Clinical trial results:
Ferumoxytol Compared to Iron Sucrose Trial (FIRST): A Randomized, Multicenter, Trial of Ferumoxytol Compared to Iron Sucrose for the Treatment of Iron Deficiency Anemia in Adult Subjects with Chronic Kidney Disease

Summary

EudraCT number	2009-015630-30
Trial protocol	BE DE GB
Global end of trial date	19 July 2011

Results information

Result version number	v1 (current)
This version publication date	21 November 2018
First version publication date	21 November 2018

Trial information

Trial identification

Sponsor protocol code	FER-CKD-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01052779
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AMAG Pharmaceuticals, Inc.
Sponsor organisation address	1100 Winter Street, Waltham, United States, 02451
Public contact	Medical Information, AMAG Pharmaceuticals, Inc., +1 877-411-2510, amag@druginfo.com
Scientific contact	Medical Information, AMAG Pharmaceuticals, Inc., +1 877-411-2510, amag@druginfo.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	19 April 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and efficacy of intravenous (IV) ferumoxytol compared to IV iron sucrose for the treatment of iron deficiency anemia (IDA) in participants with chronic kidney disease (CKD).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	United States: 97
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	162
EEA total number of subjects	44

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)	82
From 65 to 84 years	75
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

There was a 2-week Screening Period (Day -14 to -1).

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

None (Open Label)

Arms

Are arms mutually exclusive?	Yes
Arm title	Ferumoxytol

Arm description:

Participants received an IV injection of ferumoxytol (510 milligrams [mg], 17 milliliters [mL]) on Day 1 (Baseline). This was followed by a second injection of ferumoxytol (510 mg, 17 mL) 5±3 days later for a total cumulative dose of 1.02 grams (g).

Arm type	Experimental
Investigational medicinal product name	Ferumoxytol
Investigational medicinal product code	
Other name	Feraheme
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Each 20 mL single-use vial contained 17 mL of ferumoxytol that consisted of iron at a concentration of 30 mg Fe/mL, and mannitol, at a concentration of 44 mg/mL, in a black to reddish brown sterile, aqueous, colloidal, isotonic solution.

Both hemodialysis and nondialysis participants received 2 IV injections of ferumoxytol 510 mg (17 mL), the first on Day 1 and the second 5±3 days later, for a total cumulative dose of 1.02 g.

Arm title	Iron Sucrose

Arm description:

Participants received iron sucrose based on hemodialysis status. Participants on hemodialysis received either slow IV injection or IV drip infusion of 100 mg of iron sucrose on Day 1 (Baseline) and at the following 9 consecutive hemodialysis sessions for a total cumulative dose of 1.0 g.

Participants not on dialysis received either slow IV injection or IV drip infusion of 200 mg of iron sucrose on Day 1 (Baseline) and at 4 subsequent visits on nonconsecutive days over a 14-day period for a total cumulative dose of 1.0 g.

Arm type	Active comparator
Investigational medicinal product name	Iron Sucrose
Investigational medicinal product code	
Other name	Venofer
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Each mL contained 20 mg of elemental iron as iron sucrose in water for injection. The 5 mL single-use vial contained 100 mg of iron per 5 mL. The drug product contained approximately 30% sucrose (300 mg/mL). The product contained no preservatives.

Participants received iron sucrose as a slow IV injection or IV infusion based on dialysis status:

• Hemodialysis participants received 100 mg iron sucrose on Day 1 and at the following 9 consecutive hemodialysis sessions over approximately 3 weeks for a total cumulative dose of 1.0 g.

• Nondialysis participants received 200 mg iron sucrose at Day 1 and at 4 other nonconsecutive visits over a 14-day (±2 days) period for a total cumulative dose of 1.0 g.

Number of subjects in period 1	Ferumoxytol	Iron Sucrose
Started	80	82
Received at Least 1 Dose of Study Drug	80	81
Completed	75	73
Not completed	5	9
Other-Surgery	-	2
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	4
Other-Protocol Violation	1	1
Other-Missed Week 5 Visit	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Ferumoxytol
Reporting group description:	
Participants received an IV injection of ferumoxytol (510 milligrams [mg], 17 milliliters [mL]) on Day 1 (Baseline). This was followed by a second injection of ferumoxytol (510 mg, 17 mL) 5±3 days later for a total cumulative dose of 1.02 grams (g).	
Reporting group title	Iron Sucrose
Reporting group description:	
Participants received iron sucrose based on hemodialysis status. Participants on hemodialysis received either slow IV injection or IV drip infusion of 100 mg of iron sucrose on Day 1 (Baseline) and at the following 9 consecutive hemodialysis sessions for a total cumulative dose of 1.0 g. Participants not on dialysis received either slow IV injection or IV drip infusion of 200 mg of iron sucrose on Day 1 (Baseline) and at 4 subsequent visits on nonconsecutive days over a 14-day period for a total cumulative dose of 1.0 g.	

Reporting group values	Ferumoxytol	Iron Sucrose	Total
Number of subjects	80	82	162
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)	39	43	82
From 65-84 years	39	36	75
85 years and over	2	3	5
Age continuous Units: years			
arithmetic mean	61.9	63.3	
standard deviation	± 15.00	± 15.16	-
Gender categorical Units: Subjects			
Female	41	39	80
Male	39	43	82
Dialysis Status Units: Subjects			
Hemodialysis	34	36	70
Nondialysis	46	46	92

End points

End points reporting groups

Reporting group title	Ferumoxytol

Reporting group description:

Participants received an IV injection of ferumoxytol (510 milligrams [mg], 17 milliliters [mL]) on Day 1 (Baseline). This was followed by a second injection of ferumoxytol (510 mg, 17 mL) 5±3 days later for a total cumulative dose of 1.02 grams (g).

Reporting group title	Iron Sucrose

Reporting group description:

Participants received iron sucrose based on hemodialysis status. Participants on hemodialysis received either slow IV injection or IV drip infusion of 100 mg of iron sucrose on Day 1 (Baseline) and at the following 9 consecutive hemodialysis sessions for a total cumulative dose of 1.0 g.

Participants not on dialysis received either slow IV injection or IV drip infusion of 200 mg of iron sucrose on Day 1 (Baseline) and at 4 subsequent visits on nonconsecutive days over a 14-day period for a total cumulative dose of 1.0 g.

Subject analysis set title	Intent-to-Treat (ITT) Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Any randomized participant who had any exposure to study drug (IV ferumoxytol or IV iron sucrose).

Primary: Mean Change In Hemoglobin From Baseline (Day 1) To Week 5

End point title	Mean Change In Hemoglobin From Baseline (Day 1) To Week 5

End point description:

The change in hemoglobin from Baseline (Day 1) to Week 5 was calculated for each participant as:

Hemoglobin Change = Hemoglobin (Week 5) – Hemoglobin (Baseline)

The least squares mean, with standard error, is reported as g/deciliter (dL). Baseline hemoglobin for each participant was the Day 1 hemoglobin value (prior to injection of the study drug). The screening hemoglobin value was used for any participants with missing Baseline (Day 1) hemoglobin. Analysis used last observed carried forward (LOCF) imputation methods for missing values for the ITT population. Sensitivity analyses were performed without imputation for missing data and with the Markov chain Monte Carlo method.

End point type	Primary

End point timeframe:

Baseline (Day 1), Week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80[1]	82[2]		
Units: g/dL				
least squares mean (standard error)				
With LOCF Imputation	0.84 (± 0.14)	0.74 (± 0.14)		
Without Imputation (Sensitivity Analysis)	0.89 (± 0.15)	0.80 (± 0.15)		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Analysis 1 For Mean Change In Hemoglobin

Statistical analysis description:

With LOCF Imputation: The p-value and two-sided 95% confidence interval (CI) for the treatment difference in mean change in hemoglobin from Baseline (Day 1) to Week 5 were generated based on an analysis of variance (ANOVA) model adjusted for baseline hemoglobin level and hemodialysis status.

Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.515 [4]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.41

Notes:

[3] - Non-inferiority was concluded if the lower bound of the 95% CI was ≥-0.5 g/dL and superiority if the lower bound was ≥0 g/dL.
[4] - The p-value for hemoglobin change from Baseline (Day 1) was adjusted for baseline hemoglobin level and hemodialysis status.

Statistical analysis title	Analysis 2 For Mean Change In Hemoglobin

Statistical analysis description:

Without Imputation (Sensitivity Analysis): The p-value and two-sided 95% CI for the treatment difference in mean change in hemoglobin from Baseline (Day 1) to Week 5 were generated based on an ANOVA model adjusted for baseline hemoglobin level and hemodialysis status.

Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	= 0.587 [6]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.41

Notes:

[5] - Non-inferiority was concluded if the lower bound of the 95% CI was ≥-0.5 g/dL and superiority if the lower bound was ≥0 g/dL.
[6] - The p-value for hemoglobin change from Baseline (Day 1) was adjusted for baseline hemoglobin level and hemodialysis status.

Primary: Percentage Of Participants With An Increase In Hemoglobin ≥1.0 g/dL From Day 1 (Baseline) To Week 5

End point title	Percentage Of Participants With An Increase In Hemoglobin ≥1.0 g/dL From Day 1 (Baseline) To Week 5[7]

End point description:

The percentage of participants who achieved a ≥1.0 g/dL increase in hemoglobin at any time from Baseline (Day 1) up to Week 5 by treatment group is presented by study visit. Baseline hemoglobin for each participant was the Day 1 hemoglobin value (prior to injection of the study drug).

End point type	Primary

End point timeframe:

Baseline (Day 1) and up to Week 5

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Quantitative statistical analysis (for example, a p-value) was not performed for this endpoint. Only descriptive statistics are included (percentage).

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80[8]	82[9]		
Units: percent				
number (not applicable)				
Week 2	25	13.41		
Week 3	40	24.39		
Week 4	46.25	37.80		
Week 5	50	41.46		

Notes:

[8] - ITT Population

[9] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period during which adverse events were reported was defined from the time a participant signed the informed consent until the last study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Ferumoxytol

Reporting group description:

Participants received an IV injection of ferumoxytol (510 milligrams [mg], 17 milliliters [mL]) on Day 1 (Baseline). This was followed by a second injection of ferumoxytol (510 mg, 17 mL) 5±3 days later for a total cumulative dose of 1.02 grams (g).

Reporting group title	Iron Sucrose

Reporting group description:

Participants received iron sucrose based on hemodialysis status. Participants on hemodialysis received either slow IV injection or IV drip infusion of 100 mg of iron sucrose on Day 1 (Baseline) and at the following 9 consecutive hemodialysis sessions for a total cumulative dose of 1.0 g.

Participants not on dialysis received either slow IV injection or IV drip infusion of 200 mg of iron sucrose on Day 1 (Baseline) and at 4 subsequent visits on nonconsecutive days over a 14-day period for a total cumulative dose of 1.0 g.

Serious adverse events	Ferumoxytol	Iron Sucrose	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 80 (8.75%)	6 / 82 (7.32%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic haemorrhage			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			

subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal adhesions			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous graft site infection			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
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: 1 %

Non-serious adverse events	Ferumoxytol	Iron Sucrose	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 80 (43.75%)	50 / 82 (60.98%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Hypotension			
subjects affected / exposed	2 / 80 (2.50%)	8 / 82 (9.76%)	
occurrences (all)	3	17	
Poor venous access			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Catheter site erythema			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Chills			

subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Device leakage			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	2 / 80 (2.50%)	6 / 82 (7.32%)	
occurrences (all)	2	6	
Fatigue			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Feeling hot			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Injection site haematoma			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Injection site haemorrhage			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	1 / 80 (1.25%)	2 / 82 (2.44%)	
occurrences (all)	1	2	
Medical device complication			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Tenderness			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Thrombosis in device			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Social circumstances			

Treatment noncompliance			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	3 / 80 (3.75%)	0 / 82 (0.00%)	
occurrences (all)	3	0	
Dyspnoea			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Rales			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	2	
Breath sounds abnormal			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			

subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Weight increased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Burns first degree			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Humerus fracture			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Procedural hypertension			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Procedural hypotension			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	7	0	
Scratch			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Sunburn			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Vascular graft thrombosis			

subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 80 (1.25%)	2 / 82 (2.44%)	
occurrences (all)	1	2	
Dysgeusia			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Facial palsy			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	3 / 80 (3.75%)	2 / 82 (2.44%)	
occurrences (all)	3	2	
Paraesthesia			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Parosmia			
subjects affected / exposed	0 / 80 (0.00%)	4 / 82 (4.88%)	
occurrences (all)	0	31	
Unresponsive to stimuli			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	2 / 80 (2.50%)	1 / 82 (1.22%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Eye disorders			

Lacrimation increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 80 (2.50%)	3 / 82 (3.66%)	
occurrences (all)	2	3	
Diarrhoea			
subjects affected / exposed	2 / 80 (2.50%)	1 / 82 (1.22%)	
occurrences (all)	2	2	
Nausea			
subjects affected / exposed	6 / 80 (7.50%)	3 / 82 (3.66%)	
occurrences (all)	6	3	
Tooth disorder			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 80 (1.25%)	2 / 82 (2.44%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Cold sweat			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Ecchymosis			

subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Ingrowing nail			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Skin haemorrhage			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Flank pain			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Limb discomfort			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	4 / 80 (5.00%)	6 / 82 (7.32%)	
occurrences (all)	4	12	
Myalgia			
subjects affected / exposed	0 / 80 (0.00%)	2 / 82 (2.44%)	
occurrences (all)	0	2	
Neck pain			

subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 80 (1.25%)	2 / 82 (2.44%)	
occurrences (all)	1	2	
Synovial cyst			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 80 (3.75%)	2 / 82 (2.44%)	
occurrences (all)	3	2	
Sinusitis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Staphylococcal abscess			
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Urethritis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	3 / 80 (3.75%)	5 / 82 (6.10%)	
occurrences (all)	4	6	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 80 (1.25%)	3 / 82 (3.66%)	
occurrences (all)	1	3	
Hyperglycaemia			
subjects affected / exposed	1 / 80 (1.25%)	1 / 82 (1.22%)	
occurrences (all)	1	1	
Hyperkalaemia			
subjects affected / exposed	3 / 80 (3.75%)	0 / 82 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			

subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	2 / 80 (2.50%)	3 / 82 (3.66%)	
occurrences (all)	2	4	
Vitamin D deficiency			
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2010	• To ensure participant safety as well as comply with all the label requirements across countries, additional information regarding the adequate medical care needed to treat those participants who may experience a hypersensitivity reaction following administration of study drug has been added. • Bicarbonate and magnesium have been added to the list of serum chemistry analytes.
01 November 2010	• To examine the effects of ferumoxytol and iron sucrose on biomarkers of oxidative stress and tubular damage, an optional substudy has been added. This substudy will require participating participants to give additional blood samples (between 5 and 7 draws) of 8 mL each, before and after study drug administration. Since the addition of this substudy will require no change to the inclusion/exclusion criteria or to the conduct of the main study, the integrity of FER-CKD-201 will be maintained. Participants who choose to enroll in the substudy will sign an additional consent form. • The protocol has been updated to provide clarification regarding the timing of vital signs (measured from initiation of dosing) and the timing around the collection of adverse events (60 minutes from completion of dosing). These two changes were already captured in an administrative letter.

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.

None reported

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27462400

http://www.ncbi.nlm.nih.gov/pubmed/24458078