**Supplementary materials**

**Table S1 Study characteristics**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author and**  **Year** | **Treatment and Control** | **N** | **Mean Age**  **(year)** | **Female**  **(%)** | **Inclusion Criteria** | | | | | **Endpoints** | **Follow-**  **up** |
| **NYHA**  **class** | **LVEF**  **(%)** | **Hb**  **(g/dL)** | **Ferritin (μg/L)**  **and TSAT(%)** | **Others** |
| **Anker**  **2009[17]** | I.V. FCM 200 mg qd. | 304 | 67.8 ± 10.3 | 52.4 | II-III | 40% for NYHA II, 45% for NYHA III | 9.5-13.5 | ferritin< 100,  or 100-299  if TSAT < 20% |  | PGA，NYHA class,  6MWT distance，  EQ-5D score，  KCCQ score | 26  weeks |
| Placebo saline | 155 | 67.4 ± 11.1 | 54.9 |
| **Okonko**  **2008[21]** | I.V iron sucrose 200 mg qd. | 24 | 64.0 ± 14.0 | 29.2 | II-III | <45% | ＜14.5 | ferritin< 100,  or 100-300  if TSAT < 20% | PVO2 < 18ml/min/kg | PGA，NYHA class,  MLHFQ score,LVEF | 18  weeks |
| No treatment | 11 | 62.0 ± 11.0 | 27.3 |
| **Toblli**  **2007[23]** | I.V. iron sucrose 200 mg qd. | 20 | 76.0 ± 7.0 | NS | II-IV | <35% | Hb < 12.5 for men，  ＜11.5 for women | ferritin< 100 or TSAT< 20% | CrCL < 90ml/min | NYHA class,  MLHFQ score,LVEF | 6  months |
| Placebo saline | 20 | 74.0 ± 8.0 | NS |
| **Ponikowski 2015[22]** | I.V. FCM 500 or 1000 mg qd. | 150 | 69 ± 10 | 45 | II-III | <45% | ＜15 | ferritin< 100,  or 100-300  if TSAT < 20% | BNP＞100pg/ml,  NT-proBNP＞400pg/ml | PGA，NYHA class,  6MWT distance，  EQ-5D score，  KCCQ score | 52  weeks |
| Normal saline | 151 | 70 ± 9 | 49 |
| **Lewis**  **2017[20]** | P.O. iron polysaccharide | 111 | 63 | 40 | II-III | <40% | 9-15 for men，  9-13.5 for women | ferritin 15-100  or 100-299  if TSAT<20% |  | peak V˙O2,  6MWT distance，  KCCQ score | 16  weeks |
| Placebo | 114 | 63 | 32 |
| **Veldhuisen 2017[24]** | I.V. FCM | 86 | 63 ± 12 | 30 | II-III | <45% | ＜15 | ferritin< 100,  or 100-300  if TSAT < 20% | BNP＞100pg/ml,  NT-proBNP＞400pg/ml | PGA，peak VO2 ,  NYHA class | 24  weeks |
| No treatment.  Oral iron was allowed. | 86 | 64 ± 11 | 20 |

**Continued**

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| **Beck-da-**  **Silva 2013[19]** | I.V. Iron sucrose 200 mg qd. | 10 | 66.9 ± 8.3 | 33.3 | II-IV | <40% | NS | ferritin< 500 and TSAT< 20% |  | peak VO2 | 3  months |
| P.O. ferrous sulfate 200 mg qd. | 7 | 63.5 ± 16.2 | 25 |
| Placebo | 6 | 68.9 ± 10.1 | 33.3 |
| **Arutyunov 2009[18]** | I.V. iron sucrose 200 mg qd. | 38 | NS | NS | NS | NS | NS | NS |  | NS | 14  Weeks |
| I.V. FCM 200 mg qd. | 22 | NS | NS |
| NS | 19 | NS | NS |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Lita**  **2017[25]** | P.O. ferrous sulfate | 22 | NS | NS | NS | <50% | NS | Ferritin< 100 or 100-300 if TSAT< 20% |  | 6MWT distance | 3  months |
| Placebo | 19 | NS | NS |

**Table S2 Risk of bias assessment**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Random sequence generation** | **Allocation concealment** | **Blinding of participants and personnel** | **Blinding of outcome assessment** | **Incomplete outcome data** | **selective reporting** | **other bias** |
| **Anker 2009[17]** | low risks | low risks | low risks | low risks | low risks | low risks | unclear risks |
| **Okonko 2008[21]** | low risks | low risks | high risks | low risks | low risks | low risks | unclear risks |
| **Toblli 2007[23]** | low risks | unclear risks | low risks | low risks | low risks | low risks | unclear risks |
| **Ponikowski 2015[22]** | low risks | low risks | low risks | low risks | low risks | low risks | unclear risks |
| **Lewis 2017[20]** | low risks | low risks | low risks | low risks | low risks | low risks | unclear risks |
| **Veldhuisen 2017[24]** | low risks | high risks | high risks | low risks | low risks | low risks | unclear risks |
| **Beck-da-Silva 2013[19]** | low risks | low risks | low risks | low risks | low risks | low risks | unclear risks |
| **Arutyunov 2009[18]** | unclear risks | unclear risks | unclear risks | unclear risks | unclear risks | unclear risks | unclear risks |
| **Lita 2017[25]** | unclear risks | unclear risks | unclear risks | unclear risks | unclear risks | unclear risks | unclear risks |

Reference

[17]. Anker, S.D., et al., *Ferric carboxymaltose in patients with heart failure and iron deficiency.* N Engl J Med, 2009. **361**(25): p. 2436-48.

[18]. Arutyunov GP, B.N., Ivleva AY, Kobalava ZD., *The safety of intravenous (IV) ferric carboxymaltose versus IV iron sucrose in patients with chronic heart failure (CHF) and chronic kidney disease (CKD) with iron deficiency (ID).* European Journal of Heart Failure Supplements, 2009. **8**(2): p. Abstract 141.

[19]. Beck-da-Silva, L., et al., *IRON-HF study: a randomized trial to assess the effects of iron in heart failure patients with anemia.* Int J Cardiol, 2013. **168**(4): p. 3439-42.

[20]. Lewis, G.D., et al., *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.* JAMA, 2017. **317**(19): p. 1958-1966.

[21]. Okonko, D.O., et al., *Effect of intravenous iron sucrose on exercise tolerance in anemic and nonanemic patients with symptomatic chronic heart failure and iron deficiency FERRIC-HF: a randomized, controlled, observer-blinded trial.* J Am Coll Cardiol, 2008. **51**(2): p. 103-12.

[22]. Ponikowski, P., et al., *Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency.* European Heart Journal, 2014. **36**(11): p. 657-668.

[23]. Toblli, J.E., et al., *Intravenous Iron Reduces NT-Pro-Brain Natriuretic Peptide in Anemic Patients With Chronic Heart Failure and Renal Insufficiency.* Journal of the American College of Cardiology, 2007. **50**(17): p. 1657-1665.

[24]. van Veldhuisen, D.J., et al., *Effect of Ferric Carboxymaltose on Exercise Capacity in Patients With Chronic Heart Failure and Iron Deficiency.* Circulation, 2017. **136**(15): p. 1374-1383.

[25]. L.D. Suryani, S.B. Raharjo, R. Sagita et al. (2017) Oral iron therapy improves functional capacity of heart failure patients with iron deficiency anaemi. European Heart Journal Supplements 19, E17–E17

**Supplementary figure legend**

Figure S1 Forest plot showing the effect on the Quality of life parameters. (A) MLHFQ score (B)EQ-5D score.