Ferric carboxymaltose in iron deficient heart failure patients: a meta-analysis of individual-patient data from randomised clinical trials

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BACKGROUND

Despite optimal conventional therapy, many patients with chronic heart failure (CHF) are subject to high rates of hospitalisations and mortality with no well-established evidence of public health benefits and problems. The relevance and importance of non-cardiac comorbidities in CHF patients has been recently developed. 1-4

Iron deficiency (ID) is one of the most common comorbidities occurring in approximately 50% of patients with CHF. 5 Iron plays a central role in the uptake, transport, storage and metabolism of oxygen, erythropoiesis, and cellular immune response. 6 At the cellular level, ID results in reduction of enzymatic activity of both the Krebs Cycle and respiratory chain in the mitochondria. As a consequence, ID leads to disturbance in the energetic metabolism of the cell. 5 In CHF patients, ID is associated with reduced exercise capacity, impaired quality of life (QoL) and poor prognosis. 1-5,6,7

CONIFMFH and FAIR-HF, two double-blind randomised, clinical trials (RCTs) have shown improvements in functional capacity, quality of life (QoL), and cognitive function in patients with ID when treated with an intravenous (i.v) ferric carboxymaltose (FCM). 8,9 However, only limited data is available on the effect on morbidity and mortality when treating ID with i.v. iron. 3,4

Data from all double-blind RCTs in patients with systolic HF and ID and which were completed up to December 2014 are included in this meta-analysis on individual patient data to explore the effect of i.v. FCM relative to placebo on hospitalisations and mortality.

METHODS

Individual patient data were extracted from four completed RCTs comparing FCM with placebo in CHF patients with ID. The primary outcome was the composite of cardiovascular (CV) hospitalisations and CV death. Secondary outcomes included specific causes of hospitalisation and all-cause death in addition to the individual composite components.

For each RCT, hospitalisations and cause of death were independently adjudicated in a blinded manner by an adjudication committee using the same pre-defined criteria described in a detailed characerisation.

Safety outcomes

Safety outcomes focused on the incidence and frequency of adverse events and on the MedDRA System Organ Classes (SOCs) Infections and Infestations, Gastrointestinal disorders and Neoplasms benign, malignant and unspecified, in addition to the occurrence of hypersensitivity reactions.

Statistical analysis

The primary efficacy outcome was defined as all-cause hospitalisations and all-cause death. Secondary outcomes included in this meta-analysis.

RESULTS

Efficacy outcomes

Table 2 shows the baseline characteristics and concomitant medications of the pooled data for patients randomly allocated to FCM or placebo.

Table 3 shows the effect of FCM relative to placebo on hospitalisations and mortality.

Safety outcomes

Table 4 shows the proportion which experienced at least one adverse event (AE) – with an incidence rate per 100 patient-years at risk for FCM and placebo that was similar.

Table 5 shows the investigator-reported adverse events, which were sub-grouped in this meta-analysis.

CONCLUSION

Treatment with FCM compared to placebo reduces the rate of CV hospitalisations and CV mortality in ambulatory patients with systolic CHF with ID. A well-designed and adequately powered RCT is needed to confirm these findings.

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REFERENCES