Clinical trial results:
Long-term, open-label, multicenter study assessing longterm cardiovascular risks in patients treated with fingolimod

Summary

EudraCT number	2014-001241-24
Trial protocol	BE IT
Global end of trial date	24 January 2020

Results information

Result version number	v1 (current)
This version publication date	06 February 2021
First version publication date	06 February 2021

Trial information

Trial identification

Sponsor protocol code	CFTY720D2409

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02232061
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Estimate the long-term cardiovascular risk of fingolimod in patients who experienced a cardiovascular event during treatment initiation, as defined by the incidence of selected cardiovascular events over the course of the study

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	29 September 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	Belgium: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	6

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients enrolled in study FTY720D2409 who experienced a cardiovascular event within 24-hours of fingolimod treatment initiation/re-initiation which led to overnight monitoring or met serious adverse event criteria, were eligible to participate in this study.

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	Fingolimod

Arm description:

Fingolimod 0.5mg/day tablets taken orally.

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 0.5mg/day

Number of subjects in period 1	Fingolimod
Started	6
Completed	4
Not completed	2
Consent withdrawn by subject	1
Administrative problems	1

Baseline characteristics

Reporting groups	
Reporting group title	Fingolimod
Reporting group description: Fingolimod 0.5mg/day tablets taken orally.	

Reporting group values	Fingolimod	Total	
Number of subjects	6	6	
Age Categorical			
age in years			
Units: participants			
18 - 64	6	6	
Sex: Female, Male Units:			
Female	5	5	
Male	1	1	
Race/Ethnicity, Customized Units: Subjects			
Caucasian	6	6	

End points

End points reporting groups

Reporting group title	Fingolimod

Reporting group description:

Fingolimod 0.5mg/day tablets taken orally.

Primary: Percentage of patients who experienced at least one selected cardiovascular serious adverse events (SAE)

End point title	Percentage of patients who experienced at least one selected cardiovascular serious adverse events (SAE)[1]

End point description:

Patients were included who had long-term exposure to fingolimod once they had been identified as being at risk during treatment initiation in study CFTY720D2406. Selected cardiovascular events include, but are not limited to, sudden unexplained death, cardiovascular death, myocardial infarction (MI), Q-wave MI, stroke (ischemic or hemorrhagic), unstable angina requiring hospitalization, congestive heart failure requiring hospitalization, complete heart block, ventricular fibrillation, torsade de pointes, hypertensive emergency and any other suspected life threatening cardiovascular condition.

End point type	Primary

End point timeframe:

Within 6 months of qualifying event up to approximately 64 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 analysis was done

End point values	Fingolimod			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Within 6 months of qualifying event up to 64 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Initial cohort FTY720
Reporting group description: Initial cohort FTY720	

Serious adverse events	Initial cohort FTY720		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
LYMPHOPENIA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
BRONCHITIS VIRAL			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Initial cohort FTY720		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)		
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pregnancy, puerperium and perinatal conditions			
PREGNANCY			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
INSOMNIA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nervous system disorders			
MULTIPLE SCLEROSIS RELAPSE			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
HEADACHE			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
SCIATICA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
LYMPHOPENIA			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
FACET JOINT SYNDROME			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
BURSITIS			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
TENDONITIS			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
MUSCULAR WEAKNESS			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Infections and infestations NASOPHARYNGITIS subjects affected / exposed occurrences (all) TRICHOMONIASIS subjects affected / exposed occurrences (all) VIRAL PHARYNGITIS subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 3 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Metabolism and nutrition disorders FOLATE DEFICIENCY subjects affected / exposed occurrences (all) HYPERCHOLESTEROLAEMIA subjects affected / exposed occurrences (all) HYPERPHAGIA subjects affected / exposed occurrences (all) VITAMIN D DEFICIENCY subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 September 2019	Amendment was to align safety related updates to the Fingolimod label (SmPC) and to introduce administrative changes in the protocol to align with the language of D2406, the parent study from which patients were enrolled into D2409 study.

Notes:

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.

This study had no stand-alone secondary objectives. However, data from the CFTY720D2409 and D2406 studies will be pooled to supplement this study and will be appended to this record when available.

Notes: