



## Clinical trial results:

**A phase II, multicenter, open-label, randomized two-year study to evaluate the efficacy and safety of deferasirox film-coated tablet versus phlebotomy in patients with Hereditary Hemochromatosis.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2016-002529-12 |
| Trial protocol           | ES SK DE BE RO |
| Global end of trial date | 17 April 2023  |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 27 April 2024 |
| First version publication date | 27 April 2024 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CICL670F2203 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03203850 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharmaceuticals  |
| 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                       | 17 April 2023 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 17 April 2023 |
| Was the trial ended prematurely?                     | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the trial was to assess the response rate in the deferasirox FCT and phlebotomy treatment arms where response is defined by achieving target serum ferritin (SF)  $\leq 100$   $\mu\text{g/L}$  on or before 24 months.

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                          | 11 January 2018 |
| 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 | Romania: 1            |
| Country: Number of subjects enrolled | Belgium: 5            |
| Country: Number of subjects enrolled | Spain: 22             |
| Country: Number of subjects enrolled | Switzerland: 2        |
| Country: Number of subjects enrolled | Russian Federation: 8 |
| Country: Number of subjects enrolled | Slovakia: 2           |
| Country: Number of subjects enrolled | France: 5             |
| Worldwide total number of subjects   | 45                    |
| EEA total number of subjects         | 35                    |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 43 |
| From 65 to 84 years       | 2  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in 11 investigative sites in 7 countries.

### Pre-assignment

Screening details:

There was a screening period of 4 weeks to assess participants eligibility.

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Deferasirox FCT 7mg/kg |
|------------------|------------------------|

Arm description:

Deferasirox film-coated tablet 7mg/kg, oral dose daily (starting dose for the first 12 weeks)

|  |                                |
|--|--------------------------------|
| Arm type                               | Experimental                   |
| Investigational medicinal product name | Deferasirox film-coated tablet |
| Investigational medicinal product code |                                |
| Other name                             |                                |
| Pharmaceutical forms                   | Film-coated tablet             |
| Routes of administration               | Oral use                       |

Dosage and administration details:

Deferasirox film-coated tablet 7mg/kg, oral dose daily (starting dose for the first 12 weeks)

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Phlebotomy |
|------------------|------------|

Arm description:

Phlebotomy - standard of care

|          |                 |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

| <b>Number of subjects in period 1</b> | Deferasirox FCT<br>7mg/kg | Phlebotomy |
|---------------------------------------|---------------------------|------------|
| Started                               | 30                        | 15         |
| Completed                             | 22                        | 12         |
| Not completed                         | 8                         | 3          |
| Adverse event, serious fatal          | 1                         | -          |
| Adverse events                        | 3                         | -          |
| Subject/guardian decision             | 4                         | 3          |

## Baseline characteristics

### Reporting groups

|   |                        |
|---|------------------------|
| Reporting group title   | Deferasirox FCT 7mg/kg |
| Reporting group description:<br>Deferasirox film-coated tablet 7mg/kg, oral dose daily (starting dose for the first 12 weeks) |                        |
| Reporting group title   | Phlebotomy             |
| Reporting group description:<br>Phlebotomy - standard of care   |                        |

| Reporting group values                             | Deferasirox FCT 7mg/kg | Phlebotomy | Total |
|--|------------------------|------------|-------|
| Number of subjects                                 | 30                     | 15         | 45    |
| Age categorical<br>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)                               | 29                     | 14         | 43    |
| From 65-84 years                                   | 1                      | 1          | 2     |
| 85 years and over                                  | 0                      | 0          | 0     |
| Age Continuous<br>Units: years                     |                        |            |       |
| arithmetic mean                                    | 51.6                   | 52.1       | -     |
| standard deviation                                 | ± 8.20                 | ± 8.13     | -     |
| Sex: Female, Male<br>Units: participants           |                        |            |       |
| Female   | 4                      | 3          | 7     |
| Male   | 26                     | 12         | 38    |
| Race/Ethnicity, Customized<br>Units: Subjects      |                        |            |       |
| Caucasian  | 30                     | 15         | 45    |

## End points

### End points reporting groups

|                              |   |
|------------------------------|---|
| Reporting group title        | Deferasirox FCT 7mg/kg  |
| Reporting group description: | Deferasirox film-coated tablet 7mg/kg, oral dose daily (starting dose for the first 12 weeks) |
| Reporting group title        | Phlebotomy  |
| Reporting group description: | Phlebotomy - standard of care   |

### Primary: Proportion of patients achieving target SF $\leq$ 100 $\mu$ g/L for the first time

|                        |   |
|------------------------|---|
| End point title        | Proportion of patients achieving target SF $\leq$ 100 $\mu$ g/L for the first time <sup>[1]</sup>   |
| End point description: | Proportion of participants achieving target serum ferritin (SF) $\leq$ 100 $\mu$ g/L on or before Month 24. Participants were considered responders if they met response criteria (target SF $\leq$ 100 $\mu$ g/L) on or before Month 24 (Week 104) during the treatment phase. Any participant who discontinued treatment prematurely before meeting such criterion and participants with unknown or missing SF by Month 24 were counted as non-responder. |
| End point type         | Primary   |
| End point timeframe:   | Up to Month 24  |

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: only analyzed descriptively.

| End point values                  | Deferasirox FCT 7mg/kg | Phlebotomy        |  |  |
|-----------------------------------|------------------------|-------------------|--|--|
| Subject group type                | Reporting group        | Reporting group   |  |  |
| Number of subjects analysed       | 30                     | 15                |  |  |
| Units: percentage of participants |                        |                   |  |  |
| number (confidence interval 95%)  |                        |                   |  |  |
| Responder                         | 40 (22.7 to 59.4)      | 80 (51.9 to 95.7) |  |  |
| Non-Responder                     | 60 (40.6 to 77.3)      | 20 (4.3 to 48.1)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with ocular treatment emergent adverse events (AEs)

|                        |  |
|------------------------|--|
| End point title        | Number of participants with ocular treatment emergent adverse events (AEs)   |
| End point description: | Number of participants with at least one ocular treatment emergent adverse event (new or worsening from baseline). |

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 108 weeks. |           |

| End point values             | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|------------------------------|---------------------------|-----------------|--|--|
| Subject group type           | Reporting group           | Reporting group |  |  |
| Number of subjects analysed  | 30                        | 15              |  |  |
| Units: participants          |                           |                 |  |  |
| At least one ocular AE       | 9                         | 0               |  |  |
| Treatment-related ocular AEs | 2                         | 0               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with ocular treatment emergent adverse events (AEs) by preferred term

|  |  |
|--|--|
| End point title  | Number of participants with ocular treatment emergent adverse events (AEs) by preferred term |
| End point description:   |  |
| Number of participants with at least one ocular treatment emergent adverse event (new or worsening from baseline). Preferred terms are based on Medical Dictionary of Regulatory Activities (MedDRA) version 26.0. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 108 weeks.                                     |  |

| End point values            | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|-----------------------------|---------------------------|-----------------|--|--|
| Subject group type          | Reporting group           | Reporting group |  |  |
| Number of subjects analysed | 30                        | 15              |  |  |
| Units: participants         |                           |                 |  |  |
| Cataract nuclear            | 2                         | 0               |  |  |
| Glaucoma                    | 2                         | 0               |  |  |
| Blepharitis                 | 1                         | 0               |  |  |
| Cellulitis orbital          | 1                         | 0               |  |  |
| Dry eye                     | 1                         | 0               |  |  |
| Eye pain                    | 1                         | 0               |  |  |
| Eye ulcer                   | 1                         | 0               |  |  |
| Macular oedema              | 1                         | 0               |  |  |
| Open angle glaucoma         | 1                         | 0               |  |  |
| Optic nerve disorder        | 1                         | 0               |  |  |
| Panophthalmitis             | 1                         | 0               |  |  |

|                       |   |   |  |  |
|-----------------------|---|---|--|--|
| Retinal degeneration  | 1 | 0 |  |  |
| Retinal haemorrhage   | 1 | 0 |  |  |
| Visual acuity reduced | 1 | 0 |  |  |
| Vitreous haemorrhage  | 1 | 0 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

|                 |   |
|-----------------|---|
| End point title | Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs) |
|-----------------|---|

End point description:

Number of participants with treatment emergent AEs (any AE regardless of seriousness), AEs leading to study treatment discontinuation, SAEs and SAEs leading to study treatment discontinuation.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 108 weeks.

| End point values                | Deferasirox FCT 7mg/kg | Phlebotomy      |  |  |
|---------------------------------|------------------------|-----------------|--|--|
| Subject group type              | Reporting group        | Reporting group |  |  |
| Number of subjects analysed     | 30                     | 15              |  |  |
| Units: participants             |                        |                 |  |  |
| At least one AE                 | 28                     | 12              |  |  |
| At least one SAE                | 7                      | 0               |  |  |
| AEs leading to discontinuation  | 3                      | 0               |  |  |
| SAEs leading to discontinuation | 0                      | 0               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of adverse events in participants who had study treatment interrupted due to SF $\leq$ 100 $\mu$ g/L and re-initiated study treatment when $\geq$ 300 $\mu$ g/L

|                 |  |
|-----------------|--|
| End point title | Number of adverse events in participants who had study treatment interrupted due to SF $\leq$ 100 $\mu$ g/L and re-initiated study treatment when $\geq$ 300 $\mu$ g/L |
|-----------------|--|

End point description:

Number of participants who interrupt deferasirox FCT at least once due to SF level  $\leq$  100  $\mu$ g/L and re-initiate therapy at SF level  $\geq$  300  $\mu$ g/L.

There were no participants that re-initiated therapy when reached 300  $\mu$ g/L.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 24 months

| End point values            | Deferasirox<br>FCT 7mg/kg | Phlebotomy       |  |  |
|-----------------------------|---------------------------|------------------|--|--|
| Subject group type          | Reporting group           | Reporting group  |  |  |
| Number of subjects analysed | 0 <sup>[2]</sup>          | 0 <sup>[3]</sup> |  |  |
| Units: participants         |                           |                  |  |  |

Notes:

[2] - There were no participants that re-initiated therapy when reached 300 ug/L.

[3] - There were no participants that re-initiated therapy when reached 300 ug/L.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Categorical analysis of logMAR score changes from baseline to best/worst post-baseline changes in one eye with more extreme change

|                 |  |
|-----------------|--|
| End point title | Categorical analysis of logMAR score changes from baseline to best/worst post-baseline changes in one eye with more extreme change |
|-----------------|--|

End point description:

Visual acuity was measured using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart. A letter score was calculated based on the number of letters that could correctly be identified from specified distances. For low luminance and standard acuity measures, visual acuity was described on a logMAR scale for all measures. For including acuity obtained with the ETDRS letter score, the values were converted to a logMAR scale, using the following formula:  $\text{logMAR} = 1.7 - 0.02 \times \text{ETDRS score}$ . With this conversion, a difference from baseline of 0.1 logMAR = 5-letter difference in visual acuity, 0.2 logMAR = 10-letter difference, 0.3 logMAR = 15-letter difference, 0.4 logMAR = 20-letter difference, 0.5 logMAR = 25-letter difference and 0.6 logMAR = 30-letter difference. Increase in logMAR score from baseline indicates worsening in visual acuity. Decrease in logMAR score category from baseline indicates improvement in visual acuity.

|                          |           |
|--------------------------|-----------|
| End point type           | Secondary |
| End point timeframe:     |           |
| Baseline, up to Week 104 |           |

| End point values                                  | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|---|---------------------------|-----------------|--|--|
| Subject group type                                | Reporting group           | Reporting group |  |  |
| Number of subjects analysed                       | 30                        | 15              |  |  |
| Units: participants                               |                           |                 |  |  |
| Best change: Decrease <0.1                        | 9                         | 4               |  |  |
| Best change: Decrease $\geq 0.1 - <0.2$           | 9                         | 5               |  |  |
| Best change: Decrease $\geq 0.2 - <0.3$           | 1                         | 0               |  |  |
| Best change: Decrease $\geq 0.3 - <0.6$           | 0                         | 0               |  |  |
| Best change: Decrease $\geq 0.6$                  | 1                         | 0               |  |  |
| Best change: Decrease Missing baseline assessment | 2                         | 0               |  |  |
| Best change: Decrease No decrease from baseline   | 8                         | 6               |  |  |
| Worst change: Increase <0.1                       | 11                        | 11              |  |  |
| Worst change: Increase $\geq 0.1 - <0.2$          | 10                        | 2               |  |  |
| Worst change: Increase $\geq 0.2 - <0.3$          | 1                         | 2               |  |  |

|  |   |   |  |  |
|--|---|---|--|--|
| Worst change: Increase $\geq 0.3$ - $< 0.6$        | 3 | 0 |  |  |
| Worst change: Increase $\geq 0.6$                  | 0 | 0 |  |  |
| Worst change: Increase Missing baseline assessment | 2 | 0 |  |  |
| Worst change: Increase No increase from baseline   | 3 | 0 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Categorical analysis of worst post-baseline values of intraocular pressure in one eye with more extreme change

|                 |  |
|-----------------|--|
| End point title | Categorical analysis of worst post-baseline values of intraocular pressure in one eye with more extreme change |
|-----------------|--|

End point description:

Intraocular pressure was measured by tonometry. Intraocular pressure values  $> 5$  to  $\leq 21$  mmHg were considered normal.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to Week 104

| End point values                                    | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|---|---------------------------|-----------------|--|--|
| Subject group type                                  | Reporting group           | Reporting group |  |  |
| Number of subjects analysed                         | 30                        | 15              |  |  |
| Units: participants                                 |                           |                 |  |  |
| Worst post-baseline value- $\leq 5$ mmHg            | 0                         | 0               |  |  |
| Worst post-baseline value- $> 5$ to $\leq 21$ mmHg  | 27                        | 12              |  |  |
| Worst post-baseline value- $> 21$ to $\leq 30$ mmHg | 1                         | 3               |  |  |
| Worst post-baseline value- $> 30$ mmHg              | 0                         | 0               |  |  |
| missing post-baseline assessment                    | 2                         | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Categorical analysis of changes in intraocular pressure from baseline to best/worst post-baseline changes in one eye with more extreme change

|                 |   |
|-----------------|---|
| End point title | Categorical analysis of changes in intraocular pressure from baseline to best/worst post-baseline changes in one eye with more extreme change |
|-----------------|---|

End point description:

Intraocular pressure was measured by tonometry. A decrease in intraocular pressure from baseline indicated improvement.

|                          |           |
|--------------------------|-----------|
| End point type           | Secondary |
| End point timeframe:     |           |
| Baseline, up to Week 104 |           |

| End point values                                       | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|--|---------------------------|-----------------|--|--|
| Subject group type                                     | Reporting group           | Reporting group |  |  |
| Number of subjects analysed                            | 30                        | 15              |  |  |
| Units: participants                                    |                           |                 |  |  |
| Increase from baseline $\geq 5$ mmHg and<br><10 mmHg   | 4                         | 2               |  |  |
| Increase from baseline $\geq 10$ mmHg                  | 0                         | 1               |  |  |
| Decrease from baseline $\geq 5$ mmHg and<br><10 mmHg   | 6                         | 3               |  |  |
| Decrease from baseline $\geq 10$ mmHg                  | 1                         | 0               |  |  |
| No change from baseline or min. change<br>( $>5$ mmHg) | 17                        | 9               |  |  |
| Missing post-baseline values                           | 2                         | 0               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with slit lamp results for any evaluation and worst eye

|                 |  |
|-----------------|--|
| End point title | Number of participants with slit lamp results for any evaluation and worst eye |
|-----------------|--|

End point description:

Slit lamp examination was used to evaluate lids, cornea, conjunctiva, iris, anterior chamber, aqueous flare, aqueous inflammatory cells and lens. Any post-baseline abnormalities (not present at baseline) in slit lamp examination were assessed by the investigator and classified as insignificant or clinically significant. Number of participants with slit lamp results (normal, insignificant, significant, missing) for any evaluation and worst eye are reported.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to Week 104

| End point values                | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|---------------------------------|---------------------------|-----------------|--|--|
| Subject group type              | Reporting group           | Reporting group |  |  |
| Number of subjects analysed     | 30                        | 15              |  |  |
| Units: participants             |                           |                 |  |  |
| Baseline Normal                 | 12                        | 6               |  |  |
| Any post-baseline Normal        | 7                         | 3               |  |  |
| Baseline Insignificant          | 14                        | 9               |  |  |
| Any post-baseline Insignificant | 18                        | 12              |  |  |
| Baseline Significant            | 2                         | 0               |  |  |

|                               |   |   |  |  |
|-------------------------------|---|---|--|--|
| Any post-baseline Significant | 3 | 0 |  |  |
| Baseline Missing              | 2 | 0 |  |  |
| Any post-baseline Missing     | 2 | 0 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with an increase from baseline of $\geq 1$ and $\geq 2$ in LOCS III grades

|  |   |
|--|---|
| End point title  | Number of participants with an increase from baseline of $\geq 1$ and $\geq 2$ in LOCS III grades |
| End point description:   |   |
| <p>Lens Opacities Classification System III (LOCS III) grading scales include lens opacities defined as nuclear opalescence (NO), nuclear color (NC), cortical (C) cataract and posterior subcapsular (P) cataract with several degrees of extend, i.e. severity. The LOCS III scale for nuclear opalescence and for nuclear color ranges from 0 to 6. The LOCS III scale for cortical cataract and posterior subcapsular cataract opacity ranges from 0 to 5. For all scales, higher values indicate higher opacity, opalescence, or color (range: NO0/NC0/C0/P0 to NO6/NC6/C5/P5).</p> <p>Number of participants with an increase from baseline of <math>\geq 1</math> and increase of <math>\geq 2</math> in LOCS III grades is reported.</p> |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline, up to Week 104   |   |

| End point values                      | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|---------------------------------------|---------------------------|-----------------|--|--|
| Subject group type                    | Reporting group           | Reporting group |  |  |
| Number of subjects analysed           | 30                        | 15              |  |  |
| Units: participants                   |                           |                 |  |  |
| $\geq 1$ grade increase from baseline | 10                        | 5               |  |  |
| $\geq 2$ grade increase from baseline | 2                         | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with fundus oculi results for any evaluation and worst eye

|  |   |
|--|---|
| End point title  | Number of participants with fundus oculi results for any evaluation and worst eye |
| End point description:   |   |
| <p>Fundus oculi examination was used to evaluate peripheral retina, macula, optic nerve, and vitreous hemorrhage. Any post-baseline abnormalities (not present at baseline) in fundus oculi examination were assessed by the investigator and classified as insignificant or clinically significant. Number of participants with fundus oculi results (normal, insignificant, significant, missing) for any evaluation and worst eye are reported.</p> |   |
| End point type   | Secondary   |

End point timeframe:  
Baseline, up to Week 104

| <b>End point values</b>         | Deferasirox<br>FCT 7mg/kg | Phlebotomy      |  |  |
|---------------------------------|---------------------------|-----------------|--|--|
| Subject group type              | Reporting group           | Reporting group |  |  |
| Number of subjects analysed     | 30                        | 15              |  |  |
| Units: participants             |                           |                 |  |  |
| Baseline Normal                 | 15                        | 10              |  |  |
| Any post-baseline Normal        | 12                        | 10              |  |  |
| Baseline Insignificant          | 12                        | 5               |  |  |
| Any post-baseline Insignificant | 14                        | 5               |  |  |
| Baseline Significant            | 1                         | 0               |  |  |
| Any post-baseline Significant   | 2                         | 0               |  |  |
| Baseline Missing                | 2                         | 0               |  |  |
| Any post-baseline Missing       | 2                         | 0               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to response (TTR)

|   |                        |
|---|------------------------|
| End point title   | Time to response (TTR) |
| End point description:  |                        |
| <p>Time to response (TTR) is defined as the time from the date of randomization to the date of the first time the SF achieved a value <math>\leq 100 \mu\text{g/L}</math> during the treatment phase. Participants who did not achieve <math>\text{SF} \leq 100 \mu\text{g/L}</math> were censored as follows: at the last serum ferritin assessment date on or before month 24 (week 104), at the day of randomization if a subject does not have any post-baseline serum ferritin value or at the death date. TTR was analyzed using the Kaplan-Meier method. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.</p> |                        |
| End point type  | Secondary              |
| End point timeframe:  |                        |
| Up to Month 24  |                        |

| <b>End point values</b>          | Deferasirox<br>FCT 7mg/kg | Phlebotomy            |  |  |
|----------------------------------|---------------------------|-----------------------|--|--|
| Subject group type               | Reporting group           | Reporting group       |  |  |
| Number of subjects analysed      | 30                        | 15                    |  |  |
| Units: months                    |                           |                       |  |  |
| median (confidence interval 95%) | 999 (19.4 to<br>999)      | 13.6 (4.0 to<br>22.1) |  |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 108 weeks.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 26.0   |

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | DFX FCT |
|-----------------------|---------|

Reporting group description:

DFX FCT

|                       |            |
|-----------------------|------------|
| Reporting group title | Phlebotomy |
|-----------------------|------------|

Reporting group description:

Phlebotomy

| <b>Serious adverse events</b>                                       | DFX FCT         | Phlebotomy     |  |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events                   |                 |                |  |
| subjects affected / exposed   | 7 / 30 (23.33%) | 0 / 15 (0.00%) |  |
| number of deaths (all causes)                                       | 1               | 0              |  |
| number of deaths resulting from adverse events                      | 0               | 0              |  |
| Investigations  |                 |                |  |
| Blood creatinine increased  |                 |                |  |
| subjects affected / exposed   | 1 / 30 (3.33%)  | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all                     | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0          |  |
| Transaminases increased   |                 |                |  |
| subjects affected / exposed   | 1 / 30 (3.33%)  | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all                     | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0          |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                |  |
| Bladder neoplasm  |                 |                |  |
| subjects affected / exposed   | 1 / 30 (3.33%)  | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0          |  |
| Injury, poisoning and procedural complications                      |                 |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| Lower limb fracture                                  |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                             |                |                |  |
| Thoracic outlet syndrome                             |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Sudden death   |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          |  |
| Gastrointestinal disorders                           |                |                |  |
| Nausea   |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                          |                |                |  |
| Renal impairment                                     |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Infections and infestations                          |                |                |  |
| COVID-19   |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Cellulitis   |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Erysipelas   |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 30 (3.33%) | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | DFX FCT          | Phlebotomy       |  |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 23 / 30 (76.67%) | 12 / 15 (80.00%) |  |
| Vascular disorders                                    |                  |                  |  |
| Hypotension   |                  |                  |  |
| subjects affected / exposed                           | 0 / 30 (0.00%)   | 1 / 15 (6.67%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Hypertension  |                  |                  |  |
| subjects affected / exposed                           | 3 / 30 (10.00%)  | 3 / 15 (20.00%)  |  |
| occurrences (all)                                     | 4                | 3                |  |
| General disorders and administration site conditions  |                  |                  |  |
| Pyrexia   |                  |                  |  |
| subjects affected / exposed                           | 2 / 30 (6.67%)   | 0 / 15 (0.00%)   |  |
| occurrences (all)                                     | 2                | 0                |  |
| Fatigue   |                  |                  |  |
| subjects affected / exposed                           | 1 / 30 (3.33%)   | 1 / 15 (6.67%)   |  |
| occurrences (all)                                     | 1                | 1                |  |
| Asthenia  |                  |                  |  |
| subjects affected / exposed                           | 0 / 30 (0.00%)   | 1 / 15 (6.67%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Vaccination site pain                                 |                  |                  |  |
| subjects affected / exposed                           | 0 / 30 (0.00%)   | 1 / 15 (6.67%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Respiratory, thoracic and mediastinal disorders       |                  |                  |  |
| Rhinorrhoea   |                  |                  |  |
| subjects affected / exposed                           | 0 / 30 (0.00%)   | 1 / 15 (6.67%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Oropharyngeal pain                                    |                  |                  |  |

|   |                        |                      |  |
|---|------------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 1 / 30 (3.33%)<br>1    | 1 / 15 (6.67%)<br>1  |  |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 30 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1  |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 30 (3.33%)<br>1    | 3 / 15 (20.00%)<br>3 |  |
| Catarrh<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 30 (3.33%)<br>1    | 1 / 15 (6.67%)<br>1  |  |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 30 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1  |  |
| Investigations  |                        |                      |  |
| Blood uric acid increased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 30 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1  |  |
| Blood urea increased<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 30 (6.67%)<br>3    | 0 / 15 (0.00%)<br>0  |  |
| Blood lactate dehydrogenase<br>increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 30 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1  |  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                | 10 / 30 (33.33%)<br>13 | 1 / 15 (6.67%)<br>1  |  |
| Blood creatine phosphokinase<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 30 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1  |  |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all)               | 1 / 30 (3.33%)<br>1    | 1 / 15 (6.67%)<br>1  |  |
| Aspartate aminotransferase<br>increased   |                        |                      |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                       | 1 / 30 (3.33%)<br>1  | 1 / 15 (6.67%)<br>1  |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Glycosylated haemoglobin increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Vitamin D decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Injury, poisoning and procedural complications   |                      |                      |  |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Road traffic accident<br>subjects affected / exposed<br>occurrences (all)              | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Ligament sprain<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 30 (6.67%)<br>2  | 0 / 15 (0.00%)<br>0  |  |
| Cardiac disorders  |                      |                      |  |
| Sinus bradycardia<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 30 (3.33%)<br>1  | 1 / 15 (6.67%)<br>1  |  |
| Nervous system disorders   |                      |                      |  |
| Taste disorder<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                           | 4 / 30 (13.33%)<br>8 | 2 / 15 (13.33%)<br>3 |  |
| Dizziness  |                      |                      |  |

|  |  |  |  |
|--|--|--|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 30 (0.00%)<br>0  | 2 / 15 (13.33%)<br>4   |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 30 (3.33%)<br>1  | 2 / 15 (13.33%)<br>2   |  |
| Ear and labyrinth disorders<br>Deafness unilateral<br>subjects affected / exposed<br>occurrences (all)<br><br>Ear pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Phobic postural vertigo<br>subjects affected / exposed<br>occurrences (all)<br><br>Middle ear inflammation<br>subjects affected / exposed<br>occurrences (all) | 1 / 30 (3.33%)<br>1<br><br>0 / 30 (0.00%)<br>0<br><br>0 / 30 (0.00%)<br>0<br><br>0 / 30 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1 |  |
| Eye disorders<br>Glaucoma<br>subjects affected / exposed<br>occurrences (all)<br><br>Cataract nuclear<br>subjects affected / exposed<br>occurrences (all)  | 2 / 30 (6.67%)<br>2<br><br>2 / 30 (6.67%)<br>2   | 0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0   |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal distension<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastrointestinal disorder<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea   | 2 / 30 (6.67%)<br>2<br><br>1 / 30 (3.33%)<br>1<br><br>0 / 30 (0.00%)<br>0                            | 0 / 15 (0.00%)<br>0<br><br>1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1                            |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 6 / 30 (20.00%)<br>8 | 2 / 15 (13.33%)<br>3 |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 2 / 30 (6.67%)<br>2  | 0 / 15 (0.00%)<br>0  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 5 / 30 (16.67%)<br>8 | 0 / 15 (0.00%)<br>0  |  |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all)  | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Gastrointestinal pain<br>subjects affected / exposed<br>occurrences (all)   | 2 / 30 (6.67%)<br>2  | 0 / 15 (0.00%)<br>0  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 2 / 30 (6.67%)<br>3  | 0 / 15 (0.00%)<br>0  |  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 30 (3.33%)<br>1  | 1 / 15 (6.67%)<br>1  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 30 (3.33%)<br>1  | 2 / 15 (13.33%)<br>3 |  |
| Arthritis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 30 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 4 / 30 (13.33%)<br>4 | 2 / 15 (13.33%)<br>2 |  |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 30 (0.00%)<br>0  | 2 / 15 (13.33%)<br>2 |  |
| Infections and infestations   |                      |                      |  |

|                                     |                |                 |  |
|-------------------------------------|----------------|-----------------|--|
| Wound infection                     |                |                 |  |
| subjects affected / exposed         | 0 / 30 (0.00%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 0              | 1               |  |
| Urinary tract infection             |                |                 |  |
| subjects affected / exposed         | 0 / 30 (0.00%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 0              | 1               |  |
| Suspected COVID-19                  |                |                 |  |
| subjects affected / exposed         | 0 / 30 (0.00%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 0              | 1               |  |
| Sinusitis                           |                |                 |  |
| subjects affected / exposed         | 0 / 30 (0.00%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 0              | 1               |  |
| Nasopharyngitis                     |                |                 |  |
| subjects affected / exposed         | 2 / 30 (6.67%) | 3 / 15 (20.00%) |  |
| occurrences (all)                   | 2              | 5               |  |
| Escherichia urinary tract infection |                |                 |  |
| subjects affected / exposed         | 1 / 30 (3.33%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 1              | 1               |  |
| Ear infection                       |                |                 |  |
| subjects affected / exposed         | 1 / 30 (3.33%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 1              | 1               |  |
| Cystitis                            |                |                 |  |
| subjects affected / exposed         | 2 / 30 (6.67%) | 0 / 15 (0.00%)  |  |
| occurrences (all)                   | 2              | 0               |  |
| COVID-19                            |                |                 |  |
| subjects affected / exposed         | 2 / 30 (6.67%) | 0 / 15 (0.00%)  |  |
| occurrences (all)                   | 2              | 0               |  |
| Bone abscess                        |                |                 |  |
| subjects affected / exposed         | 0 / 30 (0.00%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 0              | 1               |  |
| Metabolism and nutrition disorders  |                |                 |  |
| Folate deficiency                   |                |                 |  |
| subjects affected / exposed         | 0 / 30 (0.00%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                   | 0              | 1               |  |
| Hyperglycaemia                      |                |                 |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 15 (6.67%) |  |
| occurrences (all)           | 0              | 1              |  |
| Vitamin B12 deficiency      |                |                |  |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 15 (6.67%) |  |
| occurrences (all)           | 0              | 1              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment  |
|----------------|--|
| 30 August 2018 | The purpose of this amendment is to modify the inclusion and exclusion criteria, to correct inconsistencies, typos, add some clarifications and to update withdrawal of consent language. Additionally, the local French amendment text is formally integrated in this global amendment. However, the French specific requirements remain valid for France only. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported