



Clinical trial results:

A randomized, open-label, multicenter, two arm, phase II study to investigate the benefits of an improved deferasirox formulation (film-coated tablet)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2013-004167-32 |
| Trial protocol | AT ES IT GB FR GR |
| Global end of trial date | 24 February 2016 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 |
| This version publication date | 09 September 2016 |
| First version publication date | 09 September 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CICL670F2201 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02125877 |
| 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 613421111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613421111, |

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? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 24 February 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 February 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the overall safety of deferasirox FCT and deferasirox DT formulations in patients with transfusion-dependent thalassemia or myelodysplastic syndrome at very low, low or intermediate (int) risk.

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 | 08 July 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 | Argentina: 2 |
| Country: Number of subjects enrolled | Austria: 6 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Germany: 14 |
| Country: Number of subjects enrolled | Greece: 17 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Italy: 52 |
| Country: Number of subjects enrolled | Lebanon: 20 |
| Country: Number of subjects enrolled | Malaysia: 10 |
| Country: Number of subjects enrolled | Mexico: 3 |
| Country: Number of subjects enrolled | Russian Federation: 1 |
| Country: Number of subjects enrolled | Saudi Arabia: 9 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | Thailand: 6 |
| Country: Number of subjects enrolled | United States: 7 |
| Country: Number of subjects enrolled | United Arab Emirates: 13 |
| Worldwide total number of subjects | 173 |
| EEA total number of subjects | 102 |

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) | 2 |
| Adolescents (12-17 years) | 19 |
| Adults (18-64 years) | 126 |
| From 65 to 84 years | 26 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio.

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 |
| Arm title | Deferasirox dispersible tablet (DFX-DT) |

Arm description:

Iron chelation naïve participants received DFX-DT 20 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 5 to 10 mg/kg/day, with a maximum dose of 40 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose.

| | |
|--|----------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Deferasirox (DFX-DT) |
| Investigational medicinal product code | ICL670 |
| Other name | |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Iron chelation naïve participants received DFX-DT 20 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 5 to 10 mg/kg/day, with a maximum dose of 40 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose.

| | |
|------------------|--|
| Arm title | Deferasirox film-coated tablet (DFX-FCT) |
|------------------|--|

Arm description:

Participants received DFX-FCT 14 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 3.5 to 7 mg/kg/day, with a maximum dose of 28 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Deferasirox (DFX-FCT) |
| Investigational medicinal product code | ICL670 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received DFX-FCT 14 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 3.5 to 7 mg/kg/day, with a maximum dose of 28 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose.

| Number of subjects in period 1 | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) |
|--------------------------------|---|--|
| Started | 86 | 87 |
| Pharmacokinetic analysis set | 83 | 83 |
| Pharmacokinetic subset A | 16 ^[1] | 15 ^[2] |
| Safety set | 86 | 87 |
| Completed | 73 | 77 |
| Not completed | 13 | 10 |
| Adverse event, serious fatal | - | 1 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 2 | 1 |
| Adverse event, non-fatal | 6 | 4 |
| Protocol deviation | 4 | 1 |
| Administrative problems | - | 1 |
| Participant/guardian decision | - | 2 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number at this milestone is correct.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number at this milestone is correct.

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Deferasirox dispersible tablet (DFX-DT) |
| Reporting group description: | |
| Iron chelation naïve participants received DFX-DT 20 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 5 to 10 mg/kg/day, with a maximum dose of 40 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose. | |
| Reporting group title | Deferasirox film-coated tablet (DFX-FCT) |
| Reporting group description: | |
| Participants received DFX-FCT 14 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 3.5 to 7 mg/kg/day, with a maximum dose of 28 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose | |

| Reporting group values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | Total |
|--|---|--|-------|
| Number of subjects | 86 | 87 | 173 |
| Age categorical | | | |
| 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) | 2 | 0 | 2 |
| Adolescents (12-17 years) | 8 | 11 | 19 |
| Adults (18-64 years) | 64 | 62 | 126 |
| From 65-84 years | 12 | 14 | 26 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 35.1 | 34.6 | |
| standard deviation | ± 18.6 | ± 19.97 | - |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 47 | 41 | 88 |
| Male | 39 | 46 | 85 |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Deferasirox dispersible tablet (DFX-DT) |
| Reporting group description: Iron chelation naïve participants received DFX-DT 20 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 5 to 10 mg/kg/day, with a maximum dose of 40 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose. | |
| Reporting group title | Deferasirox film-coated tablet (DFX-FCT) |
| Reporting group description: Participants received DFX-FCT 14 mg/kg/day once daily orally from weeks 1 - 4. After week 4, the dose could be adjusted by +/- 3.5 to 7 mg/kg/day, with a maximum dose of 28 mg/kg/day. Iron chelation pre-treated participants were supposed to start on a dose that was equivalent to their pre-washout dose | |

Primary: Overall safety as measured by adverse events

| | |
|---|---|
| End point title | Overall safety as measured by adverse events ^[1] |
| End point description: The percentage of participants with adverse events, serious adverse events and deaths was assessed. | |
| End point type | Primary |
| End point timeframe: 30 weeks | |

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: Statistical analysis does not apply to this primary end point.

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Adverse events | 89.5 | 89.7 | | |
| SAEs | 15.1 | 18.4 | | |
| Deaths | 0 | 1.1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Overall safety as measured by changes in laboratory values from baseline

| | |
|---|---|
| End point title | Overall safety as measured by changes in laboratory values from baseline ^[2] |
| End point description: The percentage of participants with post-baseline laboratory values meeting specified criteria for notable/extended range was assessed. The following laboratory parameters were measured: platelet | |

count, absolute neutrophils, serum creatinine , creatinine clearance, urinary protein/urinary creatinine ratio, alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Note that within data categories, creat = creatinine, cons = consecutive, ULN = upper limit of normal and urin = urinary.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| 30 weeks | |

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: Statistical analysis does not apply to this end point.

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|--|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| platelet count, notable range: $<100 \times 10^9/L$ | 9.3 | 8 | | |
| platelet count, extended range: $<50 \times 10^9/L$ | 3.5 | 5.7 | | |
| absolute neutrophils, notable range: $<1.5 \times 10^9/L$ | 8.1 | 13.8 | | |
| absolute neutrophils, extended range: $<0.5 \times 10^9/L$ | 4.7 | 0 | | |
| serum creat, 2 cons $>33\%$ inc from BL and $>ULN$ | 4.7 | 3.4 | | |
| creat clearance, notable range: 2 cons <60 mL/min | 7 | 2.3 | | |
| creat clearance, extended range: 2 cons <40 mL/min | 2.3 | 2.3 | | |
| urin protein/urin creat ratio, 2 cons >1.0 mg/mg | 2.3 | 0 | | |
| ALT, notable range: $>5 \times ULN$ and $>2 \times BL$ | 1.2 | 1.1 | | |
| ALT, extended range: $>10 \times ULN$ and $>2 \times BL$ | 1.2 | 0 | | |
| AST, notable range: $>5 \times ULN$ and $>2 \times BL$ | 0 | 1.1 | | |
| AST, extended range: $>10 \times ULN$ and $>2 \times BL$ | 1.2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of selected gastro-intestinal (GI) adverse events

| | |
|--|---|
| End point title | Frequency of selected gastro-intestinal (GI) adverse events |
| End point description: | |
| The percentage of participants with any GI adverse event, diarrhea, constipation, nausea, vomiting, abdominal pain was assessed. | |
| End point type | Secondary |

End point timeframe:

28 weeks

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Any GI adverse event | 61.6 | 58.6 | | |
| Abdominal pain | 26.7 | 26.4 | | |
| Constipation | 15.1 | 8 | | |
| Diarrhea | 34.9 | 33.3 | | |
| Nausea | 26.7 | 27.6 | | |
| Vomiting | 22.1 | 17.2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean domain scores of the modified Satisfaction with Iron Chelation Therapy (modified SICT)

| | |
|-----------------|---|
| End point title | Mean domain scores of the modified Satisfaction with Iron Chelation Therapy (modified SICT) |
|-----------------|---|

End point description:

The modified SICT consisted of 13 items that represent 3 domains: adherence, satisfaction and concerns. The adherence domain consisted of 7 items, 6 which were measured using a 5-point response scale and was calculated by summing the 6 items. The score range from 6 to 30 and higher scores indicated worse adherence. The satisfaction domain consisted of 3 items, 2 which were measured using a 5-point response scale and was calculated by summing the 2 items. The score range from 2 to 10 and higher scores indicated worse satisfaction. The concerns domain consisted of 3 items to address any concerns or worries with his/her medication. All 3 items were measured on a 5-point response scale and were calculated by summing the 3 items. The score range from 3 to 15 and higher scores indicated fewer concerns. For all three domains, the meaningful difference between two treatment arms was determined to be 1 point.

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

End point timeframe:

weeks 2, 3, 13 and 24 (end of treatment or within 7 days of last dose)

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: score on a scale | | | | |

| arithmetic mean (standard deviation) | | | | |
|--|---------------|---------------|--|--|
| week 2, adherence (n=70,70) | 10.3 (± 3.8) | 7.6 (± 2.14) | | |
| week 2, satisfaction/preference (n=70,70) | 5.2 (± 2.24) | 2.8 (± 1.37) | | |
| week 2, concerns (n=70,70) | 12.9 (± 2.94) | 13.8 (± 2.02) | | |
| week 3, adherence (n=58,51) | 10.9 (± 4.09) | 7.7 (± 2.06) | | |
| week 3, satisfaction/preference (n=58,51) | 5.4 (± 2.22) | 2.6 (± 1.05) | | |
| week 3, concerns (n=58,51) | 12.4 (± 2.73) | 14 (± 1.49) | | |
| week 13, adherence (n=59,64) | 11.2 (± 3.56) | 7.8 (± 2.05) | | |
| week 13, satisfaction/preference (n=59,64) | 5.4 (± 2.14) | 2.9 (± 1.54) | | |
| week 13, concerns (n=59,64) | 12.7 (± 2.5) | 13.6 (± 1.87) | | |
| week 24, adherence (n=63,60) | 12.5 (± 5.32) | 7.5 (± 2.41) | | |
| week 24, satisfaction/preference (n=63,60) | 5.8 (± 2.28) | 2.9 (± 1.58) | | |
| week 24, concerns (n=63,60) | 11.8 (± 3.07) | 13.7 (± 1.84) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability questionnaire score

| End point title | Palatability questionnaire score |
|--|----------------------------------|
| End point description: | |
| The palatability questionnaire consisted of 4 items. The first item measured the taste and aftertaste of the medication and were scored a on a 5-point response scale. The second item offered an additional response option of "no aftertaste". The last 2 items referred to whether the medication was taken, i.e. swallowed or vomited, and how the participant perceived the amount of medication to be taken. The palatability summary score was calculated using a scoring matrix from items 1, 3 and 4 scores and the score ranges from 0 - 11. Higher scores indicated the best palatability. A meaningful difference between two treatment arms was determined to be 1 point. | |
| End point type | Secondary |
| End point timeframe: | |
| weeks 2, 3, 13 and 24 (end of treatment or within 7 days of last dose) | |

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| week 2 (n=69,70) | 9 (± 3.01) | 10.8 (± 0.5) | | |
| week 3 (n=57,51) | 8.8 (± 3.01) | 10.8 (± 0.45) | | |
| week 13 (n=59,62) | 9.3 (± 2.84) | 10.8 (± 1.16) | | |
| week 24 (n=63,60) | 8.8 (± 3.1) | 10.9 (± 0.34) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Weekly average of daily scores of the gastrointestinal (GI) symptom diary

| | |
|-----------------|---|
| End point title | Weekly average of daily scores of the gastrointestinal (GI) symptom diary |
|-----------------|---|

End point description:

The GI symptom diary consisted of 6 items, five which were scored using a 0 - 10 rating scale with item appropriate anchors to rate the symptom, for example, Pain in your belly: 0 = no pain and 10 = worst pain. The GI diary summary score was created using the 10 point response scale for the 5 items. The GI symptom daily diary had a minimum score of 0 and a maximum score of 50. The weekly average score for the 7 days was calculated for each individual item and the GI summary score was created from these weekly averages. Higher scores indicated worse symptoms. A meaningful difference between two treatment arms was determined to be 0.3 point.

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

End point timeframe:

weeks -1, 4, 8, 12, 16, 20, 24

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| week -1 (n=69,65) | 1.4 (± 2.1) | 1.9 (± 3.69) | | |
| week 4 (n=60,64) | 1.8 (± 3.49) | 1.1 (± 2.15) | | |
| week 8 (n=59,51) | 1.4 (± 2.45) | 1.1 (± 2.16) | | |
| week 12 (n=51,45) | 1.7 (± 3.16) | 1 (± 1.78) | | |
| week 16 (n=48,41) | 1.9 (± 3.75) | 0.9 (± 1.92) | | |
| week 20 (n=40,39) | 1.5 (± 3.27) | 0.9 (± 1.44) | | |
| week 24 (n=32,26) | 1.5 (± 3.29) | 1.2 (± 1.89) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with weekly average compliance of medication consumption

| | |
|-----------------|--|
| End point title | Number of participants with weekly average compliance of |
|-----------------|--|

End point description:

A compliance questionnaire assessed whether the medication was taken. Weekly average compliance was calculated when there were at least four non-missing daily responses.

End point type

Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Participants | | | | |
| week 1 | 56 | 53 | | |
| week 2 | 64 | 64 | | |
| week 3 | 62 | 56 | | |
| week 4 | 58 | 58 | | |
| week 5 | 56 | 58 | | |
| week 6 | 62 | 51 | | |
| week 7 | 55 | 48 | | |
| week 8 | 56 | 46 | | |
| week 9 | 53 | 45 | | |
| week 10 | 52 | 46 | | |
| week 11 | 50 | 42 | | |
| week 12 | 50 | 41 | | |
| week 13 | 49 | 47 | | |
| week 14 | 51 | 42 | | |
| week 15 | 48 | 42 | | |
| week 16 | 48 | 40 | | |
| week 17 | 43 | 39 | | |
| week 18 | 43 | 38 | | |
| week 19 | 40 | 37 | | |
| week 20 | 40 | 36 | | |
| week 21 | 39 | 36 | | |
| week 22 | 38 | 34 | | |
| week 23 | 36 | 33 | | |
| week 24 | 30 | 24 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Weekly dose violation rate**End point title**

Weekly dose violation rate

End point description:

The dose violation is defined as a dose either missed completely or not taken in accordance with the timing instruction (no later than 12:00 pm. The rate was calculated as [number of dose violations/drug exposure (days)] x 100.

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

End point timeframe:

weeks 1, 4, 8, 12, 16, 20, 24

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: (number of dose violations/days)*100 | | | | |
| arithmetic mean (standard deviation) | | | | |
| week 1 (n=56,53) | 17.7 (± 31.04) | 15.8 (± 29.42) | | |
| week 4 (n=58,58) | 15.8 (± 32.51) | 6.7 (± 15.45) | | |
| week 8 (n=56,46) | 18 (± 35.38) | 8.4 (± 22.17) | | |
| week 12 (n=50,41) | 15.7 (± 34.22) | 10.7 (± 22.63) | | |
| week 16 (n=48,40) | 13.5 (± 31.08) | 10 (± 24.5) | | |
| week 20 (n=40,36) | 22.6 (± 38.38) | 11.3 (± 26.67) | | |
| week 24 (n=30,24) | 17.1 (± 34.26) | 10.1 (± 25.47) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the last quantifiable concentration (AUClast)

| | |
|-----------------|--|
| End point title | Area under the plasma concentration-time curve from time zero to the last quantifiable concentration (AUClast) |
|-----------------|--|

End point description:

Blood samples were collected to assess AUClast.

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

End point timeframe:

week 1, day 1: pre-dose (0 hour) and 1, 2, 3, 4, 8 and 24 hours post dose; week 3, day 1: pre-dose (0 hour) and 1, 2, 3, 4, 8 and 24 hours post dose

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: umol/L*h | | | | |
| arithmetic mean (standard deviation) | | | | |
| week1 (n=14,15) | 1110 (± 495) | 1040 (± 405) | | |
| week 3 (n=13,15) | 1590 (± 540) | 2110 (± 987) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Observed maximum plasma concentration following drug administration (Cmax)

| | |
|--|--|
| End point title | Observed maximum plasma concentration following drug administration (Cmax) |
| End point description: Blood samples were collected to assess Cmax. | |
| End point type | Secondary |
| End point timeframe: week 1, day 1: pre-dose (0 hour) and 1, 2, 3, 4, 8 and 24 hours post dose; week 3, day 1: pre-dose (0 hour) and 1, 2, 3, 4, 8 and 24 hours post dose | |

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: umol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| week 1 (n=14,15) | 74.6 (± 30.7) | 79.3 (± 23.5) | | |
| week 3 (n=14,15) | 118 (± 82.3) | 139 (± 57.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach the maximum plasma concentration after drug administration (Tmax)

| | |
|--|---|
| End point title | Time to reach the maximum plasma concentration after drug administration (Tmax) |
| End point description: Blood samples were collected to assess Tmax. | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| week 1, day 1: pre-dose (0 hour) and 1, 2, 3, 4, 8 and 24 hours post dose; week 3, day 1: pre-dose (0 hour) and 1, 2, 3, 4, 8 and 24 hours post dose | |

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: hour | | | | |
| median (full range (min-max)) | | | | |
| week 1 (n=14,15) | 3.57 (1.15 to 7.89) | 2 (1.15 to 15.6) | | |
| week 3 (n=14,15) | 2.85 (1.4 to 8.39) | 2.02 (1.07 to 5.06) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Dererasirox plasma concentration

| | |
|---|----------------------------------|
| End point title | Dererasirox plasma concentration |
| End point description: | |
| Blood samples were collected to assess deferasirox concentration. Dose-adjusted calculations are presented: (concentration/actual dose)*20 for participants on DFX-DT and (concentration/actual dose)*14 for participants on DFX-FCT. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 3, day 1, pre-dose (0 hour (h)) and 2 h post-dose; week 13, day 1, pre-dose (0 hour (h)) and 2 h post-dose; and week 21, day 1, pre-dose (0 hour (h)) and 2 h post-dose | |

| End point values | Deferasirox dispersible tablet (DFX-DT) | Deferasirox film-coated tablet (DFX-FCT) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 83 | | |
| Units: umol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| week 3, pre-dose (n=63,70) | 39.6 (± 48.4) | 27.3 (± 20.4) | | |
| week 3, 2 hours post-dose (n=67,76) | 80.8 (± 52.2) | 95.5 (± 53) | | |
| week 13, pre-dose (n=69,56) | 37.1 (± 37.8) | 31.3 (± 22.9) | | |
| week 13, 2 hours post-dose (n=74,59) | 78.7 (± 39.5) | 92.5 (± 39.1) | | |
| week 21, pre-dose (n=54,59) | 46.6 (± 46.4) | 43.1 (± 36.8) | | |
| week 21, 2 hours post-dose (n=59,64) | 89.8 (± 59.3) | 105 (± 51.2) | | |

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.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | DFX DT |
|-----------------------|--------|

Reporting group description:

DFX DT

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

Reporting group description:

DFX FCT

| Serious adverse events | DFX DT | DFX FCT | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 86 (15.12%) | 16 / 87 (18.39%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma pancreas | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukaemia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Face oedema | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urine protein/creatinine ratio increased | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 87 (2.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delayed haemolytic transfusion reaction | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (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 | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Autoimmune haemolytic anaemia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Haemolysis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fissure | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 87 (2.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic colitis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Biliary colic | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (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 | | | |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brucellosis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural pneumonia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 87 (2.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | DFX DT | DFX FCT | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 69 / 86 (80.23%) | 72 / 87 (82.76%) | |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 7 / 86 (8.14%) | 8 / 87 (9.20%) | |
| occurrences (all) | 7 | 11 | |
| Urine protein/creatinine ratio increased | | | |
| subjects affected / exposed | 11 / 86 (12.79%) | 17 / 87 (19.54%) | |
| occurrences (all) | 15 | 23 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 12 / 86 (13.95%) | 5 / 87 (5.75%) | |
| occurrences (all) | 30 | 5 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 8 / 86 (9.30%) | 4 / 87 (4.60%) | |
| occurrences (all) | 8 | 4 | |
| Fatigue | | | |
| subjects affected / exposed | 7 / 86 (8.14%) | 5 / 87 (5.75%) | |
| occurrences (all) | 7 | 5 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 86 (8.14%) | 7 / 87 (8.05%) | |
| occurrences (all) | 8 | 9 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 23 / 86 (26.74%) | 23 / 87 (26.44%) | |
| occurrences (all) | 33 | 33 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 10 / 87 (11.49%) | |
| occurrences (all) | 7 | 11 | |
| Constipation | | | |
| subjects affected / exposed | 13 / 86 (15.12%) | 7 / 87 (8.05%) | |
| occurrences (all) | 19 | 10 | |

| | | | |
|--|---|---|--|
| Diarrhoea subjects affected / exposed occurrences (all) | 30 / 86 (34.88%) 62 | 27 / 87 (31.03%) 55 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 2 / 86 (2.33%) 2 | 6 / 87 (6.90%) 7 | |
| Nausea subjects affected / exposed occurrences (all) | 23 / 86 (26.74%) 43 | 24 / 87 (27.59%) 43 | |
| Vomiting subjects affected / exposed occurrences (all) | 18 / 86 (20.93%) 29 | 15 / 87 (17.24%) 19 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 4 / 86 (4.65%) 4 | 7 / 87 (8.05%) 7 | |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all) Pyuria subjects affected / exposed occurrences (all) | 2 / 86 (2.33%) 2 4 / 86 (4.65%) 4 2 / 86 (2.33%) 2 | 8 / 87 (9.20%) 11 8 / 87 (9.20%) 10 6 / 87 (6.90%) 9 | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 5 | 4 / 87 (4.60%) 4 | |
| Infections and infestations Bacteriuria subjects affected / exposed occurrences (all) Gastroenteritis | 5 / 86 (5.81%) 6 | 5 / 87 (5.75%) 7 | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 86 (3.49%) 3 | 5 / 87 (5.75%) 5 | |
| Influenza subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 6 | 0 / 87 (0.00%) 0 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 6 / 86 (6.98%) 6 | 6 / 87 (6.90%) 6 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 6 / 86 (6.98%) 8 | 3 / 87 (3.45%) 3 | |
| Metabolism and nutrition disorders Hyperphosphataemia subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 7 | 4 / 87 (4.60%) 5 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 02 September 2014 | <p>The purpose of the amendment was to clarify exclusion criteria and provide guidance regarding dose modifications, concomitant medications, and contraception. The exclusion criteria and dose modification guidelines were updated to exclude patients with moderate and severe hepatic impairment (Child-Pugh Class B and C). In addition, guidance on treating patients who develop moderate hepatic impairment (Child-Pugh Class B) during the trial and immediate discontinuation if Stevens-Johnson syndrome occurs is provided, in alignment with the prescribing Exjade® information. Guidance was updated on the use of contraception. Effective contraception is required in alignment with the prescribing Exjade® information. Additional guidance was added regarding treatment discontinuation of patients with creatinine clearance <40 mL/min or serum creatinine >2 times the age appropriate ULN and caution should be used in patients with creatinine clearance between 40 and less than 60 mL/min, particularly in cases where there are additional risk factors that may impair renal function such as concomitant medications, dehydration, or severe infections in alignment with the prescribing Exjade® information. Guidance was added regarding the concomitant administration of deferasirox with CYP1A2 substrates that have a narrow therapeutic index and the concomitant use of bile acid sequestrants in alignment with the prescribing Exjade® information. An interim analysis was added to provide additional safety data to the Health Authorities during their review of the first FCT submission.</p> <p>Serum iron and total iron binding capacity (TIBC) were added to the visit evaluation schedule (VES) to further characterize Fe homeostasis status. Guidance for starting dose for patients pre-treated with deferiprone is being provided.</p> <p>In addition, clarifications were added regarding visit schedules, PK assessments and to correct typographical errors and inconsistencies.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported