Effect of ferric carboxymaltose on functional capacity in patients with heart failure and iron deficiency (CONFIRM-HF)

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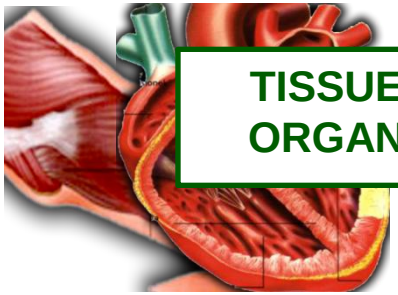
IRON IS CRITICAL FOR OPTIMAL FUNCTIONING AND SURVIVAL OF LIVING ENTITIES

CONSEQUENCES OF IRON DEFICIENCY

ORGANELLA CELLS

- MITOCHONDRIAL DYSFUNCTION
- DERANGED ACTIVITY OF ENZYMES
- ABNORMAL TRANSPORT AND STRUCTRAL PROTEINS
- CELLS DEATH – APOPTOSIS



TISSUES ORGANS

- TISSUE REMODELING
- IMPAIRED ORGAN EFFICACY

BODY POPULATIONS

- IMPAIRED EXERCISE CAPACITY
- REDUCED WORK EFFICACY
- IMPAIRED COGNITIVE PERFORMANCE AND BEHAVIOUR
- INCREASED MORBIDITY AND MORTALITY

Beard JL. J Nutr 2001
Dunn LL et al. Trends Cell Biol 2007
Anderson GJ & Vulpe CD. Cell Mol Life Sci 2009

Treatment of iron deficiency: Attractive therapeutic target in heart failure?

- Iron deficiency (ID) – frequent co-morbidity in stable HF and in patients admitted to hospital due to HF worsening
- HF complicated with ID – associated with impaired functional capacity, poor quality of life and increased mortality
- Deleterious consequences of ID in HF syndrome are irrespective of anaemia
- Correction of ID itself as an attractive therapeutic target in HF – hypothesis recently being tested in clinical studies

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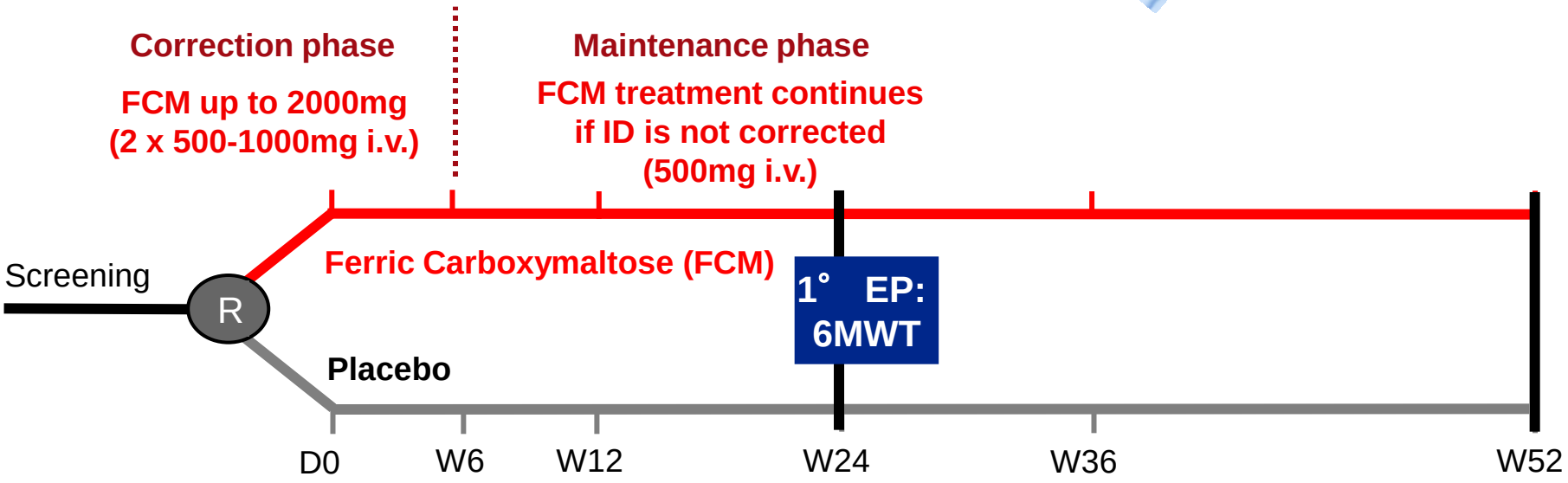
Study design

- **Design:** Multicentre, randomised (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 ng/mL or 100-300 ng/mL if TSAT <20%
  - ✓ Hb < 15 g/dL
- **Blinding:**
  - ✓ Clinical staff: unblinded and blinded personnel
  - ✓ Patients: usage of curtains and black syringes for injections



Ponikowski P et al. *ESC Heart Fail J* 2014, in press

Primary endpoint: change in 6-minutes walking test distance at Week 24

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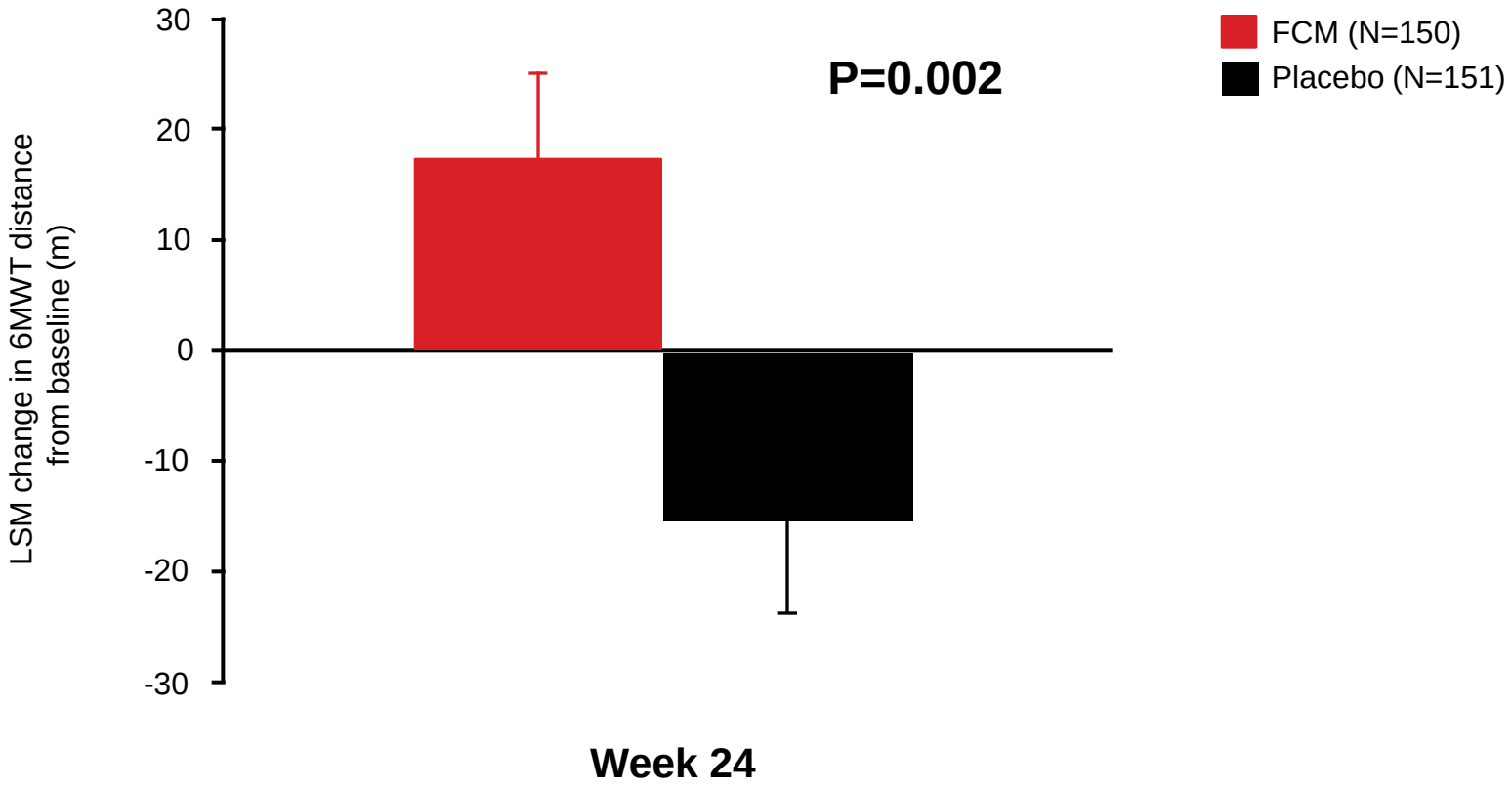
FCM improved 6MWT at week 24

FCM vs placebo: 33 ± 11 m *(least squares mean ± SE)*



Secondary endpoints: Changes in PGA & NYHA class over time

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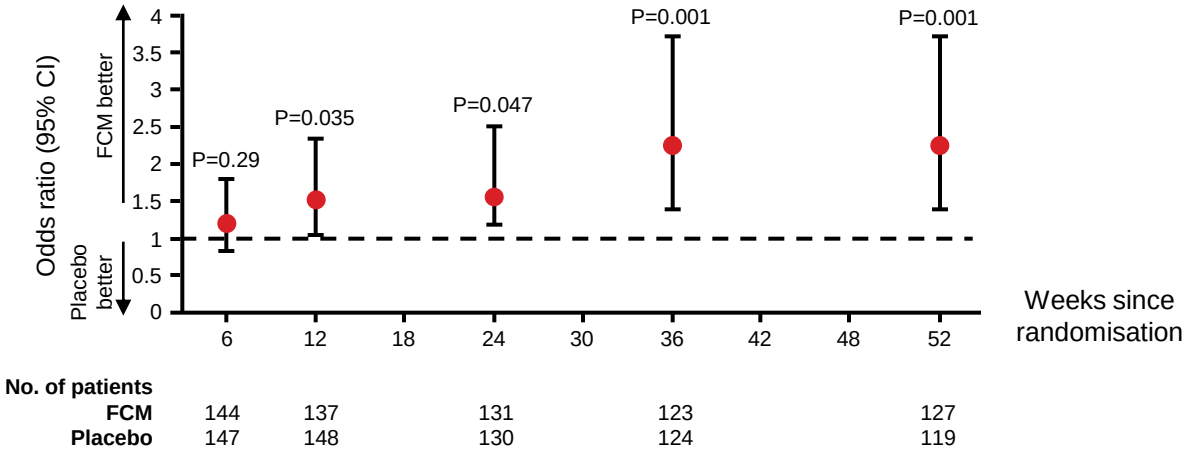
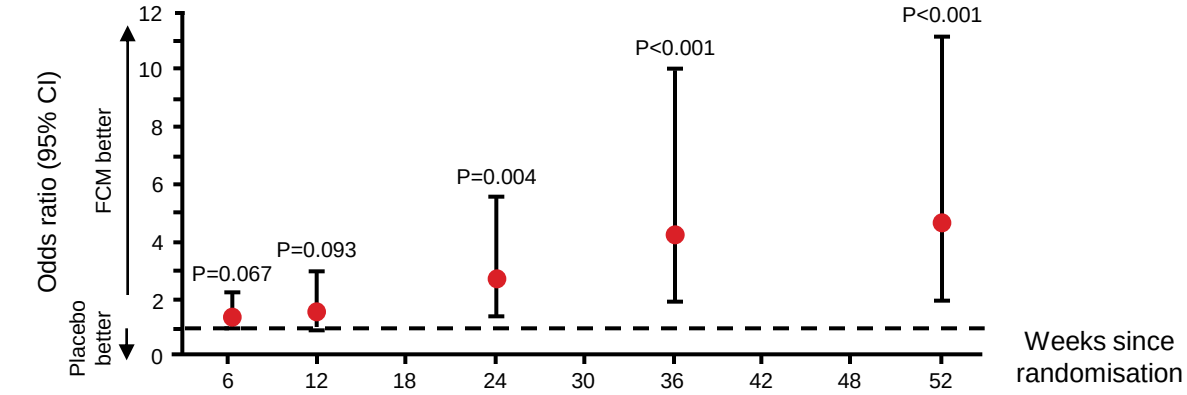
Self-reported Patient Global Assessment (PGA) score



No. of patients					
FCM	144	137	131	123	127
Placebo	147	148	130	124	119

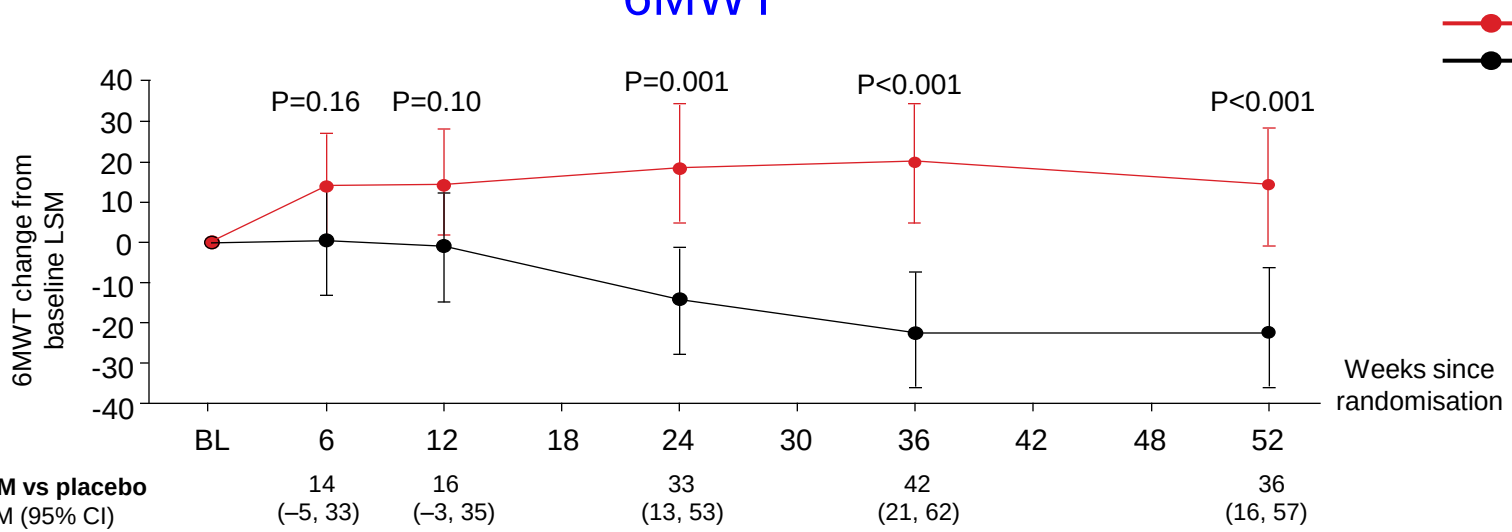
New York Heart Association Functional (NYHA) class



No. of patients					
FCM	144	137	132	123	127
Placebo	149	148	132	125	121

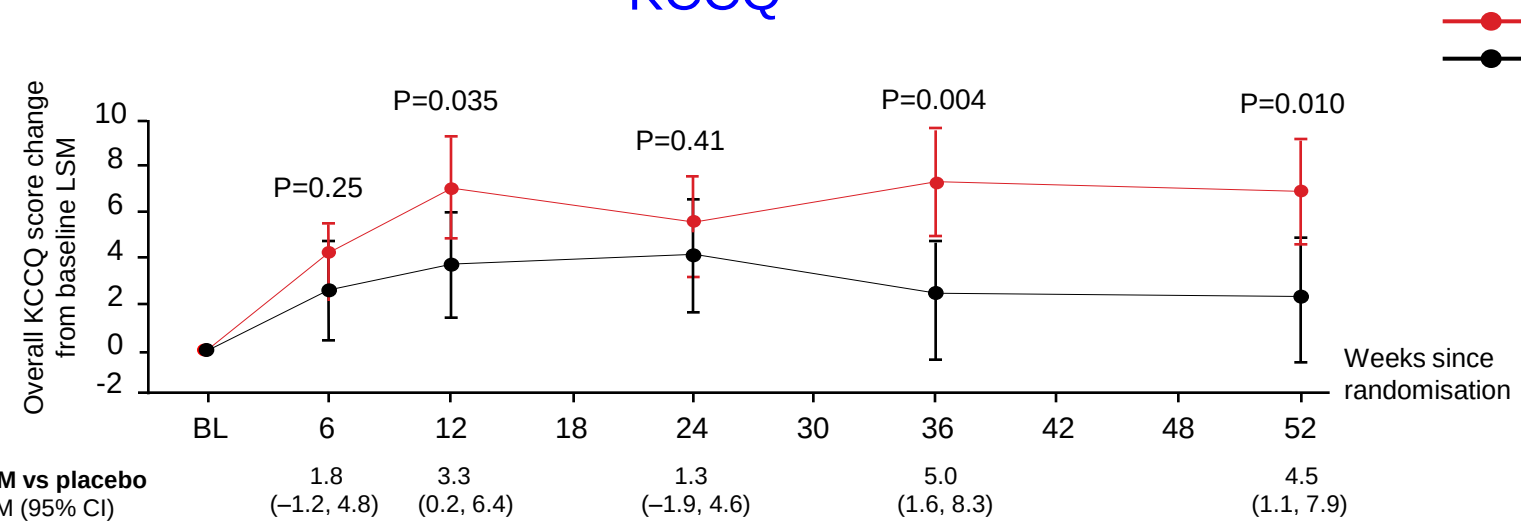
Secondary endpoints: Changes in 6MWT distance and QoL over time

6MWT



	BL	6	12	18	24	30	36	42	48	52
FCM vs placebo LSM (95% CI)		14 (–5, 33)	16 (–3, 35)		33 (13, 53)		42 (21, 62)			36 (16, 57)

KCCQ



	BL	6	12	18	24	30	36	42	48	52
FCM vs placebo LSM (95% CI)		1.8 (–1.2, 4.8)	3.3 (0.2, 6.4)		1.3 (–1.9, 4.6)		5.0 (1.6, 8.3)			4.5 (1.1, 7.9)

Secondary endpoints: Outcome events

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	FCM (N=150)		Placebo (N=151)			
End-point or event	**Total events (n)**	**Incidence/ (100 patient risk-year)**	**Total events (n)**	**Incidence/ (100 patient risk-year**	**Time to first event Hazard ratio 95% CI**	**P-value**
Death	12	12 (8.9)	14	14 (9.9)	0.89 (0.41 – 1.93)	0.77
Death for any CV reason	11	11 (8.1)	12	12 (8.5)	0.96 (0.42 – 2.16)	0.91
Hospitalisation	46	32 (26.3)	69	44 (37.0)	0.71 (0.45 – 1.12)	0.14
Hospitalisation for any CV reason	26	21 (16.6)	51	33 (26.3)	0.63 (0.37 – 1.09)	0.097
Hospitalisation due to worsening HF	**10**	**10 (7.6)**	**32**	**25 (19.4)**	**0.39 (0.19 – 0.82)**	**0.009**

FCM reduced the risk of recurrent hospitalisations due to worsening HF (post hoc):

Hazard Ratio (95% CI) – 0.30 (0.14-0.64), p=0.0019

Conclusions

In symptomatic patients with chronic heart failure and iron deficiency treatment with i.v. ferric carboxymaltose over one year period results in:

- **sustainable improvement in**
  - ✓ **functional capacity**
  - ✓ **symptoms**
  - ✓ **quality of life**
- **may reduce the risk of hospitalisations due to worsening heart failure**