UPDATED SYSTEMATIC REVIEW WITH NETWORK METAANALYSIS ON COMPARATIVE EFFICACY AND TOLERABILITY OF DIFFERENT INTRAVENOUS IRON PRODUCTS FOR THE TREATMENT OF IRON DEFICIENCY ANEMIA IN PATIENTS WITH IBD

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Background: In patients with inflammatory bowel disease (IBD), iron deficiency anemia (IDA) is a frequent complication. Causes include intestinal bleeding, reduced iron intake and impaired duodenal iron absorption due to chronic inflammation and concomitant medications (eg. 5-ASA, PPI). Reduced absorptive capacity and low therapy adherence often render oral iron therapies ineffective. Intravenous (IV) iron substitution has been shown to be more effective in IBD patients with IDA and international guidelines recommend IV iron therapy. Variances in core size, composition and shell density cause variations in the efficacy and tolerability of IV iron products.
Aims: We aimed to compare response rates and safety of ferric carboxymaltose (FCM), ferumoxytol (FOX), iron sucrose/saccharate (IS), iron isomaltoside (ISM) and iron dextran (IDX) in IBD patients with IDA by adding recent data to our 2016 network metaanalysis (NMA) and systematic review.
Methods: Using the same methodology, PUBMED, SCOPUS, Web of Science and Cochrane databases were searched in 8/2018 for articles published since 7/2016. Primary outcome was hematopoietic response (% of patients) defined as Hb normalization or increase ≥2g/dL. Secondary outcome was AE rate (safety population).
Results: We identified 151 studies including 4 prospective observational studies (2 FCM, 2 ISM), making 18 studies in total. No studies on FOX were eligible and no RCTs eligible for the NMA (4 studies) were found. In total, the updated systematic review included 7 studies (n= 798) for FCM, 2 studies (n=78) for IDX, 8 studies (n=508) for IS, and 3 studies (n=423) for ISM (infusion/bolus). Overall response rates were: FCM 599/798(78%); IDX 33/78(42%); IS 344/508(68%); ISM 265/423(63%). All IV iron products were reported to be well tolerated. Overall rates of AEs and SAEs were 66/836(7.9%), 1/836(0.1%) for FCM; 10/83(12%), 0/83 for IDX; 72/471(15.3%), 1/471(0.2%) for IS; 54/424(12.7%), 5/424(1.2%) for ISM. FCM was

significantly more effective than oral iron (OR=1.9, 95% CrI [1.1;3.2]). IS and ISM showed better response rates than oral iron (insignificant). For the node-splitting analysis of the Bayesian NMA, $p < 0.05$ indicated insignificant inconsistency.
Conclusions: Our findings indicate ferric carboxymaltose to be the most effective IV iron formulation as monotherapy, followed by IS and ISM. FCM also had fewer AEs. The totality of evidence showed that further studies are unlikely to overturn this result. FCM has not yet gained approval for use in Canada. Worldwide, FCM has been considerably more widely studied in an IBD population than its competitors. Further studies are thus needed to evaluate other IV iron products and establish their comparative efficacy and safety in patients with IBD and IDA.

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