EU Clinical Trials Register

Clinical trial results:
The effect of intravenous iron on postoperative transfusion requirements in hip fracture patients – a pilot study

Summary

EudraCT number	2011-003233-34
Trial protocol	GB
Global end of trial date	11 July 2017

Results information

Result version number	v1 (current)
This version publication date	27 February 2019
First version publication date	27 February 2019

Trial information

Trial identification

Sponsor protocol code	11048

Additional study identifiers

ISRCTN number	ISRCTN89812075
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Nottingham
Sponsor organisation address	East Atrium; Jubilee Conference Centre; Triumph Road, Nottingham, United Kingdom, NG8 1DH
Public contact	Iain Moppett, University of Nottingham, +44 01158230959, iain.moppett@nottingham.ac.uk
Scientific contact	Iain Moppett, University of Nottingham, +44 1158230959, iain.moppett@nottingham.ac.uk

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	14 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 July 2017
Global end of trial reached?	Yes
Global end of trial date	11 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether intravenous iron given in the first few days following hip fracture is effective in stimulating red cell production.

Protection of trial subjects:

No change to standard care for any participants in study, except for IMP and seven days of blood tests. Consent confirmed for each administration of IMP. All study personnel trained in trial conduct and ethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2011
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: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	0
From 65 to 84 years	53
85 years and over	27

Subject disposition

Recruitment

Recruitment details:

First participant recruited 19/7/2012
Last participant recruited 26/6/2017

Pre-assignment

Screening details:

Potential participants screened in emergency department based on age, injury and major inclusion / exclusion criteria (inability to provide own consent). Excluded (n = 1324)

Not meeting inclusion criteria (n = 1166)

Unable to give consent (n = 359)

>24 hours (n = 349)

Declined to participate (n = 158)

Other reasons (n = 0)

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Monitor, Data analyst, Investigator, Assessor[2]

Blinding implementation details:

Participants not blinded due to colour of IMP.
Assessor blinded except in case of adjudication of serious adverse reactions

Arms

Are arms mutually exclusive?	Yes
Arm title	Control

Arm description:

Control group

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Intravenous iron

Arm description:

Intravenous iron

Arm type	Experimental
Investigational medicinal product name	VENOFER
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

IMP administration

Patients allocated to IMP will receive 200mg iron sucrose (Venofer) on three separate occasions:

T1: Day 1 (within 24 hours of admission);
T2: Day 1 postop; or second morning following admission if not yet gone to theatre
T3: Day 2 postop; or third morning following admission if not yet gone to theatre

Administration of intravenous iron will be in accordance with manufacturer's recommendations. 10ml Venofer (200 mg iron) will be diluted in 100 ml 0.9% sodium chloride for injections. (Final concentration 1 mg/ml)

The infusion will be given at an infusion rate of not more than 50 ml in 15 minutes.

Oral iron is prohibited for at least 5 days following administration of intravenous iron. Given the negative results of a recent study of oral iron in hip fracture10, oral iron will not be permitted for any study participants until day 10.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: Investigators and analysts blinded to allocation. Participants not blinded due to colour of IMP.

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Investigators and analysts blinded to allocation. Participants not blinded due to colour of IMP.

Number of subjects in period 1	Control	Intravenous iron
Started	41	39
Completed	41	39

Baseline characteristics

Reporting groups

Reporting group title	Control
Reporting group description:	
Control group	
Reporting group title	Intravenous iron
Reporting group description:	
Intravenous iron	

Reporting group values	Control	Intravenous iron	Total
Number of subjects	41	39	80
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			
Age of participants at study entry			
Units: years			
arithmetic mean	82.5	81.2	
standard deviation	± 5.8	± 7.0	-
Gender categorical			
Units: Subjects			
Female	29	24	53
Male	12	15	27
Admission source			
Location participicant was admitted to hospital from			
Units: Subjects			
Home – Independent	36	36	72
Nursing care	0	1	1
Residential care	1	0	1
Warden controlled	4	2	6
Operation			
Operation type			
Units: Subjects			
AO Screws	2	1	3
DHS	14	9	23
Hemiarthroplasty	18	22	40
Nail	2	4	6
Total Hip Arthroplasty	5	3	8

Fracture type			
Type of hip fracture			
Units: Subjects			
Extracapsular	6	3	9
Intracapsular	24	26	50
Trochanteric	11	10	21
Haemoglobin concentration on admission < 120 g / L			
Number of subjects with a haemoglobin concentration level of less than 120 g / L on admission to hospital			
Units: Subjects			
Yes	15	16	31
No	26	23	49
Time to theatre			
Time from participant admission to hospital until arrival at theatre			
Units: hour			
arithmetic mean	29.8	29.7	
standard deviation	± 20	± 17	-
Haemoglobin concentration on admission			
Haemoglobin concentration on admission to hospital			
Units: g / L			
log mean	4.83	4.81	
standard deviation	± 0.11	± 0.16	-
Haemoglobin concentration on admission			
Haemoglobin concentration on admission to hospital			
Units: g / L			
arithmetic mean	125.4	122.4	
inter-quartile range (Q1-Q3)	121.4 to 129.6	116.5 to 128.6	-
Reticulocyte count day 1			
Reticulocyte count on day 1			
Units: 10^9 cells / L			
log mean	3.70	3.74	
standard deviation	± 0.28	± 0.30	-
Reticulocyte count day 1			
Reticulocyte count on day 1			
Units: 10^9 cells / L			
arithmetic mean	40.4	42.2	
inter-quartile range (Q1-Q3)	36.9 to 44.2	38.3 to 46.6	-
Reticulocyte index day 1			
Reticulocyte index on day 1			
Units: percent			
log mean	0.10	0.15	
standard deviation	± 0.32	± 0.36	-
Reticulocyte index day 1			
Reticulocyte index on day 1			
Units: percent			
arithmetic mean	1.11	1.16	
inter-quartile range (Q1-Q3)	1.00 to 1.23	1.03 to 1.3	-
Haemoglobin concentration day 1			
Haemoglobin concentration on day 1			
Units: g / L			

log mean	4.72	4.71	
standard deviation	± 0.18	± 0.20	-
Haemoglobin concentration day 1			
Haemoglobin concentration on day 1			
Units: g / L			
arithmetic mean	112.7	111.1	
inter-quartile range (Q1-Q3)	106.4 to 119.3	104.1 to 118.6	-

End points

End points reporting groups

Reporting group title	Control
Reporting group description:	
Control group	
Reporting group title	Intravenous iron
Reporting group description:	
Intravenous iron	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants randomised	

Primary: Reticulocyte count on final day following admission

End point title	Reticulocyte count on final day following admission
End point description:	
End point type	Primary
End point timeframe:	
Final day	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: 10^9 cells / L				
log mean (standard deviation)	4.28 (± 0.38)	4.49 (± 0.38)		

Statistical analyses

Statistical analysis title	Comparison of log mean final reticulocyte count
Statistical analysis description:	
Two-sided t-test to test for significance in log mean final reticulocyte count	
Comparison groups	Intravenous iron v Control
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.019
Method	t-test, 2-sided

Primary: Reticulocyte count on final day following admission

End point title	Reticulocyte count on final day following admission[1]

End point description:

End point type	Primary
End point timeframe:	
Final day	

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: Fields used to provide details for back-transformed data, analysis performed on log transformed data.

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: 10^9 cells / L				
arithmetic mean (inter-quartile range (Q1-Q3))	72.2 (63.9 to 86.4)	89.4 (78.9 to 101.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Reticulocyte index on final day following admission

End point title	Reticulocyte index on final day following admission
End point description:	

End point type	Primary
End point timeframe:	
Final day	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: percent				
log mean (standard deviation)	0.77 (± 0.42)	0.99 (± 0.35)		

Statistical analyses

Statistical analysis title	Comparison of log mean final reticulocyte index
Statistical analysis description:	
Two-sided t-test to test for significance in log mean final reticulocyte index	
Comparison groups	Control v Intravenous iron

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.022
Method	t-test, 2-sided

Primary: Reticulocyte index on final day following admission

End point title	Reticulocyte index on final day following admission[2]
End point description:	

End point type	Primary
End point timeframe:	
Final day	

Notes:

[2] - 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: Fields used to provide details for back-transformed data, analysis performed on log transformed data.

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: percent				
arithmetic mean (inter-quartile range (Q1-Q3))	2.19 (1.91 to 2.51)	2.69 (2.39 to 3.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Haemoglobin concentration on final day following admission

End point title	Haemoglobin concentration on final day following admission
End point description:	

End point type	Secondary
End point timeframe:	
Final day	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	36		
Units: g / L				
log mean (standard deviation)	4.60 (± 0.14)	4.62 (± 0.10)		

Statistical analyses

Statistical analysis title	Comparison of log mean final haemoglobin
Statistical analysis description:	
Two-sided t-test to test for significance in log mean final haemoglobin concentration	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.454
Method	t-test, 2-sided

Secondary: Haemoglobin concentration on final day following admission

End point title	Haemoglobin concentration on final day following admission
End point description:	
End point type	Secondary
End point timeframe:	
Final day	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	36		
Units: g / L				
arithmetic mean (inter-quartile range (Q1-Q3))	99.9 (95.7 to 104.2)	102.0 (98.7 to 105.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum recorded haemoglobin concentration within the first 7 days following admission

End point title	Minimum recorded haemoglobin concentration within the first 7 days following admission

End point description:

End point type	Secondary

End point timeframe:

Within first 7 days following admission

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: g / L				
log mean (standard deviation)	4.51 (± 0.16)	4.52 (± 0.14)		

Statistical analyses

Statistical analysis title	Comparison of log mean minimum haemoglobin

Statistical analysis description:

Two-sided t-test to test for significance in log mean minimum haemoglobin concentration during the first 7 days following admission to hospital

Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.638
Method	t-test, 2-sided

Secondary: Minimum recorded haemoglobin concentration within the first 7 days following admission

End point title	Minimum recorded haemoglobin concentration within the first 7 days following admission

End point description:

End point type	Secondary

End point timeframe:

Within first 7 days following admission

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: g / L				
arithmetic mean (inter-quartile range (Q1-Q3))	90.6 (86.1 to 95.2)	92.1 (88.0 to 96.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum recorded fall in haemoglobin concentration within the first 7 days following admission

End point title	Maximum recorded fall in haemoglobin concentration within the first 7 days following admission

End point description:

End point type	Secondary

End point timeframe:

Within first 7 days following admission

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: g / L				
log mean (standard deviation)	3.39 (± 0.69)	3.23 (± 0.74)		

Statistical analyses

Statistical analysis title	Comparison of log mean maximum fall in haemoglobin

Statistical analysis description:

Two-sided t-test to test for significance in log mean maximum fall in haemoglobin concentration during the first 7 days following admission to hospital

Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.344
Method	t-test, 2-sided

Secondary: Maximum recorded fall in haemoglobin concentration within the first 7

days following admission

End point title	Maximum recorded fall in haemoglobin concentration within the first 7 days following admission
End point description:	
End point type	Secondary
End point timeframe:	
Within first 7 days following admission	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: g / L				
arithmetic mean (inter-quartile range (Q1-Q3))	29.5 (23.9 to 36.5)	25.3 (20.0 to 32.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum recorded reticulocyte count within the first 7 days following admission

End point title	Maximum recorded reticulocyte count within the first 7 days following admission
End point description:	
End point type	Secondary
End point timeframe:	
Within first 7 days following admission	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: 10^9 cells / L				
log mean (standard deviation)	4.29 (± 0.34)	4.49 (± 0.36)		

Statistical analyses

Statistical analysis title	Comparison of log mean maximum reticulocyte count
Statistical analysis description:	
Two-sided t-test to test for significance in log mean maximum reticulocyte count during the first	

7 days following admission to hospital

Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.022
Method	t-test, 2-sided

Secondary: Maximum recorded reticulocyte count within the first 7 days following admission

End point title	Maximum recorded reticulocyte count within the first 7 days following admission
End point description:	
End point type	Secondary
End point timeframe:	
Within first 7 days following admission	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: 10^9 cells / L				
arithmetic mean (inter-quartile range (Q1-Q3))	72.7 (66.5 to 80.6)	88.8 (79.3 to 99.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum recorded reticulocyte index within the first 7 days following admission

End point title	Maximum recorded reticulocyte index within the first 7 days following admission
End point description:	
End point type	Secondary
End point timeframe:	
Within first 7 days following admission	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: percent				
log mean (standard deviation)	0.78 (± 0.40)	0.97 (± 0.36)		

Statistical analyses

Statistical analysis title	Comparison of log mean maximum reticulocyte index
Statistical analysis description:	
Two-sided t-test to test for significance in log mean maximum reticulocyte index during the first 7 days following admission to hospital	
Comparison groups	Intravenous iron v Control
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.022
Method	t-test, 2-sided

Secondary: Maximum recorded reticulocyte index within the first 7 days following admission

End point title	Maximum recorded reticulocyte index within the first 7 days following admission
End point description:	
End point type	Secondary
End point timeframe:	
Within first 7 days following admission	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: percent				
arithmetic mean (inter-quartile range (Q1-Q3))	2.17 (1.92 to 2.46)	2.63 (2.35 to 2.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Transferrin Receptor Concentration final day following admission

End point title	Serum Transferrin Receptor Concentration final day following admission
End point description:	
End point type	Secondary
End point timeframe:	
Final day	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: mg / L				
median (inter-quartile range (Q1-Q3))	17.4 (14.5 to 19)	16.1 (14.1 to 17.9)		

Statistical analyses

Statistical analysis title	Comparison of mean Serum Transferrin Receptor
Statistical analysis description:	
Chi-squared test for significance in mean Serum Transferrin Receptor Concentration on the final day	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.418
Method	Chi-squared

Secondary: Serum Transferrin Receptor Concentration final day following admission

End point title	Serum Transferrin Receptor Concentration final day following admission
End point description:	
End point type	Secondary
End point timeframe:	
Final day	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: mg / L				
median (full range (min-max))	17.4 (10.1 to 24.8)	16.1 (9.3 to 24.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total transfusions during admission

End point title	Total transfusions during admission
End point description:	
End point type	Secondary
End point timeframe:	
During admission	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Transfusion				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 1)		

Statistical analyses

Statistical analysis title	Comparison of total transfusions during admission
Statistical analysis description:	
Mann-Whitney test for significance of difference of total transfusions during admission to hospital	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.927
Method	Wilcoxon (Mann-Whitney)

Secondary: Total transfusions during admission

End point title	Total transfusions during admission

End point description:

End point type	Secondary

End point timeframe:

During admission

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Transfusion				
median (full range (min-max))	0 (0 to 4)	0 (0 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants transfused during admission

End point title	Participants transfused during admission

End point description:

End point type	Secondary

End point timeframe:

During admission

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Participants transfused	12	11		

Statistical analyses

Statistical analysis title	Comparison of number of participants infused

Statistical analysis description:

Chi-squared test for significance in number of participants infused during admission to hospital

Comparison groups	Intravenous iron v Control

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Chi-squared

Secondary: Total transfusions in first week

End point title	Total transfusions in first week
End point description:	
End point type	Secondary
End point timeframe:	
During first week	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Transfusions				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 1)		

Statistical analyses

Statistical analysis title	Comparison of total transfusions during first week
Statistical analysis description:	
Chi-squared test for significance in mean of total transfusions during first week in hospital	
Comparison groups	Intravenous iron v Control
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.899
Method	Chi-squared

Secondary: Total transfusions in first week

End point title	Total transfusions in first week
End point description:	
End point type	Secondary
End point timeframe:	
During the first week	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Transfusions				
median (full range (min-max))	0 (0 to 4)	0 (0 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants transfused during first week

End point title	Participants transfused during first week
End point description:	
End point type	Secondary
End point timeframe:	
During the first week	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Participants transfused	11	11		

Statistical analyses

Statistical analysis title	Comparison of number of participants infused
Statistical analysis description:	
Mann-Whitney-U test for significance in number of participants infused during the first week in hospital	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Secondary: Infective complications

End point title	Infective complications
End point description:	
End point type	Secondary
End point timeframe:	
During length of study	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Participants	12	8		

Statistical analyses

Statistical analysis title	Comparison of number of infective complications
Statistical analysis description:	
Mann-Whitney-U test for significance in number of infective complications	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.518
Method	Wilcoxon (Mann-Whitney)

Secondary: Cardiovascular complications

End point title	Cardiovascular complications
End point description:	
End point type	Secondary
End point timeframe:	
During length of study	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Participants	10	9		

Statistical analyses

Statistical analysis title	Comparison of number cardiovascular complications
Statistical analysis description:	
Mann-Whitney-U test for significance in number of cardiovascular complications	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Secondary: Cumulated ambulation score

End point title	Cumulated ambulation score
End point description:	
End point type	Secondary
End point timeframe:	
Days 1 to 3	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Score				
median (inter-quartile range (Q1-Q3))	43.5 (24 to 56)	32 (19.2 to 48)		

Statistical analyses

Statistical analysis title	Comparison of cumulated ambulation score
Statistical analysis description:	
Chi-squared test for significance in mean of cumulated ambulation score	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.137
Method	Chi-squared

Secondary: Cumulated ambulation score

End point title	Cumulated ambulation score

End point description:

End point type	Secondary
End point timeframe:	
Days 1 to 3	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Score				
median (full range (min-max))	43.5 (8 to 82)	32 (0 to 85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of hospital stay

End point title	Length of hospital stay
End point description:	

End point type	Secondary
End point timeframe:	
Duration of the study	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: day				
log mean (standard deviation)	2.66 (± 0.45)	2.60 (± 0.54)		

Statistical analyses

Statistical analysis title	Comparison of log mean length of hospital stay
Statistical analysis description:	
Two-sided t-test to test for significance in log mean length of hospital stay	
Comparison groups	Control v Intravenous iron

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.605
Method	t-test, 2-sided

Secondary: Length of hospital stay

End point title	Length of hospital stay
End point description:	
End point type	Secondary
End point timeframe:	
Duration of the study	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: day				
arithmetic mean (inter-quartile range (Q1-Q3))	14.2 (12.4 to 16.4)	13.4 (11.4 to 15.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of postoperative hospital stay

End point title	Length of postoperative hospital stay
End point description:	
End point type	Secondary
End point timeframe:	
Period remain hospitalised following operation	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: day				
log mean (standard deviation)	2.56 (± 0.48)	2.48 (± 0.59)		

Statistical analyses

Statistical analysis title	Comparison of log mean length of hospital stay
Statistical analysis description:	
Two-sided t-test to test for significance in log mean length of postoperative hospital stay	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.527
Method	t-test, 2-sided

Secondary: Length of postoperative hospital stay

End point title	Length of postoperative hospital stay
End point description:	
End point type	Secondary
End point timeframe:	
Period remain hospitalised following operation	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: day				
arithmetic mean (inter-quartile range (Q1-Q3))	12.9 (11.1 to 15)	12 (9.9 to 14.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Discharge destination

End point title	Discharge destination
End point description:	
End point type	Secondary

End point timeframe:

Discharge from hospital

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Participants				
Died	0	3		
Nursing Home	1	2		
Own Home	27	25		
Rehab hospital	11	7		
Residential Home	1	2		
Warden controlled accommodation	1	0		

Statistical analyses

Statistical analysis title	Comparison of type of discharge destination
Statistical analysis description:	
Mann-Whitney-U test for significance in type of discharge destination	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.349
Method	Wilcoxon (Mann-Whitney)

Secondary: Mortality at 30-days

End point title	Mortality at 30-days
End point description:	
End point type	Secondary
End point timeframe:	
30-days post randomisation	

End point values	Control	Intravenous iron		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Participant	0	4		

Statistical analyses

Statistical analysis title	Comparison of mortality at 30 days
Statistical analysis description:	
Chi-square test for significance in mortality at 30 days	
Comparison groups	Control v Intravenous iron
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.112
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From randomisation to the day 7 assessment	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Control
Reporting group description:	
Control group	
Reporting group title	Intravenous iron
Reporting group description:	
Intravenous iron	

Serious adverse events	Control	Intravenous iron	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 41 (9.76%)	6 / 39 (15.38%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	3	
Injury, poisoning and procedural complications			
Femoral neck fracture	Additional description: The participant independently went to the bathroom. They were heard shouting and were found lying on the floor. They had pain itn the right leg/hip and a small skin tear on their right elbow. A pelvic x-ray showed a right fractured neck of femur.		
subjects affected / exposed	1 / 41 (2.44%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive	Additional description: The participant had known congestive heart failure. They developed worsening congestive heart failure with a probable chest infection. Last dose of IMP was administered 7 days prior to event onset date.		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arrhythmia	Additional description: Participant 1: Tachycardia; hypotension. Tachycardia worsened to 146 bpm. History of SVT. Venofer given without AE. Participant 2: Developed a cardiac arrythmia, supraventricular tachycardia, resulting in hypotension		

subjects affected / exposed	0 / 41 (0.00%)	2 / 39 (5.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower respiratory tract infection	Additional description: Participant 1: Hypoxic Participant 2: Hospital acquired pneumonia. Also had heart failure. Participant 3: Known congestive heart failure. Worsened plus probable chest infection. Last dose of IMP was administered 7 days prior to event onset date.		
subjects affected / exposed	2 / 41 (4.88%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease	Additional description: Participant 1: Had a fall. Had basal crackles;tachycardia; a head injury. A chest infection deemed; antibiotics given. Resulted in infective exacerbation of COPD. Participant 2: Tachycardic post-operatively. Worsening shortness of breath		
subjects affected / exposed	0 / 41 (0.00%)	2 / 39 (5.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumonia bacterial	Additional description: The participant had abdominal discomfort; had CTPA showing pleural effusions; bi-basal consolidation with atelectasis. Received antibiotics (levofloxacin) for hospital acquired pneumonia.They had nausea (increased), constipation and shallow breathing		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus	Additional description: The participant developed vomiting and and diarrhoea (severe). It was likely a secondary norovirus infection. There had been an outbreak of norovirus on the ward where the patient was being nursed.		
subjects affected / exposed	1 / 41 (2.44%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Control	Intravenous iron	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	7 / 39 (17.95%)	
Surgical and medical procedures			
Hypotension	Additional description: The participant was hypotensive on return from surgery on day 2. Blood pressue pre-administration was 96 / 56 mmHg. Blood pressure post-administration was 99 / 63 mmHg.		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences (all)	0	1	

General disorders and administration site conditions			
Pyrexia	Additional description: Participant 1: Research team made the decision not to give study medication. Participant to be reviewed by doctor regarding pyrexia. Participant 2: IMP was not given on the grounds of patient safety. The participant will be observed.		
subjects affected / exposed	0 / 41 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Eye disorders			
Vision blurred	Additional description: Participant developed blurred vision shortly after commencing infusion. Venofer discontinued.		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea	Additional description: Participant said she felt very "queasy" following the iron infusion administered on day 1. This increased post infusion.		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus	Additional description: Participant had itching following IMP administration on day 1.No evidence of a rash post-operation.They received spinal and diamorphine in theatre. PI deems likely to be associated with analgesia. Participant withdrew from further IMP administration.		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences (all)	0	1	
Injection site irritation	Additional description: Participant declined to have third dose of Venofer. Claimed second dose stung too much and problems with cannulae were related to iron. They remained in the study and had seven day blood tests.		
subjects affected / exposed	0 / 41 (0.00%)	1 / 39 (2.56%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2013	Addition of Heart of England NHS Foundation Trust hospital in Birmingham as a second site.
28 October 2013	Temporary halt for review
13 March 2014	Study restart following temporary halt.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 October 2013	Temporay halt for review following three deaths in the treatment arm. All deaths are considered by research team to be unrelated to trial participation (the trial population is frail elderly; the causes of death are not related to intravenous iron). These death cases were independently reviewed during which time there was a temporary suspension.	10 December 2013

Notes:

Limitations and caveats

 None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24015990