



Clinical trial results:

A Double-blind, Double-dummy, Parallel, Active-controlled, Randomized and Multi-center Trial to Investigate Efficacy and Safety in Subjects With Iron Deficiency Anemia for Ferrous (II) Glycine Sulphate Complex Versus Polyferose Capsules Therapy

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-004380-20 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 14 November 2013 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 23 July 2016 |
| First version publication date | 24 May 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Removing duplicate dataset information after EudraCT return |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | SP0986 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01425463 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sanol GmbH |
| Sponsor organisation address | Alfred-Nobel-Str. 10, Monheim, Germany, 40789 |
| Public contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 1515, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 1515, clinicaltrials@ucb.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? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 19 March 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 November 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary study objective was to show non-inferiority of efficacy of Ferro Sanol Duodenal as test drug compared to Niferex as reference product after 12 weeks therapy in subjects with manifest iron deficiency anemia.

Protection of trial subjects:

Not applicable

Background therapy:

Not applicable

Evidence for comparator:

Comparison against other approved standard therapy for iron supplementation in Iron Deficiency Anemia (IDA).

| | |
|---|---------------|
| Actual start date of recruitment | 29 March 2011 |
| 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 | China: 256 |
| Worldwide total number of subjects | 256 |
| EEA total number of subjects | 0 |

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) | 1 |
| Adults (18-64 years) | 254 |
| From 65 to 84 years | 1 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

This multicenter study started to enroll subjects in March 2011 in order to end up with 16 centers in China with enrolled subjects.

Pre-assignment

Screening details:

Participant Flow refers to the Randomized Set (RS). The RS includes all subjects who have a randomization number recorded on the Case Report Form (CRF).

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

| | |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ferrous (II) Glycine Sulphate Complex |

Arm description:

Ferrous (II) Glycine Sulphate Complex treatment with 567.7 mg three times a day (t.i.d.) for 12 weeks plus Placebo to Polyferose. Ferrous (II) Glycine Sulphate Complex: Oral dose of 567.7 mg Ferrous (II) Glycine Sulphate Complex three times a day (t.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water. Placebo to Polyferose: Administered orally with water.

| | |
|--|--------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ferro Sanol® Duodenal |
| Investigational medicinal product code | |
| Other name | Ferrous (II) Glycine Sulfate Complex |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Oral dose of 567.7 mg Ferrous (II) Glycine Sulphate Complex three times a day (t.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water.

| | |
|------------------|------------|
| Arm title | Polyferose |
|------------------|------------|

Arm description:

Polyferose treatment with 150 mg twice daily (b.i.d) for 12 weeks plus Placebo to Ferrous (II) Glycine Sulphate Complex. Polyferose: Oral dose of 150 mg Polyferose Capsules twice daily (b.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water. Placebo to Ferrous (II) Glycine Sulphate Complex: Administered orally with water.

| | |
|--|-----------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Niferex |
| Investigational medicinal product code | |
| Other name | Polysaccharide Iron Complex |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Oral dose of 150 mg Polyferose Capsules twice daily (b.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water.

| Number of subjects in period 1 | Ferrous (II) Glycine Sulphate Complex | Polyferose |
|---------------------------------------|--|-------------------|
| Started | 130 | 126 |
| Safety Set | 126 | 122 |
| Full Analysis Set | 122 | 116 |
| Completed | 106 | 102 |
| Not completed | 24 | 24 |
| Consent withdrawn by subject | 7 | 5 |
| Unknown Reason | 4 | 7 |
| Non-Fatal, Serious AE(s) | 1 | 2 |
| Lost to follow-up | 5 | 2 |
| Non-Fatal, Non-Serious AE(s) | 4 | 5 |
| Protocol deviation | 2 | 2 |
| Lack of efficacy | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---------------------------------------|
| Reporting group title | Ferrous (II) Glycine Sulphate Complex |
| Reporting group description: | |
| Ferrous (II) Glycine Sulphate Complex treatment with 567.7 mg three times a day (t.i.d.) for 12 weeks plus Placebo to Polyferose. Ferrous (II) Glycine Sulphate Complex: Oral dose of 567.7 mg Ferrous (II) Glycine Sulphate Complex three times a day (t.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water. Placebo to Polyferose: Administered orally with water. | |
| Reporting group title | Polyferose |
| Reporting group description: | |
| Polyferose treatment with 150 mg twice daily (b.i.d) for 12 weeks plus Placebo to Ferrous (II) Glycine Sulphate Complex. Polyferose: Oral dose of 150 mg Polyferose Capsules twice daily (b.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water. Placebo to Ferrous (II) Glycine Sulphate Complex: Administered orally with water. | |

| Reporting group values | Ferrous (II) Glycine Sulphate Complex | Polyferose | Total |
|---------------------------|---------------------------------------|------------|-------|
| Number of subjects | 130 | 126 | 256 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | 0 | 1 | 1 |
| Adults (18-64 years) | 129 | 125 | 254 |
| From 65-84 years | 1 | 0 | 1 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 37.6 | 37.5 | |
| standard deviation | ± 8.7 | ± 7.9 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Male | 0 | 1 | 1 |
| Female | 130 | 125 | 255 |
| Weight | | | |
| Units: kilogram (kg) | | | |
| arithmetic mean | 58.3 | 58.1 | |
| standard deviation | ± 7.6 | ± 7.5 | - |
| Height | | | |
| Units: centimeter (cm) | | | |
| arithmetic mean | 161.2 | 161.2 | |
| standard deviation | ± 4.3 | ± 4.5 | - |

End points

End points reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Ferrous (II) Glycine Sulphate Complex |
|-----------------------|---------------------------------------|

Reporting group description:

Ferrous (II) Glycine Sulphate Complex treatment with 567.7 mg three times a day (t.i.d.) for 12 weeks plus Placebo to Polyferose. Ferrous (II) Glycine Sulphate Complex: Oral dose of 567.7 mg Ferrous (II) Glycine Sulphate Complex three times a day (t.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water. Placebo to Polyferose: Administered orally with water.

| | |
|-----------------------|------------|
| Reporting group title | Polyferose |
|-----------------------|------------|

Reporting group description:

Polyferose treatment with 150 mg twice daily (b.i.d) for 12 weeks plus Placebo to Ferrous (II) Glycine Sulphate Complex. Polyferose: Oral dose of 150 mg Polyferose Capsules twice daily (b.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water. Placebo to Ferrous (II) Glycine Sulphate Complex: Administered orally with water.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | PPS (Ferrous treated subjects) |
|----------------------------|--------------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Per-Protocol Set (PPS) is defined as a subset of the Full Analysis Set, excluding all subjects with protocol deviations considered important for the subjects' validity concerning the efficacy analysis.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | PPS (Polyferose treated subjects) |
|----------------------------|-----------------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Per-Protocol Set (PPS) is defined as a subset of the Full Analysis Set, excluding all subjects with protocol deviations considered important for the subjects' validity concerning the efficacy analysis.

Primary: Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 12

| | |
|-----------------|---|
| End point title | Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 12 |
|-----------------|---|

End point description:

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

End point timeframe:

From Baseline to Week 12

| End point values | PPS (Ferrous treated subjects) | PPS (Polyferose treated subjects) | | |
|--------------------------------------|--------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 95 | 92 | | |
| Units: gramm per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | 31.47 (± 23.77) | 31.92 (± 21.82) | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

| | |
|-------------------|--|
| Comparison groups | PPS (Ferrous treated subjects) v PPS (Polyferose treated |
|-------------------|--|

| | |
|---|--------------------------------|
| | subjects) |
| Number of subjects included in analysis | 187 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | LS-Mean of ANCOVA |
| Point estimate | -2.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.47 |
| upper limit | 4.09 |

Notes:

[1] - Noninferiority of the investigational drug (Ferrous (II) Glycine Sulphate Complex) to the reference drug (Polyferose) was concluded if the lower limit of the two-sided 95 % confidence interval was greater than -7.0 g/L.

Secondary: Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 2

| | |
|-----------------|--|
| End point title | Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 2 |
|-----------------|--|

End point description:

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

End point timeframe:

From Baseline to Week 2

| End point values | PPS (Ferrous treated subjects) | PPS (Polyferose treated subjects) | | |
|--------------------------------------|--------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 93 | 91 | | |
| Units: gramm per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | 12.29 (± 13.6) | 12.79 (± 13.13) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 4

| | |
|-----------------|--|
| End point title | Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 4 |
|-----------------|--|

End point description:

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

End point timeframe:

From Baseline to Week 4

| End point values | PPS (Ferrous treated subjects) | PPS (Polyferose treated subjects) | | |
|--------------------------------------|--------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 95 | 92 | | |
| Units: gramm per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | 20.37 (± 19.63) | 20.16 (± 17.46) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 8

| | |
|-----------------|--|
| End point title | Change in Hemoglobin (Hb) from Baseline (Week 0) to Week 8 |
|-----------------|--|

End point description:

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

End point timeframe:

From Baseline to Week 8

| End point values | PPS (Ferrous treated subjects) | PPS (Polyferose treated subjects) | | |
|--------------------------------------|--------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 95 | 92 | | |
| Units: gramm per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | 26.57 (± 22.67) | 28.33 (± 20.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responders at Week 12

| | |
|-----------------|-------------------------------------|
| End point title | Percentage of Responders at Week 12 |
|-----------------|-------------------------------------|

End point description:

Responders are defined as having an increment of Hemoglobin (Hb) > 15 g/L and post-treatment Hb > 120 g/L (male) or > 110 g/L (female) at Visit 6 (Week 12).

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

End point timeframe:

End of Treatment Period (Week 12)

| End point values | PPS (Ferrous treated subjects) | PPS (Polyferose treated subjects) | | |
|-----------------------------------|--------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 95 | 92 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 71.6 | 80.4 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected up to 14 weeks from Baseline to the Safety Follow-Up Visit.

Adverse event reporting additional description:

Adverse Events refer to the Safety Set (SS). SS represents all subjects included in the study who took at least one dose of study medication and have at least one safety evaluation after that.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Ferrous (II) Glycine Sulphate Complex |
|-----------------------|---------------------------------------|

Reporting group description:

Ferrous (II) Glycine Sulphate Complex treatment with 567.7 mg three times a day (t.i.d.) for 12 weeks plus Placebo to Polyferose.

Ferrous (II) Glycine Sulphate Complex: Oral dose of 567.7 mg Ferrous (II) Glycine Sulphate Complex three times a day (t.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water.

Placebo to Polyferose: Administered orally with water.

| | |
|-----------------------|------------|
| Reporting group title | Polyferose |
|-----------------------|------------|

Reporting group description:

Polyferose treatment with 150 mg twice daily (b.i.d) for 12 weeks plus Placebo to Ferrous (II) Glycine Sulphate Complex.

Polyferose: Oral dose of 150 mg Polyferose Capsules twice daily (b.i.d) for 12 weeks (equivalent to 300 mg iron element per day for 12 weeks). Administered orally with water.

Placebo to Ferrous (II) Glycine Sulphate Complex: Administered orally with water.

| Serious adverse events | Ferrous (II) Glycine Sulphate Complex | Polyferose | |
|---|---------------------------------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 126 (2.38%) | 3 / 122 (2.46%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 126 (0.00%) | 1 / 122 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Abortion induced | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 126 (1.59%) | 1 / 122 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 126 (0.00%) | 1 / 122 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Measles | | | |
| subjects affected / exposed | 1 / 126 (0.79%) | 0 / 122 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Ferrous (II) Glycine Sulphate Complex | Polyferose | |
|---|---------------------------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 22 / 126 (17.46%) | 25 / 122 (20.49%) | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 7 / 126 (5.56%) | 5 / 122 (4.10%) | |
| occurrences (all) | 9 | 6 | |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 126 (7.14%) | 11 / 122 (9.02%) | |
| occurrences (all) | 10 | 14 | |
| Melaena | | | |
| subjects affected / exposed | 6 / 126 (4.76%) | 8 / 122 (6.56%) | |
| occurrences (all) | 6 | 9 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 126 (2.38%) | 7 / 122 (5.74%) | |
| occurrences (all) | 3 | 7 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|---|--------------|
| 07 June 2011 | Investigational medicinal product (IMP) recall, due to stability failure which lead to physical unblinding. | 04 June 2012 |

Notes:

Limitations and caveats

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

| |
|----------------|
| Not applicable |
|----------------|

Notes: