

**Clinical trial results:
Changes in Myocardial Iron Content Following Administration of
Intravenous Iron
Summary**

EudraCT number	2016-004194-40
Trial protocol	ES
Global end of trial date	11 July 2018

Results information

Result version number	v1 (current)
This version publication date	10 June 2021
First version publication date	10 June 2021

Trial information**Trial identification**

Sponsor protocol code	MYOCARDIAL-IRON
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03398681
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Instituto de Investigación Sanitaria INCLIVA
Sponsor organisation address	Avd. Menéndez Pelayo 4, acc, Valencia, Spain, 46010
Public contact	Marta Peiro, Instituto de Investigación Sanitaria INCLIVA, 0034 961973536, gestioncientifica@incliva.es
Scientific contact	Marta Peiro, Instituto de Investigación Sanitaria INCLIVA, 0034 961973536, gestioncientifica@incliva.es

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	04 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 July 2018
Global end of trial reached?	Yes
Global end of trial date	11 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine and quantify the changes in myocardial iron content at 7 and 30-day after the administration of intravenous ferric carboxymaltose. Such changes will be assessed by T2* CMR.

Protection of trial subjects:

The protocol, informed consent form, participant information sheet and any applicable documents were submitted and approved by an appropriate Ethics Committee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 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	Spain: 53
Worldwide total number of subjects	53
EEA total number of subjects	53

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)	13
From 65 to 84 years	37
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Patients with established Heart Failure and left ventricular ejection fraction < 50% and iron deficiency

Pre-assignment

Screening details:

Patients with established symptomatic Heart Failure (NYHA class II-III) and iron deficiency. These patients were randomized to receive intravenous ferric carboxymaltose or placebo. All patients were recruited after signed the informed consent form.

Pre-assignment period milestones

Number of subjects started	53
Number of subjects completed	53

Period 1

Period 1 title	Randomization Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Because ferric carboxymaltose is a dark-brown solution that is easily distinguishable from the saline placebo, study personnel responsible for the preparation and administration of the study drug were aware of the group assignments and therefore, not involved in any study assessments. To ensure that patients were unaware of the study drug, materials used in drug administration were covered with aluminum foil or other opaque material and the injection site shielded from the patient view.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous ferric carboxymaltose

Arm description:

Ferric Carboxymaltose solution [Ferinject® (FCM)] will be given as a perfusion of 20 mL (which is the amount of FCM that is equivalent to 1000 mg of iron) diluted in a sterile saline solution (0.9% weight/volume (w/v) NaCl) administered over at least 15 min.

Arm type	Experimental
Investigational medicinal product name	Ferinject 50 mg / ml solution for injection and infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg

Arm title	Placebo
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Arm description:

Normal saline (0.9% weight/volume (w/v) NaCl) administered as per the instructions for active therapy

Arm type	Placebo
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Investigational medicinal product name	Normal saline (0.9% weight/volume (w/v) NaCl)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

administered as per the instructions for active therapy.

Number of subjects in period 1	Intravenous ferric carboxymaltose	Placebo
Started	27	26
Completed	27	26

Baseline characteristics

Reporting groups

Reporting group title	Intravenous ferric carboxymaltose
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Reporting group description:

Ferric Carboxymaltose solution [Ferinject® (FCM)] will be given as a perfusion of 20 mL (which is the amount of FCM that is equivalent to 1000 mg of iron) diluted in a sterile saline solution (0.9% weight/volume (w/v) NaCl) administered over at least 15 min.

Reporting group title	Placebo
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Reporting group description:

Normal saline (0.9% weight/volume (w/v) NaCl) administered as per the instructions for active therapy

Reporting group values	Intravenous ferric carboxymaltose	Placebo	Total
Number of subjects	27	26	53
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)	7	6	13
From 65-84 years	19	18	37
85 years and over	1	2	3
Gender categorical			
Units: Subjects			
Female	6	7	13
Male	21	19	40

End points

End points reporting groups

Reporting group title	Intravenous ferric carboxymaltose
Reporting group description:	Ferric Carboxymaltose solution [Ferinject® (FCM)] will be given as a perfusion of 20 mL (which is the amount of FCM that is equivalent to 1000 mg of iron) diluted in a sterile saline solution (0.9% weight/volume (w/v) NaCl) administered over at least 15 min.
Reporting group title	Placebo
Reporting group description:	Normal saline (0.9% weight/volume (w/v) NaCl) administered as per the instructions for active therapy

Primary: Changes in myocardial iron content

End point title	Changes in myocardial iron content
End point description:	Changes in myocardial iron content assessed by CMR T2* and T1-mapping evaluation on day 7 and day 30 after drug administration
End point type	Primary
End point timeframe:	Day 7 and day 30 after drug administration

End point values	Intravenous ferric carboxymaltose	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: milisec	27	26		

Statistical analyses

Statistical analysis title	Lineal Mix Model
Comparison groups	Intravenous ferric carboxymaltose v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Least square means
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	95

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Since informed consent through and including 30 calendar days after drug administration

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	4.0
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Reporting groups

Reporting group title	Intravenous ferric carboxymaltose
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Reporting group description:

Ferric Carboxymaltose solution [Ferinject® (FCM)] will be given as a perfusion of 20 mL (which is the amount of FCM that is equivalent to 1000 mg of iron) diluted in a sterile saline solution (0.9% weight/volume (w/v) NaCl) administered over at least 15 min.

Reporting group title	Placebo
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Reporting group description:

Normal saline (0.9% weight/volume (w/v) NaCl) administered as per the instructions for active therapy

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: By protocol, non-serious adverse events were recorded

Serious adverse events	Intravenous ferric carboxymaltose	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)	0 / 27 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary edema			
subjects affected / exposed	2 / 27 (7.41%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic Obstructive Pulmonary Disease Exacerbation			
subjects affected / exposed	1 / 27 (3.70%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic Kidney Disease			
subjects affected / exposed	1 / 27 (3.70%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Intravenous ferric carboxymaltose	Placebo	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 27 (0.00%)	0 / 27 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 June 2017	Inclusion/ exclusion criteria modification, including verbal and legal representative consent.

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/32067585>

<http://www.ncbi.nlm.nih.gov/pubmed/33040491>