Clinical trial results:
A Phase III, Randomized, Open-label, Active-Controlled Trial Comparing Ferumoxytol with Iron Sucrose for the Treatment of Iron Deficiency Anemia

Summary

EudraCT number	2010-018961-50
Trial protocol	LV HU FR LT DE PL GB ES IT
Global end of trial date	09 November 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	AMAG-FER-IDA-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01114204
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	09 November 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2011
Global end of trial reached?	Yes
Global end of trial date	09 November 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to evaluate the efficacy and safety of intravenous (IV) ferumoxytol compared to IV iron sucrose for the treatment of iron deficiency anemia (IDA).

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	10 August 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	Poland: 62
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 95
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Latvia: 88
Country: Number of subjects enrolled	Lithuania: 90
Country: Number of subjects enrolled	Romania: 31
Country: Number of subjects enrolled	South Africa: 64
Country: Number of subjects enrolled	Ukraine: 100
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Korea, Republic of: 46
Worldwide total number of subjects	605
EEA total number of subjects	386

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)	501
From 65 to 84 years	99
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

The study was open to enrollment for adult participants with IDA, defined as hemoglobin <10.0 grams (g)/deciliter (dL) and transferrin saturation (TSAT) <20%, and a history of unsatisfactory oral iron therapy or in whom oral iron could not be used.

Pre-assignment

Screening details:

Participants were screened for inclusion in this study up to 2 weeks (14 days) prior to the start of dosing with study drug (either ferumoxytol or iron sucrose).

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:

This is an open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ferumoxytol

Arm description:

Participants received a total of 2 doses of IV ferumoxytol 510 milligrams (mg) (17 milliliters [mL]). The first IV 510 mg dose was administered on Day 1 (Baseline) and second dose 2 to 8 (5±3) days after the first dose, for a total cumulative dose of 1.02 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:

IV injection of ferumoxytol, 510 mg (17 mL) at Baseline (Day 1) with a second dose 2 to 8 (5±3) days after Dose 1, for a total cumulative dose of 1.02 g

Arm title	Iron Sucrose

Arm description:

Participants received an IV injection or infusion of iron sucrose 200 mg (10 mL) on Day 1 (Baseline) and on 4 other non-consecutive days over a 14-day period, for a total cumulative dose of 1.0 g. Participants receiving their first ever exposure to IV iron sucrose, received a test dose on Day 1 prior to receiving the remainder of the first dose, as prescribed in the package insert for some countries.

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

Dosage and administration details:

IV injection or infusion of iron sucrose, 200 mg on Day 1 and at 4 other visits on non-consecutive days over a 14-day period, for a total cumulative dose of 1.0 g

Number of subjects in period 1	Ferumoxytol	Iron Sucrose
Started	406	199
Received at Least 1 Dose of Study Drug	406	199
Completed	385	191
Not completed	21	8
Consent withdrawn by subject	10	6
Other-Medical Monitor Request	1	-
Adverse event, non-fatal	3	2
Death	1	-
Other-Participant Request	2	-
Other-Personal Reasons	2	-
Other-Protocol Violation	1	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Ferumoxytol
Reporting group description:	
Participants received a total of 2 doses of IV ferumoxytol 510 milligrams (mg) (17 milliliters [mL]). The first IV 510 mg dose was administered on Day 1 (Baseline) and second dose 2 to 8 (5±3) days after the first dose, for a total cumulative dose of 1.02 g.	
Reporting group title	Iron Sucrose
Reporting group description:	
Participants received an IV injection or infusion of iron sucrose 200 mg (10 mL) on Day 1 (Baseline) and on 4 other non-consecutive days over a 14-day period, for a total cumulative dose of 1.0 g. Participants receiving their first ever exposure to IV iron sucrose, received a test dose on Day 1 prior to receiving the remainder of the first dose, as prescribed in the package insert for some countries.	

Reporting group values	Ferumoxytol	Iron Sucrose	Total
Number of subjects	406	199	605
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)	338	163	501
From 65-84 years	64	35	99
85 years and over	4	1	5
Age continuous Units: years			
arithmetic mean	48.0	48.9	
standard deviation	± 14.89	± 14.66	-
Gender categorical Units: Subjects			
Female	342	160	502
Male	64	39	103

End points

End points reporting groups

Reporting group title	Ferumoxytol

Reporting group description:

Participants received a total of 2 doses of IV ferumoxytol 510 milligrams (mg) (17 milliliters [mL]). The first IV 510 mg dose was administered on Day 1 (Baseline) and second dose 2 to 8 (5±3) days after the first dose, for a total cumulative dose of 1.02 g.

Reporting group title	Iron Sucrose

Reporting group description:

Participants received an IV injection or infusion of iron sucrose 200 mg (10 mL) on Day 1 (Baseline) and on 4 other non-consecutive days over a 14-day period, for a total cumulative dose of 1.0 g. Participants receiving their first ever exposure to IV iron sucrose, received a test dose on Day 1 prior to receiving the remainder of the first dose, as prescribed in the package insert for some countries.

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 (ferumoxytol or iron sucrose) and was based upon randomized treatment assignment.

Primary: Participants Who Achieved A ≥2.0 g/dL Increase In Hemoglobin At Any Time From Baseline To Week 5

End point title	Participants Who Achieved A ≥2.0 g/dL Increase In Hemoglobin At Any Time From Baseline To Week 5

End point description:

Participants who achieved a ≥2.0 g/dL increase in hemoglobin at any time from Baseline up to Week 5 are presented. Increase in hemoglobin at any time from Baseline up to Week 5 was calculated for each participant based on:
Hemoglobin Change = Hemoglobin (Week X) – Hemoglobin (Baseline), where Week X was any post-Baseline visit up to and including Week 5.
Baseline was defined as the Day 1 value (prior to injection of study drug). The screening or most recent value prior to Day 1 was used for any participant with missing Day 1 information. Participants with no post-Baseline hemoglobin values were classified as not achieving a ≥2.0 g/dL increase.
Statistical analysis was performed for data up to Week 5 only.

End point type	Primary

End point timeframe:

Baseline (Day 1) through Week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	406[1]	199[2]		
Units: Count of Participants				
Up to Week 3	291	117		
Up to Week 4	327	145		
Up to Week 5	341	162		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Participants who achieved a ≥2.0 g/dL increase in hemoglobin from Baseline up to Week 5 were analysed. Statistical comparison was performed for data up to Week 5 only.
Baseline was defined as the Day 1 value (prior to injection of study drug). The screening or most recent value prior to Day 1 was used for any participant with missing Day 1 information.

Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	605
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.2833 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.89
upper limit	9.06
Variability estimate	Standard deviation

Notes:

[3] - The 95% confidence interval (CI) was calculated using the large sample assumption. The pre-defined non-inferiority margin for testing the difference between treatment groups was -15%.
[4] - The treatment difference (ferumoxytol - iron sucrose) was expressed as a percentage.

Secondary: Mean Change In Hemoglobin From Baseline To Week 5

End point title	Mean Change In Hemoglobin From Baseline To Week 5

End point description:

Mean change in hemoglobin from Baseline to Week 5 was calculated for each participant as: Hemoglobin Change = Hemoglobin (Week 5) – Hemoglobin (Baseline).
Baseline was defined as the Day 1 value (prior to injection of study drug). The screening or most recent value prior to Day 1 was used for any participant with missing Day 1 information. If the Week 5 hemoglobin value was missing, the change from Baseline was imputed to be zero.

End point type	Secondary

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	406[5]	199[6]		
Units: g/dL				
arithmetic mean (standard deviation)	2.9 (± 1.62)	2.7 (± 1.30)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Participants Achieving A Hemoglobin Level ≥12.0 g/dL At Any Time From Baseline To Week 5

End point title	Participants Achieving A Hemoglobin Level ≥12.0 g/dL At Any Time From Baseline To Week 5

End point description:

Participants who achieved a ≥12.0 g/dL hemoglobin level at any time from Baseline up to Week 5 are presented. Increase in hemoglobin at any time from Baseline up to Week 5 was calculated for each participant based on:
Hemoglobin Change = Hemoglobin (Week X) – Hemoglobin (Baseline), where Week X was any post-Baseline visit up to and including Week 5. Baseline was defined as the Day 1 value (prior to injection of study drug). The screening or most recent value prior to Day 1 was used for any participant with missing Day 1 information. Participants without any post-Baseline hemoglobin values were treated as non-responders.

End point type	Secondary

End point timeframe:

Baseline (Day 1) through Week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	406[7]	199[8]		
Units: Count of Participants				
Up to Week 3	123	33		
Up to Week 4	210	67		
Up to Week 5	271	96		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change In TSAT From Baseline To Week 5

End point title	Mean Change In TSAT From Baseline To Week 5

End point description:

Mean change in TSAT from Baseline to Week 5 was calculated for each participant as: TSAT Change = TSAT (Week 5) – TSAT (Baseline).
Baseline was defined as the Day 1 value (prior to injection of study drug). The screening or most recent value prior to Day 1 was used for any participant with missing Day 1 information. If the Week 5 TSAT value was missing, the change from Baseline was imputed to be zero.

