Iron Deficiency in Heart Failure:

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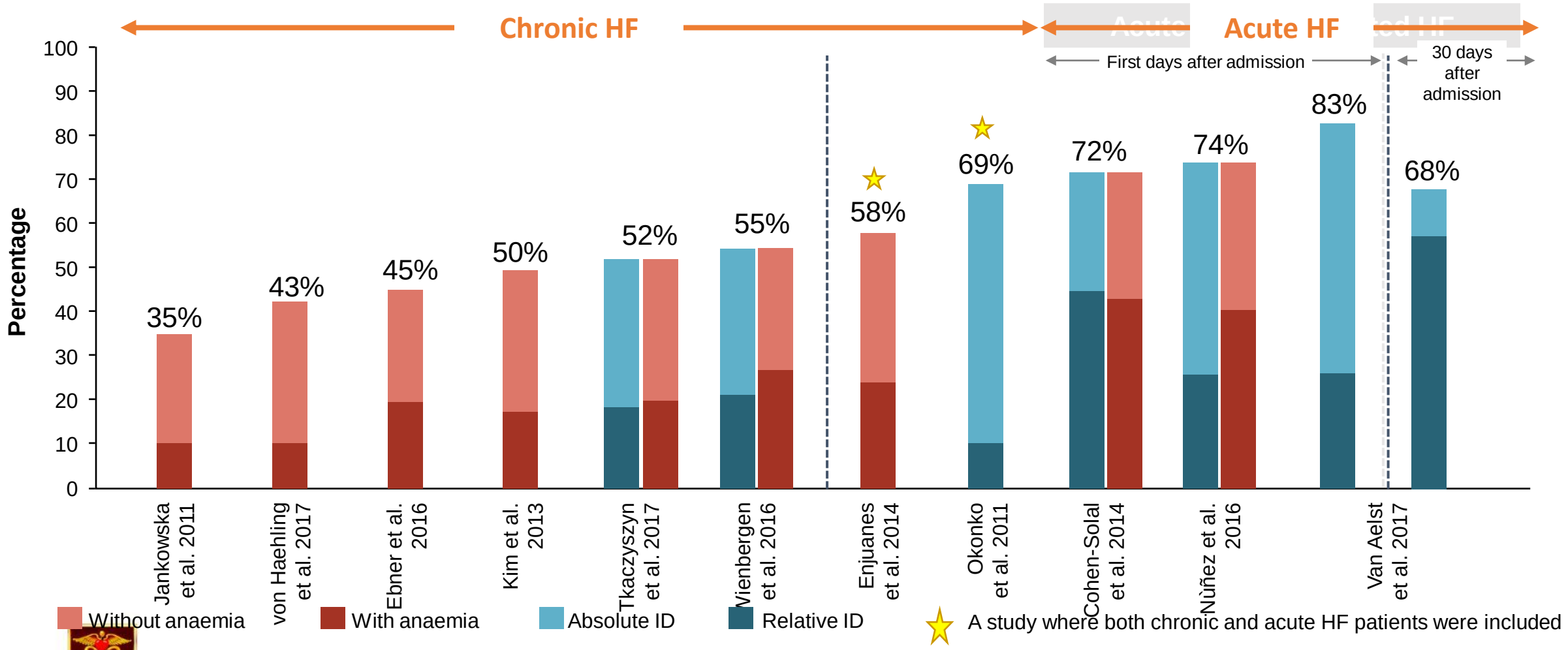
FHKAM, FHKCP, FACC, FECS

HKCC ASC 2023

Background

- HF outcome remains unsatisfactory
- HF-associated comorbidities,
  - adversely affect natural history
  - impact the management
- Iron deficiency (ID) has been recognized as a prevalent comorbidity in HF (independent of anaemia)
  - related to impaired exercise intolerance and poor quality of life
  - independently predicting poor outcome in chronic and acute settings
  - treating ID can improve the clinical outcome

ID is common in HF, especially in acute HF



Adapted from: Rocha BML, et al. J Am Coll Cardiol 2018;71:782–93

Causes of iron deficiency in HF

GI blood loss
- Anti-platelets
- Anti-coagulants
- NSAIDs
- Mucosal integrity

Malabsorption
- GI edema
- PPI
- Phospate binders

Malnutrition
- Loss of appetite
  <50% intake

Absolute Iron deficiency

Reduced iron stores:

Measured by Ferritin

Reduced iron mobilization:

Measured by TSAT

Inflammation / Pro-inflammatory activation
- Cytokines, IL-6, IL-1, TNF-α
- Hepcidin-mediated malabsorption and RES pooling

Functional Iron deficiency

Adapted from Jankowska EA et al. *Eur Heart J*.2013. 34:816-29

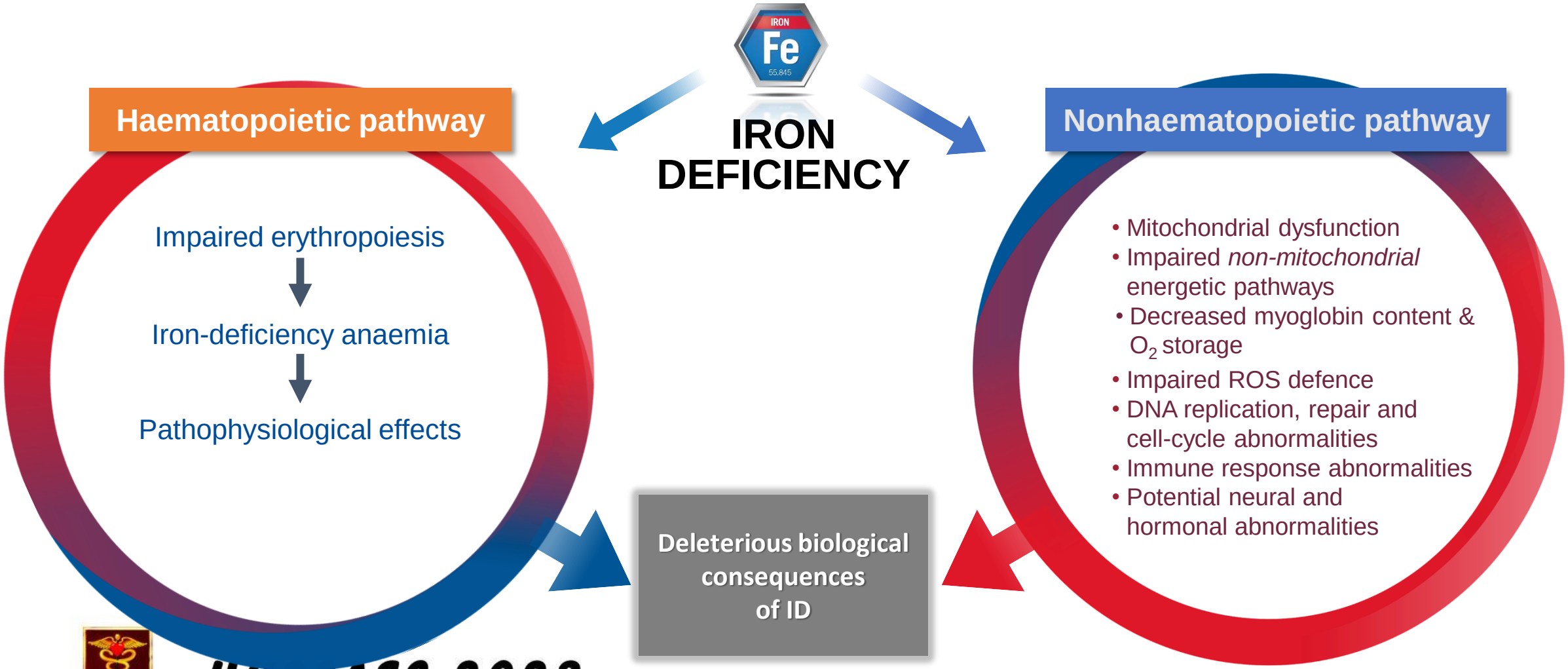
Iron deficiency in HF

ID exposes HF patients to various risks

- In the setting of HF, ID – independent of anaemia – is associated with:

Marchi G, et al. Intern Emerg Med 2021;16:167–70

Pathophysiological consequences of ID are multifactorial



Ponikowski P, et al. Eur J Heart Fail 2019;21:1651–8

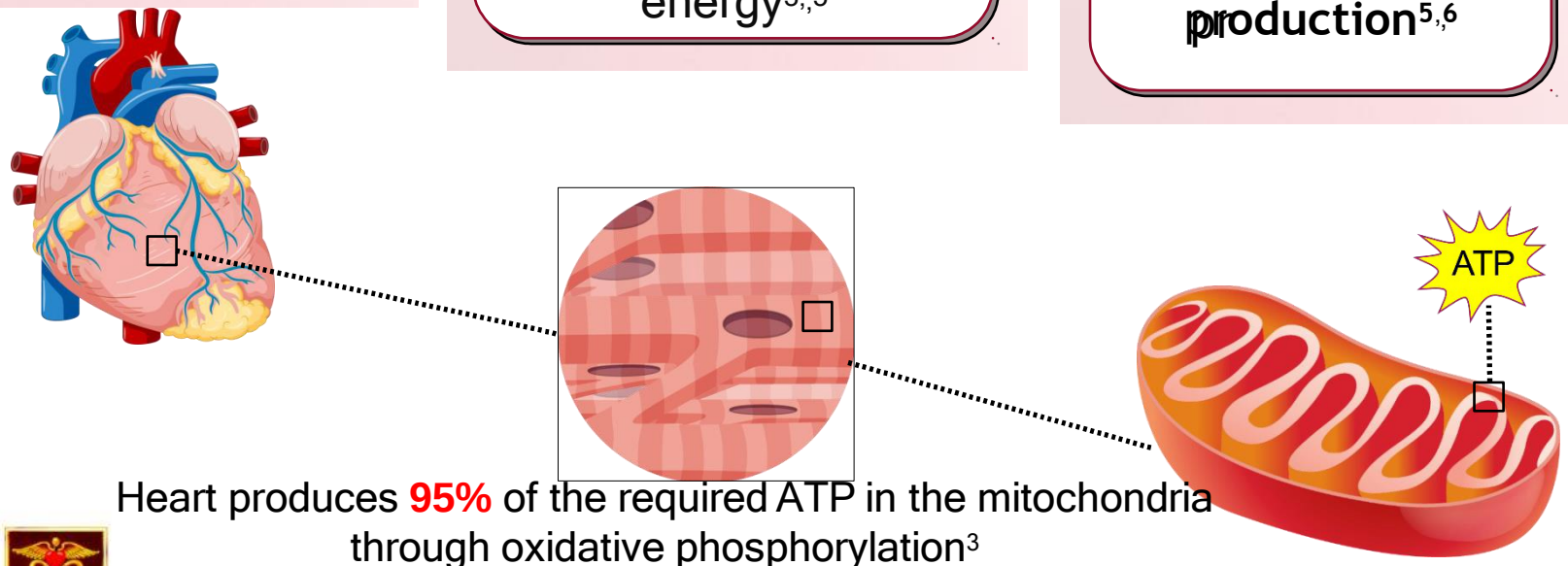
Iron matters for energy production in heart

The heart has the highest energy need of all organs in the body[2,3]

Cardiomyocytes contain many mitochondria to produce adequate energy[3,,5]

Iron is essential in mitochondrial energy production[5,6]

Cardiomyocytes are particularly sensitive to iron depletion because they have a high energy demand[1,,7]



Heart produces **95%** of the required ATP in the mitochondria through oxidative phosphorylation[3]

1. Jankowska EA *et al. Eur Heart J* 2010;31:1872–80.
2. Neubauer S. *N Engl J Med* 2007;356:1140–51.
3. Brown DA *et al. Nat Rev Cardiol* 2017;14:238–50.
4. Schaper J *et al. Circ Res* 1985;56(3):377–91.
5. Melenovsky V *et al. Eur J Heart Fail* 2017;19:522–30.
6. Dallman PR. *J Intern Med* 1989;226:367–72.
7. Jankowska EA *et al. J Card Fail* 2011;17(11):899–906.
8. Doehner W *et al. J Am Coll Cardiol* 2014;64(13):1388–400.
9. Jankowska EA, Ponikowski P. *Heart Fail Clin* 2010;6(3):295–304.
10. Von Haehling S *et al. Clin Res Cardiol* 2017;106(6):436–43.
11. Klip IT *et al. Am Heart J* 2013;165(4):575–82.
12. Martens P *et al. Acta Cardiol* 2018;73(2):115–23.
13. Comin-Colet J *et al. Eur J Heart Fail* 2013;15(10):1164–72.
14. Enjuanes C *et al. Int J Cardiol* 2014;174:268–75.
15. Wienbergen H *et al. Am J Cardiol* 2016;118(12):1875–80.
16. Yeo JT *et al. Eur J Heart Fail* 2014;16:1125–32.

ID-induced mitochondrial dysfunction may contribute to HF symptoms

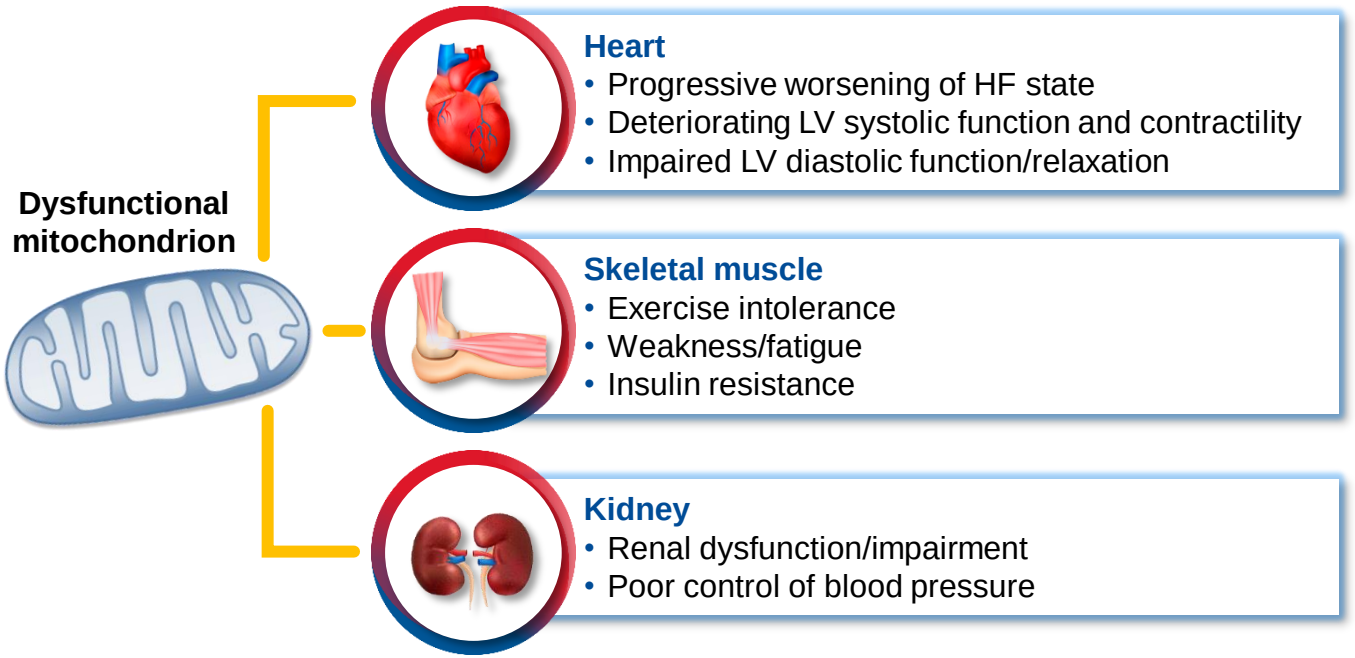
- Mitochondria are major sites of iron utilisation and accumulation[1]

Daily human energy consumption[2]

kcal/kg/day[1]	Organ/Tissue
>400	Kidney Heart
>200	Brain
>150	Liver
<50	Skeletal muscle Residual mass Adipose tissue

Metabolic rate

Dysfunctional mitochondrial energy production may account for many common HF symptoms[3]

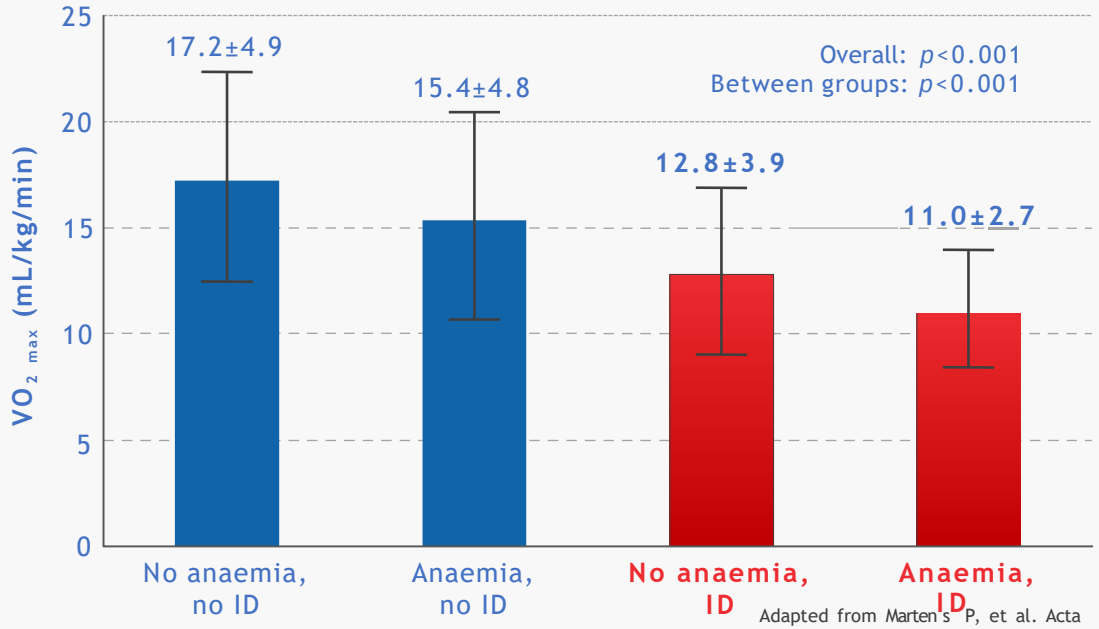


1. Paul BT, et al. Expert Rev Hematol 2017;10:65–79; 2. Boyman L, et al. Trends Mol Med 2020;26:21–39; 3. Brown D, et al. Nat Rev Cardiol 2017;14:238–50

ID is a strong determinant of impaired exercise capacity

- **Exercise capacity limitation*** was found to cluster in patients with **ID** even more than it does in patients with anaemia not caused by ID.

Figure 1. Impact of ID on exercise performance



Adapted from Martens P, et al. Acta Cardiol 2018.

reduced exercise capacity

Poor QoL

Increased risk of hospitalisation

Increased all-cause and CV mortality

Increased costs

Martens P, et al. Acta Cardiol 20

Reduced exercise capacity

Poor QoL

Increased risk of hospitalisation

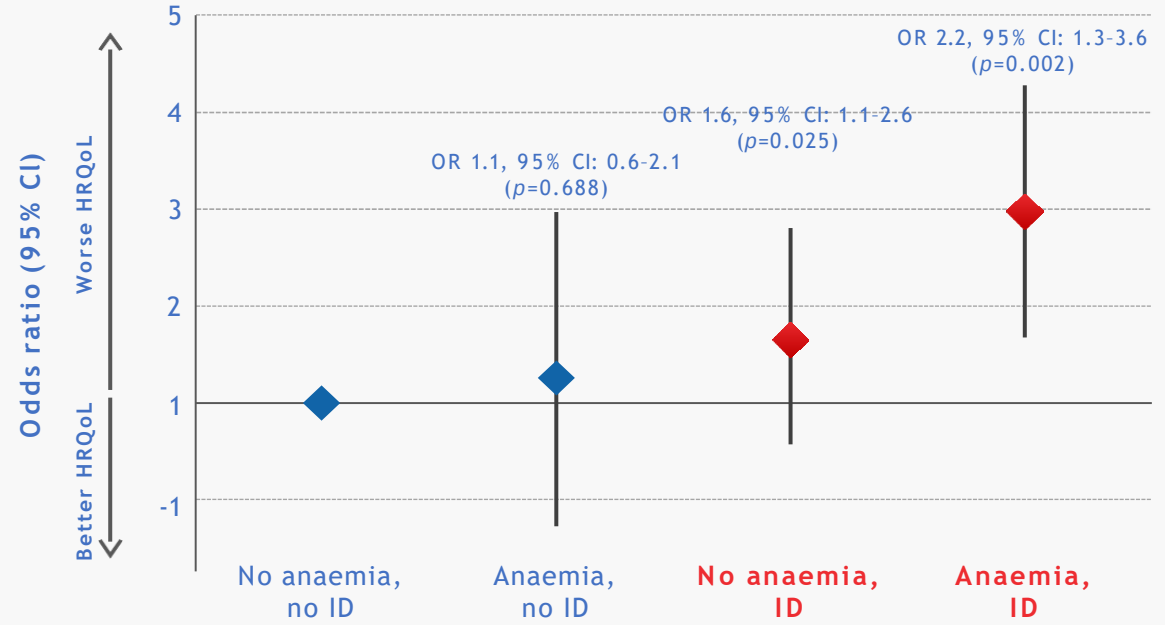
Increased all-cause and CV mortality

Increased costs

ID is associated with reduced QoL

- The presence of ID, with or without anaemia, was predictive of having a **worse QoL.**

Figure 1. Odd ratio for overall HRQoL score[1]



Adapted from Enjuanes C, et al. Int J Cardiol 2014.

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Enjuanes C, et al. Int J Cardiol 2014;174:268-75.

Reduced exercise capacity

Poor QoL

increased risk of hospitalization

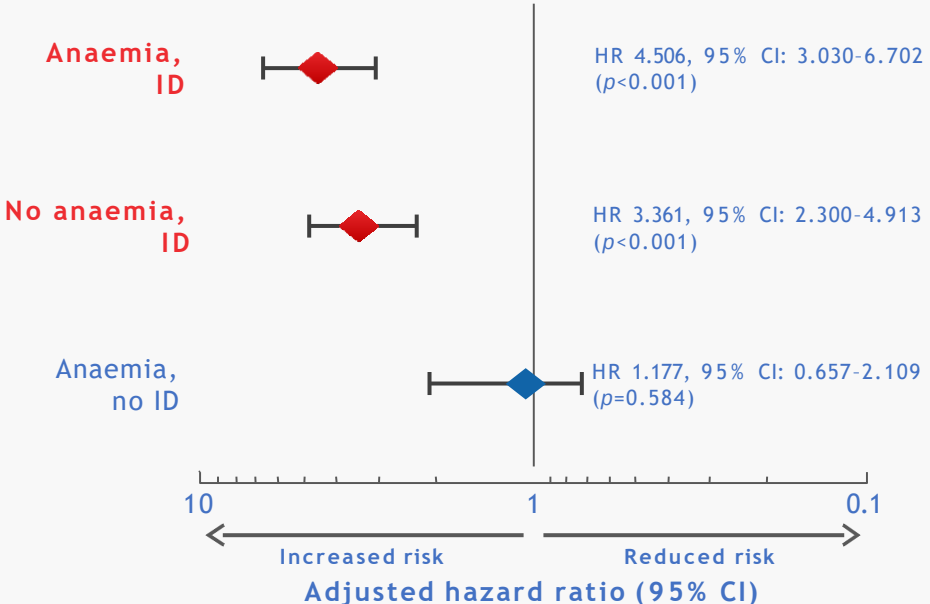
Increased all-cause and CV mortality

Increased costs

ID is associated with increased risk of hospitalization

- The presence of ID, with or without anaemia, was predictive of **increased risk of hospitalization.**

Figure 1. Risk of HF hospitalisation[1]



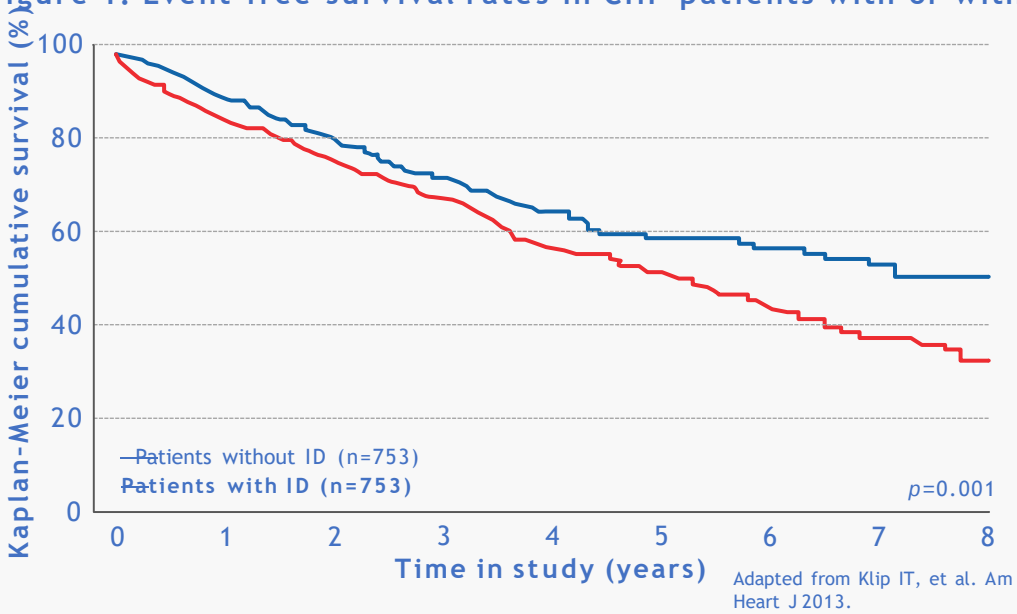
Adapted from Martens P, et al. Acta Cardiol 2018.

Martens P, et al. Acta Cardiol 2018;73(2):115-23.

ID is associated with increased mortality

- Kaplan-Meier survival analysis revealed ID as a **strong predictor for mortality** (log rank x^2 10.2, p=0.001).

Figure 1. Event-free survival rates in CHF patients with or without ID



Adapted from Klip IT, et al. Am Heart J 2013.

Reduced exercise capacity

Poor QoL

Increased risk of hospitalisation

Increased all-cause and CV mortality

Increased costs

Klip IT, et al. Am Heart J 2013;165(4):575-82.

Reduced exercise capacity

Poor QoL

Increased risk of hospitalisation

Increased all-cause and CV mortality

Increased costs

ID increases healthcare costs in the setting of HF

- For emergency admissions, the **mean length of stay (LOS) was longer** and **per capita costs were high** for patients with ID/IDA compared with those without.

Figure 1. LOS (days) in HF patients[1]

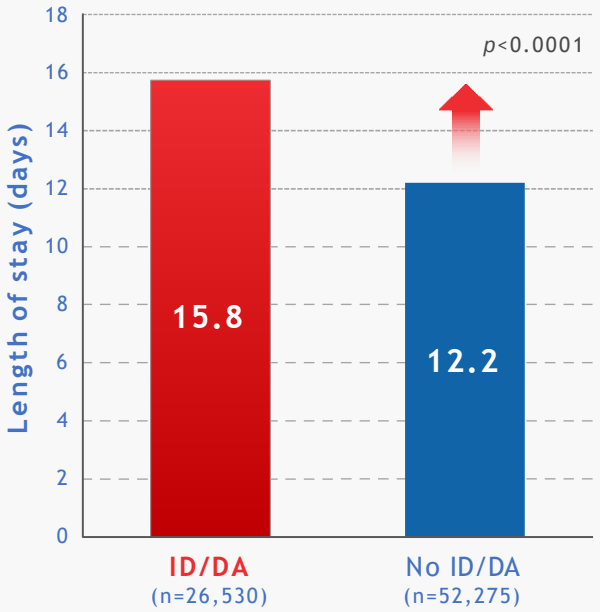
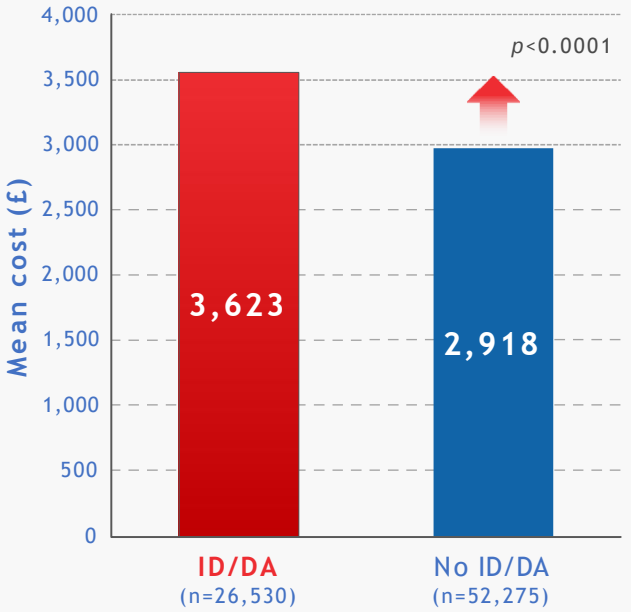


Figure 2. Per capital costs in HF patients[1]



Beattie JM, et al. Open Heart 2020;7:e001153.

Case Study

- 70-year-old female patient
- admitted for acutely decompensated heart failure
- Echocardiogram : left ventricular ejection fraction (LVEF) 35%, dilated left ventricle , and moderate functional mitral regurgitation. No significant stenosis was observed on coronary angiography. ECG: SR, normal QRS interval.
- GDMT including ACEI, beta-blockers, MRA , SGLT2 inhibitor
- Initial improvement in functional class to NYHA II; however, one month later, the patient hospitalized for an episode of decompensation of heart failure

- What would be the appropriate next steps in management?

Case Study

- up-titration of medications to guideline-targeted doses
- replacement of ACEI with angiotensin receptor/neprilysin inhibitors,
- addition of pharmacological therapy: Vericiguat
- evaluation for device therapy.
- addressing potential precipitating causes of decompensation and managing co-morbidities.

- What would be the appropriate next steps in management?

ESC 2016 guidelines on diagnosis and treatment of heart failure: screening for iron deficiency

All newly diagnosed patients with HF are recommended to be screened for iron deficiency based on serum ferritin and TSAT

Recommendations	Class [a]	Level [b]
The following diagnostic tests are recommended/should be considered for initial assessment of a patient with newly diagnosed HF in order to evaluate the patient's suitability for particular therapies, to detect reversible/treatable causes of HF and co-morbidities interfering with HF:		
- haemoglobin and WBC - sodium, potassium, urea, creatinine (with estimated GFR) - liver function tests (bilirubin, AST, ALT, GGTP) - glucose, HbA1c - lipid profile - TSH - ferritin, TSAT = (iron/TIBC)*100%	I	C
- natriuretic peptides	IIa	C

Ponikowski P, et al. Eur Heart J 2016;37:2129–200

Diagnosis of ID in HF: ESC guideline recommendations

Iron status should be checked in **ALL PATIENTS WITH SUSPECTED CHRONIC HF**[1]

ALL PATIENTS with HF should be **PERIODICALLY** screened for anaemia and iron deficiency[1]

Updated

Recommendation – Class I; Level of evidence: C[1]

Recommendations for diagnostic tests in all patients with suspected chronic HF:[1]

Routine blood tests for comorbidities, including full blood count, urea and electrolytes, thyroid function, fasting glucose and glycated haemoglobin (HbA1c), lipids, iron status (transferrin saturation [TSAT] and ferritin).[1]

I

C

Updated

Recommendation – Class I; Level of evidence: C[1]

It is recommended that all patients with HF are periodically screened for anaemia and iron deficiency with a full blood count, serum ferritin concentration and TSAT.[1]

I

C

Case Study

- Hb levels of 11.4g/dL.
- Serum ferritin : 105µg/L (normal reference >30)
- TSAT of 13.4 %
- How do we interpret these results?

Potential interference of chronic low-grade inflammation in HF with circulating ferritin

Circulating ferritin

Acute-phase reactant

Storage protein for intracellular iron

Chronic disease (inflammation)

Iron deficiency

Iron deficiency + chronic disease (inflammation)

Ferritin <30 µg/L or TSAT <20%

Ferritin <100 µg/L (Absolute ID) or Ferritin 100–299 µg/L and TSAT <20% (Functional ID)

Wish JB. Clin J Am Soc Nephrol 2006; Suppl 1:S4–8;
Nanas JN et al. J Am Coll Cardiol 2006; 19(48):2485–9.

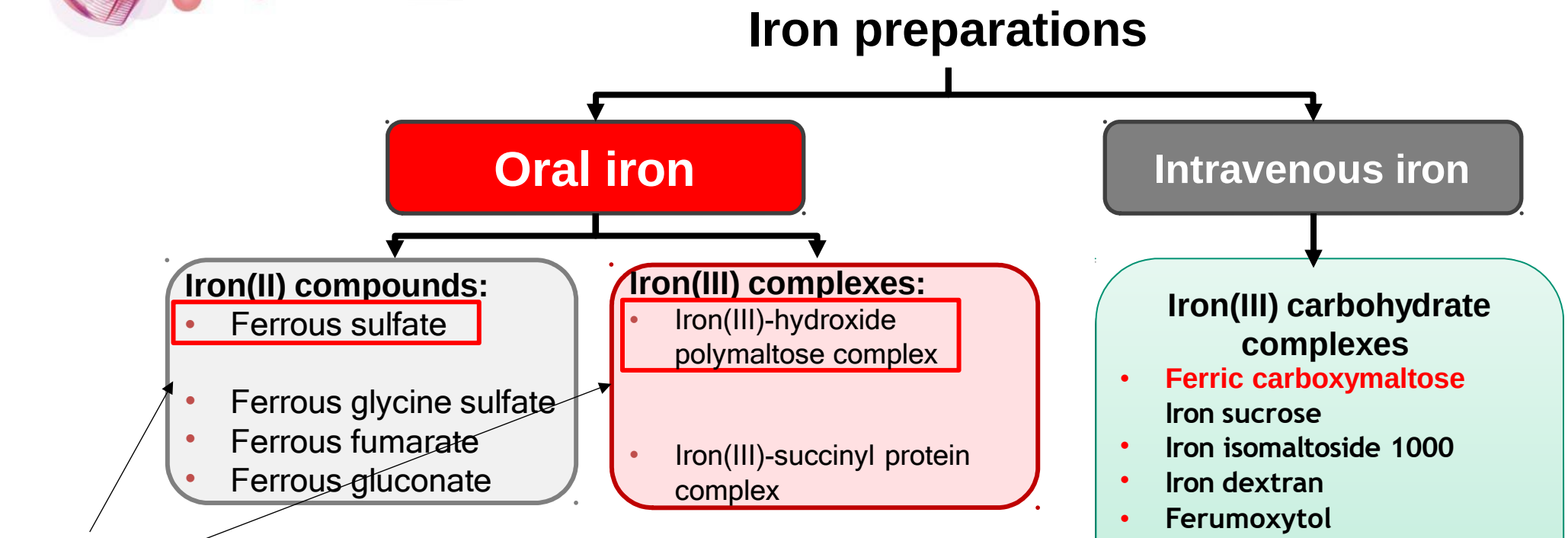
Summary of absolute and functional iron deficiency in CHF

	Absolute iron deficiency	Functional iron deficiency
Aetiology	Decreased iron intake and GI absorption; increased blood loss	Pro-inflammatory mediators, e.g. interleukin-6 in chronic inflammation, trigger up-regulation of the hepatic hormone hepcidin. This in turn causes iron sequestration in enterocytes and reticuloendothelial cells
Iron stores	Depleted	Normal or abundant but iron unavailable
Iron availability	Decreased	Decreased
Serum ferritin levels	<100 µg/L	>100 to <300 µg/L
TSAT levels	< 20%	< 20%

Case Study

- Iron deficiency (functional) diagosed
- How to replace?

Treating ID – What are the options?



Commonly available in HK

Pros:
Cheap
Convenient to take
Prescription habits
No special facilities needed

Cons:
GI track side effect
Poor absorption
Slow replenishment
Poor compliance due to taste
Low dose

Pros:
High compliance
High dose
Quick and effective replenishment
Suitable for severely anaemic or where time is limited

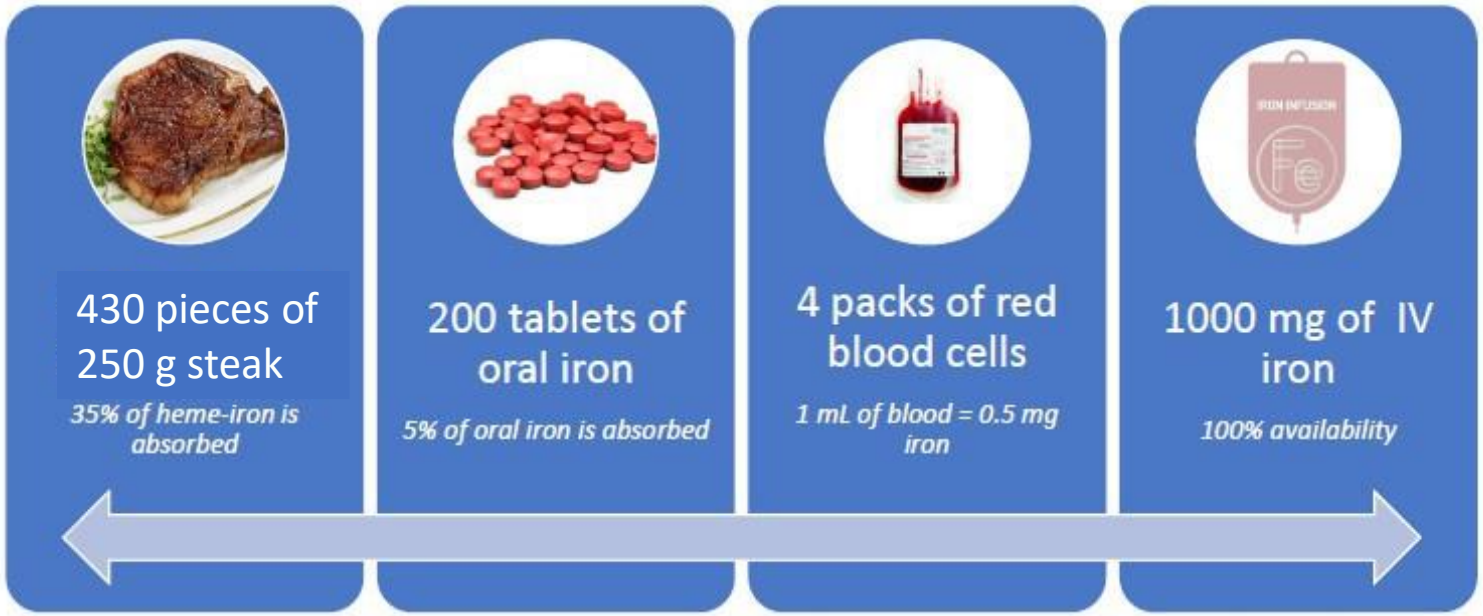
Cons:
Perceived side effects
Testing and monitoring required
Infusion facilities required

Fehr J *et al. Praxis* 2009;98:1445-1451; Gordeuk VR *et al. Am J Clin Nutr* 1987;46:1029-1034; Aapro M *et al. Ann Oncol* 2012;23:1954-1962

How to treat ID

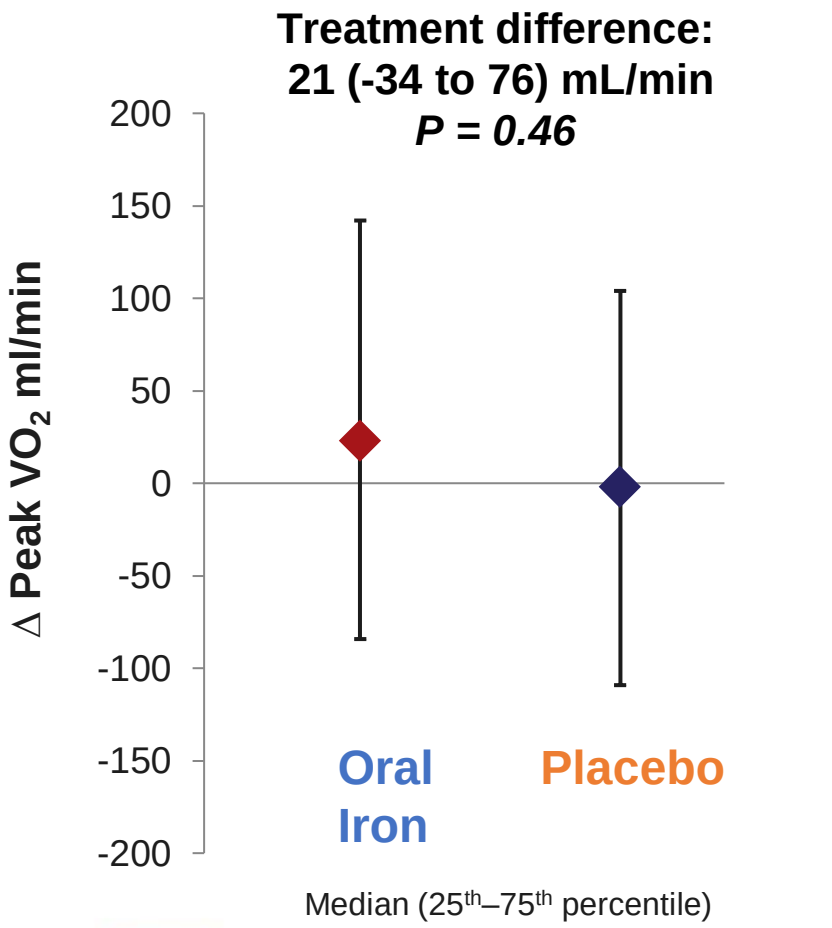
Replacing 1000 mg of iron in our bodies

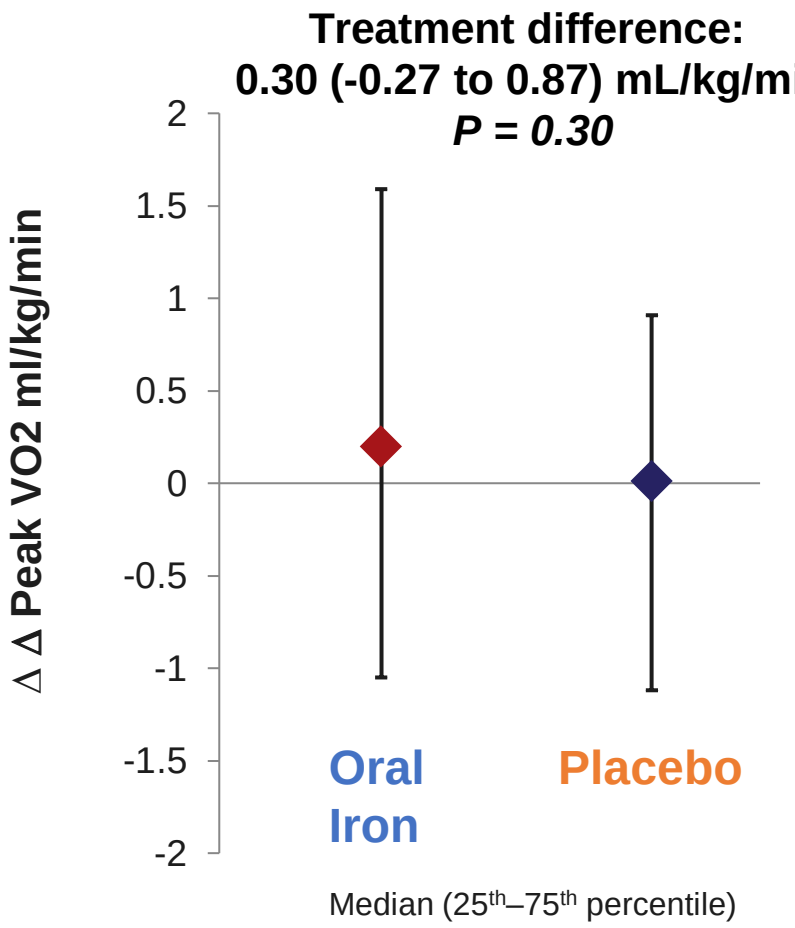
Treatment options



1. https://www.hsa.gov.sg/content/dam/HSA/BSG/Blood_Donation/Blood_Donation_Process/Iron%20Rich%20food%20Section.pdf
2. Monsen ER. J Am Diet Assoc 1988:88:786-90

IRON-OUT: oral iron (iron polysaccharide) did not improve exercise capacity in patients with HFrEF + ID





N=225 patients with HF, iron poly saccharide 150mg twice daily for 16 weeks

There is limited evidence supporting the use of oral iron for treatment of iron deficiency in HFrEF

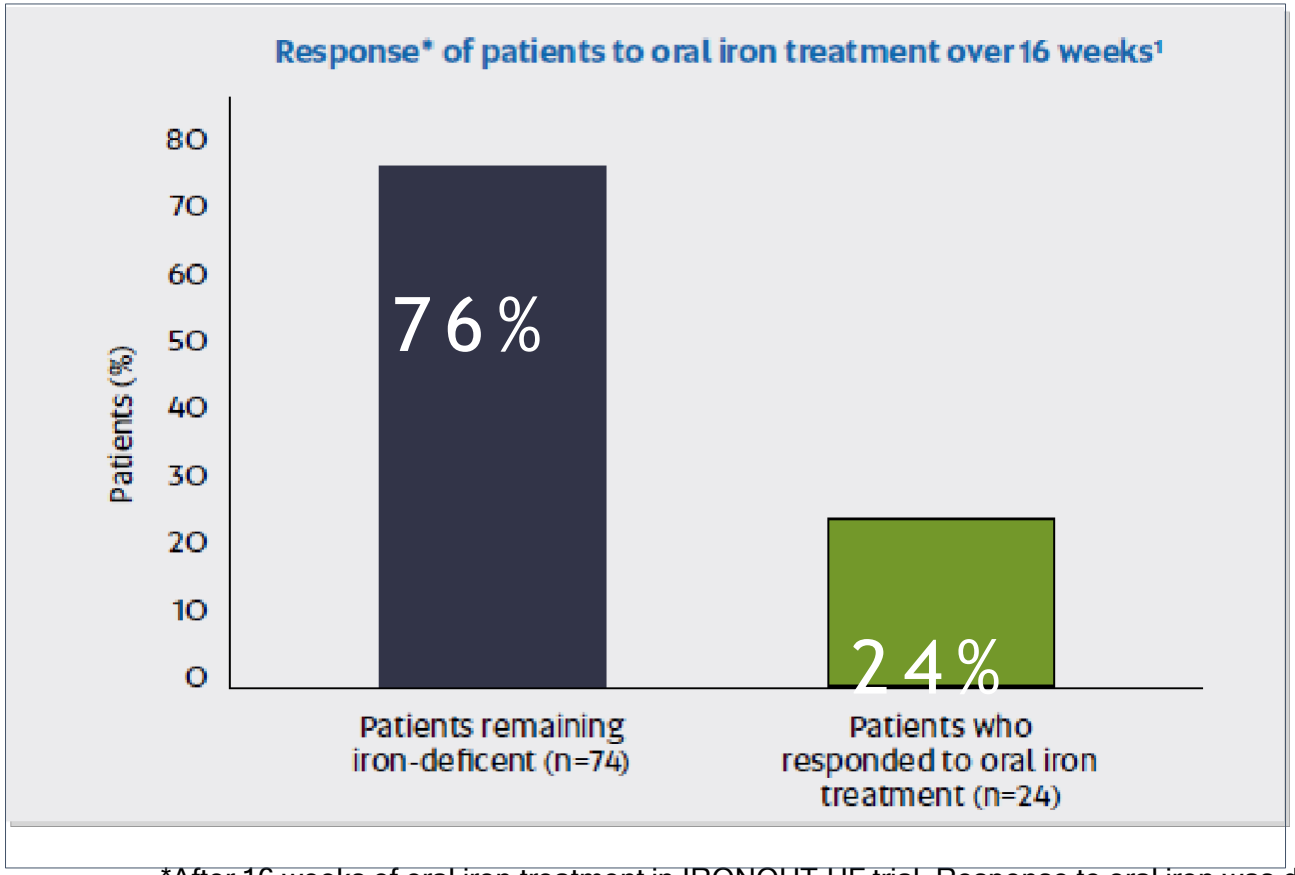
Secondary end points (all neutral, p≥0.19)

- Δ 6 MW distance at 16 weeks, meters
- Δ Mean response time, seconds
- Δ Ventilatory efficiency (VE/VCO_2 slope)
- Δ NT-BNP level, pg/ml
- Δ KCCQ score at 16 weeks

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

KCCQ, Kansas City Cardiomyopathy Questionnaire;

Most Heart failure patients with ID failed to respond to oral iron



In a post hoc analysis of the IRONOUT-HF trial to identify responders to oral iron supplementation in patients with HF, ***74 patients (76%) remained iron-deficient[1]****

*After 16 weeks of oral iron treatment in IRONOUT-HF trial. Response to oral iron was defined as ferritin level >300 ng/mL or ferritin level 100-300 ng/mL with a transferrin saturation >20% at the end of the study.

1. Ambrosy AP et al. J Cardiovasc Med 2019 Apr;20(4):223-225
2. Lewis GD, et al. *JAMA*.2017;317(19):1958-1966

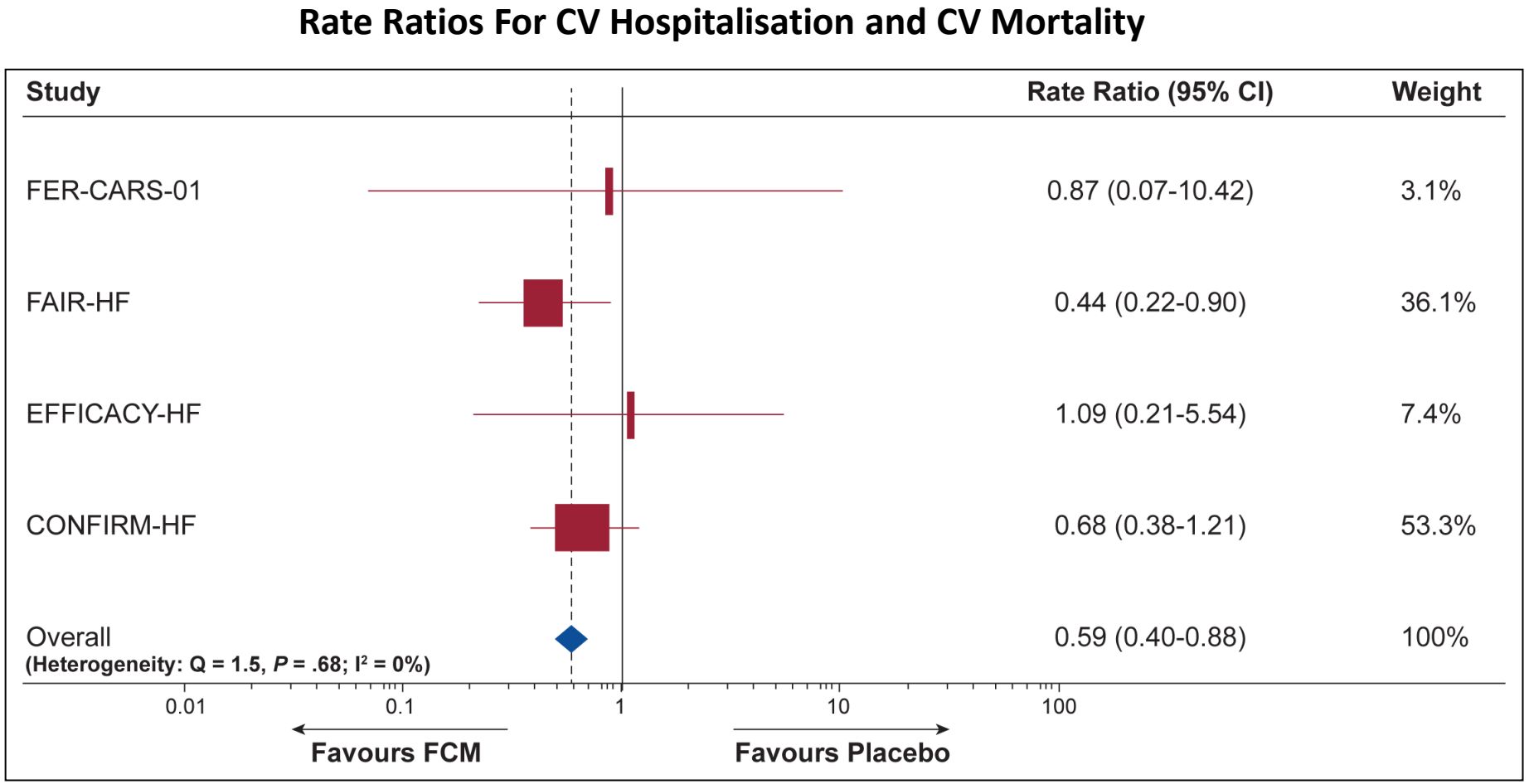
Prior IV Iron (FCM) Studies (HFrEF + HFmEF, EF<=45),

Trial	Patients	Time (weeks)	Primary endpoint
FAIR-HF	459	24	Global assessment
CONFIRM-HF	304	52	6-MWD
EFFECT-HF	172	24	Peak VO_2

Improvements in:

- Functional status (6-MWD, peak VO_2, NYHA Class)
- Biomarkers (BNP)
- Patient global assessment

Individual patient data meta-analysis of FCM in patients with HFrEF and ID



Anker SD, et al. Eur J Heart Fail 2018;20:125–33

ESC 2016 guidelines on diagnosis and treatment of heart failure: treatment of iron deficiency

Recommendations	Class [a]	Level [b]	Ref [c]
Iron deficiency			
Intravenous FCM should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100 µg/L, or ferritin between 100–299 µg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life.	IIa	A	469, 470

11.12 Iron deficiency and anaemia

Iron deficiency is common in HF, as it is with other chronic illnesses, and it can lead to anaemia and/or skeletal muscle dysfunction without anaemia.[466] Within an HF population, iron deficiency is associated with a worse prognosis.[467,468] Intravenous iron has been specifically studied in two RCTs in patients with HF and iron deficiency (serum ferritin <100 µg/L or ferritin between 100 and 299 µg/L and transferrin saturation $<20\%$)[469,470] both with and without anaemia

Ponikowski P, et al. Eur Heart J 2016;37:2129–200

AFFIRM-AHF Study Design

Key inclusion criteria

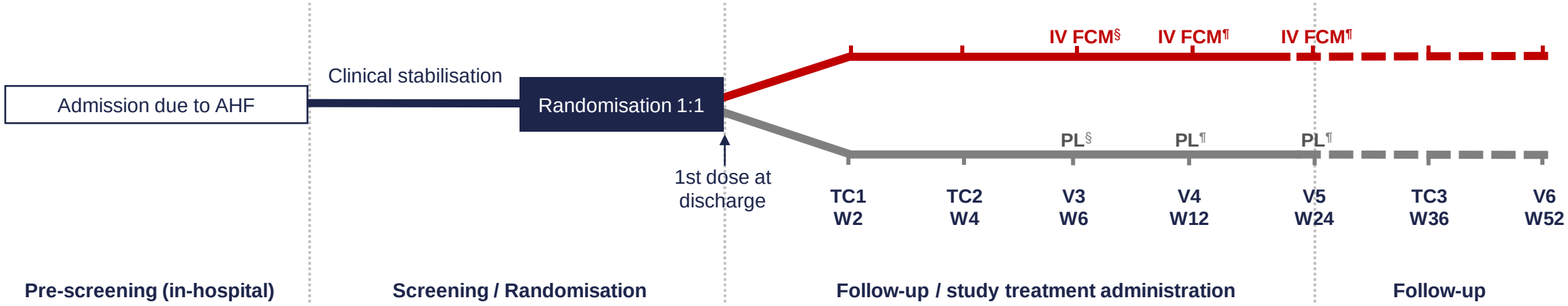
- Hospitalisation for AHF*
- ID: serum ferritin <100 ng/mL, or 100–299 ng/mL with TSAT <20%
- LVEF <50%†
- Hb ≥8 to ≤15 g/dL‡

Primary outcome

- Composite of total HF hospitalisations and CV death up to 52 weeks

Secondary and other outcomes

- Total HF hospitalisations
- CV death
- Time to first HF hospitalisation or CV death
- Composite of total CV hospitalisations and CV death
- Days lost due to HF hospitalisations or CV death
- Change from baseline in KCCQ-12 OSS and CSS
- Adverse events



*Confirmed by signs/symptoms of acute HF and elevated BNP or NT-pro-BNP levels. †Not older than 12 months prior to randomisation; ‡>10 g/dL for sites in The Netherlands, Singapore and Spain. §Repletion dose administered based on iron need assessed at the baseline visit. ¶Study treatment administered only if ID persisted.

AFFIRM-AHF Study Dosing Regimen

Week 0

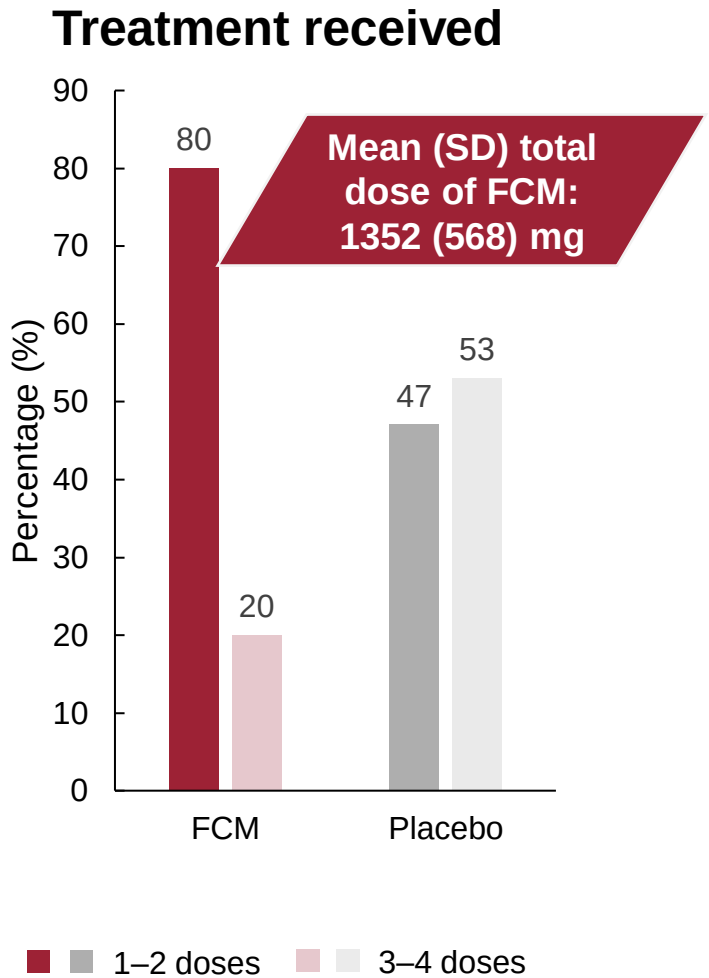
Hb 8* to ≤14 g/dL	Hb >14 to ≤15 g/dL
1000 mg FCM / placebo	500 mg FCM / placebo

Week 6

Hb 8* to ≤10 g/dL		Hb 10 to ≤14 g/dL		Hb >14 to ≤15 g/dL
<70 kg	≥70 kg	<70 kg	≥70 kg	
500 mg FCM / placebo	1000 mg FCM / placebo	No dose	500 mg FCM / placebo	No dose

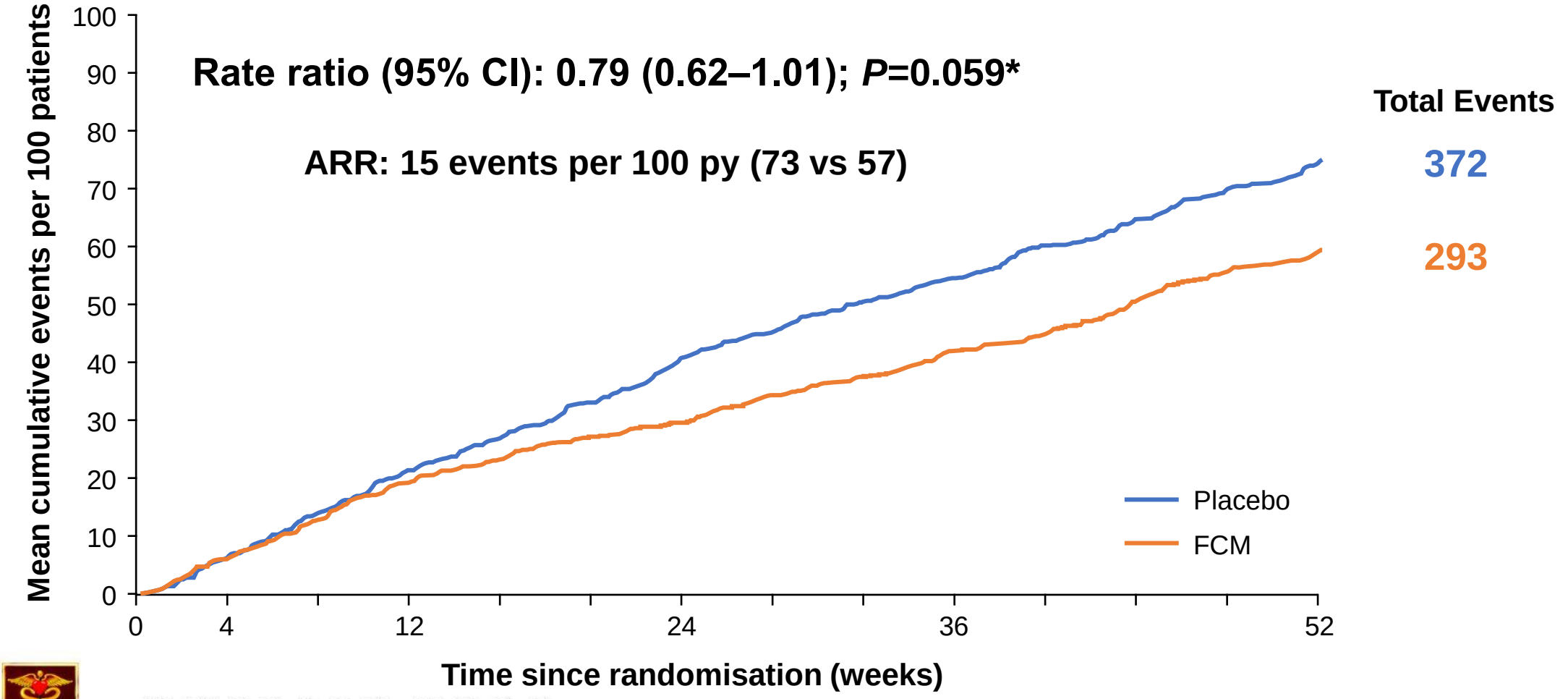
Weeks 12 + 24

Only if iron deficiency persisted
500 mg FCM / placebo



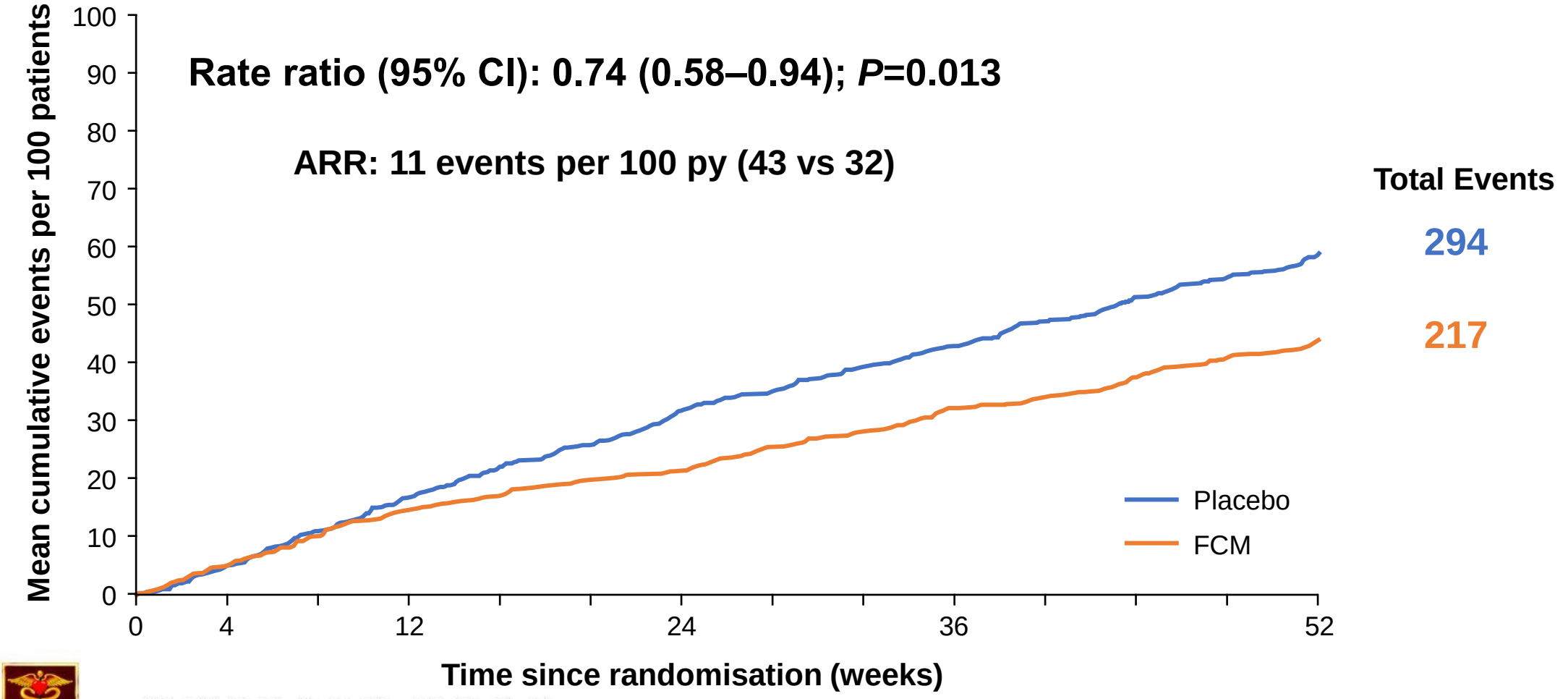
Ponikowski P et al. Eur J Heart Fail 2019;21:1651–8.

Primary endpoint: total HF hospitalisations and CV death



Ponikowski P, et al. Lancet 2020;396:1895–904

Component of primary endpoint: total HF hospitalisations



Ponikowski P, et al. Lancet 2020;396:1895–904

AFFIRM-AHF Safety overview

Adverse events (AE)	FCM (N=559)		Placebo (N=551)	
	Patients n (%)	Total Events (n)	Patients n (%)	Total Events (n)
Any AE	357 (64)	1246	360 (65)	1314
Serious AE	250 (45)	547	282 (51)	632
AE leading to withdrawal of study treatment	61 (11)	71	79 (14)	88
AE leading to study discontinuation	98 (18)	117	96 (17)	123

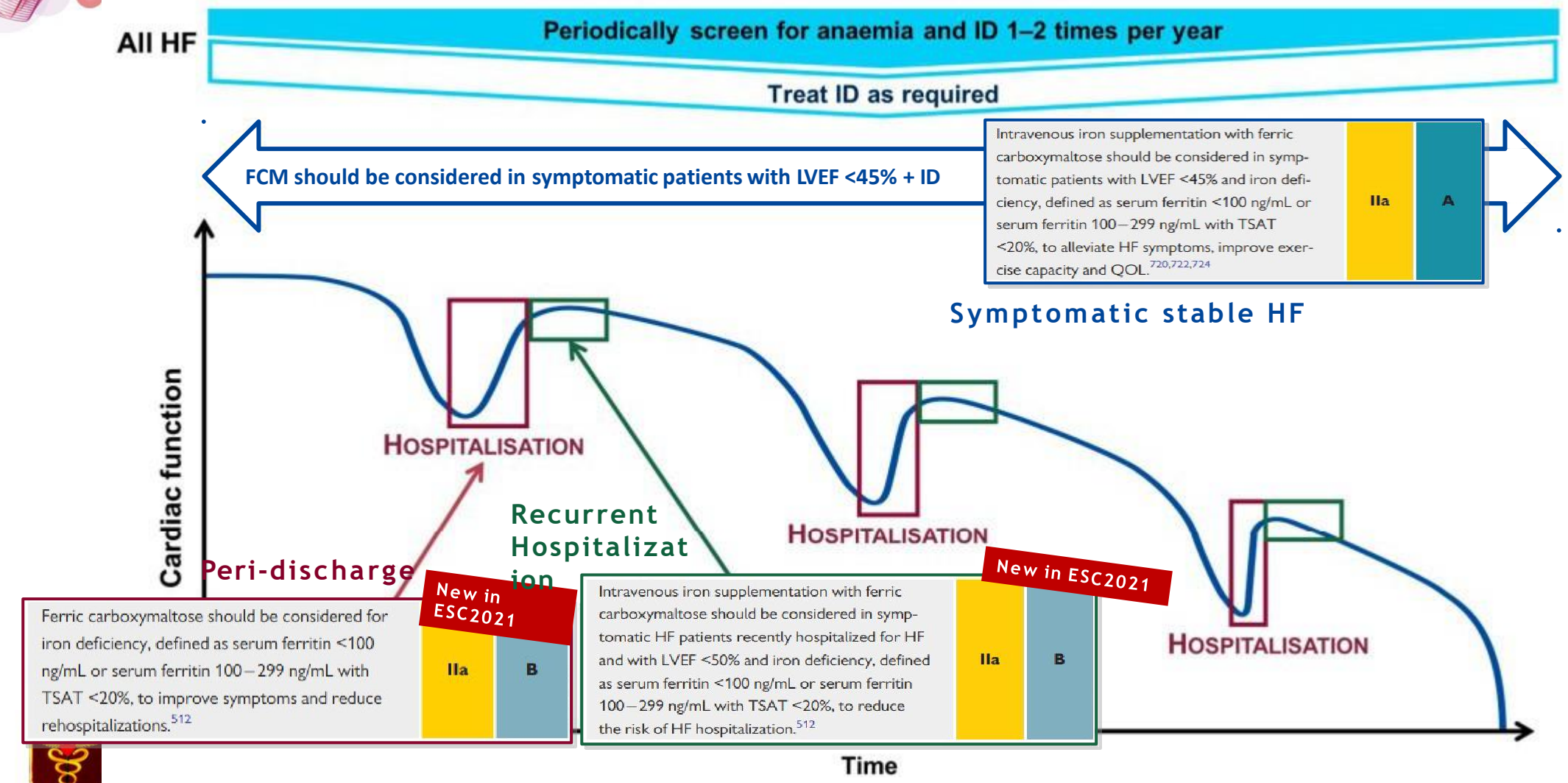
Ponikowski P, et al. Lancet 2020;396:1895–904

ESC 2021 guidelines on diagnosis and treatment of heart failure: screening for iron deficiency

Recommendations	Class[a]	Level[b]
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
Intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic patients with LVEF <45% and iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to alleviate HF symptoms, improve exercise capacity and QOL.[720,722,724]	IIa	A
Intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic HF patients recently hospitalized for HF and with LVEF <50% and iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to reduce the risk of HF hospitalization.[512]	IIa	B

- HF patients periodically screen with full blood count, serum ferritin and TSAT
- **IV FCM** should be used in symptomatic HFrEF patients with iron deficiency to alleviate symptoms, improve exercise capacity and QOL
- **IV FCM** should be used in symptomatic HFrEF patients with iron deficiency to reduce risk of HF hospitalization

Management of Iron Deficiency with FCM Across the HFrEF continuum



2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Diagnosis

Absolute ID	Ferritin < 100 ng/mL
Functional ID	Ferritin 100-300 ng/mL and TSAT < 20%

1	C-EO	2. 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.

10.1. Management of Comorbidities in Patients With HF

Recommendations for the Management of Comorbidities in Patients With HF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
Management of Anemia or Iron Deficiency		
2a	B-R	1. In patients with HFrEF and iron deficiency with or without anemia, intravenous iron replacement is reasonable to improve functional status and QOL.[1–4]
3: Harm	B-R	2. In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.[5,6]

Based on :
- The **FAIR-HF** (Ferric Carboxymaltose Assessment in Patients With Iron Deficiency and Chronic Heart Failure) trial
- The **AFFIRM-AHF** (Ferric Carboxymaltose Evaluation on Performance in Patients With Iron Deficiency in Combination with Acute Heart Failure) trial

IRONMAN

A randomized trial of intravenous ferric derisomaltose in heart failure with reduced ejection fraction. Lancet 2022; 400: 2199–209

- Study the longer-term (>12 months) efficacy and safety of IV iron in patients with heart failure

- Mean Follow-up : 2.7

Key eligibility criteria

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 (ng/L) >250 if SR / >1,000 if AF
Able and willing to provide informed consent

Exclusion criteria
Haemoglobin <9.0 g/dL
Hb >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
Disease (other than HF) with life-expectancy <2 yrs
Contra-indication to IV iron

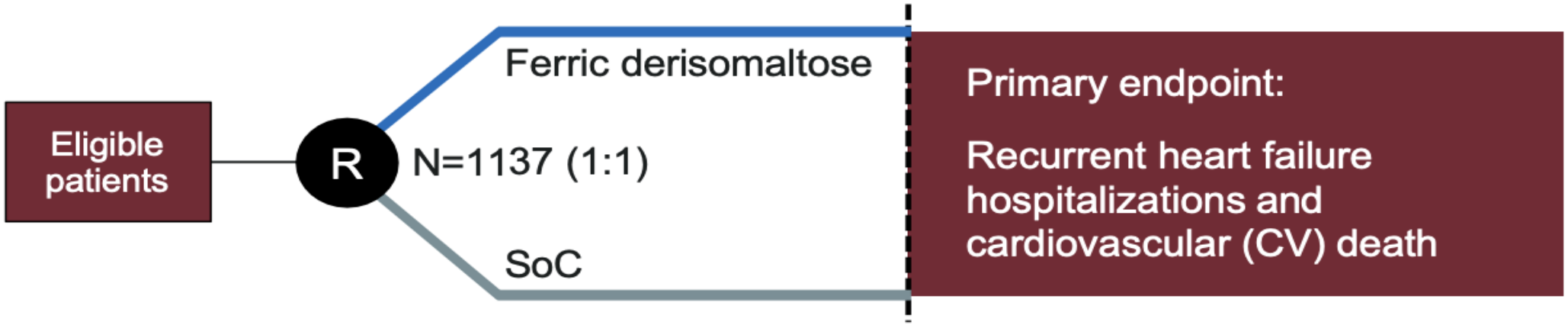
Ironman

Kalra PR et al. Heart 2022 Aug 10;heartjnl-2022-321304.

British Heart Foundation

IRONMAN

Re-dosing at week 4, month 4, and 4 monthly thereafter
if **either** ferritin <100 µg/L **or** TSAT <25% (provided ferritin was ≤400 µg/L)



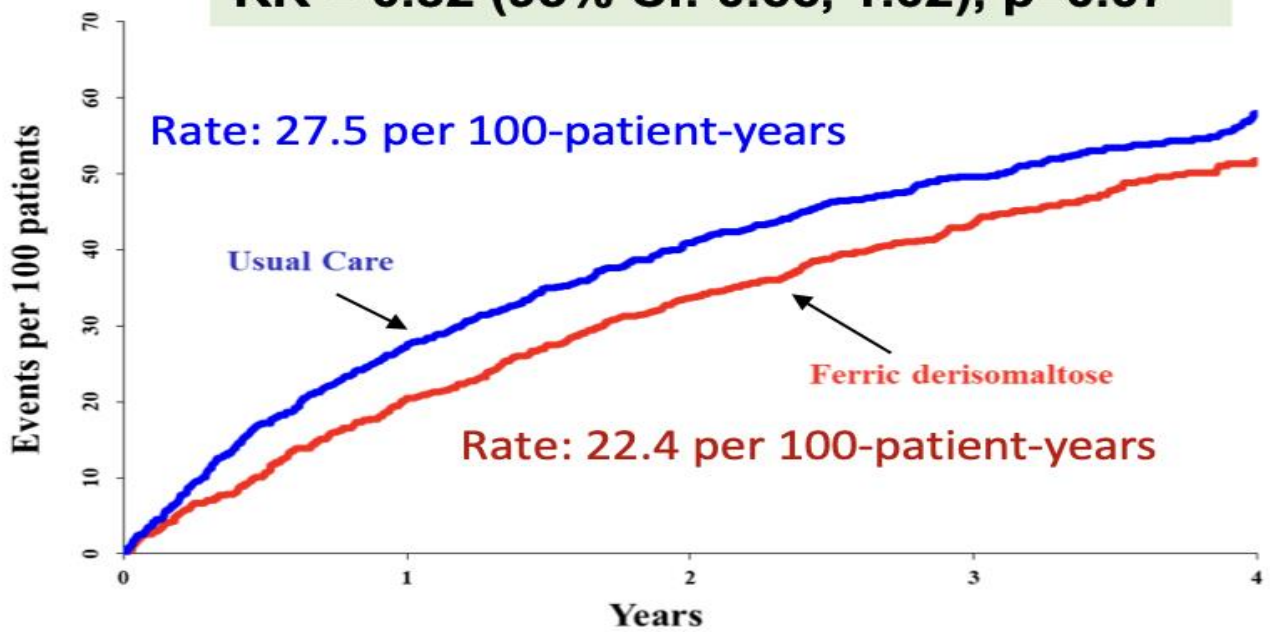
Hb	BW<50 kg	BW 50 to <70 kg	BW≥70 kg
≥10 g/dL	20 mg/kg	1000 mg	20 mg/kg up to a maximum of 1500 mg
<10 g/dL	20 mg/kg	20 mg/kg	20 mg/kg up to a maximum of 2000 mg

Kalra PR et al. Heart 2022 Aug 10;heartjnl-2022-321304.

Primary outcome:

Recurrent HF hospitalizations and CV death

RR = 0.82 (95% CI: 0.66, 1.02), p=0.07



Number at risk					
Ferric derisomaltose	569	485	405	237	86
Usual Care	568	483	406	227	87

COVID sensitivity analysis

Primary outcome	Prespecified analysis FDI (n=527) Usual care (n=536)	Post hoc analysis at 1 year FDI (n=527) Usual care (n=536)
Recurrent HF hosp. and CV death*	RR 0.76 (0.58 – 1.00) P = 0.047	RR 0.66 (0.48 – 0.91) P = 0.011
Key secondary outcomes		
Recurrent HF hospitalizations*	RR 0.76 (0.56 – 1.03) P = 0.077	RR 0.66 (0.46 – 0.94) P = 0.020
CV death, n (%)	HR 0.79 (0.57 – 1.09) P = 0.15	HR 0.67 (0.42 – 1.07) P = 0.091
First event: CV death, or hosp. for HF, MI or CVA*	HR 0.78 (0.62 – 0.98) P = 0.03	HR 0.78 (0.59 – 1.05) P = 0.097
All cause mortality	HR 0.91 (0.70 – 1.19) P = 0.48	HR 0.72 (0.48 – 1.08) P = 0.12

* no. of events (rate per 100 patient-year)

Safety

Prespecified safety outcomes	FDI (n=559)	Usual Care (n=568)	Estimated treatment effect (RR or HR, 95% CI)	P value
Hosp. due to infection*	175 (11.7)	213 (14.2)	RR 0.82 (0.62 - 1.08)	0.16
Death due to infection (%)	34 (6%)	28 (5%)	HR 1.22 (0.74 - 2.02)	0.43
Serious adverse events (MedDRA) N (%)			**Difference (95% CI)**	
All	410 (73%)	435 (77%)	-3.2 (-8.3 to 1.8)	0.21
Cardiac	200 (36%)	243 (43%)	-7.0 (-12.7 to -1.3)	0.016
Metabolism and nutrition	31 (6%)	49 (9%)	-3.1 (-6.1 to -0.1)	0.043

* no. of events (rate per 100 patient-year)

Implications for practice

The IRONMAN trial provides

- Additional evidence that correcting iron deficiency by administering high-dose IV iron improves well-being and prognosis for a broad range of patients with heart failure
- Reassurance about the long-term safety of IV ferric derisomaltose in patients with heart failure

Case Study

- Treated with i.v. iron 1000 mg ferric carboxymaltose infusion (calculated according to her weight, 58kg, and Hb level)

- At the 12-week assessment, the patient's status had improved to functional class NYHA II

  Hb 12.3. Ferritin 150. TSAT 18%

  a further dose of i.v. ferric carboxymaltose (500 mg) was administered.

- At 24-week, NYHA Class I. No longer ID.

ID in HF is underdiagnosed and undertreated

Underdiagnosed: & **Undertreated:**

10,381
total admissions for HF as primary or secondary diagnosis

158 (1.5%)
individual patients had adequate iron studies performed

109
patients met criteria for ID per guidelines

23 (21%)
patients received IV iron

Mistry R, et al. Ann Hematol 2019;98:2293–7

Conclusion

- ID is common among patients with HF, particularly in those with acute HF[1]
- ID (independent of anaemia) is associated with adverse outcomes in patients with HF: high all-cause and CV mortality, high rates of recurrent HF hospitalisations, advanced HF symptoms, poor QoL, high healthcare costs[2]
- RCTs have demonstrated the efficacy and tolerability of IV iron formulations and shown that they can improve QoL, attenuate HF symptoms and reduce the risk of HF hospitalisations[3–6]

  Oral iron and erythropoietin stimulating agents are not indicated .
- ID in HF still remains underdiagnosed and undertreated[7]

1. Rocha BML, et al. J Am Coll Cardiol 2018;71:782–93; 2. Marchi G, et al. Intern Emerg Med 2021;16:167–70; 3. Anker, et al. N Engl J Med 2009;361:2436–48; 4. Ponikowski P, et al. Eur J Heart Fail 2019;21:1651–8; 5. Van Veldhuisen, et al. Circulation 2017;136:1374–83; 6. Ponikowski P, et al. Lancet 2020;396:1895–904; 7. Mistry R, et al. Ann Hematol 2019;98:2293–7

- Thank you !