New concepts in IV iron.

Content by Joseph Shatzel MD MCR

Figures/Images by chatgpt

Disclosures

- No relevant financial disclosures.

Neurath's boat

- a ship being repaired while still afloat, symbolizing the continuous process of revising and refining knowledge.

Key Points:

Our knowledge is always revisable and incomplete.

We cannot start from a "neutral" or fully secure foundation.

We are always refining and adjusting our beliefs, theories, and methods in response to new evidence, while relying on the knowledge we already possess.

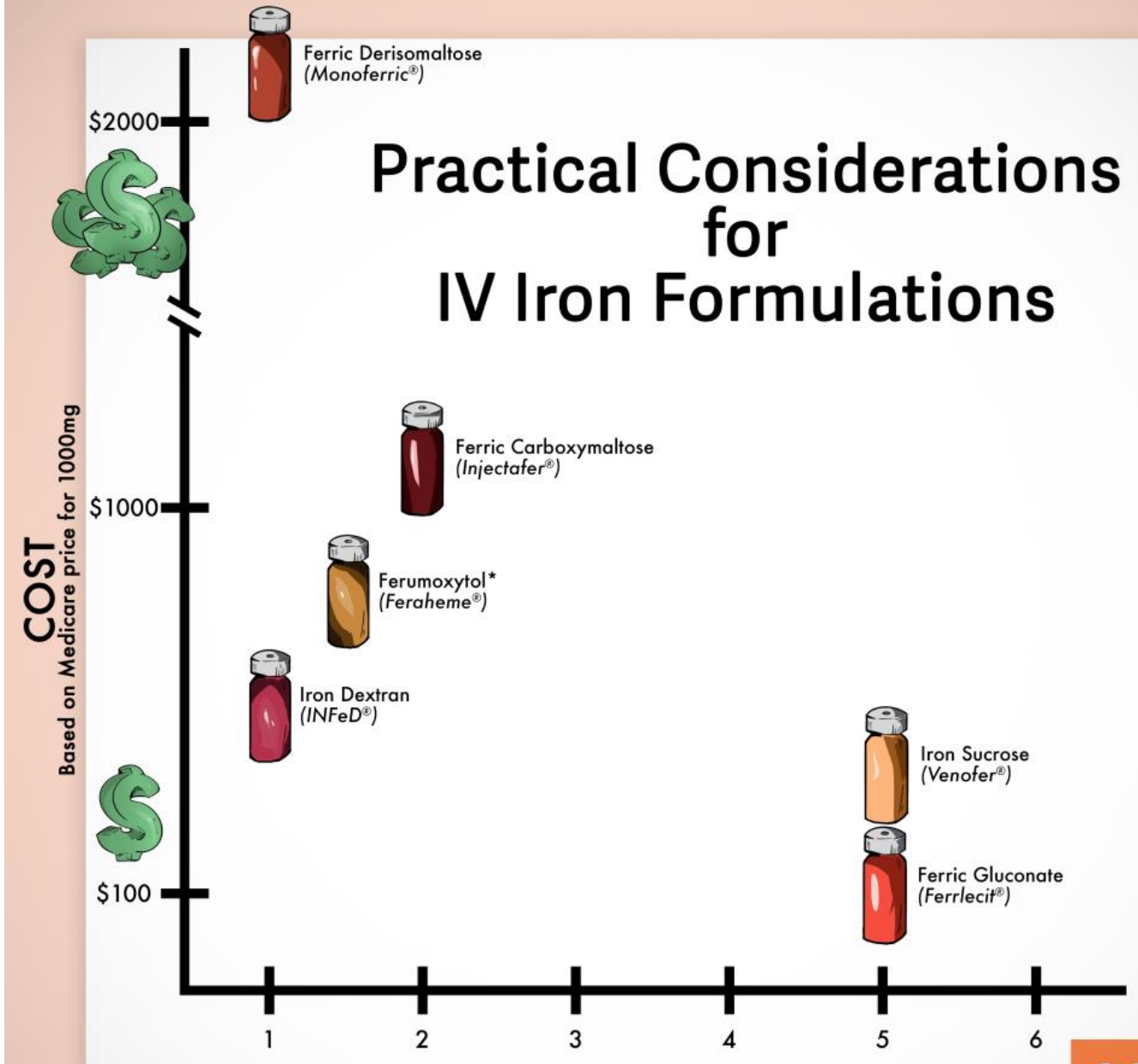
1. It’s not okay to use Venofer.

Here is the table, Joe. Good luck with your talk! You will do great!

IV Iron Product	Recommended Dose	Administration Time	Number of Doses to Make 1,000 mg
Venofer (Iron Sucrose)	200 mg per dose	2-5 minutes (slow IV push) or 15-30 min (infusion)	5
Ferrlecit (Sodium Ferric Gluconate)	125 mg per dose	1 hour (infusion)	8
Feraheme (Ferumoxytol)	510 mg per dose	15-30 minutes (infusion)	2
Injectafer (Ferric Carboxymaltose)	750 mg per dose	15 minutes (infusion)	2
Monoferric (Ferric Derisomaltose)	1,000 mg in a single dose	20 minutes (infusion)	1
Low Molecular Weight Iron Dextran (LMWID)	1,000 mg per dose	1 hour (infusion)	1

Best of luck! Let me know if you need any further tweaks or help!

Practical Considerations for IV Iron Formulations



*Can be given with 1 or 2 infusion sittings

Artwork by: @Nwachukwudexter

CORE IM

TABLE 1. Cost of IV Iron Formulations[a]

Agent	Cost per 1000 mg	4.3% add-on payment per 1000 mg	Year of FDA approval	On patent/ market exclusivity
Ferric gluconate	$205.28	$8.83	1999	No
Iron sucrose	$266.00	$11.44	2000	No
Low-molecular-weight iron dextran	$243.80	$10.48	1991	No
Ferumoxytol	$823.00	$35.39	2009	Yes
Ferric carboxymaltose	$1057.00	$45.45	2013	Yes

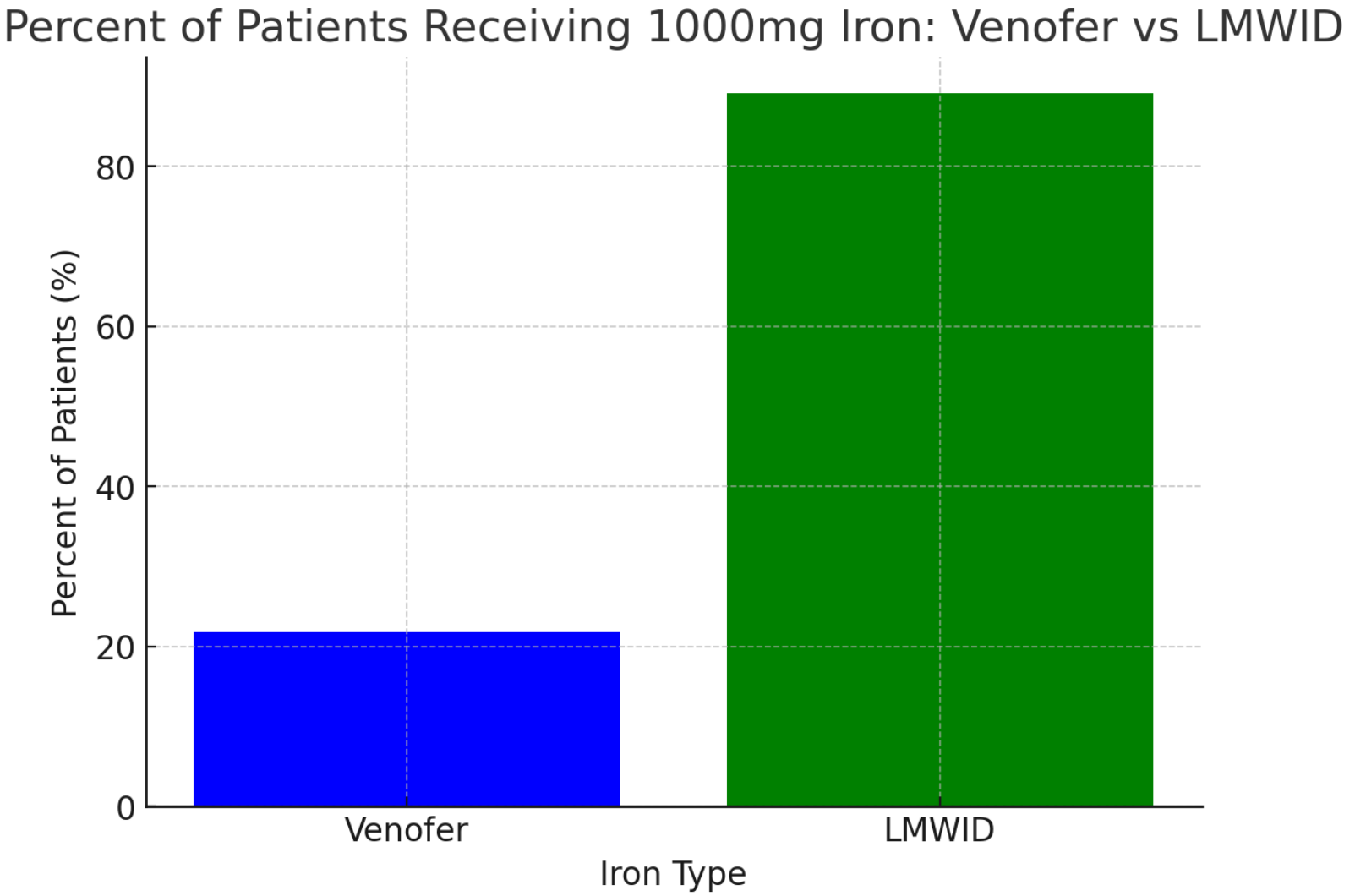
ASP, average sales price; IV, intravenous.

[a]Based upon January 2016 Medicare ASP. Ferumoxytol is available in a vial size of 510 mg, whereas ferric carboxymaltose is available in 750-mg vials. Patients requiring at least 1000 mg of IV iron supplementation would require 1020 mg of ferumoxytol and 1500 mg of ferric carboxymaltose, further increasing the cost differences depicted here. Infusion center fees outside of ASP-based reimbursement are not included.

what is the average cost of an infusion visit at a hospital in america (not the drug, just the chair time)

The average cost of an infusion visit at a hospital in the U.S., excluding the cost of the drug itself, can range from **$300 to $1,000** per visit. This includes the "chair time" or facility fees, nursing services, and other administrative costs associated with the infusion procedure.

Venofer patients are undertreated



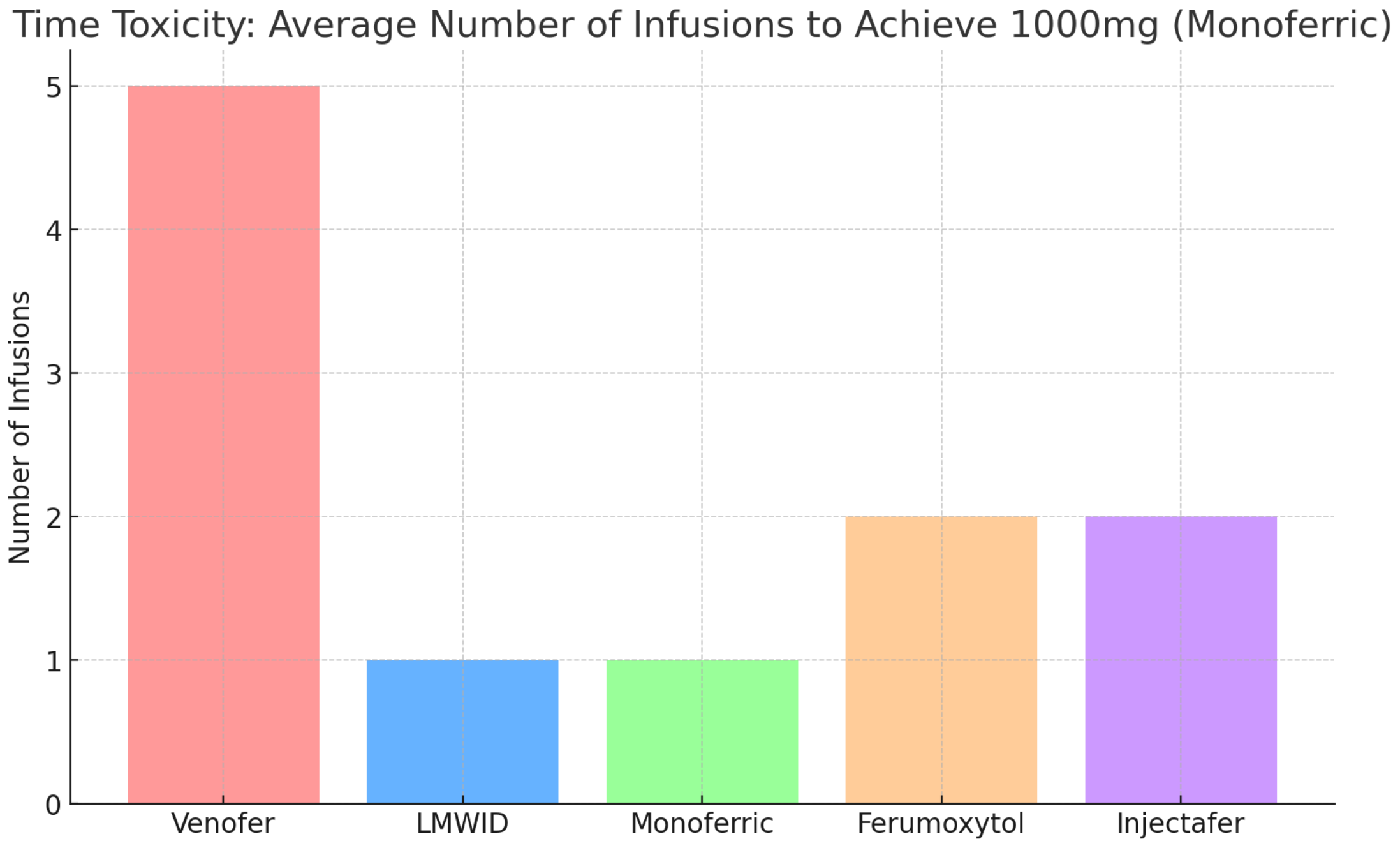
European Journal of Haematology

ORIGINAL ARTICLE

Perinatal Outcomes Following Intravenous Iron for Treatment of Iron Deficiency With and Without Anemia

Kimberly S. Ryan, Kylee L. Martens, Bharti Garg, Boris I. Chobrutskiy, Madeline A. Hedges, Olivia L. Hagen, Jean M. G. Sabile, Adam K. Lewkowitz, Methodius G. Tuuli, Thomas G. Deloughery, Joseph J. Shatzel, Jamie O. Lo, Ashley E. Benson ... See fewer authors

First published: 03 September 2024 | https://doi.org/10.1111/ejh.14298


Time Toxicity: Average Number of Infusions to Achieve 1000mg (Monoferric)
Number of Infusions
0
1
2
3
4
5
Venofer
LMWID
Monoferric
Ferumoxytol
Injectafer

Venofer

- Increased Financial toxicity
- Increased Time toxicity
- Inadequate dosing
- a poor choice

Iron is not unsafe

JAMA Network | Open™

Original Investigation | Hematology

Analysis of Adverse Events and Intravenous Iron Infusion Formulations in Adults With and Without Prior Infusion Reactions

Asad H. Arastu, MD; Benjamin K. Elstrott, BA; Kylee L. Martens, MD; Jonathan L. Cohen, PharmD; Michael H. Oakes, MD; Zhoe T. Rub, MS; Joseph E. Aslan, PhD; Thomas G. DeLoughery, MD; Joseph Shatzel, MD

Table 1. Patient Demographics, Clinical Information, and Infusion Events

Characteristic	Patients, No. (%) (N = 12 237)
Women	9480 (77.5)
Men	2757 (22.5)
Age at time of infusion, mean (SD), y	51 (20)
Documented history of allergy[a]	9677 (79.1)
Race	
American Indian/Alaska Native	119 (1.0)
Asian	338 (2.8)
Black	717 (5.9)
White	10 250 (83.7)
Unknown, declined, or other[b]	813 (6.6)
Ethnicity	
Hispanic	1026 (8.4)
Non-Hispanic	10 161 (83.0)
Unknown or declined	1050 (8.6)
Total iron infusion events, No.	35 737
Iron sucrose	22 309 (62.4)
Iron dextran full dose (with or without test)	9011 (25.2)
Iron dextran test alone	56 (0.2)
Ferumoxytol	3147 (8.8)
Ferric carboxymaltose	1214 (3.4)

[a] Inclusive of allergy to medication, food, or contact allergies.

[b] Data were not captured for specific race categories included in the other race category, which were limited to the electronic health record inputs.

12,237 patients from **6 centers** in Portland, Oregon, between January 2015 and September 2021.

Total Infusions in the Study: 35,737 infusions

Breakdown by Iron Formulation:

- **Iron Sucrose: 22,309 infusions** (62.4%)
- **Low-Molecular-Weight Iron Dextran: 9,067 infusions** (25.2%)
  - Full dose without test dose: 7,296 infusions
  - Full dose preceded by test dose: 1,715 infusions
  - Test dose alone: 56 infusions
- **Ferumoxytol: 3,147 infusions** (8.8%)
- **Ferric Carboxymaltose: 1,214 infusions** (3.4%)

- **Overall Incidence of Adverse Events:3.9%** (1,389 reactions out of 35,737 infusions)
- Reaction rates by formulation:
  - **Iron Sucrose**: 4.3%
  - **Low-Molecular-Weight Iron Dextran (LMWID)**: 3.8%
  - **Ferumoxytol**: 1.8%
  - **Ferric Carboxymaltose**: 1.4%
- **Severe Reactions** (Epinephrine use): Only **2 cases** (both associated with LMWID).

Table 2. Rates of Adverse Events Stratified by Intravenous Iron Formulation

Postinfusion medication use	Infusions, No./total No. (% of reactions)					*P* value
	Total	IS	LMWID[a]	Ferumoxytol	Ferric carboxymaltose	
Iron reactions[b]	1389/35 737 (3.9)	970/22 309 (4.3)	345/9067 (3.8)	57/3147 (1.8)	17/1214 (1.4)	<.001[c]
Epinephrine	2/1360 (0.1)	0	2	0	0	NA
Diphenhydramine	664/1360 (48.8)	400	217	34	13	NA
Famotidine	858/1360 (63.0)	601	217	30	10	NA
Hydrocortisone	245/1360 (18.0)	134	96	12	3	NA

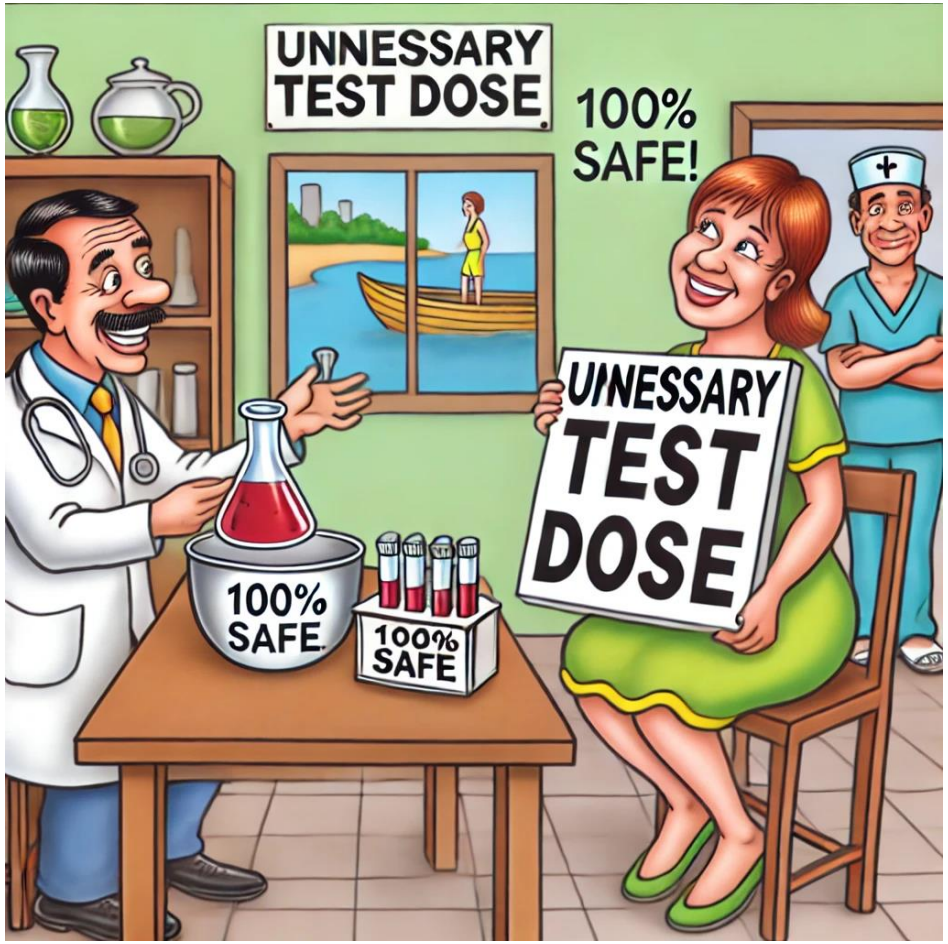
- **Premedication Use**: **23-fold higher risk** of adverse events when premedication (diphenhydramine, hydrocortisone, etc.) was used.
- Rates with premedication: **38.6%** vs. **1.7%** without premedication.
- **Management of Patients with History of Infusion Reaction**: Higher recurrence with same formulation, especially if premedicated (**68%** vs **32%**).
- Switching formulation reduced reactions
  - (**21%** with premedication, **5%** without).

Table 3. Rates of Adverse Events Among Patients Receiving Premedication or Iron Dextran Test Doses

	Total doses, No.	Infusion reaction, No. (%)	No infusion reaction, No (%).	*P* value
Rates of infusion reaction by premedication status				
Premedication given	2157	833 (38.6)	1324 (61.4)	<.001[a]
No premedication given	33 580	556 (1.7)	33 024 (98.3)	
Rates of infusion reaction in iron dextran group by test-dose status				
Full dose only	7296	279 (3.8)	7017 (96.2)	.90[a]
Test and full dose intended	1771	66 (3.7)	1705 (96.3)	
Test dose only[b]	56	29 (51.8)	27 (48.2)	NA

- **Test Doses with Low-Molecular-Weight Iron Dextran (LMWID):19.5%** of LMWID infusions were preceded by a test dose.

- **No significant difference** in adverse event rates between test dose and non-test dose groups:
  - **Full dose only**: 3.8% adverse event rate.
  - **Test dose followed by full dose**: 3.7% adverse event rate.



Key points:

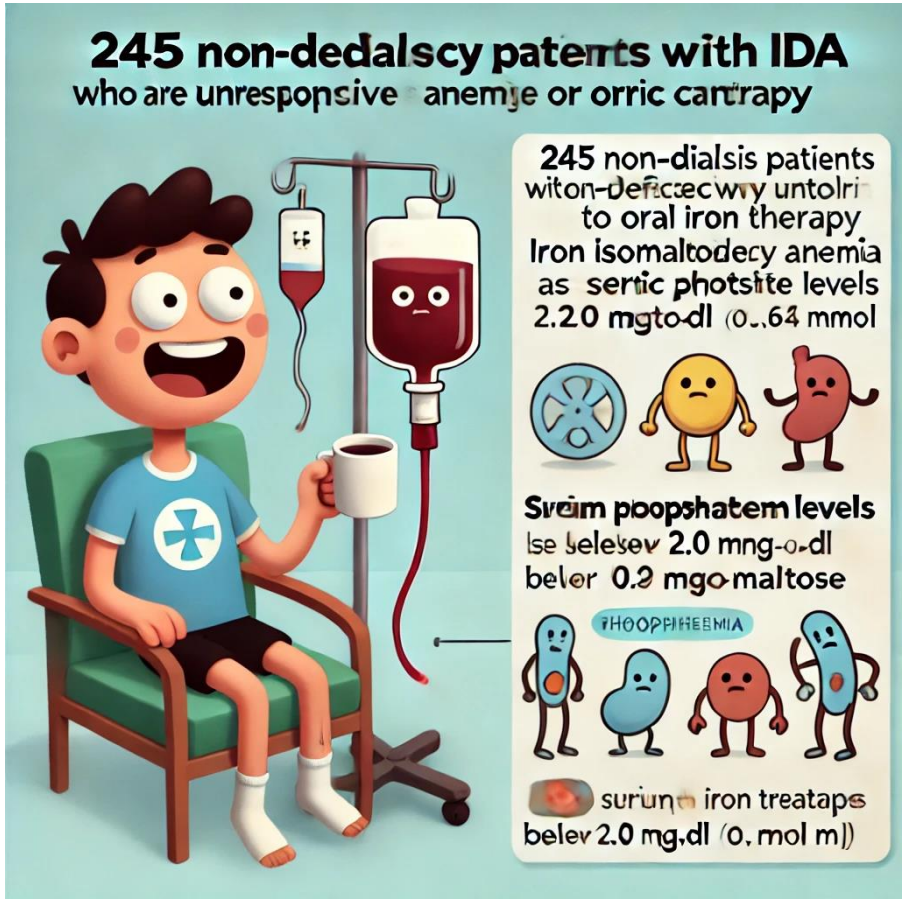
- **Iron sucrose** had the highest reaction rate (**4.3%**)
- Premedication significantly increased adverse events (**38.6%** with premedication vs. **1.7%** without),
- The use of **test doses** with low molecular weight iron dextran (LMWID) did **not reduce adverse events**,
- **Rechallenging patients** who had previous reactions with a different iron formulation was generally safe and associated with lower adverse events

3. **But Ferric Carboxymaltose may not be as safe as we thought**

The study included a total of **245 non-dialysis patients** with **iron-deficiency anemia (IDA)** who were **unresponsive or intolerant** to oral iron therapy.

These patients received intravenous iron treatments (**iron isomaltoside or ferric carboxymaltose**)

The study defined **hypophosphatemia** as **serum phosphate levels below 2.0 mg/dL (0.64 mmol/L)**.



Original Investigation

February 4, 2020

Effects of Iron Isomaltoside vs Ferric Carboxymaltose on Hypophosphatemia in Iron-Deficiency Anemia

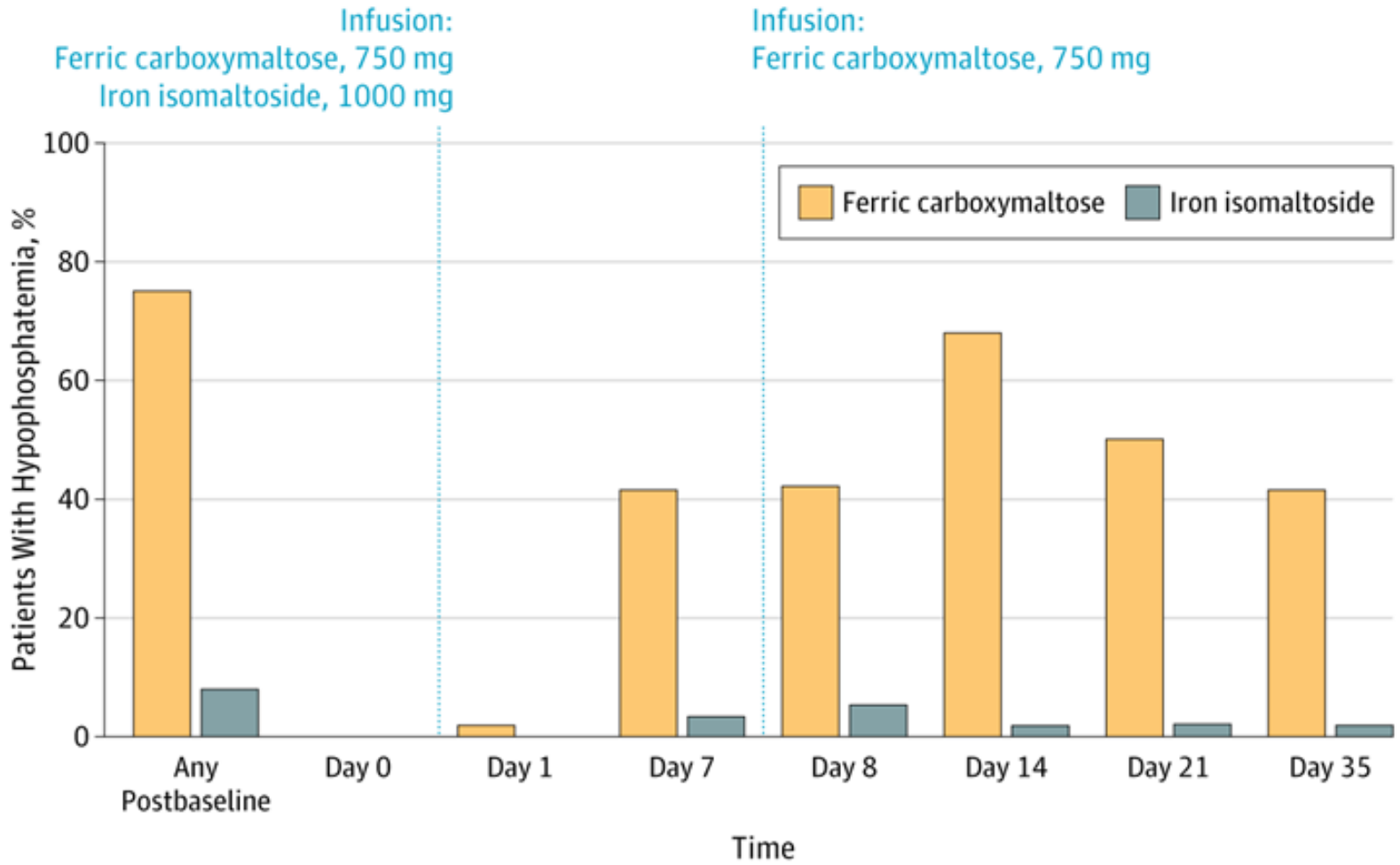
Two Randomized Clinical Trials

Myles Wolf, MD, MMSc[1]; Janet Rubin, MD[2]; Maureen Achebe, MD[3]; et al

» Author Affiliations | Article Information

JAMA. 2020;323(5):432-443. doi:10.1001/jama.2019.22450

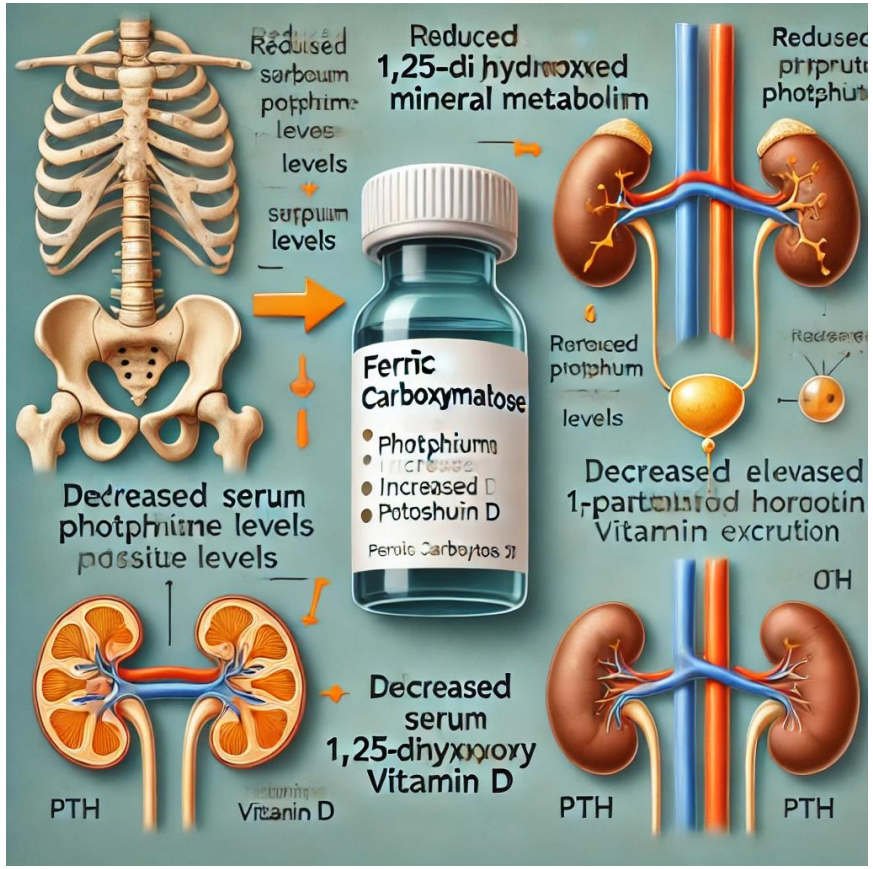
A Hypophosphatemia in trial A

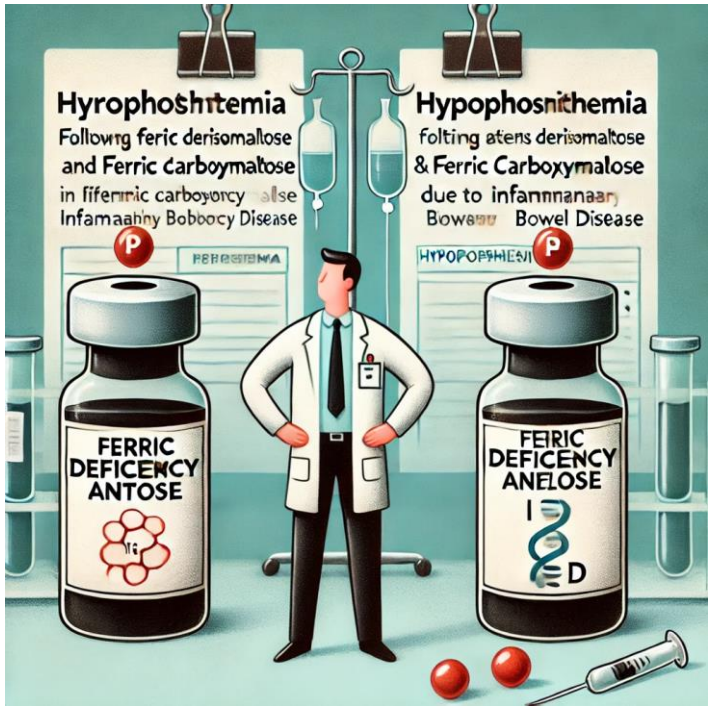


Patients, No./total No.								
Ferric carboxymaltose	45/60	0/60	1/56	24/58	24/57	38/56	28/56	24/58
Iron isomaltoside	5/63	0/63	0/59	2/60	3/57	1/58	1/54	1/59

- **Effects on Bone and Mineral Metabolism**:

- Patients treated with **ferric carboxymaltose** showed:
  - **Reduced serum phosphate** levels.
  - **Increased urinary phosphate excretion**, indicating phosphate loss through urine.
  - **Decreased serum 1,25-dihydroxyvitamin D**, leading to **secondary hyperparathyroidism**.
  - **Elevated parathyroid hormone (PTH)**, a compensatory response to hypophosphatemia.





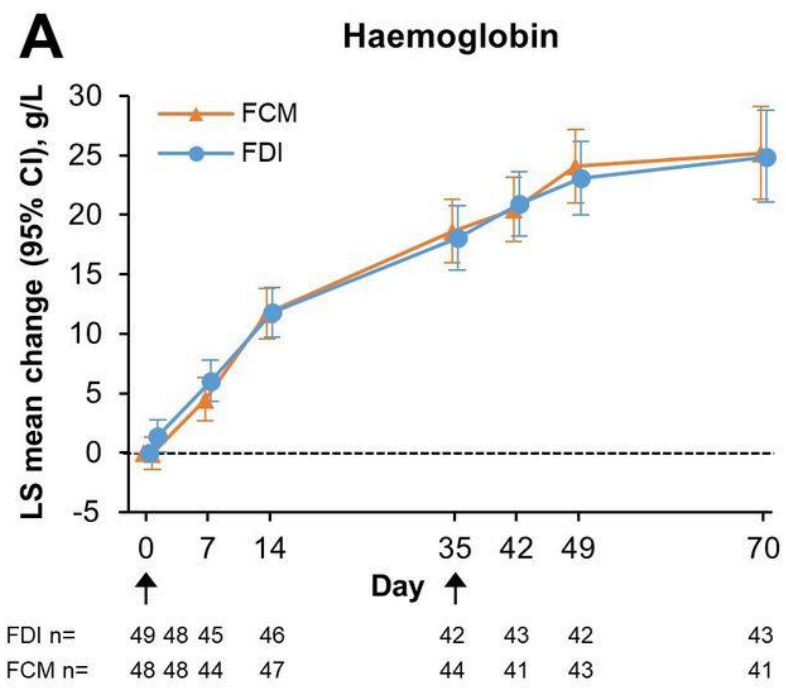
Inflammatory bowel disease
Original research

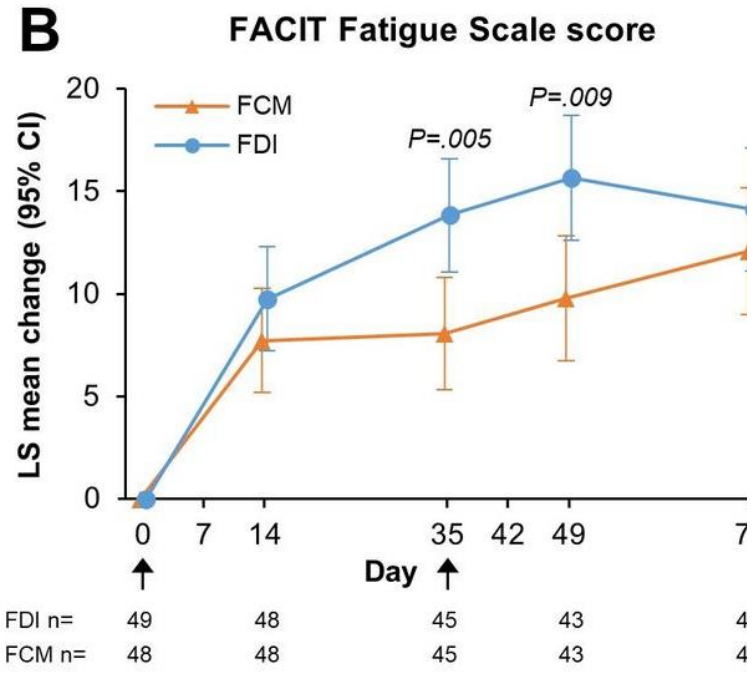
Hypophosphataemia following ferric derisomaltose and ferric carboxymaltose in patients with iron deficiency anaemia due to inflammatory bowel disease (PHOSPHARE-IBD): a randomised clinical trial