End point type	Secondary

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	406[9]	199[10]		
Units: Percentage of saturation				
arithmetic mean (standard deviation)	15.7 (± 16.80)	11.9 (± 14.41)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change In Functional Assessment Of Chronic Illness Therapy (FACIT)-Fatigue Score From Baseline To Week 5

End point title	Mean Change In Functional Assessment Of Chronic Illness Therapy (FACIT)-Fatigue Score From Baseline To Week 5

End point description:

The FACIT-Fatigue questionnaire is a 13 item questionnaire designed and validated to specifically assess the presence and impact of treatment on fatigue and related symptoms, such as tiredness, on health-related quality of life in anemic participants with cancer. The questionnaire has 13 items, each measured on a 4-point Likert scale. Scoring ranges from 0 (the most fatigued) to 52 (the least fatigued) points, with higher scores representing better functioning or less fatigue.
Mean change in FACIT-Fatigue Score from Baseline to Week 5 was calculated for each participant as: FACIT-Fatigue Score Change = FACIT-Fatigue Score (Week 5) – FACIT-Fatigue Score (Baseline). Baseline was defined as the Day 1 value (prior to first dose of study drug).The screening or most recent value prior to Day 1 was used for any participant with missing Day 1 information. If the Week 5 FACIT-Fatigue Score value was missing, the change from Baseline was imputed to be zero.

End point type	Secondary

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	399[11]	198[12]		
Units: Units on a Scale				
arithmetic mean (standard deviation)	13.1 (± 11.78)	12.4 (± 11.22)		

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Hemoglobin Increase Of ≥2.0 g/dL Or Hemoglobin Value Of ≥12.0 g/dL From Baseline

End point title	Time To Hemoglobin Increase Of ≥2.0 g/dL Or Hemoglobin Value Of ≥12.0 g/dL From Baseline

End point description:

The time to hemoglobin increase of ≥2.0 g/dL or hemoglobin value of ≥12.0 g/dL was defined as the days from Baseline (Day 1) to the first time the participant had an increase in hemoglobin of ≥2.0 g/dL

or hemoglobin value of ≥12.0 g/dL, and was calculated using a Kaplan-Meier curve. Participants who did not have a hemoglobin increase of ≥2.0 g/dL or to a hemoglobin level ≥12.0 g/dL were censored at their last visit day. Participants without any post-Baseline study visits were not included.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	406[13]	199[14]		
Units: Days				
arithmetic mean (inter-quartile range (Q1-Q3))	23.1 (15.0 to 24.0)	25.2 (21.0 to 30.0)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (after study drug administration) to Week 5 (End of Treatment)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Ferumoxytol

Reporting group description:

Participants received a total of 2 doses of IV ferumoxytol 510 mg (17 mL). The first IV 510 mg dose was administered on Day 1 (Baseline) and second dose 2 to 8 (5±3) days after the first dose, for a total cumulative dose of 1.02 g.

Reporting group title	Iron Sucrose

Reporting group description:

Participants received an IV injection or infusion of iron sucrose 200 mg (10 mL) on Day 1 (Baseline) and on 4 other non-consecutive days over a 14-day period, for a total cumulative dose of 1.0 g. Participants receiving their first ever exposure to IV iron sucrose, received a test dose on Day 1 prior to receiving the remainder of the first dose, as prescribed in the package insert for some countries.

Serious adverse events	Ferumoxytol	Iron Sucrose	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 406 (4.19%)	5 / 199 (2.51%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 406 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			
subjects affected / exposed	0 / 406 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tumour haemorrhage			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed[1]	1 / 342 (0.29%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 406 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed[2]	2 / 342 (0.58%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Road traffic accident			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 406 (0.25%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nausea			

subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (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			
Bartholin’s abscess			
subjects affected / exposed	0 / 406 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	0 / 406 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viraemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Only female participants in both arms were exposed to this adverse event.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Only female participants in both arms were exposed to this adverse event.

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	95 / 406 (23.40%)	69 / 199 (34.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 406 (0.99%)	3 / 199 (1.51%)	
occurrences (all)	4	3	
Hypotension			
subjects affected / exposed	1 / 406 (0.25%)	2 / 199 (1.01%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	9 / 406 (2.22%)	2 / 199 (1.01%)	
occurrences (all)	10	2	
Chills			
subjects affected / exposed	0 / 406 (0.00%)	4 / 199 (2.01%)	
occurrences (all)	0	4	
Fatigue			

subjects affected / exposed	3 / 406 (0.74%)	2 / 199 (1.01%)	
occurrences (all)	3	2	
Feeling hot			
subjects affected / exposed	2 / 406 (0.49%)	2 / 199 (1.01%)	
occurrences (all)	2	2	
Injection site pain			
subjects affected / exposed	0 / 406 (0.00%)	2 / 199 (1.01%)	
occurrences (all)	0	3	
Oedema peripheral			
subjects affected / exposed	3 / 406 (0.74%)	2 / 199 (1.01%)	
occurrences (all)	3	2	
Pyrexia			
subjects affected / exposed	2 / 406 (0.49%)	6 / 199 (3.02%)	
occurrences (all)	2	6	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	2 / 406 (0.49%)	2 / 199 (1.01%)	
occurrences (all)	2	2	
Hypersensitivity			
subjects affected / exposed	3 / 406 (0.74%)	2 / 199 (1.01%)	
occurrences (all)	3	2	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed[3]	3 / 342 (0.88%)	3 / 160 (1.88%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 406 (0.74%)	4 / 199 (2.01%)	
occurrences (all)	3	4	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 406 (0.99%)	4 / 199 (2.01%)	
occurrences (all)	5	4	
Aspartate aminotransferase increased			

subjects affected / exposed	3 / 406 (0.74%)	3 / 199 (1.51%)	
occurrences (all)	4	4	
Blood urea decreased			
subjects affected / exposed	2 / 406 (0.49%)	2 / 199 (1.01%)	
occurrences (all)	2	2	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 406 (0.74%)	2 / 199 (1.01%)	
occurrences (all)	3	3	
Lymphocyte count decreased			
subjects affected / exposed	4 / 406 (0.99%)	2 / 199 (1.01%)	
occurrences (all)	5	3	
White blood cell count decreased			
subjects affected / exposed	3 / 406 (0.74%)	3 / 199 (1.51%)	
occurrences (all)	3	3	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 406 (0.00%)	2 / 199 (1.01%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 406 (2.22%)	3 / 199 (1.51%)	
occurrences (all)	12	3	
Dysgeusia			
subjects affected / exposed	9 / 406 (2.22%)	13 / 199 (6.53%)	
occurrences (all)	9	34	
Headache			
subjects affected / exposed	19 / 406 (4.68%)	11 / 199 (5.53%)	
occurrences (all)	25	12	
Somnolence			
subjects affected / exposed	0 / 406 (0.00%)	2 / 199 (1.01%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 406 (0.25%)	2 / 199 (1.01%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	2 / 406 (0.49%)	2 / 199 (1.01%)	
occurrences (all)	2	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 406 (0.99%)	3 / 199 (1.51%)	
occurrences (all)	4	3	
Constipation			
subjects affected / exposed	4 / 406 (0.99%)	2 / 199 (1.01%)	
occurrences (all)	4	2	
Dry mouth			
subjects affected / exposed	6 / 406 (1.48%)	0 / 199 (0.00%)	
occurrences (all)	6	0	
Nausea			
subjects affected / exposed	11 / 406 (2.71%)	7 / 199 (3.52%)	
occurrences (all)	13	8	
Vomiting			
subjects affected / exposed	3 / 406 (0.74%)	4 / 199 (2.01%)	
occurrences (all)	4	4	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 406 (0.00%)	4 / 199 (2.01%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 406 (1.72%)	1 / 199 (0.50%)	
occurrences (all)	8	1	
Myalgia			
subjects affected / exposed	5 / 406 (1.23%)	0 / 199 (0.00%)	
occurrences (all)	6	0	
Pain in extremity			
subjects affected / exposed	1 / 406 (0.25%)	2 / 199 (1.01%)	
occurrences (all)	1	2	
Infections and infestations			
Cystitis			

subjects affected / exposed	1 / 406 (0.25%)	3 / 199 (1.51%)	
occurrences (all)	1	3	
Influenza			
subjects affected / exposed	4 / 406 (0.99%)	2 / 199 (1.01%)	
occurrences (all)	4	2	
Nasopharyngitis			
subjects affected / exposed	2 / 406 (0.49%)	2 / 199 (1.01%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	2 / 406 (0.49%)	3 / 199 (1.51%)	
occurrences (all)	2	3	

Notes:

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Only female participants in both arms were exposed to this adverse event.

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? 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/24639149