritized the global fingolimod clinical program strategy Novartis and decided to halt development of fingolimod for the treatment of ADON, resulting in the discontinuation of this study.

Notes: