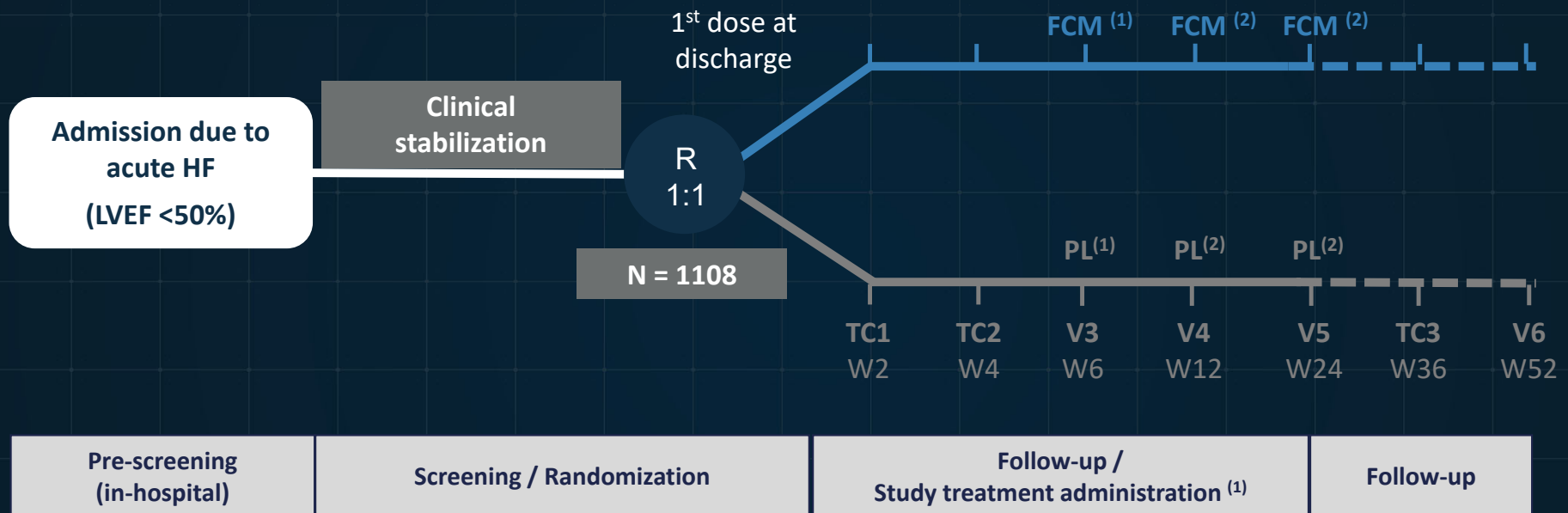


Clinical Implications of Managing Iron Deficiency from AFFIRM-AHF

AFFIRM-AHF Study Design



¹ Administered dose of study treatment based on iron need as assessed at the baseline visit.

² Study treatment administered only if iron deficiency persisted.

FCM, ferric carboxymaltose; HF, heart failure; LVEF, left ventricular ejection fraction; PL, placebo; R, randomization; TC, telephone contact; V, visit; W, week. Ponikowski P, et al. *Eur J Heart Fail.* 2019;21(12):1651-1658.

AFFIRM-AHF: Key Outcomes

	Hazard Ratio (95% CI)	P value
Modified intention-to-treat analysis		
Total heart failure hospitalizations ¹ or cardiovascular death	0.79 (0.62-1.01)	0.059
Total cardiovascular hospitalizations ¹ or cardiovascular death	0.80 (0.64-1.00)	0.050
Total heart failure hospitalizations ¹	0.74 (0.58-0.94)	0.013
Time to first heart failure hospitalization or cardiovascular death	0.80 (0.66-0.98)	0.030
COVID-19 sensitivity analysis²		
Total heart failure hospitalizations ¹ or cardiovascular death	0.75 (0.59-0.96)	0.024
Total cardiovascular hospitalizations ¹ or cardiovascular death	0.77 (0.62-0.97)	0.024
Total heart failure hospitalizations ¹	0.70 (0.55-0.90)	0.005
Time to first heart failure hospitalization or cardiovascular death	0.79 (0.65-0.97)	0.023

¹Included first and recurrent events; ²Patients were censored in each country on the date when the first patient with COVID-19 was reported in the respective country. Ponikowski P, et al. *Lancet*. 2020;396(10266):1895-1904.

Clinical Implications of AFFIRM-AHF

- Treat iron deficiency in the acute phase with FCM to reduce HF hospitalization
- Check iron status in the acute phase
 - Ferritin
 - Transferrin saturation
- Begin treatment with intravenous FCM before discharge
 - 80% will only need 1 or 2 infusions

IRONOUT HF

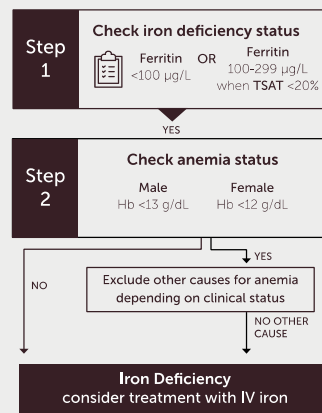
“...found that even with **giving doses of oral iron that were 15 times in excess** of daily recommended dose amounts of iron in the diet, we still found that **patients with heart failure were relatively refractory to repletion** of their iron stores...”

Chronic Heart Failure Patient Care

- Screen for iron deficiency in chronic heart failure patients who are symptomatic
- Evaluate:
 - Transferrin saturation
 - Ferritin
- If iron deficiency is diagnosed, begin treatment to modify patient risk

IRON DEFICIENCY AND ANEMIA

Diagnosis



Ferric carboxymaltose, Package leaflet, Vifor France; 2020.
 Ferric carboxymaltose, Australian product information, Vifor Pharma Pty Ltd; 2020.
 Lewis GD, et al. JAMA. 2017;317(19):1958-1966.
 McDonagh T, et al. Eur J Heart Fail. 2018;20(12):1664-1672.
 NHFA CSANZ Heart Failure Guidelines Working Group, et al. Heart Lung Circ. 2018;27(10):1123-1208.
 Penikowksi P, et al. Eur J Heart Fail. 2016;37(27):2129-2200.
 Yancy CW, et al. J Am Coll Cardiol. 2017;70(6):776-803.

Correction of Iron Deficiency*

Europe & Australia

Ferric carboxymaltose dosage forms:

- 100 mg
- 500 mg
- 1,000 mg

Hemoglobin	Patient body weight		
	g/dL	mmol/L	<35 kg 35 kg – <70 kg ≥70 kg
<10	<6.2	500 mg	1500 mg 2000 mg
10-14	6.2–8.7	500 mg	1000 mg 1500 mg
>14	>8.7	500 mg	500 mg 500 mg

United States

Ferric carboxymaltose dosage form:

- 750 mg iron per 15 mL vial
- Patients weighing ≥50 kg (≥110 lbs)
 - 2x 750 mg (1500 mg total)
 - Separated by at least 7 days
- Patients weighing <50 kg (<110 lbs)
 - 2x 15 mg/kg body weight
 - Separated by at least 7 days

*Oral iron is insufficient for the correction of iron deficiency in patients with heart failure.

Monitoring

Check ferritin + TSAT at next scheduled visit (preferably at 3 months)

Check ferritin + TSAT 1-2 times per year or if change in clinical picture or if hemoglobin decreases

Ongoing Trials in HF and ID

Study Name	IRONMAN	FAIR-HF2	HEART-FID	FAIR-HFpEF
# of Patients	1,300	1,200	3,014	200
Diagnosis	HFrEF EF <45%	HFrEF EF ≤45%	HFrEF EF ≤40%	HFpEF EF ≥45%
Blinding	Open label	Double blind	Double blind	Double blind
Study Arm	Iron (III) isomaltoside	FCM	FCM	FCM
Duration	120 weeks	Event driven + at least 12 mos f/u	Event driven + 12 mos last patient	52 weeks
Primary Endpoint	CV death or HF hospitalization	HF hospitalization + CV death	All-cause mortality + total HF hospitalization through 12 mos and Δ 6MWT after 6 mos	Δ 6MWT from baseline to Week 24
Anticipated Completion	February 2021	December 2021	June 2022	July 2021

6MWT, 6-minute walk test; CV, cardiovascular; EF, ejection fraction; FCM, ferric carboxymaltose; f/u, follow-up; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ID, iron deficiency.
von Haehling S, et al. *JACC Heart Fail.* 2019;7(1):36-46.

Take-Home Messages

- Screen for iron deficiency in HF patients with symptoms
- Acute phase patients with HF and iron deficiency:
 - Benefit from its correction
 - In turn, reduces the burden of HF hospitalization
- The most effective way to replenish iron stores is via intravenous iron