

APPROCCIO MULTIDISCIPLINARE ALL'ANEMIA SIDEROMENICA:
UNA PATOLOGIA FREQUENTE E CURABILE

Milano, 29 novembre

Anemia e carenza marziale nei pazienti con scompenso cardiaco: segni, sintomi, funzionalità cardiaca e qualità di vita del paziente



Dott Andre Pozzi
ASST-Papa Giovanni XXIII- Bergamo

Conflitto d'interesse

- Non sono un ematologo
- Non sono un ferritologo
- Non sono un esperto di ciclismo

Heart Failure: ESC definition

Syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function.

Symptoms and signs

HEAR FAILURE

Shortness of breath

Increase heart rate

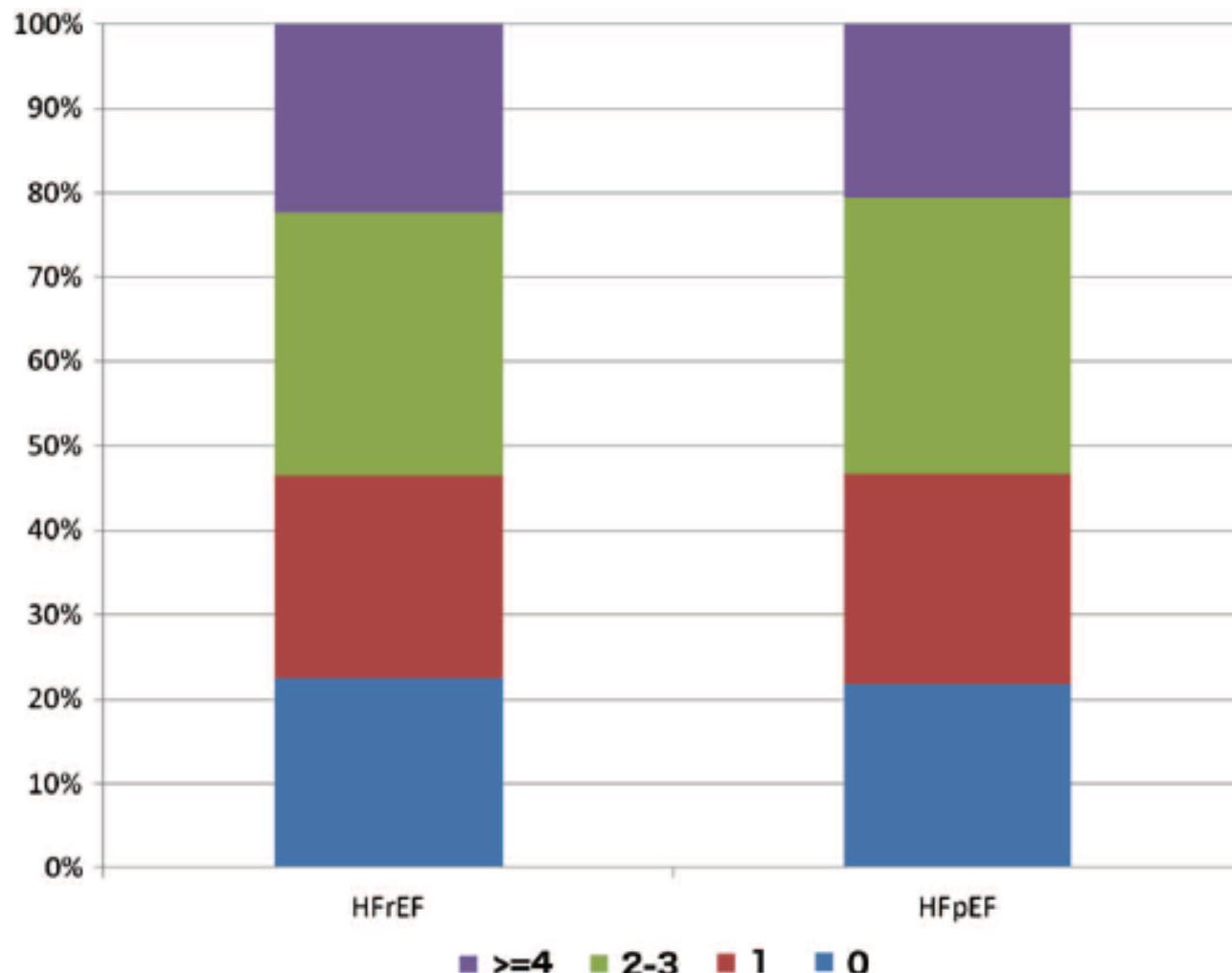
Fatigue

Loss of energy

Dizziness

ANEMIA

Comorbidities in HF



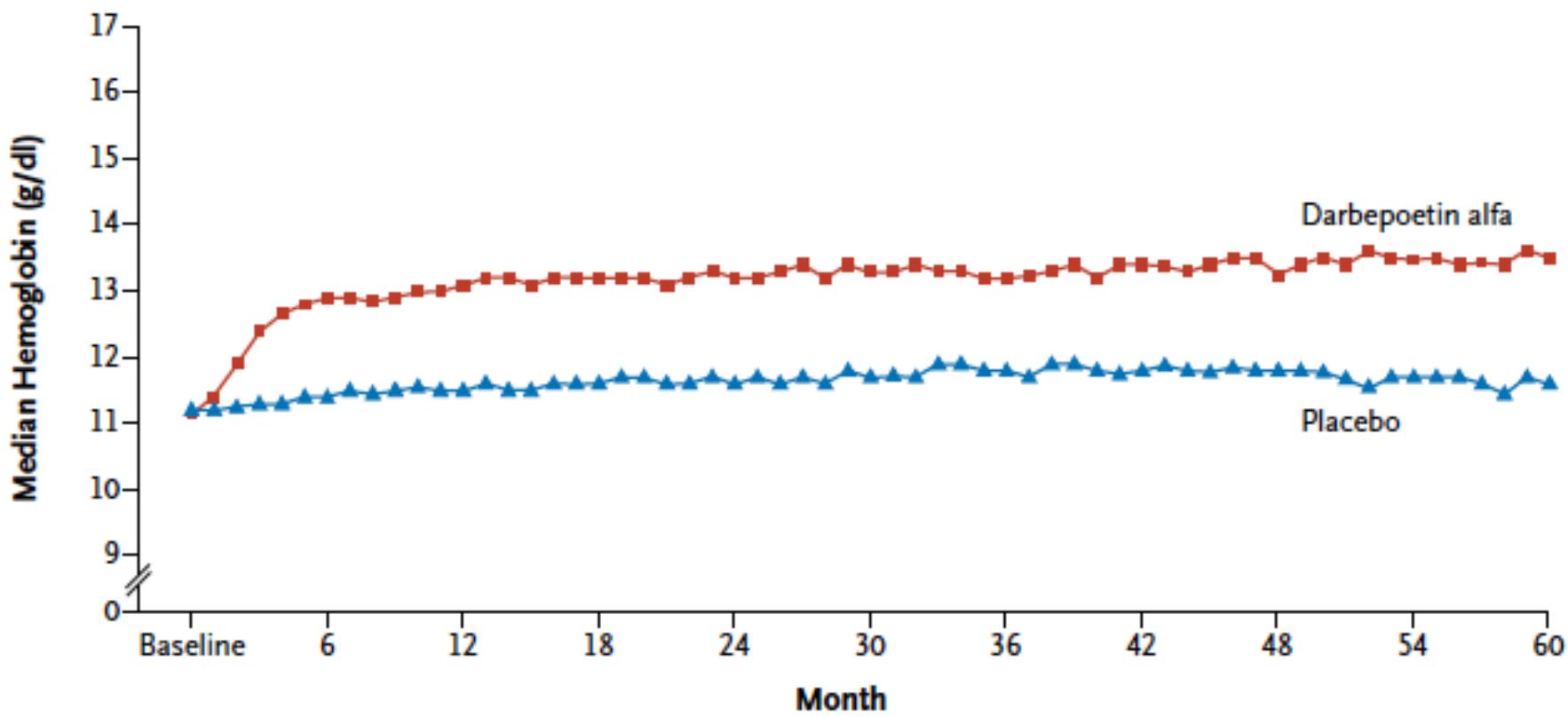
Prevalence in HF

Registries	Prevalence of Anemia
Iorio (Trieste)	25%
Koh (Swedish)	31%
Ezekowitz (Europe)	17%

Prevalence 8-62% in HF with reduced EF



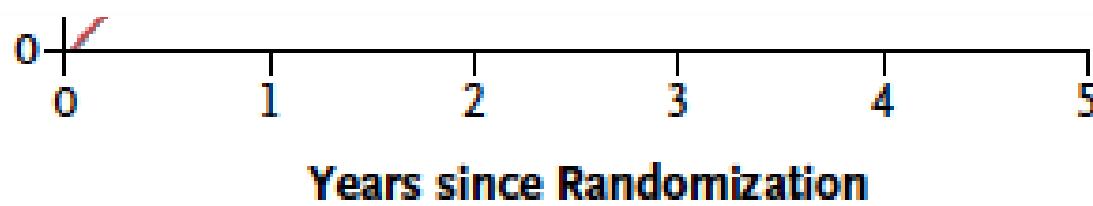
Treatment of Anemia with Darbepoetin Alfa in Systolic Heart Failure



Results and Advers Events

Primary Composite Outcome

Adverse Event	Darbepoetin Alfa (N=1133)	Placebo (N=1140)	Risk Difference (95% CI)†	P Value‡
	no. of patients (%)	percentage points		
Embolic and thrombotic events				
Any	153 (13.5)	114 (10.0)	3.5 (0.9 to 6.1)	0.009
Arterial§	87 (7.7)	73 (6.4)	1.3 (-0.8 to 3.4)	0.24
Venous¶	29 (2.6)	20 (1.8)	0.8 (-0.4 to 2.0)	0.19
Vessel type unspecified and mixed arterial and venous	51 (4.5)	27 (2.4)	2.1 (0.6 to 3.6)	0.005



Voided results from August 1998 onward

4th Overall [Vuelta a España](#)
4th Read race, [UCI Read World Read Championships](#)
1999
1st Overall [Tour de France](#)
1st Prologue, Stages 8, 9 & 19
1st Prologue [Critérium du Dauphiné Libéré](#)
1st Stage 4 [Route du Sud](#)
1st Stage 4 (ITT) [Circuit de la Sarthe](#)
1st RaboRonde Heerlen
2nd [Amstel Gold Race](#)
2000
1st Overall [Tour de France](#)
1st Stage 19 (ITT)
1st [Grand Prix des Nations](#)
1st [Grand Prix Eddy Merckx](#)
1st Stage 3 (ITT) [Critérium du Dauphiné Libéré](#)
3rd Time trial, [Olympic Games](#)
2001
1st Overall [Tour de France](#)
1st Stages 10, 11, 13 & 18
1st Overall [Tour de Suisse](#)
1st Stages 1 & 8
2nd [Amstel Gold Race](#)

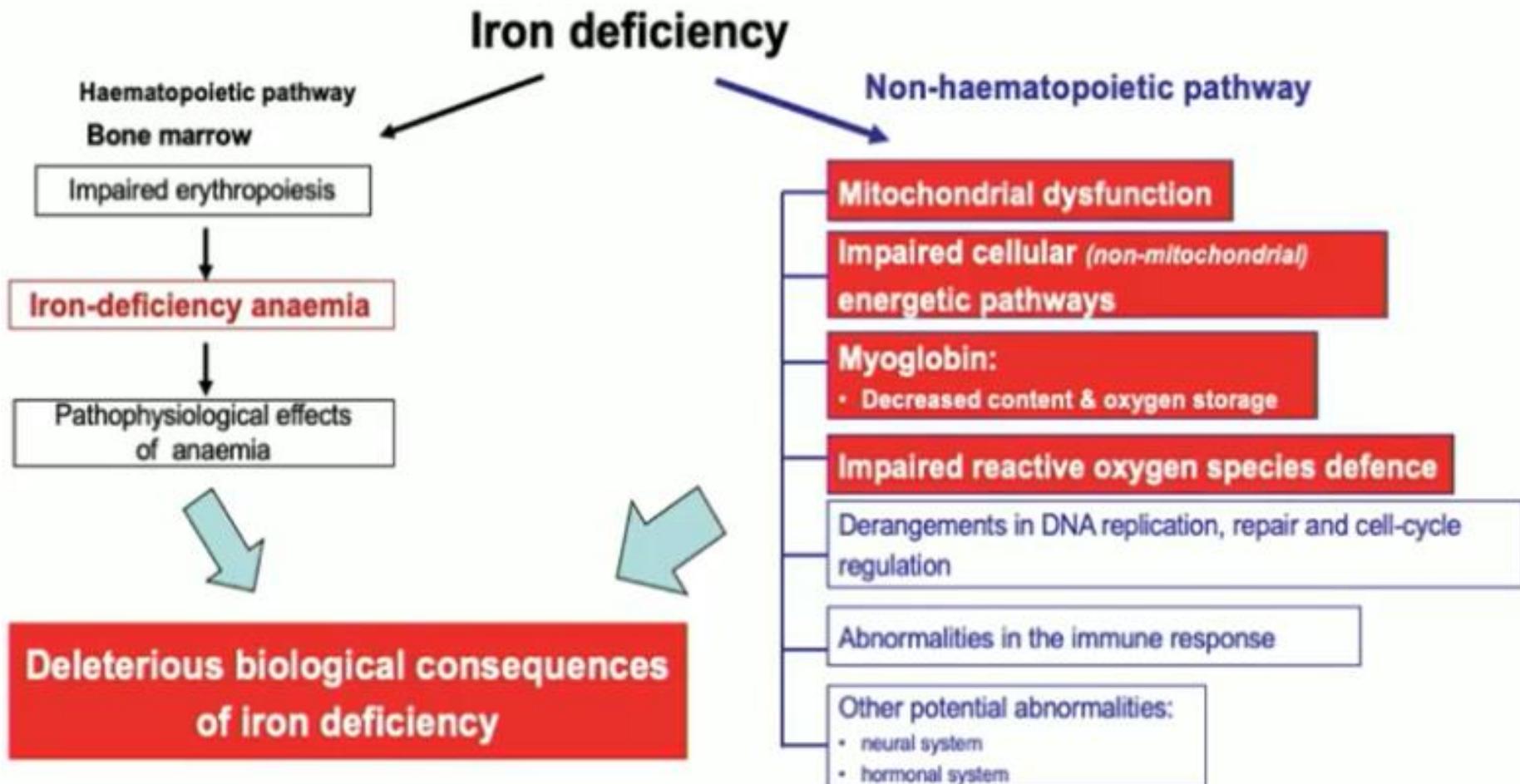
1st Stages 3 & 4
1st Stage 5 [Tour du Languedoc-Roussillon](#)
1st Stage 4 (ITT) [Volta ao Algarve](#)
1st [Profronde van Stiphout](#)
2005
1st Overall [Tour de France](#)
1st Stages 4 (TTT) & 20 (ITT)
1st Points classification [Critérium du Dauphiné Libéré](#)
2008
2nd [Leadville Trail 100 Mountain Bike Race](#)
1st 12 Hours of Snowmass
1st Individual Time Trial [Tour de Gruene](#)
1st TTT [Tour de Gruene](#)
2009
1st [Nevada City Classic](#)
1st Colorado Pro Cross-Country Championships
1st [Leadville Trail 100 Mountain Bike Race](#)
2nd Overall [Tour of the Gila](#)
3rd Overall [Tour de France](#)
1st Stage 4 (TTT)
2010
2nd Overall [Tour de Suisse](#)
3rd Overall [Tour de Luxembourg](#)
7th Overall [Vuelta a Murcia](#)

2nd [Amstel Gold Race](#)
2002
1st Overall [Tour de France](#)
1st Prologue, Stages 11, 12 & 19
1st Overall [Critérium du Dauphiné Libéré](#)
1st Stage 6
1st Overall [Grand Prix du Midi Libre](#)
1st [Profronde van Stiphout](#)
2003
1st Overall [Tour de France](#)
1st Stages 4 (TTT) & 15
1st Overall [Critérium du Dauphiné Libéré](#)
1st Stage 3 (ITT)
2004
1st Overall [Tour de France](#)
1st Stages 4 (TTT), 13, 15, 16 (ITT), 17 & 19 (ITT)
1st Overall [Tour de Georgia](#)
1st Stages 3 & 4
1st Stage 5 [Tour du Languedoc-Roussillon](#)
1st Stage 4 (ITT) [Volta ao Algarve](#)
1st [Profronde van Stiphout](#)
2005
1st Overall [Tour de France](#)
1st Stages 4 (TTT) & 20 (ITT)
1st Points classification [Critérium du](#)

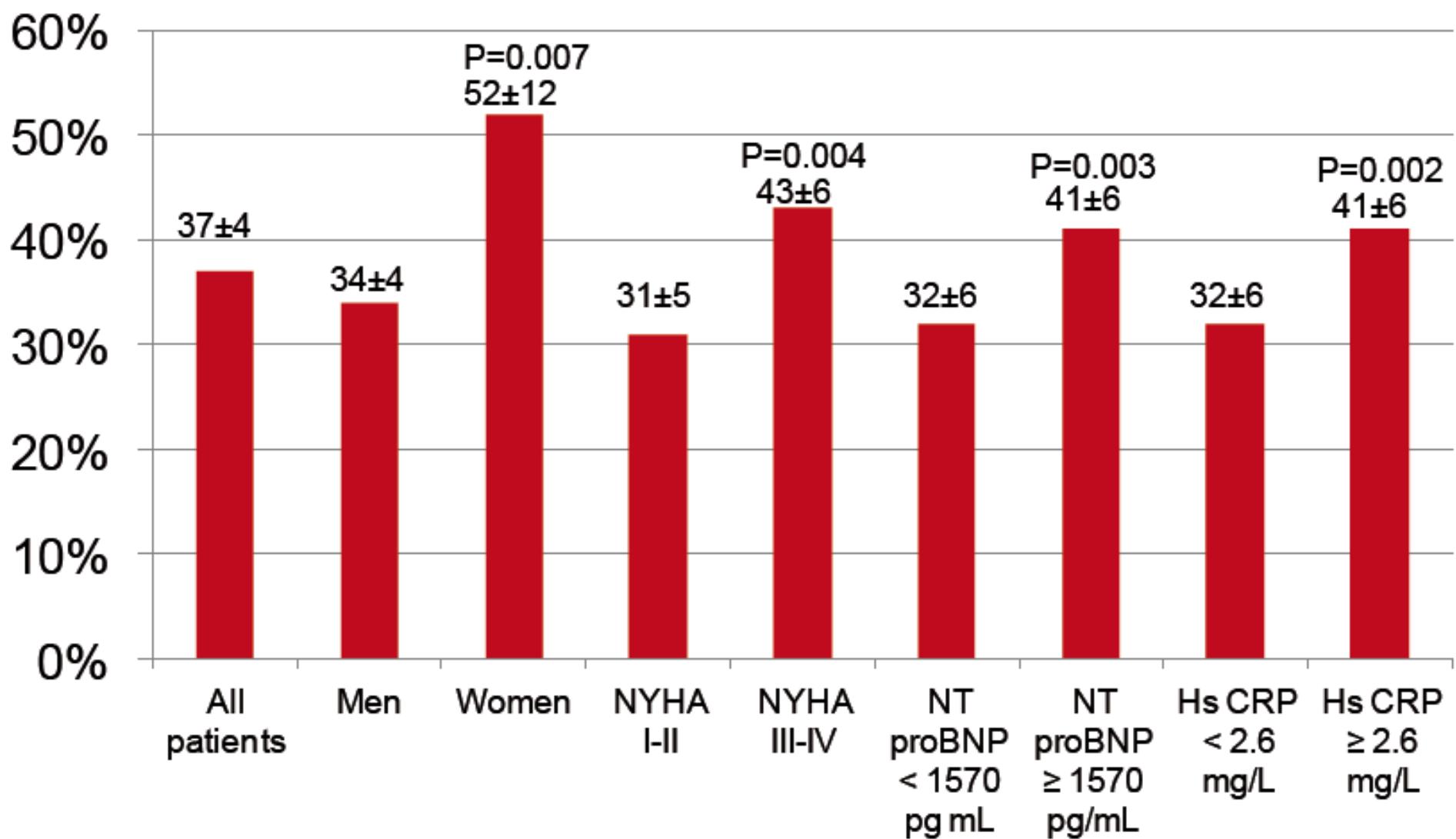


NON FISSARTI SUL PROBLEMA.....GUARDA OLTRE!!!

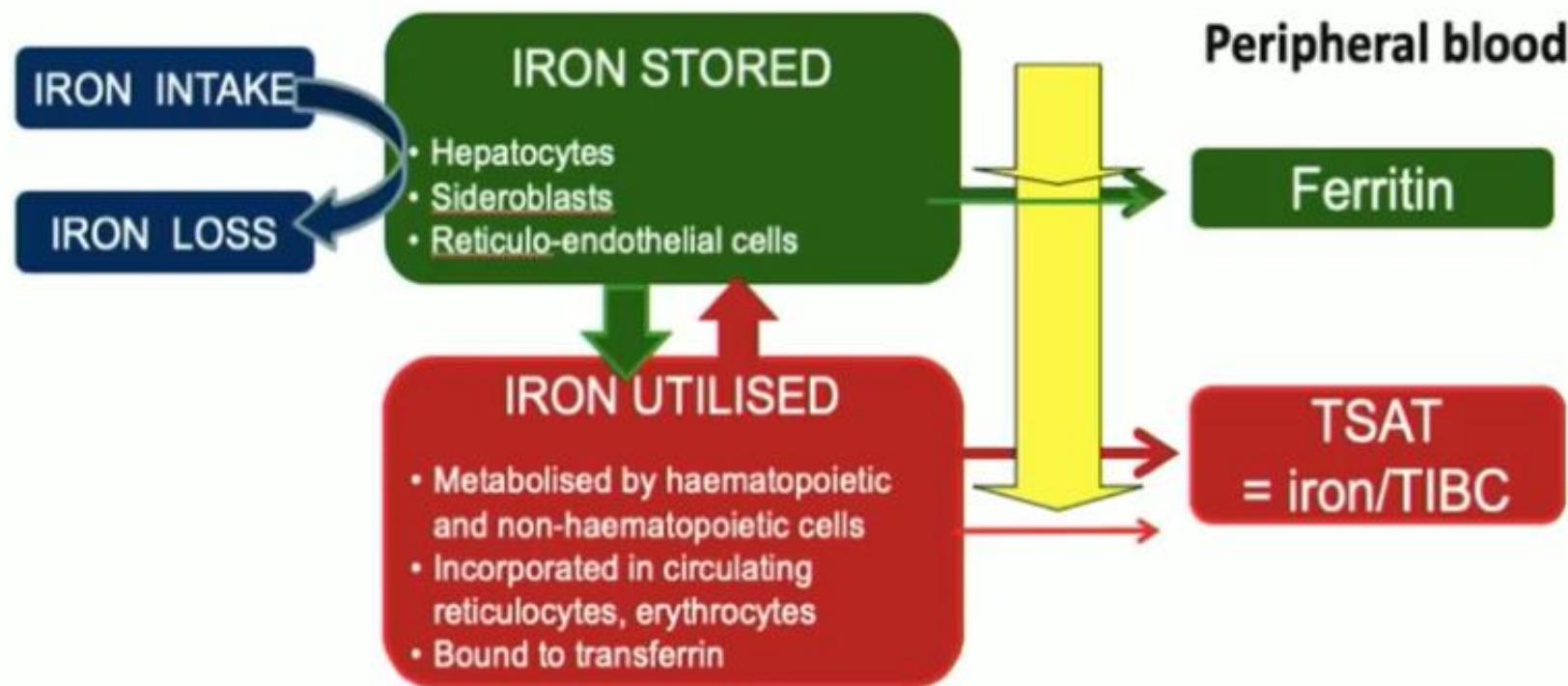
Iron Deficiency



Iron Deficiency: Prevalence in HF



Biomarkers of Iron Storage and Utilization



Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency

FAIR-HF

Anker et al New Engl J Med J 2009

Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency[†]

CONFIRM-HF

Ponikowski et al Eur Heart J 2015

Effect of Ferric Carboxymaltose on Exercise Capacity in Patients With Chronic Heart Failure and Iron Deficiency

EFFECT-HF

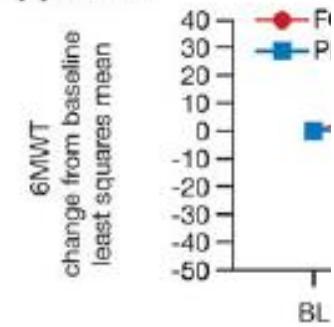
van Veldhuisen et al Circulation 2017

Which Patients?

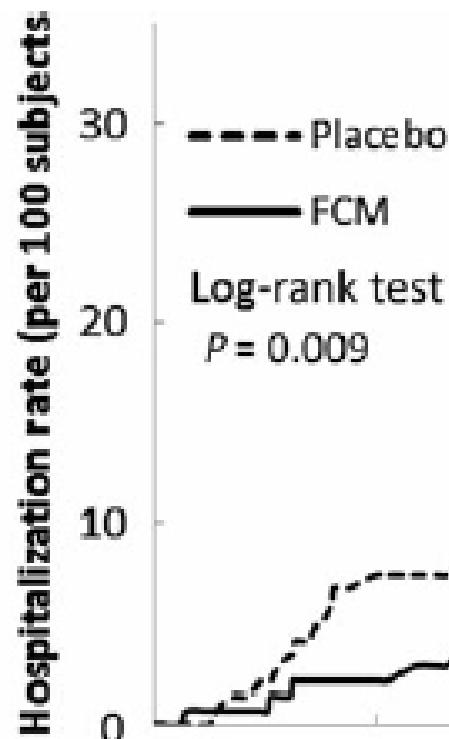
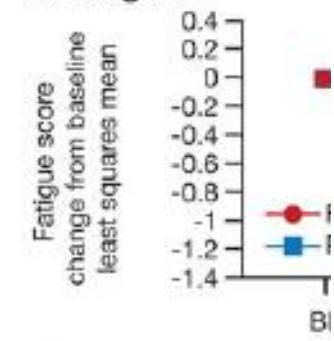
	FAIR-HF	CONFIRM-HF	EFFECT-HF
Inclusion criteria	≤40% NYHA II-III	≤45% NYHA II-III BNP	≤45% NYHA II-III BNP
Hb g/dL	9.5-13.5	< 15.0	<15.0
Iron Deficiency	Ferritin <100 Ferritin 101-299 + Tsat <20%	Ferritin <100 Ferritin 101-299 + Tsat <20%	Ferritin <100 Ferritin 101-299 + Tsat <20%
Treatment duration (w)	24	52	24
Endpoint	Self Reported NYHA 6MWT	6MWT NYHA QoL HF hosp	VO ₂ max CPET NYHA

CONFIRM-HF: Results

A 6MWT



B Fatigue



Placebo 151

138

127

117

78

FCM 150

140

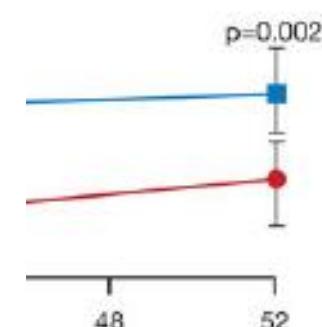
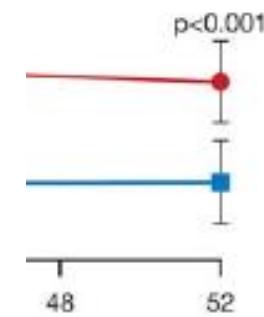
131

126

77

$p < 0.001$

$p = 0.002$



Methanalysis Ferric Carboximaltose in HF

HF hospitalisations and CV mortality

0.53 (0.33–0.86)

0.011

Outcomes	Total events, n (incidence per 100 patient-years of follow-up)	RR (95% CI)	P-value
	FCM pool (n = 504) Placebo pool (n = 335)		
HF hospitalisations	0.41 (0.23–0.73)	0.003	1
All-cause hospitalisations and all-cause mortality	-----	-----	-----
HF hospitalisations	22 (7.3)	43 (19.1)	0.003
CV hospitalisations	52 (17.4)	75 (33.3)	0.004
All-cause hospitalisations	89 (29.7)	99 (44.0)	0.056

CV hospitalisations

0.54 (0.36–0.83)

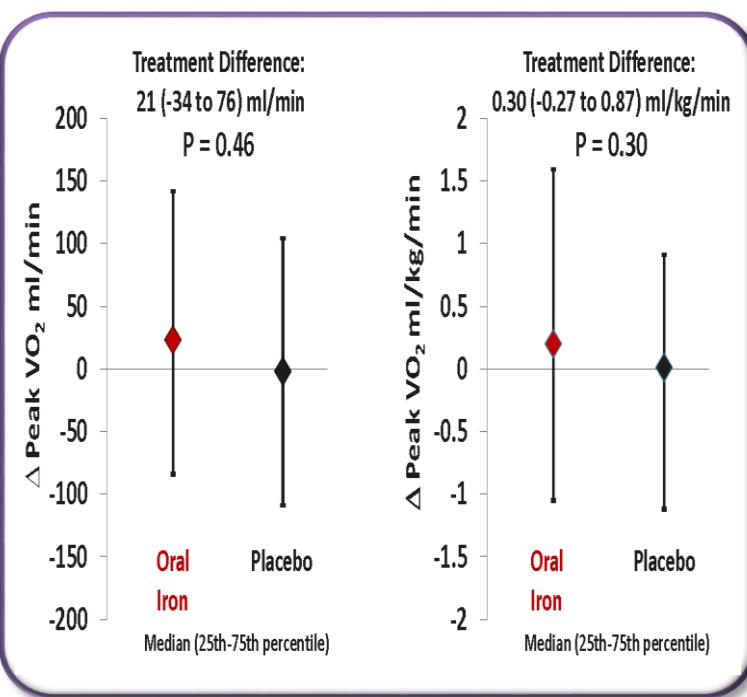
0.004

Effect of Oral Iron Repletion on Exercise Capacity in Patients with Heart Failure with Reduced Ejection Fraction and Iron Deficiency: the IRONOUT HF Randomized Clinical Trial

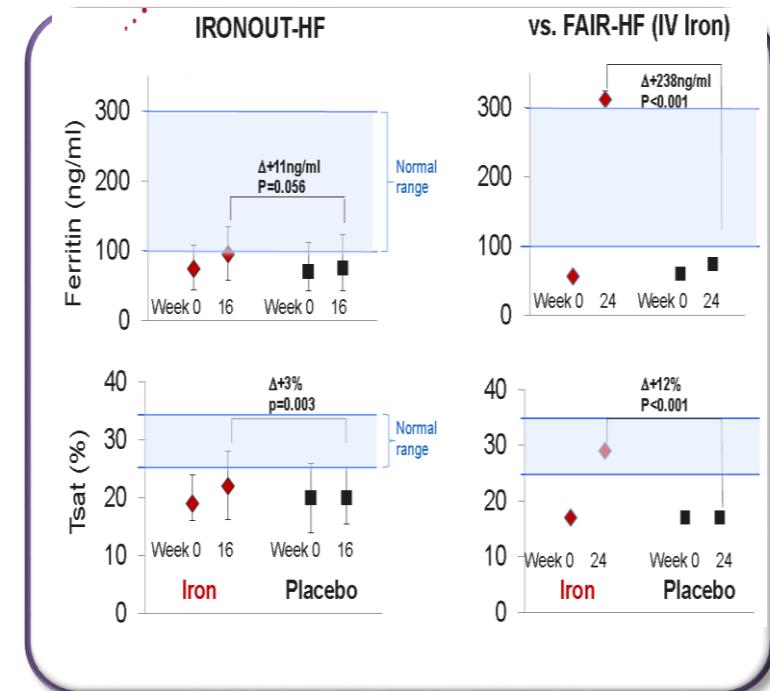
- LVEF <40%
- Iron deficiency:
 - Ferritin level 15-100 ng/ml
 - Ferritin 101-299 ng/ml and Tsat<20%
- Iron polysaccharide 150 mg bid fo 16 w
- Peak VO₂
- 6MWT, KCCQ; plasme NT-pBNP

IRONOUT-HF: results

Peak VO₂ from baseline to Week 16



Iron parameters compared to FAIR-HF (FCM)

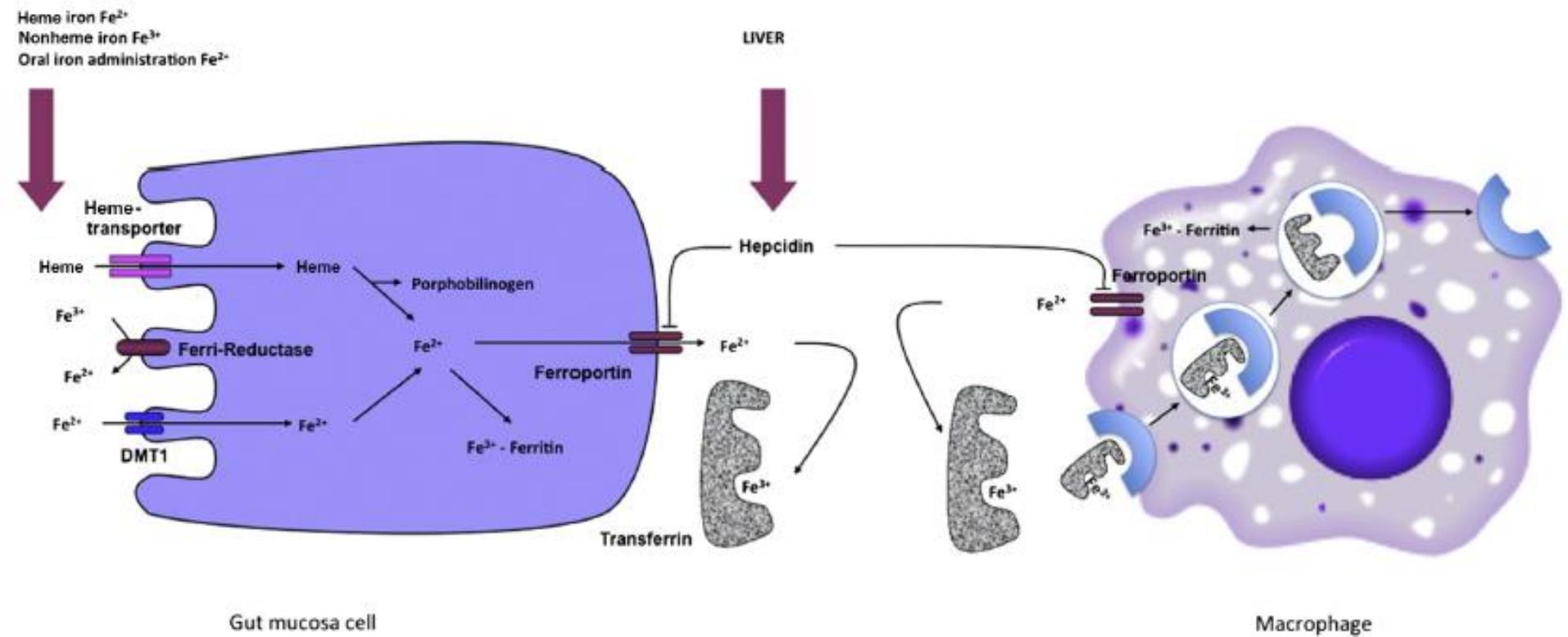


«These results do not support use of oral iron supplementation in patients with HFrEF»

IRON-OUT Results

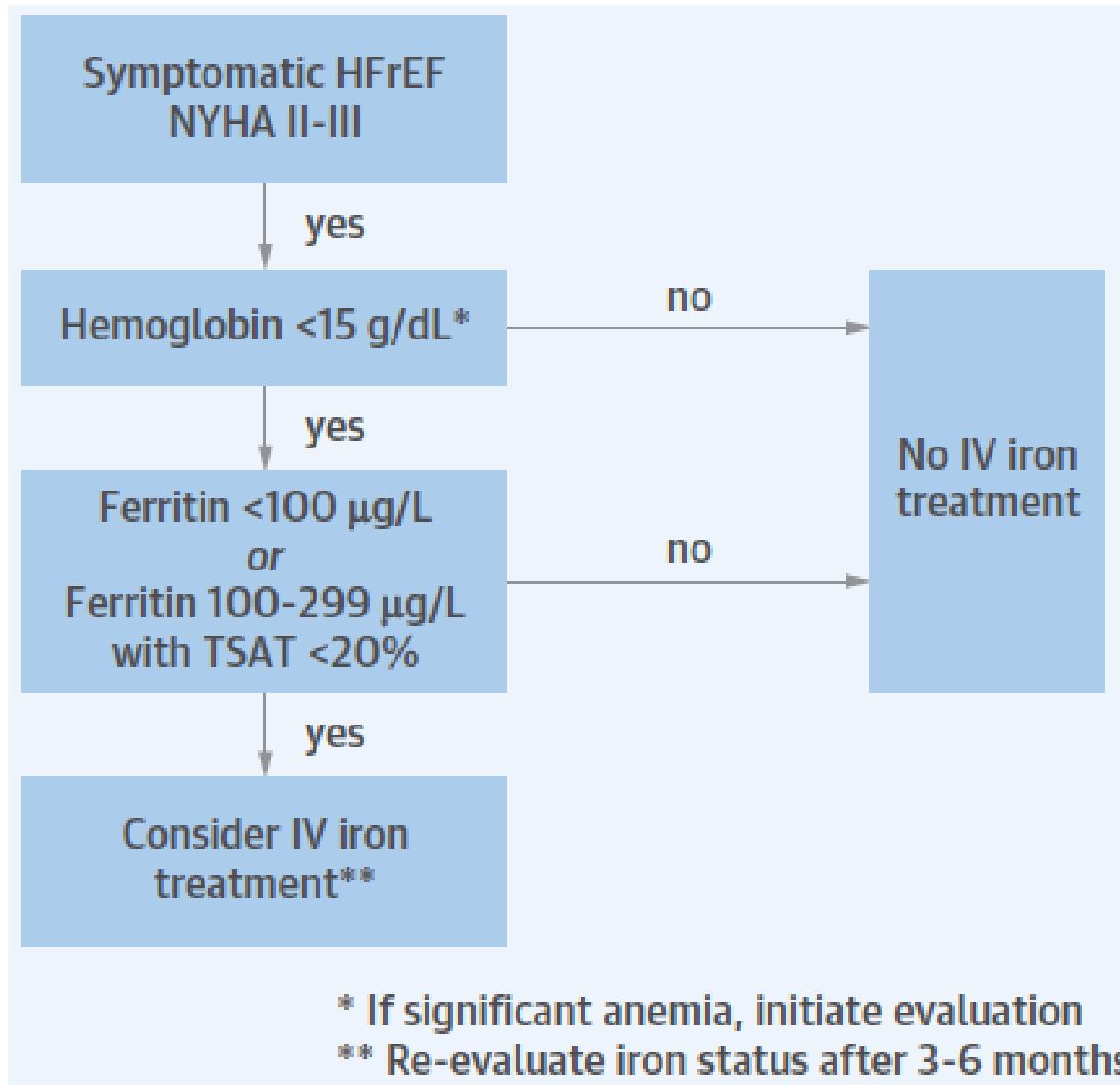
Endpoint	P value
Change Peak VO2	0.46
6MWT distance 8 w	0.95
6MWT distance 16 w	0.19
KCCQ	0.08
NT-pBNP	0.48
Death or CV hospitalization	0.64

Role of Hepcidin



Iron Deficiency in Heart Failure

An Overview



How much deficiency?

Ganzoni's Formula

Total iron deficit (TID) = Weight {kg} x (Target Hb – Actual Hb) {g/L} x 2.4 + Iron stores {mg}

How much deficiency?

Consider single doses of ferric carboxymaltose
(500–1000 mg iron) to correct iron deficiency*

Calculate total iron need using the table:

Haemoglobin		Patient body weight		
g/dL	mmol/L	<35 kg	35 kg to <70 kg	≥70 kg
<10	<6.2	500 mg	1500 mg	2000 mg
10 to <14	6.2 to <8.7	500 mg	1000 mg	1500 mg
≥14 to 15	≥8.7 to 9.3	500 mg	500 mg	500 mg

Conclusions

- Look at iron deficiency (not anemia) in all HFrEF patients
- Use ev ferric carboxymaltose
- Improve QoL and reduce HF hospitalization
- What if Armstrong used ferric carboxymaltose?