Heart Failure
More than 23 million people worldwide suffer from heart failure (HF), a progressively burdensome and debilitating condition\(^1\) with an increasing incidence and prevalence especially in the elderly (>10% prevalence).\(^2\) Despite advances in HF management, a diagnosis of HF carries a substantial risk of poor outcomes to include, hospitalisation and mortality; half of all patients diagnosed with HF will die with 4 years.\(^3\) HF is responsible for high rates of costly hospitalisations\(^4\) and around 1-2% of total healthcare expenditure in developed countries, with HF hospitalisations representing nearly 70% of these costs.\(^5\) Reducing the risk for cardiovascular hospitalisation and death remain a clinical priority in CHF.\(^6\)

Iron Deficiency in Heart Failure
Iron deficiency (ID) is a recognised comorbidity in chronic heart failure (CHF)\(^6\) and, in Europe, present in up to 50% of patients. ID, even in the absence of anaemia, is associated with high symptom burden, reduced exercise capacity, and impaired quality of life. In addition, ID is an independent risk factor for mortality.

ID therefore represents a modifiable risk factor where therapeutic intervention could provide benefit to patients and since 2012, the European Society of Cardiology Heart Failure has recommended the screening and diagnosis of ID in all patients suspected of having HF, with management a key component of overall patient care.\(^6\) ID is defined as ferritin <100 ng/mL, or ferritin 100-300 ng/mL if transferrin saturation (TSAT) <20%.
However, ID remains an under-diagnosed and under-treated co-morbidity of HF.\(^7\)

Meta-analysis Purpose and Design
Although several individual studies have evaluated intravenous (i.v.) iron therapy for ID in CHF, only studies with i.v. iron as Ferinject\(^8\) have delivered evidence supporting clinically meaningful improvements on exercise capacity, symptoms and quality of life.\(^8\)-\(^13\) One of these Ferinject\(^8\) studies, CONFIRM-HF, reported an associated reduction in hospitalisations due to HF across 301 patients when treated with Ferinject\(^8\) compared to placebo.\(^13\)

To further characterise Ferinject\(^8\) benefits on hospitalisation and mortality in ambulatory patients with systolic CHF and ID, a meta-analysis on individual patient data was performed using all the available data from 4 completed trials conducted in systolic CHF patients with ID (FER-CARS-01, FAIR-HF, EFFICACY-HF and CONFIRM-HF) which compared the i.v. iron therapy with Ferinject\(^8\) with placebo (saline). This analysis represents data from over 800 ambulatory patients with systolic CHF and ID.
All the trials were designed as double-blind, multi-centre, prospective, randomised trials and enrolled ambulatory patients with symptomatic CHF (NYHA class II/III) with left ventricular ejection fraction (LVEF) ≤ 45% and with the presence of ID (defined as ferritin < 100 ng/mL, or ferritin 100-300 ng/mL if transferrin saturation (TSAT) < 20%). A summary of these trials can be found in Table 1.

The primary efficacy outcome was the composite of all cardiovascular (CV) hospitalisations and CV deaths. Secondary outcomes included the composites: HF hospitalisation and CV death, CV hospitalisation and all-cause death and, HF hospitalisation and all-cause death in addition to the individual composite components. For all four studies, hospitalisations and cause of death were independently adjudicated in a blinded manner by an adjudication committee.

**Ferinject®**

Ferinject® (ferric carboxymaltose) is an innovative non-dextran intravenous (i.v.) iron replacement therapy discovered and developed by Vifor Pharma, a company of the Galenica Group. To date, Ferinject® has gained marketing authorisation in 68 countries worldwide for the treatment of iron deficiency where oral iron is ineffective or cannot be used. In many countries, intravenous iron replacement products are primarily used to treat dialysis patients. However, iron deficiency is also a complication of many other diseases. Vifor Pharma is evaluating new opportunities in the treatment of iron deficiency with Ferinject® in different therapeutic areas. Further clinical trials with Ferinject® in chronic kidney disease (CKD), oncology (anaemia in cancer patients), cardiology (chronic heart failure), patient blood management and women’s health are ongoing.