**Supporting Information**

**Table S1** Studies included in the pooled analysis (*n* = 41)

| **Study code** | **Therapeutic area(s)/disease state(s)** | **Patients  included in analysis** | **Duration of study (weeks)** | **Assessment of PO43– levelsa** | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **BL** | **W1** | **W2** | **W4** | **W6** | **W8** | **W12** | **W24** | **W36** | **W48** | **W52** |
| 1VIT03001 | Women’s health | 161 | 12 | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |  |
| 1VIT04002 | Women’s health | 120 | 9 | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |  |
| 1VIT04003 | Women’s health | 108 | 9 | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |  |
| 1VIT04004/5005 | NDD-CKD | 196 | 8**/44** | **X** |  | **X** | **X** |  | **X** | **X** | **X** | **X** | **X** |  |
| 1VIT05006 | GI/HD-CKD/NDD-CKD/ Women’s health/Other | 575 | 3 | **X** | **X** |  |  |  |  |  |  |  |  |  |
| 1VIT05009 | Neurology | 43 | 24 | **X** | **X** | **X** | **X** |  | **X** | **X** |  |  |  |  |
| 1VIT06011 | Women’s health | 135 | 8 | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |  |
| 1VIT07017 | Women’s health | 966 | 4 | **X** |  |  | **X** |  |  |  |  |  |  |  |
| 1VIT07018 | HD-CKD/NDD-CKD | 247 | 4 | **X** |  |  | **X** |  |  |  |  |  |  |  |
| 1VIT08019 | GI/NDD-CKD/Women’s health/Other | 340 | 7 | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |  |
| 1VIT08020 | GI/NDD-CKD/Women’s health/Other | 82 | 7 | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |  |
| 1VIT08021 | GI/NDD-CKD/Women’s health/Other | 365 | 6 | **X** | **X** |  | **X** |  |  |  |  |  |  |  |
| 1VIT08022 | Women’s health/Other | 23 | 5 | **X** | **X** |  | **X** |  |  |  |  |  |  |  |
| 1VIT08023 | Women’s health | 25 | 5 | **X** | **X** | **X** |  | **X** |  |  |  |  |  |  |
| 1VIT09030 | NDD-CKD | 1263 | 8 | **X** | **X** | **X** | **X** |  | **X** |  |  |  |  |  |
| 1VIT09031 | GI/NDD-CKD/Women’s health/Other | 493 | 20 | **X** | **X** | **X** |  | **X** |  |  |  |  |  |  |
| 1VIT13035 | GI | 98 | 6 | **X** | **X** | **X** | **X** |  |  |  |  |  |  |  |
| 1VIT14037 | Neurology | 107 | 52 | **X** | **X** | **X** |  | **X** |  |  | **X** |  |  | **X** |
| 1VIT14038 | Neurology | 40 | 6 | **X** |  |  |  | **X** |  |  |  |  |  |  |
| 1VIT14039 | Other | 119 | 18 | **X** | **X** | **X** |  | **X** |  | **X** |  |  |  |  |
| BOLINJ-08 | Other | 31 | 2 | **X** | **X** | **X** |  |  |  |  |  |  |  |  |
| FER-AOC-MM | Other | 2 | 8 | **X** | **X** | **X** | **X** | **X** | **X** |  |  |  |  |  |
| FER-ASAP-2009-01 | Other | 121 | 12 | **X** |  |  | **X** | **X** | **X** | **X** |  |  |  |  |
| FER-CARS-01 | HF | 30 | **12** | **X** | **X** | **X** | **X** | **X** | **X** | **X** |  |  |  |  |
| FER-CARS-02 | HF | 296 | 26 | **X** |  |  | **X** |  |  | **X** | **X** |  |  |  |
| FER-CARS-03 | HF | 20 | 26 | **X** |  |  | **X** |  |  | **X** | **X** |  |  |  |
| FER-CARS-04 | HF | 84 | 24 | **X** |  |  |  | **X** |  | **X** | **X** |  |  |  |
| FER-CARS-05 | HF | 148 | 52 | **X** |  |  |  | **X** |  | **X** | **X** | **X** | **X** |  |
| FER-CARS-06 | HF | 496 | 52 | **X** |  |  |  | **X** |  | **X** | **X** |  |  | **X** |
| FER-CKD-01 | NDD-CKD | 303 | 52 | **X** |  |  | **X** |  | **X** | **X** | **X** | **X** | **X** |  |
| FER-FID-CHEMO | Other | 8 | 8 | **X** |  | **X** | **X** | **X** | **X** |  |  |  |  |  |
| FER-IBD-07-COR/MAIN | GI | 286 | 12 | **X** | **X** | **X** | **X** |  | **X** | **X** |  |  |  |  |
| FER-MEC-01 | Other | 8 | 2 | **X** | **X** | **X** |  |  |  |  |  |  |  |  |
| IDNA 2009-01 | Women’s health | 138 | 10 | **X** |  |  | **X** | **X** | **X** |  |  |  |  |  |
| VIRD-VIT-45-IM | HD-CKDb | 4 | 24 | **X** |  |  |  | **X** |  | **X** | **X** |  |  |  |
| VIT-IRON-2011-003 | Other | 24 | 1 | **X** | **X** |  |  |  |  |  |  |  |  |  |
| VIT-IRON-2011-004 | Other | 187 | 8 | **X** |  | **X** | **X** | **X** | **X** |  |  |  |  |  |
| VIT-RLS-2012-013 | Neurology | 58 | 12 | **X** | **X** |  | **X** |  | **X** | **X** |  |  |  |  |
| Z213-01 | Other | 24 | 1 | **X** | **X** |  |  |  |  |  |  |  |  |  |
| Z213-02 | Women’s health | 119 | 12 | **X** | **X** | **X** | **X** | **X** | **X** | **X** |  |  |  |  |
| Z213-03 | GI | 38 | 12 | **X** | **X** | **X** | **X** | **X** | **X** | **X** |  |  |  |  |

**BL, baseline;** GI, gastrointestinal; HD-CKD, haemodialysis-dependent chronic kidney disease; HF, heart failure; NDD-CKD, non–dialysis-dependent chronic kidney disease**; W, week.**

**aIn several studies the protocol specified timepoints not reflected in this table (eg, week 3). Also, some patients had phosphate levels from biochemical assessments at additional (ie, not specified in the study protocol) timepoints. These data were included in the analysis.** bAlthough categorized as HD-CKD in the present and earlier analyses, 3 of the patients in this study did not have end-stage kidney disease.

**Table S2** FCM dosing characteristics in the pooled FCM analysis set

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | GI (*N* = 792) | HF (*N* = 1074) | NDD-CKD (*N* = 2107) | HD-CKD (*N* = 70) | Neurology (*N* = 248) | Women's health (*N* = 2839) | Other (*N* = 801) | Total (*N* = 7931) |
| FCM single dose (%) | 26.1 | 24.4 | 18.8 | 100.0 | 31.5 | 56.9 | 48.6 | 38.0 |
| FCM administrations, mean (SD) | 2.1 (1.04) | 4.3 (3.70) | 2.4 (1.54) | 1.0 (0.00) | 1.8 (0.70) | 1.5 (0.64) | 1.6 (0.64) | 2.2 (1.90) |
| FCM frequent administrations  (>1 dose within first 4 weeks) (%) | 69.6 | 31.8 | 65.3 | 0 | 68.5 | 43.1 | 51.3 | 51.4 |
| Cumulative FCM dose (mg), mean (SD) | 1393.2 (538.84) | 1530.8 (553.05) | 1522.4 (637.70) | 397.0 (343.19) | 1373.2 (432.44) | 1169.0 (350.83) | 1155.6 (423.91) | 1332.5 (532.12) |
| Cumulative FCM dose category (%) | | | | | | | | |
| ≤1000 mg | 36.1 | 30.2 | 23.0 | 100.0 | 38.3 | 61.8 | 50.2 | 43.1 |
| >1000 mg to ≤1500 mg | 46.6 | 28.3 | 60.7 | 0 | 56.9 | 27.6 | 41.4 | 40.5 |
| >1500 mg | 17.3 | 41.5 | 16.3 | 0 | 4.8 | 10.6 | 8.4 | 16.5 |
| Max single FCM dose (mg), mean (SD) | 752.5 (186.87) | 684.9 (368.54) | 764.9 (192.93) | 397.0 (343.19) | 801.1 (148.76) | 873.8 (161.73) | 774.6 (174.78) | 790.7 (227.18) |
| Max single FCM dose category (%) | | | | | | | | |
| ≤500 mg | 26.8 | 43.7 | 9.1 | 72.9 | 9.7 | 8.4 | 8.7 | 15.8 |
| >500 mg to ≤750 mg | 42.9 | 0 | 65.7 | 4.3 | 59.3 | 23.4 | 63.3 | 38.4 |
| >750 mg | 30.3 | 56.3 | 25.2 | 22.9 | 31.0 | 68.2 | 28.0 | 45.8 |

FCM, ferric carboxymaltose; GI, gastrointestinal; HD-CKD, haemodialysis-dependent chronic kidney disease; HF, heart failure; NDD-CKD, non–dialysis-dependent chronic kidney disease.

Please see *Table S1* for the duration of trials in each therapeutic area.

**Table S3** Baselinecharacteristics in the pooled HF analysis set

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | FCM (*N* = 1074) | Placebo (*N* = 809) | Comparator (*N* = 110) | | Total (*N* = 1993) |
| Female (%) | 44.8 | 47.8 | | 30.9 | 45.3 | |
| Age (y), mean (SD) | 68.7 (10.72) | 69.8 (10.63) | | 65.1 (12.12) | 69.0 (10.81) | |
| Race (%) | | | | | | |
| White | 96.7 | 96.7 | | 99.1 | 96.8 | |
| Black or African American | 0.5 | 0.4 | | 0 | 0.4 | |
| Asian | 2.4 | 2.8 | | 0 | 2.5 | |
| BMI (kg/m2), mean (SD) | 28.04 (5.213) | 28.18 (5.540) | | 27.11 (4.570) | 28.04 (5.319) | |
| Haemoglobin (g/dL), mean (SD) | 12.3 (1.49) | 12.2 (1.48) | | 12.8 (1.36) | 12.3 (1.48) | |
| Haemoglobin category (%) | | | | | | |
| <12 g/dL | 40.1 | 42.4 | | 26.4 | 40.3 | |
| ≥12 g/dL | 59.8 | 57.6 | | 73.6 | 59.7 | |
| Missing | <0.1 | 0 | | 0 | <0.1 | |
| Ferritin (mcg/L), mean (SD) | 69.7 (60.65) | 77.1 (65.63) | | 65.0 (57.75) | 72.4 (62.67) | |
| Ferritin category (%) | | | | | | |
| <30 mcg/L | 27.1 | 23.0 | | 26.4 | 25.4 | |
| 30 to <100 mcg/L | 53.9 | 53.5 | | 56.4 | 53.9 | |
| ≥100 mcg/L | 18.9 | 23.5 | | 17.3 | 20.7 | |
| Missing | <0.1 | 0 | | 0 | <0.1 | |
| Phosphorus category (%) | | | | | |
| <1 mg/dL | 0 | 0 | 0 | | 0 |
| 1 to <2 mg/dL | 0 | 0.1 | 0 | | <0.1 |
| 2 to <2.5 mg/dL | 2.0 | 2.1 | 1.8 | | 2.1 |
| 2.5 to <4.5 mg/dL | 87.2 | 84.2 | 89.1 | | 86.1 |
| ≥4.5 mg/dL | 8.6 | 11.1 | 9.1 | | 9.6 |
| Missing | 2.1 | 2.5 | 0 | | 2.2 |
| TSAT (%), mean (SD) | 17.2 (12.00) | 15.8 (8.13) | 19.1 (9.03) | | 16.8 (10.47) |
| TSAT category (%) | | | | | |
| <20% | 72.8 | 76.0 | 57.3 | | 73.3 |
| ≥20% | 26.6 | 23.6 | 42.7 | | 26.3 |
| Missing | 0.6 | 0.4 | 0 | | 0.5 |
| eGFR (CKD-EPI; mL/min/1.73 m2), mean (SD) | 60.0 (21.63) | 59.1 (22.75) | 59.6 (24.39) | | 59.6 (22.25) |
| eGFR (mL/min/1.73 m2) category (%) | | | | | |
| ≤30 | 8.7 | 9.3 | 10.9 | | 9.0 |
| >30 to ≤45 | 17.9 | 18.4 | 20.9 | | 18.3 |
| >45 to ≤60 | 20.9 | 22.2 | 21.8 | | 21.5 |
| >60 | 46.9 | 42.4 | 46.4 | | 45.1 |
| Missing | 5.6 | 7.7 | 0 | | 6.1 |

BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation; eGFR, estimated glomerular filtration rate; FCM, ferric carboxymaltose; HF, heart failure; TSAT, transferrin saturation.

**Table S4** FCM dosing in HF studies

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study Identifier** | **Patients included in analysis** | **Duration of study (weeks)** | **FCM dosing** | **FCM Exposure** |
| **FER-CARS-01** | **30** | **12** | * **200 mg weekly until repletion according to the Ganzoni formulaa** * **200 mg every 4 weeks thereafter through week 12** | **Mean (SD): 1103 (279) mg** |
| **FER-CARS-02/FAIR-HF** | **296** | **26** | * **200 mg weekly until repletion according to the Ganzoni formulaa** * **200 mg at weeks 12, 16, 20, and 24** | **Mean (SD): 1850 (433) mg** |
| **FER-CARS-03/EFFICACY-HF** | **20** | **26** | * **200 mg weekly until repletion according to the Ganzoni formulaa** * **200 mg at weeks 12, 16, 20, and 24** | **Mean (SD): 1640 (456) mg** |
| **FER-CARS-04/EFFECT-HF** | **84** | **24** | * **500-1000 mg at day 1b** * **0-1000 mg at week 6b** * **500 mg at week 12 if iron deficient** | **Mean (SD): 1204.5 (391) mg**  **42.0% of patients received 1 injection**  **54.5% of patients received 2 injections**  **3.4% of patients received 3 injections** |
| **FER-CARS-05/CONFIRM-HF** | **148** | **52** | * **500-1000 mg at day 1b** * **0-1000 mg at week 6b** * **500 mg at weeks 12, 24, and 36 if iron deficient** | **Mean (SD): 1500 (537) mg**  **24.3% of patients received 1 injection**  **51.3% of patients received 2 injections**  **17.1% of patients received 3 injections**  **7.2% of patients received 4/5 injections** |
| **FER-CARS-06/AFFIRM-AHF** | **496** | **52** | * **500-1000 mg at week 0** * **0-1000 mg at week 6b** * **500 mg at weeks 12 and 24 if iron deficient** | **Mean (SD): 1352 (568) mg**  **45.6% of patients received 1 injection**  **34.3% of patients received 2 injections**  **20% of patients received 3/4 injections** |

**FCM, ferric carboxymaltose; GI, gastrointestinal; HD-CKD, haemodialysis-dependent chronic kidney disease; HF, heart failure; NDD-CKD, non–dialysis-dependent chronic kidney disease.**

**Please see *Table S1* for the duration of trials in each therapeutic area.**

**a100 mg permitted for the last dose.**

**bIron dose dependent on screening weight and hemoglobin.**