



## Clinical trial results:

### Globifer Forte® Oral Haem and Non-haem Iron Supplementation in Heart Failure: A Randomised, DoubleBlind, Placebo Controlled, Double Dummy, Part Mechanistic Pilot Trial

#### Summary

EudraCT number	2013-004704-19
Trial protocol	GB
Global end of trial date	21 December 2020

#### Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

#### Trial information

##### Trial identification

Sponsor protocol code	GLOBIFER-HF
-----------------------	-------------

##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Dr Darlington Okonko, King's College London, +44 207848 5017, obi.okonko@kcl.ac.uk
Scientific contact	Dr Darlington Okonko, King's College London, +44 207848 5017, obi.okonko@kcl.ac.uk
Sponsor organisation name	King's College Hospital NHS Foundation Trust
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE5 9RS
Public contact	Dr Darlington Okonko, King's College London, +44 207848 5017, darlington.okonko@kcl.ac.uk
Scientific contact	Dr Darlington Okonko, King's College London, +44 207848 5017, darlington.okonko@kcl.ac.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	21 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2020
Global end of trial reached?	Yes
Global end of trial date	21 December 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effect of 3 months of Globifer Forte® treatment on exercise capacity, as quantified by the 6 minute walk distance (6MWD), in CHF patients with functional or absolute iron deficiency.

Protection of trial subjects:

All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 March 2018
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: 60
Worldwide total number of subjects	60
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)	24
From 65 to 84 years	33

85 years and over	3
-------------------	---

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Screening & Baseline Assessments

Biochemical and haematological tests

Hepcidin-25, Cytokines, NT-BNP,

Symptom status (NYHA, KCCQ, VAFS)

6MWD test, Echo

Iron absorption test & in-vivo iron transport

### Pre-assignment period milestones

Number of subjects started	60
----------------------------	----

Number of subjects completed	60
------------------------------	----

### Period 1

Period 1 title	Overall Trial (overall period)
----------------	--------------------------------

Is this the baseline period?	Yes
------------------------------	-----

Allocation method	Randomised - controlled
-------------------	-------------------------

Blinding used	Double blind
---------------	--------------

Roles blinded	Subject, Investigator
---------------	-----------------------

### Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Globifer Forte
-----------	----------------

Arm description:

1 tablet active GF twice daily + 1 tablet placebo FeSO4 twice daily

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Globifer Forte
--	----------------

Investigational medicinal product code	
--	--

Other name	
------------	--

Pharmaceutical forms	Tablet
----------------------	--------

Routes of administration	Oral use
--------------------------	----------

Dosage and administration details:

1 tablet active Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily

Investigational medicinal product name	Placebo
--	---------

Investigational medicinal product code	
--	--

Other name	
------------	--

Pharmaceutical forms	Tablet
----------------------	--------

Routes of administration	Oral use
--------------------------	----------

Dosage and administration details:

1 tablet active Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily

Arm title	FeSO4
-----------	-------

Arm description:

1 tablet placebo Globifer Forte® twice daily + 1 tablet active FeSO4 twice daily

Arm type	Active comparator
----------	-------------------

Investigational medicinal product name	FeSO4
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1 tablet placebo Globifer Forte® twice daily + 1 tablet active FeSO4 twice daily	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1 tablet placebo Globifer Forte® twice daily + 1 tablet active FeSO4 twice daily	
<b>Arm title</b>	Placebo
Arm description:	
1 tablet placebo Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1 tablet placebo Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily.	

<b>Number of subjects in period 1</b>	Globifer Forte	FeSO4	Placebo
Started	24	23	13
Completed	24	23	13

## Baseline characteristics

### Reporting groups

Reporting group title	Globifer Forte
Reporting group description: 1 tablet active GF twice daily + 1 tablet placebo FeSO4 twice daily	
Reporting group title	FeSO4
Reporting group description: 1 tablet placebo Globifer Forte® twice daily + 1 tablet active FeSO4 twice daily	
Reporting group title	Placebo
Reporting group description: 1 tablet placebo Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily.	

Reporting group values	Globifer Forte	FeSO4	Placebo
Number of subjects	24	23	13
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean standard deviation	67 ± 12	69 ± 14	70 ± 9
Gender categorical Units: Subjects			
Female	4	5	4
Male	20	18	9

Reporting group values	Total		
Number of subjects	60		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years)	0 0 0 0 0 0 0		

From 65-84 years	0		
85 years and over	0		

  

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	13		
Male	47		

## End points

### End points reporting groups

Reporting group title	Globifer Forte
Reporting group description: 1 tablet active GF twice daily + 1 tablet placebo FeSO4 twice daily	
Reporting group title	FeSO4
Reporting group description: 1 tablet placebo Globifer Forte® twice daily + 1 tablet active FeSO4 twice daily	
Reporting group title	Placebo
Reporting group description: 1 tablet placebo Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily.	

### Primary: 6 minute walking distance

End point title	6 minute walking distance
End point description:	
End point type	Primary
End point timeframe:	
6 minute walk distance (6MWD) at week 12 between patients randomised to Globifer Forte® and those allocated to placebo.	

End point values	Globifer Forte	FeSO4	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	8	
Units: metre				
arithmetic mean (standard deviation)	383 (± 133)	371 (± 105)	430 (± 100)	

### Statistical analyses

Statistical analysis title	Two-way Mixed Model ANCOVA Analysis at 12 weeks
Comparison groups	Globifer Forte v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.023
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-57



Confidence interval	
level	95 %
sides	2-sided
lower limit	-108
upper limit	16

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Number and incidence of adverse events (drug tolerance) between patients randomised to Globifer Forte® and FeSO4 from baseline to 12 weeks.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	22
--------------------	----

### Reporting groups

Reporting group title	Globifer Forte
-----------------------	----------------

Reporting group description:

1 tablet active GF twice daily + 1 tablet placebo FeSO4 twice daily

Reporting group title	FeSO4
-----------------------	-------

Reporting group description:

1 tablet placebo Globifer Forte® twice daily + 1 tablet active FeSO4 twice daily

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

1 tablet placebo Globifer Forte® twice daily + 1 tablet placebo FeSO4 twice daily.

Serious adverse events	Globifer Forte	FeSO4	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	6 / 13 (46.15%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Bowel Ischaemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Syncope	Additional description: vasovagal		
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive Heart Failure			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Acute myocardial infarction			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

<b>Non-serious adverse events</b>	Globifer Forte	FeSO4	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 23 (43.48%)	17 / 24 (70.83%)	4 / 13 (30.77%)
Vascular disorders			
Elective fem-fem bypass			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Prolonged QTc			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

drowsiness			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
loss of balance			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Deafness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
blurred vision			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Dark stools			
subjects affected / exposed	4 / 23 (17.39%)	11 / 24 (45.83%)	0 / 13 (0.00%)
occurrences (all)	4	11	0
Constipation			
subjects affected / exposed	1 / 23 (4.35%)	3 / 24 (12.50%)	1 / 13 (7.69%)
occurrences (all)	1	3	1
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	4 / 24 (16.67%)	0 / 13 (0.00%)
occurrences (all)	1	4	0
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Coryzal			
subjects affected / exposed	0 / 23 (0.00%)	2 / 24 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
shortness of breath			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 24 (4.17%) 1	0 / 13 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 24 (4.17%) 1	0 / 13 (0.00%) 0
Musculoskeletal and connective tissue disorders hip/knee pain subjects affected / exposed occurrences (all)  swollen finger subjects affected / exposed occurrences (all)  Back pain subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2  1 / 23 (4.35%) 1  1 / 23 (4.35%) 1	1 / 24 (4.17%) 1  0 / 24 (0.00%) 0  1 / 24 (4.17%) 1	1 / 13 (7.69%) 1  0 / 13 (0.00%) 0  0 / 13 (0.00%) 0
Infections and infestations toe infection subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 24 (4.17%) 1	0 / 13 (0.00%) 0
Metabolism and nutrition disorders Gout flare subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	0 / 24 (0.00%) 0	0 / 13 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 June 2018	<p>Protocol Version 2.2 to 3.0 (approved 05/07/2018):</p> <ul style="list-style-type: none"><li>• Eligibility expanded to include all patients with LVEF <math>\leq</math> 45% irrespective of degree of symptoms (NYHA class).</li><li>• Removal of need to quantify mRNA levels as excessive work given that protein levels will be measured.</li><li>• Change in comparison time for the iron absorption test from 2 to 3 days.</li><li>• Removal of 'change in' for the endpoints and safety evaluation and using 'week 12' measurements as endpoints and 'Serum iron level at 3 hours after oral' drug, in case of iron absorption test.</li><li>• Removal of alanine transaminase from liver function test list as King's College Hospital does not measure it routinely.</li><li>• Clarification that only folate and vitamin B12 levels below the lower limit of normal were an exclusion criteria as levels above the upper limit are not physiological adverse.</li><li>• Removal of cellular energetic status from the blood tests as will not be an endpoint due to it not being needed and FACS machine out of service.</li></ul> <p>GLOBIFER-HF CLINICAL STUDY REPORT 10</p> <ul style="list-style-type: none"><li>• Clarification that chronic lung disease would only be a contraindication if patients had objective measures of severe lung disease (FEV1 &lt; 50% predicted).</li><li>• Removal of chronic renal impairment with eGFR &lt; 45 as an exclusion criterion, and relaxing eGFR &lt; 30 from &lt; 65 in diabetics.</li><li>• Adding 'planning to get pregnant' to exclusion criteria.</li><li>• Clarification that functional valvular disease will not be a contraindication.</li></ul>
14 June 2019	<p>Protocol Version 3.1 to 4.0 (approved 19/06/2019):</p> <ul style="list-style-type: none"><li>• Removal of stratification of study size into groups absolute or functional iron deficiency.</li><li>• Removal of testing of Haem-carrier protein 1, and haem regulatory gene 1 from the in vitro iron transporter studies.</li><li>• Change total number of in vitro transporter studies to first 30 randomised patients from first 20 of each strata.</li><li>• Removal of allergic disorders from the exclusion criteria.</li><li>• Additional of oral haemoglobin preparations use as an exclusion criterion.</li><li>• Change of compliance check telephone calls from weeks to 2 weekly</li><li>• Removal of IL-10, and gamma interferon from the cytokine assay list.</li></ul>
09 June 2020	<p>Protocol Version 4.0 to 5.0 (approved 07/07/2020):</p> <ul style="list-style-type: none"><li>• Removal of soluble transferrin receptor as a baseline and end of study visit blood test</li><li>• Removal of TNF receptor 1&amp;2 from the cytokine list.</li><li>• Cytokines and Hcpidin-25 ELISA measurements will be outsourced to Affinity Biomarker Labs rather than be performed in King's College BHF Centre.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported