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	v1
This version publication date	08 July 2016
First version publication date	24 May 2015

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	Investigator, Assessor, Subject

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
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	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 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.

Serious adverse events	Polyferose	Ferrous (II) Glycine Sulphate Complex	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 122 (2.46%)	3 / 126 (2.38%)	
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	1 / 122 (0.82%)	0 / 126 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			

subjects affected / exposed	1 / 122 (0.82%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 122 (0.82%)	0 / 126 (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			
Measles			
subjects affected / exposed	0 / 122 (0.00%)	1 / 126 (0.79%)	
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	Polyferose	Ferrous (II) Glycine Sulphate Complex	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 122 (20.49%)	22 / 126 (17.46%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 122 (9.02%)	9 / 126 (7.14%)	
occurrences (all)	14	10	
Abdominal pain			
subjects affected / exposed	5 / 122 (4.10%)	7 / 126 (5.56%)	
occurrences (all)	6	9	
Melaena			
subjects affected / exposed	8 / 122 (6.56%)	6 / 126 (4.76%)	
occurrences (all)	9	6	
Nausea			
subjects affected / exposed	7 / 122 (5.74%)	3 / 126 (2.38%)	
occurrences (all)	7	3	

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: