Clinical trial results:
Ferroglycine Sulfate Absorption in patients with Heart Failure and Iron Deficency: an interventional before and after study.

Summary

EudraCT number	2017-000158-21
Trial protocol	SE
Global end of trial date	05 June 2020

Results information

Result version number	v1 (current)
This version publication date	09 February 2022
First version publication date	09 February 2022
Summary attachment (see zip file)	Manuscript (IronAbs Manuscript.docx)

Trial information

Trial identification

Sponsor protocol code	740220

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet, Södersjukhuset
Sponsor organisation address	Sjukhusbacken 10, Stockholm, Sweden, 118 84
Public contact	Clinical Trial Information, Karolinska Institutet, 46 733306965,
Scientific contact	Clinical Trial Information, Karolinska Institutet, 46 812363441, carin.corovic.cabrera@ki.se

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	20 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to study if heart failure with iron deficiency is associated with reduced iron absorption.

Protection of trial subjects:

Subject were given one enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+ (ATC code B03AA01) wich is a well known substans with few desciribed side effects. Venous blood samples were taken before and two hours after administration.
The study was conducted according to principles outlined in the Declaration of Helsinki and was approved by the regional Ethics Committee in Stockholm and the Swedish Medical Products Agency (EudraCT 2017-000158-21). All subjects gave their written informed consent prior to any study specific action was made. All personal data was anomymized.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2017
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	Sweden: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	6
From 65 to 84 years	36

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

We enrolled patients with ID and known and stable CHF, objectively defined as below and with no HF hospitalization or need for iv diuretics within the previous three months. ID was defined as S-Ferritin <100 µg/L, or S-Ferritin 100-299 µg/L and transferrin saturation <20%.

Pre-assignment period milestones

Number of subjects started	42
Number of subjects completed	42

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Patients with HFrEF and iron deficiency

Arm description:

Patients were divided into HF with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF)

Arm type	Experimental
Investigational medicinal product name	One enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+
Investigational medicinal product code	
Other name	ATC code B03AA01, Niferex, Erol AB
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects were instructed to fast from midnight and to abstain from medications known to interact with ferroglycin sulphate (i.e. antacids, calcium supplements) until the test was finished. In the morning they were given one enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+ (ATC code B03AA01, Niferex, Erol AB)

Arm title	Control group

Arm description:

The controls were recruited mainly from a seniors gym and had no ID and no history, symptoms or signs of HF, normal ECG and NT-pro-BNP <125 ng/L

Arm type	Experimental
Investigational medicinal product name	One enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+
Investigational medicinal product code	
Other name	ATC code B03AA01, Niferex, Erol AB
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects were instructed to fast from midnight and to abstain from medications known to interact with ferroglycin sulphate (i.e. antacids, calcium supplements) until the test was finished. In the morning they

were given one enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+ (ATC code B03AA01, Niferex, Erol AB),

Arm title	Patients with HFpEF and iron deficiency

Arm description:

We enrolled patients with ID and known and stable CHF, objectively defined as below and with no HF hospitalization or need for iv diuretics within the previous three months. ID was defined as S-Ferritin <100 µg/L, or S-Ferritin 100-299 µg/L and transferrin saturation <20%5. Patients were divided into HF with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF). Patients with left ventricular ejection fraction (LVEF) <45% were considered to have HFrEF, and patients with LVEF ≥45% with structural and/or functional abnormalities and NT-pro-BNP >125 ng/L were considered to have HFpEF.

Arm type	Experimental
Investigational medicinal product name	One enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+
Investigational medicinal product code	
Other name	ATC code B03AA01, Niferex, Erol AB
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects were instructed to fast from midnight and to abstain from medications known to interact with ferroglycin sulphate (i.e. antacids, calcium supplements) until the test was finished. In the morning they were given one enterocapsule of ferroglycin sulphate complex containing 100 mg Fe2+ (ATC code B03AA01, Niferex, Erol AB)

Number of subjects in period 1	Patients with HFrEF and iron deficiency	Control group	Patients with HFpEF and iron deficiency
Started	15	12	15
Completed	15	12	15

Baseline characteristics

Reporting groups	
Reporting group title	Patients with HFrEF and iron deficiency
Reporting group description:	
Patients were divided into HF with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF)	
Reporting group title	Control group
Reporting group description:	
The controls were recruited mainly from a seniors gym and had no ID and no history, symptoms or signs of HF, normal ECG and NT-pro-BNP <125 ng/L	
Reporting group title	Patients with HFpEF and iron deficiency
Reporting group description:	
We enrolled patients with ID and known and stable CHF, objectively defined as below and with no HF hospitalization or need for iv diuretics within the previous three months. ID was defined as S-Ferritin <100 µg/L, or S-Ferritin 100-299 µg/L and transferrin saturation <20%5. Patients were divided into HF with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF). Patients with left ventricular ejection fraction (LVEF) <45% were considered to have HFrEF, and patients with LVEF ≥45% with structural and/or functional abnormalities and NT-pro-BNP >125 ng/L were considered to have HFpEF.	

Reporting group values	Patients with HFrEF and iron deficiency	Control group	Patients with HFpEF and iron deficiency
Number of subjects	15	12	15
Age categorical Units: Subjects			
Adults (18-84 years)	15	12	15
Gender categorical Units: Subjects			
Female	5	4	6
Male	10	8	9

Reporting group values	Total		
Number of subjects	42		
Age categorical Units: Subjects			
Adults (18-84 years)	42		
Gender categorical Units: Subjects			
Female	15		
Male	27		

Subject analysis sets	
Subject analysis set title	Overall study
Subject analysis set type	Per protocol
Subject analysis set description:	
Overall study	

Reporting group values	Overall study		
Number of subjects	42		
Age categorical Units: Subjects			
Adults (18-84 years)	42		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Patients with HFrEF and iron deficiency

Reporting group description:

Patients were divided into HF with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF)

Reporting group title	Control group

Reporting group description:

The controls were recruited mainly from a seniors gym and had no ID and no history, symptoms or signs of HF, normal ECG and NT-pro-BNP <125 ng/L

Reporting group title	Patients with HFpEF and iron deficiency

Reporting group description:

We enrolled patients with ID and known and stable CHF, objectively defined as below and with no HF hospitalization or need for iv diuretics within the previous three months. ID was defined as S-Ferritin <100 µg/L, or S-Ferritin 100-299 µg/L and transferrin saturation <20%5. Patients were divided into HF with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF). Patients with left ventricular ejection fraction (LVEF) <45% were considered to have HFrEF, and patients with LVEF ≥45% with structural and/or functional abnormalities and NT-pro-BNP >125 ng/L were considered to have HFpEF.

Subject analysis set title	Overall study
Subject analysis set type	Per protocol

Subject analysis set description:

Overall study

Primary: The absolute increase of P-iron after two hours compared to baseline

End point title	The absolute increase of P-iron after two hours compared to baseline

End point description:

End point type	Primary

End point timeframe:

The absolute increase of P-iron after two hours compared to baseline

End point values	Patients with HFrEF and iron deficiency	Control group	Patients with HFpEF and iron deficiency	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	12	15	
Units: µg/dL				
median (inter-quartile range (Q1-Q3))	78 (62 to 129)	48 (31 to 62)	112 (62 to 151)	

Statistical analyses

Statistical analysis title	Mann Whitney U test

Statistical analysis description:

The non-parametric test Mann Whitney U was used for hypothesis testing and Kruskal-Wallis was used to compare differences between the three groups in baseline characteristics. A two-sided overall $\alpha<0.05$

was considered to be significant. Analyses were performed with the use of IBM SPSS Statistics 25.

Comparison groups	Patients with HFrEF and iron deficiency v Control group v Patients with HFpEF and iron deficiency
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.001
Method	Mann Whitney U tast

Notes:

[1] - The non-parametric test Mann Whitney U was used for hypothesis testing and Kruskal-Wallis was used to compare differences between the three groups in baseline characteristics. A two-sided overall $\alpha<0.05$ was considered to be significant. Analyses were performed with the use of IBM SPSS Statistics 25.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects were contacted one week after the study procedure to report any adverse events. Subjects were also encuraged to report any adverse event to the study team.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	AE report

Reporting group description: -

Serious adverse events	AE report		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (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	AE report		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 42 (11.90%)		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		

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