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RESEARCH ARTICLE

Impact of ferric carboxymaltose for iron deficiency at discharge after heart failure hospitalization: a European multinational economic evaluation

Phil McEwan[1]*, Cale Harrison[1], Rhona Binnie[1], Ruth D. Lewis[1], Alain Cohen-Solal[2], Lars H. Lund[3], Marcus Ohlsson[4], Stephan von Haehling[5], Josep Comin-Colet[6], Domingo A. Pascual-Figal[7], Sandra Wächter[8], Fabio Dorigotti[8], Antonio Ramirez de Arellano[9], Piotr Ponikowski[10], and Ewa A. Jankowska[11]

[1]Health Economics and Outcomes Research Ltd, Cardiff, UK; [2]Hospital Lariboisière, AP-HP, INSERM U948 MASCOT, Université Paris Cité, Paris, France; [3]Department of Medicine, Karolinska Institutet and Heart and Vascular Theme, Karolinska University Hospital, Stockholm, Sweden; [4]Department of Internal Medicine, Malmö University Hospital, Malmö, Sweden; [5]Department of Cardiology and Pneumology, University of Göttingen Medical Center and German Center for Cardiovascular Research (DZHK), Göttingen, Germany; [6]Cardiology Department, Hospital Universitari Bellvitge, University of Barcelona and IDIBELL, Barcelona, Spain; [7]Cardiology Department, Hospital Virgen de la Arrixaca, University of Murcia, Murcia, Spain; and Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; [8]CSL Vifor, Glattbrugg, Switzerland; [9]HEOR, CSL Vifor, Glattbrugg, Switzerland; [10]Institute of Heart Diseases, Wroclaw Medical University, Wrocław, Poland; and [11]Institute of Heart Diseases, University Hospital, Wrocław, Poland

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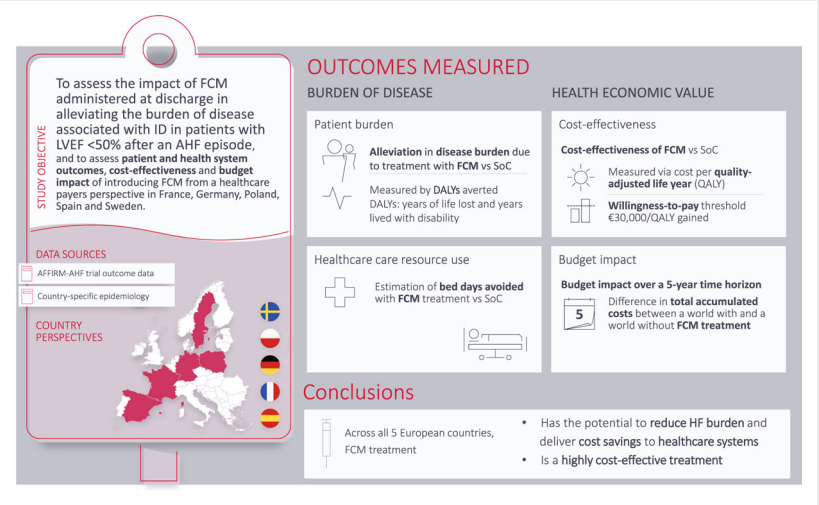
Aims Iron deficiency (ID) is comorbid in up to 50% patients with heart failure (HF) and exacerbates disease burden. Ferric carboxymaltose (FCM) reduced HF hospitalizations and improved quality of life when used to treat ID at discharge in patients hospitalized for acute HF with left ventricular ejection fraction <50% in the AFFIRM-AHF trial. We quantified the effect of FCM on burden of disease and the wider pharmacoeconomic implications in France, Germany, Poland, Spain and Sweden.

Methods and results The per country eligible population was calculated, aligning with the 2021 European Society of Cardiology (ESC) HF guidelines and the AFFIRM-AHF trial. Changes in burden of disease with FCM versus standard of care (SoC) were represented by disability-adjusted life years (DALYs), hospitalization episodes and bed days, using AFFIRM-AHF data. A Markov model was adapted to each country to estimate cost-effectiveness and combined with epidemiology data to calculate the impact on healthcare budgets. Between 335 (Sweden) and 13 237 (Germany) DALYs were predicted to be avoided with FCM use annually. Fewer hospitalizations and shorter lengths of stay associated with FCM compared to SoC were projected to result in substantial annual savings in bed days, from 5215 in Sweden to 205 630 in Germany. In all countries, FCM was predicted to be dominant (cost saving with gains in quality-adjusted life years), resulting in net savings to healthcare budgets within 1 year.

Conclusions This comprehensive evaluation of FCM therapy highlights the potential benefits that could be realized through implementation of the ESC HF guideline recommendations regarding ID treatment.

*Corresponding author. Health Economics and Outcomes Research Ltd, Rhymney House, Unit A Copse Walk, Cardiff Gate Business Park, Cardiff, CF23 8RB, UK. Tel: +44 2920 399146, Email: phil.mcewan@heor.co.uk

Graphical Abstract



Methods used to capture the burden of disease and pharmacoeconomic evaluation of ferric carboxymaltose (FCM). AHF, acute heart failure; ID, iron deficiency; HF, heart failure; LVEF, left ventricular ejection fraction; SoC, standard of care.

Keywords Ferric carboxymaltose • Heart failure • Iron deficiency • Burden of disease • Cost-effectiveness • Budget impact

Introduction

Heart failure (HF) remains a global public health problem, affecting 1–2% of the adult population in developed countries.[1] It is most common in the elderly and due to an ageing population HF incidence continues to rise.[1] The high prevalence and incidence of HF significantly impacts on healthcare expenditure, consuming around 1–2% of the total healthcare budget, with the highest proportion of costs due to hospitalization, drugs and interventions.[2] HF comorbidities also drive high healthcare costs, and result in increased mortality, morbidity and hospitalizations.[3]

Iron deficiency (ID), defined as serum ferritin <100 ng/ml or serum ferritin 100–299 ng/ml with transferrin saturation <20%, is frequently present in HF patients; in up to 55% of chronic HF and in up to 80% of acute HF (AHF).[1] ID may be present with or without anaemia, and prevalence of both anaemia and ID increase with higher New York Heart Association class.[4] ID may be absolute or functional and possible underlying causes in HF include: nutritional deficiencies, loss of blood through the gastrointestinal system, reduction in iron absorption, inflammation and chronic kidney disease.[5] Irrespective of the presence of anaemia, ID is an independent predictor of recurrent hospitalizations and mortality,[1,4] reduces exercise capacity,[1,5,6] and worsens quality of life (QoL) in HF patients.[7]

The burden of ID in HF highlights an unmet clinical need in these patients and the requirement for a new treatment strategy in this patient population. Ferric carboxymaltose (FCM), provided as intravenous (IV) iron therapy, has been recommended by the European Society of Cardiology (ESC) for consideration for the treatment of ID in HF patients to alleviate symptoms, improve exercise capacity and QoL and reduce HF rehospitalizations.[1] Based on an extensive clinical trial programme, FCM has been shown to be well tolerated and effective in improving symptoms, exercise capacity and QoL in HF patients with ID. In the AFFIRM-AHF trial, treatment of ID with FCM has been demonstrated to reduce the risk of HF hospitalizations, with no apparent effect on cardiovascular (CV) mortality, in patients with left ventricular ejection fraction (LVEF) <50% stabilized after an episode of AHF.[8]

Using data from AFFIRM-AHF, this study aimed to assess the impact of FCM administered at discharge in alleviating the burden of disease associated with ID in patients with LVEF <50% after an AHF episode, and to assess patient and health system outcomes, cost-effectiveness and budget impact of introducing FCM from a healthcare payers perspective in five European countries: France, Germany, Poland, Spain and Sweden.

Methods

An illustrative summary of the methods used to capture the burden of disease and pharmacoeconomic evaluation of FCM is provided in the *Graphical Abstract*.

AFFIRM-AHF trial design and patient population

AFFIRM-AHF (NCT02937454) was a randomized, double-blind, placebo-controlled trial which assessed the efficacy of IV FCM for the treatment of ID in adults hospitalized for AHF with LVEF <50% and stabilized after treatment with at least 40 mg IV furosemide (or equivalent).[9] Patients received either FCM or placebo shortly before discharge, with a second dose at week 6 and up to two subsequent doses if clinically indicated until week 24. Follow-up was for 52 weeks. The rate ratio for the primary endpoint, a composite of CV death and total HF hospitalizations was 0.79 (95% confidence interval 0.62–1.01; $p = 0.059$). In the present analysis, AFFIRM-AHF trial outcome data were used to perform a multinational analysis to explore and predict the impact of FCM treatment compared to standard of care (SoC) on burden of disease, cost-effectiveness and budget impact in five country settings: France, Germany, Poland, Spain and Sweden. The placebo arm of AFFIRM-AHF was assumed to represent SoC. Treatment efficacy and the incidence of events and adverse events (AEs) were assumed as equivalent across all countries; over 60% of trial participants were enrolled from Europe and therefore were assumed to be generalizable across country settings. Baseline characteristics used in the modelling have been reported previously.[10]

Eligible population

The eligible population was defined by the inclusion criteria of AFFIRM-AHF[8] and aligned with the 2021 ESC guidelines: ID patients discharged after an episode of AHF with LVEF <50%.[1] A targeted literature review was undertaken in order to determine an estimate of the incident population eligible for FCM treatment per country setting (see online supplementary *Appendix S1* for further information). Calculation of the eligible population for each country is shown in supplementary *Table S1* and summary of epidemiology inputs sourced are shown in supplementary *Tables S2* and *S3*.

Burden of disease analyses

This study considered two components of disease burden. The first quantified the clinical burden on patients, represented by disability-adjusted life years (DALYs). DALYs were calculated as a composite of years of life lost (YLL) due to premature mortality and years lived with disability (YLD). AFFIRM-AHF data were used to simulate monthly mortality for each study arm, with country-specific life expectancy data for the general population at the age of death used to calculate YLL. Disability weights specific to ID were not available, therefore the effect of treatment of ID in the eligible population was estimated using disability weights for HF, stratified by severity. Disability weights for patients receiving SoC were estimated as the average of the weights for patients with moderate and severe HF, with the improvement in QoL due to treatment with FCM represented by an average of improvements by one severity class.[11] These disability weights were applied to the total number of living patients and the average duration of disability used to calculate YLD for each study arm. The impact of uncertainties around these assumptions for disability weights was explored in scenario analysis. Additional scenario analyses were conducted on the upper and lower bounds of the eligible population estimates as described above.

The second component of disease burden considered healthcare resource use at the country system level. Differences in length of stay (LOS) and total hospitalization for HF (HHF) events during first year between treatment arms reported in AFFIRM-AHF were used to derive estimations of hospital bed days avoided through FCM treatment compared to SoC within each healthcare system.

Cost-effectiveness modelling

The cost-effectiveness model (CEM) has been described previously[10] and is summarized in online supplementary *Appendix S1*. To adapt the CEM for each setting, country-specific life tables were used to extract CV death proportions from overall mortality curves, and country-specific event costs and AE costs were also applied (online supplementary *Table S4*). No data were identified to inform healthcare resource use stratified by Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score quartile, therefore a country-specific background HF management cost was applied equally across health states. In the case of Spain, a review of sources returned differing estimations of background HF costs. Therefore, the Spanish base case used an average of the figures reported for primary care visits and background HF medication to account for differences in included healthcare resource cost components between input estimates and the impact of this assumption was explored in scenario analysis.

Ferric carboxymaltose acquisition costs were calculated using the average dosage of 1354 mg from AFFIRM-AHF, by applying 1000 mg and 354 mg infusions in the first- and second- month cycles, respectively. FCM acquisition costs for each country setting were derived from the literature for France,[12] Germany[13] and Spain.[14] Published FCM costs for Poland and Sweden could not be identified; these were supplied by CSL Vifor.

Standard of care was assumed to have no associated costs. All direct medical costs were indexed to 2021 prices. Currency conversion using local exchange rates was applied where relevant to express all prices in Euros. Country-specific annual discount rates were also applied: Germany, Spain, and Sweden, 3%; France, 4% for the first 30 years and 2% thereafter; and Poland, 5% (costs) and 3.5% (benefits).[15]

The primary outcome measure of the CEM was the incremental cost-effectiveness ratio (ICER), calculated as the cost per life year or quality-adjusted life year (QALY) gained. A uniform willingness-to-pay threshold of €30 000/QALY gained was used for all countries. Analysis was performed from the payer perspective.

Budget impact modelling

The budget impact of FCM treatment within each healthcare system was estimated across a time horizon of up to 5 years, calculated as the difference in total accumulated costs between a world with versus world without FCM treatment, based on the predicted eligible population within each country setting (vide infra). The analysis was performed from the payer perspective.

Country-specific costs, as described for the CEM, were calculated as the aggregate total costs of drug acquisition, hospitalization events, AEs and CV deaths over the period.

Market share growth proportions were implemented to replicate predicted annual uptake of FCM treatment, with applied market figures validated by an expert panel (online supplementary *Table S5*). A more conservative estimate of FCM market shares for each country was evaluated in scenario analysis.

Sensitivity analysis

Sensitivity analysis tested the robustness of model assumptions and application of key parameters within the models, including drug and

event costs, clinical efficacy and survival inputs, and target population epidemiology values. Deterministic sensitivity analyses (DSA) were conducted to demonstrate the impact of individual input values, by varying the parameter value (mean) applied in the base case: upper bound +20% and lower bound −20%. Probabilistic sensitivity analysis (PSA) was performed with 1000 runs, whereby each parameter was varied according to respective distribution around the point estimate.

Results

Estimation of population eligible for ferric carboxymaltose treatment

The base case population comprised patients hospitalized for AHF with LVEF <50% with concomitant ID. The eligible patient population for FCM treatment was estimated as follows: 71 770 in France; 197 919 in Germany; 72 727 in Poland; 44 863 in Spain; and 5019 in Sweden. These populations were used to calculate the magnitude of the country-specific burden of disease and the predicted impact on healthcare budget of introducing FCM treatment.

Ferric carboxymaltose is predicted to reduce burden of disease

Comorbid ID is associated with worse prognosis, functional capacity and QoL, exacerbating the burden of disease in patients with HF. Treatment with FCM was predicted to result in a reduction in annual DALYs across all populations: 5055 for France; 13 238 for Germany; 4203 for Poland; 3142 for Spain; and 335 for Sweden, representing a reduction in the burden of disease (*Table 1*, *Figure 1A*, *B*).

The burden of disease can also be considered in terms of impact on healthcare resource use. In AFFIRM-AHF, FCM treatment was associated with a shorter LOS upon instances of HHF (3.8 vs. 6.2 days) and a reduction in the number of subsequent HHF.[8] Across all countries FCM treatment was predicted to result in 63.8 hospitalizations being avoided per 1000 population, over 1 year, compared to SoC. This corresponds to 4581 hospitalizations avoided annually in France; 12 633 in Germany; 4642 in Poland; 2912 in Spain; and 321 in Sweden (*Figure 1C* and online supplementary *Table S6*). The averted hospitalizations and reported shortened LOS associated with FCM treatment result in an improvement of hospital capacity: an avoided total 74 566 in France in the first year; 205 630 in Germany; 75 561 in Poland; 47 398 in Spain; and 5215 in Sweden (*Figure 1D*).

The scenario analysis around epidemiology figures varied prevalences of LVEF <50% and ID within the AHF population to assess the impact on scale of burden outcomes, while variation around the disability weights evaluated the impact on YLD. Variation in ID proportions was demonstrated to have a larger influence on DALY and hospitalization output in terms of epidemiology figures, while disability weights affecting the untreated population was the dominating parameter overall. Scenario output is listed in online supplementary *Table S7*.

Ferric carboxymaltose is projected to be highly cost-effective

The base case results indicated that FCM was not only cost-effective but dominant (more effective and less costly) compared to SoC in all country settings over a lifetime horizon (*Table 2*). In comparison to SoC, FCM treatment was associated with a QALY gain and cost savings of 0.430 and €597 in France; 0.444 and €173 in Germany; 0.419 and €390 in Poland; 0.448 and €80 in Spain; and 0.430 and €703 in Sweden (*Table 2*). These cost savings were predominantly due to fewer HHF events in patients receiving FCM. Disaggregated results can be found in online supplementary *Table S8*. Scenario analysis was performed to investigate the impact on the results of uncertainty around the background HF cost in Spain. The application of the upper bound estimate of primary care and HF medication costs returned an ICER of €652/QALY gained, meaning that at the upper bound FCM is predicted to remain highly cost-effective (online supplementary *Table S9*).

Table 1 Components of disability-adjusted burden of disease outcomes at 1 year across eligible incident population

Component	France			Germany			Poland			Spain			Sweden		
	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ
Per 1000 population															
YLD	15	30	−15	15	30	−15	15	30	−15	15	30	−15	15	30	−15
YLL	767	822	−55	718	769	−52	591	633	−43	745	799	−54	716	767	−51
DALYs averted	782	852	−70	732	799	−67	606	663	−58	760	829	−69	730	797	−67
Per eligible population															
YLD	1057	2153	−1096	2916	5938	−3022	1071	2182	−1111	672	1369	−697	74	151	−77
YLL	55 046	59 006	−3959	142 016	152 231	−10 215	42 979	46 071	−3091	34 002	36 448	−2446	3591	3850	−258
DALYs averted	56 104	61 159	−5055	144 931	158 169	−13 238	44 050	48 253	−4203	34 674	37 816	−3142	3665	4000	−335

DALY, disability-adjusted life year; FCM, ferric carboxymaltose; YLD, years lived with disability; YLL, years of life lost; SoC, standard of care.
Incremental represents the possible averted outcomes by use of FCM.

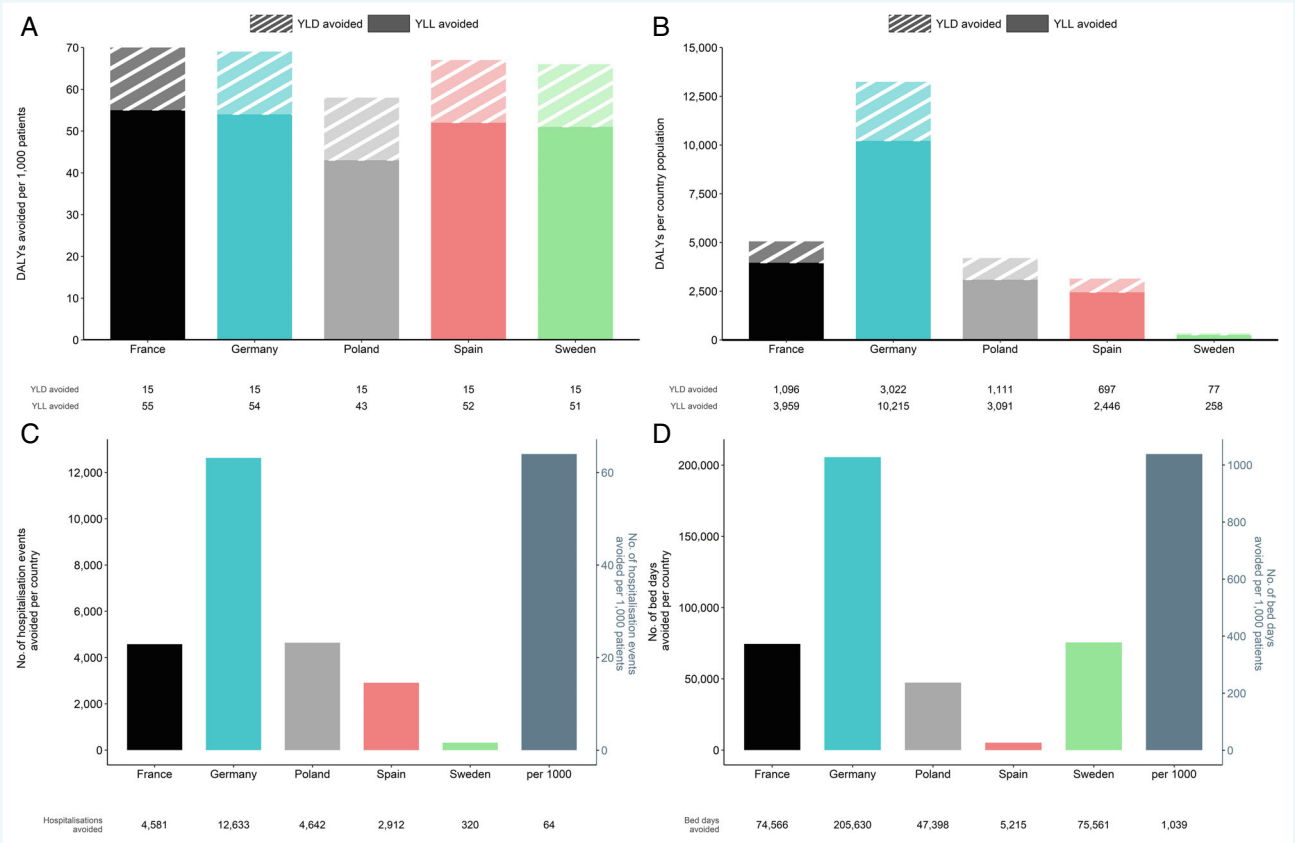


Figure 1 Effect of ferric carboxymaltose (FCM) treatment in reducing the burden of disease for patients and the healthcare system. (*A*) Disability-adjusted life years (DALYs) avoided associated with FCM treatment per 1000 people by country. (*B*) DALYs avoided associated with FCM treatment per country. (*C*). Avoided hospitalization events associated with FCM treatment per country population and per 1000 population. (*D*) Avoided bed days associated with FCM treatment per country and per 1000 people. All projections are for the first year of treatment. YLD, years lived with disability; YLL, years of life lost.

Table 2 **Ferric carboxymaltose is predicted to be dominant in all country settings**

	France			Germany			Poland			Spain			Sweden		
	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ
Costs (€)	18 091	18 688	−597	29 332	29 505	−173	7357	7748	−390	15 086	15 166	−80	13 669	14 373	−703
LYs	4.238	3.755	0.483	4.266	3.764	0.502	4.165	3.695	0.470	4.284	3.776	0.508	4.235	3.753	0.482
QALYs	2.962	2.531	0.430	2.981	2.537	0.444	2.910	2.491	0.419	2.994	2.545	0.448	2.959	2.530	0.430
ICER (cost/LYG)	Dominant			Dominant			Dominant			Dominant			Dominant		
ICER (cost/QALY gained)	Dominant			Dominant			Dominant			Dominant			Dominant		

FCM, ferric carboxymaltose; ICER, incremental cost-effectiveness ratio; LY, life year; LYG, life years gained; QALY, quality-adjusted life year; SoC, standard of care.
A dominant result indicates that FCM is predicted to be associated with both cost savings and LY or QALY gains.

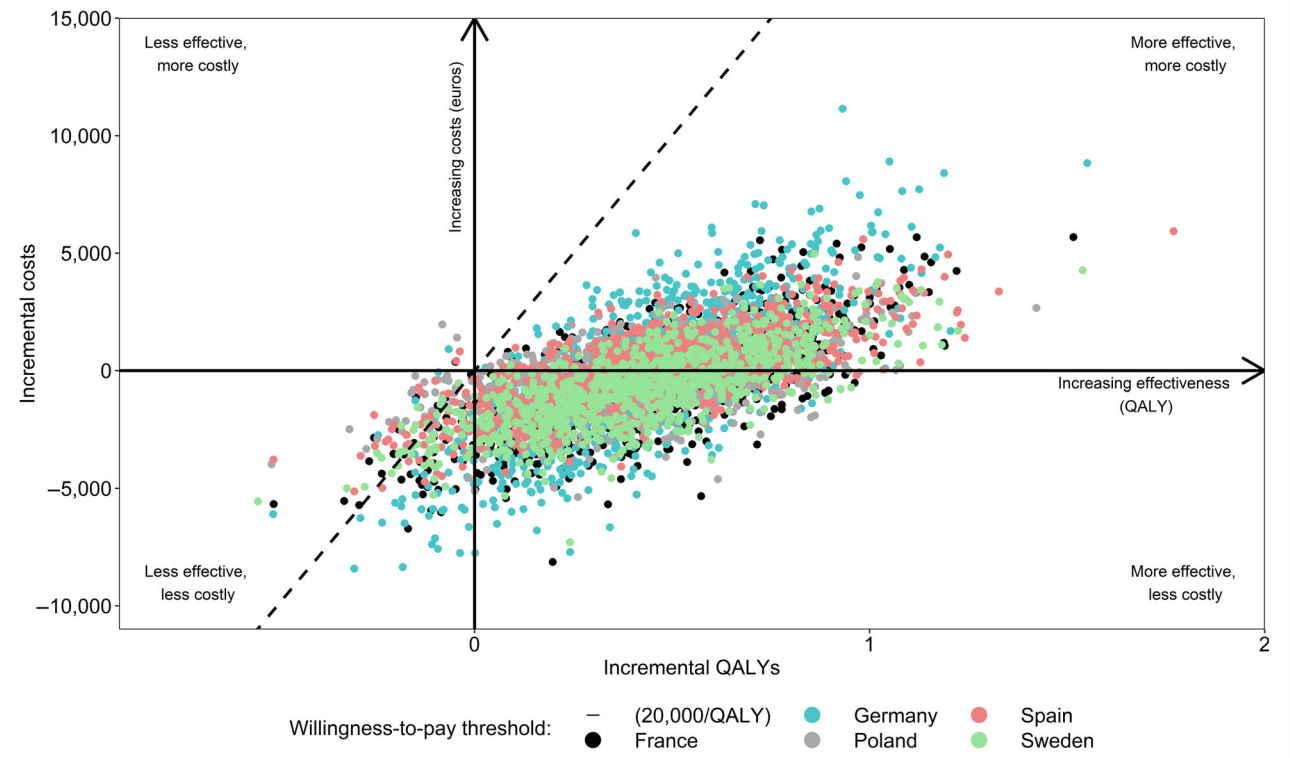


Figure 2 Cost-effectiveness plane based on probabilistic sensitivity analysis. Cost-effectiveness plane showing incremental costs and benefits associated with ferric carboxymaltose treatment for each country. Inset illustrates outcome by quadrant. QALY, quality-adjusted life year.

The two most influential parameters in the DSA were background costs and the discount rate for cost (online supplementary *Table S10*). Increasing background costs to 120% of the mean, or using 0% discounting for costs, resulted in ICERs which were cost-effective, rather than dominant, in Germany and Spain. Variation across all other parameters and in other country cases returned dominant results, indicating that the cost-effectiveness results are robust to uncertainty in the input parameters. PSA indicated that the probability that FCM is cost-effective at €30 000/QALY gained is 96.9%, 96.2%, 98.3%, 96.3% and 95.7% in France, Germany, Poland, Spain and Sweden, respectively (*Figure 2*). Costs and benefits generated in PSA for each country are presented in online supplementary *Table S11*. Cost-effectiveness planes and cost-effectiveness acceptability curves are depicted for each country in online supplementary *Figures S1–S10*.

Introduction of ferric carboxymaltose is predicted to provide net savings to healthcare budgets

Overall the net budget impact of introducing FCM, versus no FCM, in France, Germany, Poland, Spain and Sweden over 5 years resulted in cost savings of €49 767 439 in France; €81 319 417 in Germany; €9 120 523 in Poland; €2 011 304 in Spain; and €2 347 447 in Sweden (*Table 3*, *Figure 3*). The large discrepancy in cost savings observed between France or Germany versus Poland, Spain or Sweden is due to differences in overall population size, percentage market share, cost of FCM and event costs between countries, impacting cumulative incremental costs.

The market share for the scenario analysis was set at 5% for year 1, 10% for year 2, 15% for year 3, 20% for year 4%, and 25% for year 5. From cumulative budget impact, at year 5 savings were made: €14 563 903 in France; €53 017 792 in Germany; € 4 560 262 in Poland; €469 562 in Spain; and €1 076 775 in Sweden (online supplementary *Table S12*).

Across all countries, the cost of FCM in the first month was one of the three most influential parameters in DSA (online supplementary *Table S13* and *Figures S11–S15*). Other influential parameters include HHF (in France, Poland, Spain and Sweden), CV death (in France, Germany and Spain), costs associated with AEs (sepsis: Germany and Poland) and ID prevalence (in Sweden).

Discussion

The burden of HF is well documented,[16–18] and there is a need for evidence-based therapy to prolong life, increase QoL and reduce hospitalizations in this vulnerable patient population in order to benefit patients and reduce the burden on healthcare systems. Pharmacoeconomic analysis of novel therapeutics typically evaluates cost-effectiveness; the results presented in this study demonstrate that the introduction of FCM in all five European

Table 3 Modelled outcomes, associated costs and net budget impact over 5 years

Outcome	France			Germany			Poland			Spain			Sweden		
	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ	FCM	SoC	Δ
Events															
Hospitalizations															
HHF	109 520	121 486	−11 966	320 100	335 018	−14 918	115 955	123 106	−7151	67 672	77 223	−9551	7961	8496	−535
HnHF	75 079	77 521	−2442	210 733	213 777	−3044	77 095	78 555	−1459	47 328	49 277	−1949	5312	5422	−109
CV death	39 747	44 922	−5175	117 429	123 880	−6451	42 428	45 521	−3092	24 425	28 555	−4130	2910	3142	−232
Adverse events															
AF	4644	2443	2201	9481	6737	2744	3791	2476	1316	3310	1553	2201	269	171	99
Pneumonia	8260	9853	−1593	25 185	27 170	−1986	9032	9984	−952	4992	6263	−1593	618	689	−71
AKI	4005	3060	945	9617	8439	1178	3666	3101	565	2700	1945	945	256	214	42
Sepsis	4890	5519	−629	14 436	15 219	−783	5217	5592	−376	3007	3508	−628	358	386	−28
Total	21 799	20 975	824	58 719	57 565	1154	21 706	21 153	553	14 009	13 269	740	1501	1460	41
Costs (€)															
Treatment	46 286 271	0	46 286 271	90 788 430	0	90 788 430	23 428 456.12	0	23 428 456.12	59 048 151	0	59 048 151	1 104 069	0	1 104 069
Hospitalizations															
HHF	514 777 408	570 267 638	−55 490 230	1 487 976 651	1 555 933 611	−67 956 961	211 559 277	224 606 165	−13 046 888	212 807 936	242 369 946	−29 562 010	39 479 868	42 092 934	−2 613 066
HnHF	352 568 219	363 891 538	−11 323 320	1 058 488 685	1 073 482 140	−14 993 455	57 581 619	58 671 493	−1 089 874	55 089 177	57 325 138	−2 235 962	10 936 980	11 158 499	−221 519
CV death	228 860 604	258 249 434	−29 388 830	1 590 286 046	1 675 889 935	−85 603 889	206 594 577.01	221 652 423.01	−15 057 846	169 581 827	197 796 796	−28 214 968	5 543 364	5 977 328	−433 964
Adverse events	181 738 813	181 590 144	148 669	281 331 975	284 885 517	−3 553 542	118 860 851	122 215 222	−3 354 372	48 249 798	49 296 313	−1 046 515	6 247 868	6 430 837	−182 968
Overall															
With FCM costs	1 324 231 315	1 373 998 754	−49 767 439	4 508 871 786	4 590 191 204	−81 319 417	618 024 780	627 145 303	−9 120 523	544 776 889	546 788 193	−2 011 304	63 312 150	65 659 597	−2 347 447
Without FCM costs	1 277 945 044	1 373 998 754	−96 053 710	4 418 083 356	4 590 191 204	−172 107 848	594 596 323.80	627 145 303	−32 548 980	485 728 738	546 788 193	−61 059 455	62 208 081	65 659 597	−3 451 516

AF, atrial fibrillation; AKI, acute kidney injury; CV, cardiovascular; FCM, ferric carboxymaltose; HHF, hospitalization for heart failure; HnHF, hospitalization not for heart failure; SoC, standard of care.

countries evaluated is expected to be highly cost effective, with FCM actually dominating SoC, due primarily to the substantial cost savings associated with the reduction in HHF events. These results are consistent with a number of other health economic studies, demonstrating that FCM for the treatment of ID in a range of HF indications is either cost-saving or cost-effective in comparison to placebo.[10,19–23] Nevertheless, cost-effectiveness analysis does not necessarily capture all the potential impacts of a new intervention, therefore this study also focused on the burden of disease at both the patient and healthcare system level, and on the overall projected impact on healthcare budgets.

This study is the first to estimate the impact of FCM treatment at discharge on the burden of ID in patients with HF and LVEF <50% following hospitalization for AHF. The burden of disease on patients was quantified using DALYs; one DALY represents the loss of 1 year of full health, combining lost years due to premature mortality with lost years of healthy life due to disability.[24] This measure was introduced by the World Health Organization (WHO) Global Burden of Disease (GBD) studies as a unified metric of disease burden. Patients receiving FCM in AFFIRM-AHF reported a greater increase in health-related QoL measured by KCCQ, compared to placebo.[25] This is reflected in the modelling presented in this study, which predicted that in the SoC arm more patients are in the most severe KCCQ quartile after a year (20% vs. 14% in the FCM arm) and fewer in the least severe quartile (39% vs. 45% in the FCM arm). Other studies have demonstrated that small improvements in KCCQ have a clinically meaningful impact on HF symptoms, including in patients treated for ID.[26] It is important to stress in this context that few of the available non-invasive guideline-recommended HF treatments have been shown to carry beneficial effects on QoL.[27] The FCM-related improvements seen in AFFIRM-AHF can be represented by a change in disability weights, in addition to the projected impact on YLL, leading to an estimated 58–70 DALYs averted per 1000 population, depending on country-specific life expectancy.

AFFIRM-AHF data showed that FCM treatment in patients at discharge after AHF is also associated with a reduction in both the number of HHF and the average hospital LOS, leading to a combined saving in hospital bed days in the first year following treatment initiation. Considering the increasing prevalence of HF, the needs of this patient population have significant ongoing implications for healthcare budgets and system capacity. The analysis presented in this study illustrates the benefits that could be realized by adherence to the recommendations on screening and treatment for ID in symptomatic HF patients recently hospitalized with LVEF <50% in the 2021 ESC HF guidelines.[1] Beyond the potential cost savings to healthcare budgets quantified here, releasing hospital capacity would help alleviate the ongoing challenge in healthcare resourcing. Other uncaptured benefits of reducing HHF events in this vulnerable population include reducing the risk of hospital-associated complications including nosocomial infections, deconditioning and hospital-induced delirium, which can have profound impacts on patient QoL and ongoing healthcare and social care resource requirements.

Herein, we quantify the budget savings projected to be associated with the introduction of FCM in the eligible population,

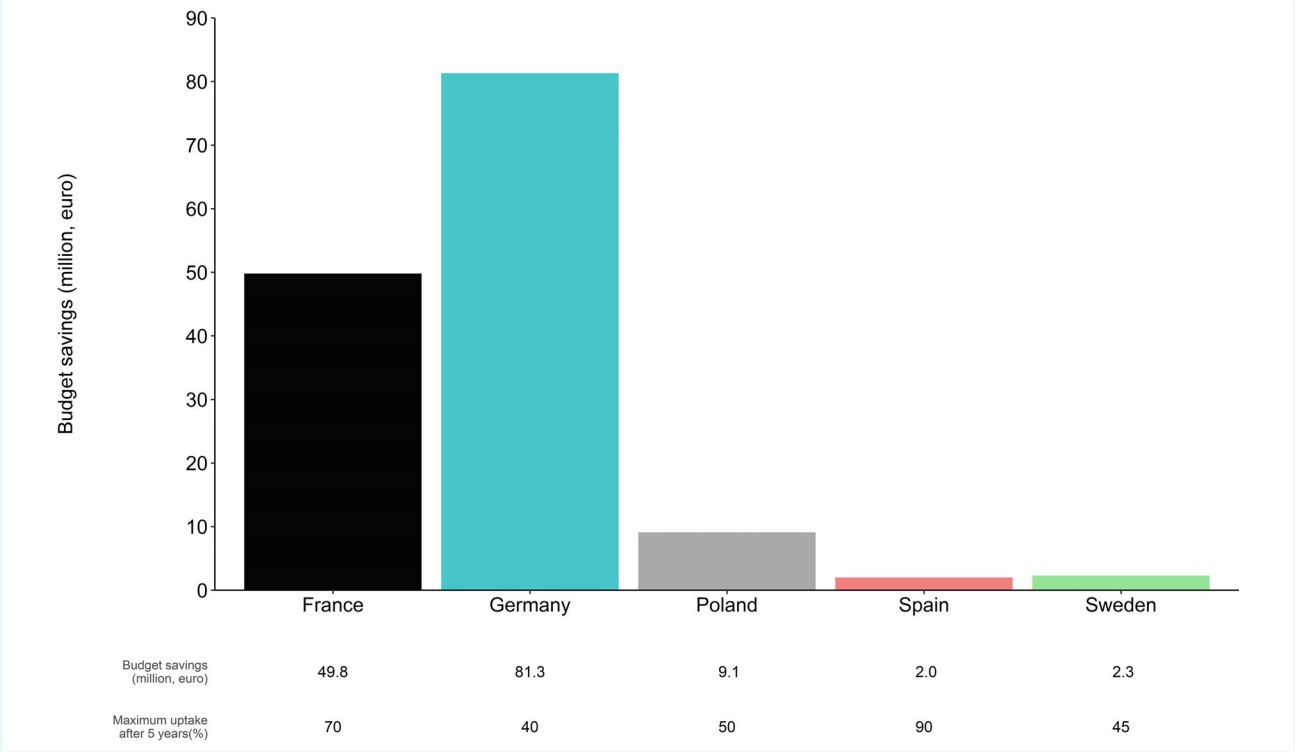


Figure 3 Cumulative 5-year budget savings of introducing ferric carboxymaltose. Cumulative 5-year budget savings associated with introducing ferric carboxymaltose in France, Germany, Poland, Spain and Sweden, based on the maximum percentage uptake of treatment predicted for each country after 5 years.

highlighting the health economic value of adherence to the 2021 ESC guidelines for HF management, in addition to the clinical benefits.[1] This is consistent with other published budget impact studies, which have also shown either cost savings, or modest cost increases, associated with FCM therapy in HF patients across many European countries.[12,20,28–30] A Spanish budget impact study, using data from CONFIRM-HF, reported an annual cost saving of €534.80 per patient with FCM treatment versus non-iron treatment, driven by a decrease in hospitalizations.[30] Similarly, a French budget impact analysis extrapolating data from the CONFIRM-HF trial demonstrated cumulative cost savings of €0.8 m with FCM compared to no treatment.[12] These savings were driven by reduced hospitalization costs, associated with worsening HF, and decreased follow-up costs.

There are however some limitations to our study. Although every effort was made to ensure the use of appropriate inputs within the country adaptations, inputs were subject to availability of data from published literature and required calculation or use of proxies in several cases. Although the AFFIRM-AHF was a multinational trial including Europe, South America and Asia, the efficacy data per country were not sufficiently large to enable reliable country-specific analysis. Hence, the results from each country adaptation, where clinical parameters were unchanged, may not fully represent the treatment guidelines and diversity of clinical outcomes for each local setting. Additionally, QoL elicitation applied throughout the models was standardized to the UK setting and may not represent exact predictions of output in each respective setting.

Another limitation is that GBD disability weights are not published specifically for ID, therefore the effect of FCM treatment on disability weights was approximated via the reported effects of FCM treatment on QoL and HF-related symptoms in relevant populations. Furthermore, the analysis does not account for any potential differences in background healthcare use between patients at different stages of the HF disease pathway or between treatment groups. This is a conservative assumption as more patients in the placebo arm spend greater time in more severe disease states compared to the FCM arm, which may result in uncaptured higher resource use and higher costs for comparator.

In conclusion, FCM for the treatment of ID at discharge in patients hospitalized for AHF with LVEF <50% has the potential to reduce HF burden and deliver cost savings to healthcare systems, and is estimated to be a highly cost-effective treatment across all five countries. This comprehensive evaluation of the pharmacoeconomic impacts of FCM therapy highlights the range of potential benefits that could be realized through implementation of the 2021 ESC HF guideline recommendations, which require not only improved treatment rates but also an increase in ascertainment of ID. Given the prevalence of ID in the eligible population, the index of clinical suspicion should be high, and implementation of routine screening may be required to deliver the full potential of this treatment to patients and healthcare systems.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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