Clinical trial results:
Repetitive blood donations and endurance sport performance: does iron supplementation limit the negative effects on hematological parameters?

Summary

EudraCT number	2017-003406-40
Trial protocol	BE
Global end of trial date	31 May 2018

Results information

Result version number	v1 (current)
This version publication date	20 April 2019
First version publication date	20 April 2019

Trial information

Trial identification

Sponsor protocol code	RK2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Université catholique de Louvain
Sponsor organisation address	Place de l'Université 1, Louvain-La-Neuve, Belgium, 1348
Public contact	Louise Deldicque, Université catholique de Louvain, 0032 10474443, louise.deldicque@uclouvain.be
Scientific contact	Louise Deldicque, Université catholique de Louvain, 0032 10474443, louise.deldicque@uclouvain.be

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	01 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2018
Global end of trial reached?	Yes
Global end of trial date	31 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We propose to measure the impact of 3 blood donations, interspersed by 3 months, on blood parameters and on performance during a maximal incremental test and to see whether iron supplementation can limit or even reverse the negative effects of donations on blood parameters reflecting iron status.

Protection of trial subjects:

* At the Rode Kruis Vlanderen, during the blood donation, numerous physicians were present in case of emergency. At the Faculty of Motor Science (Louvain-La-Neuve), during the exercise test, the hemoglobin mass measurement and the blood sample collection, there was always a physician present in case of emergency.
* Plasma ferritin concentrations was checked before starting and during the whole study (1 week before iron supplementation and at day 2, 7, 14, 28 after the beginning of iron supplementation, day 28 being the last day of supplementation. Analyses were repeated at each iron supplementation following blood donation). If a value above 300µg/l ferritin would have been measured, iron supplementation would have been immediately stopped.
* Exercise testing: a medical screening was performed before the beginning of the experiment to ensure that the participants were able to perform maximal exercise tests. In addition, participants were told that they can stop exercising at any time. A test was terminated if a subject shows any untoward signs and symptoms, including pallor, severe nausea and dizziness.
* Subjects were asked to report every adverse events to the investigator until 2 months after the end of the trial and therefore the iron supplementation, even in case of premature clinical trial termination. Every adverse events reported by the subjects was recorded by the Principal investigator and the promotor. The physician evaluated the seriousness and the causality with the product and decided the action to take.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2017
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	Belgium: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	44
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment between September 2017 and November 2017

Pre-assignment

Screening details:

Inclusion criteria:
- age between 18-50 years
- BMI between 20-28 kg/m2
- hours sport per week between 1-6
Screening of 50 subjects. 6 screening failure

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

* Blood donation: subjects were isolated from each other and were blinded using a sterile field so that theywere not be able to see their arm. Moreover, they listened to music through a headphone, . They were all stitched by a needle but no blood was collected for the control-control group
* No information was added on the pill to allow subject to recognize iron or glucose supplementation

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo group

Arm description:

- No blood donation
- Glucose supplementation during 4 weeks following each blood donations for the other groups

Arm type	Placebo
Investigational medicinal product name	Glucose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

400mg/capsule, 1 capsule per day during 4 weeks following each blood donation

Arm title	Donation - placebo group

Arm description:

- Blood donation (3 blood donations with three months of interval)
- Glucose supplementation 4 weeks after each blood donations

Arm type	Placebo
Investigational medicinal product name	Glucose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

400mg/capsule, 1 capsule per day during 4 weeks following each blood donation

Arm title	Donation - 20mg iron group

Arm description:

- Blood donation (three blood donations with three months of interval)
- Iron supplementation: 173.72mg of ferrous gluconate per day during 4 weeks following each blood donation

Arm type	Experimental
Investigational medicinal product name	Losferron 1/4
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Effervescent tablet
Routes of administration	Oral use

Dosage and administration details:

1/4 losferron tablet (173.72 mg of ferrous gluconate) per day during 4 weeks following each blood donation.

Arm title	Donation - 80mg iron group

Arm description:

- Blood donation (three blood donations with three months of interval
- iron supplementation : 695mg of ferrous gluconate per day during 4 weeks following each blood donation

Arm type	Experimental
Investigational medicinal product name	Losferron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Effervescent tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet of losferron per day (695mg of ferrous gluconate) during 4 weeks following each blood donation

Number of subjects in period 1	Placebo group	Donation - placebo group	Donation - 20mg iron group
Started	8	12	12
Completed	7	11	11
Not completed	1	1	1
Adverse event, non-fatal	-	1	-
Lost to follow-up	1	-	1

Number of subjects in period 1	Donation - 80mg iron group
Started	12
Completed	11
Not completed	1
Adverse event, non-fatal	-
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo group
Reporting group description:	
- No blood donation - Glucose supplementation during 4 weeks following each blood donations for the other groups	
Reporting group title	Donation - placebo group
Reporting group description:	
- Blood donation (3 blood donations with three months of interval) - Glucose supplementation 4 weeks after each blood donations	
Reporting group title	Donation - 20mg iron group
Reporting group description:	
- Blood donation (three blood donations with three months of interval) - Iron supplementation: 173.72mg of ferrous gluconate per day during 4 weeks following each blood donation	
Reporting group title	Donation - 80mg iron group
Reporting group description:	
- Blood donation (three blood donations with three months of interval - iron supplementation : 695mg of ferrous gluconate per day during 4 weeks following each blood donation	

Reporting group values	Placebo group	Donation - placebo group	Donation - 20mg iron group
Number of subjects	8	12	12
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	12	12
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	24.3	21.5	22.5
full range (min-max)	18 to 32	18 to 33	19 to 33
Gender categorical Units: Subjects			
Female	0	0	0
Male	8	12	12

Reporting group values	Donation - 80mg iron group	Total	
Number of subjects	12	44	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	44	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	24		
full range (min-max)	19 to 31	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	12	44	

End points

End points reporting groups

Reporting group title	Placebo group
Reporting group description:	
- No blood donation - Glucose supplementation during 4 weeks following each blood donations for the other groups	
Reporting group title	Donation - placebo group
Reporting group description:	
- Blood donation (3 blood donations with three months of interval) - Glucose supplementation 4 weeks after each blood donations	
Reporting group title	Donation - 20mg iron group
Reporting group description:	
- Blood donation (three blood donations with three months of interval) - Iron supplementation: 173.72mg of ferrous gluconate per day during 4 weeks following each blood donation	
Reporting group title	Donation - 80mg iron group
Reporting group description:	
- Blood donation (three blood donations with three months of interval - iron supplementation : 695mg of ferrous gluconate per day during 4 weeks following each blood donation	

Primary: peak oxygen consumption

End point title	peak oxygen consumption
End point description:	
Measurement of this endpoint at several time points: - 1 week before first blood donation - 2 days after first blood donation - 1 week after first blood donation - 2 weeks after first blood donation - 4 weeks after first blood donation - 1 week before second blood donation - 2 days after second blood donation - 1 week after second blood donation - 2 weeks after second blood donation - 4 weeks after second blood donation - 1 week before third blood donation - 2 days after third blood donation - 1 week after third blood donation - 2 weeks after third blood donation - 4 weeks after third blood donation	
End point type	Primary
End point timeframe:	
4 weeks after the third blood donation	

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: mL/min/kg				
arithmetic mean (standard error)	56.4 (± 4.3)	48.6 (± 1.7)	47.4 (± 3.5)	53.5 (± 2.4)

Statistical analyses

Statistical analysis title	mixed ANOVA model

Statistical analysis description:

A mixed ANOVA model (SAS Statistical Software) was used with the subjects as a random variable and groups (placebo, donation alone, donation + 20mg iron and donation + 80mg iron) and condition (time) as fixed independent variables. Contrast analyses were performed to compare means, applying a Sidak correction. Statistical significance was set at $p < 0.05$

Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Variability estimate	Standard error of the mean

Secondary: hemoglobin

End point title	hemoglobin

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: g/dL				
arithmetic mean (standard error)	14.6 (± 0.4)	14.5 (± 0.3)	14.4 (± 0.3)	14.1 (± 0.2)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: red blood cells

End point title	red blood cells

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: 10E12/L				
arithmetic mean (standard error)	4.6 (± 0.1)	4.7 (± 0.1)	4.6 (± 0.1)	4.6 (± 0.1)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Iron

End point title	Iron

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: µg/dL				
arithmetic mean (standard error)	102 (± 15)	85 (± 13)	97 (± 7)	116 (± 12)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Transferrin

End point title	Transferrin

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: g/L				
arithmetic mean (standard error)	2.5 (± 0.03)	2.79 (± 0.09)	2.72 (± 0.09)	2.61 (± 0.09)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Ferritin

End point title	Ferritin

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: µg/L				
arithmetic mean (standard error)	64 (± 8)	28 (± 9)	31 (± 4)	36 (± 6)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Hepcidin

End point title	Hepcidin

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: pg/mL				
arithmetic mean (standard error)	18698 (± 6770)	3824 (± 1095)	7859 (± 2827)	7851 (± 2875)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Eryhtropoietin

End point title	Eryhtropoietin

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: mIU/mL				
arithmetic mean (standard error)	8 (± 1.6)	10.8 (± 1.4)	7.4 (± 0.6)	9.9 (± 1.0)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Soluble transferrin receptor

End point title	Soluble transferrin receptor

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: mg/L				
arithmetic mean (standard error)	2.15 (± 0.24)	2.72 (± 0.19)	2.24 (± 0.18)	2.18 (± 0.19)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Hemoglobin mass

End point title	Hemoglobin mass

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- the day of the first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- the day of the second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- the day of the third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	6	5
Units: g/kg				
arithmetic mean (standard error)	13.59 (± 1.16)	12.22 (± 0.91)	12.36 (± 0.55)	12.75 (± 0.36)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Lactate max

End point title	Lactate max

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after thrid blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: mM				
arithmetic mean (standard error)	8.8 (± 1.5)	7.4 (± 1.1)	11.1 (± 1.1)	9.1 (± 0.9)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Heart rate max

End point title	Heart rate max

End point description:

Measurement of this endpoint at several time points:
- 1 week before first blood donation
- 2 days after first blood donation
- 1 week after first blood donation
- 2 weeks after first blood donation
- 4 weeks after first blood donation
- 1 week before second blood donation
- 2 days after second blood donation
- 1 week after second blood donation
- 2 weeks after second blood donation
- 4 weeks after second blood donation
- 1 week before third blood donation
- 2 days after third blood donation
- 1 week after third blood donation
- 2 weeks after third blood donation
- 4 weeks after third blood donation

End point type	Secondary

End point timeframe:

4 weeks after third blood donation

End point values	Placebo group	Donation - placebo group	Donation - 20mg iron group	Donation - 80mg iron group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	11	11	11
Units: bpm				
arithmetic mean (standard error)	180 (± 4)	184 (± 3)	191 (± 3)	180 (± 3)

Statistical analyses

Statistical analysis title	mixed ANOVA model
Comparison groups	Placebo group v Donation - placebo group v Donation - 20mg iron group v Donation - 80mg iron group
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

- 1 week before blood donation
- blood donation
- 2 days fater blood donation
- 1 week after blood donation
- 2 weeks after blood donation
- 4 weeks after blood donation

Repeated at every 3 blood donations, interval 3 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Donation - 80mg iron group
Reporting group description: -	
Reporting group title	Donation - placebo group
Reporting group description: -	
Reporting group title	Placebo group
Reporting group description: -	
Reporting group title	Donation - 20mg iron group
Reporting group description: -	

Serious adverse events	Donation - 80mg iron group	Donation - placebo group	Placebo group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Donation - 20mg iron group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Donation - 80mg iron group	Donation - placebo group	Placebo group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	2 / 11 (18.18%)	1 / 7 (14.29%)
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	1 / 7 (14.29%)
occurrences (all)	14	1	1
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Non-serious adverse events	Donation - 20mg iron group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	3		
Discomfort			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported