Clinical trial results:
A prospective randomisd open label study to determine the effects of intravenous iron administration on markers of acute kidney injury in chronic kidney disease (CKD)

Summary

EudraCT number	2010-020452-64
Trial protocol	GB
Global end of trial date	08 March 2019

Results information

Result version number	v1 (current)
This version publication date	08 May 2022
First version publication date	08 May 2022
Summary attachment (see zip file)	The comparative effect of intravenous iron on oxidative stress and inflammation in patients with Chronic Kidney Disease (CKD) and iron deficiency - A randomized controlled-pilot study. Short title: IR ([KRCP-20-120].docx)

Trial information

Trial identification

Sponsor protocol code	version2.0

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hull University Teaching Hospitals NHS Trust
Sponsor organisation address	Castle Road, Cottingham, United Kingdom, HU16 5JQ
Public contact	Research and Development, Hull University Teaching Hospitals NHS Trust, +44 01482 461903, research.development@hey.nhs.uk
Scientific contact	Academic Renal Research, Hull University Teaching Hospitals NHS Trust, +44 01482 605260, sunil.bhandari@hey.nhs.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	08 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2019
Global end of trial reached?	Yes
Global end of trial date	08 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether three preparations of intravenous iron therapy affect markers of kidney injury including NGAL levels in serum and urine as a result of intravenous Iron therapy in patients with chronic kidney disease (CKD).
The primary objective of this study is to:
•To assess the effects of three preparations of intravenous (IV) iron in a cohort of CKD patients with biochemical functional or absolute iron deficiency (ferritin level less than 200 microg/l or/and transferrin saturation of <20%) on measures renal injury.
•To determine whether iron isomaltoside, iron sucrose and iron dextran differ in their effects on markers of renal injury in comparison to baseline measures during the lead in period.
•To determine whether IVI iron leads to potential transient AKI from assessment of changes in markers of renal injury from baseline markers prior to iron administration.
To determine for iron isomaltoside if there is a difference related to dose of drug (low dose and normal dose)

Protection of trial subjects:

Robust eligibility criteria to ensure that potential participants who could not successfully complete the required protocol assessments were not entered into the trial.
Blood value ranges were specified to ensure only participants who require iron infusions and would contribute to the primary and secondary outcomes of the trial.
Women who were pregnant, intending to become pregnant or lactating were excluded from the trial.
Certain medical conditions excluded participants so they were unnecessarily enrolled in a trial that would neither benefit them or the outcome of the trial.

Background therapy:

There were no other treatments given that were not test or comparators for the trial.

Evidence for comparator:

- To assess the effects of three preparations of intravenous (IV) iron in a cohort of CKD patients with biochemical functional or absolute iron deficiency (ferritin level less than 200 g/l or/and transferrin saturation of <20%) on measures renal injury.
- To determine whether iron sucrose, iron isomaltoside and iron dextran differ in their effects on markers of renal injury in comparison to baseline measures during the lead in period.
- To determine whether IVI iron leads to potential transient AKI from assessment of changes in markers of renal injury from baseline markers prior to iron administration.
- To determine if changes in the above measurements vary between low dose and normal dose Iron isomaltoside

Actual start date of recruitment	25 April 2014
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: 40
Worldwide total number of subjects	40
EEA total number of subjects	0

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)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In this randomized open-label explorative single center study in the U.K, non-dialysis-dependent CKD patients with iron deficiency were randomized (1:1:1:1) to a single infusion of 200 mg Iron Dextran, or Iron Sucrose (IS) or 200 mg or 1000 mg Ferric Derisomaltose (FDI) and were followed up for 3 months.

Pre-assignment

Screening details:

Patients will be evaluated at baseline and according to the schedule after administration of iron replacement therapy. They will then receive routine clinical care until the end of the study. After one year a clinical check of their medical records will made to identify any hospital admissions, any treatment with dialysis, morbidities and mortalit

Period 1

Period 1 title	Screening
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	single infusion of 200 mg iron dextran

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	single infusion of 200 mg iron sucrose

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)

Arm title	Single infusion of 200mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Number of subjects in period 1	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose
Started	10	10	10
Completed	10	10	10

Number of subjects in period 1	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10
Completed	10

Period 2

Period 2 title	Baseline (V2a)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	single infusion of 200 mg iron dextran
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 200mg ferric derisomaltose (FDI)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	single infusion of 200 mg iron sucrose
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)

Number of subjects in period 2	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10	10	10
Completed	10	10	10

Number of subjects in period 2	single infusion of 200 mg iron sucrose
Started	10
Completed	10

Period 3

Period 3 title	2hr Post Iron (V2b)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	single infusion of 200 mg iron dextran

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	single infusion of 200 mg iron sucrose

Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)

Arm title	Single infusion of 200mg ferric derisomaltose (FDI)

Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Number of subjects in period 3	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose
Started	10	10	10
Completed	10	10	10

Number of subjects in period 3	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10
Completed	10

Period 4

Period 4 title	1 Day post Iron infusion (V3a)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	single infusion of 200 mg iron dextran
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	single infusion of 200 mg iron sucrose
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)

Arm title	Single infusion of 200mg ferric derisomaltose (FDI)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Number of subjects in period 4	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose
Started	10	10	10
Completed	10	10	10

Number of subjects in period 4	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10
Completed	10

Period 5	
Period 5 title	1 week post Iron infusion (V3b)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	single infusion of 200 mg iron dextran
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution	
Arm title	single infusion of 200 mg iron sucrose
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)	
Arm title	Single infusion of 200mg ferric derisomaltose (FDI)

Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)

Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Number of subjects in period 5	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10	10	10
Completed	10	10	10
Not completed	0	0	0
Adverse event, serious fatal	-	-	-

Number of subjects in period 5	Single infusion of 1000mg ferric derisomaltose (FDI)
Started	10
Completed	9
Not completed	1
Adverse event, serious fatal	1

Period 6

Period 6 title	1 month post Iron infusion (V4)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	single infusion of 200 mg iron dextran

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	single infusion of 200 mg iron sucrose

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)

Arm title	Single infusion of 200mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Number of subjects in period 6	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10	10	10
Completed	10	10	10

Number of subjects in period 6	Single infusion of 1000mg ferric derisomaltose (FDI)
Started	9
Completed	9

Period 7

Period 7 title	3 months post Iron infusion (V5)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	single infusion of 200 mg iron dextran

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Investigational medicinal product name	Cosmofer 200mg IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	Single infusion of 1000mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Monofer 1000mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Arm title	single infusion of 200 mg iron sucrose

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Venofer 200mg IV
Investigational medicinal product code	
Other name	Iron sucrose
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France)

Arm title	Single infusion of 200mg ferric derisomaltose (FDI)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Monofer 200mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were recruited and randomly allocated in a 1:1:1:1 ratio to receive a single infusion of either 200 mg IS (Venofer, Vifor Pharma, Paris, France), 200 mg ID (Cosmofer, Pharmacosmos A/S, Holbaek, Denmark), or 200 mg or 1,000 mg FDI (Monofer, Pharmacosmos A/S) as per summary product characteristics and standard practice in our institution

Number of subjects in period 7	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose
Started	10	9	10
Completed	10	7	10
Not completed	0	2	0
Physician decision	-	1	-
Pregnancy	-	1	-

Number of subjects in period 7	Single infusion of 200mg ferric derisomaltose (FDI)
Started	10
Completed	10
Not completed	0
Physician decision	-
Pregnancy	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	single infusion of 200 mg iron dextran
Reporting group description: -	
Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron sucrose
Reporting group description: -	
Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron dextran
Reporting group description: -	
Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron sucrose
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron dextran
Reporting group description: -	
Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron sucrose
Reporting group description: -	
Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron dextran
Reporting group description: -	
Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron sucrose
Reporting group description: -	
Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron dextran
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron sucrose
Reporting group description: -	
Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron dextran
Reporting group description: -	
Reporting group title	single infusion of 200 mg iron sucrose
Reporting group description: -	
Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)
Reporting group description: -	
Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)

Reporting group description: -

Reporting group title	single infusion of 200 mg iron dextran

Reporting group description: -

Reporting group title	Single infusion of 1000mg ferric derisomaltose (FDI)

Reporting group description: -

Reporting group title	single infusion of 200 mg iron sucrose

Reporting group description: -

Reporting group title	Single infusion of 200mg ferric derisomaltose (FDI)

Reporting group description: -

Subject analysis set title	Oxidative Stress and labile plasma iron
Subject analysis set type	Per protocol

Subject analysis set description:

Administration of IV iron resulted in a rise in mean TBARS level within 2 hours (pre-infusion: 1,083.0 ± 117.1 nM, 2 hours post-infusion: 1,552.6 ± 156.0 nM; p = 0.060, all groups combined) (Fig. 2). The increased levels returned to baseline within 1 week. The greatest rise in TBARS was noted in the 1,000 mg FDI group, which was not statistically significant (pre-infusion: 846.0 ± 108.9 nM, 2 hours post-infusion: 1,865.0 ± 203.2 nM; p = 0.250). There was a non-statistically significant increase with IS that occurred 1 week post-infusion (pre-infusion: 906.3 ± 140.9 nM, 1 week post-infusion: 1,261.3 ± 369.3 nM; p = 0.990). There were no statistically significant differences for the effect on TBARS between products used or between the high-dose and low-dose FDI.

Subject analysis set title	Labile plasma iron (LBI)
Subject analysis set type	Per protocol

Subject analysis set description:

Mean LPI levels increased significantly within 2 hours of infusion and returned to baseline within 1 week (pre-infusion: 1.4 ± 0.5 ΔFU/min, 2 hours post-infusion: 7.4 ± 2.4 ΔFU/min; p = 0.006, all groups combined) (Fig. 3). LPI increased in the ID and IS groups, but these did not reach statistical significance. The concentration of LPI with 200 mg FDI remained constant and similar to the baseline level throughout the study. There was a significant increase in LPI with 1,000 mg FDI (pre-infusion: 0.33 ± 0.2 ΔFU/min, 2 hours post-infusion: 19.6 ± 7.1 ΔFU/min; p < 0.001), and the level at 2 hours post-infusion was significantly higher when compared to the 200 mg FDI group (19.6 ± 7.1 ΔFU/min vs. 1.6 ± 0.8 ΔFU/min; p < 0.001). These changes resolved within 1 week.

Subject analysis set title	CRP level (Inflammation)
Subject analysis set type	Per protocol

Subject analysis set description:

There was a rise in mean CRP level within a day of infusion, which returned to baseline levels within 1 month (pre-infusion: 7.5 ± 1.6 mg/L, 1 day post-infusion: 17.6 ± 8.0 mg/L; p = 0.400/ 1 month post-infusion: 7.5 ± 1.7 mg/L; p > 0.999, all groups combined). This rise was more evident in patients receiving IS (pre-infusion: 8.1 ± 3.3 mg/L, 1 day post-infusion: 36.1 ± 27.0 mg/L; p = 0.550). The changes in CRP did not reach statistical significance for FDI at any dose (Fig. 4).

Subject analysis set title	Interleukin concentrations
Subject analysis set type	Per protocol

Subject analysis set description:

A transient fall in IL-10 within one month and a rise in IL-8 within 1 week of IV iron infusion were observed across the treatment groups; IL-6 was unaffected. IL-1β did not reach detectable levels during the study. A transient rise in IL-10 within 2 hours of infusion was noted with IS

Subject analysis set title	Haemoglobin concentration
Subject analysis set type	Per protocol

Subject analysis set description:

For all groups combined, hemoglobin concentration rose to its maximal level after one month and was sustained until the end of the study at 3 months (p > 0.999). The increase in hemoglobin concentration was not significantly different between the iron compounds, and no statistically significant difference was noted between high-dose and low-dose FDI (p > 0.999 throughout study)

Subject analysis set title	TSAT
Subject analysis set type	Per protocol

Subject analysis set description:

TSAT increased within 2 hours post-infusion (up to 80%, all groups combined) and returned to baseline level by the first week (Fig. 5). This transient rise from baseline to 2 hours post-infusion was statistically significant in both the 1,000 mg FDI (17.8% to 98.7%; p < 0.001) and IS groups (21.1% to 91.4%; p < 0.001). High-dose FDI produced a significant change in TSAT at 2 hours and 1 day post-infusion when

compared with low-dose FDI that persisted for 1 week (FDI of 1,000 mg vs. 200 mg; 2 hours post-infusion: 98.7% vs. 58.3%, p = 0.005; 1 day post-infusion: 100% vs. 51.8%, p < 0.001). There was no statistically significant difference between the different iron preparations at 2 hours post-infusion.

Subject analysis set title	Serrum ferritin
Subject analysis set type	Per protocol

Subject analysis set description:

The mean SF level rose within 2 hours post-infusion to achieve its maximal mean concentration at 1 week (pre-infusion: 68.8 ± 8.0 µg/L, 1 week post-infusion: 216.2 ± 36.6 µg/L, 3 months post-infusion: 122.6 ± 23.1 µg/L; all groups combined) (Fig. 6). The 1,000 mg FDI group produced the greatest and longest-lasting iron repletion (pre-infusion: 69.1 ± 18.4 µg/L, 1 week post-infusion: 505.9 ± 105.5 µg/L, 3 months post-infusion: 271.0 ± 83.3 µg/L), which remained significantly higher than baseline throughout the study (baseline to 1 week post-infusion, p < 0.001; baseline to 3 months post-infusion, p = 0.007). The 1,000 mg FDI dose achieved a statistically significantly greater change in SF when compared to the 200 mg FDI dose throughout the study (p < 0.001).

Subject analysis set title	PWV
Subject analysis set type	Per protocol

Subject analysis set description:

There was a trend for a reduction in mean PWV throughout the study across all groups, which did not reach statistical significance (pre-infusion: 7.5 ± 0.4 m/sec, 3 months post-infusion: 6.7 ± 0.4 m/sec; p > 0.999). There was no significant difference between the compound used and improvement in PWV. No difference was noted between high-dose and low-dose FDI. A similar improvement tendency was observed for augmentation index

Subject analysis set title	E-selectin and P-selectin
Subject analysis set type	Per protocol

Subject analysis set description:

IV iron did not significantly affect E-selectin during the study, regardless of iron preparation or dose. A non-statistically significant decrease in mean P-selectin level was seen (pre-infusion: 75.0 ± 6.4 ng/mL; 2 hours post-infusion: 72.4 ± 6.5 ng/mL; 3 months post-infusion: 68.7 ± 6.9 ng/mL; p > 0.999, all groups combined); no significant differences in P-selectin were seen between the different IV iron groups or between different doses of FDI

Subject analysis set title	SF-36 Quality of Life Questionnaire
Subject analysis set type	Per protocol

Subject analysis set description:

There was a trend for improvement in all domains of the SF-36 following iron administration for all iron treatment groups combined and with each compound separately through the completion of the study. This was not statistically significant

Subject analysis set title	Augementation Index (%)
Subject analysis set type	Per protocol

Subject analysis set description:

An indirect measure of arterial stiffness and increases with age.

Primary: SF-36 Questionnaire

End point title	SF-36 Questionnaire

End point description:

End point type	Primary

End point timeframe:

Baseline, 1 month, 3 months

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	10	10
Units: quantitative units				
arithmetic mean (standard error)				
Physical Status Component	41.0 (± 2.4)	35.3 (± 3.6)	36.0 (± 3.6)	38.5 (± 4.5)
Mental status component	43.9 (± 4.1)	45.9 (± 4.5)	41.6 (± 3.8)	40.3 (± 2.7)
Physical functioning	59.5 (± 8.5)	40.6 (± 10.1)	47.0 (± 11.0)	54.5 (± 11.6)
Role limitations due to physical functioning	47.5 (± 10.5)	43.8 (± 11.4)	44.4 (± 13.4)	49.4 (± 11.5)
Bodily pain	62.9 (± 10.1)	51.9 (± 9.7)	51.8 (± 9.0)	54.9 (± 10.7)
General health	42.7 (± 5.3)	34.2 (± 6.4)	24.4 (± 6.1)	25.8 (± 7.4)
Vitality	36.9 (± 6.2)	40.3 (± 5.5)	26.3 (± 8.9)	23.8 (± 5.9)
Social function	60.0 (± 10.0)	58.3 (± 11.4)	56.3 (± 10.4)	58.8 (± 8.8)
Role limitations due to emotional functioning	60.8 (± 10.5)	62.0 (± 11.9)	55.0 (± 13.0)	51.7 (± 10.3)
Mental health	70.0 (± 7.5)	67.2 (± 10.0)	64.5 (± 6.8)	58.5 (± 4.2)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: quantitative units				
arithmetic mean (standard error)				
Physical Status Component	45.0 (± 3.3)	38.7 (± 4.2)	37.1 (± 4.9)	38.6 (± 4.5)
Mental status component	47.1 (± 3.3)	48.7 (± 4.8)	45.5 (± 4.7)	45.4 (± 4.4)
Physical functioning	66.7 (± 7.4)	43.8 (± 12.6)	52.1 (± 16.2)	48.9 (± 12.9)
Role limitations due to physical functioning	65.3 (± 8.4)	53.1 (± 12.0)	40.2 (± 14.6)	52.8 (± 13.3)
Bodily pain	69.4 (± 8.3)	73.0 (± 9.8)	61.4 (± 13.2)	56.6 (± 9.6)
General health	49.9 (± 6.0)	35.1 (± 9.9)	28.0 (± 8.9)	37.8 (± 11.0)
Vitality	46.5 (± 6.6)	49.2 (± 8.0)	42.9 (± 9.9)	34.7 (± 6.6)
Social function	70.8 (± 8.1)	64.1 (± 11.7)	60.7 (± 12.9)	69.4 (± 11.2)
Role limitations due to emotional functioning	75.0 (± 8.4)	62.5 (± 13.9)	60.7 (± 14.5)	67.4 (± 11.5)
Mental health	70.6 (± 6.3)	77.5 (± 9.2)	69.3 (± 9.3)	64.4 (± 7.5)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	9

Units: quantitative units				
arithmetic mean (standard error)				
Physical Status Component	42.5 (± 3.7)	35.7 (± 3.6)	32.9 (± 4.0)	40.1 (± 4.2)
Mental status component	44.1 (± 3.0)	41.9 (± 6.2)	44.5 (± 6.4)	44.3 (± 4.9)
Physical functioning	59.4 (± 11.0)	39.0 (± 15.2)	42.5 (± 16.1)	52.5 (± 11.1)
Role limitations due to physical functioning	54.9 (± 10.2)	40.0 (± 13.8)	32.3 (± 15.8)	56.3 (± 11.8)
Bodily pain	62.8 (± 9.6)	53.6 (± 8.6)	43.2 (± 11.6)	62.3 (± 9.5)
General health	43.7 (± 7.7)	30.4 (± 12.3)	25.7 (± 9.0)	35.4 (± 11.3)
Vitality	45.1 (± 7.5)	33.8 (± 12.6)	36.5 (± 11.0)	32.0 (± 8.6)
Social function	63.9 (± 9.2)	55.0 (± 14.0)	60.4 (± 16.6)	68.8 (± 9.7)
Role limitations due to emotional functioning	58.3 (± 12.4)	43.3 (± 15.2)	54.2 (± 16.1)	68.7 (± 12.0)
Mental health	68.9 (± 4.8)	68.0 (± 13.9)	65.0 (± 12.6)	63.1 (± 7.4)

Attachments (see zip file)	SF-36.pdf

Statistical analyses

Statistical analysis title	Quality of life

Statistical analysis description:

There was a trend for improvement in all domains of the SF-36 following iron administration for all iron treatment groups combined and with each compound separately through the completion of the study. This was not statistically significant

Comparison groups	single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v Single infusion of 1000mg ferric derisomaltose (FDI)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.999
Method	Chi-squared
Parameter estimate	No parameter estimated.

Primary: P-Selectin

End point title	P-Selectin

End point description:

End point type	Primary

End point timeframe:

Baseline, 2hr, 1 day, 1 week, 1 month, 3 months

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	10	10
Units: ng/ml				
arithmetic mean (standard error)	92.9 (± 18.5)	61.1 (± 6.1)	76.4 (± 15.1)	69.0 (± 7.6)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	92.4 (± 18.1)	64.1 (± 7.3)	77.5 (± 17.1)	59.9 (± 8.4)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	86.4 (± 15.4)	83.3 (± 14.2)	65.9 (± 16.9)	56.9 (± 6.1)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	83.0 (± 17.2)	60.1 (± 8.4)	96.2 (± 18.7)	70.2 (± 8.5)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose	Single infusion of 1000mg ferric

			(FDI)	derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	79.7 (± 9.1)	67.2 (± 9.7)	62.1 (± 9.1)	92.7 (± 34.2)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	9
Units: ng/ml				
arithmetic mean (standard error)	88.0 (± 24.8)	68.2 (± 9.7)	54.9 (± 4.7)	64.2 (± 6.2)

Statistical analyses

Statistical analysis title	Endovascular function

Statistical analysis description:

IV iron did not significantly affect E-selectin during the study, regardless of iron preparation or dose. A non-statistically significant decrease in mean P-selectin level was seen (pre-infusion: 75.0 ± 6.4 ng/mL; 2 hours post-infusion: 72.4 ± 6.5 ng/mL; 3 months post-infusion: 68.7 ± 6.9 ng/mL; p > 0.999, all groups combined); no significant differences in P-selectin were seen between the different IV iron groups or between different doses of FDI

Comparison groups	single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v Single infusion of 1000mg ferric derisomaltose (FDI)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [1]
Method	Chi-squared
Parameter estimate	No parameter estimated.

Notes:

[1] - Non-statistically significant.

Primary: E-selectin

End point title	E-selectin

End point description:

End point type	Primary

End point timeframe:

Baseline, 2hr, 1 day, 1 week, 1 month, 3 months

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	10	10
Units: ng/ml				
arithmetic mean (standard error)	59.8 (± 10.6)	68.3 (± 12.7)	67.9 (± 16.5)	68.5 (± 9.3)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	61.1 (± 9.7)	72.6 (± 11.8)	73.0 (± 15.4)	76.9 (± 10.1)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	61.7 (± 10.2)	68.6 (± 9.3)	72.1 (± 16.5)	79.2 (± 11.2)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10

Units: ng/ml				
arithmetic mean (standard error)	66.6 (± 12.1)	72.8 (± 10.6)	86.1 (± 20.0)	74.4 (± 10.7)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: ng/ml				
arithmetic mean (standard error)	62.7 (± 11.2)	72.4 (± 10.8)	60.8 (± 15.9)	69.0 (± 8.4)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	9
Units: ng/ml				
arithmetic mean (standard error)	60.9 (± 13.2)	51.5 (± 6.8)	71.3 (± 18.9)	81.4 (± 14.2)

Attachments (see zip file)	j-krcp-20-120suppl5.pdf

Statistical analyses

Statistical analysis title	Endovascular function
Comparison groups	single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v Single infusion of 1000mg ferric derisomaltose (FDI) v single infusion of 200 mg iron dextran v single infusion of 200 mg iron sucrose v Single infusion of 200mg ferric derisomaltose (FDI) v Single infusion of 1000mg ferric derisomaltose (FDI)

Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.999
Method	Chi-squared
Parameter estimate	No parameter estimated.

Secondary: Pulse wave velocity

End point title	Pulse wave velocity

End point description:

End point type	Secondary

End point timeframe:

Across all timepoints on all arms.

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	10	10
Units: m/sec				
arithmetic mean (standard error)	8.3 (± 0.9)	6.9 (± 1.0)	6.9 (± 0.6)	8.1 (± 0.6)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: m/sec				
arithmetic mean (standard error)	7.2 (± 1.2)	8.1 (± 0.9)	6.8 (± 0.6)	6.3 (± 0.8)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: m/sec				
arithmetic mean (standard error)	7.2 (± 1.0)	7.4 (± 1.0)	6.6 (± 0.8)	7.7 (± 0.4)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: m/sec				
arithmetic mean (standard error)	7.1 (± 0.7)	7.5 (± 1.2)	6.5 (± 0.6)	7.7 (± 0.4)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: m/sec				
arithmetic mean (standard error)	6.4 (± 0.7)	6.9 (± 1.4)	7.1 (± 0.6)	7.4 (± 1.0)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	9
Units: m/sec				
arithmetic mean (standard error)	6.8 (± 1.1)	6.5 (± 0.7)	6.5 (± 0.7)	6.9 (± 0.8)

End point values	PWV			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: m/sec				
arithmetic mean (standard error)	7.1 (± 0.4)			

Attachments (see zip file)	j-krcp-20-120suppl5.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Augmentation Index

End point title	Augmentation Index

End point description:

End point type	Secondary

End point timeframe:

Baseline, 2hrs, 1 day, 1 week, 1 month, 3 months

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	10	10
Units: %				
arithmetic mean (standard error)	24.4 (± 4.1)	20.2 (± 4.8)	19.8 (± 2.3)	19.7 (± 3.4)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: %				
arithmetic mean (standard error)	21.6 (± 5.0)	23.5 (± 3.8)	17.1 (± 3.6)	18.4 (± 3.9)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: %				
arithmetic mean (standard error)	14.4 (± 5.6)	24.4 (± 4.5)	19.1 (± 2.8)	16.3 (± 3.0)

End point values	single infusion of 200 mg iron dextran	Single infusion of 1000mg ferric derisomaltose (FDI)	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: %				
arithmetic mean (standard error)	17.0 (± 4.2)	21.3 (± 4.9)	17.6 (± 2.7)	19.1 (± 3.3)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: %				
arithmetic mean (standard error)	19.1 (± 5.6)	16.6 (± 4.5)	15.6 (± 2.6)	20.4 (± 2.7)

End point values	single infusion of 200 mg iron dextran	single infusion of 200 mg iron sucrose	Single infusion of 200mg ferric derisomaltose (FDI)	Single infusion of 1000mg ferric derisomaltose (FDI)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	9
Units: %				
arithmetic mean (standard error)	16.0 (± 4.5)	19.4 (± 3.5)	14.4 (± 4.4)	24.7 (± 3.3)

Attachments (see zip file)	j-krcp-20-120suppl5.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The AE reporting period for this trial begins at visit 1, and ends 30 days after the patients final research study visit.

Adverse event reporting additional description:

Each trial subject will be questioned about adverse events at each visit. The investigator will record all directly observed AEs and all AEs spontaneously reported by the trial subject.
A pre-existing condition (i.e. a disorder present before the AE reporting period started and noted on the pre-treatment medical history/physical examination form/

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Adverse events shown within Subject Disposition at the time it occurs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 July 2012	Revision of trial protocol. Study has not commenced but this revision is to include a third treatment option arm. Therefore patients will be randomised to one of four arms. the initial study arms remain but the two additional arms include use of the iron preparation Monofer (iron isomaltoside) which is currently on the hospital formula and in clinical use in the United kingdom and locally in Hull and East Yorkshire Hospitals NHS Trust. The reason for the amendment is the increasing use of Monofer (iron isomaltoside) within the department but data remains lacking in comparison to the two conventional iron preparations and the mechanistic data is lacking in all three preparations. Therefore this revised study which is more comprehensive will in the future allow a more evidenced based approach to optimal treatment with parenteral iron therapy and also may lead to cost savings within the health service
08 February 2018	Reduction of recruitment numbers from 100 to 40
16 November 2018	The removal of the 1 year post-infusion check of medical records with no negative consequences to the patients who have already completed the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30947751