

**Clinical trial results:**

A Phase IV, multi-centre, randomized, open label study to investigate the efficacy and safety of Floradix® mit Eisen and ferro sanol® duodenal mite 50 mg in pregnant women with diagnosed iron deficiency

Summary

EudraCT number	2010-018940-15
Trial protocol	DE
Global end of trial date	28 November 2013

Results information

Result version number	v1 (current)
This version publication date	13 August 2022
First version publication date	13 August 2022

Trial information**Trial identification**

Sponsor protocol code	FLDX-001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	SALUS Haus GmbH & Co. KG
Sponsor organisation address	Bahnhofstraße 24, Bruckmühl, Germany, 83052
Public contact	Dr. med. vet. Jana D'Alascio, Medical Consulting Dr. Schlichtinger GmbH Nußbaumstraße 10 80336 München Germany, 0049 89 673 7916,
Scientific contact	Dr. med. Claus A.Hanusch, Rotkreuzklinikum München - Frauenklinik Taxisstraße 3 80637 München Germany, 0049 89 157 06 620,

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	05 December 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To gather information on the efficacy and safety profile of a long-term treatment with Floradix® mit Eisen and to compare descriptively against a treatment with ferro sanol® duodenal mite 50mg

Protection of trial subjects:

none

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 October 2010
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	Germany: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

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)	26
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

4 sites should recruit a total of 40 randomized patients, i.e. female caucasians with mean gestation duration of 26 weeks.

Early termination of recruitment: A nearly 50% screening failure rate resulted in the fact that after 3 and a half year field phase only 26 patients could be randomised. The sponsor then decided to terminate recruitment.

Pre-assignment

Screening details:

Age (years): 32.8 +/- 5.6

Height (cm): 165.0 +/- 6.3

Weight (kg): 66.5 +/- 11.3

BMI (kg/m²): 24.4 +/- 3.9

Pre-assignment period milestones

Number of subjects started	49 ^[1]
Number of subjects completed	26

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failures: 23
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 49 patients were screened, 26 of them were randomized.

Period 1

Period 1 title	Randomization visit
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Floradix mit Eisen (baseline)
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Floradix mit Eisen
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for infusion
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Routes of administration	Oral use
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Dosage and administration details:

Oral intake of solution

Floradix mit Eisen: 3 x 15 ml per day

Arm title	Ferro sanol duodenal mite 50 mg (baseline)
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	ferro sanol duodenal mite 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Oral intake of capsule

1 capsule per day

Number of subjects in period 1	Floradix mit Eisen (baseline)	Ferro sanol duodenal mite 50 mg (baseline)
	Started	13
Completed	13	13

Period 2

Period 2 title	Treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Floradix mit Eisen
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Floradix mit Eisen
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for infusion
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Routes of administration	Oral use
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Dosage and administration details:

Oral intake of solution

Floradix mit Eisen: 3 x 15 ml per day

Arm title	Ferro sanol duodenal mite 50 mg
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Arm description: -

Arm type	multicentre, open label
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Investigational medicinal product name	Ferro sanol duodenal mite 50 mg
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

Oral intake of capsule

1 capsule per day

Number of subjects in period 2	Floradix mit Eisen	Ferro sanol duodenal mite 50 mg
Started	13	13
Completed	11	11
Not completed	2	2
change of physician	1	-
Adverse event, non-fatal	1	-
Lack of efficacy	-	1
lack of compliance	-	1

Baseline characteristics

Reporting groups

Reporting group title	Floradix mit Eisen (baseline)
Reporting group description: -	
Reporting group title	Ferro sanol duodenal mite 50 mg (baseline)
Reporting group description: -	

Reporting group values	Floradix mit Eisen (baseline)	Ferro sanol duodenal mite 50 mg (baseline)	Total
Number of subjects	13	13	26
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	13	26
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	13	13	26
Male	0	0	0

End points

End points reporting groups

Reporting group title	Floradix mit Eisen (baseline)
Reporting group description: -	
Reporting group title	Ferro sanol duodenal mite 50 mg (baseline)
Reporting group description: -	
Reporting group title	Floradix mit Eisen
Reporting group description: -	
Reporting group title	Ferro sanol duodenal mite 50 mg
Reporting group description: -	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set included all enrolled patients who received at least 1 dose of study drug and had at least 1 valid post-baseline Hb measurement.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Set included all enrolled patients who received at least 1 dose of study drug.	

Primary: Baseline change of haemoglobin (Hb) measurements (w12 - w0)

End point title	Baseline change of haemoglobin (Hb) measurements (w12 - w0)
End point description: Values displayed here are the ones from study week12 compared to baseline w0. For Hb changes (vs. baseline) calculated for previous visits, please refer to attached document. For Hb values recorded for w14 and after birth, please also refer to attacher overview. Changes of Hb w14-w0 were not calculated due to low number of patients in each arm. Changes of Hb after birth-w0 were not calculated due to missing values for w14-w0.	
End point type	Primary
End point timeframe: Hb measurements were done prior to randomisation (visit 1, visit 2 (= baseline, i.e. week 0) and after 4, 6, 8, 10, 12, 14 weeks and at a last measurement 6 -8 weeks after birth.	

End point values	Floradix mit Eisen	Floradix mit Eisen (baseline)	Ferro sanol duodenal mite 50 mg (baseline)	Ferro sanol duodenal mite 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	12	9
Units: Haemoglobin (g/dl)				
arithmetic mean (standard deviation)	1.72 (± 1.35)	0 (± 0)	0 (± 0)	1.27 (± 0.84)

Statistical analyses

Statistical analysis title	Baseline difference w12-w0, Floradix mit Eisen
Statistical analysis description: Changes of Hb values at w12 (11 patients) compared to w0 (12 patients).	
Comparison groups	Floradix mit Eisen v Floradix mit Eisen (baseline)
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.0018
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	2.63
Variability estimate	Standard deviation
Dispersion value	1.35

Notes:

[1] - Superiority W12 vs. w0.

The present study was designed as a prospective exploratory study to demonstrate by means of a trend analysis whether:

- the efficacy of both iron preparations is satisfactory in this patient population and whether there are hints for potential differences in the efficacy profile

Statistical analysis title	Baseline difference w12-w0, Ferro sanol duodenal
Statistical analysis description: Changes of Hb values at w12 (9 patients) compared to w0 (12 patients).	
Comparison groups	Ferro sanol duodenal mite 50 mg v Ferro sanol duodenal mite 50 mg (baseline)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.0019
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.91
Variability estimate	Standard deviation
Dispersion value	0.84

Notes:

[2] - Superiority W12 vs. w0.

The present study was designed as a prospective exploratory study to demonstrate by means of a trend analysis whether:

- the efficacy of both iron preparations is satisfactory in this patient population and whether there are hints for potential differences in the efficacy profile

Statistical analysis title	Mean group difference w12-w0
Comparison groups	Floradix mit Eisen v Ferro sanol duodenal mite 50 mg
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.374
Method	t-test f unequal var. (Satterthwaite)
Parameter estimate	Mean difference (net)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	1.54
Variability estimate	Standard deviation

Notes:

[3] - The primary aim of this was to establish whether a solution is preferable regarding therapeutic effect as compared to a solid oral formulation.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring during the clinical study have to be recorded in source documents and CRF. In case an adverse event becomes known to the investigator within 2 weeks after the end of treatment it has still to be reported by the investigator.

Adverse event reporting additional description:

All adverse events occurring during the clinical study have to be recorded in the source documents and the CRF. Where they are not based on diagnostic data, such events should be evaluated in standardized fashion through the investigator's neutral question: "Have you noticed any changes or complaints since your last visit?"

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Floradix mit Eisen
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Reporting group description:

In the study protocol, an adverse event (AE) was defined as any adverse change from the patients` s condition at screening, whether or not considered to be related to the investigational product.

Reporting group title	Ferro sanol duodenal mite 50 mg
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Reporting group description: -

Serious adverse events	Floradix mit Eisen	Ferro sanol duodenal mite 50 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)	1 / 13 (7.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Postpartum haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature labour			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical incompetence			

subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (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: 1.7 %

Non-serious adverse events	Floradix mit Eisen	Ferro sanol duodenal mite 50 mg
Total subjects affected by non-serious adverse events		
subjects affected / exposed	9 / 13 (69.23%)	11 / 13 (84.62%)
Vascular disorders		
Vascular disorder		
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Surgical and medical procedures		
Surgical and medicinal procedures		
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	1
Pregnancy, puerperium and perinatal conditions		
Pregnancy etc.		
subjects affected / exposed	3 / 13 (23.08%)	2 / 13 (15.38%)
occurrences (all)	4	2
General disorders and administration site conditions		
General disorders		
subjects affected / exposed	1 / 13 (7.69%)	2 / 13 (15.38%)
occurrences (all)	1	2
Reproductive system and breast disorders		
Reproductive tract disorder		
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	1	1
Respiratory, thoracic and mediastinal disorders		
Respiratory disorder etc.		
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	1	1
Injury, poisoning and procedural complications		

Injury etc. subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Nervous system disorders Nervous system disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Gastrointestinal disorders Gastrointestinal disorders e.g. Gastroenteritis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 13 (30.77%) 4	
Skin and subcutaneous tissue disorders Oedema etc. subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Musculoskeletal and connective tissue disorders Musculoskeletal disorder etc. subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Infections and infestations Infections and infestations e.g. Bacterial abdominal infection; subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 4	3 / 13 (23.08%) 4	
Metabolism and nutrition disorders Metabolic disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2010	Amendment 1 (Protocol v3.0), dated 29 March 2010, was the initially approved version by BfArM and CEC, based on which the study was initiated. The amendment newly introduced the U1 and U2 data from the new-born and a final blood draw at study end.
30 July 2010	Amendment 2 (Protocol v4.0), dated 30 July 2010, was introduced to widen the inclusion time window and allow to include patients from gestation week 20 to 28 (both inclusive).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported