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LETTER

Economic Analysis of Intravenous Iron in Patients with Iron Deficiency Anemia Due to Inflammatory Bowel Disease: Considerations for Clinicians [Letter]

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Dear editor

We read, with interest, the recently published article by Aksan et al (2021),[1] which presents the results of an economic analysis comparing the cost-effectiveness of intravenous (IV) iron products in the treatment of iron deficiency anemia (IDA) associated with inflammatory bowel disease (IBD), in the UK setting. The authors concluded that ferric carboxymaltose (FCM; Vifor Pharma, Glattbrugg, Switzerland) is likely to be the least costly, and most effective, IV iron therapy compared with ferric derisomaltose (FDI; previously known as iron isomaltoside; Pharmacosmos A/S, Holbæk, Denmark) and iron sucrose (IS; Vifor Pharma, Glattbrugg, Switzerland).[1] We would like to share our experience of health economics in the field of IV iron therapy to present some important considerations for clinicians when interpreting these findings, to ensure rational and evidence-based treatment decisions.

Firstly, the clinical effectiveness inputs used in the Aksan et al (2021) analysis were based on the results of an earlier network meta-analysis (NMA) comparing the efficacy and tolerability of different IV iron products (including FDI, FCM, and IS) in patients with IDA due to IBD (published by Aksan et al in 2017).[1,2] The NMA showed no statistically significant differences in efficacy (treatment response: hemoglobin [Hb] normalization or increase in Hb ≥2 g/dL) between FDI and FCM.[2] The shortcomings of this NMA have been detailed in a previous communication,[3] but the Aksan et al (2021) analysis does not seem to incorporate changes to overcome these short-falls.

Secondly, in the Aksan et al (2021) analysis, the authors acknowledge the weakness of using indirect evidence to obtain the data for the clinical effectiveness inputs, justifying this approach by the lack of direct evidence from head-to-head trials conducted in a relevant patient population.[1] Indeed, Aksan et al (2021) did not include the data from the head-to-head PHOSPHARE-IDA trial showing comparable efficacy (iron and anemia parameters, assessed as secondary endpoints) between FCM and FDI, on the basis that the IDA was due to a gynecological condition, not to IBD.[1,4] Evidence is now available from the head-to-head PHOSPHARE-IBD trial, which was conducted, specifically, in patients with IBD (n=96); equivalent doses of FCM and FDI (initial dose of 1000 mg at baseline followed by 500 mg or 1000 mg after 5 weeks) were compared, with assessment of Hb as a secondary endpoint.[5] As shown in Table 1, the PHOSPHARE-IBD trial showed no statistically significant difference between FCM and FDI in the post-treatment Hb changes from baseline.[5]

The evidence from PHOSPHARE-IBD provides confirmation of equivalent hematological efficacy of FCM and FDI in an IBD population with IDA.[5] Therefore, the suggestion that FCM is more effective than FDI (as was concluded for the Aksan et al (2017) NMA),[2] is not completely borne out by published evidence.

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Table 1 Mean Change from Baseline in Hb Following Treatment with FCM or FDI

	FDI (n=49)	FCM (n=48)	p-value
Day 1	0.13 (0.45) (n=48)	−0.01 (0.50) (n=48)	0.1165
Week 1	0.58 (0.73) (n=45)	0.47 (0.71) (n=44)	0.2293
Week 2	1.16 (0.87) (n=46)	1.18 (0.94) (n=47)	0.9393
Week 5	1.77 (1.01) (n=42)	1.84 (1.06) (n=44)	0.7778
Week 6	2.08 (1.07) (n=43)	2.06 (1.13) (n=41)	0.8295
Week 7	2.36 (1.27) (n=42)	2.38 (1.23) (n=43)	0.6428
Week 10	2.51 (1.41) (n=43)	2.44 (1.49) (n=41)	0.9257

Notes: Data presented are mean (SD). Adapted from EU Clinical Trials Register. Clinical Trial Results: A randomized, double-blinded, comparative trial comparing the incidence of hypophosphatemia in relation to repeated treatment courses of iron isomaltoside and ferric carboxymaltose in subjects with iron deficiency anaemia due to inflammatory bowel disease. EudraCT number: 2017-002452-87. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-002452-87/results.[5]
Abbreviations: FCM, ferric carboxymaltose; FDI, ferric derisomaltose; Hb, hemoglobin; SD, standard deviation.

Thirdly, the Aksan et al (2021) analysis acknowledged that the impact of safety issues on cost and clinical outcomes was not considered, and that such information should be captured in future cost-effectiveness studies.[1] This is, indeed, an important reflection given that the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency considers there to be a possible causal relationship between hypophosphatemic osteomalacia and FCM, specifically[6] – it is not a class effect for all IV iron products. In November 2020, the regulatory authorities in the UK published an update to the product information for FCM to include a requirement for serum phosphate monitoring in patients who receive multiple administrations of FCM at higher doses, or long-term FCM treatment (and in those with existing risk factors for hypophosphatemia, including IBD).[7] The cost of this additional monitoring is particularly relevant to the Aksan et al (2021) analysis, given that it was focused on a population of IBD patients in the UK.[1]

We hope that the issues highlighted in this letter will give a broader perspective to the findings of the Aksan et al (2021) economic analysis for prescribing clinicians and decision-makers in the UK. Of particular importance for real-world clinical practice are the recent changes to the FCM product label, which translate into an additional economic impact of FCM treatment in the management of IDA due to IBD.

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