Clinical trial results:
A Phase III, Open-Label Extension Trial of the Safety and Efficacy of Ferumoxytol for the Episodic Treatment of Iron Deficiency Anemia

Summary

EudraCT number	2011-001866-17
Trial protocol	LV PL
Global end of trial date	23 April 2013

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-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01114217
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	24 September 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 April 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of ferumoxytol for the episodic 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	27 July 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: 48
Country: Number of subjects enrolled	India: 75
Country: Number of subjects enrolled	United States: 465
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Latvia: 24
Worldwide total number of subjects	634
EEA total number of subjects	46

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)	578
From 65 to 84 years	50
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Participants who previously enrolled in and completed AMAG-FER-IDA-301 [2011-001865-42], received any dose of study drug, and met the inclusion/exclusion criteria were eligible to enroll in this Extension Study AMAG-FER-IDA-303.

Pre-assignment

Screening details:

Participants enrolled in AMAG-FER-IDA-301, received any dose of study drug, completed study, and met the inclusion/exclusion criteria were eligible to enroll in Extension Study, AMAG-FER-IDA-303. Participants could be screened for eligibility and be enrolled in AMAG-FER-IDA-303 at the AMAG-FER-IDA-301 Week 5 visit or up to 2 weeks after that visit.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Received Ferumoxytol in IDA-303

Arm description:

Participants received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42]. Participants enrolled in AMAG-FER-IDA-303 who were found to have persistent or recurrent IDA, defined as hemoglobin <11.0 grams per deciliter (g/dL) and transferrin saturation (TSAT) <20% at any monthly evaluation visit (with the exception of the Study Termination visit), began a 5-week Treatment Period (TP) and received a total of 2 doses of ferumoxytol 510 milligrams (mg) intravenously (IV). The first IV 510 mg dose was administered on TP Day 1 (Baseline) and second dose 2 to 8 (5±3) days after Dose 1, for a total cumulative dose of 1.02 grams (g).

Arm type	Experimental
Investigational medicinal product name	Ferumoxytol in IDA-303
Investigational medicinal product code	
Other name	Feraheme
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The first IV 510 mg dose was administered on TP Day 1 (Baseline) and second dose 2 to 8 (5±3) days after Dose 1, for a total cumulative dose of 1.02 g.

Arm title	Did Not Receive Ferumoxytol in IDA-303

Arm description:

Participants who received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42] and did not receive ferumoxytol during AMAG-FER-IDA-303.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Received Ferumoxytol in IDA-303	Did Not Receive Ferumoxytol in IDA-303
Started	337	297
Received at Least 1 Dose of Ferumoxytol	337	0 [1]
Completed	262	199
Not completed	75	98
Other - Withdrawal by Subject	1	1
Other - Lost to Follow-up	1	-
Other - Clerical Error	3	-
Other - Site stopped communicating	2	-
Other - Physician Decision	1	1
Consent withdrawn by subject	21	28
Other - Protocol Violation	1	3
Other - Lack of Efficacy	1	-
Adverse event, non-fatal	5	3
Other - Sponsor decision	10	12
Other - Study Termination	-	1
Other - Pregnancy	2	4
Other - Early Termination	6	10
Other - Procedure	1	1
Lost to follow-up	17	33
Other - Non-Compliance	2	-
Other - Study Withdrawn	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: No investigational medicinal product was assigned in this arm.

Baseline characteristics

Reporting groups	
Reporting group title	Received Ferumoxytol in IDA-303
Reporting group description:	
Participants received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42]. Participants enrolled in AMAG-FER-IDA-303 who were found to have persistent or recurrent IDA, defined as hemoglobin <11.0 grams per deciliter (g/dL) and transferrin saturation (TSAT) <20% at any monthly evaluation visit (with the exception of the Study Termination visit), began a 5-week Treatment Period (TP) and received a total of 2 doses of ferumoxytol 510 milligrams (mg) intravenously (IV). The first IV 510 mg dose was administered on TP Day 1 (Baseline) and second dose 2 to 8 (5±3) days after Dose 1, for a total cumulative dose of 1.02 grams (g).	
Reporting group title	Did Not Receive Ferumoxytol in IDA-303
Reporting group description:	
Participants who received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42] and did not receive ferumoxytol during AMAG-FER-IDA-303.	

Reporting group values	Received Ferumoxytol in IDA-303	Did Not Receive Ferumoxytol in IDA-303	Total
Number of subjects	337	297	634
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)	304	274	578
From 65-84 years	29	21	50
85 years and over	4	2	6
Age continuous Units: years			
arithmetic mean	46.0	43.8	
standard deviation	± 13.33	± 13.26	-
Gender categorical Units: Subjects			
Female	304	269	573
Male	33	28	61

End points

End points reporting groups

Reporting group title	Received Ferumoxytol in IDA-303

Reporting group description:

Participants received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42]. Participants enrolled in AMAG-FER-IDA-303 who were found to have persistent or recurrent IDA, defined as hemoglobin <11.0 grams per deciliter (g/dL) and transferrin saturation (TSAT) <20% at any monthly evaluation visit (with the exception of the Study Termination visit), began a 5-week Treatment Period (TP) and received a total of 2 doses of ferumoxytol 510 milligrams (mg) intravenously (IV). The first IV 510 mg dose was administered on TP Day 1 (Baseline) and second dose 2 to 8 (5±3) days after Dose 1, for a total cumulative dose of 1.02 grams (g).

Reporting group title	Did Not Receive Ferumoxytol in IDA-303

Reporting group description:

Participants who received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42] and did not receive ferumoxytol during AMAG-FER-IDA-303.

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

Subject analysis set description:

Participants who received at least 1 dose of ferumoxytol and had evaluable data for hemoglobin at TP Baseline and TP Week 5 in AMAG-FER-IDA-303.

Primary: Mean Change In Hemoglobin From TP Baseline To TP Week 5 Following The First Course Of Ferumoxytol

End point title	Mean Change In Hemoglobin From TP Baseline To TP Week 5 Following The First Course Of Ferumoxytol[1][2]

End point description:

Mean change in hemoglobin from TP Baseline (Day 1) to TP Week 5 following the first dose of ferumoxytol was calculated as: Hemoglobin Change = Hemoglobin (TP Week 5) – Hemoglobin (TP Baseline) TP Baseline was the most recent value measured on/after the screening or the closest monthly evaluation visit prior to Day 1 dosing of Course 1.
Change from Baseline used an imputed value of 0 for missing values at the post-baseline visit.
Statistical analysis (t-test, 2-sided, with a p-value of <0.0001) was performed.

End point type	Primary

End point timeframe:

TP Baseline (Day 1), TP Week 5

Notes:

[1] - 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: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	151[3]			
Units: g/dL				
arithmetic mean (standard deviation)	2.6 (± 1.55)			

Notes:

[3] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change In Hemoglobin Following Each Course Of Ferumoxytol From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol After The First Course

End point title	Mean Change In Hemoglobin Following Each Course Of Ferumoxytol From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol After The First Course[4]

End point description:

Mean change in hemoglobin from TP Baseline to TP Week 5 following each course of ferumoxytol after the first course was calculated for each participant as:
Hemoglobin Change = Hemoglobin (TP Week 5) – Hemoglobin (TP Baseline) The first course of treatment with ferumoxytol for participants who had previously received placebo in AMAG-FER-IDA-301 was considered Course 1. The first course of treatment with ferumoxytol for participants who had previously received ferumoxytol in AMAG-FER-IDA-301 was considered Course 2; subsequent treatment courses were serially numbered.

End point type	Secondary

End point timeframe:

TP Baseline (Day 1), TP Week 5 for Courses 1, 2, and 3

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	337[5]			
Units: g/dL				
arithmetic mean (standard deviation)				
Course 1, 151 Participants	2.6 (± 1.55)			
Course 2, 244 Participants	1.5 (± 1.28)			
Course 3, 69 Participants	1.1 (± 1.30)			

Notes:

[5] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Of Participants With An Increase In Hemoglobin ≥2.0 g/dL At Any Time From TP Baseline To TP Week 5

End point title	Percentage Of Participants With An Increase In Hemoglobin ≥2.0 g/dL At Any Time From TP Baseline To TP Week 5[6]

End point description:

Proportion of participants with an increase in hemoglobin ≥2.0 g/dL at any time from TP Baseline to TP Week 5 following each course of ferumoxytol. The first course of treatment with ferumoxytol for participants who had previously received placebo in AMAG-FER-IDA-301 was considered Course 1. The first course of treatment with ferumoxytol for participants who had previously received ferumoxytol in AMAG-FER-IDA-301 was considered Course 2; subsequent treatment courses were serially numbered.

End point type	Secondary

End point timeframe:

TP Baseline (Day 1), TP Week 5 for Courses 1, 2, and 3

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	337[7]			
Units: Percentage of Participants				
number (not applicable)				
Course 1, 151 Participants	78.8			
Course 2, 244 Participants	43.9			
Course 3, 69 Participants	37.7			

Notes:

[7] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Of Participants Who Achieved A Hemoglobin Level ≥12.0 g/dL At Any Time From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol

End point title	Percentage Of Participants Who Achieved A Hemoglobin Level ≥12.0 g/dL At Any Time From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol[8]

End point description:

Proportion of participants who achieved a hemoglobin level ≥12.0 g/dL at any time from TP Baseline to TP Week 5 following each course of ferumoxytol. The first course of treatment with ferumoxytol for participants who had previously received placebo in AMAG-FER-IDA-301 was considered Course 1. The first course of treatment with ferumoxytol for participants who had previously received ferumoxytol in AMAG-FER-IDA-301 was considered Course 2; subsequent treatment courses were serially numbered.

End point type	Secondary

End point timeframe:

TP Baseline (Day 1), TP Week 5 for Courses 1, 2, and 3

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	337[9]			
Units: Percentage of Participants				
number (not applicable)				
Course 1, 151 Participants	38.4			
Course 2, 244 Participants	57.0			
Course 3, 69 Participants	40.6			

Notes:

[9] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change In TSAT Following Each Course Of Ferumoxytol From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol

End point title	Mean Change In TSAT Following Each Course Of Ferumoxytol From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol[10]

End point description:

Mean change in TSAT from TP Baseline to TP Week 5 following each course of ferumoxytol.

End point type	Secondary

End point timeframe:

TP Baseline (Day 1), TP Week 5 for Courses 1, 2, and 3

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	337[11]			
Units: Percentage of Saturation				
arithmetic mean (standard deviation)				
Course 1, 151 Participants	12.8 (± 10.19)			
Course 2, 244 Participants	11.7 (± 12.47)			
Course 3, 69 Participants	7.5 (± 9.13)			

Notes:

[11] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Participant-reported Outcome Measure: Mean Change In Functional Assessment Of Chronic Illness Therapy (FACIT)-Fatigue Questionnaire From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol

End point title	Participant-reported Outcome Measure: Mean Change In Functional Assessment Of Chronic Illness Therapy (FACIT)-Fatigue Questionnaire From TP Baseline To TP Week 5 Following Each Course Of Ferumoxytol[12]

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 questionnaire from TP Baseline to TP Week 5 following each course of ferumoxytol was calculated as:
FACIT-Fatigue Score Change = FACIT-Fatigue Score (Week 5) – FACIT-Fatigue Score (Baseline).
TP Baseline was the most recent value measured on/after the screening or the closest monthly evaluation visit prior to Day 1 dosing in each course.
If the TP Week 5 FACIT-Fatigue Score value was missing, the change from TP Baseline was conservatively imputed as zero.

End point type	Secondary

End point timeframe:

TP Baseline (Day 1), TP Week 5 for Courses 1, 2, and 3

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	337[13]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Course 1, 151 Participants	6.9 (± 9.57)			
Course 2, 244 Participants	4.1 (± 8.58)			
Course 3, 69 Participants	1.5 (± 6.87)			

Notes:

[13] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

End point title	Time To Hemoglobin Increase Of ≥2.0 g/dL Or To A Hemoglobin Level Of ≥12.0 g/dL From Baseline[14]

End point description:

Days to event was defined as the days from Baseline to the first time the participant met the criteria. Participants without any post-Baseline study visits were not included in this analysis.
The first course of treatment with ferumoxytol for participants who had previously received placebo in AMAG-FER-IDA-301 was considered Course 1. The first course of treatment with ferumoxytol for participants who had previously received ferumoxytol in AMAG-FER-IDA-301 was considered Course 2; subsequent treatment courses were serially numbered. Ranges were determined for 25%, 50%, and 75% of events. Course 3, 69 participants, is not reported due to the limitations of the EudraCT database, which requires actual numbers. The arithmetic mean for Course 3 was 30.7, with the inter-quartile (Q1-Q3) range of 22.0 to "not applicable" because there was an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

TP Baseline (Day 1) up to TP Week 5 for Courses 1, 2, and 3

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for all efficacy endpoints were performed only on the Reporting Group

receiving ferumoxytol.

End point values	Received Ferumoxytol in IDA-303			
Subject group type	Reporting group			
Number of subjects analysed	337[15]			
Units: Days				
arithmetic mean (inter-quartile range (Q1-Q3))				
Course 1, 151 Participants	27.8 (22.0 to 36.0)			
Course 2, 244 Participants	30.6 (22.0 to 37.0)			

Notes:

[15] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment Period Baseline (Day 1) through TP Week 5	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups	
Reporting group title	Received Ferumoxytol in IDA-303

Reporting group description:

Participants received ferumoxytol or placebo during AMAG-FER-IDA-301 [2011-001865-42]. Participants enrolled in AMAG-FER-IDA-303 who were found to have persistent or recurrent IDA, defined as hemoglobin <11.0 g/dL and TSAT <20% at any monthly evaluation visit (with the exception of the Study Termination visit), began a 5-week TP and received a total of 2 doses of ferumoxytol 510 mg IV. The first IV 510 mg dose was administered on TP Day 1 (Baseline) and second dose 2 to 8 (5±3) days after Dose 1, for a total cumulative dose of 1.02 g.

Serious adverse events	Received Ferumoxytol in IDA-303		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 337 (6.53%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer metastatic			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon cancer stage III			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon neoplasm			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stridor			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vocal cord disorder			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Incisional hernia			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haematoma			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative fever			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Procedural pain			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Vocal cord paralysis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 337 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Small intestinal stenosis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cirrhosis alcoholic			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			

subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngitis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	1 / 337 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Received Ferumoxytol in IDA-303		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 337 (27.60%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 337 (1.19%)		
occurrences (all)	9		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 337 (1.48%)		
occurrences (all)	5		
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	11 / 337 (3.26%) 11		
Dysgeusia subjects affected / exposed occurrences (all)	4 / 337 (1.19%) 7		
Headache subjects affected / exposed occurrences (all)	24 / 337 (7.12%) 28		
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	9 / 337 (2.67%) 9		
Oedema peripheral subjects affected / exposed occurrences (all)	6 / 337 (1.78%) 6		
Pyrexia subjects affected / exposed occurrences (all)	5 / 337 (1.48%) 5		
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	5 / 337 (1.48%) 6		
Constipation subjects affected / exposed occurrences (all)	7 / 337 (2.08%) 8		
Diarrhoea subjects affected / exposed occurrences (all)	10 / 337 (2.97%) 10		
Nausea subjects affected / exposed occurrences (all)	17 / 337 (5.04%) 20		
Vomiting subjects affected / exposed occurrences (all)	10 / 337 (2.97%) 12		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	7 / 337 (2.08%)		
occurrences (all)	8		
Dyspnoea			
subjects affected / exposed	4 / 337 (1.19%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 337 (1.78%)		
occurrences (all)	8		
Back pain			
subjects affected / exposed	9 / 337 (2.67%)		
occurrences (all)	9		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 337 (2.97%)		
occurrences (all)	10		
Sinusitis			
subjects affected / exposed	5 / 337 (1.48%)		
occurrences (all)	6		
Upper respiratory tract infection			
subjects affected / exposed	6 / 337 (1.78%)		
occurrences (all)	6		
Urinary tract infection			
subjects affected / exposed	19 / 337 (5.64%)		
occurrences (all)	20		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	7 / 337 (2.08%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2011	• Addition of optional cognitive function testing and exercise tolerance testing at United States sites for additional measures of clinical benefit outcomes following improvement in hemoglobin/anemia. • Addition of 2 new exploratory endpoints to account for the addition of the new clinical benefit outcomes assessments.

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/26572233