



Clinical trial results:

Is intravenous iron and darbepoetin more effective than oral iron in reducing blood transfusion requirements for patients undergoing cardiac surgery

Summary

EudraCT number	2011-003695-36
Trial protocol	GB
Global end of trial date	11 November 2019

Results information

Result version number	v1 (current)
This version publication date	31 January 2020
First version publication date	31 January 2020
Summary attachment (see zip file)	INITIATE Clinical study summary report (INITIATE - SUMMARY REPORT.pdf)

Trial information

Trial identification

Sponsor protocol code	11/LO/1310
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Additional study identifiers

ISRCTN number	ISRCTN41421863
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Brighton and Sussex University Hospitals Trust
Sponsor organisation address	Royal Sussex County Hospital Eastern Road, Brighton, United Kingdom, BN2 5BE
Public contact	Mr Scott Harfield, Brighton and Sussex University Hospitals, 044 01273 696955, Scott.Harfield@bsuh.nhs.uk
Scientific contact	Mr Scott Harfield, Brighton and Sussex University Hospitals, 044 01273 696955, Scott.Harfield@bsuh.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	11 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 November 2019
Global end of trial reached?	Yes
Global end of trial date	11 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In patients who have a low haemoglobin level before surgery, will treatment using a combination of intravenous iron and darbepoetin result in less blood transfusion after heart surgery than treatment using iron tablets alone.

Protection of trial subjects:

Patients were given full advice and information through the participation information sheet before being asked if they wished to participate in the study and once involved they were asked at each visit whether they wished to continue and were free to withdraw from the study. After treatment the patients were monitored to ensure they were in no distress and all was well before being told that they were free to return home. They were given the contact numbers of the research staff in case they had any queries and also the contact details of the Patient Advice and Liaison Service

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 170
Worldwide total number of subjects	170
EEA total number of subjects	170

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)	170
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details:

Intervention group analysed: 79
Standard care group analysed: 77
Total randomised: 170

Pre-assignment

Screening details:

2799 patients undergoing elective cardiac surgery at the centre were screened for eligibility. An Hb concentration between 100 and 130 g/L (inclusive) was required for inclusion

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Intervention
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Arm description:

Participants in the intervention group received a total dose infusion of iron (III) isomaltoside 1000 (Monofer®). The dose of 1000mg (or 20mg/kg if body weight less than 50kg) was infused

Arm type	Experimental
Investigational medicinal product name	iron (III) isomaltoside 1000 (Monofer®).
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Participants in the intervention group received a total dose infusion of iron (III) isomaltoside 1000 (Monofer®). The dose of 1000mg (or 20mg/kg if body weight less than 50kg) was infused according to the manufacturer's recommended protocol via a peripheral vein

Arm title	Standard of care
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Arm description:

Participants randomised to Standard Care were instructed to see their GP as soon as possible. The participant was given a prescription for 2 week supply of ferrous sulphate and prescribed the maximum tolerated dose of oral ferrous sulphate (starting at 200mg x 3 per day) until the day of surgery. Participants who do not tolerate this dose will be asked to reduce the dose to 200mg x2 or 200mg x1 per day. Concurrent deficiencies in vitamin B12 or folate or abnormal thyroid function will be treated according to standard practice.

Arm type	Active comparator
Investigational medicinal product name	ferrous sulphate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants randomised to Standard Care were instructed to see their GP as soon as possible. The participant was given a prescription for 2 week supply of ferrous sulphate and prescribed the maximum tolerated dose of oral ferrous sulphate (starting at 200mg x 3 per day) until the day of surgery. Participants who do not tolerate this dose will be asked to reduce the dose to 200mg x2 or 200mg x1 per day. Concurrent deficiencies in vitamin B12 or folate or abnormal thyroid function will be treated

according to standard practice.

Number of subjects in period 1	Intervention	Standard of care
Started	86	84
Completed	79	77
Not completed	7	7
Physician decision	7	7

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
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Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	170	170	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	74		
inter-quartile range (Q1-Q3)	68 to 79	-	
Gender categorical			
Units: Subjects			
Female	85	85	
Male	85	85	

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: Participants in the intervention group received a total dose infusion of iron (III) isomaltoside 1000 (Monofer®). The dose of 1000mg (or 20mg/kg if body weight less than 50kg) was infused	
Reporting group title	Standard of care
Reporting group description: Participants randomised to Standard Care were instructed to see their GP as soon as possible. The participant was given a prescription for 2 week supply of ferrous sulphate and prescribed the maximum tolerated dose of oral ferrous sulphate (starting at 200mg x 3 per day) until the day of surgery. Participants who do not tolerate this dose will be asked to reduce the dose to 200mg x2 or 200mg x1 per day. Concurrent deficiencies in vitamin B12 or folate or abnormal thyroid function will be treated according to standard practice.	

Primary: Did participant receive one red cell transfusion on days 0-5

End point title	Did participant receive one red cell transfusion on days 0-5 ^[1]
End point description:	
End point type	Primary
End point timeframe: 0-5 days post surgery	
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: See attached documents for results	

End point values	Intervention	Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	63		
Units: Yes or No	53	63		

Attachments (see zip file)	INITIATE Analysis/INITIATE analysis 1.0.pdf
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

For the duration of the study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18
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Frequency threshold for reporting non-serious adverse events: 0 %

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: See attached documents for adverse events

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2013	Addition to, and clarification of, the exclusion criteria and stipulation of SAE reporting process
06 September 2013	<ol style="list-style-type: none">1. Clarification that a change in Hb count prior to randomisation will not necessarily result in the participant becoming ineligible for the study.2. Indicating that the intravenous iron infusions may be done in CIRU.3. Clarifying that the end of study visit may not necessarily be 6-weeks after surgery, but whenever the post-operative outpatient appointment takes place.4. Amending the AE and SAE reporting to suggest that all AEs will only require recording for trial purposes between IMP administration and surgery, and not post-surgery. SAEs and recognised complications during and after surgery should not be recorded if listed as expected in table 14.3.5. Updating Hb measurement to the new guidelines (g/l instead of g/dl)
29 September 2016	Allowance for interim analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported