Safety and Efficacy of Intravenous Ferric Derisomaltose Compared to Iron Sucrose for Iron Deficiency Anemia in Patients with Chronic Kidney Disease With and Without Heart Failure

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Ferric derisomaltose (FDI) is an intravenous (IV) high-dose iron formulation approved in the US for the treatment of iron deficiency anemia in adults who are intolerant of/have had an unsatisfactory response to oral iron, or who have non-dialysis-dependent chronic kidney disease (NDD-CKD). FERWON-NEPHRO was a randomized, open-label, multicenter clinical trial evaluating the safety and efficacy of a single infusion of FDI 1,000 mg versus up to 5 doses of iron sucrose (IS) 200 mg (recommended cumulative dose, 1,000 mg) over 8 weeks in patients with NDD-CKD and iron deficiency anemia. Of 1,525 patients included in the safety analysis, 244 (16%) had a history of heart failure (HF). Overall, the rate of serious or severe hypersensitivity reactions was low and did not differ between treatment groups. Cardiovascular adverse events (AEs) were reported for 9.4% of patients who had HF and 4.2% who did not. Time to first cardiovascular AE was longer following administration of FDI compared with IS (hazard ratio: 0.59 [95% CI: 0.37, 0.92]; p=0.0185), a difference that was similar in patients with or without HF (p=0.908 for interaction). Patients achieved a faster hematological response (assessed by changes in hemoglobin and ferritin concentrations, and increase in transferrin saturation) with FDI versus IS. In conclusion, in patients with NDD-CKD, a single infusion of FDI was safe, well tolerated, and was associated with fewer cardiovascular AEs and a faster hematological response, compared to multiple doses of IS. These effects were similar for patients with and without HF. **(Am J Cardiol 2021;152:138−145)**

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Ferric derisomaltose (FDI), previously known as iron isomaltoside, is an intravenous (IV) high-dose iron formulation. Since its approval by the European Medicines Agency in 2009, FDI has been commercially available for the treatment of iron deficiency in several European countries. In 2020, the US Food and Drug Administration (FDA) approved FDI for the treatment of iron deficiency anemia in adults who are either intolerant of or have had an unsatisfactory response to oral iron, or who have non-dialysis-dependent chronic kidney disease (NDD-CKD). FDA approval was based on two randomized, open-label, multicenter trials, FERWON-IDA[1] and FERWON-NEPHRO.[2] FERWON-IDA included younger patients (mean age 44 years) with iron deficiency anemia, mainly women (89%),[1] and only 16 had heart failure (HF) (unpublished data). FERWON-NEPHRO reported that, in patients with NDD-CKD, a single dose of FDI resulted in a rapid hematological response (improvements in iron indices and hemoglobin), was well-tolerated, and was associated with fewer cardiovascular adverse events (AEs) compared with multiple doses of iron sucrose (IS).[2] For patients with HF, iron deficiency and anemia are common and associated with more severe symptoms, poorer quality of life, reduced exercise capacity, impaired renal function and a worse prognosis.[3-9] Randomized controlled trials conducted in patients with HF

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and a reduced ejection fraction (HFrEF) have shown that IV iron improves symptoms and exercise capacity, and may reduce hospitalizations for worsening HF; the effects on mortality are less certain.[10-13] In response, many clinical practice guidelines[14-17] recommend that IV iron should (or may) be considered in order to improve health-related quality of life and functional status in patients with symptomatic HFrEF and iron deficiency, whether or not accompanied by anemia. The objective of this *post hoc* analysis of the FERWON-NEPHRO trial was to investigate the safety and hematological efficacy of FDI versus IS in patients with NDD-CKD and iron deficiency anemia, with or without a history of HF.

Methods

FERWON-NEPHRO (NCT02940860) was a randomized, open-label, multicenter trial to evaluate the safety and efficacy of FDI (Monofer®/Monoferric®, Pharmacosmos A/S, Holbæk, Denmark) versus IS (Venofer®, American Regent, Shirley, NY, USA) in 1,538 patients with NDD-CKD and iron deficiency anemia.[2] CKD was defined by either: (i) estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 at screening (as calculated by the Modification of Diet in Renal Disease formula), or (ii) eGFR <90 mL/min/1.73 m^2 at screening, a medical record of abnormal urine composition, and/or increased risk of cardiovascular disease based on the Framingham model.[2] Iron deficiency anemia was defined as hemoglobin ≤11 g/dL and a serum ferritin ≤100 ng/mL (or ≤300 ng/mL if the transferrin saturation [TSAT] was ≤30%).[2] When used, the dose of erythropoiesis-stimulating agents had to be stable for 4 weeks prior to randomization.[2] Patients were randomized 2:1 to receive treatment with FDI (single dose of 1,000 mg) or IS (200 mg administered up to 5 times within the first 2 weeks, according to the product label, with a recommended cumulative dose of 1,000 mg) and were followed up for 8 weeks to assess the incidence of serious or severe hypersensitivity reactions and the change in hemoglobin, as co-primary endpoints.[2] Symptoms of fatigue were evaluated as a secondary efficacy endpoint.[2] Secondary safety endpoints included the incidence of a composite of cardiovascular AEs, and the incidence of hypophosphatemia (defined as serum phosphate <2 mg/dL).[2] The methodology and findings of the main analyses have already been reported.[2] The safety analysis set included 1,525 randomized patients who received ≥1 dose of trial medication.[2] The full analysis set included 1,510 randomized patients who received ≥1 dose of trial medication and who had ≥1 post-baseline measurement of hemoglobin.[2]

For this *post hoc* analysis, data from FERWON-NEPHRO were analyzed according to whether or not a medical history of HF was recorded in the case report form at screening. HF was coded using the Medical Dictionary for Regulatory Activities (MedDRA) preferred term 'cardiac failure congestive'. The incidences of all-cause AEs, including serious or severe hypersensitivity reactions, and cardiovascular AEs, were calculated. Hypersensitivity reactions and cardiovascular AEs were adjudicated by a Clinical Endpoint Committee, blinded to treatment allocation. Differences between FDI and IS were analyzed for the safety analysis set using Fisher's exact test. The time to first cardiovascular AE was estimated using the Kaplan−Meier method and significance was tested using a log-rank test. For each outcome, a logistic regression analysis was performed, with allocated iron preparation and presence of HF as factors. Changes from baseline to Weeks 1, 2, 4, and 8 in hemoglobin, ferritin, and TSAT were measured and change in fatigue was evaluated at Weeks 1, 2, and 8 using the Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale (higher scores indicate less fatigue). Differences in response between FDI and IS were analyzed for the full analysis set using a mixed model for repeated measures with treatment, subgroups, and week as factors, treatment-by-subgroup-by-week interactions, and baseline value as a covariate. Interaction tests were performed to assess possible differences in response in hemoglobin, ferritin, TSAT, and FACIT Fatigue Scale for FDI compared to IS in patients with and without HF. A 5% level of significance was used for all analyses. Statistical analyses were performed using SAS Version 9.4 (Cary, North Carolina, USA).

Results

Of 1,538 patients randomized,[2] 244 (16%) had a history of HF at screening (Table 1). Compared to patients without HF, patients with HF were more likely to be men, less likely to be white, had a higher body mass index (BMI), more severe fatigue and were more often prescribed β-blockers, mineralocorticoid receptor antagonists, sacubitril-valsartan, digoxin, and loop diuretics. Angiotensin converting-enzyme inhibitors/angiotensin receptor blockers were prescribed for a similar proportion of patients with and without HF. The mean total dose (standard deviation) of IV iron (FDI or IS) administered was similar for patients with HF (FDI: 980 [128] mg; IS: 887 [201] mg) and without HF (FDI: 996 [54] mg; IS: 902 [198] mg).

The incidence of serious or severe hypersensitivity reactions was low after administration of FDI in patients with HF (n=2) and without HF (n=1); no events were reported following administration of IS. The incidence of all-cause treatment-emergent AEs and serious AEs was higher in patients with HF compared to those without HF, but was similar for each iron formulation (Supplementary tables 1 and 2). Time to first cardiovascular AE was longer following administration of FDI compared with IS (hazard ratio: 0.59 [95% confidence intervals {CI}: 0.37, 0.92]; p=0.0185) (Figure 1). The effect was similar in patients with HF or without HF (hazard ratio: 0.57 [95% CI: 0.25, 1.29] and 0.60 [95% CI: 0.35, 1.03], respectively; test for interaction of treatment effect and presence or absence of HF [p=0.908]) and driven by fewer hospitalizations for HF (Table 2). Overall, the incidence of adverse drug reactions was low regardless of treatment administered (Table 3), although numerically higher in patients with HF (odds ratio=1.98 [95% CI: 0.54, 7.20]; p=0.300). The most common adverse drug reactions were nausea and pruritus in patients with HF, and hypertension and pruritus in patients without HF (Table 3). Hypophosphatemia was rare after administration of either FDI or IS (Supplementary table 3).

Table 1
Baseline demographics and clinical characteristics

Variable	Patients with HF		Patients without HF	
	FDI (n=158)	IS (n=86)	FDI (n=861)	IS (n=420)
Age (years)	69 (62−80)	70 (60−77)	69 (61−76)	71 (64−78)
Women	87 (55%)	44 (51%)	540 (63%)	283 (67%)
White	105 (66%)	60 (70%)	622 (72%)	314 (75%)
Black	49 (31%)	23 (27%)	211 (25%)	91 (22%)
Asian	2 (1%)	1 (1%)	14 (2%)	9 (2%)
Other	2 (1%)	2 (2%)	14 (2%)	6 (1%)
Weight (kg)	93 (73−111)	86 (74−101)	82 (69−97)[a]	78 (68−92)
BMI (kg/m^2)	32.6 (27.7−38.9)	31.9 (26.6−35.9)	29.8 (26.0−35.0)[a]	29.3 (25.7−33.4)
CKD stage				
2	6 (4%)	2 (2%)	126 (15%)	63 (15%)
3A	20 (13%)	9 (10%)	143 (17%)	71 (17%)
3B	45 (28%)	18 (21%)	244 (28%)	97 (23%)
4	73 (46%)	43 (50%)	257 (30%)	148 (35%)
5	14 (9%)	14 (16%)	91 (11%)	41 (10%)
Coronary artery disease	58 (37%)	33 (38%)	155 (18%)	72 (17%)
Diabetes mellitus	125 (79%)	67 (78%)	562 (65%)	285 (68%)
Hemoglobin (g/dL)	9.6 (8.7−10.1)	9.5 (8.7−10.1)	9.8 (9.0−10.5)[b]	9.8 (9.1−10.5)
Ferritin (ng/mL)	70 (29−124)	58 (28−122)	52 (23−111)	60 (25−124)
TSAT (%)	14 (11−19)	14 (10−19)	16 (11−21)[b]	17 (12−21)[c]
FACIT Fatigue Scale score	26.5 (16−35)	26 (17−37)	29 (20−39)[d]	28.5 (18−38)
Serum phosphate (mg/dL)	4.0 (3.5−4.6)[e]	4.1 (3.7−4.6)[f]	3.9 (3.4−4.4)[g]	3.8 (3.4−4.4)[h]
Serum creatinine (mg/dL)	2.1 (1.6−3.0)	2.3 (1.7−3.3)	1.7 (1.2−2.6)	1.7 (1.2−2.5)
Urea nitrogen (mg/dL)	41 (30−56)[e]	46 (32−60)[f]	33 (23−46)[g]	33 (22−47)[h]
ACE inhibitor/ARB	85 (54%)	41 (48%)	510 (59%)	256 (61%)
Beta-blocker	118 (75%)	68 (79%)	430 (50%)	217 (52%)
Digoxin	5 (3%)	4 (5%)	9 (1%)	2 (<1%)
Loop diuretics	123 (78%)	68 (79%)	334 (39%)	147 (35%)
Mineralocorticoid receptor antagonist	18 (11%)	10 (12%)	32 (4%)	17 (4%)
Sacubitril-valsartan	3 (2%)	3 (3%)	3 (<1%)	2 (1%)
SGLT2 inhibitors	–	–	6 (1%)	1 (<1%)
Thiazides	8 (5%)	5 (6%)	130 (15%)	53 (13%)

Data are median (IQR), unless otherwise stated; safety analysis set

[a] n=858; [b] n=860; [c] n=418; [d] n=859; [e] n=151; [f] n=80; [g] n=814; [h] n=398

HF defined as patients with medical history terms coded as MedDRA preferred term, 'cardiac failure congestive'

For patients with a baseline TSAT level >100% (an indication that the IV iron infusion had occurred before the baseline blood sample was taken), the screening value was used as baseline in the data analysis

Definitions of CKD stage (based on estimated GFR): Stage 1, normal or high GFR (GFR >90 mL/min/1.73 m^2); Stage 2, mild CKD (GFR=60−89 mL/min/1.73 m^2); Stage 3A, moderate CKD (GFR=45−59 mL/min/1.73 m^2); Stage 3B, moderate CKD (GFR=30−44 mL/min/1.73 m^2); Stage 4, severe CKD (GFR=15−29 mL/min/1.73 m^2); Stage 5, end-stage CKD (GFR <15 mL/min/1.73 m^2)

FACIT Fatigue Scale score range: 0−52; higher scores denote a better quality of life; a score <30 indicates severe fatigue

ACE=angiotensin-converting enzyme; ARB=angiotensin receptor blocker; BMI=body mass index; CKD=chronic kidney disease; FACIT=Functional Assessment of Chronic Illness Therapy; FDI=ferric derisomaltose; GFR=glomerular filtration rate; HF=heart failure; IQR=interquartile range; IS=iron sucrose; IV=intravenous; MedDRA=Medical Dictionary for Regulatory Activities; SGLT2=sodium−glucose co-transporter-2; TSAT=transferrin saturation

Within 1 week of treatment, patients who received FDI had a greater increase in hemoglobin, ferritin, and TSAT, than those who received IS (Figure 2). No heterogeneity was observed between patients with or without HF (p>0.05 for interaction tests for each measure, at every time point; Supplementary table 4). FACIT Fatigue Scale scores improved from baseline in both treatment groups, regardless of HF status (p<0.001; Table 4).

Discussion

This analysis of the FERWON-NEPHRO trial provides further information on the safety and efficacy of a single infusion of FDI, compared to multiple administrations of IS, in patients with NDD-CKD, iron deficiency anemia, and HF. The overall incidence of AEs and serious AEs was similar regardless of iron preparation, but the time to first cardiovascular AE was longer in those assigned to FDI, with a similarly favorable effect in patients with or without HF. This difference was largely driven by a reduction in HF hospitalizations, independent of HF status at baseline. Among patients with HF, the incidence of adverse drug reactions or hypophosphatemia, was low after the administration of FDI and IS. Regardless of HF status, the hematological response was faster to FDI than to IS, but similar effects were achieved by 4 to 8 weeks.

This is the first analysis to examine the effects of FDI in patients with HF using data from a substantial randomized

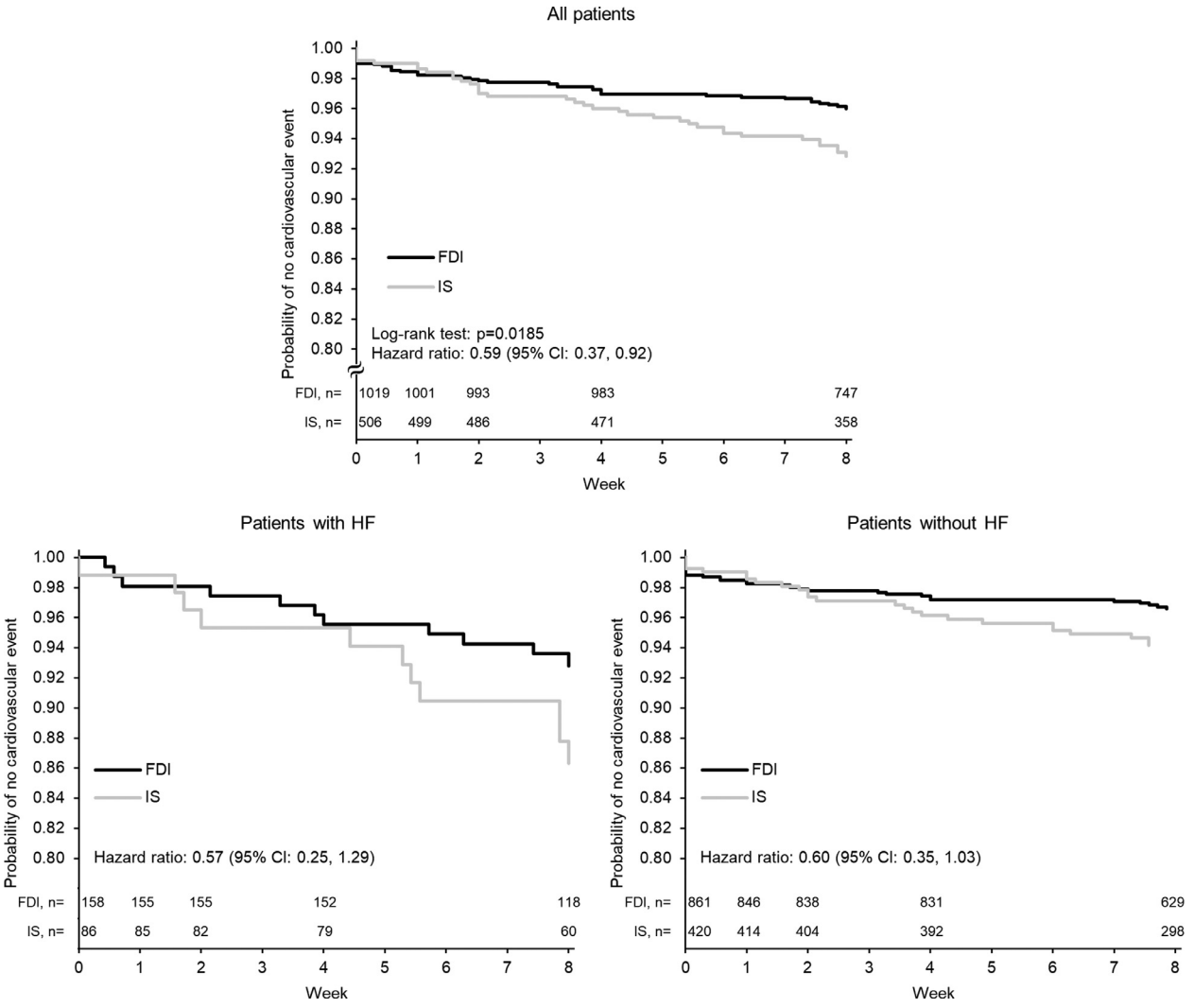

Figure 1. Time to first composite cardiovascular adverse event.
Safety analysis set; Kaplan−Meier analysis
HF defined as patients with medical history terms coded as MedDRA preferred term, 'cardiac failure congestive'
The 'All patients' Kaplan−Meier plot is adapted from Bhandari et al. (2021).[2] The log-rank test compared FDI versus IS for patients with HF and without HF. Interaction analysis tested for differences in outcome according to assigned treatment (FDI or IS) in the presence and absence of HF (p=0.908)
AE=adverse event; CI=confidence interval; FDI=ferric derisomaltose; HF=heart failure; IS=iron sucrose; MedDRA=Medical Dictionary for Regulatory Activities

controlled trial. The rate of cardiovascular AEs was higher for patients with HF compared to those without HF. However, in relative terms, the reduction in the incidence of cardiovascular AEs with FDI compared to IS was similar whether the patient had HF (hazard ratio: 0.57) or did not have HF (hazard ratio: 0.60), suggesting a greater absolute benefit for patients with HF (5.2% absolute risk reduction) compared to those without HF (2.2% absolute risk reduction). Atrial fibrillation is an important precipitant of HF and was reported in fewer FDI- than IS-treated patients. Interestingly, the FERRIC-HF II trial[18] found that treatment with FDI reduced P wave dispersion, a possible marker of the risk of atrial fibrillation (Jaumdally et al. Abstract at the 68th American Congress of Cardiology 2019).

The AFFIRM-AHF trial has shown that amongst patients with a left ventricular ejection fraction <50% and iron deficiency recovering from acute HF, treatment with ferric carboxymaltose (FCM; another high-dose IV iron formulation) reduced the risk of hospitalization for HF, but had little effect on cardiovascular mortality.[13] Meta-analyses of randomized trials also suggest that, compared to placebo/control arm, IV iron reduces the risk of hospitalizations for HF.[19,20] Furthermore, cardiology guidelines document an improvement in well-being with IV iron.[15] Several other pivotal trials (ClinicalTrials.gov identifiers: NCT02642562 [IRONMAN]; NCT03036462 [FAIR-HF2]; and NCT03037931 [HEART-FID]) are currently evaluating the effect of IV iron on morbidity and mortality in patients with HF.

FDI and IS had a good safety profile and were well tolerated in patients with and without a history of HF. Furthermore, FDI can be safely administered as a single IV infusion, which delivers a more rapid response, is more

Table 2
Incidence of adjudicated and confirmed treatment-emergent composite cardiovascular AEs, by type of CV event

n (%)	Patients with HF			Patients without HF		
	FDI (n=158)	IS (n=86)	p-value	FDI (n=861)	IS (n=420)	p-value
Any event	12 (7.6)	11 (12.8)	0.251	30 (3.5)	24 (5.7)	0.075
Hospitalization for HF	4 (2.5)	6 (7.0)	0.172	8 (0.9)	7 (1.7)	0.273
Arrhythmia	4 (2.5)	3 (3.5)	0.700	3 (0.3)	5 (1.2)	0.123
Hypertension	2 (1.3)	1 (1.2)	1.000	15 (1.7)	9 (2.1)	0.662
Hypotension	1 (0.6)	1 (1.2)	1.000	1 (0.1)	1 (0.2)	0.548
Acute coronary syndrome	1 (0.6)	0 (0.0)	1.000	3 (0.3)	1 (0.2)	1.000
Fatal event not otherwise classified[a]	2 (1.3)	0 (0.0)	0.542	0 (0.0)	3 (0.7)	0.035
Cannot be classified	0 (0.0)	1 (1.2)	0.352	0 (0.0)	0 (0.0)	–
Stroke	1 (0.6)	0 (0.0)	1.000	2 (0.2)	1 (0.2)	1.000
Sudden death	0 (0.0)	0 (0.0)	–	1 (0.1)	0 (0.0)	1.000
Transient ischemic attack	0 (0.0)	0 (0.0)	–	1 (0.1)	0 (0.0)	1.000

p-values were obtained using Fisher's exact test; safety analysis set

[a] Cellulitis was experienced by 1 patient, which progressed to septic shock and the patient died – both events were classified as a 'Fatal event not otherwise classified' and captured in the table. However, the classification of cellulitis event as a fatal CV event in the adjudicated data was made in error; therefore, septic shock was the only fatal CV event to have occurred among patients

HF defined as patients with medical history terms coded as MedDRA preferred term, 'cardiac failure congestive'

AE=adverse event; CV=cardiovascular; FDI=ferric derisomaltose; HF=heart failure; IS=iron sucrose; MedDRA=Medical Dictionary for Regulatory Activities

convenient for patients and clinical staff and, therefore, potentially increases efficiency and reduces costs. The safety of FDI is further supported by a meta-analysis of 21 prospective studies including 8,599 patients, which suggested a lower risk of serious or severe hypersensitivity reactions with FDI compared to FCM, or to IS.[21] FDI also causes a smaller increase in urinary phosphate excretion, and a lower incidence of hypophosphatemia, than FCM.[22,23] Currently, the importance of FCM-associated hypophosphatemia on symptoms, exercise capacity, and on bone metabolism are uncertain, but one report suggests that hypophosphatemia can be persistent and prolong hospital stay.[24] CKD may attenuate renal phosphate wasting triggered by FCM and reduce the risk of hypophosphatemia.[25] However, in a published clinical trial, hypophosphatemia was reported in 21.5% of patients with CKD receiving FCM.[26]

Our analysis has several limitations. A history of HF was based on the investigator's opinion and was not specifically defined. Neither an assessment of the severity of symptoms nor cardiac imaging to assess left ventricular function and left atrial volume was required. The diagnosis of HF is often missed by those with no special training in the management of HF.[27] The rate of hospitalization for HF was numerically lower for FDI versus IS, even amongst patients who had no prior diagnosis of HF; some of these patients might have had undiagnosed HF. The lack of imaging data means that the proportion of patients with HFrEF is unknown. However, the median age of patients with HF was 70 years, most patients had an eGFR of 15 to 44 mL/min/1.73 m^2, 54% were women, BMI was high, and pharmacological therapy as recommended for HFrEF was relatively low. Therefore, it can be reasonably surmised that a substantial proportion of patients with HF had a preserved left ventricular ejection fraction. Finally, this analysis was not powered to detect differences in clinical outcomes within subgroups. All findings with respect to the incidence of composite cardiovascular AEs within subgroups should be properly viewed as hypothesis-generating and require prospective confirmation in large-scale randomized controlled trials.

In conclusion, this *post hoc* analysis of FERWON-NEPHRO found that a single infusion of FDI was well tolerated and safe. Compared with multiple doses of IS, FDI

Table 3
ADRs occurring with an incidence of ≥1%, by preferred term

n (%)	Patients with HF			Patients without HF		
	FDI (n=158)	IS (n=86)	p-value	FDI (n=861)	IS (n=420)	p-value
Any ADR	11 (7.0)	4 (4.7)	0.584	37 (4.3)	23 (5.5)	0.398
Nausea	3 (1.9)	1 (1.2)	1.000	1 (0.1)	2 (0.5)	0.252
Pruritus	2 (1.3)	1 (1.2)	1.000	3 (0.3)	3 (0.7)	0.400
Blood pressure – systolic increased	0 (0.0)	1 (1.2)	0.352	0 (0.0)	0 (0.0)	–
Chest discomfort	0 (0.0)	1 (1.2)	0.352	1 (0.1)	0 (0.0)	1.000
Dyspnea	0 (0.0)	1 (1.2)	0.352	1 (0.1)	0 (0.0)	1.000
Headache	1 (0.6)	1 (1.2)	1.000	3 (0.3)	0 (0.0)	0.555
Hypertension	0 (0.0)	0 (0.0)	–	3 (0.3)	5 (1.2)	0.123

p-values were obtained using Fisher's exact test; safety analysis set

ADR=adverse drug reaction; FDI=ferric derisomaltose; HF=heart failure; IS=iron sucrose

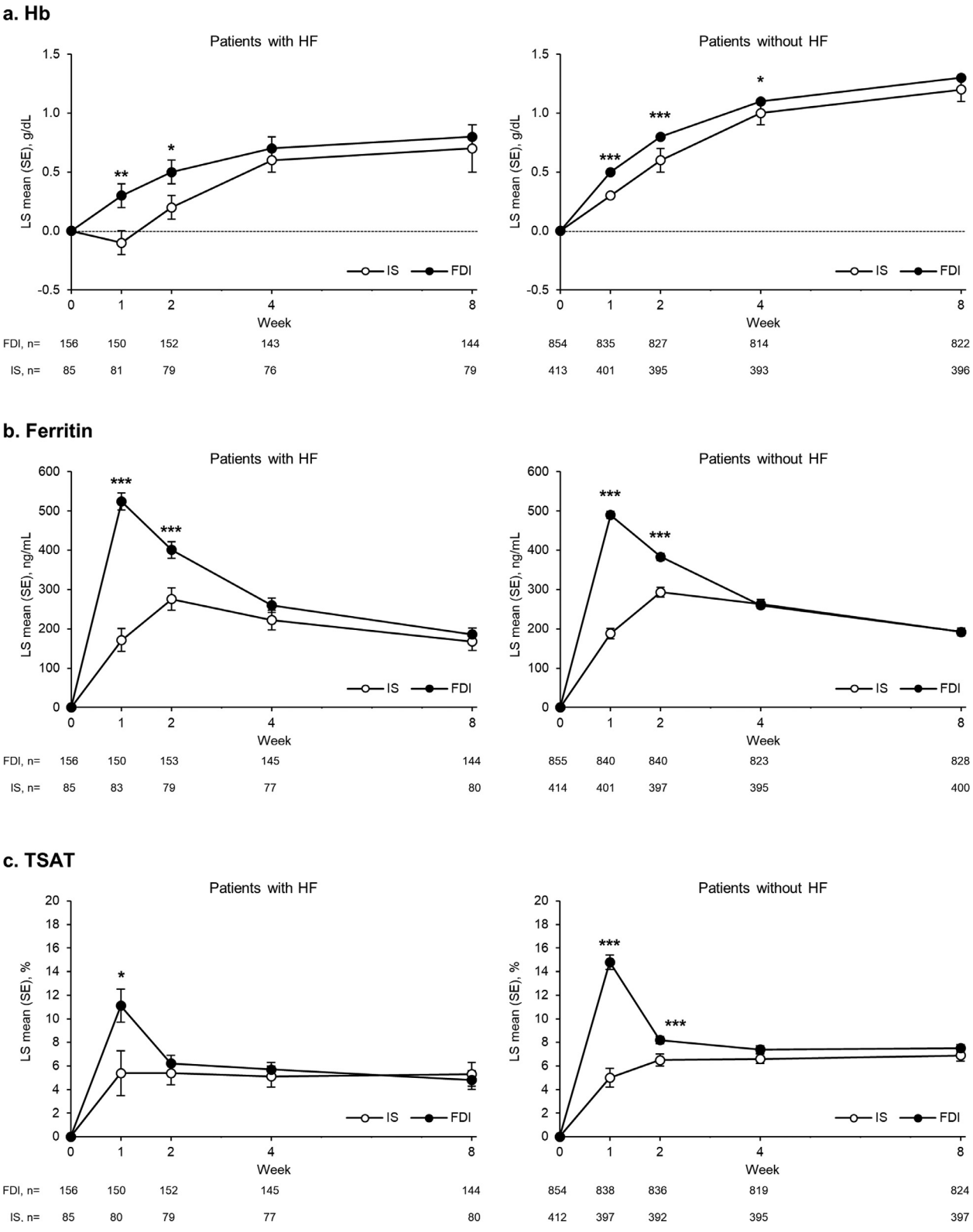

Figure 2. Change from baseline in hemoglobin, ferritin, and transferrin saturation.
*p<0.05, **p<0.01, ***p≤0.001 versus IS, MMRM; full analysis set
HF defined as patients with medical history terms coded as MedDRA preferred term, 'cardiac failure congestive'
For patients with a baseline TSAT >100% (an indication that the IV iron infusion had occurred before the baseline blood sample was taken), the screening value was used as baseline in the data analysis
FDI=ferric derisomaltose; Hb=hemoglobin; HF=heart failure; IS=iron sucrose; IV=intravenous; LS=least squares; MedDRA=Medical Dictionary for Regulatory Activities; MMRM=mixed model for repeated measures; SE=standard error; TSAT=transferrin saturation

Table 4
Change from baseline in FACIT Fatigue Scale score

	Patients with HF				Patients without HF				Interaction test (HF versus non-HF)	
	n	LS mean (95% CL)	p-value vs baseline	p-value FDI vs IS	n	LS mean (95% CL)	p-value vs baseline	p-value FDI vs IS	LS mean (95% CL)	p-value
Week 1										
FDI	149	5.7 (4.4, 6.9)	<0.001	–	838	4.9 (4.3, 5.4)	<0.001	–	–	–
IS	84	4.4 (2.8, 6.1)	<0.001	–	406	5.0 (4.2, 5.7)	<0.001	–	–	–
FDI versus IS		1.2 (-0.8, 3.3)	–	0.248		-0.1 (-1.0, 0.8)	–	0.828	1.3 (-0.9, 3.6)	0.252
Week 2										
FDI	152	7.3 (6.0, 8.6)	<0.001	–	839	7.3 (6.8, 7.9)	<0.001	–	–	–
IS	81	6.2 (4.5, 8.0)	<0.001	–	398	7.7 (6.9, 8.5)	<0.001	–	–	–
FDI versus IS		1.0 (-1.2, 3.2)	–	0.364		-0.4 (-1.3, 0.6)	–	0.479	1.4 (-1.0, 3.8)	0.264
Week 8										
FDI	142	8.4 (6.9, 9.8)	<0.001	–	827	9.3 (8.7, 9.9)	<0.001	–	–	–
IS	80	7.2 (5.2, 9.2)	<0.001	–	403	9.3 (8.4, 10.2)	<0.001	–	–	–
FDI versus IS		1.2 (-1.3, 3.7)	–	0.345		0.0 (-1.0, 1.1)	–	0.937	1.1 (-1.6, 3.8)	0.405

MMRM; full analysis set

HF defined as patients with medical history terms coded as MedDRA preferred term, 'cardiac failure congestive'

FACIT Fatigue Scale score range: 0−52; higher scores denote a better quality of life; a score <30 indicates severe fatigue

CL=confidence limit; FACIT=Functional Assessment of Chronic Illness Therapy; FDI=ferric derisomaltose; HF=heart failure; IS=iron sucrose; LS=least squares; MedDRA=Medical Dictionary for Regulatory Activities; MMRM=mixed model for repeated measures

led to an early hematological response in patients with NDD-CKD, iron deficiency anemia, and HF.

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Andrew P Ambrosy: conceptualization, methodology, writing − original draft, writing − review and editing, visualization, supervision.

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Supplementary Materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.04.042.

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