



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 |
|-----------------------|-----------|

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 |
|-----------|----------------------|

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 |
|-----------------------|-----------|

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 |
|-----------------------|----------------------|

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 |
|-----------------------|-----------|

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 |
|-----------------------|----------------------|

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 |
|-----------------|---------------|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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 |
|-----------------|--------------------------------|

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 |
|----------------|---------|

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 |
|----------------------------|-------------------|

| | |
|-------------------|----------------------------------|
| Comparison groups | FerInject v Oral Fe substitution |
|-------------------|----------------------------------|

| | |
|---|----|
| Number of subjects included in analysis | 53 |
|---|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|----------|
| P-value | = 0.5862 |
|---------|----------|

| | |
|--------|--------------|
| Method | Fisher exact |
|--------|--------------|

Secondary: Time to response

| | |
|-----------------|------------------|
| End point title | Time to response |
|-----------------|------------------|

End point description:

The median time to response in both arms was 3.0 month

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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 |
|-----------------------------------|----------------------|

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 |
|-----------------------------------|----------------------|

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 |
|-----------------|------------|

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | FerInject |
|-----------------------|-----------|

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 |
|-----------------------|----------------------|

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) | 4 / 31 (12.90%) | 4 / 30 (13.33%) | |
| | 5 | 7 | |
| | | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 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