



Clinical trial results:

Intravenous ferric carboxymaltose vs. oral iron substitution in patients with metastatic colorectal cancer (CRC) and iron deficiency anemia: a randomized multicenter treatment optimization study.

Summary

EudraCT number	2014-000246-30
Trial protocol	DE
Global end of trial date	04 May 2020

Results information

Result version number	v1 (current)
This version publication date	21 September 2023
First version publication date	21 September 2023

Trial information

Trial identification

Sponsor protocol code	FERINJECT
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest
Sponsor organisation address	Steinbacher Hohl 2-26, Frankfurt am Main Mitte-West, Frankfurt am Main, Germany, 60488
Public contact	Prof. Al-Batran, Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest, info@ikf-khnw.de
Scientific contact	Prof. Al-Batran, Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest, info@ikf-khnw.de

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	27 October 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to estimate the treatment response of intravenous iron carboxymaltose versus oral iron replacement in patients with metastatic colorectal cancer (CRC) and iron deficiency anemia. The primary endpoint was the response rate defined as proportion of patients with either an increase in serum hemoglobin by 2 g/dl or normalization of serum hemoglobin (12 g/dl) within 12 weeks from baseline.

Secondary objectives of the trial were to further compare intravenous iron carboxymaltose versus oral iron replacement in terms of efficacy and safety.

Protection of trial subjects:

This clinical study was designed and shall be implemented and reported in accordance with the protocol, the AMG (Arzneimittelgesetz), the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations (including European Directive 2001/20/EC), and with the ethical principles laid down in the Declaration of Helsinki. The trial was authorized/approved by the competent authority (Paul-Ehrlich-Institut, PEI) and the competent ethics committee responsible for the trial ("federführende Ethikkommission").

Before recruitment into the clinical trial, each patient was informed that participation in the study is completely voluntary, and that he or she may withdraw his or her participation in the trial at any time without any declaration of reasons, which will not lead to any disadvantage for the respective patient. The eligibility of a new patient was determined by the local investigator during regular clinical visits. The examinations for the study and the inclusion of the patient were done after detailed written and oral education about aims, methods, anticipated benefits and potential hazards of the study by use of the informed consent forms and after given written consent of the patient.

Safety of the trial treatment was monitored continuously by careful monitoring of all adverse events (AEs) and serious adverse events (SAEs) reported. An independent data safety monitoring board (DSMB) was responsible for assessment of reports summarizing safety data or study results and gave recommendations for planned protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 May 2015
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	Germany: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	27
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between May 2015 and Feb 2019, 64 patients from 12 centers in Germany were enrolled. Eligible patients were stratified by ferritin (≤ 30 versus >30 ng/ml), ECOG (0 versus 1/2) and palliative treatment line (1 versus ≥ 2) and randomized 1:1.

Pre-assignment

Screening details:

Main criteria for inclusion: Metastatic or inoperable colorectal carcinoma, no curative therapy available, current palliative chemotherapy, Iron deficiency anemia: hemoglobin ≤ 10.5 g/dl and transferrin saturation $< 20\%$ and/or serum ferritin < 20 ng/mL, body weight ≥ 40 kg

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
Arm title	FerInject

Arm description:

Patients received once intravenous substitution with ferric carboxymaltose (Ferinject); max. 2000 mg over 2 weeks (max. 1000 mg per week).

In addition, oral folic acid and vitamin B-12 substitution was applied in both study arms. Folic acid 400 μ g per day and vitamin B-12 10 μ g per day.

Arm type	Experimental
Investigational medicinal product name	Ferinject
Investigational medicinal product code	
Other name	ferric carboxymaltose
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Infusion , Injection

Dosage and administration details:

Patients with 40-69 kg body weight: Hb < 10 g/dL --> 1500 mg Ferinject; Hb ≥ 10 g/dL --> 1000 mg Ferinject

Patients with ≥ 70 kg body weight: Hb < 10 g/dL --> 2000 mg Ferinject; Hb ≥ 10 g/dL --> 1500 mg Ferinject

Infusion over at least 6 min (500 mg) or respectively 15 min (1000 mg). The maximum recommended cumulative dose of Ferinject was 1000 mg per week, total dose was applied within a maximum of 2 weeks.

Arm title	Oral Fe substitution
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Arm description:

Patients received 200 mg oral per day over 12 weeks.

In addition, oral folic acid and vitamin B-12 substitution was applied in both study arms. Folic acid 400 μ g per day and vitamin B-12 10 μ g per day.

Arm type	Experimental
Investigational medicinal product name	Ferro sanol duodenal
Investigational medicinal product code	
Other name	Eisen(II)-glycin-sulfat-Komplex
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

200 mg per day (2 capsule per 100 mg) on empty stomach (e.g. in the morning and evening 1 hour before meals)

Number of subjects in period 1	FerInject	Oral Fe substitution
Started	32	32
Completed	26	20
Not completed	6	12
Physician decision	-	2
Patient's wish	1	3
Adverse event, non-fatal	-	3
Death	1	-
Other	4	4

Baseline characteristics

Reporting groups

Reporting group title	FerInject
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Reporting group description:

Patients received once intravenous substitution with ferric carboxymaltose (Ferinject); max. 2000 mg over 2 weeks (max. 1000 mg per week).

In addition, oral folic acid and vitamin B-12 substitution was applied in both study arms. Folic acid 400 µg per day and vitamin B-12 10 µg per day.

Reporting group title	Oral Fe substitution
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Reporting group description:

Patients received 200 mg oral per day over 12 weeks.

In addition, oral folic acid and vitamin B-12 substitution was applied in both study arms. Folic acid 400 µg per day and vitamin B-12 10 µg per day.

Reporting group values	FerInject	Oral Fe substitution	Total
Number of subjects	32	32	64
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			
median	67.5	67.5	
full range (min-max)	31 to 81	41 to 80	-
Gender categorical Units: Subjects			
Female	13	15	28
Male	19	17	36
ECOG performance status Units: Subjects			
ECOG 0	10	10	20
ECOG 1	19	20	39
ECOG 2	3	2	5
Primary localisation Units: Subjects			
Colon	19	19	38
Rectum	12	13	25
Missing	1	0	1
T stage Units: Subjects			

T0	1	0	1
T2	2	2	4
T3	16	17	33
T4	9	6	15
Tx	3	6	9
Missing	1	1	2
N stage			
Units: Subjects			
N0	5	7	12
N1	10	6	16
N2	10	12	22
Nx	6	6	12
Missing	1	1	2
M stage			
Units: Subjects			
M0	5	2	7
M1	27	29	56
Missing	0	1	1
Number prior palliative therapy lines			
without current therapy			
Units: Subjects			
Zero	14	13	27
One	10	13	23
Two	4	4	8
Three	2	1	3
Four	2	0	2
Six	0	1	1
Prior Fe substitution within last 6 months			
Units: Subjects			
Yes	1	2	3
No	31	30	61
Substitution with packed red blood cells			
Median number of red blood cells substitution was 2.0 (2-8) in the Ferinject Arm and 2.0 (1-8) in the Oral Fe Arm			
Units: Subjects			
Yes	5	5	10
No	26	27	53
Missing	1	0	1
Substitution with erythropoietin			
Units: Subjects			
Yes	0	0	0
No	31	31	62
Missing	1	1	2

End points

End points reporting groups

Reporting group title	FerInject
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Reporting group description:

Patients received once intravenous substitution with ferric carboxymaltose (Ferinject); max. 2000 mg over 2 weeks (max. 1000 mg per week).

In addition, oral folic acid and vitamin B-12 substitution was applied in both study arms. Folic acid 400 µg per day and vitamin B-12 10 µg per day.

Reporting group title	Oral Fe substitution
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Reporting group description:

Patients received 200 mg oral per day over 12 weeks.

In addition, oral folic acid and vitamin B-12 substitution was applied in both study arms. Folic acid 400 µg per day and vitamin B-12 10 µg per day.

Primary: Response Rate

End point title	Response Rate
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End point description:

End point type	Primary
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End point timeframe:

The response rate defined as proportion of patients with either an increase in serum hemoglobin by 2 g/dl or normalization of serum hemoglobin (12 g/dl) within 12 weeks from baseline

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: subjects				
Yes	18	13		
No	13	19		
Missing	1	0		

Statistical analyses

Statistical analysis title	Fishers Exact Test
Comparison groups	FerInject v Oral Fe substitution
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.211
Method	Fisher exact

Primary: Response Rate Per-Protocol Set

End point title	Response Rate Per-Protocol Set
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End point description:

This set contains all eligible patients, who fulfilled all inclusion/exclusion criteria, and received at least one application of protocol treatment and for whom baseline hemoglobin (Hb) data as well as further Hb-data after at least 4 weeks of start of protocol treatment were available.

End point type	Primary
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End point timeframe:

within 12 weeks from baseline

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	25		
Units: Subjects				
Yes	17	13		
No	11	12		
Missing	0	0		

Statistical analyses

Statistical analysis title	Fisher Exact Test
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Comparison groups	FerInject v Oral Fe substitution
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Number of subjects included in analysis	53
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 0.5862
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Method	Fisher exact
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Secondary: Time to response

End point title	Time to response
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End point description:

The median time to response in both arms was 3.0 month

End point type	Secondary
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End point timeframe:

Calculated from the date of study enrolment until the date of increase or normalization of hemoglobin. Only subjects with an event were analyzed.

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Subjects				
Response	18	13		
No Response	13	19		

Attachments (see zip file)	Time to response.png
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Statistical analyses

Statistical analysis title	Log Rank Test
Comparison groups	Oral Fe substitution v FerInject
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1875
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.658
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.322
upper limit	1.345

Secondary: Overall survival

End point title	Overall survival
End point description:	
Median Overalls survival was 13 months [95% CI 9,25] in the FerInject Arm and 21 months [14, not estimable] in the aral FE substitution arm	
End point type	Secondary
End point timeframe:	
from time of randomization to date of last follow-up	

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: Subjects				
Death	19	16		
Alive	13	16		

Attachments (see zip file)	Overall survival.png
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Statistical analyses

Statistical analysis title	Log Rank Test
Comparison groups	Oral Fe substitution v FerInject
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2573
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.682
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.345
upper limit	1.347

Secondary: Hand force measurements

End point title	Hand force measurements
End point description:	
End point type	Secondary
End point timeframe:	
from baseline till end of treatment	

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: Units				
arithmetic mean (standard deviation)				
Baseline	31.5 (± 5.9)	30.9 (± 12.2)		
Change over baseline on Visit 7/EOT	0.9 (± 4.8)	0.9 (± 4.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Nutrition Risk Score

End point title	Nutrition Risk Score
End point description: nutrition risk score indicates a nutrition risk by a score of 3 and higher	
End point type	Secondary
End point timeframe: from baseline till end of treatment	

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: unit(s)				
arithmetic mean (standard deviation)				
Baseline	2 ($\pm$ 1.3)	2.1 ($\pm$ 0.9)		
Change over baseline at visit 7/EOT	0 ($\pm$ 0.8)	0.3 ($\pm$ 2.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC QLQ C30 - Mean change from baseline at EOT

End point title	EORTC QLQ C30 - Mean change from baseline at EOT
End point description:	
End point type	Secondary
End point timeframe: from baseline till end of treatment	

End point values	FerInject	Oral Fe substitution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	27		
Units: unit(s)				
arithmetic mean (standard deviation)				
Global Health Status	3.2 ($\pm$ 20.7)	4.9 ($\pm$ 22.1)		
Physical Functioning	2.8 ($\pm$ 21.1)	1.4 ($\pm$ 16.6)		
Role Functioning	3.2 ($\pm$ 33.3)	-3.6 ($\pm$ 30.5)		
Emotional Functioning	-0.2 ($\pm$ 22.4)	2.2 ($\pm$ 15.3)		
Cognitive Functioning	-2.6 ($\pm$ 19.8)	0.7 ($\pm$ 16.3)		
Social Functioning	13.5 ($\pm$ 30.9)	4.3 ($\pm$ 23.1)		
Fatigue	-7.9 ($\pm$ 24.8)	-11.6 ($\pm$ 21.6)		

Nausea/Vomiting	2.6 (± 22)	-1.4 (± 11.1)		
Pain	0 (± 36.5)	-2.2 (± 25.8)		
Dyspnea	-13.3 (± 25.5)	1.5 (± 26.2)		
Insomnia	5.1 (± 36.1)	0 (± 20.1)		
Appetite Loss	-5.1 (± 41.8)	-10.1 (± 32.5)		
Constipation	-4 (± 35.1)	-6.1 (± 43.2)		
Diarrhea	-6.7 (± 34.7)	-4.3 (± 30.7)		
Financial Difficulties	-2.6 (± 20.9)	-10.1 (± 21.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were monitored from baseline till end of treatment

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	FerInject
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Reporting group description:

Patients received once intravenous substitution with ferric carboxymaltose (Ferinject); max. 2000 mg over 2 weeks (max. 1000 mg per week).

In addition, oral folic acid and vitamin B-12 substitution is applied in both study arms. Folic acid 400 µg per day and vitamin B-12 10 µg per day.

Reporting group title	Oral Fe substitution
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Reporting group description:

Patients receive 200 mg oral per day over 12 weeks.

In addition, oral folic acid and vitamin B-12 substitution is applied in both study arms. Folic acid 400 µg per day and vitamin B-12 10 µg per day.

Serious adverse events	FerInject	Oral Fe substitution	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 31 (29.03%)	8 / 30 (26.67%)	
number of deaths (all causes)	1	16	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Arteria femoralis superficialis stenose			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac Insufficiency			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Stroke			

subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
	Additional description: with gastrointestinal bleeding		
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 31 (6.45%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vomiting			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ileus			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure	Additional description: progressive disease		
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bile duct stenosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Inflammation	Additional description: toe interdigits inflamed		
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lumboischialgia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection of port system			

subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (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	FerInject	Oral Fe substitution	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	29 / 30 (96.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 31 (3.23%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	4 / 31 (12.90%)	0 / 30 (0.00%)	
occurrences (all)	4	0	
Edema limbs			
subjects affected / exposed	6 / 31 (19.35%)	3 / 30 (10.00%)	
occurrences (all)	6	3	
Fatigue			
subjects affected / exposed	11 / 31 (35.48%)	8 / 30 (26.67%)	
occurrences (all)	12	12	
General physical health deterioration			
subjects affected / exposed	5 / 31 (16.13%)	2 / 30 (6.67%)	
occurrences (all)	5	2	
Pain			

subjects affected / exposed occurrences (all)	7 / 31 (22.58%) 9	4 / 30 (13.33%) 5	
Weight decreased subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	1 / 30 (3.33%) 1	
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	7 / 31 (22.58%) 7	5 / 30 (16.67%) 5	
Dyspnoea subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	4 / 30 (13.33%) 6	
Epistaxis subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 10	2 / 30 (6.67%) 2	
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	0 / 30 (0.00%) 0	
Investigations			
Neutrophil count decreased subjects affected / exposed occurrences (all)	8 / 31 (25.81%) 11	3 / 30 (10.00%) 3	
White blood cell count decreased subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 5	1 / 30 (3.33%) 1	
C-reactive protein increased subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 3	1 / 30 (3.33%) 1	
Nervous system disorders			
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	7 / 31 (22.58%) 7	5 / 30 (16.67%) 5	
Dizziness subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	2 / 30 (6.67%) 2	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 31 (25.81%)	3 / 30 (10.00%)	
occurrences (all)	11	4	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 31 (3.23%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 31 (9.68%)	2 / 30 (6.67%)	
occurrences (all)	3	2	
Constipation			
subjects affected / exposed	5 / 31 (16.13%)	5 / 30 (16.67%)	
occurrences (all)	7	5	
Diarrhoea			
subjects affected / exposed	9 / 31 (29.03%)	8 / 30 (26.67%)	
occurrences (all)	9	15	
Mucositis oral			
subjects affected / exposed	3 / 31 (9.68%)	4 / 30 (13.33%)	
occurrences (all)	3	5	
Nausea			
subjects affected / exposed	10 / 31 (32.26%)	7 / 30 (23.33%)	
occurrences (all)	12	7	
Vomiting			
subjects affected / exposed	5 / 31 (16.13%)	0 / 30 (0.00%)	
occurrences (all)	5	0	
Ascites			
subjects affected / exposed	1 / 31 (3.23%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Asthenia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 31 (9.68%)	2 / 30 (6.67%)	
occurrences (all)	3	2	

Dry skin subjects affected / exposed occurrences (all)	7 / 31 (22.58%)	3 / 30 (10.00%)	
	8	5	
Rash acneiform subjects affected / exposed occurrences (all)	4 / 31 (12.90%)	1 / 30 (3.33%)	
	4	1	
Palmar-plantar erythrodysesthesia syndrome subjects affected / exposed occurrences (all)	1 / 31 (3.23%)	2 / 30 (6.67%)	
	1	2	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	3 / 31 (9.68%)	0 / 30 (0.00%)	
	4	0	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	2 / 31 (6.45%)	0 / 30 (0.00%)	
	2	0	
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	4 / 31 (12.90%)	4 / 30 (13.33%)	
	5	7	
	4 / 31 (12.90%)	1 / 30 (3.33%)	
	4	2	

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