

# **SUPPLEMENTAL MATERIAL**

**Table S1. Inclusion and exclusion criteria.**

<b>Inclusion criteria</b>
<ul style="list-style-type: none"><li>▪ Outpatients with chronic HF</li><li>▪ Older than 18 years</li><li>▪ NYHA II-III with optimal medical treatment in the last 4 weeks, without dose changes of HF treatment in the last 2 weeks (except for diuretics)</li><li>▪ NT-proBNP &gt;400 pg/mL</li><li>▪ LVEF &lt;50% in the last 12 months</li><li>▪ ID, defined as: serum ferritin &lt;100µg/L, or 100-299µg/L if TSAT &lt;20% and Hemoglobin &lt;15 g/dL</li><li>▪ Participants are willing and able to give informed consent for participation in the study</li></ul>
<b>Exclusion criteria</b>
<ul style="list-style-type: none"><li>▪ Known intolerance to FCM</li><li>▪ History of acquired iron overload</li><li>▪ Severe valve disease or cardiac surgery scheduled in the next 30 days</li><li>▪ ACS, TIA, or ictus in the 3 previous months</li><li>▪ CABG, major surgery, or cardiac, cerebrovascular or aortic percutaneous intervention (diagnostic angiography is allowed) in the 3 previous months</li><li>▪ Scheduled revascularization in the next 30 days</li><li>▪ Scheduled CRTD implantation in the next 30 days</li><li>▪ Active bleeding in the last 30 days</li><li>▪ Active infection or malignancy</li></ul>

- Immediate need for transfusion or hemoglobin  $\geq 15\text{g/dL}$
- Anemia for reasons other than ID
- Immunosuppressive therapy or dialysis
- History of treatment with erythropoietin, intravenous iron, or transfusion in the previous 12 weeks
- Treatment with oral iron at doses  $>100\text{mg/day}$  in the previous week
- Contraindications to MRI, including non-compatible pacemakers or defibrillators, cochlear implants, cerebral aneurysm clips, claustrophobia, or abdominal obesity not allowing the realization of the test due to a physical space problem.
- Pregnant or lactating women
- Subject of childbearing age who is unwilling to use adequate contraceptive measures during the study and up to 5 half-lives after the administration of study treatment
- Participation in another trial at the time of inclusion or in the previous 30 days
- Any disorder that compromises the ability to sign informed consent and/or comply with study procedures

ACS: acute coronary syndrome; CABG: coronary artery by-pass surgery, CRTD: cardiac resynchronization therapy device; HF: heart failure; NT-proBNP: amino-terminal pro-brain natriuretic peptide; FCM: ferric carboxymaltose, ID: iron deficiency; LVEF: left ventricle ejection fraction; NYHA: New York Heart Association; TIA: transient ischemic attack, TSAT: transferrin saturation.

**Table S2. Patients' characteristics by visit.**

Patients' characteristics	Baseline			7-day visit			30-day visit			Omnibus p-value
	Placebo (n=26)	Iron (n=27)	p-value	Placebo (n=26)	Iron (n=27)	p-value	Placebo (n=26)	Iron (n=27)	p-value	
CMR T1-mapping, msec	1071.5 (1030, 1116)	1082 (1052, 1122)	0.395	1071 (1038, 1112)	1064 (1048, 1095)	0.919	1068.5 (1040, 1088)	1081 (1066, 1109)	0.471	<0.001
CMR T2*, msec	37 (31, 42)	40 (34, 45)	0.217	39 (35, 42)	38 (35, 41)	0.644	38.5 (34, 45)	38 (36, 42)	0.769	0.001
CMR LVEF, %	36 (31, 45)	44 (36, 49)	0.242	39 (34, 49)	43 (35, 53)	0.365	40 (31, 46)	45 (38, 53)	0.129	0.017
6MWT, m	273 (228, 342)	312 (221, 383)	0.869	286.5 (240, 360)	306 (240, 362)	0.881	297.5 (264, 384)	312 (228, 372)	0.738	0.014
KCCQ, overall summary score	72.7 (54.3, 91.1)	75.0 (63.0, 92.2)	0.426	78.3 (53.6, 88.3)	82.3 (70.5, 94.3)	0.300	75.3 (51.0, 86.3)	84.4 (68.8, 91.7)	0.140	0.012
TSAT, %	15.4 (9.6, 20.0)	15.7 (12.0, 19.2)	0.472	15.0 (11.0, 21.7)	39.0 (27.0, 44.8)	0.001	14.8 (10.0, 20.0)	27.2 (23.0, 36.8)	<0.001	0.001
Ferritin, pg/mL	47.8 (23.0, 73.0)	73.0 (56.0, 94.0)	0.217	45.5 (21.0, 70.0)	944.0 (790.8, 1097.2)	<0.001	55.5 (29.3, 81.7)	447.0 (294.0, 599.9)	<0.001	<0.001

	114.0)	126.0)		109.0)	1356.0)		107.0)	632.3)		
Hemoglobin, g/dL	13.4 (12.7, 14.6)	13.1 (11.9, 13.4)	0.267	13.3 (12.6, 14.4)	12.6 (12.1, 13.6)	0.315	13.1 (12.3, 14.1)	13.1 (12.5, 14.2)	0.943	0.178
NT-proBNP, pg/mL	1213.5 (1010, 2667)	1990 (976, 2830)	0,960	1328.5 (821, 3268)	1790 (1009, 2973)	0,422	1409 (805, 2978)	2111 (858, 3122)	0.500	0.856

CMR: cardiac magnetic resonance; KCCQ: Kansas City Cardiomyopathy Questionnaire; LVEF: left ventricle ejection fraction; *NT-proBNP*: amino-terminal pro-brain natriuretic peptide; TSAT: transferrin saturation; 6MWT: 6-minute walking test.

Continuous values are expressed as median (interquartile range).