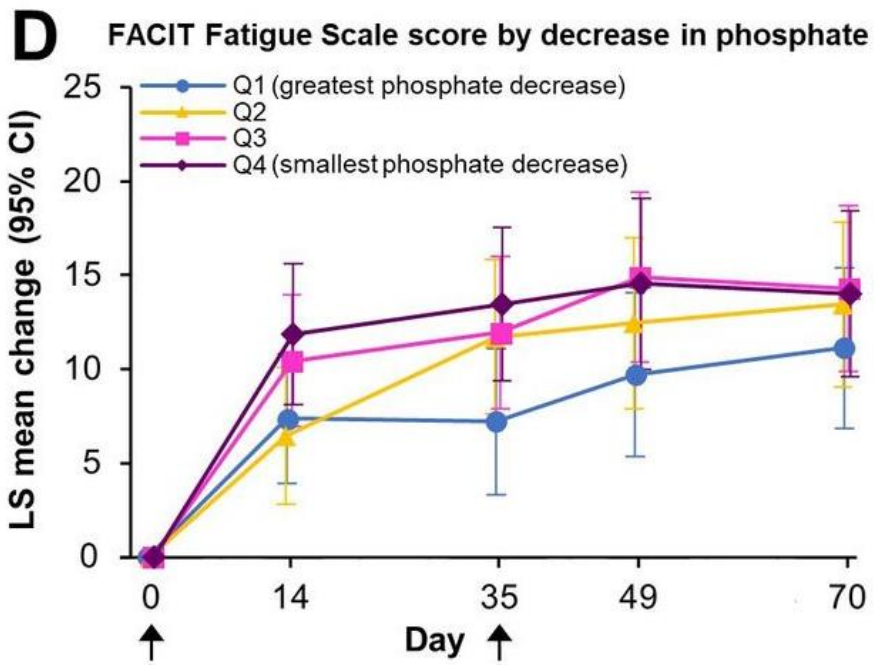
Heinz Zoller [1], Myles Wolf [2], Irina Blumenstein [3], Christian Primas [4], Stefan Lindgren [5], Lars L Thomsen [6], Walter Reinisch [7], Tariq Iqbal [8]

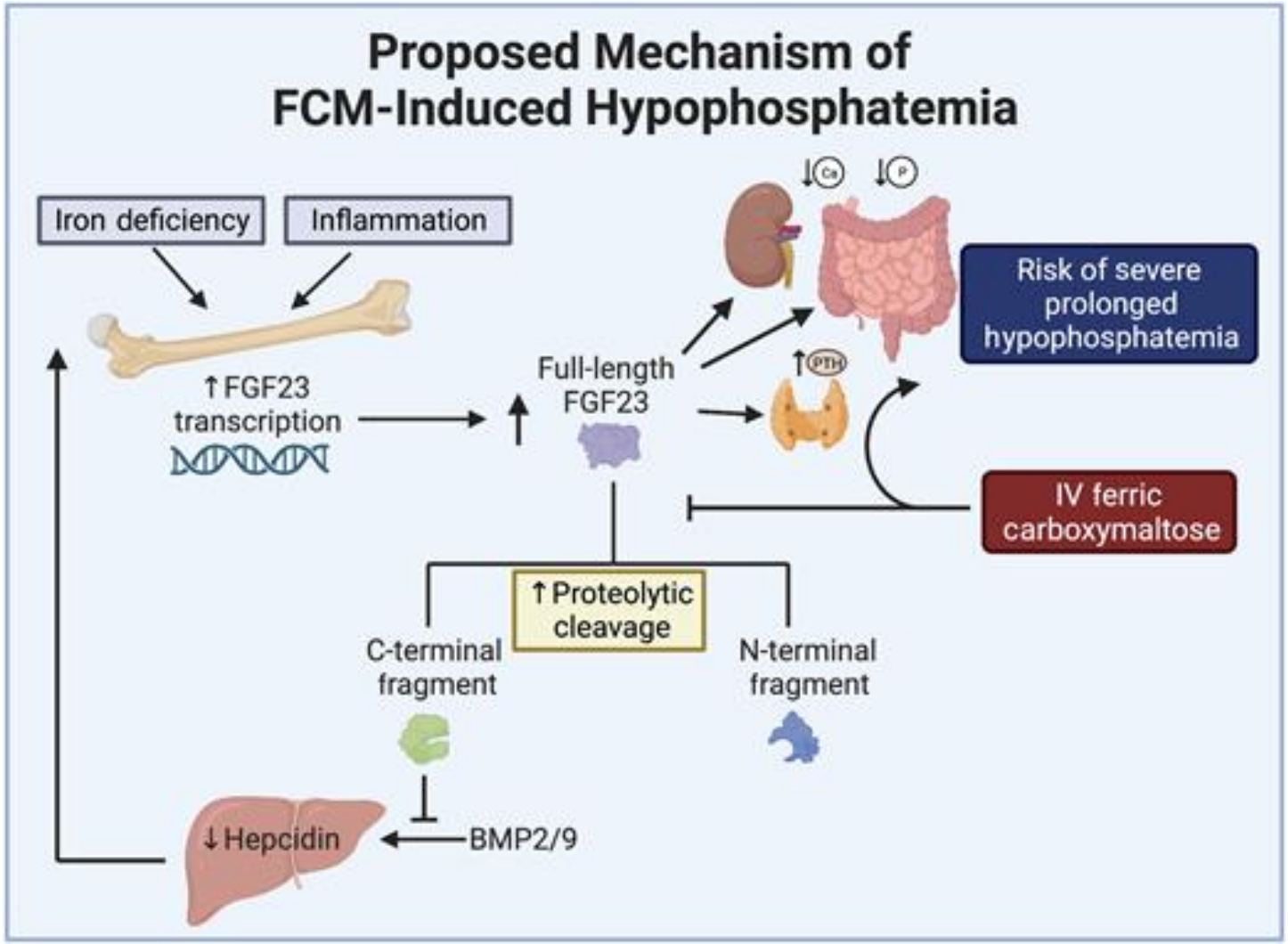
Correspondence to Dr Heinz Zoller, Department of Medicine I and Christian Doppler Laboratory on Iron and Phosphate Biology, Medical University of Innsbruck, Innsbruck, Tirol, Austria; heinz.zoller@i-med.ac.at

Undertreatment of fatigue







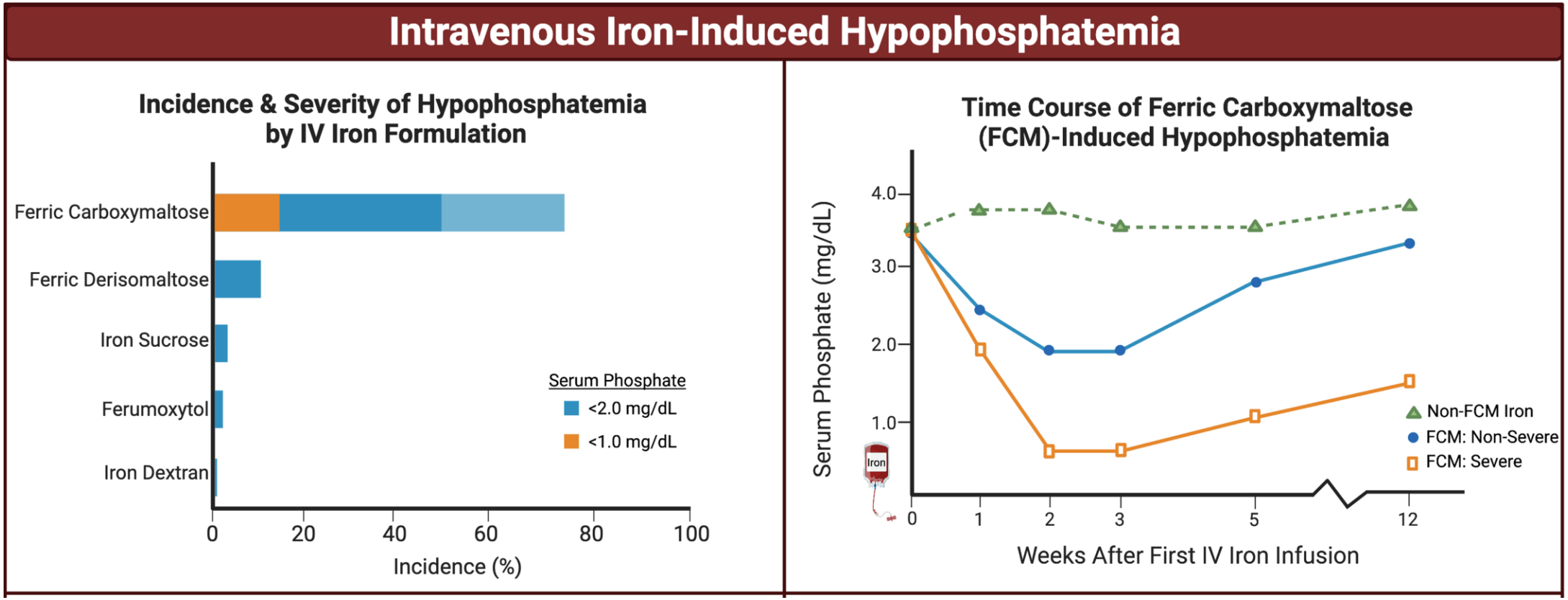


EVIDENCE-BASED MINIREVIEW | DECEMBER 8, 2023

Incidence, mechanism, and consequences of IV iron–induced hypophosphatemia

Evidence-Based Minireview

Kylee L. Martens, Myles Wolf

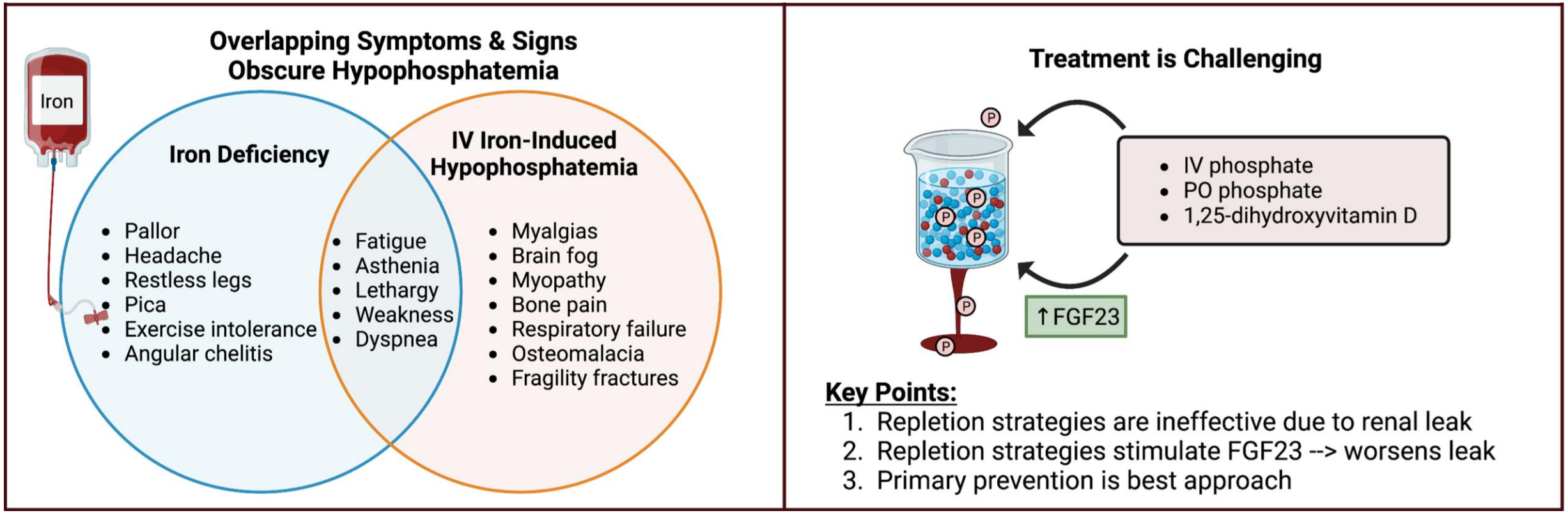


EVIDENCE-BASED MINIREVIEW | DECEMBER 8, 2023

Incidence, mechanism, and consequences of IV iron–induced hypophosphatemia

Evidence-Based Minireview

Kylee L. Martens, Myles Wolf



EVIDENCE-BASED MINIREVIEW | DECEMBER 8, 2023

Incidence, mechanism, and consequences of IV iron–induced hypophosphatemia

Evidence-Based Minireview

Kylee L. Martens, Myles Wolf

Conclusion

- It’s not okay to use Venofer.
- Iron is not unsafe
- But, Ferric Carboxymaltose may not be as safe as we thought