Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Inclusion and Exclusion Criteria, and Main Revisions to the Trial Protocols

Inclusion and exclusion criteria, and changes implemented during the trial conduct
Inclusion criteria 1. Men or women >18 years with IDA caused by different etiologies,[a] such as abnormal uterine bleeding, gastrointestinal diseases, cancer, bariatric procedures (gastric bypass operations), and other conditions leading to significant blood loss. 2. Hb ≤11 g/dl. 3. Body weight >50 kg. 4. Serum ferritin ≤100 ng/ml. 5. Estimated glomerular filtration rate ≥65 ml/min/1.73 m^2. 6. Serum phosphate >2.5 mg/dl. 7. Documented history of intolerance or unresponsiveness to oral iron therapy[b] for at least one month[c] prior to trial enrollment. 8. Willingness to participate and signing the Informed Consent Form.
Exclusion criteria 1. Acute bleeding >500 ml within 72 hours. 2. Anaemia predominantly caused by factors other than IDA according to Investigator's judgment. 3. Hemochromatosis or other iron storage disorders. 4. Known hypersensitivity reaction to any component of IIM or FCM. 5. Previous serious hypersensitivity reactions to any IV iron compounds. 6. Treatment with IV iron within the last 30 days prior to screening. 7. Treatment with erythropoietin or erythropoietin-stimulation agents, red blood cell transfusion, radiotherapy, and/or chemotherapy within the last 30 days prior to screening. 8. Received an investigational drug within the last 30 days prior to screening. 9. Planned surgical procedure within the trial period. 10. Alanine aminotransferase and/or aspartate aminotransferase >3 times upper limit of normal (e.g., decompensated liver cirrhosis or active hepatitis). 11. Surgery under general anaesthesia within the last 30 days prior to screening. 12. Any non-viral infection within the last 30 days prior to screening. 13. Alcohol or drug abuse within the past 6 months. 14. Untreated hyperparathyroidism. 15. Kidney transplantation. 16. Estimated life expectancy of <6 months or, for cancer patients, an Eastern Cooperative Oncology Group (ECOG) performance status >1. 17. Conditions that interfere with the subject's ability to understand the requirements of the trial and/or presumable non-compliance. 18. Any other laboratory abnormality, medical condition, or psychiatric disorders which, in the opinion of the Investigator, will put the subject's disease management at risk or may result in the subject being unable to comply with the trial requirements. 19. Pregnant or nursing women. In order to avoid pregnancy, women of childbearing potential have to use adequate contraception (e.g., intrauterine devices, hormonal contraceptives, or double barrier method) during the entire trial period and 7 days after the last dosing.
Main revisions made to the trial protocols
The original protocols were amended once during the trials. Besides minor editing and administrative changes, the following amendments were made to the original protocol: • Text was updated to show that alkaline phosphatase was measured in serum and not in plasma. • The pyridinoline test – an exploratory end point with limited value – was omitted. • Exclusion criteria changes: Surgery under anesthesia was changed to surgery under general anesthesia; measurement of vitamin D prior to IV iron treatment was deleted as this is not standard; exclusion of oncology patients was a mistake and therefore this exclusion criterion was replaced with an inclusion criterion of life expectancy of at least 6 months; and psychological illness or seizures were omitted since neither were contraindicated or warned of in the prescribing information.

Main revisions made to the trial protocols (continued)
• "Documented history" was defined with the subject's own description of their illness deemed adequate to be entered in the medical file as source. Thus, no medical files from the referring physician or other were considered necessary. • Prohibited medications and non-drug therapies – erythropoietin or erythropoietin-stimulation agents, radiotherapy, and chemotherapy – were clarified as prohibited by alignment with exclusion criteria and prohibited medications. • Functional team positions within two internal teams – the TCT and GCP Quality Steering Committee – were expanded to reflect the updated team constitutions. • The description of trial summary data for posting in public registries was simplified to reflect updated requirements of the FDA "Final Rule".

[a] The etiology for IDA was documented in the medical history and verified in the source documents; if the etiology was unknown, this was also documented.

[b] Intolerance and non-response to oral iron treatment, along with the accompanying signs and symptoms, were documented in the medical history and verified in the source documents.

[c] Intolerance or unresponsiveness to ≥1 month of prescribed oral iron therapy according to the Investigator's judgment within the last 9 months was documented; these patients would not be candidates for oral iron again.

GCP, Good Clinical Practice; Hb, hemoglobin; FCM, ferric carboxymaltose; IDA, iron deficiency anemia; IIM iron isomaltoside 1000/ferric derisomaltose; IV, intravenous; TCT, Trial Core Team.

eTable 2. Listing of All Secondary Safety and Efficacy End Points

Secondary end point	Reported in manuscript?
Safety end points[a]	
Proportion of patients with hypophosphatemia at day 35	Yes
Absolute change in serum phosphate from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Relative change in serum phosphate from baseline to days 1, 7, 8, 14, 21, and 35	No
Change in fractional urinary phosphate excretion from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in intact fibroblast growth factor 23 from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in C-terminal fibroblast growth factor 23 from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in 1,25-Dihydroxyvitamin D from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in 24,25-Dihydroxyvitamin D from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in 25-Hydroxyvitamin D from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in ionized calcium from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in intact parathyroid hormone from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Incidence of serum phosphate <1.0 mg/dl at any time from baseline to day 35	Yes[b]
Time with hypophosphatemia (serum phosphate <2.0 mg/dl) from baseline to day 35	No
Type and incidence of adverse events	Yes
Serious or severe hypersensitivity reactions (i.e., treatment-emergent)	Yes
Efficacy end points	
Change in hemoglobin per gram of iron from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in ferritin from baseline to days 1, 7, 8, 14, 21, and 35	Yes
Change in transferrin saturation from baseline to days 1, 7, 8, 14, 21, and 35	Yes

[a] In addition, physical examinations and measurements of vital signs, height, weight, electro-cardiogram, and safety laboratory parameters were measured as part of standard safety assessments.

[b] The pre-specified secondary endpoint for severe hypophosphatemia was <1.0 mg/dl, whereas ≤1.0 mg/dl is reported in the manuscript. This modification of the definition of severe hypophosphatemia was enacted to account for rounding of values measured in mmol/l to two decimal places, into mg/dl reported to one decimal place, which caused values of 0.99 mg/dl (0.32 mmol/l) to be rounded to equal to rather than less than 1.0 mg/dl.

eTable 3. Biochemical Assays

Biochemical/ bone marker	Assay	Manufacturer	Precision (%CV)	
			Intra-assay	Inter-assay
Hemoglobin	Flow cytometry	Siemens ADVIA 2120i Hematology System	0.9–1.1	0.9–1.8
Serum phosphate	Photometric analysis	Roche Diagnostics	0.5–0.9	1.2–1.4
Urine phosphorus	Colorimetric	Roche Cobas 8000 Modular Analyzer	0.5–0.8	1.3–1.4
Ferritin	Chemiluminescence immunoassay	Beckman Coulter Inc.	2.6–3.9	4.1–6.3
Transferrin	Chemiluminescence immunoassay	Siemens BN II Nephelometer	2.7	2.3
Serum creatinine	Automated clinical chemistry	Roche Cobas 8000 Modular Analyzer	0.9–2.5	1.7–3.7
Urine creatinine	Colorimetric	Roche Cobas 8000 Modular Analyzer	1.1–2.1	1.7–2.2
Intact FGF23	ELISA	Immutopics, Inc.	2.0–4.1	3.5–9.1
C-terminal FGF23	ELISA	Immutopics, Inc.	1.4–2.4	2.4–4.7
25-Hydroxyvitamin D	LC-MS/MS	SCIEX	D2: 2.5–3.1 D3: 1.5–4.0	D2: 2.9–5.4 D3: 2.8–4.4
1,25-Dihydroxyvitamin D	Chemiluminescence immunoassay	DiaSorin	3.5–7.8	3.6–6.6
24,25-Dihydroxyvitamin D	LC-MS/MS	Danaher-SCIEX API5000	D2: 2.3–5.9 D3: 3.1–7.8	D2: 3.3–6.2 D3: 3.0–6.5
Ionized calcium	Ion-selective electrode	Instrumentation Laboratory	Not specified	Not specified
Intact parathyroid hormone	Chemiluminescence immunoassay	Siemens Healthcare Diagnostics	3.4–5.2	1.5–5.8
Alkaline phosphatase	Photometric analysis	Roche Diagnostics	0.4–0.5	0.67
Bone-specific alkaline phosphatase	Chemiluminescence immunoassay	Beckman Coulter Inc.	1.5–2.6	3.6–6.4
N-terminal propeptide of Type I collagen	Electrochemiluminescence immunoassay	Roche Diagnostics	1.6–2.1	4.2–4.4
Carboxy-terminal collagen crosslinks	Elecsys β-CrossLaps serum assay	Roche Diagnostics	1.3–2.3	4.6–6.5

Urinary fractional excretion of phosphate was calculated as: [urinary phosphate * serum creatinine] / [serum phosphate * urinary creatinine] * 100. Transferrin saturation was calculated as: [total serum iron (μmol/l) * 5.586] / [transferrin (g/l) *100] * 70.9.

CV, coefficient of variation; ELISA, enzyme-linked immunosorbent assay; FGF23, fibroblast growth factor; LC-MS/MS, liquid chromatography and tandem mass spectrometry.

eTable 4. Prevalence of Hypophosphatemia at Each Time Point – Trial A, Trial B and Pooled Data for Trials A and B

	Day						
	0 **n/N (%)**	**1** **n/N (%)**	**7** **n/N (%)**	**8** **n/N (%)**	**14** **n/N (%)**	**21** **n/N (%)**	**35** **n/N (%)**
Trial A							
IIM	0/63 (0.0)	0/59 (0.0)	2/60 (3.3)	3/57 (5.3)	1/58 (1.7)	1/54 (1.9)	1/59 (1.7)
FCM	0/60 (0.0)	1/56 (1.8)	24/58 (41.4)	24/57 (42.1)	38/56 (67.9)	28/56 (50.0)	24/58 (41.4)
Rate difference (95% CI)	–	–1.8 (–5.3, 1.7)[a]	–37.9 (–50.9, –22.9)	–36.2 (–49.6, –20.9)	–65.9 (–76.8, –48.9)	–47.2 (–60.1, –30.0)	–39.2 (–52.2, –23.3)
P value	–	*P* = .30	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Rate difference, overall incidence (95% CI)	–67.0 (–77.4, –51.5)						
P value	*P* < .001						
Site-adjusted rate difference, overall incidence (95% CI)[b]	–67.5 (–78.5, –49.8)						
P value	*P* < .001						
Trial B							
IIM	0/62 (0.0)	0/61 (0.0)	2/60 (3.3)	3/59 (5.1)	3/58 (5.2)	1/56 (1.8)	0/58 (0.0)
FCM	0/57 (0.0)	0/53 (0.0)	14/55 (25.5)	22/53 (41.5)	33/53 (62.3)	28/55 (50.9)	25/56 (44.6)
Rate difference (95% CI)	–	–	–22.0 (–35.1, –7.5)	–38.4 (–52.2, –22.5)	–57.1 (–69.5, –40.3)	–48.6 (–61.4, –31.6)	–44.6 (–57.7, –31.6)[a]
P value	–	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Rate difference, overall incidence (95% CI)	–65.8 (–76.6, –49.8)						
P value	*P* < .001						
Site-adjusted rate difference, overall incidence (95% CI)[b]	–69.2 (–79.8, –51.3)						
P value	*P* < .001						

	Day						
	0 **n/N (%)**	**1** **n/N (%)**	**7** **n/N (%)**	**8** **n/N (%)**	**14** **n/N (%)**	**21** **n/N (%)**	**35** **n/N (%)**
Pooled data for Trial A and Trial B							
IIM	0/125 (0.0)	0/120 (0.0)	4/120 (3.3)	6/116 (5.2)	4/116 (3.4)	2/110 (1.8)	1/117 (0.9)
FCM	0/117 (0.0)	1/109 (0.9)	38/113 (33.6)	46/110 (41.8)	71/109 (65.1)	56/111 (50.5)	49/114 (43.0)
Rate difference (95% CI)	–	–0.9 (–2.7, 0.9)[a]	–30.1 (–39.5, –20.5)	–37.3 (–47.1, –26.8)	–61.5 (–70.1, –50.8)	–48.1 (–57.4, –37.4)	–41.7 (–50.9, –31.1)
P value	–	*P* = .29	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Rate difference, overall incidence (95% CI)	–66.4 (–74.4, –55.8)						
P value	*P* < .001						
Site-adjusted rate difference, overall incidence (95% CI)[b]	–68.3 (–76.5, –56.5)						
P value	*P* < .001						

Data are presented for the safety analysis set. *P* values are for between-group comparisons. Rate differences with 95% Newcombe CI adjusted for stratum (and trial, in the pooled analyses) using the Cochran-Mantel-Haenszel method, unless otherwise stated. [a] Rate difference with 95% Newcombe CI adjusted for stratum (and trial, in the pooled analyses) using the Cochran-Mantel-Haenszel method could not be estimated due to lack of events. Unadjusted treatment difference and 95% CI presented. [b] Rate difference with 95% Newcombe CI adjusted for site using the Cochran-Mantel-Haenszel method (*post-hoc* analysis).

CI, confidence interval; FCM, ferric carboxymaltose; FGF, fibroblast growth factor; IIM, iron isomaltoside 1000/ferric derisomaltose.

eTable 5. Secondary and Additional Safety End Points – Trial A, Trial B, and Pooled Data for Trials A and B

End point		Day 0 Mean (SD) n	1 Mean (SD) n	7 Mean (SD) n	8 Mean (SD) n	14 Mean (SD) n	21 Mean (SD) n	35 Mean (SD) n
Trial A								
Serum phosphate (mg/dl)	IIM	3.3 (0.6) (n=63)	3.6 (0.5) (n=59)	3.2 (0.6) (n=60)	3.2 (0.6) (n=57)	3.2 (0.6) (n=58)	3.4 (0.6) (n=54)	3.5 (0.6) (n=59)
	FCM	3.3 (0.5) (n=60)	3.1 (0.5) (n=56)	2.2 (0.5) (n=58)	2.2 (0.6) (n=57)	1.9 (0.8) (n=56)	2.3 (1.0) (n=56)	2.4 (0.9) (n=58)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Urinary fractional excretion of phosphate (%)	IIM	11.1 (6.7) (n=40)	10.3 (6.4) (n=41)	11.8 (5.7) (n=43)	12.1 (6.7) (n=40)	11.1 (5.8) (n=44)	11.6 (6.5) (n=42)	10.3 (4.7) (n=49)
	FCM	10.3 (4.7) (n=42)	12.8 (5.0) (n=40)	18.8 (8.2) (n=42)	19.4 (9.4) (n=42)	21.8 (11.3) (n=46)	18.7 (10.2) (n=47)	15.2 (9.2) (n=48)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* = .001
Intact FGF23 (pg/ml)	IIM	59.0 (39.8) (n=59)	61.1 (58.2) (n=58)	69.0 (44.4) (n=60)	64.2 (32.4) (n=54)	51.2 (40.4) (n=57)	56.0 (49.1) (n=54)	48.2 (26.1) (n=58)
	FCM	46.2 (20.5) (n=57)	151.2 (90.1) (n=55)	118.1 (79.7) (n=56)	343.6 (257.7) (n=56)	151.0 (111.4) (n=56)	111.9 (94.2) (n=55)	79.0 (62.3) (n=57)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
C-terminal FGF23 (RU/ml)	IIM	847.1 (811.6) (n=60)	137.7 (72.3) (n=57)	119.1 (41.1) (n=55)	129.6 (93.3) (n=55)	107.2 (39.0) (n=57)	105.0 (47.3) (n=51)	109.2 (44.9) (n=53)
	FCM	631.2 (672.6) (n=55)	218.0 (122.1) (n=53)	161.6 (72.9) (n=55)	304.3 (172.4) (n=55)	193.6 (128.8) (n=55)	138.6 (64.7) (n=53)	122.2 (58.2) (n=57)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* = .14
1,25-Dihydroxyvitamin D (pg/ml)	IIM	58.9 (18.2) (n=62)	63.2 (23.9) (n=59)	39.2 (18.4) (n=60)	42.4 (19.0) (n=58)	55.2 (14.0) (n=58)	55.8 (15.5) (n=56)	55.2 (16.3) (n=59)
	FCM	63.9 (19.4) (n=60)	43.3 (17.2) (n=58)	25.1 (21.0) (n=58)	24.4 (25.3) (n=58)	24.9 (22.4) (n=57)	34.9 (28.4) (n=56)	46.0 (23.4) (n=58)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* = .004
24,25-Dihydroxyvitamin D (ng/ml)	IIM	2.1 (1.1) (n=61)	2.1 (0.9) (n=59)	2.4 (1.2) (n=60)	2.3 (1.2) (n=58)	2.2 (1.1) (n=58)	2.2 (1.3) (n=56)	2.2 (1.2) (n=59)
	FCM	2.4 (1.2) (n=56)	2.5 (1.3) (n=58)	3.2 (1.6) (n=58)	3.2 (1.6) (n=58)	3.5 (1.6) (n=56)	3.3 (1.5) (n=55)	3.1 (1.5) (n=58)
	P	–	*P* = .06	*P* = .002	*P* < .001	*P* < .001	*P* < .001	*P* = .001

End point		Day 0 Mean (SD) n	Day 1 Mean (SD) n	Day 7 Mean (SD) n	Day 8 Mean (SD) n	Day 14 Mean (SD) n	Day 21 Mean (SD) n	Day 35 Mean (SD) n
Trial A (continued)								
25-Hydroxyvitamin D (ng/ml)	IIM	23.2 (7.6) (n=62)	23.7 (7.4) (n=59)	24.5 (7.9) (n=60)	23.9 (7.8) (n=58)	24.2 (8.0) (n=58)	24.2 (8.2) (n=55)	23.4 (8.1) (n=59)
	FCM	25.9 (7.8) (n=60)	26.2 (8.0) (n=58)	25.3 (8.2) (n=57)	26.2 (8.3) (n=58)	25.1 (8.5) (n=57)	25.5 (7.6) (n=57)	26.0 (6.5) (n=56)
	P	–	*P* = .56	*P* = .01	*P* = .61	*P* = .04	*P* = .24	*P* = .83
Ionized calcium (mg/dl)	IIM	5.08 (0.21) (n=59)	5.12 (0.22) (n=56)	5.10 (0.19) (n=55)	5.11 (0.20) (n=54)	5.09 (0.22) (n=56)	5.13 (0.20) (n=54)	5.10 (0.24) (n=51)
	FCM	5.08 (0.21) (n=60)	5.08 (0.23) (n=56)	5.02 (0.17) (n=56)	5.05 (0.20) (n=56)	5.00 (0.20) (n=53)	5.03 (0.23) (n=50)	5.05 (0.24) (n=55)
	P	–	*P* = .27	*P* = .004	*P* = .05	*P* = .005	*P* = .006	*P* = .13
Intact parathyroid hormone (pg/ml)	IIM	55.1 (26.4) (n=62)	52.8 (25.6) (n=57)	50.8 (27.6) (n=58)	55.7 (32.4) (n=55)	59.5 (33.9) (n=55)	54.6 (29.4) (n=53)	55.5 (28.3) (n=54)
	FCM	51.6 (26.4) (n=59)	54.1 (23.5) (n=54)	58.5 (29.7) (n=57)	54.8 (28.7) (n=56)	68.3 (37.5) (n=57)	68.0 (34.7) (n=56)	72.7 (45.2) (n=57)
	P	–	*P* = .74	*P* = .04	*P* = .92	*P* = .06	*P* < .001	*P* = .003
Alkaline phosphatase (IU/l) (exploratory end point)	IIM	70.0 (26.9) (n=62)	70.3 (25.8) (n=59)	72.1 (22.4) (n=60)	72.7 (21.7) (n=57)	71.5 (22.0) (n=57)	71.3 (21.0) (n=56)	73.5 (25.4) (n=59)
	FCM	72.4 (27.5) (n=58)	72.1 (30.6) (n=54)	74.6 (28.2) (n=58)	78.8 (30.9) (n=58)	78.6 (32.0) (n=56)	81.9 (30.0) (n=56)	81.9 (31.0) (n=58)
	P	–	*P* = .96	*P* = .69	*P* = .14	*P* = .13	*P* = .005	*P* = .03
N-terminal propeptide of Type I collagen (ng/ml)	IIM	56.5 (26.3) (n=62)	55.0 (27.4) (n=59)	48.4 (21.5) (n=60)	48.7 (21.1) (n=58)	51.2 (25.6) (n=58)	53.4 (23.2) (n=56)	53.8 (25.7) (n=59)
	FCM	57.3 (28.9) (n=60)	54.8 (28.4) (n=58)	44.6 (23.0) (n=58)	45.2 (21.9) (n=57)	37.3 (17.9) (n=56)	38.4 (17.9) (n=54)	45.0 (19.1) (n=58)
	P	–	*P* = .92	*P* = .02	*P* = .03	*P* < .001	*P* < .001	*P* = .001
Carboxy-terminal collagen crosslinks (ng/ml)	IIM	0.33 (0.16) (n=61)	0.37 (0.19) (n=59)	0.31 (0.15) (n=59)	0.35 (0.18) (n=55)	0.34 (0.20) (n=57)	0.37 (0.21) (n=55)	0.37 (0.21) (n=57)
	FCM	0.29 (0.15) (n=58)	0.28 (0.15) (n=55)	0.25 (0.13) (n=57)	0.25 (0.12) (n=55)	0.24 (0.11) (n=56)	0.27 (0.13) (n=55)	0.30 (0.17) (n=58)
	P	–	*P* = .01	*P* = .02	*P* < .001	*P* < .001	*P* < .001	*P* = .10

End point		Day 0 Mean (SD) n	1 Mean (SD) n	7 Mean (SD) n	8 Mean (SD) n	14 Mean (SD) n	21 Mean (SD) n	35 Mean (SD) n
Trial B								
Serum phosphate (mg/dl)	IIM	3.4 (0.5) (n=62)	3.6 (0.5) (n=61)	3.0 (0.6) (n=60)	3.0 (0.6) (n=59)	3.1 (0.6) (n=58)	3.3 (0.5) (n=56)	3.5 (0.5) (n=58)
	FCM	3.3 (0.5) (n=57)	3.1 (0.4) (n=53)	2.5 (0.7) (n=55)	2.2 (0.7) (n=53)	1.8 (0.7) (n=53)	2.1 (0.9) (n=55)	2.3 (0.9) (n=56)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Urinary fractional excretion of phosphate (%)	IIM	9.4 (4.9) (n=38)	10.2 (6.1) (n=38)	10.8 (5.8) (n=44)	12.4 (6.1) (n=43)	10.3 (4.9) (n=45)	10.0 (4.0) (n=46)	10.9 (5.7) (n=52)
	FCM	10.2 (4.5) (n=37)	11.4 (4.3) (n=36)	14.9 (6.5) (n=39)	15.7 (6.0) (n=37)	18.4 (10.0) (n=41)	16.9 (7.9) (n=44)	15.5 (8.4) (n=50)
	P	–	*P* = .21	*P* = .004	*P* = .001	*P* < .001	*P* < .001	*P* = .007
Intact FGF23 (pg/ml)	IIM	60.9 (50.3) (n=60)	55.6 (50.1) (n=61)	77.7 (62.9) (n=60)	69.4 (50.0) (n=59)	55.7 (45.9) (n=57)	52.8 (44.3) (n=56)	51.7 (46.6) (n=58)
	FCM	53.6 (35.3) (n=57)	147.8 (104.2) (n=54)	87.1 (73.1) (n=56)	311.6 (222.5) (n=54)	127.5 (104.5) (n=56)	107.9 (84.9) (n=56)	64.7 (49.4) (n=55)
	P	–	*P* < .001	*P* = .11	*P* < .001	*P* < .001	*P* < .001	*P* = .004
C-terminal FGF23 (RU/ml)	IIM	835.4 (802.2) (n=55)	136.5 (77.6) (n=61)	130.5 (126.7) (n=61)	108.4 (49.2) (n=57)	96.7 (45.2) (n=53)	96.7 (47.8) (n=55)	104.9 (63.4) (n=53)
	FCM	1060.9 (1799.4) (n=49)	239.0 (120.1) (n=52)	141.3 (85.4) (n=55)	319.3 (152.5) (n=48)	158.1 (88.8) (n=55)	143.9 (64.5) (n=53)	115.4 (85.7) (n=55)
	P	–	*P* = .12	*P* = .55	*P* < .001	*P* = .35	*P* = .20	*P* = .44
1,25-Dihydroxyvitamin D (pg/ml)	IIM	55.6 (16.4) (n=61)	61.0 (16.8) (n=60)	38.6 (17.9) (n=61)	41.6 (16.1) (n=59)	54.6 (17.6) (n=58)	55.3 (14.9) (n=57)	55.7 (15.1) (n=58)
	FCM	59.6 (19.6) (n=57)	42.6 (18.2) (n=56)	36.0 (30.6) (n=56)	25.0 (22.9) (n=55)	23.8 (21.7) (n=56)	35.9 (25.5) (n=55)	46.7 (22.9) (n=55)
	P	–	*P* < .001	*P* = .29	*P* < .001	*P* < .001	*P* < .001	*P* = .03
24,25-Dihydroxyvitamin D (ng/ml)	IIM	2.0 (1.6) (n=53)	2.0 (1.5) (n=54)	2.3 (1.7) (n=53)	2.1 (1.6) (n=50)	2.1 (1.6) (n=50)	2.0 (1.6) (n=52)	2.1 (1.6) (n=50)
	FCM	1.9 (1.1) (n=47)	2.0 (1.0) (n=46)	2.2 (1.1) (n=47)	2.3 (1.1) (n=45)	2.5 (1.2) (n=46)	2.4 (1.2) (n=46)	2.2 (0.9) (n=45)
	P	–	*P* = .51	*P* = .76	*P* = .32	*P* = .002	*P* < .001	*P* = .11

End point		Day 0 Mean (SD) n	Day 1 Mean (SD) n	Day 7 Mean (SD) n	Day 8 Mean (SD) n	Day 14 Mean (SD) n	Day 21 Mean (SD) n	Day 35 Mean (SD) n
Trial B (continued)								
25-Hydroxyvitamin D (ng/ml)	IIM	23.2 (11.0) (n=56)	22.6 (10.2) (n=54)	22.6 (10.3) (n=55)	22.3 (10.4) (n=51)	22.1 (10.1) (n=51)	22.2 (10.1) (n=51)	23.7 (9.7) (n=50)
	FCM	23.8 (10.0) (n=48)	23.9 (10.0) (n=47)	24.8 (10.3) (n=47)	25.3 (10.2) (n=45)	24.8 (10.4) (n=46)	24.4 (9.6) (n=45)	23.8 (8.1) (n=44)
	P	–	*P* = .69	*P* = .10	*P* = .02	*P* = .02	*P* = .10	*P* = .89
Ionized calcium (mg/dl)	IIM	5.11 (0.21) (n=54)	5.11 (0.20) (n=57)	5.13 (0.21) (n=55)	5.12 (0.21) (n=56)	5.05 (0.51) (n=52)	5.14 (0.19) (n=56)	5.13 (0.24) (n=56)
	FCM	5.07 (0.22) (n=51)	5.13 (0.22) (n=47)	5.07 (0.21) (n=51)	5.07 (0.22) (n=49)	5.01 (0.23) (n=48)	5.07 (0.23) (n=53)	5.05 (0.23) (n=50)
	P	–	*P* = .30	*P* = .16	*P* = .13	*P* = .94	*P* = .04	*P* = .24
Intact parathyroid hormone (pg/ml)	IIM	55.4 (26.5) (n=62)	55.7 (25.3) (n=60)	54.6 (24.4) (n=59)	53.9 (27.5) (n=57)	62.3 (32.2) (n=56)	56.4 (30.8) (n=56)	54.0 (29.0) (n=57)
	FCM	59.9 (33.9) (n=57)	53.3 (28.5) (n=54)	62.1 (34.7) (n=55)	58.2 (31.3) (n=54)	83.4 (40.5) (n=54)	83.4 (45.2) (n=56)	83.5 (45.5) (n=55)
	P	–	*P* = .22	*P* = .30	*P* = .92	*P* = .003	*P* < .001	*P* < .001
Alkaline phosphatase (IU/l) (exploratory end point)	IIM	71.8 (18.5) (n=60)	72.0 (17.8) (n=61)	72.1 (16.5) (n=60)	72.3 (16.6) (n=59)	69.6 (16.8) (n=58)	68.4 (17.4) (n=56)	70.8 (18.0) (n=58)
	FCM	76.9 (26.8) (n=55)	79.0 (27.7) (n=51)	78.8 (28.7) (n=55)	79.9 (29.3) (n=53)	81.7 (37.9) (n=53)	83.4 (50.5) (n=55)	83.8 (39.7) (n=56)
	P	–	*P* = .32	*P* = .22	*P* = .08	*P* = .05	*P* = .16	*P* = .04
N-terminal propeptide of Type I collagen (ng/ml)	IIM	58.4 (25.4) (n=60)	56.6 (23.3) (n=61)	49.8 (19.9) (n=60)	50.0 (20.8) (n=59)	50.1 (21.4) (n=57)	53.6 (22.0) (n=57)	55.6 (21.1) (n=58)
	FCM	65.6 (39.4) (n=57)	59.7 (30.3) (n=56)	53.8 (30.2) (n=56)	52.2 (29.0) (n=55)	48.3 (27.2) (n=53)	49.2 (33.2) (n=56)	53.2 (35.4) (n=56)
	P	–	*P* = .35	*P* = .83	*P* = .18	*P* < .001	*P* < .001	*P* = .01
Carboxy-terminal collagen crosslinks (ng/ml)	IIM	0.33 (0.15) (n=61)	0.37 (0.20) (n=61)	0.32 (0.18) (n=61)	0.33 (0.19) (n=59)	0.32 (0.16) (n=57)	0.35 (0.16) (n=56)	0.34 (0.17) (n=57)
	FCM	0.38 (0.22) (n=57)	0.34 (0.17) (n=56)	0.34 (0.21) (n=56)	0.28 (0.15) (n=54)	0.31 (0.17) (n=56)	0.34 (0.19) (n=56)	0.39 (0.21) (n=56)
	P	–	*P* = .01	*P* = .34	*P* < .001	*P* = .06	*P* = .15	*P* = .74

End point		Day 0 Mean (SD) n	Day 1 Mean (SD) n	Day 7 Mean (SD) n	Day 8 Mean (SD) n	Day 14 Mean (SD) n	Day 21 Mean (SD) n	Day 35 Mean (SD) n
Pooled data for Trial A and Trial B								
Serum phosphate (mg/dl)	IIM	3.4 (0.5) (n=125)	3.6 (0.5) (n=120)	3.1 (0.6) (n=120)	3.1 (0.6) (n=116)	3.2 (0.6) (n=116)	3.3 (0.6) (n=110)	3.5 (0.6) (n=117)
	FCM	3.3 (0.5) (n=117)	3.1 (0.5) (n=109)	2.3 (0.6) (n=113)	2.2 (0.6) (n=110)	1.9 (0.7) (n=109)	2.2 (1.0) (n=111)	2.4 (0.9) (n=114)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Urinary fractional excretion of phosphate (%)	IIM	10.3 (5.9) (n=78)	10.2 (6.2) (n=79)	11.3 (5.7) (n=87)	12.3 (6.4) (n=83)	10.7 (5.4) (n=89)	10.7 (5.4) (n=88)	10.6 (5.2) (n=101)
	FCM	10.3 (4.6) (n=79)	12.2 (4.7) (n=76)	16.9 (7.7) (n=81)	17.7 (8.1) (n=79)	20.2 (10.8) (n=87)	17.8 (9.2) (n=91)	15.4 (8.8) (n=98)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Intact FGF23 (pg/ml)	IIM	59.9 (45.2) (n=119)	58.3 (54.0) (n=119)	73.3 (54.4) (n=120)	66.9 (42.4) (n=113)	53.5 (43.1) (n=114)	54.4 (46.5) (n=110)	49.9 (37.7) (n=116)
	FCM	49.9 (29.0) (n=114)	149.5 (96.9) (n=109)	102.6 (77.7) (n=112)	327.9 (240.5) (n=110)	139.2 (108.2) (n=112)	109.9 (89.3) (n=111)	72.0 (56.5) (n=112)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
C-terminal FGF23 (RU/ml)	IIM	841.5 (803.6) (n=115)	137.0 (74.8) (n=118)	125.1 (95.9) (n=116)	118.8 (74.6) (n=112)	102.2 (42.2) (n=110)	100.7 (47.5) (n=106)	107.0 (54.7) (n=106)
	FCM	833.7 (1338.9) (n=104)	228.4 (121.0) (n=105)	151.5 (79.7) (n=110)	311.3 (162.8) (n=103)	175.8 (111.6) (n=110)	141.3 (64.4) (n=106)	118.8 (72.8) (n=112)
	P	–	*P* < .001	*P* = .14	*P* < .001	*P* < .001	*P* < .001	*P* = .40
1,25-Dihydroxyvitamin D (pg/ml)	IIM	57.3 (17.3) (n=123)	62.1 (20.6) (n=119)	38.9 (18.1) (n=121)	42.0 (17.6) (n=117)	54.9 (15.9) (n=116)	55.6 (15.1) (n=113)	55.5 (15.6) (n=117)
	FCM	61.8 (19.5) (n=117)	43.0 (17.6) (n=114)	30.5 (26.6) (n=114)	24.7 (24.1) (n=113)	24.3 (21.9) (n=113)	35.4 (26.9) (n=111)	46.4 (23.1) (n=113)
	P	–	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001
24,25-Dihydroxyvitamin D (ng/ml)	IIM	2.0 (1.4) (n=114)	2.0 (1.3) (n=113)	2.3 (1.5) (n=113)	2.2 (1.4) (n=108)	2.2 (1.4) (n=108)	2.1 (1.4) (n=108)	2.1 (1.4) (n=109)
	FCM	2.2 (1.2) (n=103)	2.3 (1.2) (n=104)	2.7 (1.5) (n=105)	2.8 (1.5) (n=103)	3.0 (1.5) (n=102)	2.9 (1.4) (n=101)	2.7 (1.4) (n=103)
	P	–	*P* = .07	*P* = .04	*P* < .001	*P* < .001	*P* < .001	*P* < .001

End point		Day 0 Mean (SD) n	Day 1 Mean (SD) n	Day 7 Mean (SD) n	Day 8 Mean (SD) n	Day 14 Mean (SD) n	Day 21 Mean (SD) n	Day 35 Mean (SD) n
Pooled data for Trial A and Trial B (continued)								
25-Hydroxyvitamin D (ng/ml)	IIM	23.2 (9.4) (n=118)	23.2 (8.8) (n=113)	23.6 (9.1) (n=115)	23.2 (9.1) (n=109)	23.2 (9.0) (n=109)	23.3 (9.2) (n=106)	23.6 (8.8) (n=109)
	FCM	25.0 (8.9) (n=108)	25.2 (9.0) (n=105)	25.1 (9.1) (n=104)	25.8 (9.1) (n=103)	24.9 (9.3) (n=103)	25.0 (8.5) (n=102)	25.0 (7.3) (n=100)
	P	–	*P* = .46	*P* = .35	*P* = .30	*P* = .71	*P* > .99	*P* = .94
Ionized calcium (mg/dl)	IIM	5.09 (0.21) (n=113)	5.11 (0.21) (n=113)	5.11 (0.20) (n=110)	5.12 (0.21) (n=110)	5.07 (0.39) (n=108)	5.13 (0.20) (n=110)	5.12 (0.24) (n=107)
	FCM	5.08 (0.22) (n=111)	5.10 (0.22) (n=103)	5.04 (0.19) (n=107)	5.06 (0.21) (n=105)	5.00 (0.21) (n=101)	5.05 (0.23) (n=103)	5.05 (0.24) (n=105)
	P	–	*P* = .87	*P* = .003	*P* = .01	*P* = .21	*P* < .001	*P* = .06
Intact parathyroid hormone (pg/ml)	IIM	55.3 (26.3) (n=124)	54.3 (25.4) (n=117)	52.7 (26.0) (n=117)	54.8 (29.9) (n=112)	60.9 (32.9) (n=111)	55.5 (30.0) (n=109)	54.7 (28.5) (n=111)
	FCM	55.7 (30.5) (n=116)	53.7 (26.0) (n=108)	60.3 (32.1) (n=112)	56.4 (29.9) (n=110)	75.6 (39.5) (n=111)	75.7 (40.9) (n=112)	78.0 (45.5) (n=112)
	P	–	*P* = .44	*P* = .02	*P* = .93	*P* < .001	*P* < .001	*P* < .001
Alkaline phosphatase (IU/l) (exploratory end point)	IIM	70.9 (23.1) (n=122)	71.1 (22.0) (n=120)	72.1 (19.6) (n=120)	72.5 (19.2) (n=116)	70.5 (19.5) (n=115)	69.9 (19.3) (n=112)	72.1 (22.0) (n=117)
	FCM	74.6 (27.1) (n=113)	75.5 (29.3) (n=105)	76.6 (28.4) (n=113)	79.3 (30.0) (n=111)	80.1 (34.9) (n=109)	82.7 (41.2) (n=111)	82.8 (35.4) (n=114)
	P	–	*P* = .64	*P* = .29	*P* = .02	*P* = .01	*P* = .003	*P* = .002
N-terminal propeptide of Type I collagen (ng/ml)	IIM	57.4 (25.7) (n=122)	55.8 (25.3) (n=120)	49.1 (20.7) (n=120)	49.3 (20.9) (n=117)	50.6 (23.5) (n=115)	53.5 (22.5) (n=113)	54.7 (23.4) (n=117)
	FCM	61.4 (34.5) (n=117)	57.2 (29.3) (n=114)	49.1 (27.0) (n=114)	48.7 (25.8) (n=112)	42.6 (23.4) (n=109)	43.9 (27.2) (n=110)	49.0 (28.5) (n=114)
	P	–	*P* = .36	*P* = .07	*P* = .01	*P* < .001	*P* < .001	*P* < .001
Carboxy-terminal collagen crosslinks (ng/ml)	IIM	0.33 (0.16) (n=122)	0.37 (0.19) (n=120)	0.32 (0.16) (n=120)	0.34 (0.18) (n=114)	0.33 (0.18) (n=114)	0.36 (0.19) (n=111)	0.36 (0.19) (n=114)
	FCM	0.34 (0.20) (n=115)	0.31 (0.16) (n=111)	0.29 (0.18) (n=113)	0.26 (0.14) (n=109)	0.28 (0.14) (n=112)	0.31 (0.17) (n=111)	0.35 (0.20) (n=114)
	P	–	*P* < .001	*P* = .04	*P* < .001	*P* < .001	*P* < .001	*P* = .23

Data are presented for the safety analysis set. *P* values are for between-group comparisons from a mixed model for repeated measures analysis with treatment, day, treatment-by-day, trial (in the pooled analysis) and stratum as fixed effects and baseline value and baseline value-by-day as covariates.

CI, confidence interval; FCM, ferric carboxymaltose; FGF, fibroblast growth factor; IIM, iron isomaltoside 1000/ferric derisomaltose; SD, standard deviation.

eTable 6. Least Squares Mean Changes From Baseline in Biochemical and Bone Markers – Trial A, Trial B, and Pooled Data for Trials A and B

Trial A

Biochemical/bone marker	IIM	FCM	Difference between IIM and FCM (95% CI)	P Value
Serum phosphate (mg/dl)				
Day 1	0.24	–0.23	0.48 (0.31,0.65)	< .001
Day 7	–0.07	–1.13	1.06 (0.85,1.27)	< .001
Day 8	–0.09	–1.12	1.03 (0.81,1.25)	< .001
Day 14	–0.08	–1.42	1.35 (1.10,1.60)	< .001
Day 21	0.02	–1.02	1.03 (0.75,1.32)	< .001
Day 35	0.22	–0.91	1.13 (0.86,1.39)	< .001
Fractional urinary excretion of phosphate (%)				
Day 1	–1.6	2.3	–3.9 (–5.9,–1.9)	< .001
Day 7	0.9	7.9	–7.1 (–10.3,–3.8)	< .001
Day 8	1.5	8.9	–7.3 (–11.2,–3.5)	< .001
Day 14	0.7	11.2	–10.4 (–14.9,–6.0)	< .001
Day 21	0.7	8.7	–8.1 (–12.2,–3.9)	< .001
Day 35	–1.3	4.5	–5.8 (–9.2,–2.4)	.001
Intact FGF23 (pg/ml)				
Day 1	–2.1	103.6	–105.7 (–131.0,–80.5)	< .001
Day 7	8.6	69.4	–60.8 (–83.0,–38.6)	< .001
Day 8	13.4	306.6	–293.2 (–368.2,–218.3)	< .001
Day 14	–5.9	111.5	–117.5 (–151.6,–83.3)	< .001
Day 21	–0.2	71.0	–71.2 (–101.8,–40.6)	< .001
Day 35	–6.7	30.4	–37.2 (–54.9,–19.4)	< .001
C-terminal FGF23 (RU/ml)				
Day 1	–586.1	–487.0	–99.1 (–136.42,–61.76)	< .001
Day 7	–597.5	–548.2	–49.3 (–72.80,–25.90)	< .001
Day 8	–588.0	–396.7	–191.3 (–242.47,–140.09)	< .001
Day 14	–610.0	–509.3	–100.7 (–137.19,–64.20)	< .001
Day 21	–613.2	–564.8	–48.4 (–71.78,–24.96)	< .001
Day 35	–604.6	–589.7	–15.0 (–35.04, 5.06)	.14
Ionized calcium (mg/dl)				
Day 1	0.04	0.01	0.04 (–0.03, 0.10)	.27
Day 7	0.02	–0.06	0.09 (0.03,0.14)	.004
Day 8	0.04	–0.03	0.06 (0.00,0.13)	.05
Day 14	0.02	–0.09	0.10 (0.03,0.17)	.01
Day 21	0.06	–0.04	0.10 (0.03,0.17)	.01
Day 35	0.02	–0.03	0.06 (–0.02, 0.13)	.13
Parathyroid hormone (pg/ml)				
Day 1	–1.0	0.2	–1.1 (–8.0,5.7)	.74
Day 7	–3.4	6.4	–9.7 (–18.8,–0.6)	.04
Day 8	1.9	2.4	–0.5 (–10.6, 9.6)	.92
Day 14	5.1	16.3	–11.2 (–22.8, 0.5)	.06
Day 21	–1.9	16.3	–18.2 (–28.7,–7.7)	< .001
Day 35	1.8	21.6	–19.8 (–32.8,–6.8)	.003

Biochemical/bone marker	IIM	FCM	Difference between IIM and FCM (95% CI)	P Value
25-Hydroxyvitamin D (ng/ml)				
Day 1	0.1	0.3	–0.2 (–1.1,0.6)	.56
Day 7	0.8	–1.0	1.8 (0.4,3.1)	.01
Day 8	0.4	–0.0	0.4 (–1.2,2.0)	.61
Day 14	0.9	–1.2	2.1 (0.1,4.1)	.04
Day 21	0.5	–0.7	1.2 (–0.8,3.1)	.24
Day 35	–0.5	–0.3	–0.2 (–2.2,1.8)	.83
1,25-Dihydroxyvitamin D (pg/ml)				
Day 1	4.3	–20.0	24.3 (18.8,29.7)	< .001
Day 7	–21.4	–37.2	15.8 (8.8,22.7)	< .001
Day 8	–17.7	–37.8	20.1 (12.1,28.2)	< .001
Day 14	–5.4	–37.6	32.2 (25.5, 39.0)	< .001
Day 21	–4.9	–27.8	22.9 (14.8,31.0)	< .001
Day 35	–5.7	–16.3	10.6 (3.4,17.8)	.004
24,25-Dihydroxyvitamin D (ng/ml)				
Day 1	–0.03	0.14	–0.17 (–0.34, 0.00)	.06
Day 7	0.33	0.69	–0.37 (–0.60, –0.13)	.002
Day 8	0.18	0.69	–0.51 (–0.80, –0.21)	< .001
Day 14	0.14	0.94	–0.80 (–1.11, –0.49)	< .001
Day 21	0.10	0.75	–0.64 (–1.01, –0.28)	< .001
Day 35	0.03	0.62	–0.59 (–0.94, –0.23)	.001
Alkaline phosphatase (IU/l)				
Day 1	0.3	0.4	–0.1 (–3.9,3.7)	.96
Day 7	1.6	2.5	–0.9 (–5.5,3.7)	.69
Day 8	2.9	6.6	–3.6 (–8.4,1.2)	.14
Day 14	1.4	5.6	–4.2 (–9.8,1.3)	.13
Day 21	0.3	8.7	–8.4 (–14.2, –2.6)	.005
Day 35	2.3	9.6	–7.3 (–13.7, –0.9)	.03
Bone-specific alkaline phosphatase (µg/l)				
Day 1	0.4	0.3	0.1 (–0.4,0.7)	.67
Day 7	–0.1	0.6	–0.7 (–1.3,–0.1)	.03
Day 8	0.0	1.3	–1.3 (–2.1, –0.5)	.002
Day 14	–0.1	0.8	–1.0 (–2.0,0.1)	.07
Day 21	–0.1	1.5	–1.6 (–2.7, –0.6)	.003
Day 35	0.5	2.3	–1.8 (–2.8,–0.7)	< .001
N-terminal propeptide of Type I collagen (ng/ml)				
Day 1	–1.8	–2.0	0.2 (–3.6,3.9)	.92
Day 7	–7.0	–11.8	4.8 (0.7,8.9)	.02
Day 8	–6.7	–11.4	4.7 (0.4,8.9)	.03
Day 14	–4.9	–19.5	14.6 (9.2,20.1)	< .001
Day 21	–2.2	–17.3	15.1 (9.6,20.5)	< .001
Day 35	–1.7	–11.4	9.7 (3.9,15.5)	.001
Carboxy-terminal collagen crosslinks (ng/ml)				
Day 1	0.05	–0.01	0.05 (0.01,0.10)	.01
Day 7	0.00	–0.04	0.05 (0.01,0.09)	.02
Day 8	0.03	–0.05	0.08 (0.04,0.12)	< .001
Day 14	0.02	–0.06	0.08 (0.04,0.13)	< .001
Day 21	0.06	–0.04	0.10 (0.05,0.15)	< .001
Day 35	0.05	0.00	0.05 (–0.01, 0.10)	0.10

Data presented are for the safety analysis set.

Estimates are derived from a mixed model for repeated measurements with treatment, day, treatment-by-day interaction, and randomized strata as fixed effects, and baseline value and baseline value-by-day interactions as covariates.

CI, confidence interval; FCM, ferric carboxymaltose; FGF23, fibroblast growth factor; IIM, iron isomaltoside 1000/ferric derisomaltose.

Trial B

Biochemical/bone marker	IIM	FCM	Difference between IIM and FCM (95% CI)	P Value
Serum phosphate (mg/dl)				
Day 1	0.23	–0.23	0.46 (0.30, 0.62)	< .001
Day 7	–0.38	–0.92	0.54 (0.32, 0.76)	< .001
Day 8	–0.40	–1.13	0.73 (0.49,0.96)	< .001
Day 14	–0.28	–1.50	1.22 (0.99,1.46)	< .001
Day 21	–0.05	–1.30	1.24 (0.98,1.51)	< .001
Day 35	0.15	–1.02	1.17 (0.91,1.43)	< .001
Fractional urinary excretion of phosphate (%)				
Day 1	0.3	1.7	–1.4 (–3.5,0.8)	.21
Day 7	1.2	5.0	–3.9 (–6.4,–1.3)	.004
Day 8	2.2	6.4	–4.2 (–6.7,–1.7)	.001
Day 14	–0.2	8.4	–8.6 (–12.0, –5.2)	< .001
Day 21	–0.0	6.5	–6.5 (–9.2,–3.8)	< .001
Day 35	1.0	5.3	–4.3 (–7.4,–1.2)	.007
Intact FGF23 (pg/ml)				
Day 1	–4.6	92.3	–96.8 (–119.8, –73.8)	< .001
Day 7	17.1	32.8	–15.7 (–34.9, 3.4)	.11
Day 8	6.2	257.9	–251.7 (–307.2, –196.2)	< .001
Day 14	–5.9	73.2	–79.1 (–103.7, –54.5)	< .001
Day 21	–8.5	53.3	–61.8 (–83.0, –40.5)	< .001
Day 35	–8.7	9.3	–18.0 (–30.1, –5.9)	.004
C-terminal FGF23 (RU/ml)				
Day 1	–796.2	–738.7	–57.5 (–131.1, 16.1)	.12
Day 7	–807.2	–827.9	20.7 (–49.7, 91.0)	.55
Day 8	–816.7	–661.0	–155.7 (–234.7, –76.6)	< .001
Day 14	–835.8	–808.5	–27.3 (–86.0, 31.5)	.35
Day 21	–848.2	–823.9	–24.3 (–62.3, 13.7)	.20
Day 35	–840.9	–852.2	11.3 (–18.6, 41.2)	.44
Ionized calcium (mg/dl)				
Day 1	0.01	0.04	–0.03 (–0.10, 0.03)	.30
Day 7	0.04	–0.01	0.05 (–0.02, 0.13)	.16
Day 8	0.02	–0.03	0.05 (–0.02, 0.12)	.13
Day 14	–0.08	–0.07	–0.01 (–0.17, 0.16)	.94
Day 21	0.04	–0.03	0.07 (0.00,0.14)	.04
Day 35	0.02	–0.02	0.05 (–0.03, 0.12)	.24
Parathyroid hormone (pg/ml)				
Day 1	–0.9	–5.5	4.6 (–2.7,11.9)	.22
Day 7	–2.5	2.2	–4.6 (–13.5,4.2)	.30
Day 8	–1.9	–2.3	0.4 (–7.8,8.6)	.92
Day 14	6.9	22.6	–15.7 (–26.1, –5.3)	.003
Day 21	0.8	23.3	–22.5 (–33.9, –11.2)	< .001
Day 35	–1.8	23.0	–24.8 (–35.4, –14.2)	< .001

Biochemical/bone marker	IIM	FCM	Difference between IIM and FCM (95% CI)	P Value
25-Hydroxyvitamin D (ng/ml)				
Day 1	–0.5	–0.3	–0.2 (–1.1, 0.7)	.69
Day 7	–0.4	0.6	–1.0 (–2.3, 0.2)	.10
Day 8	–0.9	0.8	–1.6 (–3.0, –0.3)	.02
Day 14	–1.2	0.7	–1.9 (–3.5, –0.3)	.02
Day 21	–1.3	0.1	–1.4 (–3.0, 0.3)	.10
Day 35	–0.3	–0.5	0.1 (–1.8, 2.0)	.89
1,25-Dihydroxyvitamin D (pg/ml)				
Day 1	5.4	–16.5	21.8 (17.7, 26.0)	< .001
Day 7	–17.9	–22.5	4.6 (–4.1, 13.3)	.29
Day 8	–14.0	–33.5	19.6 (12.4, 26.7)	< .001
Day 14	–1.4	–34.5	33.1 (26.0, 40.1)	< .001
Day 21	–0.9	–22.7	21.8 (14.2, 29.4)	< .001
Day 35	–0.6	–9.7	9.0 (1.2, 16.9)	.03
24,25-Dihydroxyvitamin D (ng/ml)				
Day 1	0.02	0.08	–0.06 (–0.22, 0.11)	.51
Day 7	0.30	0.26	0.04 (–0.24, 0.32)	.76
Day 8	0.24	0.38	–0.14 (–0.41, 0.14)	.32
Day 14	0.09	0.56	–0.47 (–0.76, –0.18)	.002
Day 21	0.00	0.51	–0.50 (–0.77, –0.24)	< .001
Day 35	0.01	0.23	–0.23 (–0.50, 0.05)	.11
Alkaline phosphatase (IU/l)				
Day 1	0.4	1.4	–1.0 (–3.0, 1.0)	.32
Day 7	0.7	2.4	–1.7 (–4.5, 1.1)	.22
Day 8	0.8	3.6	–2.8 (–6.1, 0.4)	.08
Day 14	–0.5	4.5	–5.0 (–10.0, –0.0)	.05
Day 21	–0.4	5.2	–5.6 (–13.3, 2.2)	.16
Day 35	1.1	6.9	–5.8 (–11.2, –0.3)	.04
Bone-specific alkaline phosphatase (µg/l)				
Day 1	–0.0	0.3	–0.4 (–1.2, 0.4)	.34
Day 7	–0.2	0.3	–0.5 (–1.1, 0.1)	.10
Day 8	–0.3	0.6	–0.9 (–1.7, –0.1)	.03
Day 14	–0.3	1.1	–1.3 (–2.4, –0.3)	.01
Day 21	–0.2	1.2	–1.4 (–2.5, –0.3)	.01
Day 35	–0.1	2.1	–2.3 (–3.2, –1.3)	< .001
N-terminal propeptide of Type I collagen (ng/ml)				
Day 1	–3.4	–4.9	1.5 (–1.7, 4.7)	.35
Day 7	–10.0	–10.5	0.5 (–3.9, 4.9)	.83
Day 8	–9.5	–12.4	2.9 (–1.4, 7.1)	.18
Day 14	–9.4	–16.4	6.9 (3.2, 10.7)	< .001
Day 21	–5.3	–15.4	10.1 (4.7, 15.5)	< .001
Day 35	–2.8	–11.2	8.3 (1.8, 14.8)	.01
Carboxy-terminal collagen crosslinks (ng/ml)				
Day 1	0.03	–0.03	0.06 (0.01, 0.11)	.01
Day 7	–0.01	–0.04	0.02 (–0.03, 0.08)	.34
Day 8	0.00	–0.09	0.09 (0.04, 0.14)	< .001
Day 14	–0.02	–0.06	0.04 (–0.00, 0.09)	.06
Day 21	0.01	–0.03	0.04 (–0.01, 0.09)	.15
Day 35	0.01	0.02	–0.01 (–0.06, 0.04)	.74

Data presented are for the safety analysis set.

Estimates are derived from a mixed model for repeated measurements with treatment, day, treatment-by-day interaction, and randomized strata as fixed effects, and baseline value and baseline value-by-day interactions as covariates.

CI, confidence interval; FCM, ferric carboxymaltose; FGF23, fibroblast growth factor; IIM, iron isomaltoside 1000/ferric derisomaltose.

Pooled data for Trial A and Trial B

Biochemical/bone marker	IIM	FCM	Difference between IIM and FCM (95% CI)	P Value
Serum phosphate (mg/dl)				
Day 1	0.24	–0.23	0.47 (0.36, 0.58)	< .001
Day 7	–0.22	–1.03	0.81 (0.66, 0.96)	< .001
Day 8	–0.25	–1.13	0.88 (0.72,1.04)	< .001
Day 14	–0.18	–1.46	1.29 (1.12,1.46)	< .001
Day 21	–0.02	–1.15	1.13 (0.94,1.33)	< .001
Day 35	0.18	–0.96	1.14 (0.96,1.32)	< .001
Fractional urinary excretion of phosphate (%)				
Day 1	–0.7	2.1	–2.8 (–4.2,–1.3)	< .001
Day 7	0.9	6.7	–5.7 (–7.9,–3.6)	< .001
Day 8	1.7	7.8	–6.1 (–8.4,–3.7)	< .001
Day 14	0.2	9.9	–9.7 (–12.6, –6.9)	< .001
Day 21	0.2	7.8	–7.6 (–10.2, –5.1)	< .001
Day 35	–0.3	5.0	–5.3 (–7.7,–2.9)	< .001
Intact FGF23 (pg/ml)				
Day 1	–3.9	98.4	–102.2 (–119.1, –85.4)	< .001
Day 7	12.8	51.3	–38.6 (–53.4, –23.8)	< .001
Day 8	7.8	282.2	–274.4 (–320.1, –228.6)	< .001
Day 14	–6.6	92.1	–98.7 (–119.2, –78.2)	< .001
Day 21	–5.2	61.4	–66.6 (–84.8, –48.5)	< .001
Day 35	–8.3	20.1	–28.4 (–39.1, –17.6)	< .001
C-terminal FGF23 (RU/ml)				
Day 1	–688.4	–606.0	–82.4 (–122.1, –42.6)	< .001
Day 7	–704.3	–682.9	–21.4 (–50.2, 7.4)	.14
Day 8	–702.4	–525.4	–177.0 (–217.6, –136.4)	< .001
Day 14	–721.0	–653.6	–67.4 (–97.9, –36.9)	< .001
Day 21	–728.7	–690.1	–38.6 (–57.7, –19.5)	< .001
Day 35	–721.6	–714.7	–6.9 (–22.9,9.2)	.40
Ionized calcium (mg/dl)				
Day 1	0.03	0.02	0.00 (–0.04. 0.05)	.87
Day 7	0.03	–0.04	0.07 (0.03,0.12)	.003
Day 8	0.03	–0.03	0.06 (0.01,0.10)	.01
Day 14	–0.02	–0.08	0.05 (–0.03, 0.14)	.21
Day 21	0.05	–0.03	0.09 (0.04,0.14)	< .001
Day 35	0.02	–0.03	0.05 (-0.00, 0.10)	.06
Parathyroid hormone (pg/ml)				
Day 1	–0.9	–2.8	1.9 (–3.0,6.8)	.44
Day 7	–2.9	4.3	–7.2 (–13.5, –1.0)	.02
Day 8	–0.1	0.1	–0.3 (–6.7,6.1)	.93
Day 14	5.9	19.7	–13.8 (–21.6, –6.0)	< .001
Day 21	–0.9	20.1	–21.1 (–28.8, –13.4)	< .001
Day 35	–0.3	22.6	–22.8 (–31.1, –14.6)	< .001

Biochemical/bone marker	IIM	FCM	Difference between IIM and FCM (95% CI)	P Value
25-Hydroxyvitamin D (ng/ml)				
Day 1	–0.2	0.0	–0.2 (–0.8,0.4)	.46
Day 7	0.2	–0.2	0.4 (–0.5,1.4)	.35
Day 8	–0.2	0.3	–0.6 (–1.6,0.5)	.30
Day 14	–0.1	–0.4	0.2 (–1.0,1.5)	.71
Day 21	–0.4	–0.4	0.0 (–1.3,1.3)	1.0
Day 35	–0.4	–0.4	–0.1 (–1.4,1.3)	.94
1,25-Dihydroxyvitamin D (pg/ml)				
Day 1	4.8	–18.3	23.1 (19.7,26.5)	< .001
Day 7	–19.7	–30.0	10.3 (4.7,15.8)	< .001
Day 8	–15.8	–35.7	19.8 (14.5,25.2)	< .001
Day 14	–3.4	–36.1	32.7 (27.9, 37.6)	< .001
Day 21	–2.9	–25.3	22.4 (17.0,27.9)	< .001
Day 35	–3.2	–13.1	9.9 (4.7,15.1)	< .001
24,25-Dihydroxyvitamin D (ng/ml)				
Day 1	–0.00	0.11	–0.11 (–0.23, 0.01)	.07
Day 7	0.31	0.50	–0.20 (–0.38, –0.01)	.04
Day 8	0.20	0.56	–0.36 (–0.56, –0.15)	< .001
Day 14	0.12	0.77	–0.65 (–0.86, –0.44)	< .001
Day 21	0.06	0.64	–0.58 (–0.80, –0.36)	< .001
Day 35	0.02	0.44	–0.43 (–0.66, –0.20)	< .001
Alkaline phosphatase (IU/l)				
Day 1	0.4	0.9	–0.5 (–2.7,1.7)	.64
Day 7	1.1	2.6	–1.5 (–4.2,1.3)	.29
Day 8	1.8	5.2	–3.4 (–6.3,–0.5)	.02
Day 14	0.3	5.3	–5.0 (–8.8, –1.1)	.01
Day 21	–0.7	7.5	–8.2 (–13.4, –2.9)	.003
Day 35	1.4	8.6	–7.1 (–11.5, –2.8)	.002
Bone-specific alkaline phosphatase (µg/l)				
Day 1	0.2	0.3	–0.1 (–0.6,0.4)	.62
Day 7	–0.2	0.4	–0.6 (–1.0,–0.1)	.01
Day 8	–0.1	1.0	–1.1 (–1.7, –0.5)	< .001
Day 14	–0.2	1.0	–1.2 (–1.9,–0.4)	.002
Day 21	–0.2	1.3	–1.5 (–2.3, –0.8)	< .001
Day 35	0.2	2.2	–2.0 (–2.7,–1.3)	< .001
N-terminal propeptide of Type I collagen (ng/ml)				
Day 1	–2.3	–3.5	1.2 (–1.4,3.7)	.36
Day 7	–8.5	–11.2	2.7 (–0.2,5.7)	.07
Day 8	–8.1	–11.9	3.8 (0.8,6.7)	.01
Day 14	–7.1	–18.0	10.9 (7.5,14.2)	< .001
Day 21	–3.8	–16.3	12.5 (8.6,16.3)	< .001
Day 35	–2.4	–11.2	8.8 (4.5,13.1)	< .001
Carboxy-terminal collagen crosslinks (ng/ml)				
Day 1	0.04	–0.02	0.07 (0.03,0.10)	< .001
Day 7	–0.00	–0.04	0.03 (0.00,0.07)	.04
Day 8	0.02	–0.07	0.09 (0.06,0.12)	< .001
Day 14	0.01	–0.06	0.07 (0.04,0.10)	< .001
Day 21	0.04	–0.03	0.07 (0.04,0.10)	< .001
Day 35	0.03	0.01	0.02 (–0.02, 0.06)	.23

Data presented are for the safety analysis set.

Estimates are derived from a mixed model for repeated measurements with treatment, day, treatment-by-day interaction, trial, and randomized strata as fixed effects, and baseline value and baseline value-by-day interactions as covariates.

CI, confidence interval; FCM, ferric carboxymaltose; FGF23, fibroblast growth factor; IIM, iron isomaltoside 1000/ferric derisomaltose.

eTable 7. Secondary Efficacy End Points – Trial A, Trial B, and Pooled Data for Trial A and Trial B

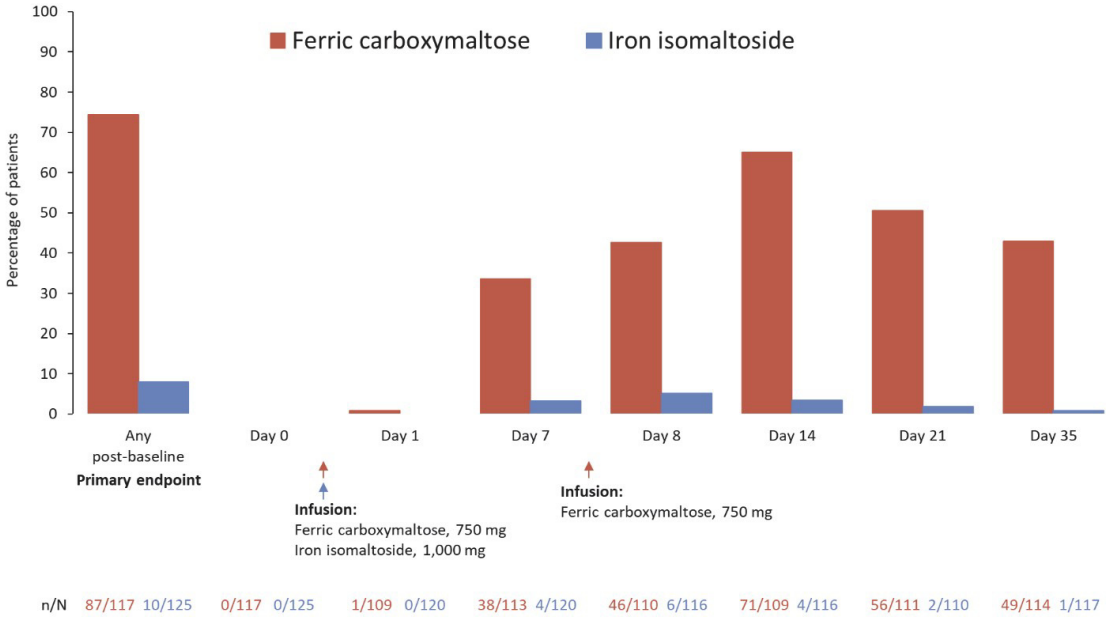
End point		Day 0 Mean (SD) n	1 Mean (SD) n	7 Mean (SD) n	8 Mean (SD) n	14 Mean (SD) n	21 Mean (SD) n	35 Mean (SD) n
Trial A								
Hemoglobin per gram of iron in actual dose (g/dl)[a,b]	IIM	–	–0.3 (1.2) (n=46)	0.6 (0.9) (n=48)	0.5 (1.2) (n=47)	1.5 (1.5) (n=48)	1.6 (1.4) (n=47)	2.1 (1.6) (n=49)
	FCM	–	0.3 (2.0) (n=42)	0.9 (1.6) (n=47)	0.6 (0.8) (n=45)	1.1 (0.9) (n=45)	1.4 (0.9) (n=46)	1.9 (1.0) (n=45)
	P	–	*P* = .24	*P* = .24	*P* = .74	*P* = .09	*P* = .009	*P* = .11
Hemoglobin (g/dl) (exploratory end point)	IIM	9.8 (1.3) (n=62)	9.7 (1.2) (n=54)	10.5 (0.9) (n=54)	10.4 (0.8) (n=54)	11.3 (1.1) (n=53)	11.6 (0.8) (n=53)	12.1 (1.0) (n=56)
	FCM	9.6 (1.3) (n=61)	9.8 (1.8) (n=52)	10.3 (1.2) (n=58)	10.6 (1.2) (n=55)	11.4 (1.0) (n=54)	11.9 (1.0) (n=56)	12.5 (1.1) (n=56)
	P	–	*P* = .37	*P* = .73	*P* = .12	*P* = .46	*P* = .24	*P* = .01
Ferritin (ng/ml)	IIM	15.7 (31.7) (n=62)	97.0 (52.0) (n=58)	277.3 (173.2) (n=59)	264.8 (171.3) (n=57)	149.9 (98.4) (n=57)	111.0 (122.3) (n=55)	63.4 (54.0) (n=58)
	FCM	11.7 (29.4) (n=61)	108.1 (80.1) (n=58)	301.3 (170.4) (n=59)	337.5 (214.5) (n=59)	364.6 (216.1) (n=57)	191.3 (126.4) (n=57)	120.6 (103.3) (n=59)
	P	–	*P* = .19	*P* = .56	*P* = .05	*P* < .001	*P* = .001	*P* < .001
Transferrin saturation (%)	IIM	16.6 (31.2) (n=61)	136.6 (41.9) (n=58)	27.4 (14.1) (n=59)	24.1 (13.0) (n=57)	22.2 (10.3) (n=57)	22.3 (14.0) (n=55)	20.8 (10.2) (n=57)
	FCM	7.0 (6.7) (n=60)	94.2 (36.1) (n=58)	20.0 (12.5) (n=59)	68.2 (40.0) (n=59)	23.5 (9.1) (n=57)	23.8 (9.9) (n=56)	21.7 (9.3) (n=59)
	P	–	*P* < .001	*P* = .009	*P* < .001	*P* = .37	*P* = .48	*P* = .36
Trial B								
Hemoglobin per gram of iron in actual dose (g/dl)[a,b]	IIM	–	0.2 (0.8) (n=48)	1.0 (1.1) (n=51)	1.1 (1.2) (n=51)	1.7 (1.1) (n=53)	1.9 (0.9) (n=53)	2.2 (1.2) (n=54)
	FCM	–	0.5 (1.2) (n=47)	1.4 (1.1) (n=51)	0.8 (0.7) (n=51)	1.3 (0.9) (n=53)	1.6 (0.9) (n=54)	2.0 (0.9) (n=53)
	P	–	*P* = .08	*P* = .17	*P* = .06	*P* = .004	*P* = .02	*P* = .10
Hemoglobin (g/dl) (exploratory end point)	IIM	9.6 (1.2) (n=61)	9.7 (1.4) (n=54)	10.6 (1.5) (n=57)	10.6 (1.5) (n=56)	11.3 (1.3) (n=56)	11.4 (1.2) (n=56)	11.8 (1.4) (n=57)
	FCM	9.3 (1.4) (n=61)	9.6 (1.7) (n=50)	10.4 (1.4) (n=54)	10.5 (1.4) (n=54)	11.3 (1.1) (n=55)	11.8 (1.0) (n=57)	12.3 (1.2) (n=56)
	P	–	*P* = .23	*P* = .99	*P* = .66	*P* = .42	*P* = .003	*P* = .001

End point		Day 0 Mean (SD) n	Day 1 Mean (SD) n	Day 7 Mean (SD) n	Day 8 Mean (SD) n	Day 14 Mean (SD) n	Day 21 Mean (SD) n	Day 35 Mean (SD) n
Trial B (continued)								
Ferritin (ng/ml)	IIM	10.5 (13.4) (n=61)	84.3 (82.9) (n=60)	263.0 (165.4) (n=60)	230.1 (150.4) (n=58)	154.8 (101.8) (n=57)	109.4 (95.1) (n=56)	66.7 (74.2) (n=57)
	FCM	17.9 (40.5) (n=61)	101.1 (83.7) (n=57)	297.9 (214.6) (n=57)	332.5 (227.7) (n=56)	398.2 (279.5) (n=57)	251.3 (213.9) (n=57)	144.9 (164.0) (n=57)
	P	–	*P* = .66	*P* = .49	*P* = .01	*P* < .001	*P* < .001	*P* = .004
Transferrin saturation (%)	IIM	8.4 (8.1) (n=61)	132.3 (48.8) (n=60)	23.5 (9.8) (n=60)	20.9 (9.3) (n=58)	18.9 (7.6) (n=56)	19.2 (9.2) (n=56)	18.3 (10.5) (n=57)
	FCM	9.2 (10.0) (n=59)	99.3 (33.1) (n=56)	22.3 (28.6) (n=57)	83.0 (29.3) (n=56)	26.2 (12.1) (n=57)	25.5 (9.8) (n=56)	23.9 (11.3) (n=56)
	P	–	*P* = .05	*P* = .58	*P* < .001	*P* < .001	*P* < .001	*P* = .004
Pooled data for Trial A and Trial B								
Hemoglobin per gram of iron in actual dose (g/dl)[a,b]	IIM	–	–0.0 (1.1) (n=94)	0.8 (1.0) (n=99)	0.8 (1.2) (n=98)	1.6 (1.3) (n=101)	1.8 (1.2) (n=100)	2.2 (1.4) (n=103)
	FCM	–	0.4 (1.6) (n=89)	1.2 (1.4) (n=98)	0.7 (0.7) (n=96)	1.2 (0.9) (n=98)	1.5 (0.9) (n=100)	2.0 (0.9) (n=98)
	P	–	*P* = .01	*P* = .09	*P* = .08	*P* < .001	*P* < .001	*P* = .02
Hemoglobin (g/dl) (exploratory end point)	IIM	9.7 (1.3) (n=123)	9.7 (1.3) (n=108)	10.5 (1.2) (n=111)	10.5 (1.2) (n=110)	11.3 (1.2) (n=109)	11.5 (1.0) (n=109)	11.9 (1.2) (n=113)
	FCM	9.5 (1.4) (n=122)	9.7 (1.7) (n=102)	10.3 (1.3) (n=112)	10.6 (1.3) (n=109)	11.3 (1.1) (n=109)	11.8 (1.0) (n=113)	12.4 (1.1) (n=112)
	P	–	*P* = .08	*P* = .72	*P* = .24	*P* = .50	*P* = .003	*P* < .001
Ferritin (ng/ml)	IIM	13.1 (24.4) (n=123)	90.5 (69.4) (n=118)	270.1 (168.7) (n=119)	247.3 (161.4) (n=115)	152.4 (99.7) (n=114)	110.2 (108.9) (n=111)	65.0 (64.5) (n=115)
	FCM	14.8 (35.4) (n=122)	104.6 (81.6) (n=115)	299.6 (192.6) (n=116)	335.1 (220.1) (n=115)	381.4 (249.3) (n=114)	221.3 (177.5) (n=114)	132.6 (136.5) (n=116)
	P	–	*P* = .25	*P* = .27	*P* < .001	*P* < .001	*P* < .001	*P* < .001
Transferrin saturation (%)	IIM	12.5 (23.1) (n=122)	134.4 (45.4) (n=118)	25.4 (12.2) (n=119)	22.5 (11.4) (n=115)	20.6 (9.1) (n=113)	20.7 (11.8) (n=111)	19.5 (10.4) (n=114)
	FCM	8.1 (8.5) (n=119)	96.7 (34.6) (n=114)	21.1 (21.9) (n=116)	75.4 (35.8) (n=115)	24.8 (10.7) (n=114)	24.7 (9.8) (n=112)	22.8 (10.3) (n=115)
	P	–	*P* < .001	*P* = .11	*P* < .001	*P* < .001	*P* = .004	*P* = .003

Data are presented for the randomized analysis set, unless otherwise stated as [a] all patients in the randomized data set, who received at least one dose of trial drug, had at least one post-baseline hemoglobin assessment, and who did not have a major protocol deviation. [b] Values are mean (SD) change in hemoglobin.

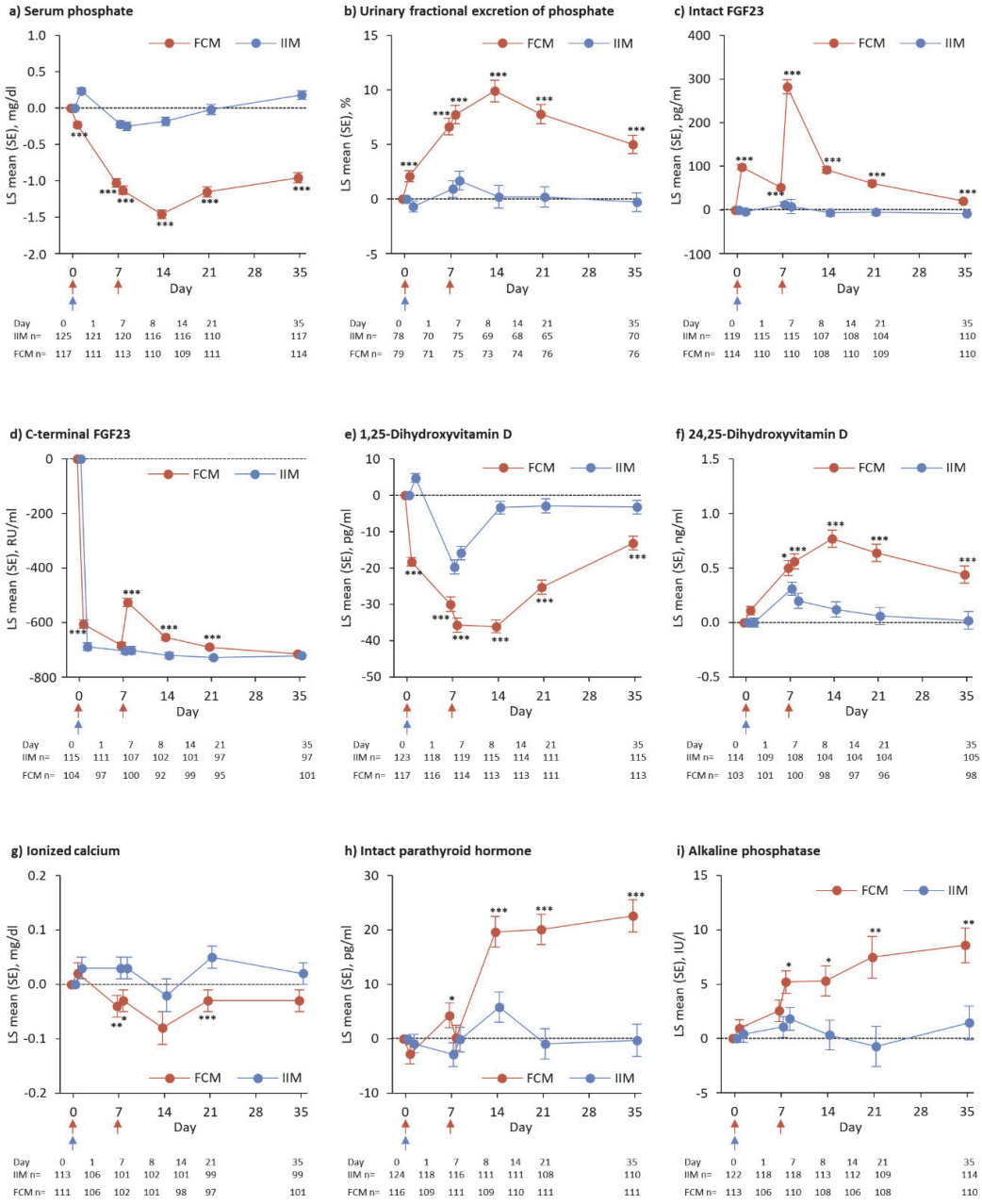
P values are for between-group comparisons from a mixed model for repeated measures analysis with treatment, day, treatment-by-day, trial (in the pooled analysis) and stratum as fixed effects and baseline value and baseline value-by-day, as covariates. FCM, ferric carboxymaltose; IIM, iron isomaltoside 1000/ferric derisomaltose; SD, standard deviation.

eFigure 1. Incidence of Hypophosphatemia (Serum Phosphate <2.0 mg/dl) Overall and Prevalence of Hypophosphatemia at Each Time Point – Pooled Data for Trial A and Trial B



The leftmost columns correspond to the primary outcome of incident hypophosphatemia at any time during the trial. The remaining columns correspond to the proportions of patients with serum phosphate <2.0 mg/dl at each individual time point.
Safety analysis set.

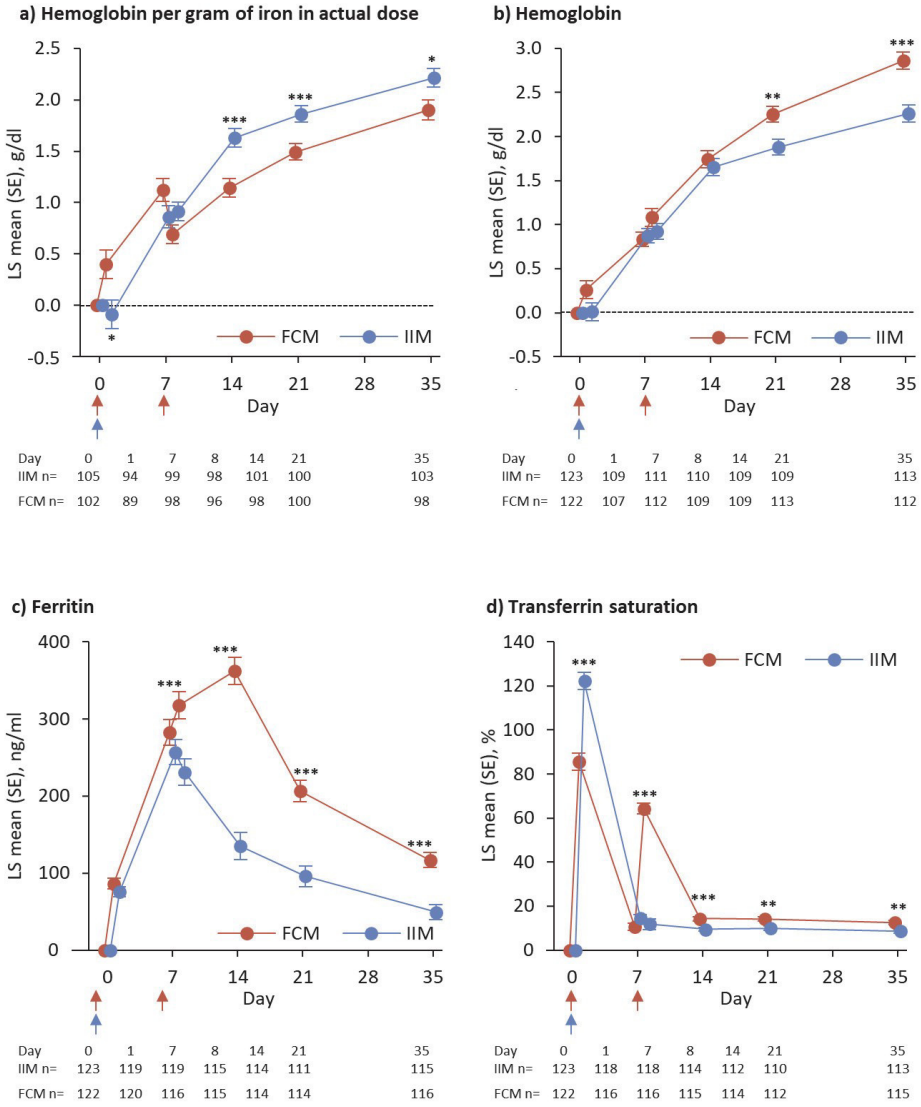
eFigure 2. Least Squares Mean Changes From Baseline in Biomarkers of Mineral and Bone Homeostasis According to Iron Treatment – Pooled Data for Trial A andTrial B



Red arrows indicate infusion of ferric carboxymaltose, 750 mg; blue arrows indicate infusion of iron isomaltoside, 1000 mg.
*$P < .05$, **$P < .01$, ***$P < .001$ between-group comparisons from a mixed model for repeated measures analysis with treatment, day, treatment-by-day, trial and stratum as fixed effects and baseline value and baseline value-by-day as covariates; safety analysis set.

FCM, ferric carboxymaltose; FGF23, fibroblast growth factor 23; IIM iron isomaltoside 1000/ferric derisomaltose; LS, least squares; SE, standard error.

eFigure 3. Least Squares Mean Changes From Baseline in Iron Parameters – Pooled Data for Trial A and Trial B



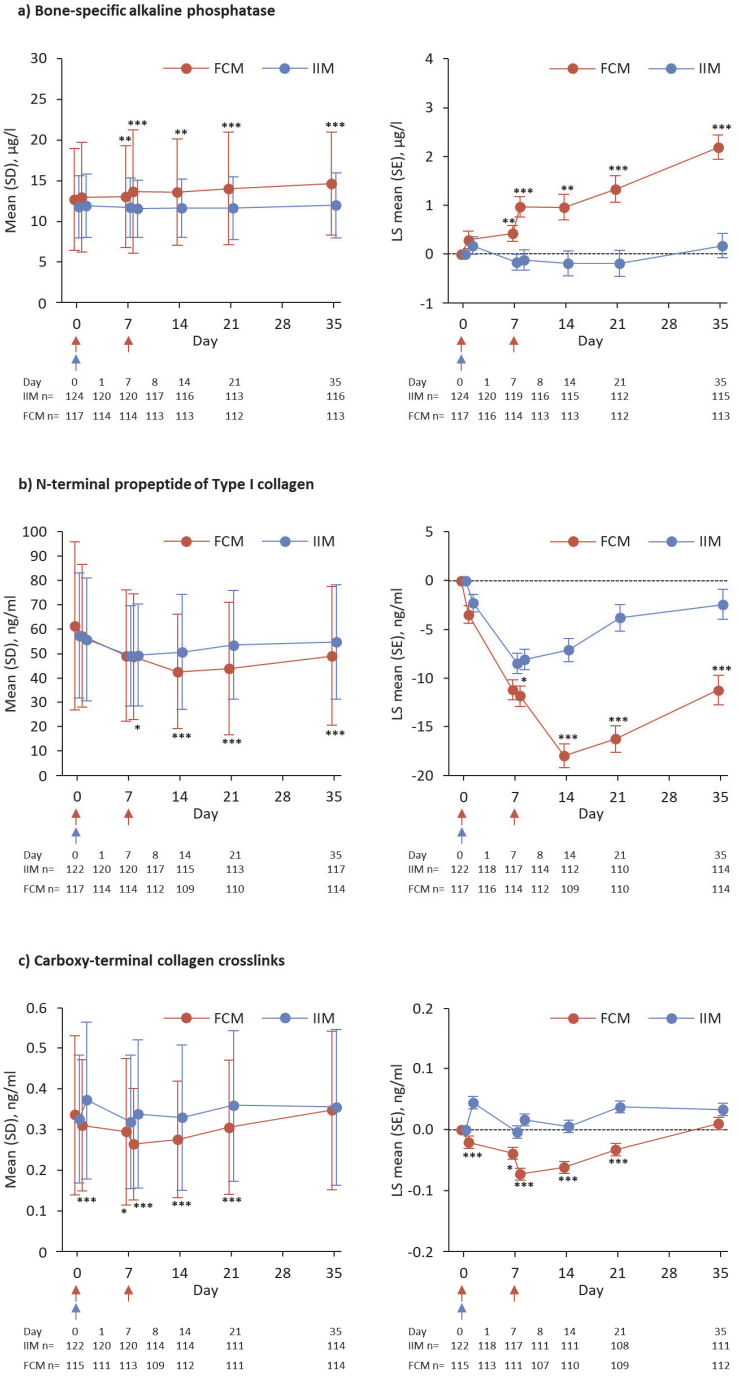
Red arrows indicate infusion of FCM, 750 mg; blue arrows indicate infusion of IIM, 1000 mg.

*$P < .05$, **$P < .01$, ***$P < .001$ between-group comparison from a mixed model for repeated measurements with treatment, day, treatment-by-day, trial and stratum as fixed effects, and baseline value and baseline value-by-day as covariates; randomized data set; part a) is all patients in the randomized data set, who received at least one dose of trial drug, had at least one post baseline hemoglobin assessment, and who did not have a major protocol deviation.

Transferrin saturation was calculated as: [total serum iron (µmol/l) * 5.586] / [transferrin (g/l) *100] * 70.9. In accordance with the pharmacokinetics of IIM, on day 1 after the infusion of 1000 mg of the drug, when TSAT was >100%, a proportion of the drug was still present in the circulation and this is also measured with the serum iron assay and causes the calculated TSAT to exceed 100%.

FCM, ferric carboxymaltose; IIM iron isomaltoside 1000/ferric derisomaltose; LS, least squares; SE, standard error.

eFigure 4. Changes in Bone Turnover Markers – Pooled Data for Trial A and Trial B



Left-hand figures show mean absolute values; right-hand figures show LS mean change from baseline values.

Red arrows indicate infusion of FCM, 750 mg; blue arrows indicate infusion of IIM, 1000 mg.

*$P < .05$, **$P \leq .01$, ***$P < .001$ between-group comparison from a mixed model for repeated measures analysis with treatment, day, treatment-by-day, trial and stratum as fixed effects and baseline value and baseline value-by-day as covariates; safety analysis set.

FCM, ferric carboxymaltose; IIM, iron isomaltoside 1000/ferric derisomaltose; LS, least squares; SD, standard deviation; SE, standard error.