Efficacy and safety of intravenous iron repletion in patients with heart failure: a systematic review and meta-analysis

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Introduction: AFFIRM-AHF and IRONMAN demonstrated lower rates of the combined endpoint recurrent heart failure (HF) hospitalizations and cardiovascular death (CVD) by using intravenous (IV) ferric carboxymaltose (FCM) and ferric derisomaltose (FDI), respectively in patients with HF and iron deficiency (ID) utilizing prespecified COVID-19 analyses.

Material and methods: We meta-analyzed efficacy, between trial heterogeneity and data robustness for the primary endpoint and CVD in AFFIRM-AHF and IRONMAN. As sensitivity analysis, we analyzed data from all eligible exploratory trials investigating FCM/FDI in HF.

Results: FCM/FDI reduced the primary endpoint (RR = 0.81, 95% CI 0.69-0.95, p = 0.01, I2 = 0%), with the number needed to treat (NNT) being 7. Power was 73% and findings were robust with fragility index (FI) of 94 and fragility quotient (FQ) of 0.041. Effects of FCM/FDI were neutral concerning CVD (OR = 0.88, 95% CI 0.71-1.09, p = 0.24, I2 = 0%). Power was 21% while findings were fragile with reverse FI of 14 and reversed FQ of 0.006. The sensitivity analysis from all eligible trials (n = 3,258) confirmed positive effects of FCM/FDI on the primary endpoint (RR = 0.77, 95% CI 0.66-0.90, p = 0.0008, I2 = 0%), with NNT being 6. Power was 91% while findings were robust (FI of 147 and FQ of 0.045). Effect on CVD was neutral (RR = 0.87, 95% CI 0.71-1.07, p = 0.18, I2 = 0%). Power was 10% while findings were fragile (reverse FI of 7 and reverse FQ of 0.002). Rate of infections (OR = 0.85, 95% CI 0.71-1.02, p = 0.09, I2 = 0%), vascular disorder (OR = 0.84, 95% CI 0.57-1.25, p = 0.34, I2 = 0%) and general or injection-site related disorders (OR = 1.39, 95% CI 0.88-1.29, p = 0.16, I2 = 30%) were comparable between groups. There was no relevant heterogeneity (I2>50%) between the trials for any of the analyzed outcomes.

Conclusions: Use of FCM/FDI is safe and reduces the composite of recurrent HF hospitalizations and CVD without benefit on CVD. Findings concerning composite outcomes exhibit a high level of robustness without heterogeneity between trials with FCM and FDI.