



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

| | | | |
|---|--|--|--|
| 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: