



Clinical trial results:

An open-label, phase II, randomized, pilot study to assess the effect in terms of erythroid improvement of deferasirox combined with erythropoietin compared to erythropoietin alone in patients with low- and int-1-risk myelodysplastic syndrome

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-000981-12 |
| Trial protocol | IT SE GB ES |
| Global end of trial date | 22 March 2017 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 06 April 2018 |
| First version publication date | 06 April 2018 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CICL670A2421 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01868477 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 22 March 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 March 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the effect of treatment with deferasirox (DFX) + erythropoietin (EPO) vs. erythropoietin (EPO) alone on erythropoiesis after 12 weeks of treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 28 January 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 | Canada: 2 |
| Country: Number of subjects enrolled | China: 6 |
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Italy: 3 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Spain: 3 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 14 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |

| | |
|--|----|
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 3 |
| From 65 to 84 years | 20 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Twenty-three patients were randomized into the trial

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 | Erythropoietin alpha |

Arm description:

Starting dose was erythropoietin 40,000 units/week. If after 4 weeks erythroid improvement was inadequate, dose was escalated to 60,000 units/week. If after 12 weeks of treatment, erythroid improvement was inadequate, participants were switched to the combination arm. At any time when erythroid response was achieved, erythropoietin treatment was stopped until end of study.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Erythropoietin alpha |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Erythropoietin alpha (EPO): provided as available in the respective country and is delivered subcutaneous injection

| | |
|------------------|------------------------------------|
| Arm title | Deferasirox + Erythropoietin alpha |
|------------------|------------------------------------|

Arm description:

Starting dose was deferasirox dispersible tablet (DT) 10 mg/kg/day or deferasirox film-coated tablet (FCT) 7 mg/kg/day in combination with erythropoietin 40,000 units/week. If after 4 weeks erythroid improvement was inadequate, erythropoietin dose was escalated to 60,000 units/week. If after 12 weeks of treatment, erythroid improvement was inadequate, participants were discontinued from the study. At any time when erythroid response was achieved, erythropoietin treatment was stopped study and Deferasirox treatment was continued until end of study

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | deferasirox dispersible tablets |
| Investigational medicinal product code | DFX DT |
| Other name | |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

supplied in 125, 250, 500 mg dispersible tablets

| | |
|--|---------------------------------|
| Investigational medicinal product name | deferasirox film-coated tablets |
| Investigational medicinal product code | |
| Other name | DFX FCT |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:
supplied in 90,180, 360 mg film-coated tablets

| Number of subjects in period 1 | Erythropoietin alpha | Deferasirox + Erythropoietin alpha |
|---------------------------------------|----------------------|---------------------------------------|
| Started | 12 | 11 |
| Completed | 8 | 6 |
| Not completed | 4 | 5 |
| Consent withdrawn by subject | 1 | - |
| Disease progression | 1 | 1 |
| Adverse event, non-fatal | 2 | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Erythropoietin alpha |
|-----------------------|----------------------|

Reporting group description:

Starting dose was erythropoietin 40,000 units/week. If after 4 weeks erythroid improvement was inadequate, dose was escalated to 60,000 units/week. If after 12 weeks of treatment, erythroid improvement was inadequate, participants were switched to the combination arm. At any time when erythroid response was achieved, erythropoietin treatment was stopped until end of study.

| | |
|-----------------------|------------------------------------|
| Reporting group title | Deferasirox + Erythropoietin alpha |
|-----------------------|------------------------------------|

Reporting group description:

Starting dose was deferasirox dispersible tablet (DT) 10 mg/kg/day or deferasirox film-coated tablet (FCT) 7 mg/kg/day in combination with erythropoietin 40,000 units/week. If after 4 weeks erythroid improvement was inadequate, erythropoietin dose was escalated to 60,000 units/week. If after 12 weeks of treatment, erythroid improvement was inadequate, participants were discontinued from the study. At any time when erythroid response was achieved, erythropoietin treatment was stopped study and Deferasirox treatment was continued until end of study

| Reporting group values | Erythropoietin alpha | Deferasirox + Erythropoietin alpha | Total |
|--|----------------------|------------------------------------|-------|
| Number of subjects | 12 | 11 | 23 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 74.5 | 71.1 | |
| standard deviation | ± 5.84 | ± 7.54 | - |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 8 | 5 | 13 |
| Male | 4 | 6 | 10 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Caucasian | 8 | 7 | 15 |
| Asian | 4 | 4 | 8 |

End points

End points reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Erythropoietin alpha |
|-----------------------|----------------------|

Reporting group description:

Starting dose was erythropoietin 40,000 units/week. If after 4 weeks erythroid improvement was inadequate, dose was escalated to 60,000 units/week. If after 12 weeks of treatment, erythroid improvement was inadequate, participants were switched to the combination arm. At any time when erythroid response was achieved, erythropoietin treatment was stopped until end of study.

| | |
|-----------------------|------------------------------------|
| Reporting group title | Deferasirox + Erythropoietin alpha |
|-----------------------|------------------------------------|

Reporting group description:

Starting dose was deferasirox dispersible tablet (DT) 10 mg/kg/day or deferasirox film-coated tablet (FCT) 7 mg/kg/day in combination with erythropoietin 40,000 units/week. If after 4 weeks erythroid improvement was inadequate, erythropoietin dose was escalated to 60,000 units/week. If after 12 weeks of treatment, erythroid improvement was inadequate, participants were discontinued from the study. At any time when erythroid response was achieved, erythropoietin treatment was stopped and Deferasirox treatment was continued until end of study

| | |
|----------------------------|--------------------|
| Subject analysis set title | EPO+DFX (12 weeks) |
|----------------------------|--------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Patients randomized to EPO alone with inadequate response at 12 weeks who had been switched over to combination EPO+DFX

| | |
|----------------------------|----------------|
| Subject analysis set title | EPO (24 weeks) |
|----------------------------|----------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Patients who were in EPO alone group and were not switched to EPO+DFX after 12 weeks,

| | |
|----------------------------|---------------|
| Subject analysis set title | EPO+DFX at 12 |
|----------------------------|---------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Patients randomized to EPO alone with inadequate response at 12 weeks who had been switched over to combination EPO+DFX

| | |
|----------------------------|---------------------|
| Subject analysis set title | EPO+DFX at 12 weeks |
|----------------------------|---------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

This analysis included patients randomized either to EPO or DFX+EPO at baseline as well as patients who did not have erythroid response at week 12 in the EPO group and switched to combination therapy. The time-course of Hb and its absolute changes from baseline was summarized by descriptive statistics by visit and erythroid response. Patients randomized to EPO and not switching after 12 weeks to EPO+DFX would consist of only responders

Primary: Summary of erythroid response within 12 weeks, by treatment group (Full Analysis Set)

| | |
|-----------------|---|
| End point title | Summary of erythroid response within 12 weeks, by treatment group (Full Analysis Set) |
|-----------------|---|

End point description:

Difference in percentage of patients achieving an erythroid response within 12 weeks of treatment between the two arms according to modified IWG 2006 criteria increase in hemoglobin (Hb) ≥ 1.5 g/dL. Erythroid response is defined as the increase in Hb from baseline ≥ 1.5 g/dL. Patients achieving erythroid response at least once within 12 weeks were considered responders

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

End point timeframe:

Baseline up to 12 weeks

| End point values | Erythropoietin alpha | Deferasirox + Erythropoietin alpha | | |
|-----------------------------------|----------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 11 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 41.7 (15.2 to 72.3) | 27.3 (6.02 to 61.0) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | EPO vs EPO + DFX |
| Comparison groups | Erythropoietin alpha v Deferasirox + Erythropoietin alpha |
| Number of subjects included in analysis | 23 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 14.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -24 |
| upper limit | 48.16 |

Secondary: Summary of hematologic response in patients randomized to EPO+DFX and EPO alone, within 24 weeks of treatment (Full Analysis Set)

| | |
|-------------------------|---|
| End point title | Summary of hematologic response in patients randomized to EPO+DFX and EPO alone, within 24 weeks of treatment (Full Analysis Set) |
| End point description: | Hematological response criteria defined as: Erythroid response: hemoglobin (Hb) increase from baseline ≥ 1.5 g/dL (baseline < 11 g/dL), neutrophil response: increase from baseline $\geq 100\%$ and increase $> 0.5 \times 10^9/L$ (baseline $< 1 \times 10^9/L$), platelet response: increase from baseline $\geq 30 \times 10^9/L$ (baseline $< 100 \times 10^9/L$) according to modified IWG 2006 criteria |
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to 24 weeks | |

| End point values | Erythropoietin alpha | Deferasirox + Erythropoietin alpha | | |
|--------------------------------------|----------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 11 | | |
| Units: participants | | | | |
| arithmetic mean (standard deviation) | 1.8 (± 0.21) | 2.1 (± 0.61) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of hematologic improvement in patients randomized to EPO+DFX and EPO alone, within 24 weeks of treatment (Full Analysis Set)

| | |
|------------------------|---|
| End point title | Summary of hematologic improvement in patients randomized to EPO+DFX and EPO alone, within 24 weeks of treatment (Full Analysis Set) |
| End point description: | Percentage of participants achieving an hematologic improvement defined as: neutrophil improvement: increase from baseline $>0.5 \times 10^9/L$ (baseline = $1.0 \times 10^9/L$), platelet improvement: increase from baseline $\geq 30 \times 10^9/L$ (baseline = $100 \times 10^9/L$), hemoglobin improvement: Hb increase from baseline $\geq 1 \text{ g/dL}$ (baseline $<11 \text{ g/dL}$) |
| End point type | Secondary |
| End point timeframe: | Baseline up to 24 weeks |

| End point values | Erythropoietin alpha | Deferasirox + Erythropoietin alpha | | |
|-----------------------------------|----------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 11 | | |
| Units: percentage of participants | | | | |
| Hematologic improvement | 100 | 46 | | |
| Neutropil improvement | 67 | 80 | | |
| Platelet improvement | 50 | 80 | | |
| Hemoglobin improvement | 67 | 60 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in hemoglobin values up to 24 weeks

| | |
|------------------------|--|
| End point title | Absolute change in hemoglobin values up to 24 weeks |
| End point description: | Absolute change in hemoglobin values for patients showing improvement: Hemoglobin improvement Hb increase from baseline $\geq 1 \text{ g/dL}$ (baseline $<11 \text{ g/dL}$) |
| End point type | Secondary |

End point timeframe:
Baseline up to 24 weeks

| End point values | Erythropoietin alpha | Deferasirox + Erythropoietin alpha | | |
|--------------------------------------|----------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 3 | | |
| Units: g/dL | | | | |
| arithmetic mean (standard deviation) | 1.3 (± 0.37) | 1.4 (± 0.55) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in platelets and neutrophil levels up to 24 weeks

| | |
|-----------------|---|
| End point title | Absolute change in platelets and neutrophil levels up to 24 weeks |
|-----------------|---|

End point description:

Absolute change in platelets and neutrophil levels for patients showing improvement: neutrophil improvement: increase from baseline $>0.5 \times 10^9/L$ (baseline = $1.0 \times 10^9/L$), platelet improvement: increase from baseline $\geq 30 \times 10^9/L$ (baseline = $100 \times 10^9/L$)

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

End point timeframe:

Baseline up to 24 weeks

| End point values | Erythropoietin alpha | Deferasirox + Erythropoietin alpha | | |
|--------------------------------------|----------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 11 | | |
| Units: $10^9/L$ | | | | |
| arithmetic mean (standard deviation) | | | | |
| Platelets n=6,4 | 58.7 (± 23.93) | 66.3 (± 22.74) | | |
| Neutrophils n=8,4 | 1.2 (± 1.16) | 2.4 (± 1.57) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of erythroid response in participants randomized to EPO alone at baseline and switched to EPO+DFX after 12 weeks of treatment (Full Analysis Set)

| | |
|--|---|
| End point title | Summary of erythroid response in participants randomized to EPO alone at baseline and switched to EPO+DFX after 12 weeks of treatment (Full Analysis Set) |
| End point description: Erythroid response: hemoglobin increase from baseline ≥ 1.5 g/dL (baseline <11 g/dL). Percentages are based on N. Confidence intervals are calculated using Clopper-Pearson method. Hemoglobin value is at time of first response | |
| End point type | Secondary |
| End point timeframe: Week 13 up to 24 weeks | |

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | EPO+DFX (12 weeks) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: participants | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of erythroid response within 24 weeks in participants randomized to EPO at baseline and not switched to EPO+DFX after 12 weeks of treatment (Full Analysis set)

| | |
|--|---|
| End point title | Summary of erythroid response within 24 weeks in participants randomized to EPO at baseline and not switched to EPO+DFX after 12 weeks of treatment (Full Analysis set) |
| End point description: Erythroid response: hemoglobin increase from baseline ≥ 1.5 g/dL (baseline <11 g/dL). Percentages are based on N. Confidence intervals are calculated using Clopper-Pearson method. Hemoglobin value is at time of first response | |
| End point type | Secondary |
| End point timeframe: baseline up to 24 weeks | |

| | | | | |
|-----------------------------------|----------------------|--|--|--|
| End point values | EPO (24 weeks) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 71.4 (47.8 to 100.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in serum ferritin up to 24 weeks for erythropoietin alpha arm (Full Analysis Set)

| | |
|-----------------|--|
| End point title | Absolute change in serum ferritin up to 24 weeks for erythropoietin alpha arm (Full Analysis Set) ^[1] |
|-----------------|--|

End point description:

Absolute change in serum ferritin from baseline

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

End point timeframe:

Baseline up to 24 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was done

| End point values | Erythropoietin alpha | | | |
|-------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 7 | | | |
| Units: ng/mL | | | | |
| median (full range (min-max)) | | | | |
| Responders - Week 5 n=5 | -98.5 (-323 to -73.5) | | | |
| Responders - Week 9 n=5 | -79.0 (-381 to 54.0) | | | |
| Responders - Week 13 n=4 | 24.8 (-179 to 104) | | | |
| Responders - Week 17 n=4 | -57.8 (-140 to 258.0) | | | |
| Responders - Week 21 n=2 | -39.8 (-44.0 to -35.5) | | | |
| Non-responders - Week 5 n=2 | -352 (-523 to -182) | | | |
| Non-responders - Week 9 n=2 | -189 (-572 to 194.5) | | | |
| Non-responders - Week 13 n=2 | -44.5 (-621 to 531.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in serum ferritin up to 24 weeks for Deferasirox + erythropoietin alpha arm (Full Analysis Set)

| | |
|-----------------|--|
| End point title | Absolute change in serum ferritin up to 24 weeks for Deferasirox + erythropoietin alpha arm (Full Analysis Set) ^[2] |
|-----------------|--|

End point description:

Absolute change in serum ferritin from baseline

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

End point timeframe:

Baseline up to 24 weeks

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was done

| End point values | Deferasirox + Erythropoietin alpha | | | |
|-------------------------------|------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: ng/mL | | | | |
| median (full range (min-max)) | | | | |
| Responders - Week 5 n=3 | -82.5 (-243 to 1068) | | | |
| Responders - Week 9 n=3 | -139 (-292 to 702.0) | | | |
| Responders - Week 13 n=3 | -121 (-338 to 0.0) | | | |
| Responders - Week 17 n=3 | 16.5 (-143 to 722.0) | | | |
| Responders - Week 21 n=3 | -95.5 (-189 to 173.0) | | | |
| Non-responders - Week 5 n=7 | -38.0 (-315 to 111.0) | | | |
| Non-responders - Week 9 n=4 | -144 (-435 to 1.0) | | | |
| Non-responders - Week 13 n=3 | -155 (-225 to -127) | | | |
| Non-responders - Week 17 n=2 | -123 (-154 to -91.0) | | | |
| Non-responders - Week 21 n=1 | -291 (-291 to -291) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in serum ferritin up to 24 weeks for EPO+DFX at 12 weeks arm (Full Analysis Set)

| | |
|---|--|
| End point title | Absolute change in serum ferritin up to 24 weeks for EPO+DFX at 12 weeks arm (Full Analysis Set) |
| End point description: | |
| Absolute change in serum ferritin from baseline | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline up 24 weeks | |

| End point values | EPO+DFX at 12 | | | |
|-------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: ng/mL | | | | |
| median (full range (min-max)) | | | | |
| Responders - Week 5 n=1 | -116 (-116 to -116) | | | |
| Responders - Week 9 n=1 | -136 (-136 to -136) | | | |
| Responders - Week 13 n=1 | 59.5 (59.5 to 59.5) | | | |
| Responders - Week 17 n=1 | 74.5 (74.5 to 74.5) | | | |
| Non-responders - Week 5 n=4 | -68.3 (-144 to 221.3) | | | |
| Non-responders - Week 9 n=3 | -148 (-319 to 321.3) | | | |
| Non-responders - Week 13 n=4 | 220.4 (-228 to 635.3) | | | |
| Non-responders - Week 17 n=2 | -16.6 (-28.5 to -4.7) | | | |
| Non-responders - Week 21 n=3 | -10.5 (-463 to 367.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in hemoglobin (Hb) from baseline for erythropoietin alpha arm (Full Analysis Set)

| | |
|-----------------|--|
| End point title | Absolute change in hemoglobin (Hb) from baseline for erythropoietin alpha arm (Full Analysis Set) ^[3] |
|-----------------|--|

End point description:

This analysis included patients randomized either to EPO or DFX+EPO at baseline as well as patients who did not have erythroid response at week 12 in the EPO group and switched to combination therapy. The time-course of Hb and its absolute changes from baseline was summarized by descriptive statistics by visit and erythroid response. Patients randomized to EPO and not switching after 12 weeks to EPO+DFX, would consist of only responders.

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

End point timeframe:

Baseline up to 24 weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analysis was done

| End point values | Erythropoietin alpha | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 7 | | | |
| Units: g/dL | | | | |
| median (full range (min-max)) | | | | |
| Responders - Week 5 n=5 | 1.5 (1.1 to 3.2) | | | |
| Responders - Week 9 n=5 | 1.9 (1.3 to 4.4) | | | |

| | | | | |
|------------------------------|---------------------|--|--|--|
| Responders - Week 13 n=4 | 1.7 (1.5 to 3.4) | | | |
| Responders - Week 17 n=4 | 1.6 (-0.3 to 1.8) | | | |
| Responders - Week 21 n=3 | 0.8 (-0.7 to 1.8) | | | |
| Non-responders - Week 5 n=2 | -0.9 (-1.7 to -0.1) | | | |
| Non-responders - Week 9 n=2 | -1.7 (-2.0 to -1.4) | | | |
| Non-responders - Week 13 n=2 | -2.5 (-2.8 to -2.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in hemoglobin (Hb) from baseline for Deferasirox + erythropoietin alpha arm (Full Analysis Set)

| | |
|-----------------|--|
| End point title | Absolute change in hemoglobin (Hb) from baseline for Deferasirox + erythropoietin alpha arm (Full Analysis Set) ^[4] |
|-----------------|--|

End point description:

This analysis included patients randomized either to EPO or DFX+EPO at baseline as well as patients who did not have erythroid response at week 12 in the EPO group and switched to combination therapy. The time-course of Hb and its absolute changes from baseline was summarized by descriptive statistics by visit and erythroid response. Patients randomized to EPO and not switching after 12 weeks to EPO+DFX would consist of only responders.

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

End point timeframe:

Baseline up to 24 weeks

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was done

| End point values | Deferasirox + Erythropoietin alpha | | | |
|-------------------------------|------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: g/dL | | | | |
| median (full range (min-max)) | | | | |
| Responders - Week 5 n= n=3 | 0.7 (0.6 to 2.0) | | | |
| Responders - Week 9 n=3 | 1.6 (1.0 to 2.6) | | | |
| Responders - Week 13 n=3 | 2.9 (2.8 to 3.0) | | | |
| Responders - Week 17 n=3 | 2.4 (0.6 to 3.0) | | | |
| Responders - Week 21 n=3 | 1.7 (-1.3 to 2.4) | | | |
| Non-responders - Week 5 n=7 | -0.1 (-2.3 to 0.1) | | | |
| Non-responders - Week 9 n=4 | 0.0 (-0.8 to 0.5) | | | |
| Non-responders - Week 13 n=3 | 0.2 (0.1 to 0.5) | | | |
| Non-responders - Week 17 n=1 | -0.5 (-0.5 to 0.5) | | | |

| | | | | |
|------------------------------|--------------------|--|--|--|
| Non-responders - Week 21 n=1 | -0.6 (-0.6 to 0.6) | | | |
|------------------------------|--------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in hemoglobin (Hb) from baseline for EPO+DFX at 12 weeks arm (Full Analysis Set)

| | |
|--|--|
| End point title | Absolute change in hemoglobin (Hb) from baseline for EPO+DFX at 12 weeks arm (Full Analysis Set) |
| End point description: This analysis included patients randomized either to EPO or DFX+EPO at baseline as well as patients who did not have erythroid response at week 12 in the EPO group and switched to combination therapy. The time-course of Hb and its absolute changes from baseline was summarized by descriptive statistics by visit and erythroid response. Patients randomized to EPO and not switching after 12 weeks to EPO+DFX would consist of only responders. | |
| End point type | Secondary |
| End point timeframe: Baseline up to 24 weeks | |

| End point values | EPO+DFX at 12 weeks | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: g/dL | | | | |
| median (full range (min-max)) | | | | |
| Responders - Week 5 n= n=1 | 1.2 (1.2 to 1.2) | | | |
| Responders - Week 9 n=1 | 1.8 (1.8 to 1.8) | | | |
| Responders - Week 13 n=1 | 0.7 (0.7 to 0.7) | | | |
| Responders - Week 17 n=1 | -0.6 (-0.6 to -0.6) | | | |
| Non-responders - Week 5 n=4 | 0.3 (-0.5 to 0.6) | | | |
| Non-responders - Week 9 n=3 | 0.5 (-0.4 to 0.8) | | | |
| Non-responders - Week 13 n=3 | 0.4 (0.2 to 1.0) | | | |
| Non-responders - Week 17 n=3 | 0.0 (-0.1 to 0.9) | | | |
| Non-responders - Week 21 n=3 | 0.0 (-0.7 to 0.8) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit up to approximately 24 weeks

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | EPO a |
|-----------------------|-------|

Reporting group description:

EPO alpha

| | |
|-----------------------|------------|
| Reporting group title | EPO+DFX DT |
|-----------------------|------------|

Reporting group description:

EPO+DFX DT

| | |
|-----------------------|-------------|
| Reporting group title | EPO+DFX FCT |
|-----------------------|-------------|

Reporting group description:

EPO+DFX FCT

| | |
|-----------------------|------------------------------------|
| Reporting group title | Switched to DFX+EPO after 12 weeks |
|-----------------------|------------------------------------|

Reporting group description:

Switched to DFX+EPO after 12 weeks

| Serious adverse events | EPO a | EPO+DFX DT | EPO+DFX FCT |
|---|----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 10 (10.00%) | 1 / 1 (100.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |

| | | | |
|--|----------------|----------------|-----------------|
| Tachycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 1 / 1 (100.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Diverticulitis | | | |

| | | | |
|---|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 1 / 1 (100.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|------------------------------------|--|--|
| Serious adverse events | Switched to DFX+EPO after 12 weeks | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | EPO a | EPO+DFX DT | EPO+DFX FCT |
|---|----------------|-------------------|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 10 / 10 (100.00%) | 1 / 1 (100.00%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |

| | | | |
|--|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 10 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gravitational oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Anal fissure subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 10 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 1 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 3 / 10 (30.00%) 3 | 1 / 1 (100.00%) 1 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 1 (0.00%) 0 |
| Inguinal hernia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Hepatobiliary disorders Hepatic function abnormal subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 1 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 1 (0.00%) 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes zoster | | | |

| | | | |
|------------------------------------|----------------|-----------------|---------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 10 (10.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 10 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|--|--|--|
| Non-serious adverse events | Switched to DFX+EPO after 12 weeks | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 5 (100.00%) | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 1 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 1 | | |
| Blood creatinine increased | | | |

| | | | |
|---|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Blood uric acid increased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Heart rate increased subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Gravitational oedema subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Injection site bruising subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 2 | | |
| Ear and labyrinth disorders | | | |

| | | | |
|--|---------------------|--|--|
| Vertigo subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 2 | | |
| Anal fissure subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Constipation subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Inguinal hernia subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Toothache subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Hepatobiliary disorders Hepatic function abnormal subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Alopecia | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash maculo-papular</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p> <p>0 / 5 (0.00%)</p> <p>0</p> | | |
| <p>Renal and urinary disorders</p> <p>Renal impairment</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 5 (20.00%)</p> <p>1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neck pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p> <p>1 / 5 (20.00%)</p> <p>1</p> <p>0 / 5 (0.00%)</p> <p>0</p> | | |
| <p>Infections and infestations</p> <p>Conjunctivitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastroenteritis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Herpes zoster</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hordeolum</p> | <p>0 / 5 (0.00%)</p> <p>0</p> <p>0 / 5 (0.00%)</p> <p>0</p> <p>0 / 5 (0.00%)</p> <p>0</p> | | |

| | | | |
|------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences (all) | 0 | | |
| Localised infection | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | | |
| occurrences (all) | 2 | | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 2 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 26 November 2013 | <ul style="list-style-type: none">- Change inclusion criteria of lower hemoglobin (Hb) threshold value of > 6 g/dl to ≥ 8 g/dL- Clarify that patients with performance status (PS) > 2 must not be enrolled in the study- Clarify that patients with need of transfusion must not be enrolled in the study and they must be withdrawn from the study anytime when transfusion as rescue therapy is needed- Delete prophylactic hydrocortisone to prevent transfusion reaction from the list of allowed concurrent therapy- Standardize term for trial design from exploratory to pilot- Addition of inflammatory biomarkers IL-1, IL-6 and IFN-γ |
| 14 November 2014 | <ul style="list-style-type: none">- Changed the inclusion criterion of upper limit of documented diagnosis of MDS disease from < 2 years to < 3 years- Changed the inclusion criterion of lower limit of creatinine clearance from ≥ 60 mL/min to above the concentration limit in locally approved prescribing information- Inclusion of patients with stable steroid treatment for other chronic medical conditions than adrenal failure was allowed- Excluded patients with hepatic impairment fulfilling criteria of Child-Pugh Class B or C- Guidance on treating patients with Stevens-Johnson syndrome- Guidance on concomitant administration of deferasirox with CYP1A2 substrates that have a narrow therapeutic index and the concomitant use of bile acid sequestrates- Introduction of Per Protocol set, grouping for safety analyses and supportive analyses- Revision of analysis sets of primary and secondary objectives |
| 06 August 2015 | <ul style="list-style-type: none">- Addition of DFX FCT as optional study medication- Patients with creatinine clearance between 40 mL/min and < 60 mL/min, who do not present with additional risk factors that may impair renal function, might have been eligible at the discretion of the investigator.- Changed the inclusion criterion of upper limit of Serum Ferritin from 1,000 ng/mL to 1,500 ng/mL (Values within 10% difference above 1500 ng/mL or 10% difference below 300 ng/mL might have been accepted at discretion of the investigator if the patient represented the investigational population. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study did not meet the original enrollment objective of 60 patients and was terminated without extending enrollment past original planned LPFV of 31-Oct-2016.

Notes:

