Addressing and Treating Iron Deficiency to Improve Symptoms and Outcomes in Patients with Heart Failure

Javed Butler, MD, MPH, MBA
President, Baylor Scott and White Research Institute
Maxwell A. and Gayle H. Clampitt Endowed Chair
Dallas, TX
Distinguished Professor of Medicine , University of Mississippi,
Jackson, MS

Gurusher Panjrath, MD, FACC, FAHA
Professor of Medicine
Director, Heart Failure and Mechanical Support Program
George Washington University School of Medicine and Health Sciences
Washington D.C.

Ileana L Piña, MD, MPH, FAHA, FACC, FHFSA
Professor of Medicine, Thomas Jefferson University
Quality Chief for the CV Line
Clinical Professor of Medicine, Central Michigan University College of Medicine
Adjunct Professor of Epidemiology and Biostats, Case Western University,
Population & Quantitative Health Sciences
Senior Staff Fellow, Medical Officer FDA, CDRH

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Agenda

- Opening remarks and introductions
- Screening and Diagnosis of Iron Deficiency (ID) in Heart Failure (HF)
- Treatment of ID in HF
- Challenging Cases & Panel Discussion: Diagnosis & Treatment of ID in HF

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Screening and Diagnosis of Iron Deficiency in Heart Failure

Gurusher Panjrath, MD FACC FAHA

Professor of Medicine

Director, Heart Failure and Mechanical Support Program

George Washington University School of Medicine and Health Sciences

Washington D.C.

@PanjrathG

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Agenda

- Burden of ID in HF
- Causes of ID in HF
- Clinical manifestations
- Screening and diagnosis of ID in HF

Iron Deficiency in Heart Failure

- Iron deficiency (ID) and anemia -frequent comorbidities in HF
  - *Both are independently associated with worse clinical status and outcome*
  - Do not necessarily coexist

- ID is poorly linked with red cell indices in HF
  - Should be seen independently of erythropoietic status
  - Prevalence is high
    - ➢ Ambulatory HF - 59% in non-anemic
    - ➢ Acute HF- 57% in men and 79% in women

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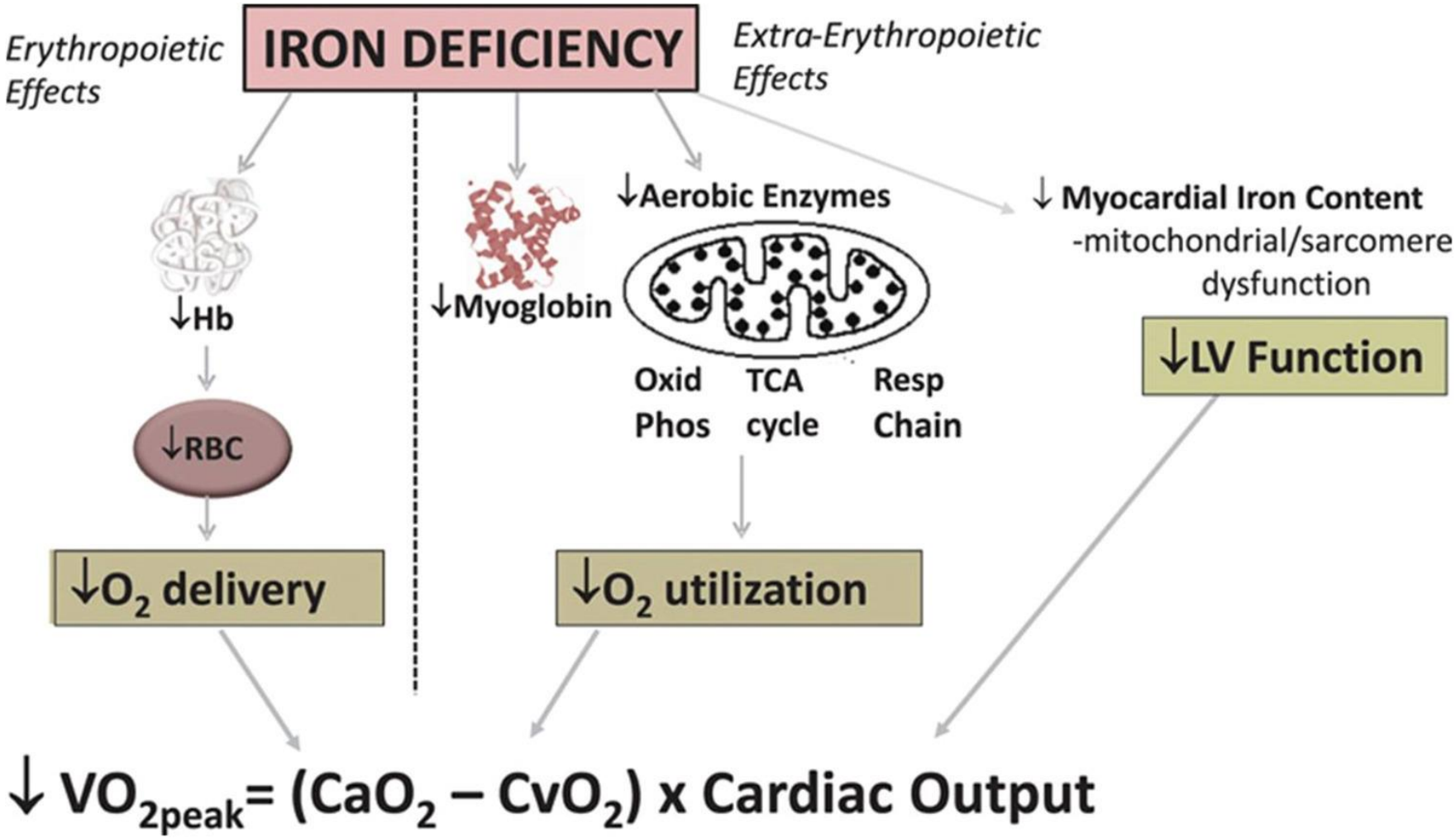
Detrimental Effects of Iron Deficiency



Beavers CJ, et al. *J Cardiac Failure* 2023; 29.7: 1059-1077
Lewis GD , et al. Circ Heart Failure 2016; 9.5: e000345

Iron Deficiency Has Significant Impact on Patient Outcomes and Quality of Life, Even in the Absence of Anemia

Mitochondrial dysfunction, deranged enzyme activity, abnormal transport and structural proteins, apoptosis	Tissue remodeling, impaired organ efficacy	Impaired exercise capacity, reduced work efficacy	Impaired cognitive performance and behavior	Increased morbidity and mortality

.

Jankowska EA, et al. *Eur Heart J*. 2013;34(11):816-829.

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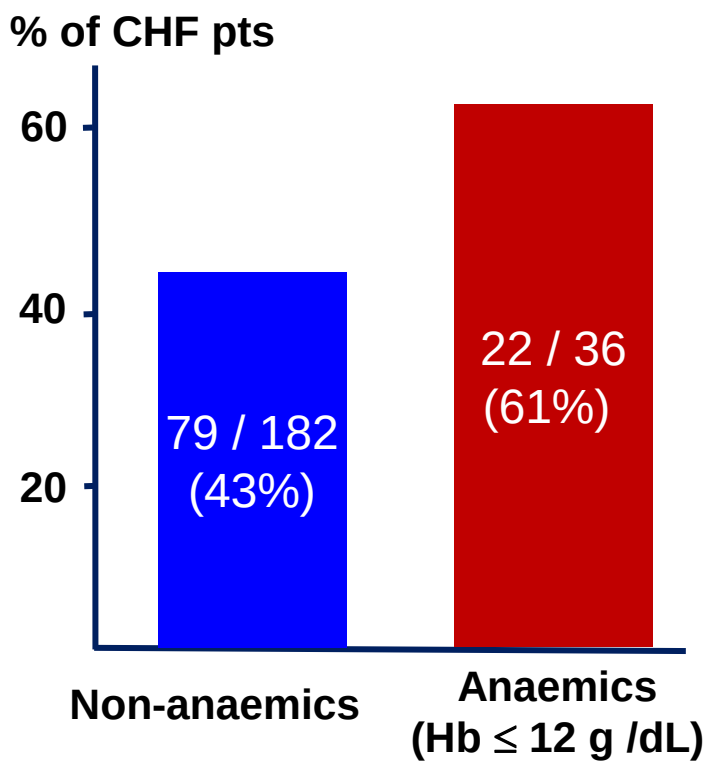
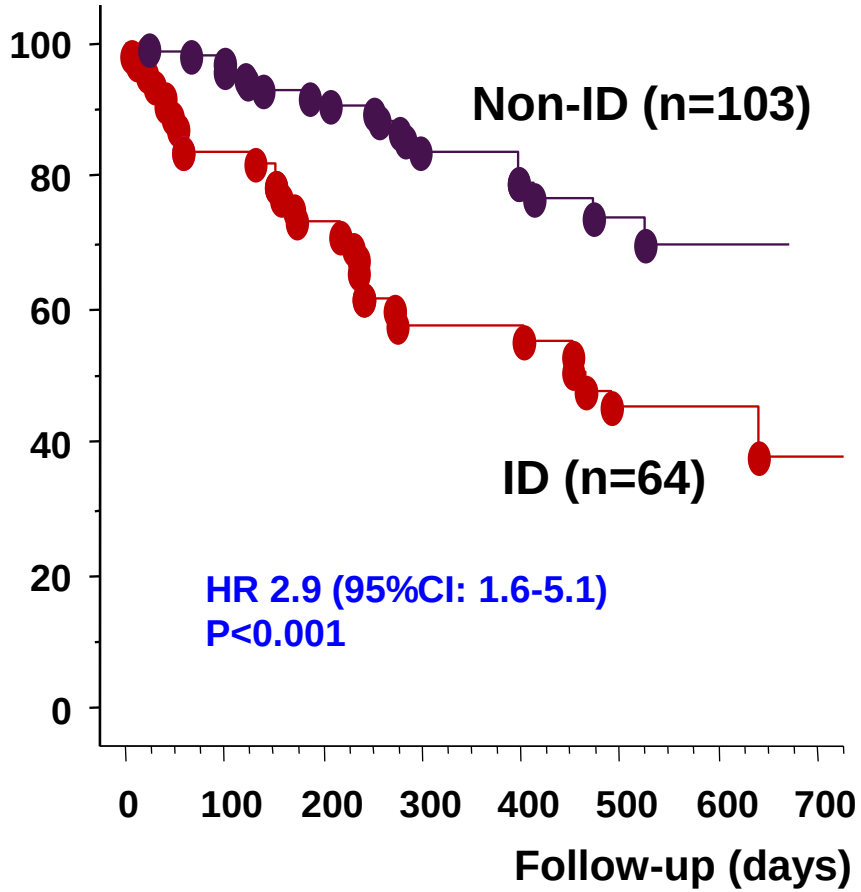
Functional Iron Deficiency = poor Prognosis

definition: serum ferritin <100 µg/L or <300 µg/L, if TSAT <20%

Prevalence of ID in CHF patients



Endpoint:
Death & HF hospitalisation



Jankowska et al., EHJ 2010
Grzeslo A et al. (abstract at HFA 2006)

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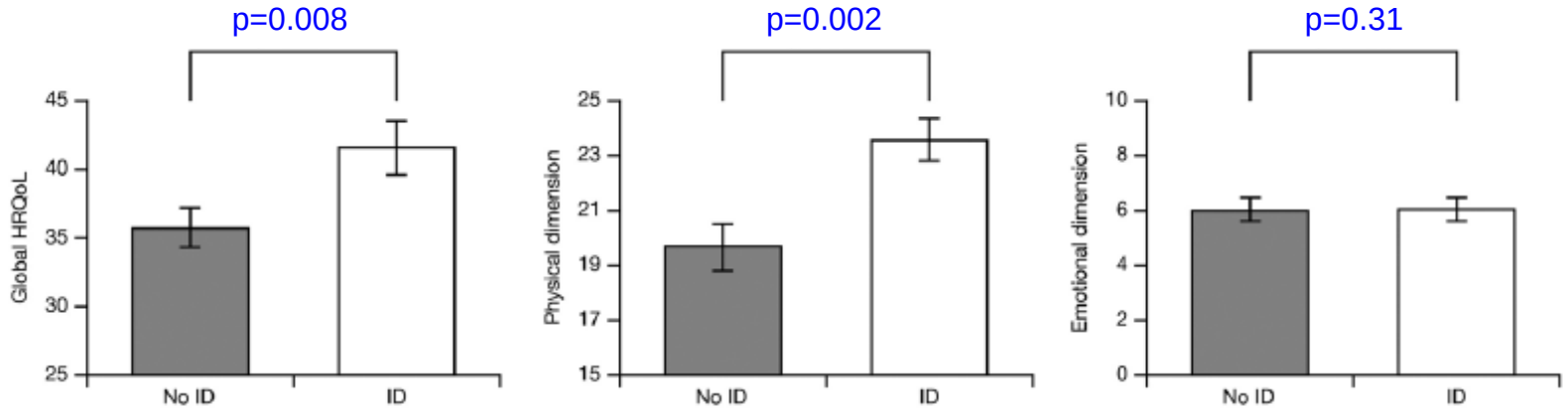
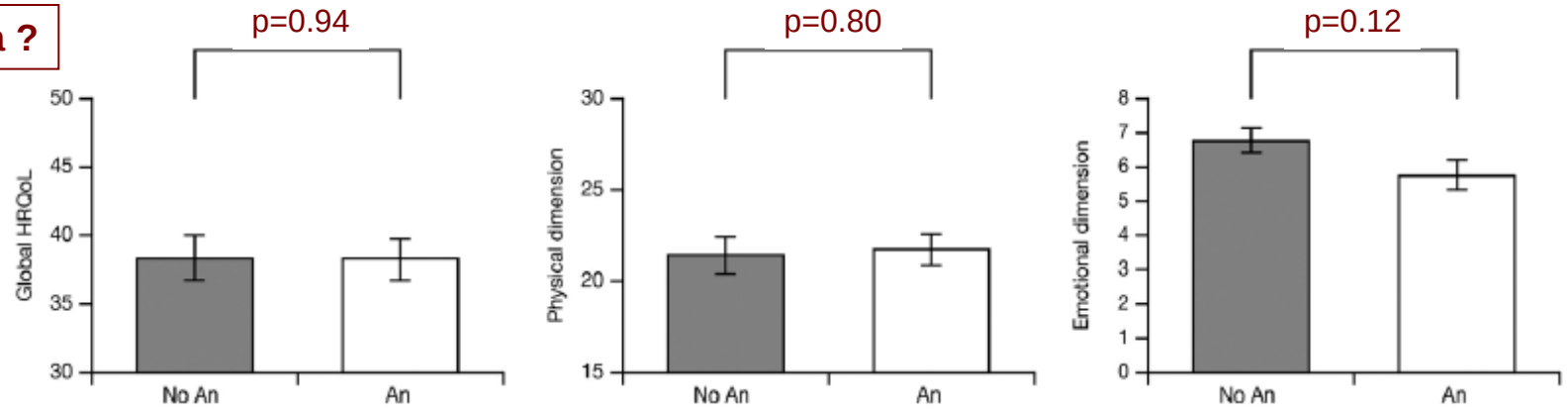
Iron Deficiency is Associated with Reduced QoL in CHF patients

- HRQoL test: Minnesota Living with Heart Failure Questionnaire (MLHFQ)
- Results adjusted for anaemia, ID and other covariates

ID ?



Anemia ?



Comin-Colet et al. Eur J Heart Fail 2013

Iron Deficiency in Heart Failure

- Two Distinct Forms
  - *Absolute Iron Deficiency*
  - *Functional Iron Deficiency*

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Absolute Iron Deficiency – depleted stores

- **Poor nutrition**

- **Physiological and functional changes to the intestinal wall**
  - ***-mucosal edema***
  - ***-reduced gastrointestinal blood flow***
  - ***-impaired iron uptake from the gut***

- **Iron loss secondary to:**
  - ***-gastritis or ulceration***
  - ***-proteinuria from chronic renal disease***
  - ***-bleeding due to antiplatelet drugs or anticoagulation***

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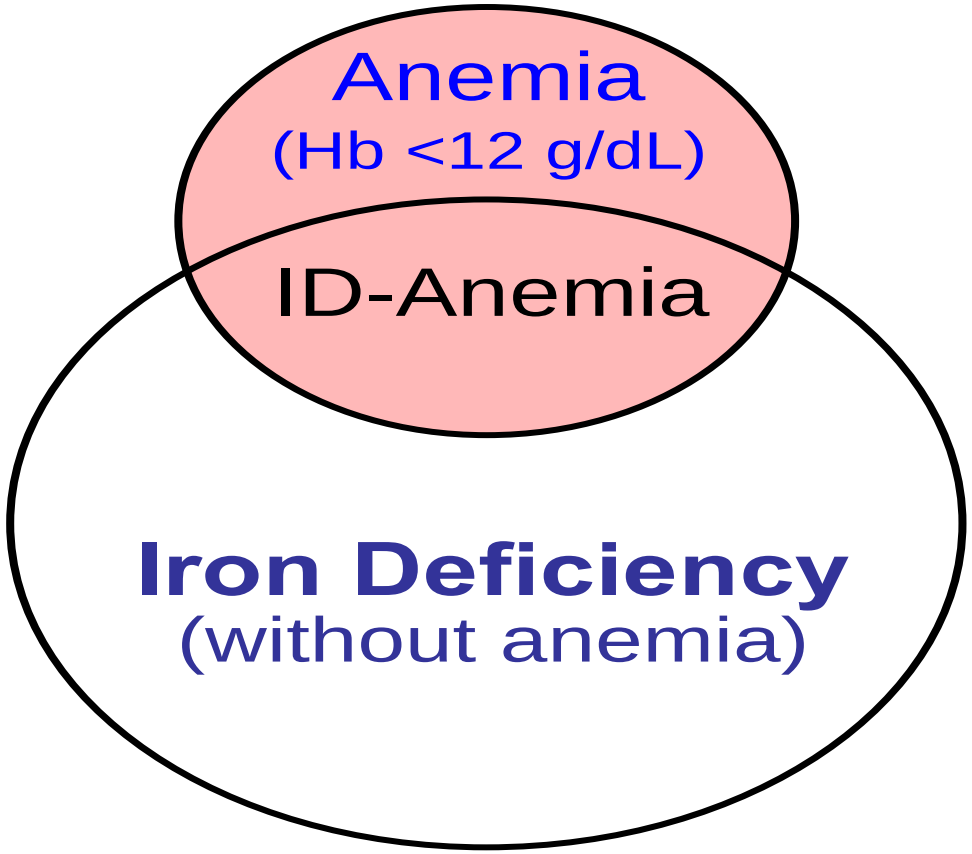


1. Absolute iron deficiency
(Reduction in iron stores)

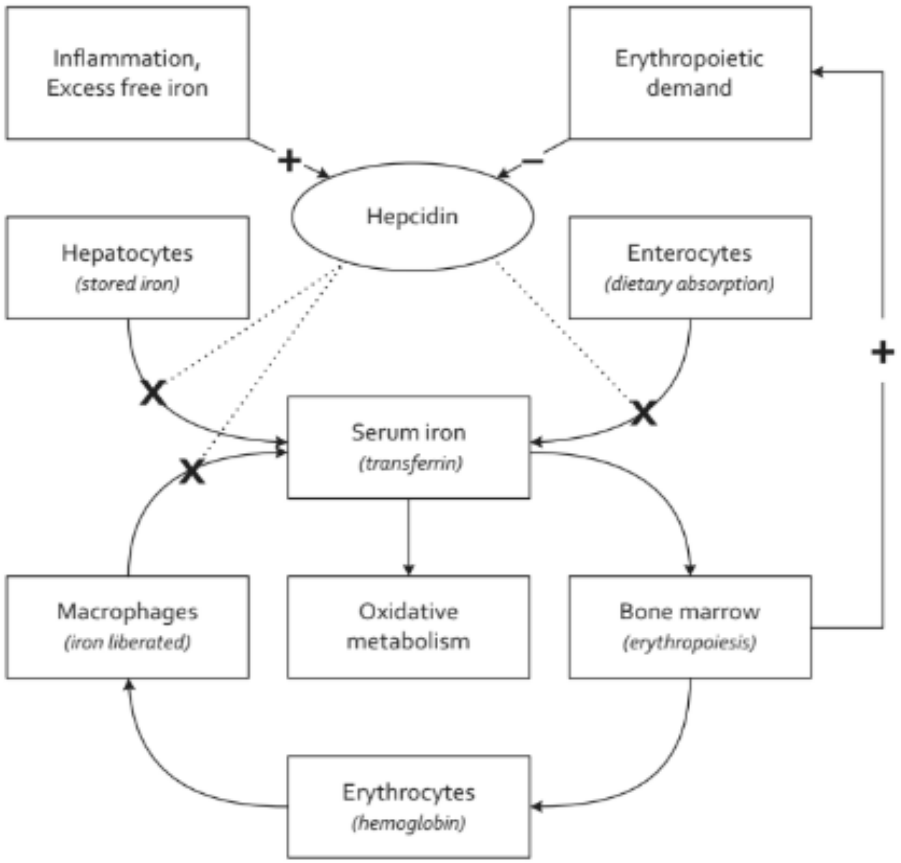
- Causes: chronic blood loss (aspirin), malnutrition, malabsorption
- Diagnosis: low serum ferritin level <30 µg/L

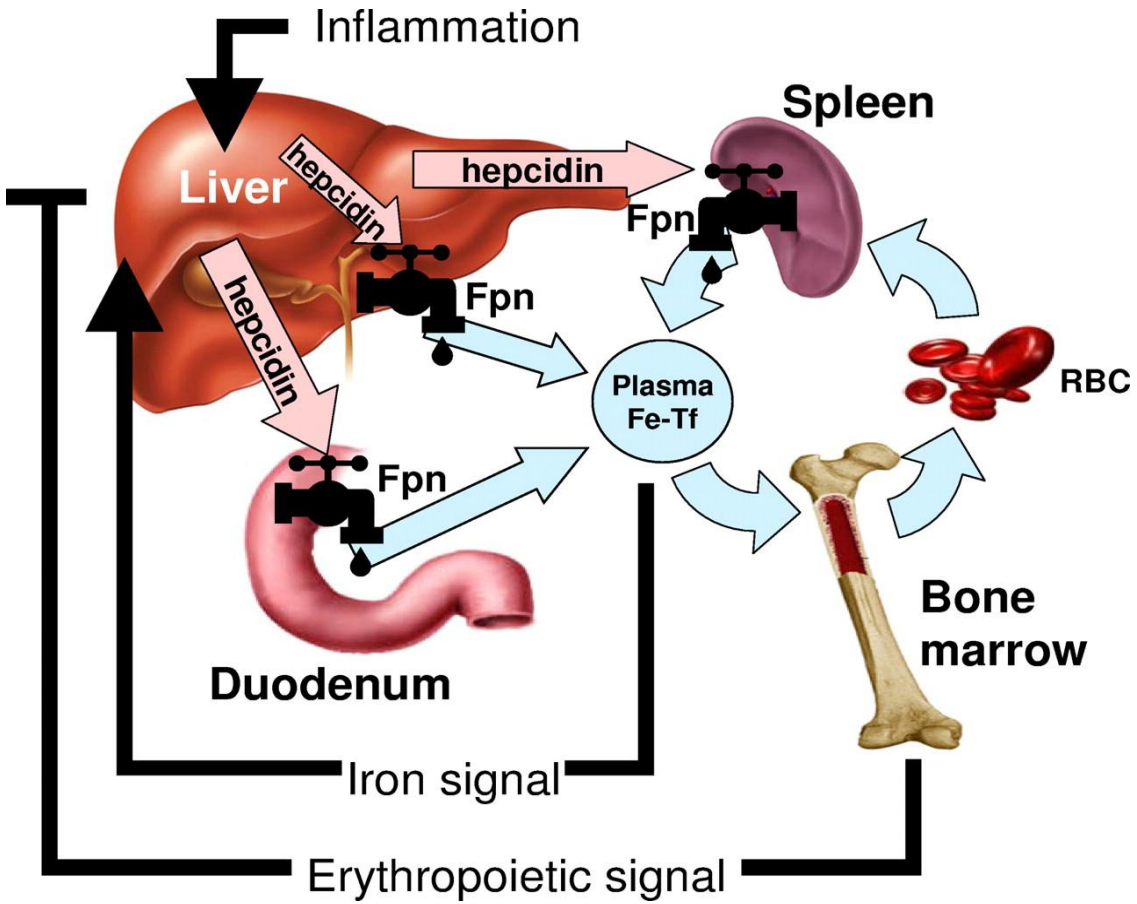
2. Functional iron deficiency
(Disturbed iron metabolism in bone marrow; iron stores =/↓)

- Causes: chronic inflammation & kidney dysfunction
- Diagnosis: serum ferritin 30–99 µg/L or serum ferritin 100–299 µg/L and TSAT<20%

1. Wish JB. *Clin J Am Soc Nephrol* 2006;1:S4–8. 2. Muñoz M, et al. *World J Gastroenterol* 2009;15:4617–26.

Functional Iron Deficiency – reduced availability





Generalized inflammatory state ↑ *levels of proinflammatory cytokines such as IL-6*

↑ *production and release of hepcidin*- an acute phase protein synthesized in the liver

Hepcidin regulates the release of stored iron from enterocytes and hepatocytes

Degradation of the iron transporter protein, ferroportin

High levels of hepcidin can 'trap' iron in storage

Hematol Oncol Clin North Am. 2014 August ; 28(4): 671–681.
Beavers CJ, et al. *Pharmacotherapy* 2014;34(7):719–732.

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Features of Iron Deficiency Anemia (IDA)

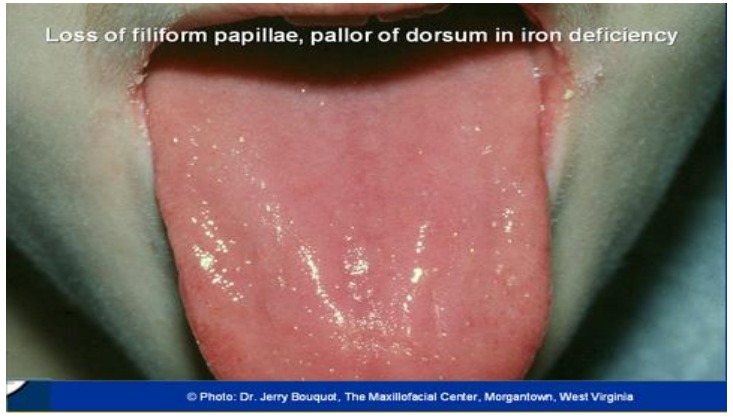
- **Depends on the degree and the rate of development of anemia**
- **Symptoms common to all anemias:**
  - ***pallor, fatigability, weakness, dizziness, irritability***

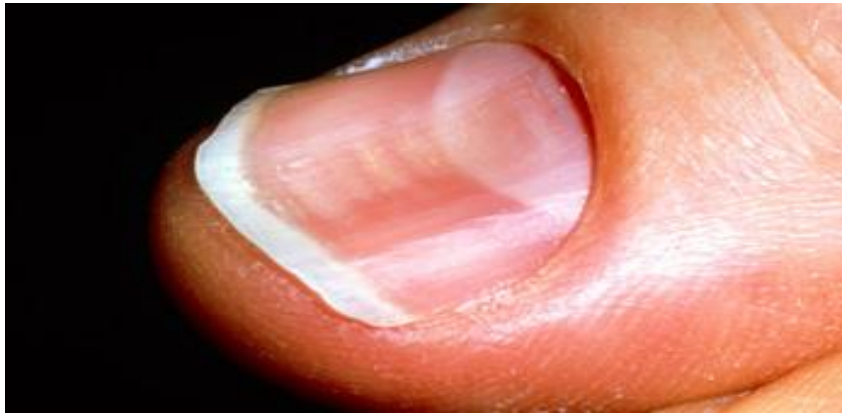
Iron Deficiency: Clinical Manifestations

- **Symptoms of anemia**
- **Reduced exercise capacity, dyspnea on exertion**
- **Pica/Pagophagia-craving for peculiar food or non-food substances e.g ice, dirt, chalk**
- **Dysphagia, esophageal web, glossitis (Plummer-Vinson or Patterson-Kelly Sx)-very rare**

Other Features of IDA

- Glossitis - smooth tongue
- Restless Legs
- Angular stomatitis - cracking of corners of mouth
- Koilonychia - thin, brittle, spoon-shaped fingernails





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Tests for Iron Deficiency

- Peripheral blood smear
- Red cell indices (MCV, MCH)
- Serum ferritin
- Serum iron / transferrin = iron saturation
- Bone marrow iron stain (Prussian blue)

- **Serum hepcidin (correlates with iron stores more precisely than ferritin)**

- **Soluble transferrin receptor (sTfR) (facilitates intracellular import of iron; ID induces the expression and release of the transferrin receptor to the circulation)**
  - Lack of assay standardization restricts its implementation in clinical routines

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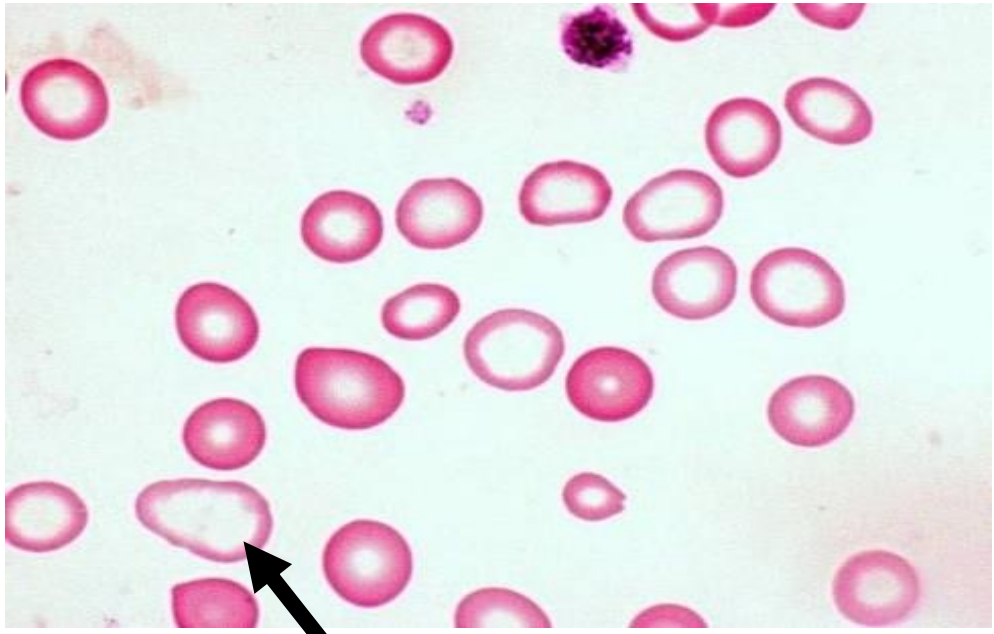
Am. J. Clin. Nutr. 2017;106:1606S–1614S

Fe Deficiency: Lab Findings

- **CBC**
  - ***↑RDW (anisocytosis), platelets***
  - ***↓MCV (<80 fl), MCH, MCHC (<32 g/dl) , RBC, Hb, Hct***
- **Blood smear**
  - ***Microcytosis***
  - ***Hypochromasia widening of the central pallor accounting for >1/3 of the total RBC diameter***
  - ***Anisocytosis***
- **Retic count not increased**



Marked hypochromasia

https://www.pathologystudent.com/microcytosis-and-hypochromasia/

Fe Deficiency: Lab Findings

- **Serum tests**
  - ***↓Fe***
  - ***↓iron sat (ratio of serum iron to TIBC (< 20%),***
  - ***↓Ferritin***
  - ***↑Total iron-binding capacity (TIBC): maximum amount of iron needed to saturate plasma or serum transferrin, transferrin receptor***

- Ganzoni equation: Iron deficit (mg) = body weight (kg) x (15 – actual Hgb) (g/dl) x 2.4 + 500 (mg).

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Definition of Iron Deficiency

Ferritin level <100 µg/L (AID)

OR

Ferritin (100 to 300 µg/L) + transferrin saturation (TSAT) <20% (FID)

*sensitivity of 82.4% and a specificity of 72% for detecting ID in patients with HF
*Serum iron (≤13 µmol/L) and TSAT (≤19.8%) maybe better cutoffs

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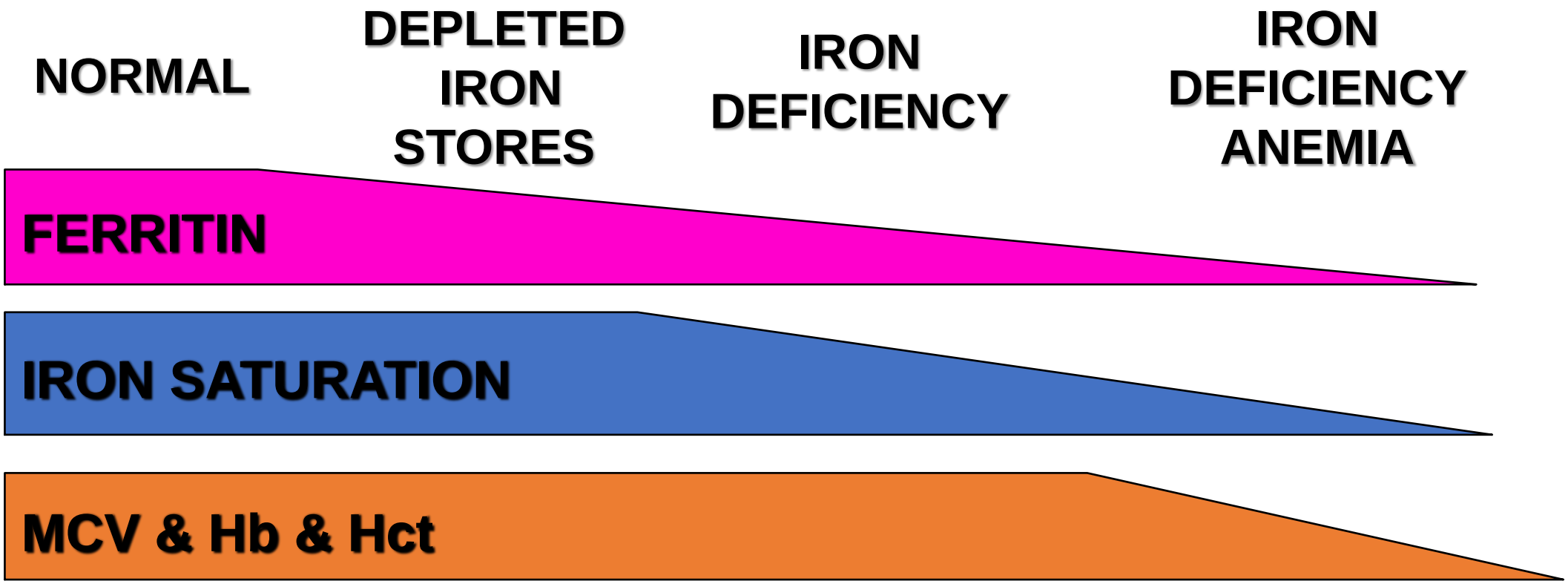
McDonagh T.A. et al . *Eur. Heart J.* 2021;42:3599–3726.
HFSA Scientific Statement. J Cardiac Failure, 29, ISSUE 7, P1059-1077

Sequential Changes in IDA



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Stages of Iron Deficiency

	Stage I Prelatent	Stage II Latent	Stage III Anemia
BM Iron	↓	Absent	Absent
S.Ferritin	↓	<12 ug/L	<12 ug/L
Hb	Normal	Normal	↓
MCV	Normal	Normal	↓
Symptoms	+/-	+/-	+

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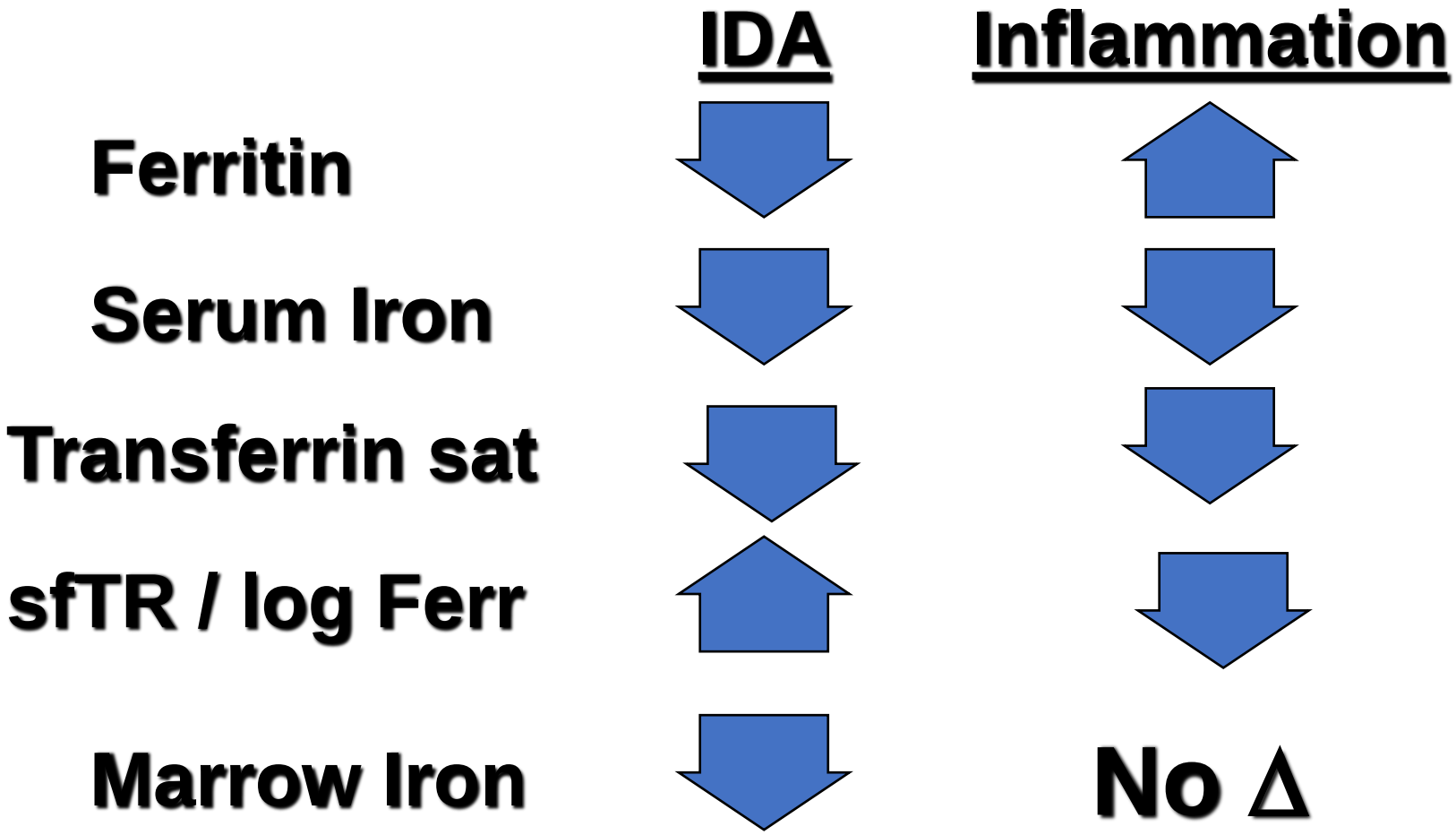
IDA vs. Inflammation



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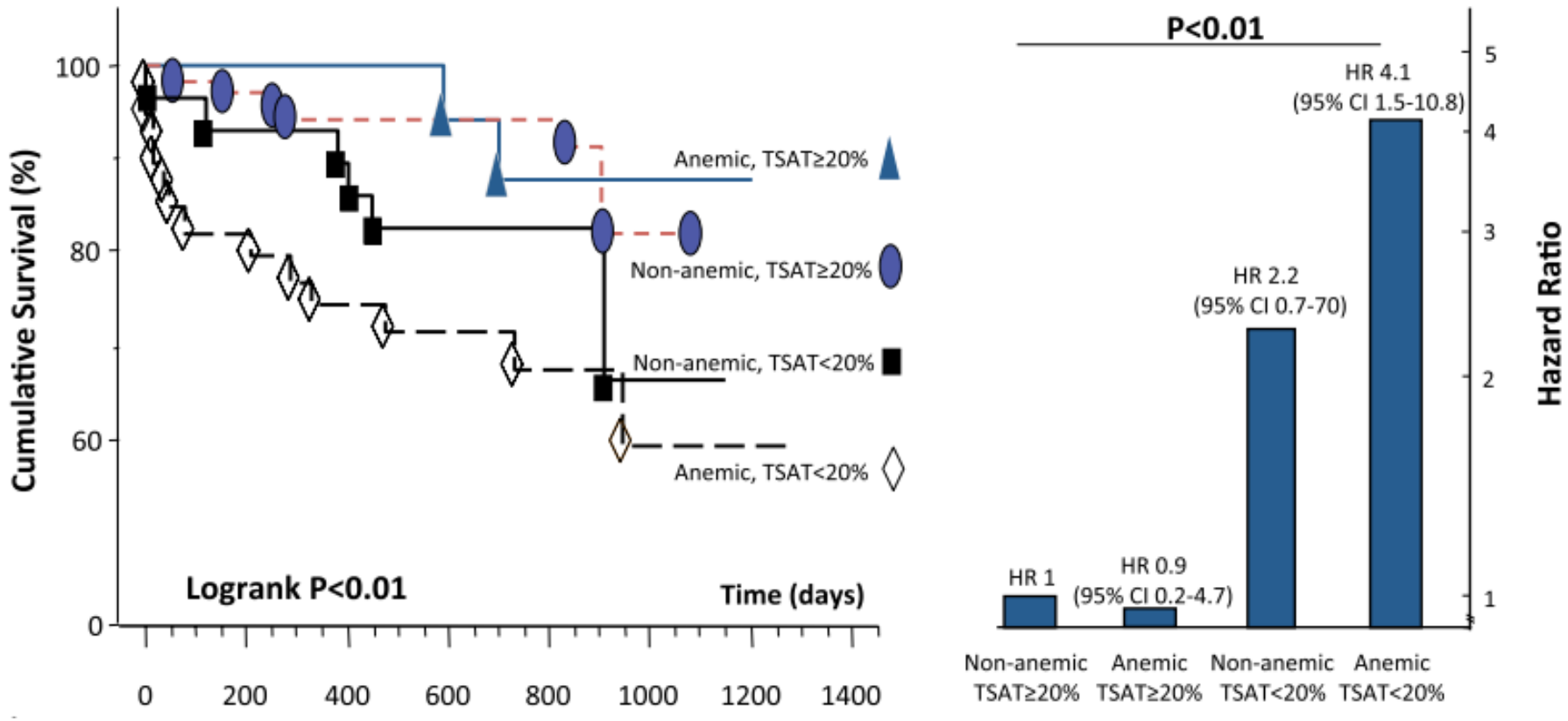
Prognostic Association of Varying Hematological Groups



Patients with IDA had a 2-fold greater risk for death than those with nonanemic iron deficiency and a 4-fold greater risk for death than iron-replete patients with or without anemia.

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Okono , et al. *JACC*. 2011;58:1241-51.

Response to Therapy

- Peak reticulocyte count 7 - 10 d
- Increased Hb and Hct 14 - 21 d
- Normal Hb and Hct 2 months
- Normal iron stores 4 - 5 months

- **Continue therapy to <u>replenish iron stores</u>**

- <u>Monitoring-</u> **NO GOLD Standards exist**

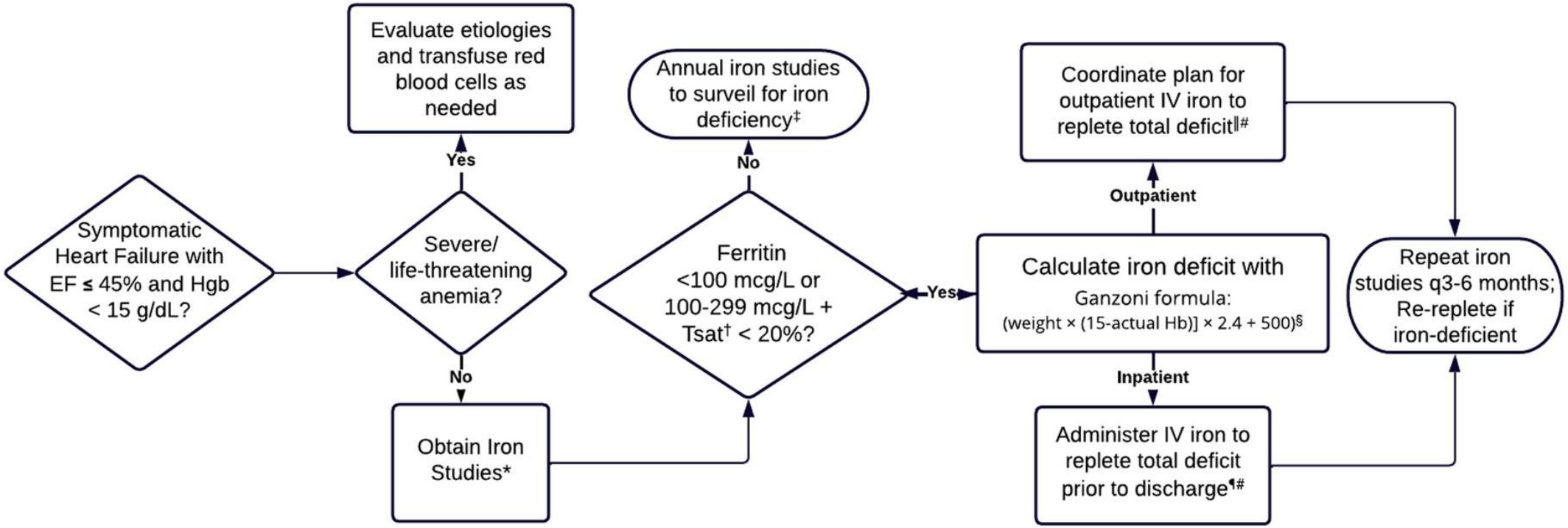
1. Check ferritin/TSAT at 3 months

2. Check ferritin/TSAT:
   - ➢ *if change in clinical picture*
   - ➢ *Hb decrease*
   - ➢ *1–2 times/year*

European Journal of Heart Failure (2018) **20**, 1664–1672

European Journal of Heart Failure (2015) **17**, 248–262

Diagnosis of ID in HF – 2023 HFSA Statement



*Iron studies consist of iron, total iron binding capacity (TIBC) and ferritin and can be measured from the same green-top tube used for a basic metabolic panel at a cost of ~$10.
†Tsat, transferrin saturation, derived from iron/TIBC
‡If a patient newly develops anemia, mycrocytosis (MCV < 80 fL) or RDW >14.5%, implement earlier re-screening of iron studies.
§Substitute ideal body weight for actual body weigh in obese indivuduals.
‖Agent used based on coverage, patient preference, and facilitation or administration schedule
¶Agent used based on institutional formulary
#Number of doses depends on formulation used (Table 1). To correct and maintain iron parameters above the thresholds for iron deficiency the mean and median dose of IV iron over 1-yer enrollment of CONFIRM-HF was 1500 mg per subject delivered in 2 infusions.

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Beavers CJ, et al. *J Cardiac Failure* 2023; 29.7: 1059-1077

Summary of ESC and Practical Guideline Recommendations: In whom and when?

Recommendation	Class	Level
It is recommended that all patients with HF be periodically screened for anaemia and iron deficiency with a full blood count, serum ferritin concentration, and TSAT.	**I**	**C**

- Iron status evaluation is also recommended in patients with existing CHF, particularly if they are symptomatic

- Iron parameters should be evaluated at least once a year

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2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal (2021) 42, 35993726

2022 AHA/ACC/HFSA HF Guidelines

1	C-EO

For patients who are diagnosed with HF, laboratory evaluation should include complete blood count, urinalysis, serum electrolytes, blood urea nitrogen, serum creatinine, glucose, lipid profile, liver function tests, **iron studies**, and thyroid-stimulating hormone to optimize management.

- ☑ Serum iron
- ☑ Serum ferritin
- ☑ Transferrin saturation

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Heidenreich PA, et al. *Circulation* 2022; 145: e895-e1032

Summary

- Iron deficiency may be present in absence of anemia
- Hepcidin plays an important role in iron homeostasis
  - *may be the biomarker to test in the future*
- Serum transferrin and ferritin are different in IDA compared to ACD
- Symptoms may resolve prior to laboratory indices
- Ongoing monitoring is advised

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Treatment of Iron Deficiency in Heart Failure

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President, Baylor Scott and White Research Institute

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Dallas, TX

Distinguished Professor of Medicine

University of Mississippi

Jackson, MS

Consultant: American Regent, Amgen, Applied Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, CVRx, Cardior, Cytokinetics, Imbria, Impulse Dynamics, Innolife, Janssen, Lexicon, Medtronic, Merck, Novartis, Novo Nordisk, Occlutech, Roche, Secretome, Sequana, Tricog, Vifor

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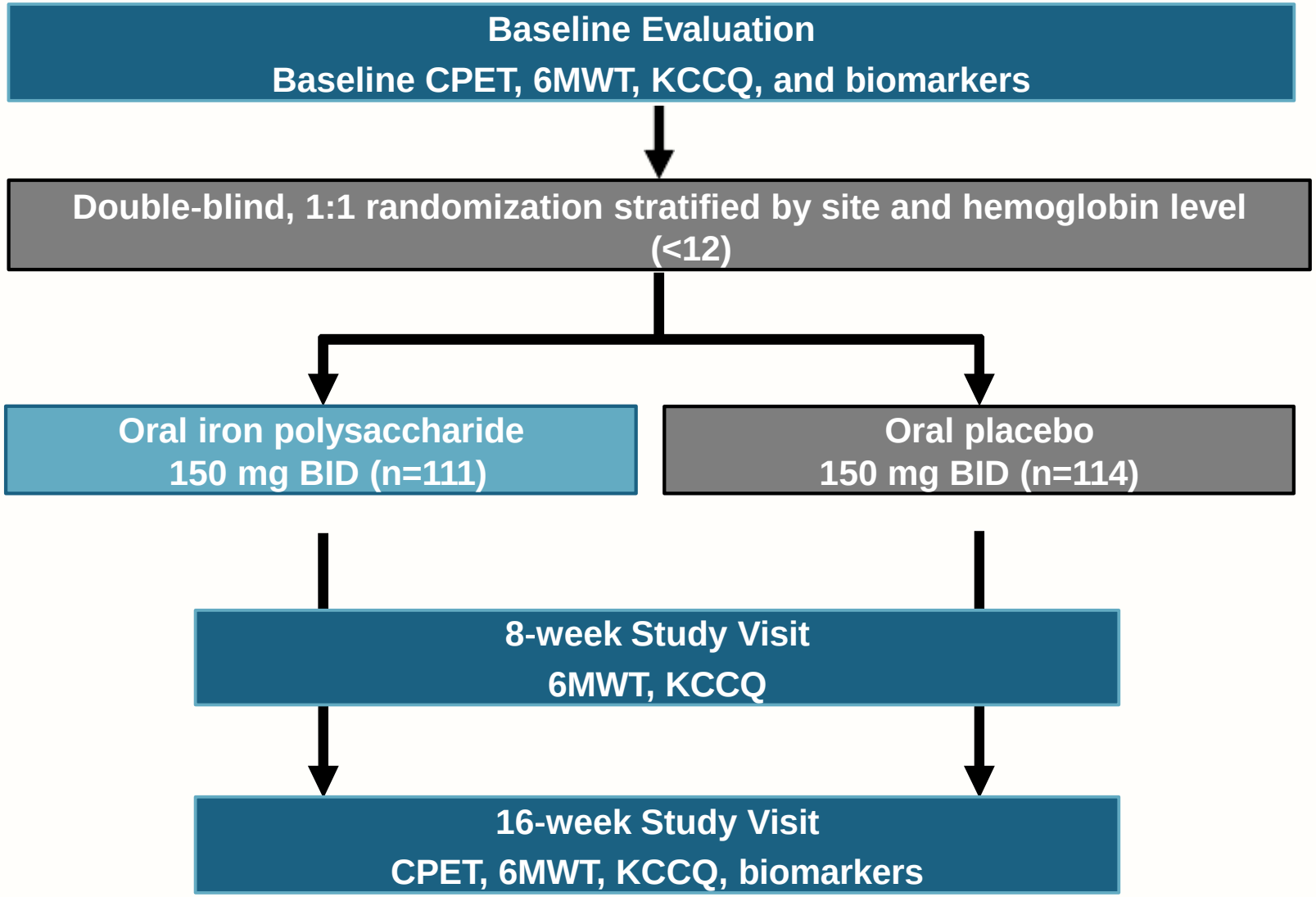
ORAL IRON THERAPY

IRONOUT-HF* (Phase 2)

- LVEF <40% and NYHA II/III
  - Median age 63 yrs.
  - 36% women
  - 6MWT 363 m
  - Median time w HF: 5.7 yrs.
- Ferritin 15–100 µg/L or <300 µg/L with TSAT<20% and Hgb 9–15.0 (men) /9–13.5 (women)
- Primary outcome: peak exercise capacity

*, Iron Repletion Effects on Oxygen Uptake in Heart Failure



Lewis GD, et al. JAMA. 2017;317:1958-66.

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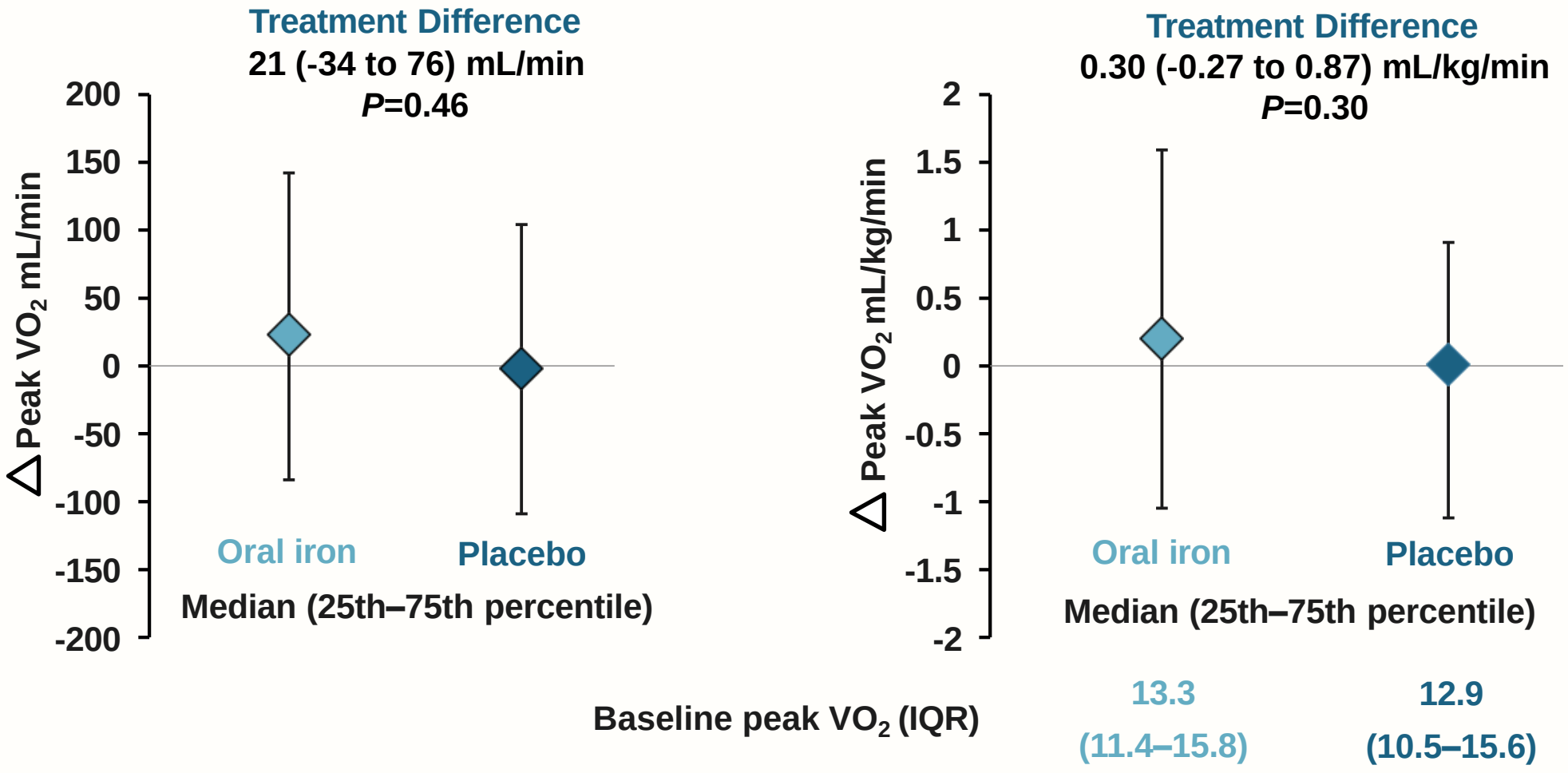
IRONOUT-HF

N = 225; Oral iron: No Change in exercise capacity



KNOW ID in HF

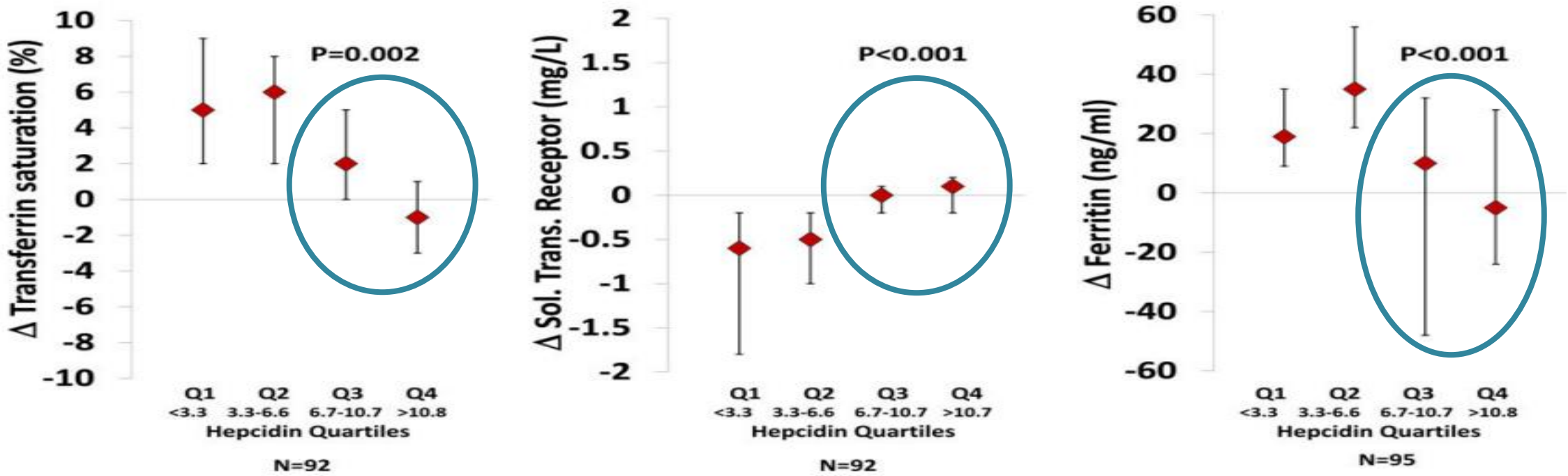
Lewis GD, et al. JAMA. 2017;317:1958-66.

High Hepcidin Levels Predict Poor Responsiveness to Oral Iron

Hepcidin: chronically elevated in proinflammatory conditions (like HF)

Hepcidin: a protein synthesized & secreted in hepatocytes; controls the activity of ferroportin

Ferroportin, a protein responsible for iron export out of the gut enterocytes & hepatocytes/macrophages of the liver's reticuloendothelial system



Higher baseline hepcidin levels were related to:

↓ Δ iron bioavailability:	Δ TSAT	r = –0.29	*P*=0.004
↓ Δ cellular iron levels:	Δ sTfR*	r = 0.48	*P*<0.001
↓ Δ iron stores:	Δ Ferritin	r = –0.30	*P*=0.004

*, Sol. Trans., soluble transferrin receptor (a measure of functional iron status)
-- Levels are increased as a response to depleted tissue iron

Lewis GD, et al. JAMA. 2017;317:1958-66.

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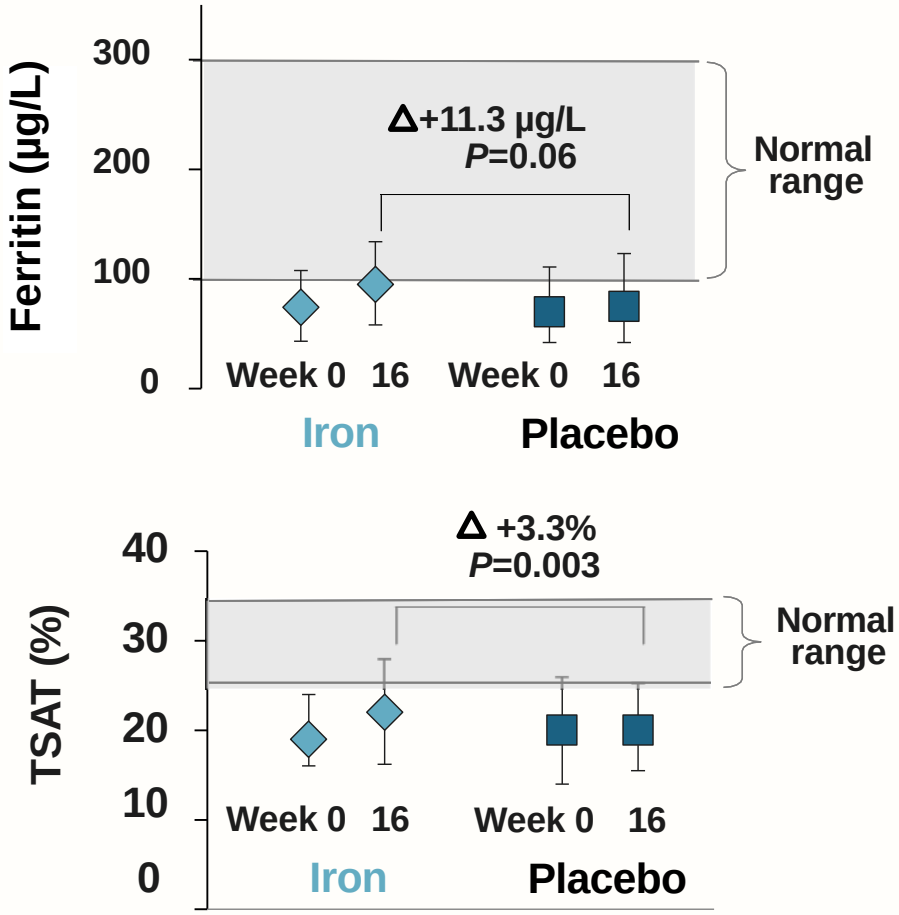
IRONOUT-HF

No Substantial Increase in Ferritin or TSAT in Iron Studies with Oral Iron in HF



PO

Inexpensive

- **High frequency of GI adverse events**
- **Drug-drug and drug-food interactions**

Utility in heart failure:
IRONOUT-HF did not show improvement in exercise capacity; very limited role, if any

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Lewis GD, et al. JAMA. 2017;317:1958-66.

Intravenous Iron Formulations

Formulation	Test Dose	Maximum Dose	FDA Indication	Evidence in HF
Iron Dextran	Yes	100 mg	ID, blood loss	Retrospective, observational studies
Iron Sucrose	No	200 mg	CKD	Small RCTs; prospective observational trials
Ferric Gluconate	No	250 mg	CKD-dialysis	Retrospective, observational trials
Ferumoxytol	No	510 mg	CKD, IDA	None to date
Ferric Carboxymaltose	No	1000 mg	CKD, IDA, **HF**	RCTs specifically conducted in patients with HFrEF
Ferric Derisomaltose	No	1-2000 mg	CKD, IDA	Subanalysis of RCT that included some HF patients; 1 large RCT

CKD, chronic kidney disease; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ID, iron deficiency; IDA, iron deficiency anemia; RCT, randomized controlled trial

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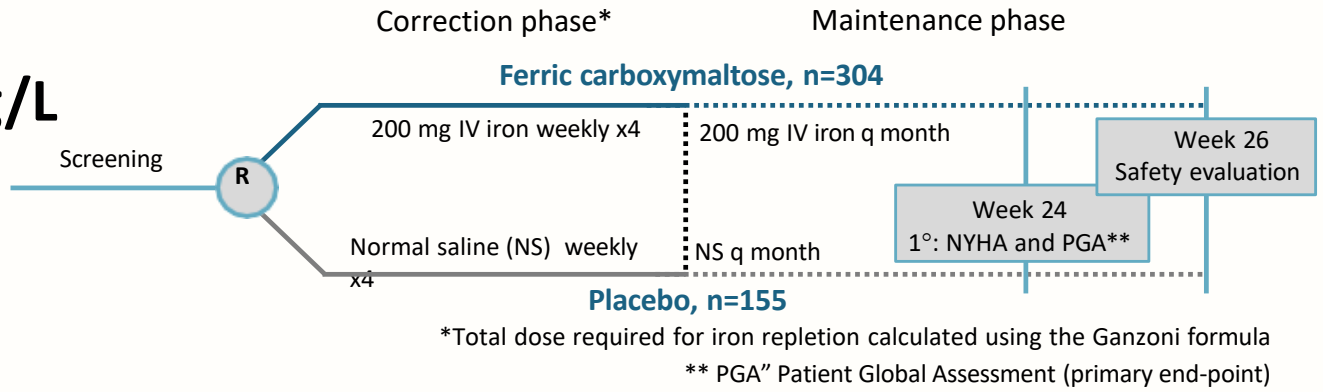
Beavers CJ, et al. *J Cardiac Failure* 2023; 29.7: 1059-1077

IV IRON -- FAIR-HF Trial Study Design

- **Main inclusion criteria**
  - **NYHA class II/III, LVEF ≤ 40% (NYHA II) or ≤ 45% (NYHA III)**
  - **Hgb: 9.5–13.5 g/dL**
  - **Iron deficiency: serum ferritin <100 µg/L or <300 µg/L, if TSAT <20%**
- **Treatment adjustment algorithm**
  - **Interruption: Hgb >16.0 g/dL or ferritin >800 µg/L or ferritin >500 µg/L, if TSAT >50%**
  - **Restart: Hb <16.0 g/dL and serum ferritin <400 µg/L and TSAT <45%**
- **Blinding**
  - **Clinical staff: unblinded and blinded personnel**
  - **Patients: used curtains and black syringes for injections**



*Total dose required for iron repletion calculated using the Ganzoni formula

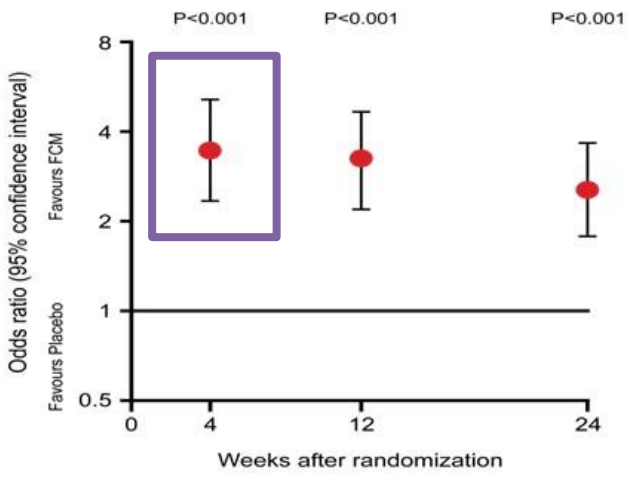
** PGA" Patient Global Assessment (primary end-point)

Anker SD, et al. *Eur J Heart Fail.* 2009;11:1084-91.
Anker SD, et al. *N Engl J Med.* 2009;361:2436-48.

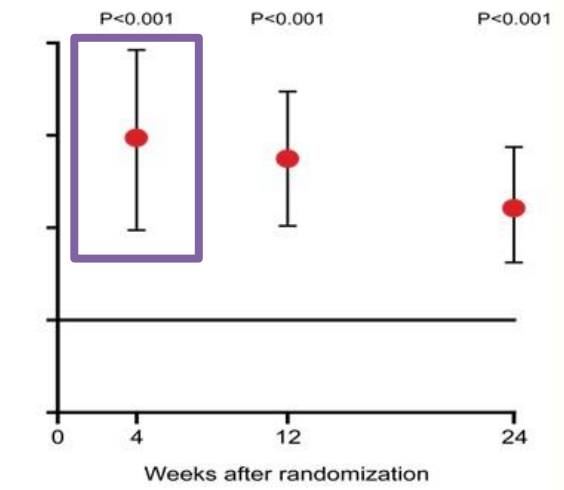
FAIR-HF

NYHA Class, Self-reported Patient Global Assessment, Quality of Life, and 6-minute Walking Test

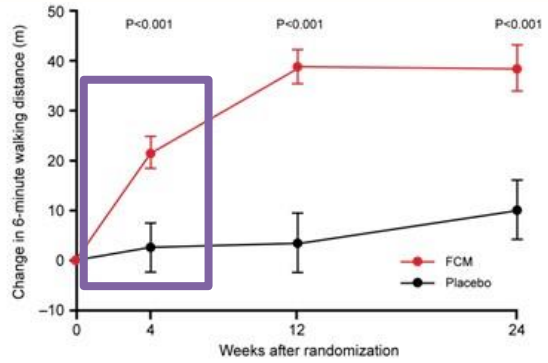
Self-reported Patient Global Assessment



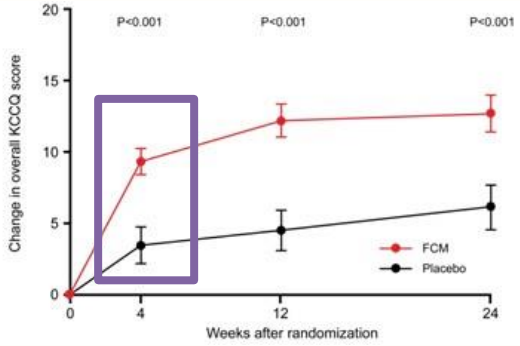
NYHA Functional Class



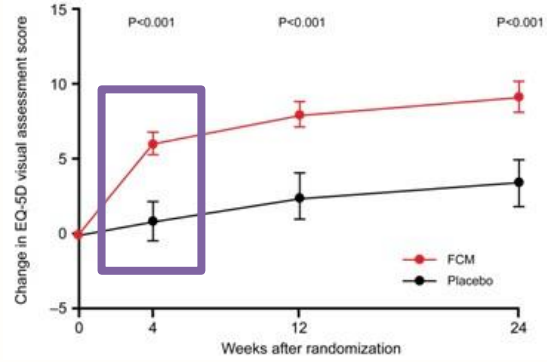
6-minute Walking Test



KCCQ Overall Score



EQ-5D VAS Score



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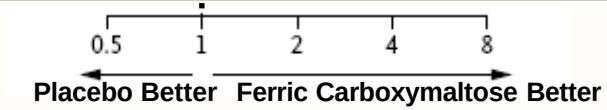
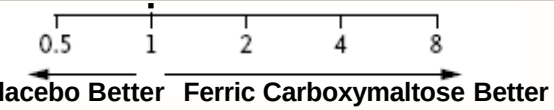
Anker SD, et al. *N Engl J Med.* 2009;361:2436-48.

FAIR-HF

IV FCM Improves Patient Global Assessment, NYHA Class, and Key Iron Indices in HF Patients *with and without Anemia*

Subgroup	Self-reported Patient Global Assessment				NYHA Functional Class			
	FCM	Placebo	Odds Ratio (95% CI)	*P*-value for Interaction	FCM	Placebo	Odds Ratio (95% CI)	*P*-value for Interaction
	# patients				*# patients*			
Hemoglobin				0.98				0.51
≤12.0 (g/dL)	146	74			148	74		
>12.0 (g/dL)	146	75			146	75		





Week 24 Results	FCM	Placebo	*P*-value*
Patients with anemia at baseline			
Serum ferritin (µg/L)	275 ± 18	68 ± 11	<0.001
TSAT (%)	29 ± 1	17 ± 1	<0.001
Hemoglobin (g/dL)	12.7 ± 1	11.8 ± 2	<0.001
Patients without anemia at baseline			
Serum ferritin (µg/L)	349 ± 19	80 ± 11	<0.001
TSAT (%)	30 ± 1	22 ± 1	<0.001
Hemoglobin (g/dL)	13.3 ± 1	13.2 ± 1	0.21

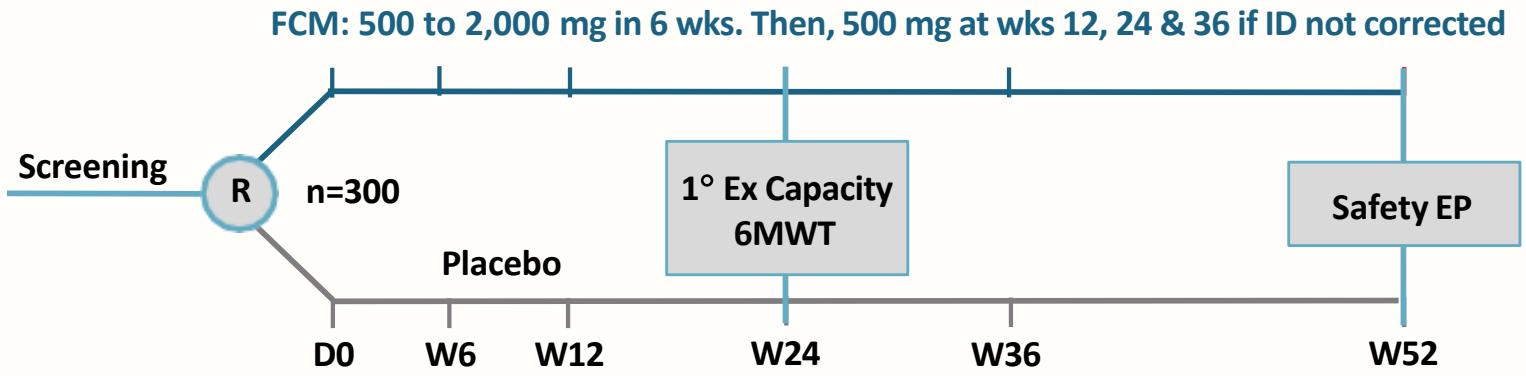
*Mean treatment effect, adjusted for the baseline value

KNOW ID in HF

Anker SD, et al. *N Engl J Med*. 2009;361:2436-48.

CONFIRM-HF - Design

- **Design:** multicenter, randomized (1:1), double- blind, placebo-controlled
- **Main inclusion criteria**
  - NYHA class II/III, LVEF ≤45%
  - BNP >100 pg/mL or NT-proBNP >400 pg/mL
  - Iron deficiency: serum ferritin <100 µg/L or <300 µg/L, if TSAT <20%; Hgb ≤15 g/dL
- **Primary endpoint**
  - Exercise capacity: change in 6MWT distance from baseline to week 24
- **Secondary endpoints**
  - Change in biomarkers for iron deficiency, cardiac biomarkers, NYHA FC, PGA, and QoL
  - Overall safety

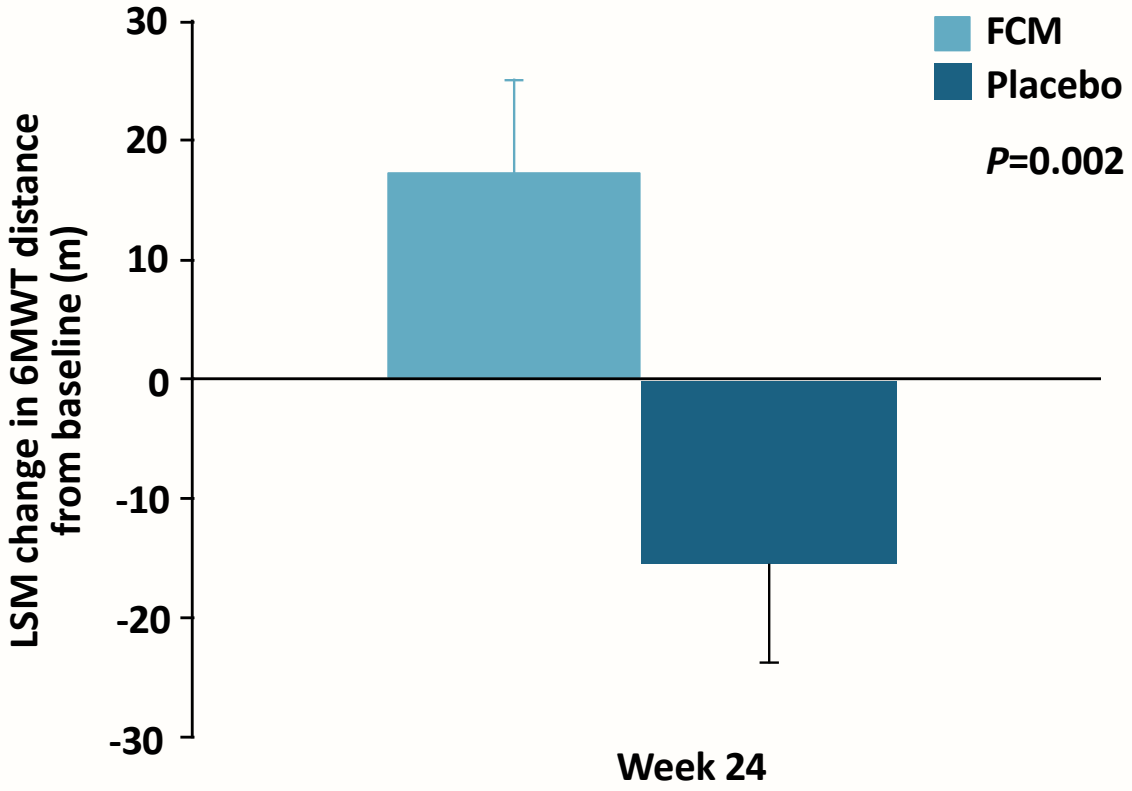


Ponikowski P, et al. *Eur Heart J.* 2015;36:657-68.

CONFIRM-HF

Improved 6-minute Walking Distance At Week 24

- **FCM improved 6MWT at week 24**
- **FCM vs placebo: 33 ± 11 m (least squares mean ± SE)**



Ponikowski P, et al. *Eur Heart J.* 2015;36:657-68.

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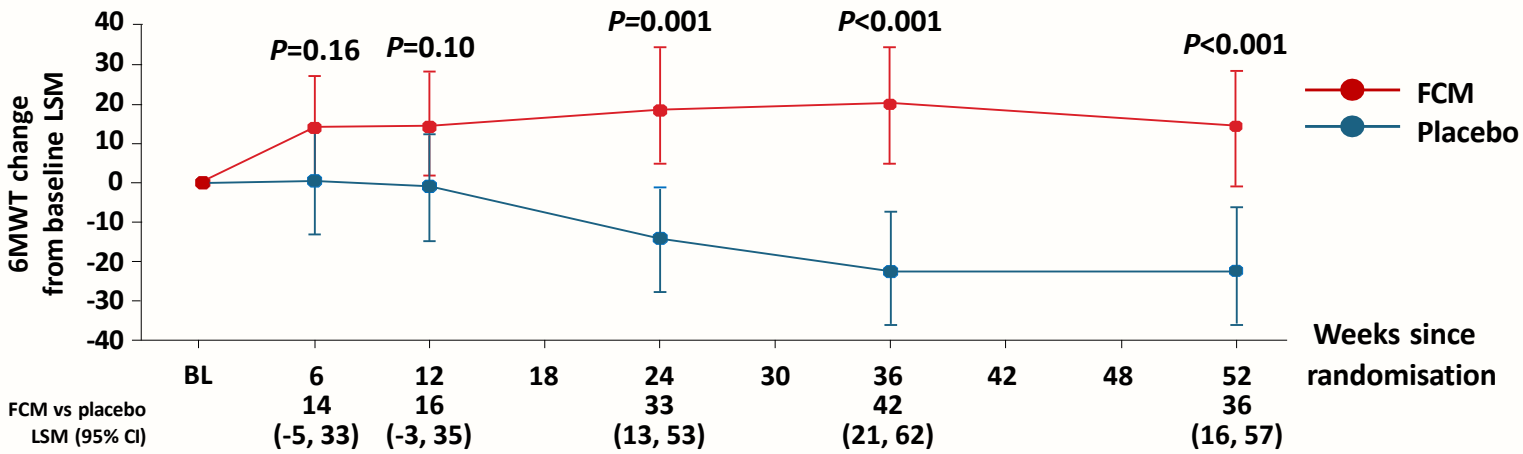
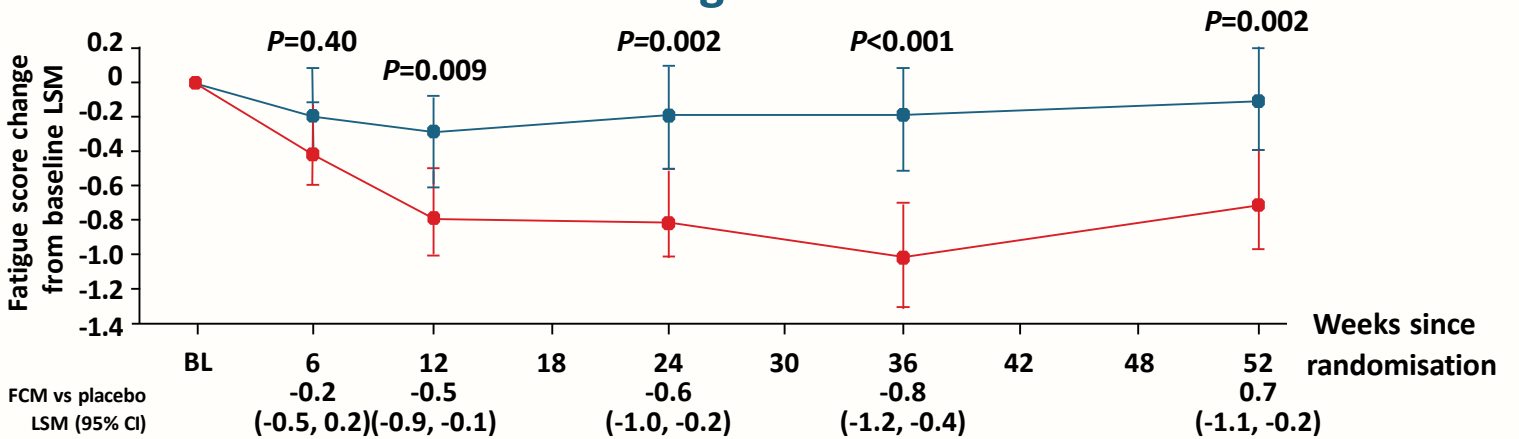
CONFIRM-HF

Improved 6-minute Walking Test and Fatigue Score over Time

6-minute Walking Test Distance



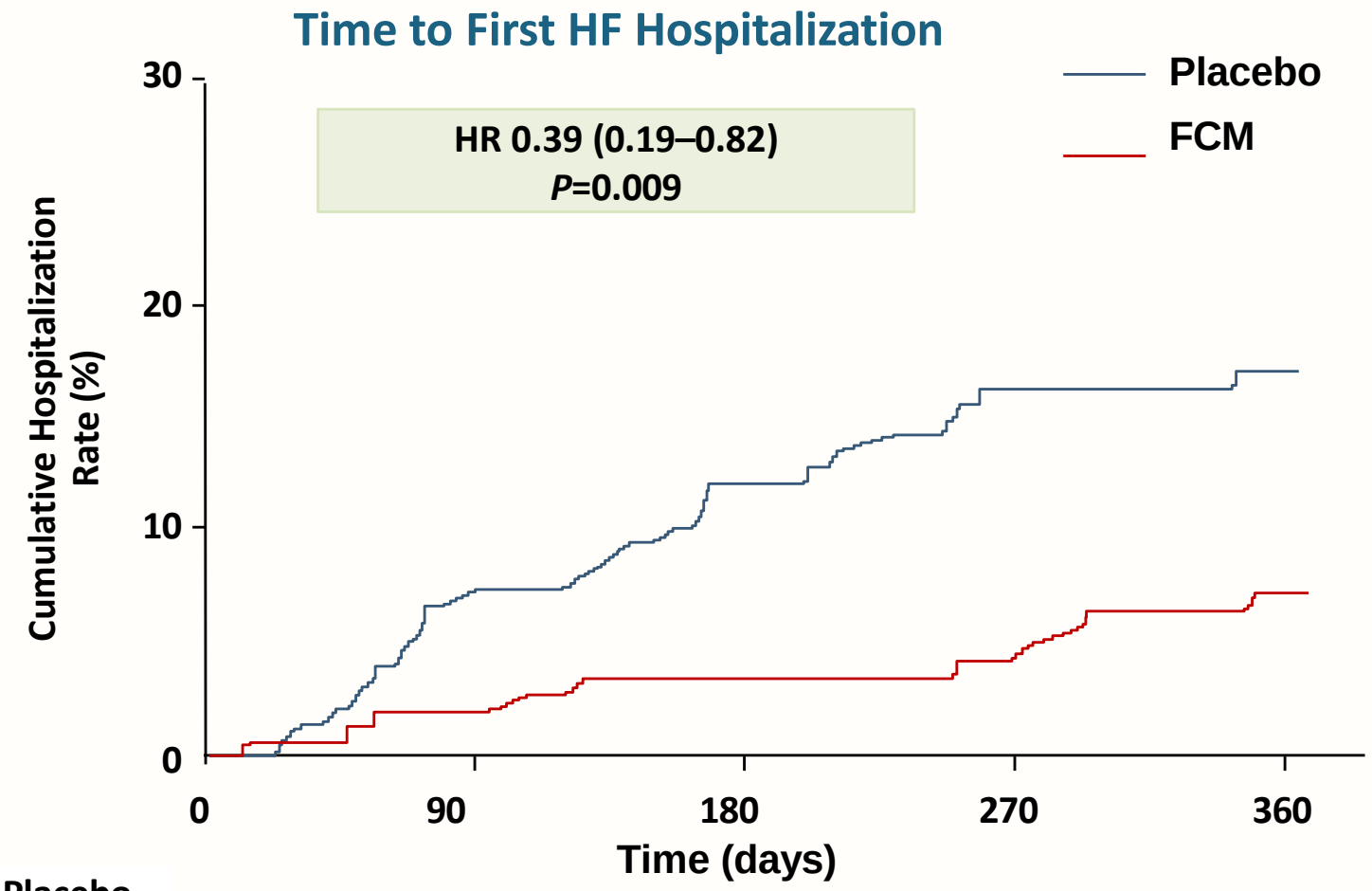
Fatigue Score



Ponikowski P, et al. *Eur Heart J.* 2015;36:657-68.

CONFIRM-HF

Secondary Outcome: Lower Worsening HF Events?



Ponikowski P, et al. *Eur Heart J.* 2015;36:657-68.

KNOW ID in HF

Pooled Analysis of FAIR-HF and CONFIRM-HF

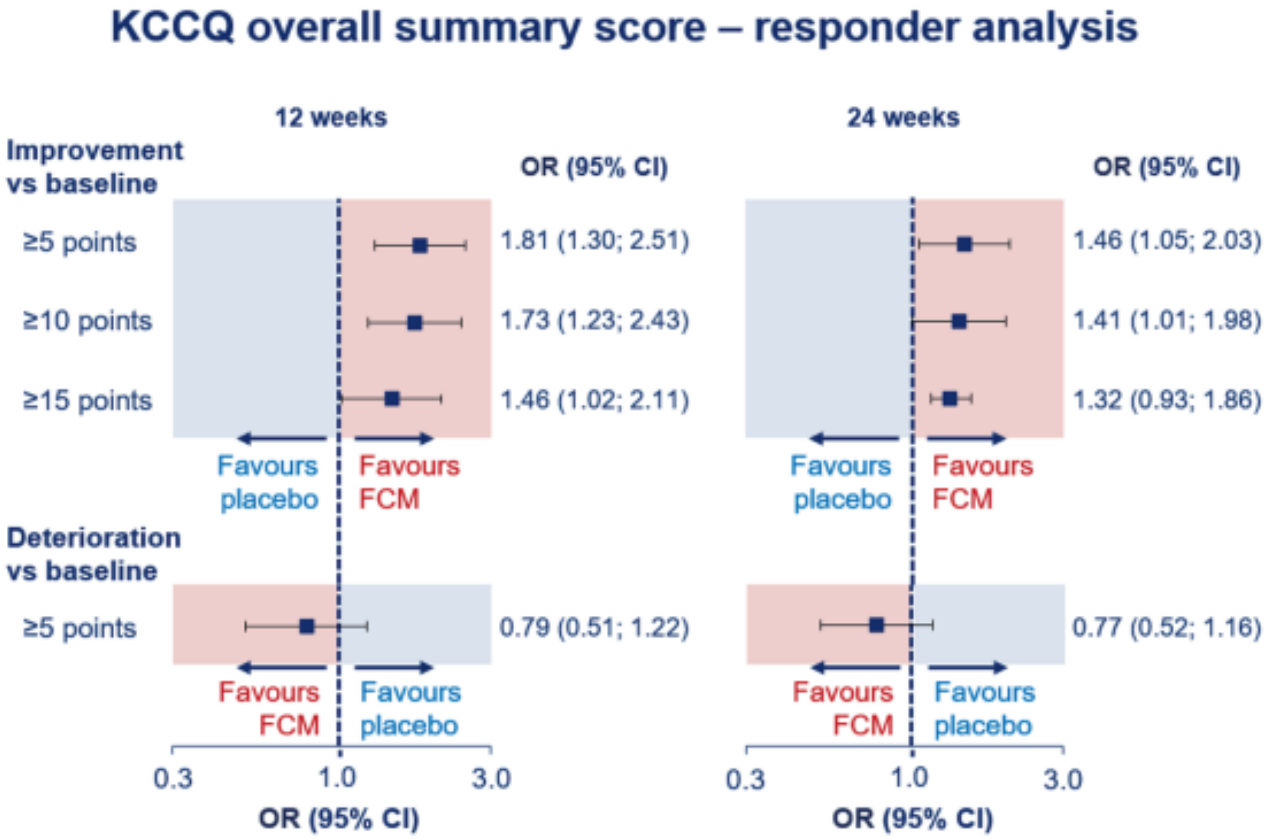
Sustained KCCQ Improvements At Individual Level

Aim: to explore the likelihood of individual improvement or deterioration in KCCQ domains with FCM vs placebo and evaluate the stability of this response over time

FAIR-HF
CONFIRM-HF
→ N=760
FCM n=454
Placebo n=306

Key outcome: likelihood of experiencing a clinically meaningful change vs baseline in KCCQ OSS, CSS and TSS

Assessed vs baseline at weeks 12 and 24

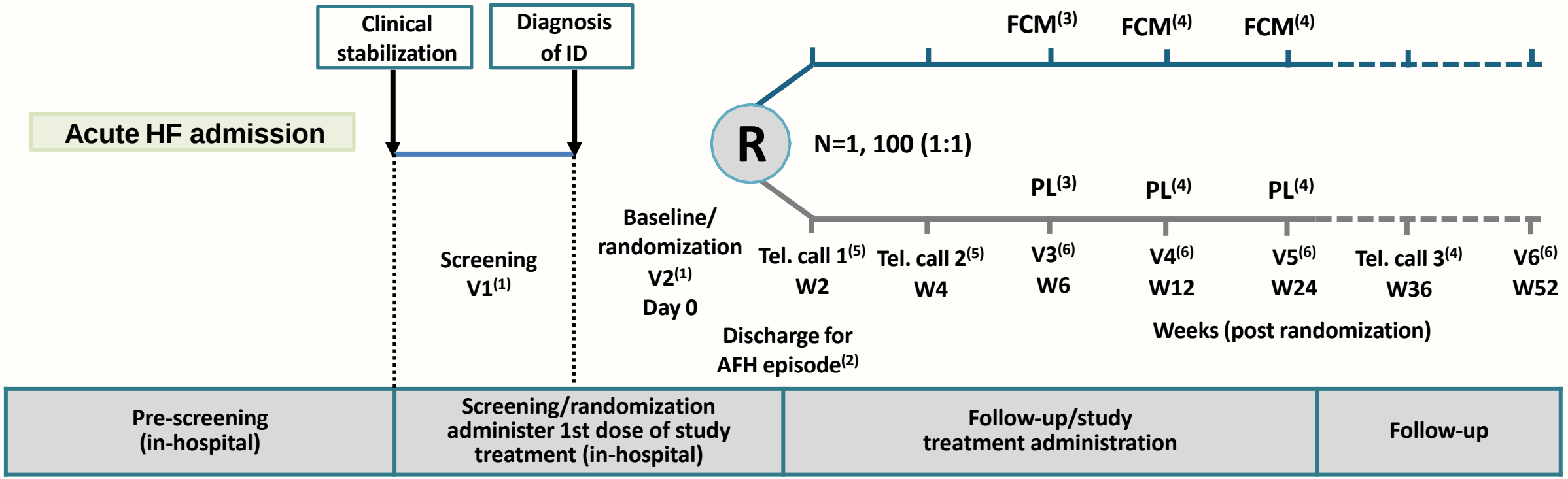


CSS, clinical summary score; KCCQ: Kansas City Cardiomyopathy Questionnaire; OR, odds ratio; OSS, overall summary score; TSS, total symptom score

KNOW ID in HF

Butler J, et al. *Eur J Heart Fail.* 2022.24:821-32.

AFFIRM-AHF Trial



Key Inclusion

- Hospitalized for acute HF; LVEF <50%;
- Iron deficiency: ferritin <100 µg/L or ferritin 100–299 µg/L with TSAT <20%

KNOW ID in HF

Ponikowski P, et al. *Eur J Heart Fail*. 2019.21:1651-58.

AFFIRM-AHF Trial

Primary Outcome: Total Heart Failure Hospitalizations and Cardiovascular Death

Total CV hospitalizations AND CV deaths:

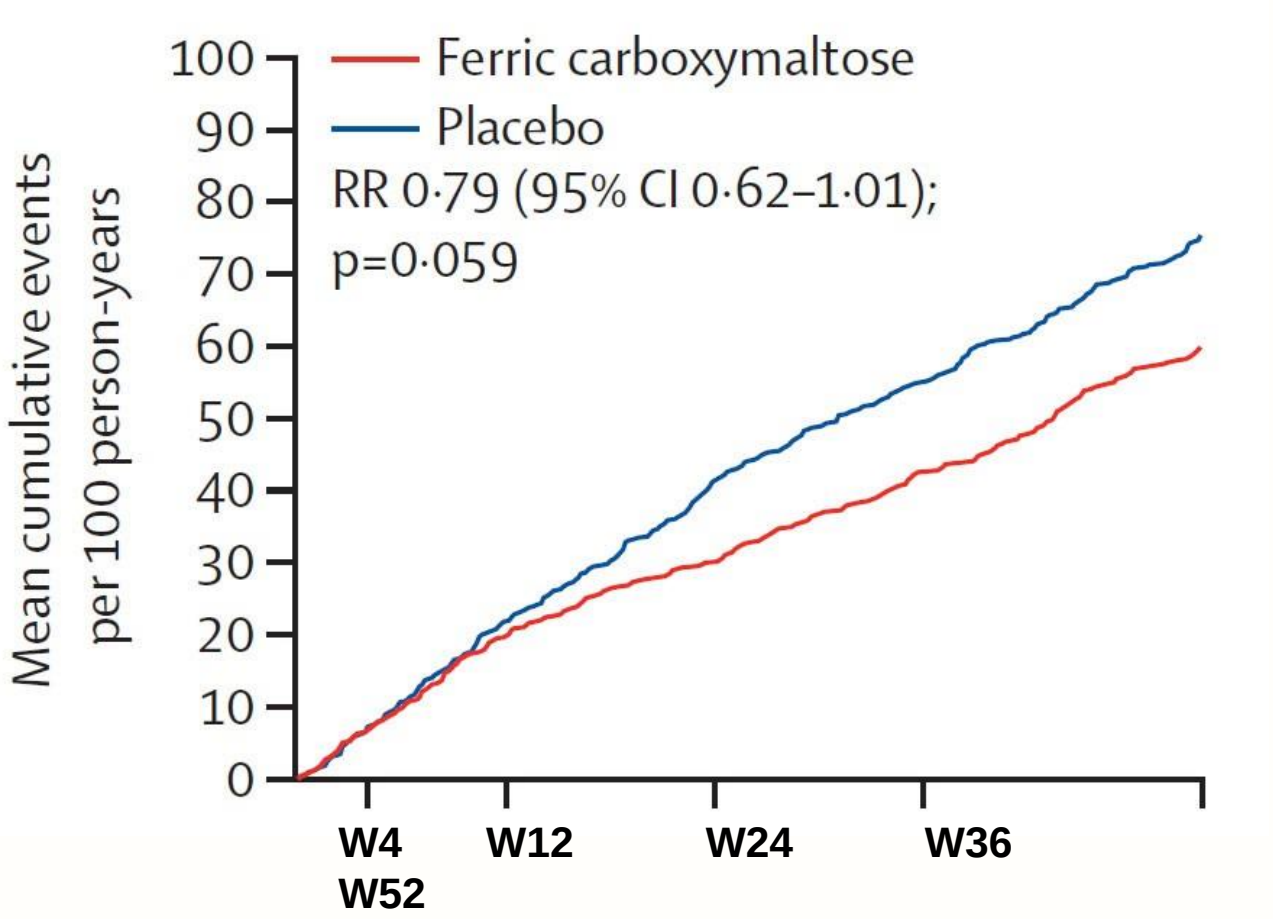
- 370 in FCM group
- 451 in the placebo group
  - RR: 0.80, 95% CI 0.64, 1.00; *p*=0.05

CV deaths:

- 77 of 558 (14%) in FCM group
- 78 of 550 (14%) in the placebo group
  - HR: 0.96, 95% CI 0.70, 1.32; *p*=0.81

HF hospitalizations:

- 217 in FCM group
- 294 in the placebo group
  - RR: 0.74, 95% CI 0.58, 0.94; *p*=0.03



Ferric carboxymaltose group: 293 primary events (57.2 per 100 patient-years)
Placebo group: 372 primary events (72.5 per 100 patient-years)

Ponikowski P, et al. *Lancet.* 2020;396:1895-1904.

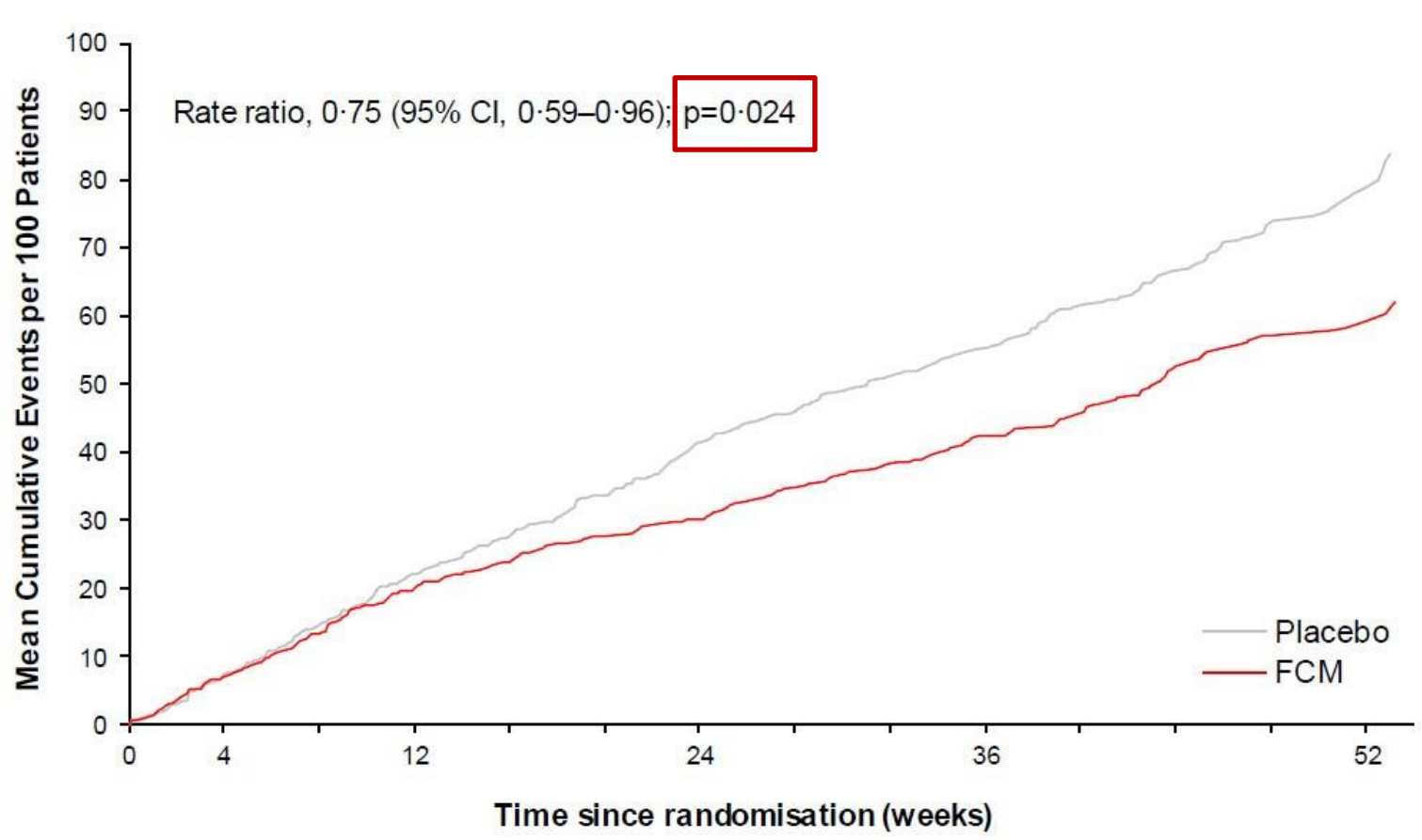
KNOW ID in HF

AFFIRM-AHF Trial

COVID-19 Sensitivity Analysis

COVID-19 Sensitivity Analysis

How might COVID-19 affect trial outcomes?
Study completion, 07/21/2020



Ponikowski P, et al. *Lancet.* 2020;396:1895-1904.

KNOW ID in HF

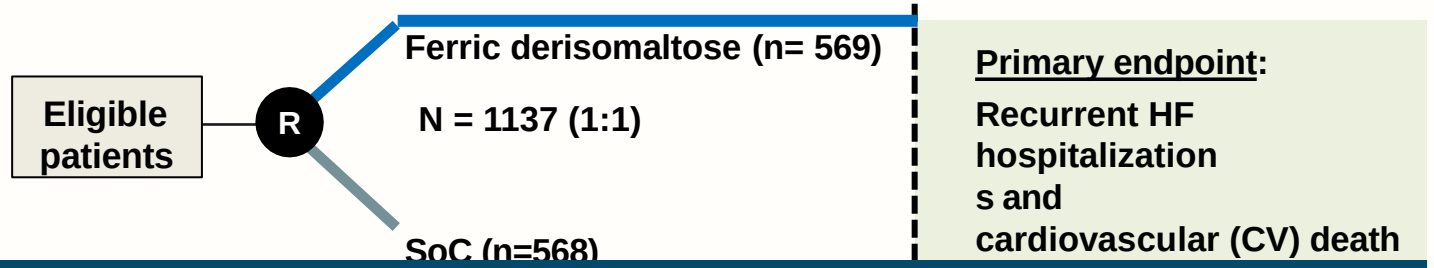
IRONMAN (IV Ferric Derisomaltose)

- **Eligibility**

Inclusion criteria
Age ≥ 18 years
LVEF ≤ 45% within the last 2 years
NYHA class II – IV
TSAT <20% or ferritin <100 ug/L
Increased risk of CV events, with either • Current or recent (<6 months) HF hosp. or • NT-proBNP (pg/mL) >250 if SR / >1,000 if AF
Able and willing to provide informed consent

Exclusion criteria
Hemoglobin <9.0 g/dL
Hgb >13 g/dL in women or >14g/dL in men
Ferritin > 400ug/L
eGFR < 15ml/min/1.73m^2
MI, stroke or cardiac procedure in prior 3 mnth
• Planned cardiac surgery or revascularization
• Cardiac transplant or LVAD (planned or received)
Active infection
Non-HF disease with life-expectancy <2 yrs
Contraindication to IV iron

- **Design**



Hb	BW<50 kg	BW 50 to <70 kg	BW≥70 kg
≥10 g/dL	20 mg/kg	1000 mg	20 mg/kg up to a maximum of 1500 mg
<10 g/dL	20 mg/kg	20 mg/kg	20 mg/kg up to a maximum of 2000 mg

KNOW ID in HF

Kalra PR, et al. *Lancet.* 2022 Dec 17;400(10369):2199-2209.

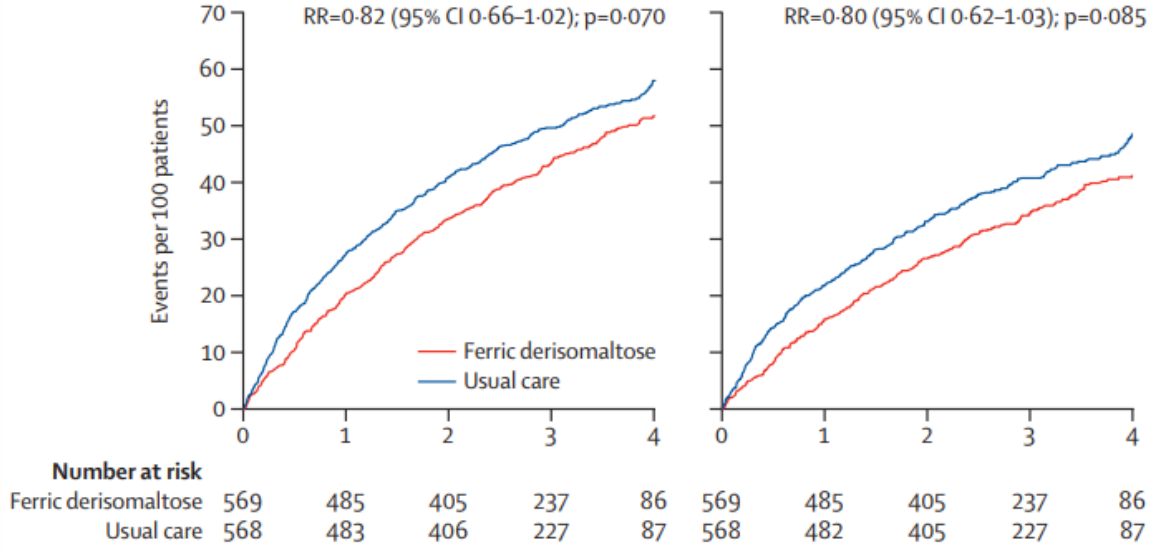
IRONMAN (IV Ferric Derisomaltose) Outcomes

Median age, 73 years [IQR 63-79]
Female, 300 (26%)
Recruited during hospital admission, 164 (14%)
Admission for HF in previous 6 months, 208 (18%)
Enrolled from OPD clinics and had elevated BNP biomarker, 765 (67%)

All but 2% were NYHA FC II-III

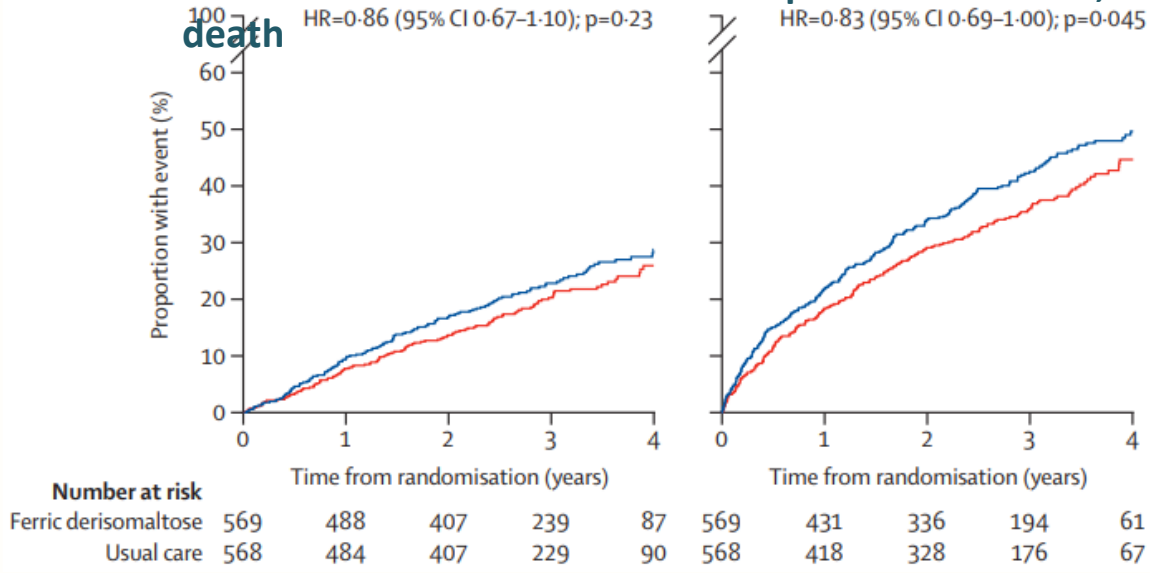
Principal cause of HF: ICM (57%)

All HF hosp. & CV Death



All HF Hospitalizations

CV Deaths



Hospitalization for HF, stroke, MI or CV death

Kalra PR, et al. *Lancet.* 2022 Dec 17;400(10369):2199-2209.

IRONMAN (IV Ferric Derisomaltose) Outcomes Censoring follow-up on Sept 30, 2020 (COVID-19)

	Ferric derisomaltose group (n=527)	Usual care group (n=536)	Estimated treatment effect (95% CI)	p value
Primary endpoint				
Cardiovascular death and hospital admission for heart failure, number of events (rate per 100 patient-years)	210 (22·3)	280 (29·3)	0·76 (0·58–1·00)*	0·047
Secondary endpoints				
Hospital admissions for heart failure, number of events (rate per 100 patient-years)	163 (17·3)	218 (22·8)	0·76 (0·56–1·03)*	0·077
Cardiovascular hospital admission, n (%)	177 (34%)	205 (38%)	0·86 (0·70–1·05)†	0·14
Cardiovascular death or hospital admission for heart failure, n (%)	127 (24%)	160 (30%)	0·80 (0·63–1·01)†	0·055
Cardiovascular death, n (%)	67 (13%)	86 (16%)	0·79 (0·57–1·09)†	0·15
Cardiovascular death or hospital admission for stroke, myocardial infarction, or heart failure, n (%)	137 (26%)	175 (33%)	0·78 (0·62–0·98)†	0·030
All-cause mortality, n (%)	103 (20%)	115 (21%)	0·91 (0·70–1·19)†	0·48
All-cause hospital admission, n (%)	260 (49%)	288 (54%)	89 (0·75–1·05)†	0·18
All-cause mortality or all-cause unplanned hospital admission, n (%)	271 (51%)	303 (57%)	0·89 (0·75 to 1·04)†	0·15

KNOW ID in HF

Kalra PR, et al. *Lancet.* 2022 Dec 17;400(10369):2199-2209.

Meta-Analysis Comparing FCM with FDI in HF w Iron Deficiency

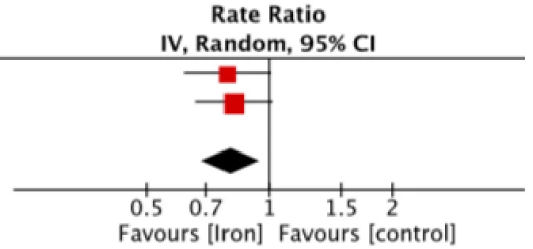
Ferric carboxymaltose (AFFIRM-AHF) and Ferric derisomaltose (IRONMAN)

Vukadinovic D, et al. *Clin Research in Cardiol.* 2023; Apr 19:1-13. Online ahead of print.

A **Composite of recurrent heart failure hospitalizations and cardiovascular death**

Study or Subgroup	log[Rate Ratio]	SE	Iron Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
AFFIRM-AHF	-0.2357	0.1253	558	550	44.1%	0.79 [0.62, 1.01]
IRONMAN	-0.1985	0.1114	569	568	55.9%	0.82 [0.66, 1.02]
Total (95% CI)			**1127**	**1118**	**100.0%**	**0.81 [0.69, 0.95]**

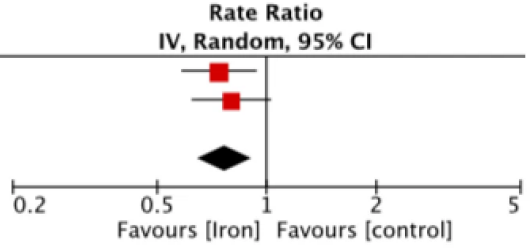
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.05$, df = 1 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 2.58 (P = 0.010)



B **Total heart failure hospitalizations**

Study or Subgroup	log[Rate Ratio]	SE	Iron Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
AFFIRM-AHF	-0.3011	0.1221	558	550	52.7%	0.74 [0.58, 0.94]
IRONMAN	-0.2231	0.1289	569	568	47.3%	0.80 [0.62, 1.03]
Total (95% CI)			**1127**	**1118**	**100.0%**	**0.77 [0.65, 0.91]**

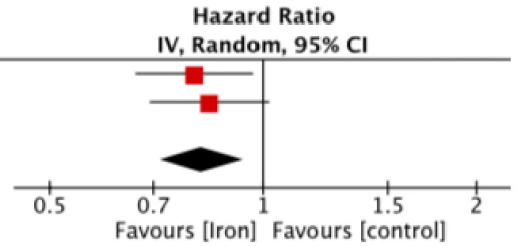
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.19$, df = 1 (P = 0.66); $I^2 = 0\%$
Test for overall effect: Z = 2.98 (P = 0.003)



C **Time to first heart failure hospitalizations or cardiovascular death**

Study or Subgroup	log[Hazard Ratio]	SE	Iron Total	Control Total	Weight	Hazard Ratio IV, Random, 95% CI
AFFIRM-AHF	-0.2231	0.0982	558	550	50.5%	0.80 [0.66, 0.97]
IRONMAN	-0.1744	0.0991	569	568	49.5%	0.84 [0.69, 1.02]
Total (95% CI)			**1127**	**1118**	**100.0%**	**0.82 [0.71, 0.94]**

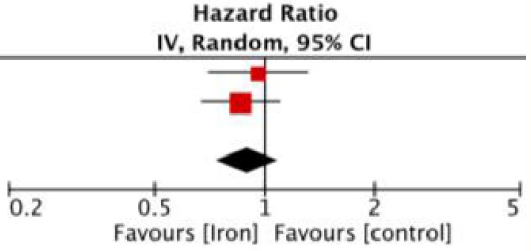
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.12$, df = 1 (P = 0.73); $I^2 = 0\%$
Test for overall effect: Z = 2.85 (P = 0.004)



D **Time to cardiovascular death**

Study or Subgroup	log[Hazard Ratio]	SE	Iron Total	Control Total	Weight	Hazard Ratio IV, Random, 95% CI
AFFIRM-AHF	-0.0408	0.1612	558	550	38.4%	0.96 [0.70, 1.32]
IRONMAN	-0.1508	0.1274	569	568	61.6%	0.86 [0.67, 1.10]
Total (95% CI)			**1127**	**1118**	**100.0%**	**0.90 [0.74, 1.09]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.29$, df = 1 (P = 0.59); $I^2 = 0\%$
Test for overall effect: Z = 1.09 (P = 0.28)



KNOW ID in HF

2022 AHA/ACC/HFSA HF Guidelines

Recommendations for management of patients with HF & anemia / iron deficiency

COR	LOE	AHA/ACC/HFSA Recommendations
2a	B-R	In patients with HFrEF and iron deficiency with or without anemia, intravenous iron replacement *is reasonable* to improve functional status and QoL.
3 Harm	B-R	In patients with HF and anemia, erythropoietin-stimulating agents *should not be used* to improve morbidity and mortality.

Heidenreich P, et al. *J Am Coll Cardiol.* 2022;79:e263-421.

ESC HF Management Recommendations	COR	LOE
All patients with HF be periodically screened for anemia and iron deficiency with a full blood count, serum ferritin concentration, and TSAT.	I	C
IV iron supplementation with FCM *should be considered* in symptomatic patients with LVEF <45% and iron deficiency, defined as serum ferritin <100 µg/L or serum ferritin 100–299 µg/L with TSAT <20%, to alleviate HF symptoms, improve exercise capacity, and QoL.	IIa	A
IV iron supplementation with FCM *should be considered* in symptomatic HF patients recently hospitalized for HF and with LVEF <50% and iron deficiency, defined as serum ferritin <100 µg/L or serum ferritin 100–299 µg/L with TSAT <20%, to reduce the risk of HF hospitalization.	IIa	B

McDonagh TA, et al. *Eur Heart J.* 2021;42:3599-3726.

ID Theme	2022 AHA/ACC/HFSA Guidelines	2021 ESC Guidelines
Target population	HFrEF with ID (with or without anemia)	Symptomatic HFrEF / recent HF hospitalization
Goal	To improve functional status and QoL	To alleviate HF symptoms, improve exercise capacity, enhance QoL, and reduce the risk of HF hospitalization

KNOW ID in HF

2023 ESC HF Guideline Focused Update

Recommendations	Class[a]	Level[b]
Intravenous iron supplementation is recommended in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to alleviate HF symptoms and improve quality of life.[c]	I	A
Intravenous iron supplementation with ferric carboxymaltose or ferric derisomaltose should be considered in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to reduce the risk of HF hospitalization.[c]	IIa	A

HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction.

[a]Class of recommendation.

[b]Level of evidence.

[c]Most of the evidence refers to patients with left ventricular ejection fraction ≤45%.

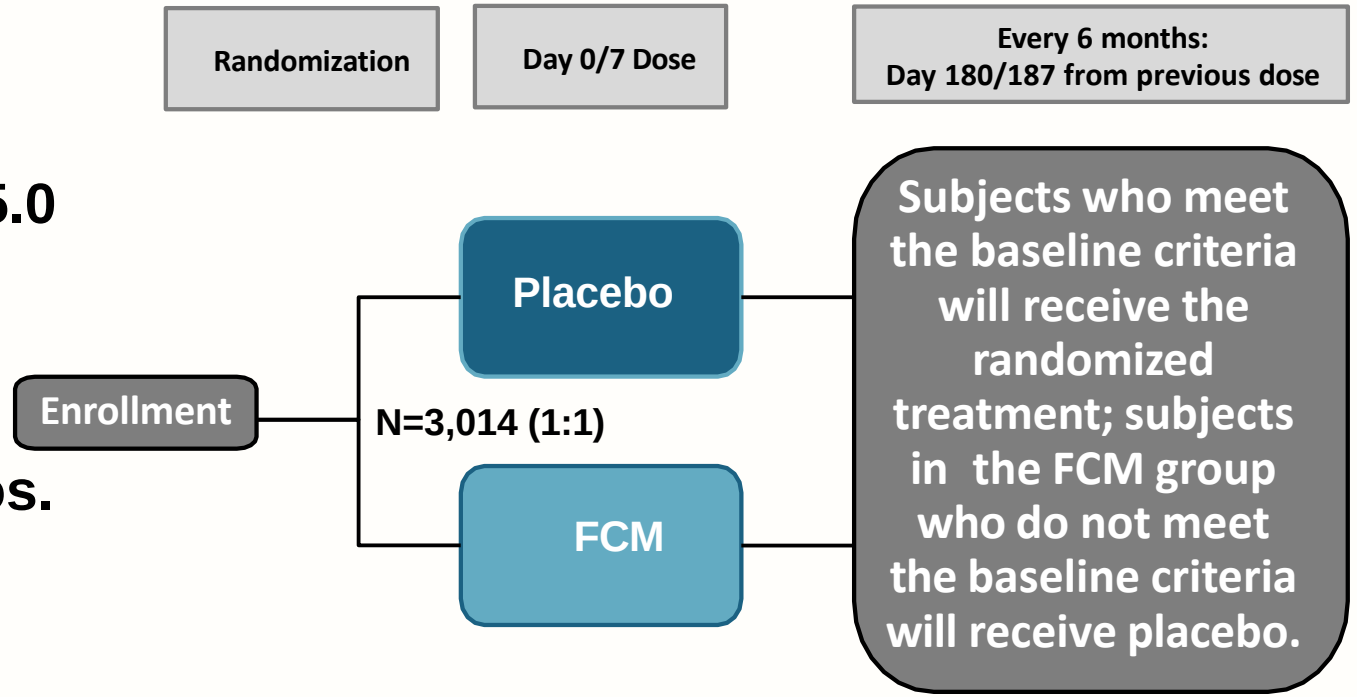
KNOW ID in HF

McDonagh TA. European Heart Journal 2023, 44(37): 3627-3639

HEART-FID Trial

To Assess IV Iron on Clinical Outcomes in HF

- Stable HFrEF
- NYHA II–IV on max-tolerated med Tx
- Hgb >9.0 g/dL and <13.5 g/dL (F) or <15.0 g/dL (M)
- Serum ferritin: <100 µg/L
  or 100–300 µg/L + TSAT <20%
- Documented hosp. for HF within 12 mos.
  or elevated NPs at screening
- Primary endpoints
  - Death
  - # hospitalizations for HF at 1 year
  - Change in 6MWT at 6 months



- FCM administered as 2 doses IV of 15 mg/kg to a maximum individual dose of 750 mg 7 days apart and a maximum combined dose of 1,500 mg
- Repeated every 6 months if ferritin <100 ng/mL or 100–300 ng/mL + TSAT <20%) and hemoglobin <13.5/15.0 g/dL

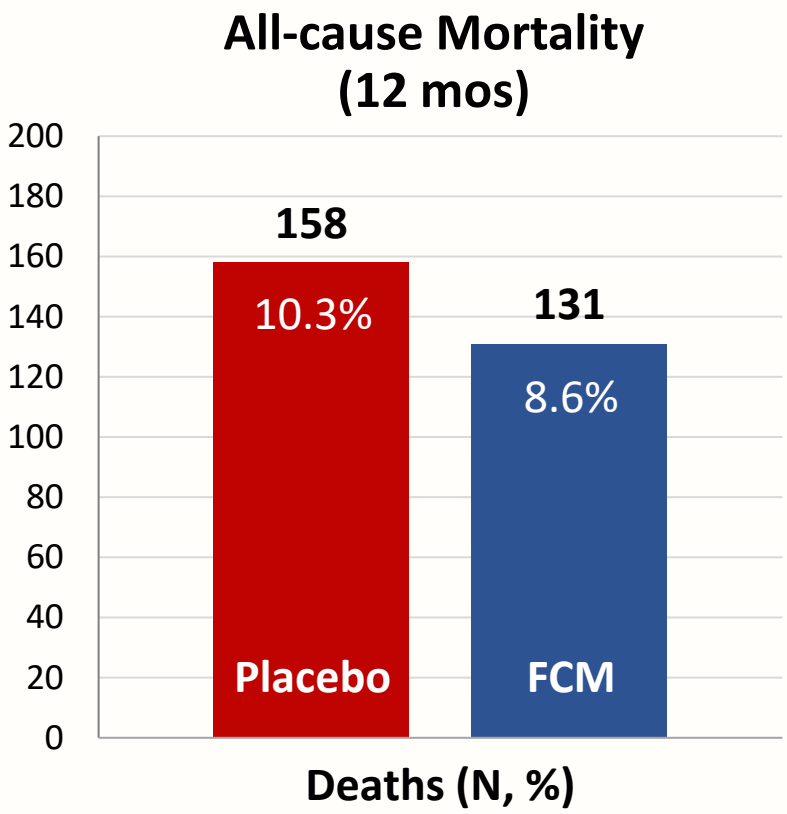
KNOW ID in HF

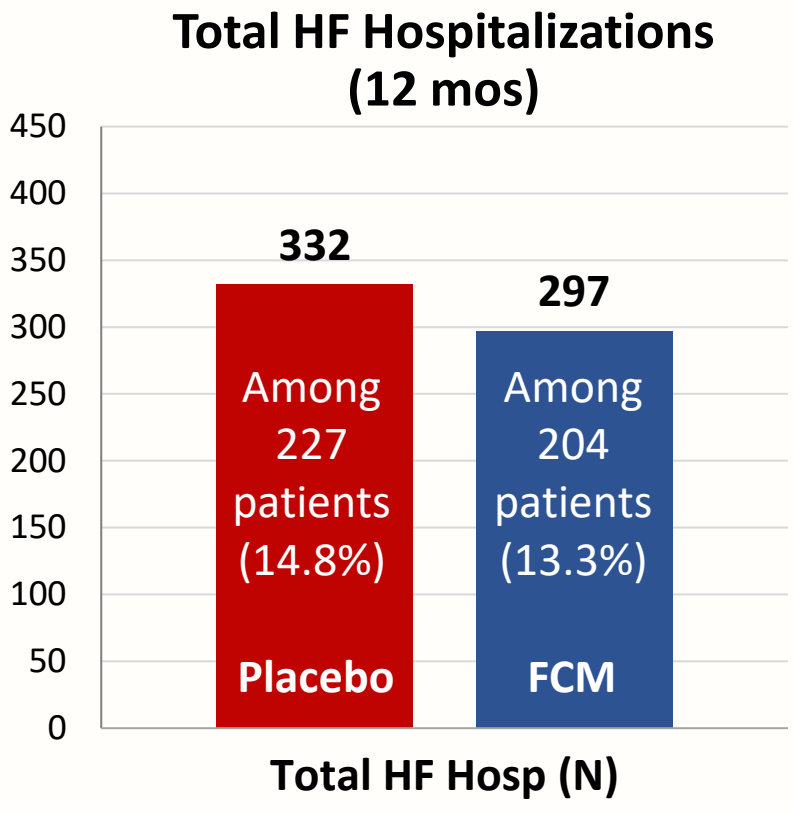
Mentz R, et al. *Circ Heart Fail.* 2021;14(5):008100.

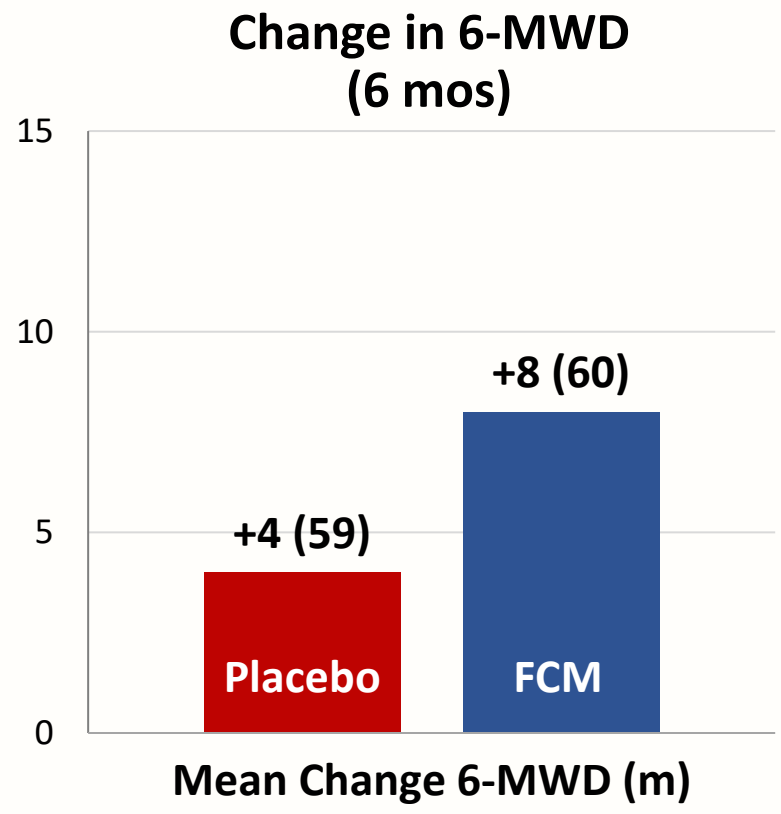
Primary Hierarchical Endpoint

P-value = 0.019 (target <0.01)

Win Ratio (99%CI) = 1.10 (0.99, 1.23)







1.7% ARR (20% more wins)

270 fewer HF hospitalization days

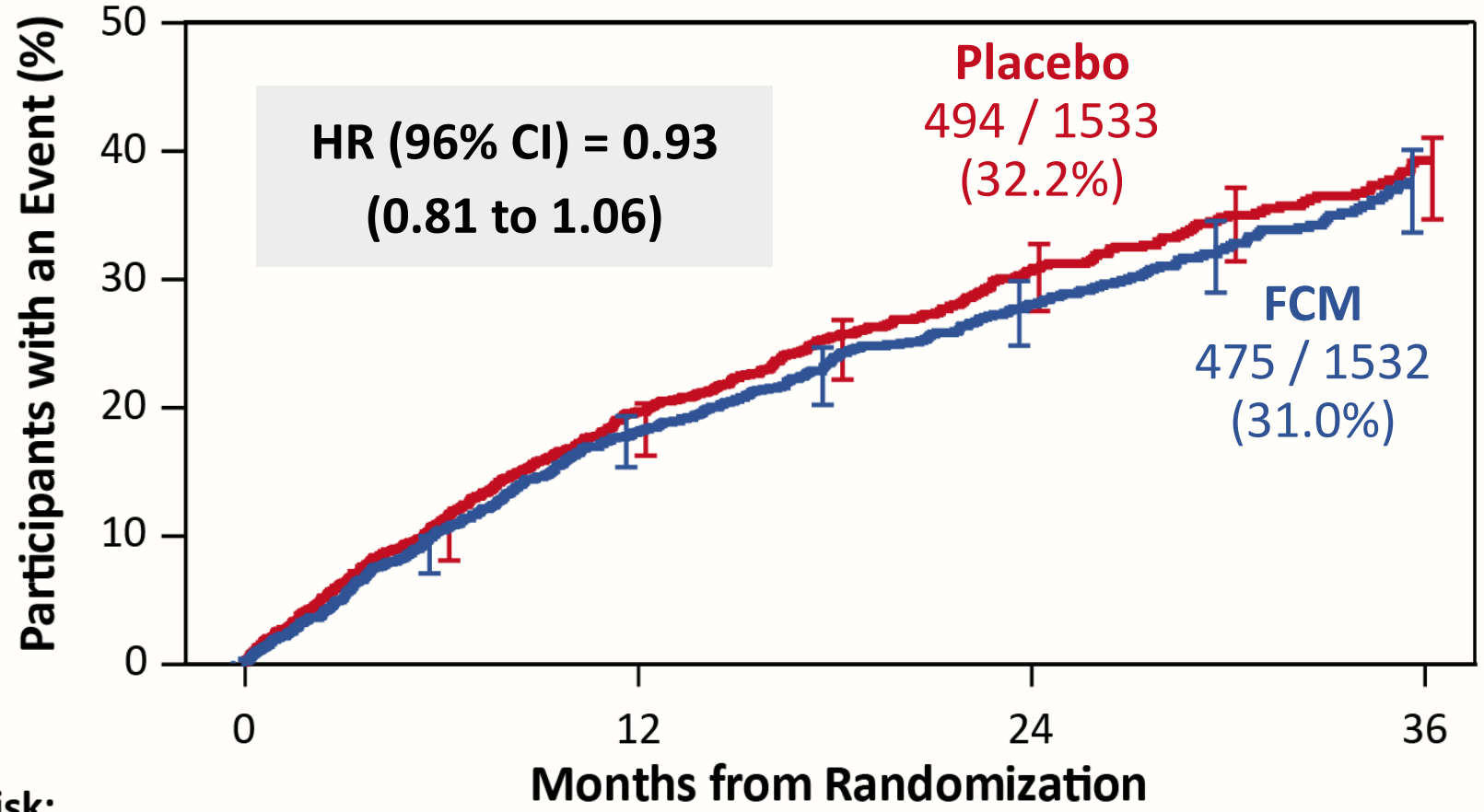
+4 meter benefit (11% more wins)

Mentz RJ, *et al. NEJM* 2023

KNOW ID in HF

Top Secondary Endpoint

Time to Cardiovascular Death or First HF Hospitalization



17.3 (PBO) vs. 16.0 (FCM) events per 100 patient years

Number at Risk:

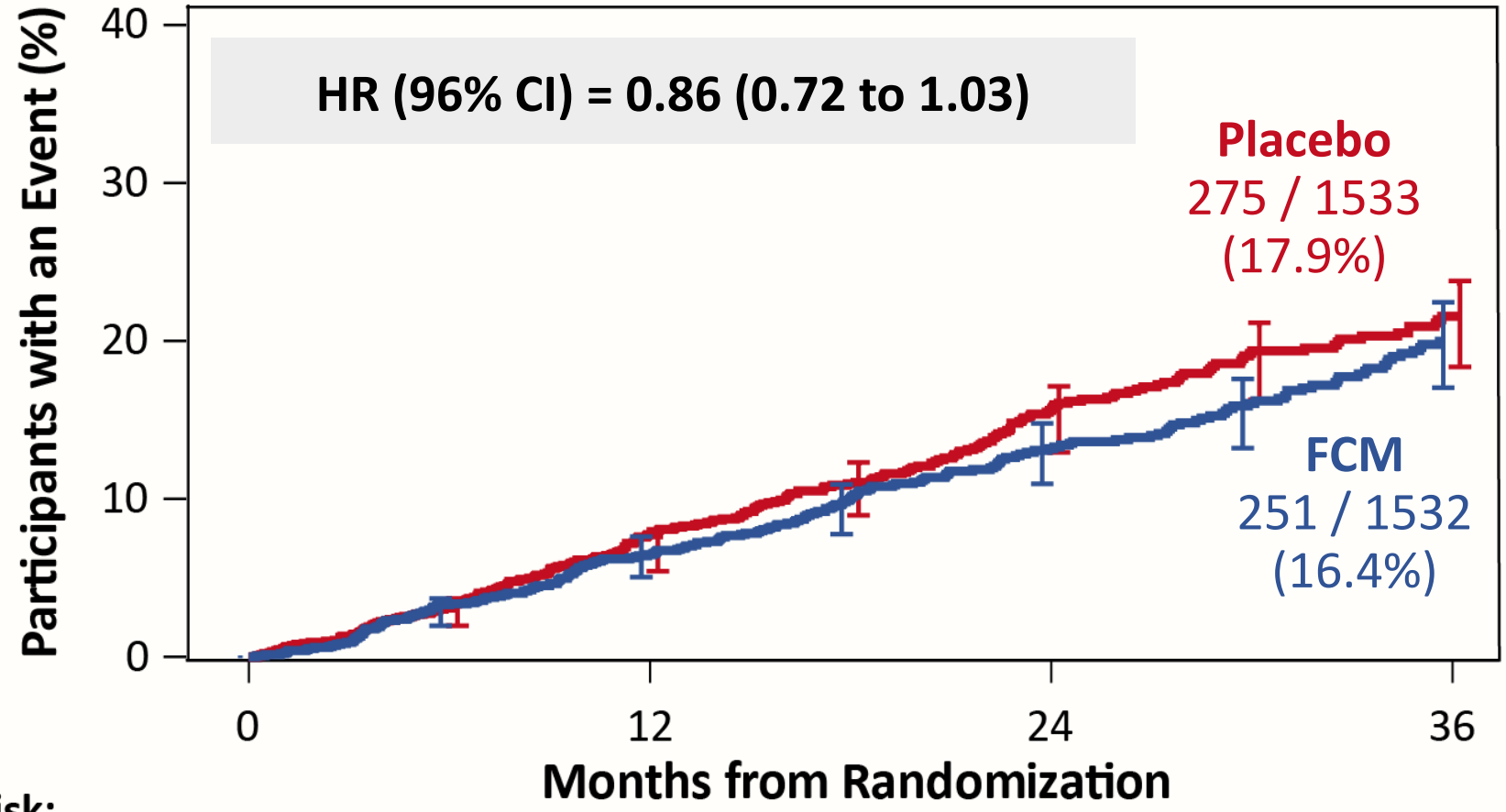
FCM	1532	1390	1219	913	642	429	314
Placebo	1533	1369	1189	872	610	410	291

Median Follow-up of **1.9 years** (IQR, 1.3 to 3.0)

Mentz RJ, *et al. NEJM* 2023

KNOW ID in HF

Time to CV Death



8.2 (PBO) vs. 7.2 (FCM) events per 100 patient years

Number at Risk:

FCM	1532	1474	1380	1076	792	558	423
Placebo	1533	1470	1352	1037	747	516	387

Median Follow-up of **1.9 years** (IQR, 1.3 to 3.0)

Mentz RJ, *et al. NEJM* 2023

Pre-specified Responder Analysis
Change in 6-minute walk distance

	FCM	Placebo	Odds Ratio (95% CI) vs. Placebo
Change from Baseline at 6 Months			
Improved ≥ 10 m	41%	36%	**1.24 (1.08, 1.44)**
Improved ≥ 20 m	31%	26%	**1.27 (1.09, 1.49)**
Change from Baseline at 12 Months			
Improved ≥ 10 m	38%	31%	**1.32 (1.13, 1.53)**
Improved ≥ 20 m	30%	26%	**1.24 (1.06, 1.45)**

≥24% increase in the Odds of Response with FCM

KNOW ID in HF

Mentz RJ, *et al. NEJM* 2023

Efficacy of Ferric carboxymaltose in heart failure with iron deficiency

An individual participant data meta-analysis

Ponikowski P, Mentz RJ, Hernandez AF, Butler J, Khan MS, van Veldhuisen DJ, Roubert B, Blackman N, Friede T, Jankowska EA, Anker SD.

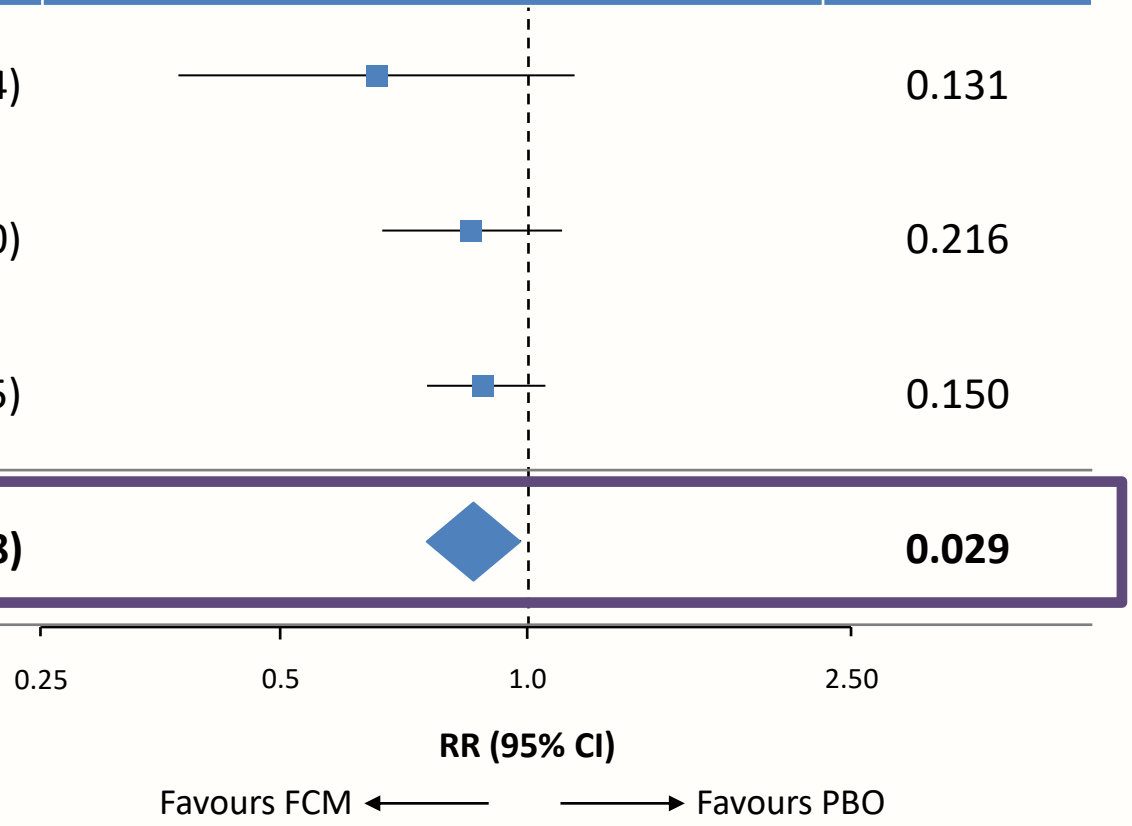
Ponikowski P, Mentz RJ, *et al. Eur Heart J* 2023

KNOW ID in HF

• Co-Primary Endpoint: Total CV Hospitalisations + CV Death

Study	FCM n/N (%)	PBO n/N (%)	Rate ratio (95% CI)	*P*-value
CONFIRM-HF	28/150 (18.7)	38/151 (25.2)	0.65 (0.37–1.14)	0.131
AFFIRM-AHF	218/558 (39.1)	252/550 (45.8)	0.85 (0.66–1.10)	0.216
HEART-FID	371/1529 (24.3)	391/1532 (25.5)	0.88 (0.75–1.05)	0.150
Overall	**617/2237 (27.6)**	**681/2233 (30.5)**	**0.86 (0.75–0.98)**	**0.029**

Cochran *Q*: 0.008; *P*=0.996.



Rate ratios and *P*-values are estimated using a negative binomial model on the number of events, including treatment, region, haemoglobin level at baseline (fixed covariates), and (random covariate) study.
CV=cardiovascular; FCM=ferric carboxymaltose; PBO=placebo; RR=rate ratio.

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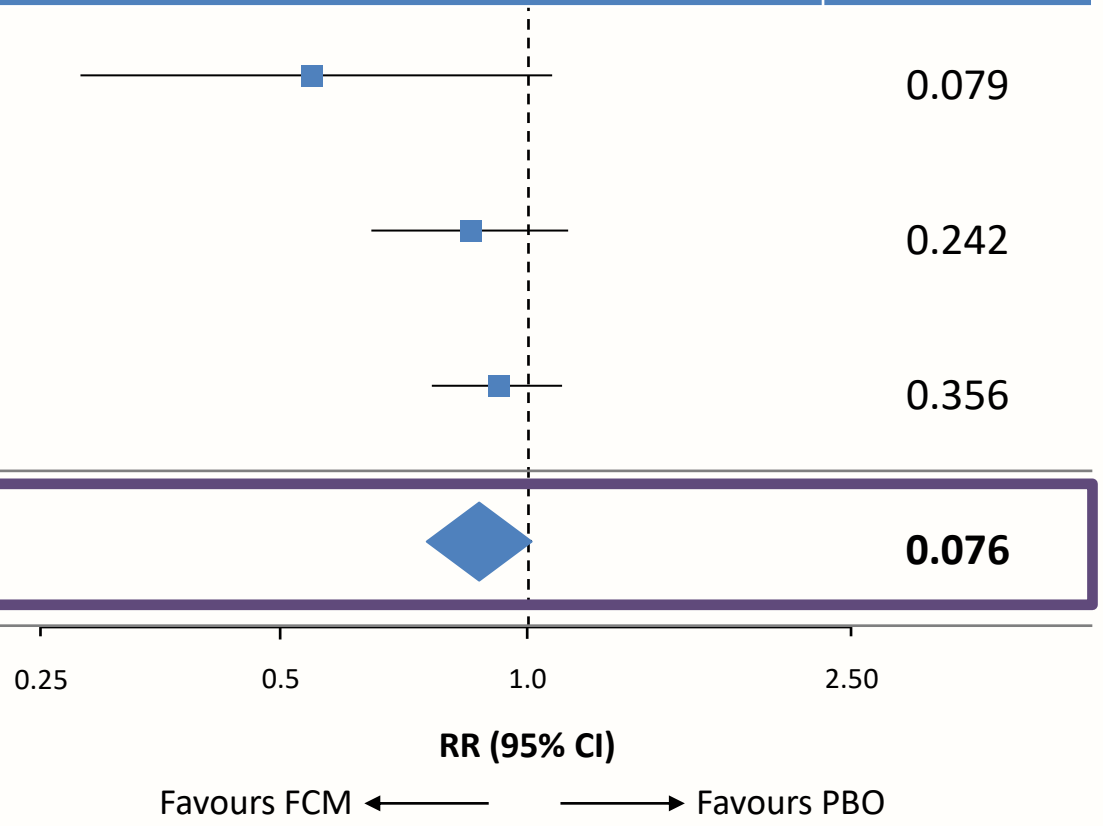
• Co-Primary Endpoint: Total HF Hospitalisations + CV Death

Study	FCM n/N (%)	PBO n/N (%)	Rate ratio (95% CI)	*P*-value
CONFIRM-HF	18/150 (12.0)	31/151 (20.5)	0.54 (0.28–1.07)	0.079
AFFIRM-AHF	189/558 (33.9)	216/550 (39.3)	0.85 (0.64–1.12)	0.242
HEART-FID	296/1529 (19.4)	316/1532 (20.6)	0.92 (0.76–1.10)	0.356
Overall	**503/2237 (22.5)**	**563/2233 (25.2)**	**0.87 (0.75–1.01)**	**0.076**

Cochran *Q*: 0.008; *P*=0.996.



Rate ratios and *P*-values are estimated using a negative binomial model on the number of events, including treatment, region, haemoglobin level at baseline (fixed covariates), and (random covariate) study.
CV=cardiovascular; FCM=ferric carboxymaltose; HF=heart failure; PBO=placebo; RR=rate ratio.

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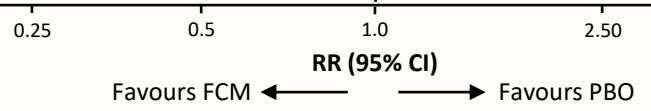
Ponikowski P, Mentz RJ, *et al. Eur Heart J* 2023

• Subgroup Analyses: Total CV Hospitalisations + CV Death

		FCM n/N (%)	PBO n/N (%)	RR (95% CI)	*P*-value	*P*-int
Age, years	<66	209/766 (27.3)	229/784 (29.2)	0.83 (0.66–1.05)	0.114	
	≥66 and <75	187/737 (25.4)	219/706 (31.0)	0.77 (0.61–0.99)	0.038	0.355
	≥75	221/734 (30.1)	233/743 (31.4)	0.99 (0.78–1.25)	0.901	
HF aetiology	Non-ischaemic	222/819 (27.1)	241/868 (27.8)	0.96 (0.77–1.20)	0.745	0.209
	Ischaemic	373/1325 (28.2)	418/1282 (32.6)	0.81 (0.68–0.96)	0.015	
TSAT, %	<20	380/1140 (33.3)	456/1183 (38.5)	0.80 (0.67–0.95)	0.012	0.100
	≥20	232/1079 (21.5)	215/1032 (20.8)	1.00 (0.81–1.23)	0.989	
TSAT, %	<15	222/678 (32.7)	292/697 (41.9)	0.72 (0.57–0.91)	0.006	0.019
	≥15 and <24	216/739 (29.2)	244/790 (30.9)	0.87 (0.69–1.09)	0.223	
	≥24	173/802 (21.6)	135/728 (18.5)	1.17 (0.91–1.50)	0.213	
eGFR, mL/min/1.73 m²	<47.5	251/723 (34.7)	261/677 (38.6)	0.81 (0.65–1.02)	0.071	0.525
	≥47.5 and <68.3	184/700 (26.3)	187/699 (26.8)	0.94 (0.74–1.20)	0.619	
	≥68.3	129/682 (18.9)	165/720 (22.9)	0.77 (0.60–1.00)	0.053	
Haemoglobin, g/dL	<11.9	217/729 (29.8)	271/750 (36.1)	0.73 (0.58–0.92)	0.007	0.099
	≥11.9 and <13.2	195/690 (28.3)	221/752 (29.4)	0.83 (0.65–1.05)	0.122	
	≥13.2	201/803 (25.0)	185/720 (25.7)	1.04 (0.82–1.32)	0.729	
NYHA functional class	≤ class II	286/1146 (25.0)	319/1160 (27.5)	0.83 (0.68–1.00)	0.052	0.919
	≥ class III	331/1090 (30.4)	362/1070 (33.8)	0.84 (0.69–1.02)	0.073	
Ferritin, ng/mL	<100	513/1906 (26.9)	546/1866 (29.3)	0.84 (0.73–0.98)	0.025	0.501
	≥100	100/318 (31.4)	132/361 (36.6)	0.96 (0.68–1.35)	0.807	
Sex	Male	421/1420 (29.6)	481/1379 (34.9)	0.85 (0.72–1.01)	0.061	0.818
	Female	196/817 (24.0)	200/854 (23.4)	0.88 (0.70–1.11)	0.293	
Hospitalisation for HF in the prior year	Yes	290/929 (31.2)	329/902 (36.5)	0.83 (0.68–1.01)	0.064	0.759
	No	256/1005 (25.5)	275/1015 (27.1)	0.87 (0.71–1.06)	0.171	
Overall		**617/2237 (27.6)**	**681/2233 (30.5)**	**0.86 (0.75–0.98)**	**0.029**	



Rate ratio and *P*-value estimated using a negative binomial model on the number of events, including (fixed covariates) treatment, region, baseline haemoglobin level (where applicable), interaction between subgroup and treatment, and (random covariate) study.
CV=cardiovascular; eGFR=estimated glomerular filtration rate; FCM=ferric carboxymaltose; HF=heart failure; NYHA=New York Heart Association; PBO=placebo; RR=rate ratio; TSAT=transferrin saturation.

KNOW ID in HF

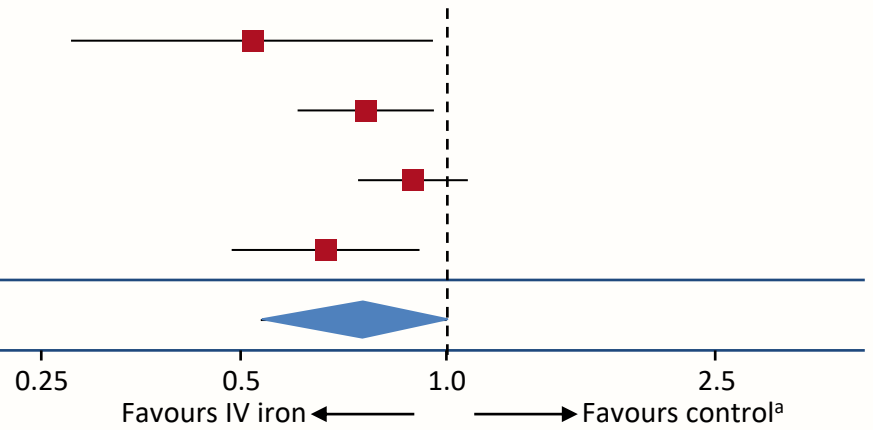
Ponikowski P, Mentz RJ, *et al. Eur Heart J* 2023

• Sensitivity Analysis (3 FCM Studies + IRONMAN) Total HF Hospitalisations + CV Death

Censored at 52 weeks

Study	Rate ratio (95% CI)
CONFIRM-HF	0.51 (0.28–0.95)
AFFIRM-AHF	0.76 (0.60–0.96)
HEART-FID	0.89 (0.74–1.07)
IRONMAN	0.66 (0.48–0.91)
Overall	**0.76 (0.53–1.00)**

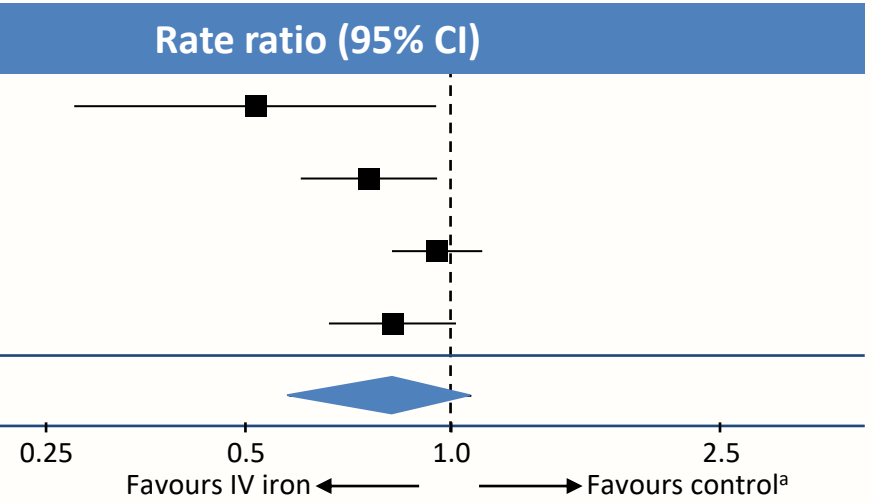
Tau=0.16 (95% CI: 0.00–0.53)



All data
1 year
1 year
1.9 years (median)
2.7 years (median)

Study	Rate ratio (95% CI)
CONFIRM-HF	0.51 (0.28–0.95)
AFFIRM-AHF	0.76 (0.60–0.96)
HEART-FID	0.96 (0.82–1.11)
IRONMAN	0.82 (0.66–1.02)
Overall	**0.82 (0.58–1.07)**

Tau=0.16 (95% CI: 0.00–0.53)



[a]Placebo or standard of care. Standardised trial level analyses were performed using the semiparametric LWYY model, including treatment and region as factors. Analysis used Bayesian random-effects meta-analysis.
CI=credible interval; CV=cardiovascular; FCM=ferric carboxymaltose; HF=heart failure; IV=intravenous.

KNOW ID in HF

Ponikowski P, Mentz RJ, *et al. Eur Heart J* 2023

FDA-Approval for FCM in Heart Failure

Additional indication (06/2023)	To treat iron deficiency in adult patients with heart failure and New York Heart Association class II/III to improve exercise capacity
Dosage and administration	For patients weighing 50 kg or more, the recommended dosage is 750 mg intravenously in two doses separated by at least 7 days for a total cumulative dose of 1,500 mg of iron per course. For adult patients weighing 50 kg or more, an alternative dose of 15 mg/kg body weight up to a maximum of 1,000 mg intravenously may be administered as a single-dose per course For patients weighing less than 50 kg, the recommended dosage is 15 mg/kg body weight intravenously in two doses separated by at least 7 days per course
Contraindications	Hypersensitivity to FCM or any of its inactive components
Warning and precautions	Hypersensitivity, symptomatic hypophosphatemia, and hypertension
Adverse reactions	The most common adverse reactions in adult patients (>2%) are nausea, hypertension, flushing, injection site reactions, erythema, hypophosphatemia, and dizziness

Recommended dosage in patients with ID with HF	Weight > 70 kg			Weight ≥ 70 kg		
	Hb (g/dL)			Hb (g/dL)		
	< 10	10 to 14	>14 to <15	< 10	10 to 14	>14 to <15
Day 1	1,000 mg	1,000 mg	500 mg	1,000 mg	1,000 mg	500 mg
Week 6	500 mg	No dose	No dose	1,000 mg	500 mg	No dose

KNOW ID in HF

FCM product label, accessed November 6, 2023

Overall Conclusion & Clinical Application

- **In HEART-FID, FCM appeared safe and resulted in modest improvement for the hierarchical endpoint of all-cause mortality, HF hospitalizations and 6-MWD.**
- **A simultaneous publication at ESC combining HEART-FID with CONFIRM-HF and AFFIRM-AHF demonstrated the following with FCM among 4,501 patients (52 weeks):**
  - **Reduced the composite of CV death or total CV hosp – 14% Reduction**
  - **Trend toward reduction of CV death or total HF hosp – 13% Reduction (non-signif)**

Messages:

- **Totality of evidence supports safety and clinical benefits with IV FCM in HFrEF + ID.**
- **In this exciting time of quadtherapy for HFrEF – IV FCM is an effective therapy that is not another daily pill but rather a straightforward injection in the clinic or hospital – *"one and done"* injection to benefit many patients.**
- **FCM is another "*tool in our toolkit*" to help patients with HFrEF + Iron Deficiency.**

Mentz RJ, *et al. N Engl J Med.* 2023
Ponikowski P, Mentz RJ, *et al. Eur Heart J* 2023

KNOW ID in HF

FAIR-HF2

- **Design:** multicenter, Phase 4, RCT (1:1), double-blind, N = 1,200 (1,000-1,800)
- **Main inclusion criteria**
  - HF with LVEF ≤45% and NYHA class II/III
  - HF hospitalization within 6 months or BNP/NT-proBNP >100/>300 pg/mL or MRproANP >120 mmol/L
  - Iron deficiency: serum ferritin <100 µg/L or ferritin 100–299 µg/L with TSAT <20%
  - Hgb: 9.5 - 14.0 g/dL
- **Treatment group**
  - FCM 1,000 mg (up to 2 doses in 4 weeks); then 500 mg q 4 months (x 12 mo) if hemoglobin < 16 g/dL or ferritin < 800 µg/L
- **Primary endpoint**
  - Rate of recurrent hospitalizations for HF or CV death during follow-up
- **Secondary endpoints**
  - CV/HF hospitalization, CV death (recurrent events, time-to-first event)
  - Change in NYHA functional class, EQ-5D, and PGA

Estimated Study Completion Date: 2024-2025

KNOW ID in HF

ClinicalTrials.gov, NCT03036462

FAIR-HFpEF

- **Design:** multicenter, Phase 2 RCT (1:1), double-blind, N = 200
- **Main inclusion criteria**
  - NYHA class II/III, LVEF ≥45%
  - In sinus rhythm, BNP/NT-proBNP >100/>300 pg/mL or MR-proANP >120 mmol/L (if in AF, 2x values listed)
  - 6MWT <450 m
  - Evidence of diastolic dysfunction
  - Iron deficiency: serum ferritin <100 µg/L or TSAT <20%; Hgb: 9.0–14.5 g/dL
- **Primary endpoint**
  - Change in 6MWT *at week 24*
- **Secondary endpoints**
  - Change in biomarkers for iron deficiency, renal function, cardiac function, NYHA functional class, PGA, and QoL
  - Overall safety over the treatment period

KNOW ID in HF

ClinicalTrials.gov, NCT03074591

Challenging Cases & Panel Discussion: Diagnosis & Treatment of ID in HF

KNOW ID in HF

Case #1

- Mr MFG is a 73 y.o. man with hx of CAD/MI and CABG
- Managed with EF 35% on Lisinopril 5 mg daily and 6.25 carvedilol bid Since 2019

4-28-21

1. Moderate to severe LV systolic dysfunction with EF estimated at 25-30%
2. Inferior/posterior LV segment akinesis; All other LV segments are moderately hypokinetic
3. Moderate LA dilatation; Moderate MR

HGB 13.7 4/17/19
13.1 7/21/19
13.5 9/25/19

Admitted for ADHF 6/23/22

		06/24/22	04/06/23	04/25/23	06/06/23	07/25/23	09/22/23
Iron	50 - 180 mcg/dL	28 (L)	21 (L)	71	69	37 (L)	94
Iron Binding Cap	250 - 425 mcg/dL (calc)	468 (H)	446 (H)	376	437 (H)	411	343
Iron Saturation	20 - 55 %	6 (L)	5 (L)				
% Saturation - Q	20 - 48 % (calc)	19 (L)	16 (L)	9 (L)	27		
Ferritin	24 - 380 ng/mL	40	14 (L)	77	32	14 (L)	283

6/24/22

1. Severe LV systolic dysfunction with estimated ejection fraction 20-25% with predominantly global LV wall hypokinesis. There is discrete inferolateral akinesis from prior infarction.
2. Abnormal mitral inflow pattern due to presence atrial fibrillation 3. Severe left atrial and moderate right atrial
6. Severe tricuspid regurgitation

KNOW ID in HF

Case 1 – Question 1

Disease	Iron	TIBC/Transferrin	UIBC	%Transferrin Saturation	Ferritin
Iron Deficiency	Low	High	High	Low	Low
Hemochromatosis	High	Low	Low	High	High
Chronic Illness	Low	Low	Low/Normal	Low	Normal/High
Hemolytic Anemia	High	Normal/Low	Low/Normal	High	High
Sideroblastic Anemia	Normal/High	Normal/Low	Low/Normal	High	High
Iron Poisoning	High	Normal	Low	High	Normal

Which combination of lab findings lead to a diagnosis of iron deficiency?

A. Low iron, High transferrin saturation and high ferritin
B. Low iron, low transferrin saturation and high ferritin
C. Low iron, high TIBC, low transferrin saturation and low ferritin
D. High iron, high TIBC, low transferring saturation and high ferritin.

KNOW ID in HF

Case 1 – Question 2

The patient presented had near normal hemoglobin for several years. Which is a TRUE statement?

A. The minimally low abnormal Hgb was part of a chronic disease diagnosis with heart failure
B. A normal or near normal Hgb does not rule out iron deficiency
C. The prevalence of iron deficiency in patients with heart failure is low
D. It is difficult to measure iron deficiency

Case #2

- 65 yo AA woman with HFimpEF EF 40% previously 25%
- On ARNI 97-103, SGLT2i, Bisoprolol 10 mg qd, spironolactone 25 mg qd
- Continues to feel fatigued especially in the afternoons. Denies true dyspnea
- Labs show Cr 1.8 (stable); K 4.8 (stable)
- CBC Hgb of 10 noted in charts up to 4 years previously. On FeSO4 daily for 4 years. Diagnosis is anemia of chronic disease.
- On careful GYN history, she reports menorrhagia for several years during the menopausal period. On no HRT.

Case 2 – Question

For women patients with heart failure and persistent fatigue which of the following is/are recommended:

A. A detailed history of reproductive health including menopause followed by iron studies
B. Informing the patient that anemia of chronic disease is common in patients with HF
C. Continuing oral iron with assurance that the Hgb will improve.
D. Informing the patient that Hgb drops with age and more commonly, in women
E. A and C are correct

Labs

• **Iron**	50 - 180 mcg/dL	28 (L)
• **Iron Binding Cap**	250 - 425 mcg/dL (calc)	401 (H)
• **Iron Saturation**	20 - 55 %	6 (L)
• **% Saturation - Q**	20 - 48 % (calc)	9 (L)
• **Ferritin**	24 - 380 ng/mL	24

What would you do next?

A. Start oral iron
B. Start intravenous iron
C. Start an erythropoietic stimulating agent (ESA)
D. Unsure/other

- Ferric carboxymaltose infusion x 3 with an increase in iron to 80.
- Pt feeling better. No ADHF for 1 year.

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