

IV Iron & Bone Health

CORNERSTONE CLINICAL TOOL

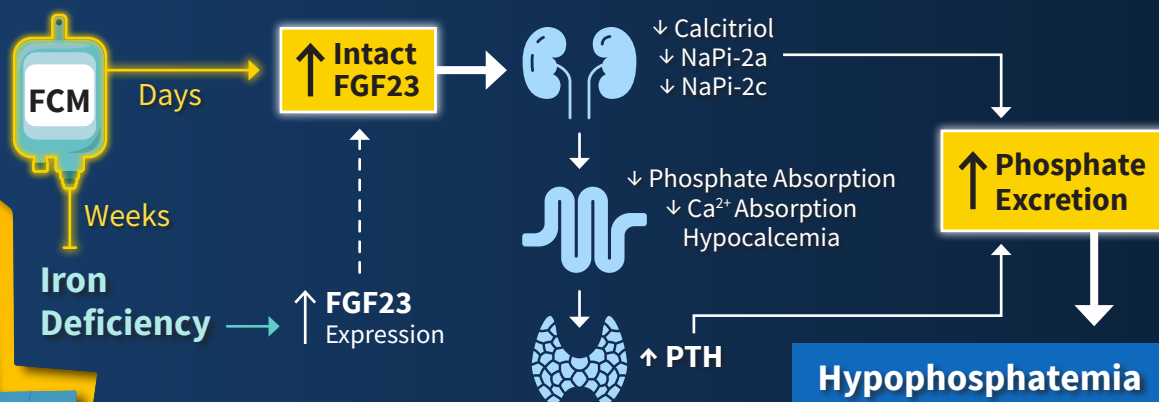
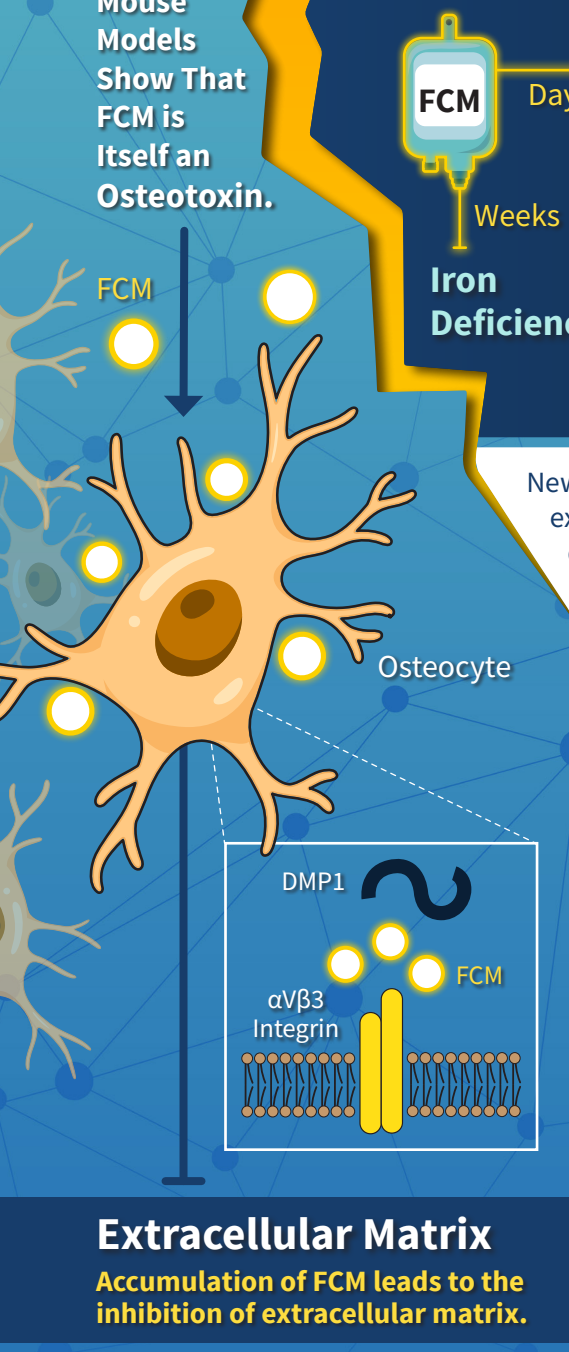


A Closer Look at Fracture Risk

In HHT, **chronic blood loss frequently results in iron deficiency (ID) and ID anemia (IDA)**, and IV iron is an important component of management when oral iron is ineffective, poorly absorbed, or not tolerated, or when anemia is severe; ongoing bleeding may necessitate regularly scheduled infusions. Historically, the principal skeletal concern with ferric carboxymaltose (FCM) has been **FGF23-mediated hypophosphatemia** and its downstream effects on bone mineralization.

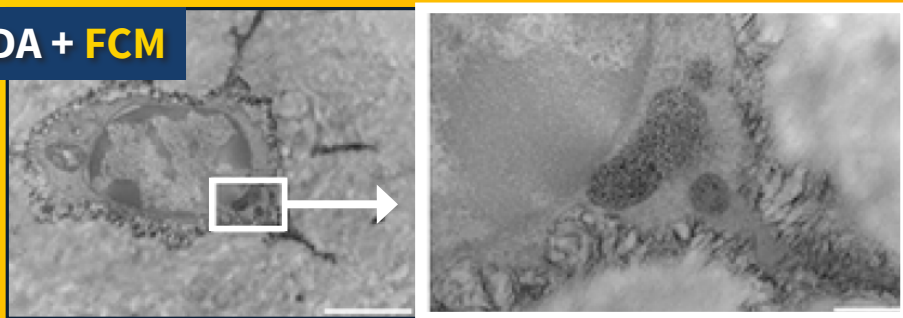
More Than Phosphate?

Mouse Models Show That FCM is Itself an Osteotoxin.

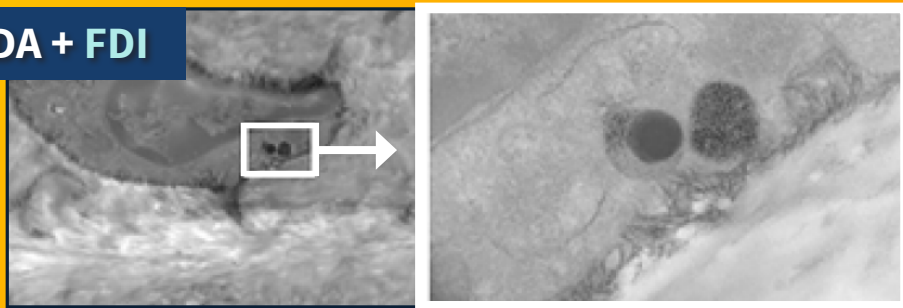


New evidence from mouse models show **direct osteotoxic effects of FCM** that extend **beyond hypophosphatemia**. As shown below in a comparison with ferric derisomaltose (FDI), **FCM preferentially accumulates** in bone and disrupts pathways involved in osteocyte function.

IDA + FCM



IDA + FDI



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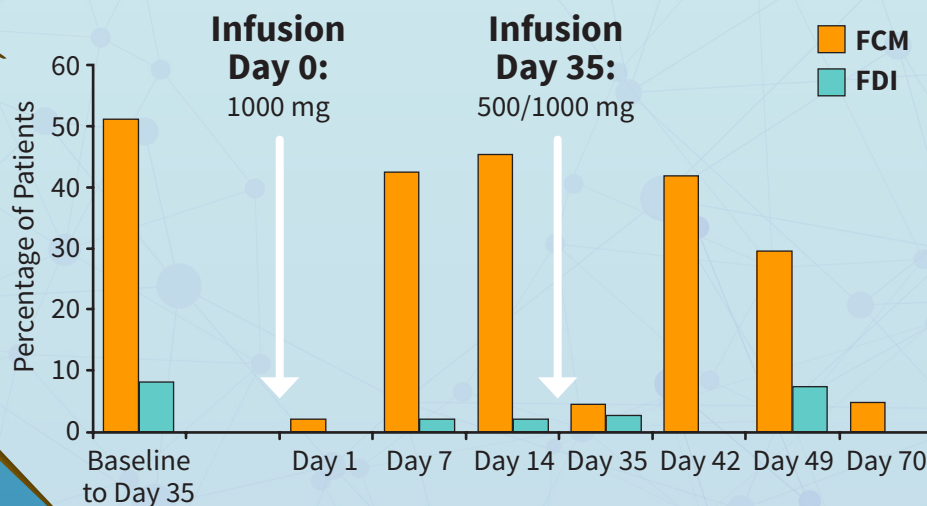
Examining the Evidence Regarding FCM Safety

Although emerging evidence shows that FCM can impair bone health independent of phosphate levels, **hypophosphatemia remains a major contributor to FCM-associated morbidity**. The effects of FCM can be severe, prolonged, and clinically difficult to manage.

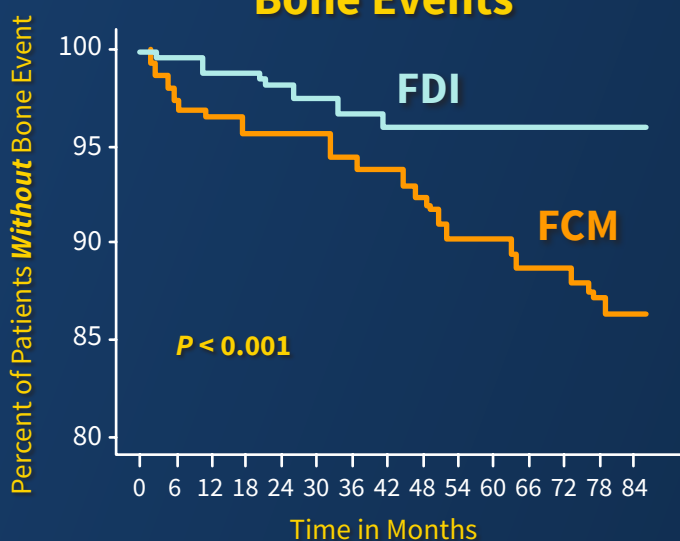
PHOSPHARE-IBD Trial: Primary Outcome of Incident Hypophosphatemia



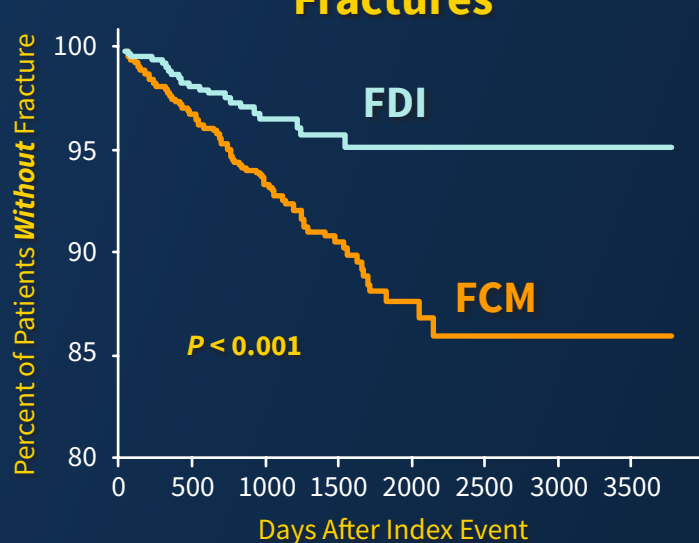
FCM has a Black Box Warning for “Symptomatic Hypophosphatemia” on its label, which can happen after ONE dose!



Bone Events



Fractures



Although **comparably effective** in treating IDA, the risks of hypophosphatemia, difficult-to-treat mineral disturbances, **direct osteotoxicity**, and **increased fracture risk distinguish FCM from other IV iron options** and warrant careful consideration when deciding on a therapeutic approach to managing ID or IDA, regardless of the underlying cause.

Sources: Wagner SA, Panzer M, Pertler E, et al. Blood. 2026;148(1):15-30; Finberg KE, Auerbach M. Blood. 2026;148(1):1-2; Zoller H, Wolf M, Blumenstein I, et al. Gut. 2023;72(4):644-653; Auerbach M, Henry D, DeLoughery TG. Am J Hematol. 2021;96(6):727-734; Wolf M, Koch TA, Bregman DB. J Bone Miner Res. 2013;28(8):1793-1803; Schaefer B, Tobiasch M, Wagner S, et al. Bone. 2022;154:116202.



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