



Clinical trial results:

A Phase III, Randomized, Multicenter, Double-Blind, Safety Study of Ferumoxytol Compared to Ferric Carboxymaltose for the Treatment of Iron Deficiency Anemia (IDA)

Summary

EudraCT number	2016-000831-41
Trial protocol	HU LV LT PL
Global end of trial date	17 July 2017

Results information

Result version number	v1 (current)
This version publication date	29 November 2018
First version publication date	29 November 2018

Trial information

Trial identification

Sponsor protocol code	AMAG-FER-IDA-304
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02694978
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	16 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2017
Global end of trial reached?	Yes
Global end of trial date	17 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of 1.020 grams (g) of intravenous (IV) ferumoxytol compared to 1.500 g of IV ferric carboxymaltose (FCM).

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	29 February 2016
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: 34
Country: Number of subjects enrolled	Hungary: 34
Country: Number of subjects enrolled	Latvia: 122
Country: Number of subjects enrolled	Lithuania: 111
Country: Number of subjects enrolled	United States: 1661
Country: Number of subjects enrolled	Canada: 35
Worldwide total number of subjects	1997
EEA total number of subjects	301

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)	1343
From 65 to 84 years	553
85 years and over	101

Subject disposition

Recruitment

Recruitment details:

Participants with IDA, <12.0 g per deciliter (dL) for females and <14.0 g/dL for males within 60 days of dosing and transferrin saturation <20% or Ferritin ≤100 nanograms per milliliter (mL) within 60 days of dosing 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 either on or up to 30 days prior to the start of dosing with study drug (either ferumoxytol or FCM).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind ^[1]
Roles blinded	Subject, Data analyst, Carer, Assessor

Blinding implementation details:

This study was double blind with respect to treatment assignment; all study participants (study participant, study staff, including the physician, and all non-study individuals) with the exception of the test article preparer and the unblinded monitor were blinded to the treatment assigned to each participant.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ferumoxytol

Arm description:

Participants received an IV infusion of ferumoxytol 510 milligrams (mg) diluted (17 mL) in 233 mL 0.9% sodium chloride injection, United States Pharmacopeia (USP) (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.020 g.

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

Dosage and administration details:

Intravenous infusion of ferumoxytol 510 mg diluted (17 mL) in 233 mL 0.9% sodium chloride injection, USP (normal saline) to a final volume of 250 mL, over at least 15 minutes with a second dose 7-8 days after Dose 1, for a total cumulative dose of 1.020 g.

Arm title	Ferric Carboxymaltose (FCM)
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Arm description:

Participants received an IV infusion of FCM 750 mg diluted (15 mL) in 235 mL 0.9% sodium chloride injection, USP (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.500 g.

Arm type	Active comparator
Investigational medicinal product name	Ferric Carboxymaltose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of FCM 750 mg diluted (15 mL) in 235 mL 0.9% sodium chloride injection, USP (normal saline) to a final volume 250 mL, over at least 15 minutes with a second dose 7-8 days after Dose 1, for a total cumulative dose of 1.500 g.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: This study was double blind with respect to treatment assignment; all study participants (study participant, study staff, including the physician, and all non-study individuals) with the exception of the test article preparer and the unblinded monitor were blinded to the treatment assigned to each participant.

Number of subjects in period 1	Ferumoxytol	Ferric Carboxymaltose (FCM)
Started	997	1000
Received at Least 1 Dose of Study Drug	997	1000
Completed	935	948
Not completed	62	52
Adverse event, serious fatal	4	1
Consent withdrawn by subject	22	19
Other-Decision of Participant	6	1
Adverse event, non-fatal	10	9
Other-Unable To Be Reached	-	1
Other-Investigator's Decision	1	-
Other-Personal Reasons	3	3
Other-Protocol Noncompliant	2	1
Lost to follow-up	14	17

Baseline characteristics

Reporting groups

Reporting group title	Ferumoxytol
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Reporting group description:

Participants received an IV infusion of ferumoxytol 510 milligrams (mg) diluted (17 mL) in 233 mL 0.9% sodium chloride injection, United States Pharmacopeia (USP) (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.020 g.

Reporting group title	Ferric Carboxymaltose (FCM)
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Reporting group description:

Participants received an IV infusion of FCM 750 mg diluted (15 mL) in 235 mL 0.9% sodium chloride injection, USP (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.500 g.

Reporting group values	Ferumoxytol	Ferric Carboxymaltose (FCM)	Total
Number of subjects	997	1000	1997
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)	657	686	1343
From 65-84 years	286	267	553
85 years and over	54	47	101
Age continuous Units: years			
arithmetic mean	55.6	54.8	
standard deviation	± 17.30	± 17.02	-
Gender categorical Units: Subjects			
Female	743	776	1519
Male	254	224	478

End points

End points reporting groups

Reporting group title	Ferumoxytol
Reporting group description: Participants received an IV infusion of ferumoxytol 510 milligrams (mg) diluted (17 mL) in 233 mL 0.9% sodium chloride injection, United States Pharmacopeia (USP) (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.020 g.	
Reporting group title	Ferric Carboxymaltose (FCM)
Reporting group description: Participants received an IV infusion of FCM 750 mg diluted (15 mL) in 235 mL 0.9% sodium chloride injection, USP (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.500 g.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: Any randomized participant who received any amount of study drug. Treatment group was based on actual treatment.	
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, based on randomized treatment assignment.	

Primary: Participants With Treatment-Emergent (TE) Moderate To Severe Hypersensitivity Reactions (Rxns), Including Anaphylaxis, Or Moderate To Severe Hypotension

End point title	Participants With Treatment-Emergent (TE) Moderate To Severe Hypersensitivity Reactions (Rxns), Including Anaphylaxis, Or Moderate To Severe Hypotension
End point description: All IV iron formulations carry some risk of serious hypersensitivity reactions or anaphylaxis. Signs and symptoms potentially representing hypersensitivity were recorded and adjudicated by a blinded Clinical Events Committee (CEC). Hypotension is defined as a >30% drop in systolic blood pressure from baseline or decrease of >20 mmHg for systolic blood pressure. Statistical analysis was only performed on composite data. A summary of serious and all other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.	
End point type	Primary
End point timeframe: Day 1 (after first dosing) through Week 5	

End point values	Ferumoxytol	Ferric Carboxymaltose (FCM)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	997 ^[1]	1000 ^[2]		
Units: Participants				
Moderate hypersensitivity reaction	3	6		
Severe hypersensitivity reaction	1	0		
Anaphylaxis	0	0		
Moderate hypotension	2	1		

Severe hypotension	0	0		
Any TE moderate to severe hypersensitivity rxn	6	7		

Notes:

[1] - Safety Population

[2] - Safety Population

Statistical analyses

Statistical analysis title	Ferumoxytol/Ferric Carboxymaltose (FCM)
Statistical analysis description:	
Statistical analysis was only performed on composite reaction data (that is, the "Any TE moderate to severe hypersensitivity rxn" row in the data table)	
Comparison groups	Ferumoxytol v Ferric Carboxymaltose (FCM)
Number of subjects included in analysis	1997
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Wald large sample assumption
Parameter estimate	Treatment difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.61

Secondary: Participants With Moderate To Severe Hypersensitivity Reactions, Including Anaphylaxis, Serious Cardiovascular Events, And Death

End point title	Participants With Moderate To Severe Hypersensitivity Reactions, Including Anaphylaxis, Serious Cardiovascular Events, And Death
End point description:	
All IV iron formulations carry some risk of serious hypersensitivity reactions or anaphylaxis. Signs and symptoms potentially representing hypersensitivity were recorded and adjudicated by a blinded CEC. A summary of serious and all other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.	
End point type	Secondary
End point timeframe:	
Day 1 (after first dosing) through Week 5	

End point values	Ferumoxytol	Ferric Carboxymaltose (FCM)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	997 ^[3]	1000 ^[4]		
Units: Participants				
Moderate hypersensitivity reaction	3	6		
Severe hypersensitivity reaction	1	0		

Anaphylaxis	0	0		
Serious cardiovascular event	6	13		
Death	4	2		
Any moderate to severe hypersensitivity rxn	13	20		

Notes:

[3] - Safety Population

[4] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change In Hemoglobin From Baseline To Week 5

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

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Week 5

End point values	Ferumoxytol	Ferric Carboxymaltose (FCM)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	997 ^[5]	1000 ^[6]		
Units: g/dL				
arithmetic mean (standard deviation)				
Mean Change In Hemoglobin From Baseline To Week 5	1.38 (± 1.351)	1.63 (± 1.535)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change In Hemoglobin Per Gram Of Iron Administered From Baseline To Week 5

End point title	Mean Change In Hemoglobin Per Gram Of Iron Administered From Baseline To Week 5
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End point description:

Mean change in hemoglobin per g of iron administered from Baseline (Day 1) 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.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Week 5

End point values	Ferumoxytol	Ferric Carboxymaltose (FCM)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	997 ^[7]	1000 ^[8]		
Units: g/dL				
arithmetic mean (standard deviation)				
Mean Change In Hemoglobin Per Gram Of Iron Adminis	1.35 (± 1.353)	1.10 (± 1.050)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (after first dosing) through Week 5

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Ferumoxytol
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Reporting group description:

Participants received an IV infusion of ferumoxytol 510 mg diluted (17 mL) in 233 mL 0.9% sodium chloride injection, USP (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.020 g.

Reporting group title	Ferric Carboxymaltose (FCM)
-----------------------	-----------------------------

Reporting group description:

Participants received an IV infusion of FCM 750 mg diluted (15 mL) in 235 mL 0.9% sodium chloride injection, USP (normal saline) (final volume 250 mL) over at least 15 minutes with a second dose 7-8 days after the first dose, for a total cumulative dose of 1.500 g.

Serious adverse events	Ferumoxytol	Ferric Carboxymaltose (FCM)	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 997 (3.61%)	35 / 1000 (3.50%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 997 (0.10%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metastatic uterine cancer			
subjects affected / exposed ^[1]	0 / 743 (0.00%)	1 / 776 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed hepatocellular cholangiocarcinoma			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed ^[2]	1 / 743 (0.13%)	0 / 776 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed ^[3]	1 / 743 (0.13%)	0 / 776 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
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 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			

subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic ulcer			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Post-procedural haemorrhage subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris subjects affected / exposed	0 / 997 (0.00%)	2 / 1000 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation subjects affected / exposed	0 / 997 (0.00%)	2 / 1000 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure chronic subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive subjects affected / exposed	1 / 997 (0.10%)	3 / 1000 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiorespiratory arrest subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Left ventricular failure			

subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restless legs syndrome			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 997 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	3 / 997 (0.30%)	3 / 1000 (0.30%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia vitamin B12 deficiency			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	2 / 997 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 997 (0.10%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenal ulcer			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Hepatitis acute			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculopapular			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (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 kidney injury			
subjects affected / exposed	2 / 997 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (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			
Anal abscess			

subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 997 (0.10%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 997 (0.30%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 997 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 997 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis syndrome			

subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 997 (0.10%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 997 (0.10%)	0 / 1000 (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.

[3] - 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	Ferric Carboxymaltose (FCM)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	186 / 997 (18.66%)	245 / 1000 (24.50%)	
Vascular disorders			
Flushing			
subjects affected / exposed	11 / 997 (1.10%)	16 / 1000 (1.60%)	
occurrences (all)	11	16	
Hypertension			
subjects affected / exposed	7 / 997 (0.70%)	15 / 1000 (1.50%)	
occurrences (all)	7	15	

Nervous system disorders			
	Dizziness		
	subjects affected / exposed	25 / 997 (2.51%)	40 / 1000 (4.00%)
	occurrences (all)	31	40
	Headache		
	subjects affected / exposed	60 / 997 (6.02%)	82 / 1000 (8.20%)
	occurrences (all)	70	90
General disorders and administration site conditions			
	Chest discomfort		
	subjects affected / exposed	8 / 997 (0.80%)	11 / 1000 (1.10%)
	occurrences (all)	9	11
	Chest pain		
	subjects affected / exposed	10 / 997 (1.00%)	4 / 1000 (0.40%)
	occurrences (all)	10	4
	Fatigue		
	subjects affected / exposed	30 / 997 (3.01%)	36 / 1000 (3.60%)
	occurrences (all)	32	38
	Pyrexia		
	subjects affected / exposed	7 / 997 (0.70%)	22 / 1000 (2.20%)
	occurrences (all)	7	23
Gastrointestinal disorders			
	Abdominal pain		
	subjects affected / exposed	17 / 997 (1.71%)	21 / 1000 (2.10%)
	occurrences (all)	18	23
	Constipation		
	subjects affected / exposed	14 / 997 (1.40%)	13 / 1000 (1.30%)
	occurrences (all)	14	13
	Diarrhoea		
	subjects affected / exposed	29 / 997 (2.91%)	33 / 1000 (3.30%)
	occurrences (all)	29	37
	Nausea		
	subjects affected / exposed	35 / 997 (3.51%)	60 / 1000 (6.00%)
	occurrences (all)	39	69
	Vomiting		
	subjects affected / exposed	11 / 997 (1.10%)	13 / 1000 (1.30%)
	occurrences (all)	11	15

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 997 (1.50%)	13 / 1000 (1.30%)	
occurrences (all)	17	14	
Dyspnoea			
subjects affected / exposed	11 / 997 (1.10%)	18 / 1000 (1.80%)	
occurrences (all)	11	19	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	12 / 997 (1.20%)	11 / 1000 (1.10%)	
occurrences (all)	15	11	
Urticaria			
subjects affected / exposed	3 / 997 (0.30%)	13 / 1000 (1.30%)	
occurrences (all)	3	13	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 997 (1.40%)	12 / 1000 (1.20%)	
occurrences (all)	16	12	
Back pain			
subjects affected / exposed	19 / 997 (1.91%)	16 / 1000 (1.60%)	
occurrences (all)	23	16	
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	0 / 997 (0.00%)	18 / 1000 (1.80%)	
occurrences (all)	0	18	

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/29417614>

<http://www.ncbi.nlm.nih.gov/pubmed/29033620>