



Clinical trial results:

An open label study to evaluate the safety and efficacy of 12 week treatment with CFZ533 in patients with Graves' disease

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-005564-41 |
| Trial protocol | DE |
| Global end of trial date | 24 April 2017 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 09 May 2018 |
| First version publication date | 09 May 2018 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CCFZ533X2205 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02713256 |
| 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, 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 April 2017 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 April 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the effects of CFZ533 on thyroid function in Graves' disease after 12 week 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.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 19 April 2016 |
| 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 | Germany: 13 |
| Country: Number of subjects enrolled | United States: 2 |
| Worldwide total number of subjects | 15 |
| EEA total number of subjects | 13 |

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) | 14 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 15 patients were enrolled and all of them completed the 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 | CFZ533 10 mg/kg |
|-----------|-----------------|

Arm description:

CFZ533 intravenously over approximately one hour

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | CFZ533 |
| Investigational medicinal product code | CFZ533 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

CFZ533 10mg/kg intravenous (iv) over approximately one hour on Study Days 1, 15, 29, 57 and 85.

| | |
|---------------------------------------|-----------------|
| Number of subjects in period 1 | CFZ533 10 mg/kg |
| Started | 15 |
| Completed | 15 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | CFZ533 10 mg/kg |
|-----------------------|-----------------|

Reporting group description:

CFZ533 intravenously over approximately one hour

| Reporting group values | CFZ533 10 mg/kg | Total | |
|--|-----------------|-------|--|
| Number of subjects | 15 | 15 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 14 | 14 | |
| From 65-84 years | 1 | 1 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 44.3 | | |
| standard deviation | ± 12.9 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 13 | 13 | |
| Male | 2 | 2 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 1 | 1 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 14 | 14 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|--|-----------------|
| Reporting group title | CFZ533 10 mg/kg |
| Reporting group description: CFZ533 intravenously over approximately one hour | |

Primary: Percentage of participants whose thyroid stimulating hormone (TSH) levels normalize after 12 week treatment

| | |
|-----------------|--|
| End point title | Percentage of participants whose thyroid stimulating hormone (TSH) levels normalize after 12 week treatment ^[1] |
|-----------------|--|

End point description:

Normalization of TSH is defined as TSH level greater than 0.35 mU/L after 12 week treatment (Day 85).
No statistical analysis was planned for this primary outcome

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

12 week (DAY 85)

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 statistical analysis was planned for this primary outcome

| | | | | |
|-----------------------------------|-----------------|--|--|--|
| End point values | CFZ533 10 mg/kg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 | | | |
| Units: percentage of participants | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants whose total triiodothyronine (total T3) levels decrease after 12 week treatment

| | |
|-----------------|---|
| End point title | Percentage of participants whose total triiodothyronine (total T3) levels decrease after 12 week treatment ^[2] |
|-----------------|---|

End point description:

Percentage of participants whose total triiodothyronine (total T3) levels decrease after 12 week treatment. A decrease is when total T3 level is below Upper limit of normal (ULN) ≤ 2.79 nmol/L
No statistical analysis was planned for this primary outcome

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

12 week (DAY 85)

Notes:

[2] - 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 statistical analysis was planned for this primary outcome

| | | | | |
|-----------------------------------|-----------------|--|--|--|
| End point values | CFZ533 10 mg/kg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 38.5 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants whose free thyroxine (free T4) levels decrease after 12 week treatment

| | |
|-----------------|--|
| End point title | Percentage of participants whose free thyroxine (free T4) levels decrease after 12 week treatment ^[3] |
|-----------------|--|

End point description:

Percentage of participants whose free thyroxine (free T4) levels decrease after 12 weeks of treatment (DAY85). A decrease is when free T4 level is below Upper limit of normal (ULN) ≤ 22.7 pmol/L

No statistical analysis was planned for this primary outcome

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

12 week (DAY 85)

Notes:

[3] - 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 statistical analysis was planned for this primary outcome

| | | | | |
|-----------------------------------|-----------------|--|--|--|
| End point values | CFZ533 10 mg/kg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 30.8 | | | |

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 | 20.0 |

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | CFZ533 10 mg/kg |
|-----------------------|-----------------|

Reporting group description:

CFZ533 10 mg/kg

| Serious adverse events | CFZ533 10 mg/kg | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | CFZ533 10 mg/kg | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 15 (80.00%) | | |
| Investigations | | | |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| CARDIAC MURMUR | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| ELECTROCARDIOGRAM QT PROLONGED | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| PALPITATIONS | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| FATIGUE | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | | |
| occurrences (all) | 2 | | |
| Ear and labyrinth disorders | | | |
| VERTIGO | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| CONSTIPATION | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| DRY MOUTH | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | | |
| occurrences (all) | 1 | | |
| NAUSEA | | | |

| | | | |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>VOMITING</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 15 (13.33%)</p> <p>2</p> <p>1 / 15 (6.67%)</p> <p>2</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>COUGH</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 15 (6.67%)</p> <p>1</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>ALOPECIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>HYPERHIDROSIS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>PRURITUS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>URTICARIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> | | |
| <p>Psychiatric disorders</p> <p>INSOMNIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>SLEEP DISORDER</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 15 (13.33%)</p> <p>2</p> <p>1 / 15 (6.67%)</p> <p>1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>MUSCULOSKELETAL PAIN</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>OSTEOPENIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> | | |

| | | | |
|---|---|--|--|
| Infections and infestations CYSTITIS subjects affected / exposed occurrences (all) SKIN INFECTION subjects affected / exposed occurrences (all) UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all) VIRAL UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all) | 3 / 15 (20.00%) 5 1 / 15 (6.67%) 1 2 / 15 (13.33%) 3 2 / 15 (13.33%) 2 | | |
|---|---|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 16 March 2016 | Amendment 1: The purpose of this amendment was to address comments received from the US Food and Drug Administration (FDA) in the advice/information request letter following submission of the investigational new drug (IND) application. Additional changes included, other administrative changes or clarifications. |
| 18 May 2016 | Amendment 2: The purpose of this amendment was to revise the inclusion criteria to be more reflective of the patient characteristics based on the feedback received from the study investigators. Due to the mechanistic nature of the study, newly diagnosed patients with GD were the target population for more homogeneity of the disease states. However, this treatment option could provide more benefit for patients relapsing from ATD treatments in the real world based on communication with the investigators, therefore, patients did not necessarily need to be newly diagnosed with GD (within 6 months of screening) to participate in the study. Few other changes and clarifications are also made in the enrollment criteria. Additionally, other administrative changes were made throughout the document. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported