Clinical trial results:
Ferumoxytol for Anemia of CKD Trial (FACT): A Phase IV, Open-Label, Multicenter Trial, with MRI Substudy, of Repeated Doses of Ferumoxytol Compared with Iron Sucrose for the Treatment of Iron Deficiency Anemia (IDA) in Chronic Kidney Disease (CKD) Patients on Hemodialysis

Summary

EudraCT number	2010-022133-28
Trial protocol	GB
Global end of trial date	24 February 2016

Results information

Result version number	v1 (current)
This version publication date	25 November 2017
First version publication date	25 November 2017

Trial information

Trial identification

Sponsor protocol code	AMAG-FER-CKD-401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01227616
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AMAG Pharmaceuticals Inc.
Sponsor organisation address	1100 Winter St., Waltham, United States, MA 02451
Public contact	FACT Study Info, AMAG Pharmaceuticals Inc., factstudyinfo@amagpharma.com
Scientific contact	FACT Study Info, AMAG Pharmaceuticals Inc., factstudyinfo@amagpharma.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	17 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that 1.02 g courses of ferumoxytol (delivered as either an undiluted IV injection or diluted IV infusion of 510 mg each) are noninferior to 1.0 g courses of iron sucrose (delivered either as slow IV undiluted injections or IV diluted infusions of 100 mg each) in raising hemoglobin after each treatment period in hemodialysis-dependent CKD subjects with IDA over a one-year period

Protection of trial subjects:

Female subjects of childbearing potential who are not on an effective method of birth control or female subjects who are pregnant or intend to become pregnant, breastfeeding, within 2 weeks postpartum, or have a positive serum or urine pregnancy test will not be allowed to participate in this study.

For those subjects not previously exposed to iron sucrose, a test dose will be administered
o For IV drip infusion the first 20-25 mg of iron should be infused over a period of approximately 15 minutes. If no adverse reactions occur during this time then the remaining portion of the infusion should be given at an infusion rate of not more than 100 mg over 15 minutes
o For a slow IV injection, a test dose of 1 mL (~20 mg of iron) should be injected slowly over a period of approximately 1 minute. If no adverse reactions occur within 15 minutes of completing the test dose, then the remaining portion of the injection may be given

Background therapy: -

Evidence for comparator:

Iron sucrose for injection is currently approved in over 79 countries, including the US, EU and Canada as an IV iron replacement therapy for patients with CKD and IDA. Iron sucrose for injection is currently the most frequently prescribed IV iron therapy worldwide. The 100 mg dose of iron sucrose to be administered in this trial is consistent with the approved and marketed doses of iron sucrose worldwide. It has been shown to significantly increase hemoglobin levels as early as 15 days after dosing, with a mean change in hemoglobin of 1.0-1.3 g/dL from Baseline to Week 8.

Actual start date of recruitment	19 August 2013
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	United Kingdom: 11
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	United States: 275
Worldwide total number of subjects	293
EEA total number of subjects	11

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)	192
From 65 to 84 years	95
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

A total of 296 hemodialysis patients with IDA who met the entry criteria were enrolled and randomized (ferumoxytol: n=197; iron sucrose: n=99). One subject in the ferumoxytol group and 2 subjects in the iron sucrose group withdrew prior to receiving study drug

Pre-assignment

Screening details:

2-week Screening Period, male and female hemodialysis subjects ≥18 years of age with IDA and CKD, with screening hemoglobin values of <11.5 g/dL and TSAT <30% who met the other inclusion criteria and did not satisfy any exclusion criteria were eligible for the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ferumoxytol

Arm description: -

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

Dosage and administration details:

Subjects assigned to the ferumoxytol treatment group will receive ferumoxytol as a diluted IV infusion as follows: 510 mg ferumoxytol on Day 1 and then a second dose 2 to 8 days later (TP Day 3 to 9), for a total cumulative dose of 1.02 g

Arm title	Iron Sucrose

Arm description: -

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

Dosage and administration details:

iron sucrose treatment group received iron sucrose as a slow undiluted IV injection or diluted IV infusion as follows: 100 mg iron sucrose on Day 1 and at the following 9 consecutive hemodialysis sessions over approximately 3 weeks for a total cumulative dose of 1.0 g.

Number of subjects in period 1	Ferumoxytol	Iron Sucrose
Started	196	97
Evaluable Population	181	83
Completed	142	74
Not completed	54	23
Consent withdrawn by subject	10	7
Adverse event, non-fatal	8	2
Other	20	8
Death	13	5
Lost to follow-up	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Ferumoxytol
Reporting group description: -	
Reporting group title	Iron Sucrose
Reporting group description: -	

Reporting group values	Ferumoxytol	Iron Sucrose	Total
Number of subjects	196	97	293
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	59.3	57.6	
standard deviation	± 14.13	± 13.62	-
Gender categorical Units: Subjects			
Female	114	57	171
Male	82	40	122
Race Units: Subjects			
White	101	47	148
Black or African American	62	26	88
Asian	15	13	28
American Indian or Alaska Native	10	4	14
Other/Multiracial	6	4	10
Native Hawaiian or Other Pacific Islander	2	3	5
Ethnicity Units: Subjects			
Hispanic and/or Latino	68	40	108
Not Hispanic or Latino	128	57	185
Height Units: cm			
arithmetic mean	168.3	167.2	
standard deviation	± 10.49	± 10.39	-
Weight Units: kilogram(s)			

arithmetic mean	86.8	83.2	
standard deviation	± 23.4	± 20.95	-

End points

End points reporting groups

Reporting group title	Ferumoxytol
Reporting group description: -	
Reporting group title	Iron Sucrose
Reporting group description: -	
Subject analysis set title	Evaluable Population- Ferumoxytol
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Any randomized subjects who met the following criteria:
• Did not have any significant protocol violations/deviations considered to impact study integrity
• Received 2 doses of ferumoxytol or all 10 doses of iron sucrose in TP1
• Had data for hemoglobin (primary endpoint) at TP1 Baseline and Week 5
• Confirmatory analyses for the primary efficacy were performed in the Evaluable Population.

Subject analysis set title	Evaluable Population- Iron Sucrose
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Any randomized subjects who met the following criteria:
• Did not have any significant protocol violations/deviations considered to impact study integrity
• Received 2 doses of ferumoxytol or all 10 doses of iron sucrose in TP1
• Had data for hemoglobin (primary endpoint) at TP1 Baseline and Week 5
• Confirmatory analyses for the primary efficacy were performed in the Evaluable Population.

Primary: Mean Change in Hemoglobin at Week 5: TP1

End point title	Mean Change in Hemoglobin at Week 5: TP1

End point description:

Mean change in hemoglobin from TP Baseline (defined as the hemoglobin level immediately prior to each treatment course) to Week 5 was non-inferior for ferumoxytol compared to iron sucrose in treatment period 1.

End point type	Primary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose	Evaluable Population- Ferumoxytol	Evaluable Population- Iron Sucrose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	195	94	180	82
Units: gram(s)/decilitre				
arithmetic mean (standard deviation)	0.5 (± 0.97)	0.4 (± 0.97)	0.5 (± 0.96)	0.5 (± 0.89)

Statistical analyses

Statistical analysis title	LS mean and 95% Confidence Interval for difference
Comparison groups	Ferumoxytol v Iron Sucrose

Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.2811
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.36

Notes:

[1] - The study protocol defined the margin for non-inferiority as 0.5 g/dL meaning non–inferiority would be established in a TP if the lower
limit of the 95% confidence limit for the difference between ferumoxytol and iron sucrose mean change was ≥0.5 g/dL.

Statistical analysis title	Copy of LS mean and 95% Confidence Interval for...
Comparison groups	Evaluable Population- Ferumoxytol v Evaluable Population- Iron Sucrose
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.6968
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.29

Notes:

[2] - The study protocol defined the margin for non-inferiority as 0.5 g/dL meaning non–inferiority would be established in a TP if the lower
limit of the 95% confidence limit for the difference between ferumoxytol and iron sucrose mean change was ≥0.5 g/dL.

Primary: Mean Change in Hemoglobin at Week 5: TP2

End point title	Mean Change in Hemoglobin at Week 5: TP2

End point description:

Mean change in hemoglobin from TP Baseline (defined as the hemoglobin level immediately prior to each treatment course) to Week 5 was non-inferior for ferumoxytol compared to iron sucrose in treatment period 2.

End point type	Primary

End point timeframe:

Baseline (start of treatment period) to week 5

End point values	Ferumoxytol	Iron Sucrose	Evaluable Population- Ferumoxytol	Evaluable Population- Iron Sucrose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	167	88	159	76
Units: gram(s)/decilitre				
arithmetic mean (standard deviation)	0.6 (± 0.96)	0.3 (± 1.03)	0.5 (± 0.96)	0.3 (± 1.1)

Statistical analyses

Statistical analysis title	LS mean and 95% Confidence Interval for difference
Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0158
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.55

Statistical analysis title	Copy of LS mean and 95% Confidence Interval for...
Comparison groups	Evaluable Population- Ferumoxytol v Evaluable Population- Iron Sucrose
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0347
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.55

Primary: Mean Change in Hemoglobin at Week 5: TP3

End point title	Mean Change in Hemoglobin at Week 5: TP3

End point description:

Mean change in hemoglobin from TP Baseline (defined as the hemoglobin level immediately prior to

each treatment course) to Week 5 was non-inferior for ferumoxytol compared to iron sucrose in treatment period 3.

End point type	Primary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose	Evaluable Population-Ferumoxytol	Evaluable Population-Iron Sucrose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	130	64	124	58
Units: gram(s)/decilitre				
arithmetic mean (standard deviation)	0.6 (± 1.1)	0.4 (± 0.87)	0.6 (± 1.09)	0.5 (± 0.83)

Statistical analyses

Statistical analysis title	LS mean and 95% Confidence Interval for difference
Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0592
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.56

Primary: Mean Change in Hemoglobin at Week 5: TP4

End point title	Mean Change in Hemoglobin at Week 5: TP4

End point description:

Mean change in hemoglobin from TP Baseline (defined as the hemoglobin level immediately prior to each treatment course) to Week 5 was non-inferior for ferumoxytol compared to iron sucrose in treatment period 4.

End point type	Primary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose	Evaluable Population-Ferumoxytol	Evaluable Population-Iron Sucrose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	81	32	78	28
Units: gram(s)/decilitre				
arithmetic mean (standard deviation)	0.5 (± 1.12)	0.6 (± 1.11)	0.5 (± 1.13)	0.7 (± 1.14)

Statistical analyses

Statistical analysis title	LS mean and 95% Confidence Interval for difference
Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3134
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.2

Primary: Mean Change in Hemoglobin at Week 5: TP5

End point title	Mean Change in Hemoglobin at Week 5: TP5

End point description:

Mean change in hemoglobin from TP Baseline (defined as the hemoglobin level immediately prior to each treatment course) to Week 5 was non-inferior for ferumoxytol compared to iron sucrose in treatment period 5.

End point type	Primary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose	Evaluable Population-Ferumoxytol	Evaluable Population-Iron Sucrose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	48	17	47	13
Units: gram(s)/decilitre				
arithmetic mean (standard deviation)	0.4 (± 1.14)	0.3 (± 0.96)	0.5 (± 1.15)	0.3 (± 0.54)

Statistical analyses

Statistical analysis title	LS mean and 95% Confidence Interval for difference
Comparison groups	Ferumoxytol v Iron Sucrose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8745
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.63

Primary: Mean Change in Hemoglobin at Week 5: TP6

End point title	Mean Change in Hemoglobin at Week 5: TP6
End point description:	
Mean change in hemoglobin from TP Baseline (defined as the hemoglobin level immediately prior to each treatment course) to Week 5 was non-inferior for ferumoxytol compared to iron sucrose in treatment period 6.	
End point type	Primary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose	Evaluable Population-Ferumoxytol	Evaluable Population-Iron Sucrose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	22	8	21	7
Units: gram(s)/decilitre				
arithmetic mean (standard deviation)	0.5 (± 1.21)	-0.3 (± 1)	0.6 (± 1.23)	-0.3 (± 1.07)

Statistical analyses

Statistical analysis title	LS mean and 95% Confidence Interval for difference
Comparison groups	Ferumoxytol v Iron Sucrose

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2253
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	1.69

Secondary: Mean Change in TSAT at Week 5- TP1

End point title	Mean Change in TSAT at Week 5- TP1
End point description:	
Mean change in TSAT from TP Baseline to Week 5 for treatment period 1	
End point type	Secondary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	95		
Units: percent				
arithmetic mean (standard deviation)	6.6 (± 9.2)	9.5 (± 11.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in TSAT at Week 5- TP2

End point title	Mean Change in TSAT at Week 5- TP2
End point description:	
Mean change in TSAT from TP Baseline to Week 5 for treatment period 2	
End point type	Secondary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	88		
Units: percent				
arithmetic mean (standard deviation)	8.2 (± 12.95)	11.3 (± 14.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in TSAT at Week 5- TP3

End point title	Mean Change in TSAT at Week 5- TP3
End point description:	
Mean change in TSAT from TP Baseline to Week 5 for treatment period 3	
End point type	Secondary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	63		
Units: percent				
arithmetic mean (standard deviation)	8.5 (± 10.56)	9.1 (± 11.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in TSAT at Week 5- TP4

End point title	Mean Change in TSAT at Week 5- TP4
End point description:	
Mean change in TSAT from TP Baseline to Week 5 for treatment period 4	
End point type	Secondary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	32		
Units: percent				
arithmetic mean (standard deviation)	9.8 (± 14.76)	10 (± 14.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in TSAT at Week 5- TP5

End point title	Mean Change in TSAT at Week 5- TP5
End point description:	
Mean change in TSAT from TP Baseline to Week 5 for treatment period 5	
End point type	Secondary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	17		
Units: percent				
arithmetic mean (standard deviation)	6.3 (± 9.77)	14.4 (± 17.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in TSAT at Week 5- TP6

End point title	Mean Change in TSAT at Week 5- TP6
End point description:	
Mean change in TSAT from TP Baseline to Week 5 for treatment period 6	
End point type	Secondary
End point timeframe:	
Baseline to week 5	

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	8		
Units: percent				
arithmetic mean (standard deviation)	7.1 (± 16.62)	5.1 (± 12.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP1

End point title	Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP1

End point description:

Proportion of subjects with an increase in hemoglobin of ≥1.0 g/dL at any time from TP Baseline to Week 5 for treatment period 1

End point type	Secondary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	97		
Units: percent				
number (not applicable)	28.1	23.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP2

End point title	Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP2

End point description:

Proportion of subjects with an increase in hemoglobin of ≥1.0 g/dL at any time from TP Baseline to Week 5 for treatment period 2

End point type	Secondary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	88		
Units: percent				
number (not applicable)	31.8	14.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP3

End point title	Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP3

End point description:

Proportion of subjects with an increase in hemoglobin of ≥1.0 g/dL at any time from TP Baseline to Week 5 for treatment period 3

End point type	Secondary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	65		
Units: percent				
number (not applicable)	31.6	29.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP4

End point title	Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP4

End point description:

Proportion of subjects with an increase in hemoglobin of ≥1.0 g/dL at any time from TP Baseline to Week 5 for treatment period 4

End point type	Secondary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	33		
Units: percent				
number (not applicable)	23.5	30.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP5

End point title	Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP5

End point description:

Proportion of subjects with an increase in hemoglobin of ≥1.0 g/dL at any time from TP Baseline to Week 5 for treatment period 5

End point type	Secondary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	18		
Units: percent				
number (not applicable)	26.5	16.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP6

End point title	Subjects with an increase in hemoglobin of ≥1 g/dL at any time from TP baseline to Week 5- TP6

End point description:

Proportion of subjects with an increase in hemoglobin of ≥1.0 g/dL at any time from TP Baseline to Week 5 for treatment period 6

End point type	Secondary

End point timeframe:

Baseline to week 5

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	8		
Units: percent				
number (not applicable)	22.7	12.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Treatment-Emergent Adverse Events by Treatment Group

End point title	Summary of Treatment-Emergent Adverse Events by Treatment Group

End point description:

The incidence of treatment-emergent AEs (TEAEs) in various categories by treatment group and in the total study population. A TEAE was defined as an event with an onset date and time on or after the first dosing start date and time, or on or after the first dosing start date if the onset time was missing.

End point type	Secondary

End point timeframe:

on or after the first dosing start date and time

End point values	Ferumoxytol	Iron Sucrose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	97		
Units: number				
All AEs	158	81		
Related AEs	9	4		
SAEs	93	49		
Related SAEs	0	0		
AEs of Special Interest protocol defined	25	26		
Cardiovascular AEs	29	25		
AEs resulting in temp discontinuation of IMP	2	3		
AEs resulting in permanent discontinuation of IMP	8	0		
AEs resulting in study discontinuation	20	7		
Death	15	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The time a subject signs the informed consent until the last study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	tbc

Reporting groups	
Reporting group title	Ferumoxytol
Reporting group description: -	
Reporting group title	Iron Sucrose
Reporting group description: -	

Serious adverse events	Ferumoxytol	Iron Sucrose	
Total subjects affected by serious adverse events			
subjects affected / exposed	93 / 196 (47.45%)	49 / 97 (50.52%)	
number of deaths (all causes)	15	6	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
subjects affected / exposed	2 / 196 (1.02%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	12 / 196 (6.12%)	13 / 97 (13.40%)	
occurrences causally related to treatment / all	0 / 14	0 / 14	
deaths causally related to treatment / all	0 / 2	0 / 1	
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	9 / 196 (4.59%)	6 / 97 (6.19%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Immune system disorders			
subjects affected / exposed	2 / 196 (1.02%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	21 / 196 (10.71%)	6 / 97 (6.19%)	
occurrences causally related to treatment / all	0 / 27	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	6 / 196 (3.06%)	2 / 97 (2.06%)	
occurrences causally related to treatment / all	0 / 11	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Investigation			
subjects affected / exposed	0 / 196 (0.00%)	2 / 97 (2.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poinsoning and procedural complications			
subjects affected / exposed	18 / 196 (9.18%)	16 / 97 (16.49%)	
occurrences causally related to treatment / all	0 / 22	0 / 20	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	20 / 196 (10.20%)	15 / 97 (15.46%)	
occurrences causally related to treatment / all	0 / 31	0 / 27	
deaths causally related to treatment / all	0 / 5	0 / 3	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	13 / 196 (6.63%)	9 / 97 (9.28%)	
occurrences causally related to treatment / all	0 / 16	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Blood and lymphatic system disorders			
subjects affected / exposed	7 / 196 (3.57%)	5 / 97 (5.15%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 4	0 / 0	
Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	0 / 196 (0.00%)	2 / 97 (2.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	25 / 196 (12.76%)	12 / 97 (12.37%)	
occurrences causally related to treatment / all	0 / 32	0 / 21	
deaths causally related to treatment / all	0 / 3	0 / 0	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	1 / 196 (0.51%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	3 / 196 (1.53%)	3 / 97 (3.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and infestations			
subjects affected / exposed	38 / 196 (19.39%)	17 / 97 (17.53%)	
occurrences causally related to treatment / all	0 / 49	0 / 24	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			

subjects affected / exposed	17 / 196 (8.67%)	10 / 97 (10.31%)	
occurrences causally related to treatment / all	0 / 18	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Ferumoxytol	Iron Sucrose	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 196 (33.16%)	48 / 97 (49.48%)	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	26 / 196 (13.27%)	11 / 97 (11.34%)	
occurrences (all)	63	24	
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	48 / 196 (24.49%)	15 / 97 (15.46%)	
occurrences (all)	77	31	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	20 / 196 (10.20%)	12 / 97 (12.37%)	
occurrences (all)	47	21	
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	12 / 196 (6.12%)	5 / 97 (5.15%)	
occurrences (all)	19	8	
Investigations			
Investigations			
subjects affected / exposed	11 / 196 (5.61%)	11 / 97 (11.34%)	
occurrences (all)	12	19	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	43 / 196 (21.94%)	26 / 97 (26.80%)	
occurrences (all)	113	81	
Cardiac disorders			

Cardiac disorders subjects affected / exposed occurrences (all)	10 / 196 (5.10%) 33	3 / 97 (3.09%) 6	
Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all)	22 / 196 (11.22%) 32	15 / 97 (15.46%) 36	
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	7 / 196 (3.57%) 12	1 / 97 (1.03%) 1	
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	49 / 196 (25.00%) 131	24 / 97 (24.74%) 64	
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	18 / 196 (9.18%) 31	9 / 97 (9.28%) 13	
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	37 / 196 (18.88%) 121	22 / 97 (22.68%) 78	
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	26 / 196 (13.27%) 63	16 / 97 (16.49%) 37	
Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	15 / 196 (7.65%) 33	5 / 97 (5.15%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 August 2014	Amendment 1 allowed physicians to choose between delivering ferumoxytol as either an IV injection over 1 minute or an IV infusion over a minimum of 15 minutes. Amendment 1 also updated the AE reporting rates with current postmarketing information and changed the collection of prior prescription medications at Screening to the collection of all prior medications at Screening.
09 April 2015	Amendment 2 required all subjects to receive ferumoxytol as a 15-minute infusion and updated safety information with warnings regarding serious hypersensitivity/anaphylaxis reactions and a new contraindication regarding history of allergy to any IV iron product. The changes were instituted to align the protocol with changes in the Prescribing Information (PI) for ferumoxytol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported