Efficacy and Safety of Oral Ferric Maltol (FM) in Treating Iron-Deficiency Anemia (IDA) in Patients with Chronic Kidney Disease (CKD): Randomized, Controlled Trial

Nelson Kopyt DO, FASN, FACP
Lehigh Valley Health Network, Nelson.Kopyt@lvhn.org

Published In/Presented At

Kopyt, N. (2018, October 26). *Efficacy and Safety of Oral Ferric Maltol (FM) in Treating Iron-Deficiency Anemia (IDA) in Patients with Chronic Kidney Disease (CKD): Randomized, Controlled Trial*. Presentation Presented at: ASN Kidney Week, San Diego, CA.

Efficacy and Safety of Oral Ferric Maltol (FM) in Treating Iron-Deficiency Anemia (IDA) in Patients with Chronic Kidney Disease (CKD): Randomized, Controlled Trial

Nelson P. Kopyt

Lehigh Valley Hospital, Allentown, PA, USA

On behalf of the AEGIS-CKD Study Group

The AEGIS-CKD trial was sponsored by Shield TX (UK) Ltd, Gateshead Quays, UK.

Ferric maltol is not currently licensed for the treatment of IDA in CKD in the United States.

Disclosures

- Principal investigator in the AEGIS-CKD phase III trial, which was sponsored by Shield TX (UK) Ltd, Gateshead Quays, UK
- The speaker retained full control over all content
  - The speaker wishes to thank Succinct Medical Communications for editorial and studio assistance in the preparation of this presentation
- Other disclosures:
  - Honoraria previously received from Mallinckrodt, Otsuka, Astra Zeneca, Amgen
  - Steering Committee member for Sandoz

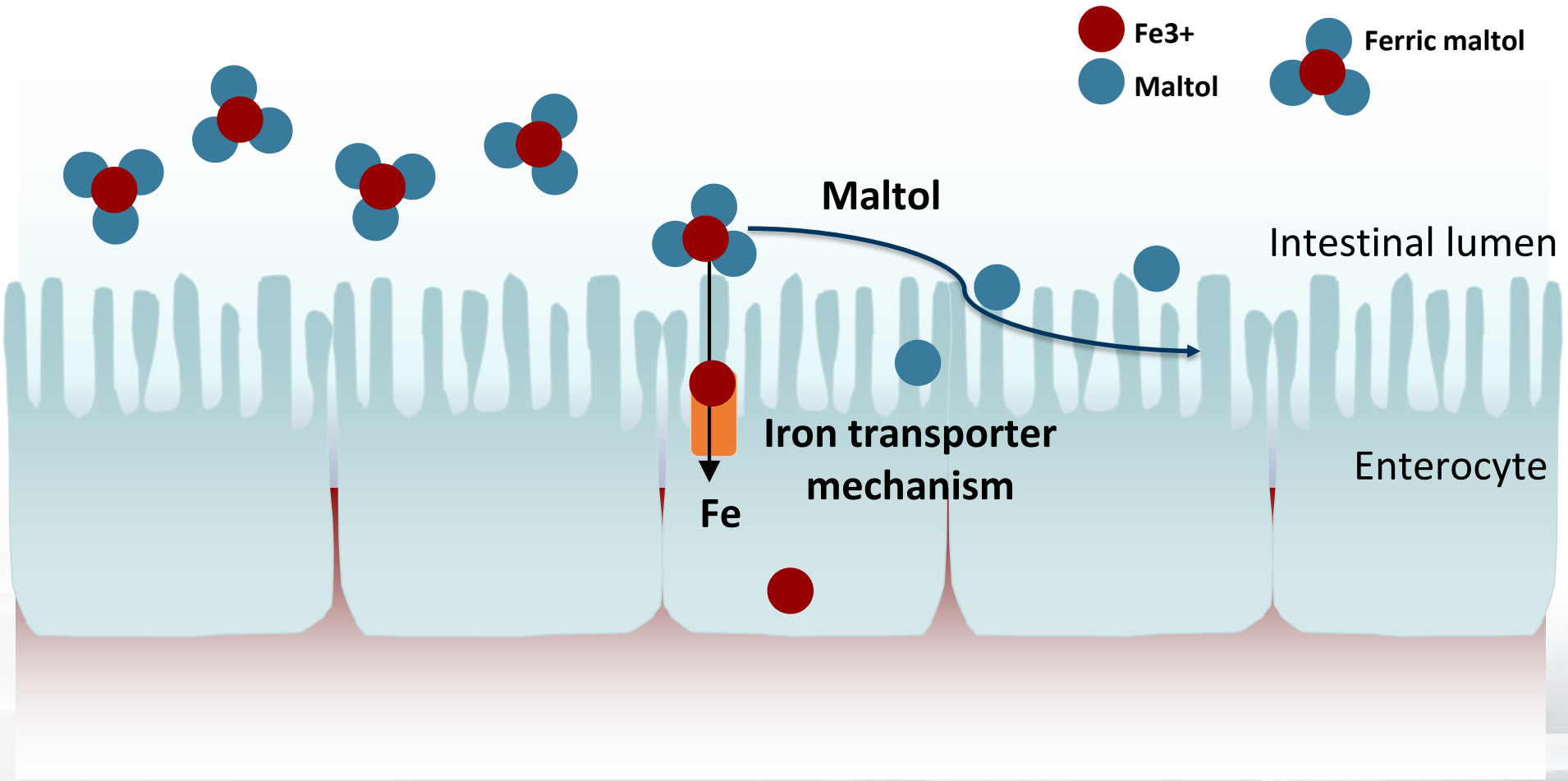
Rationale

- Anemia is prevalent in CKD, worsening with its progression[1,2]
  - A substantial proportion of people with CKD lack sufficient iron stores to support erythropoiesis
- Current treatment options for IDA have limitations:
  - Oral ferrous products may be poorly tolerated because of GI AEs[3]
  - Intravenous iron administration can be inconvenient and risks iron overload and allergic reactions[4,5]
- Ferric maltol is an oral iron-replacement therapy for IDA formulated to improve GI absorption

AE, adverse event; CKD, chronic kidney disease; GI, gastrointestinal; IDA, iron-deficiency anemia.

1. Hsu CY et al. J Am Soc Nephrol 2002;13:504–510. 2. Stauffer ME, Fan T. Plos One 2014;9:e84943. 3. Zhu A et al. Dig Dis Sci 2010;55:548–559. 4. Horl WH. J Am Soc Nephrol 2007; 18:382–393. 5. Del Vecchio L et al. Clin Kidney J 2016;9:260–267.

Mechanism of action of oral ferric maltol



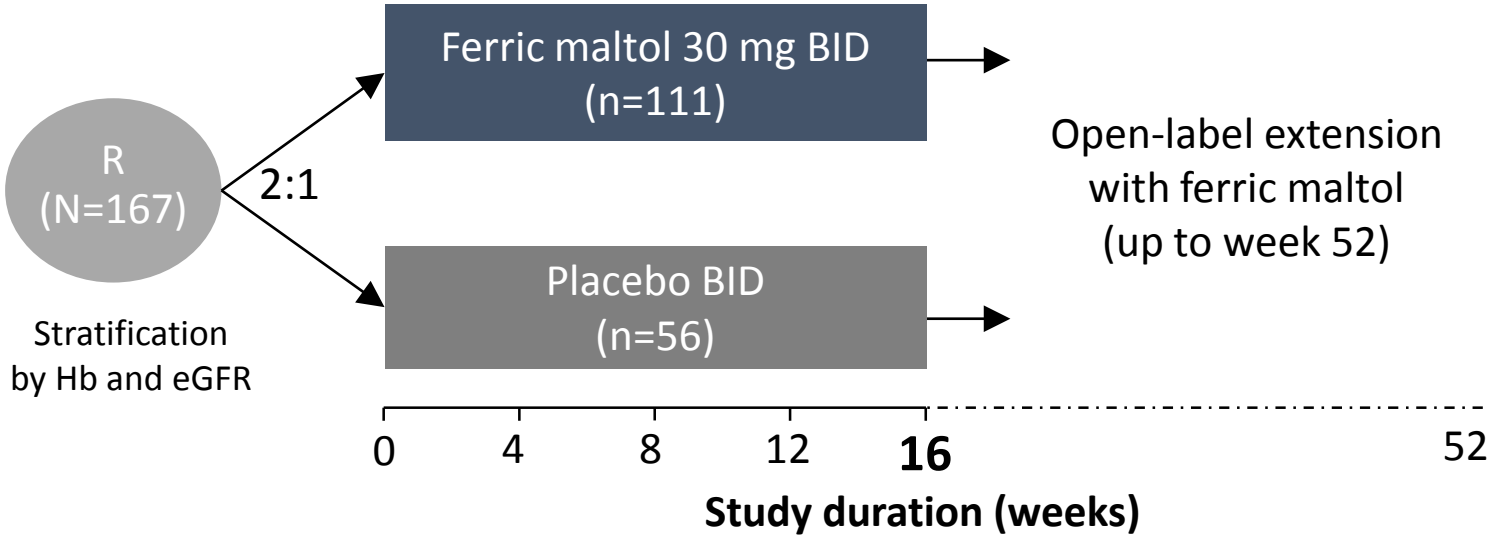
1. Andrews AC. Nat Rev Genet 2000;1:208–217; 2. Barrand MA, Callingham BA. Br J Pharmacol 1991;102:408–414; 3. Barrand MA et al. Br J Pharmacol 1991;102:723–729; 4. Barrand MA et al. J Pharm Pharmacol 1987;39:203–211; 5. Barrand MA et al. J Pharm Pharmacol 1990;42:279–282; 6. Bokemeyer B. Drug Discov Today 2015;20:1037–1039; 7. European Medicines Agency. Feraccru®. Assessment report, 17 December 2015; 8. Singh S, Hider RC. Anal Biochem 1988;171:47–54; 9. Stallmach A, Büning C. Expert Opin Pharmacother 2015;16:2859–2867.

AEGIS-CKD: phase III trial to evaluate the efficacy of oral ferric maltol vs placebo to treat IDA in patients with stage 3 or 4 CKD

Multicenter double-blind, randomized controlled trial (NCT02968368)

Key inclusion criteria:

- **eGFR ≥15 to <60 mL/min/1.73 m²**
- **Hb ≥8.0 to <11.0 g/dL**
  and **ferritin <250 µg/L + TSAT <25%**
  or **ferritin <500 µg/L + TSAT <15%**



Primary efficacy endpoint	Secondary efficacy endpoints include:
• **Change in Hb concentration from baseline to week 16**	• ≥1 g/dL and ≥2 g/dL Hb increases at week 16 • Hb ≥11 g/dL at week 16 • Hb changes from baseline to week 4 and week 8 • Changes in ferritin, TSAT and serum iron • Treatment-emergent AEs and SAEs

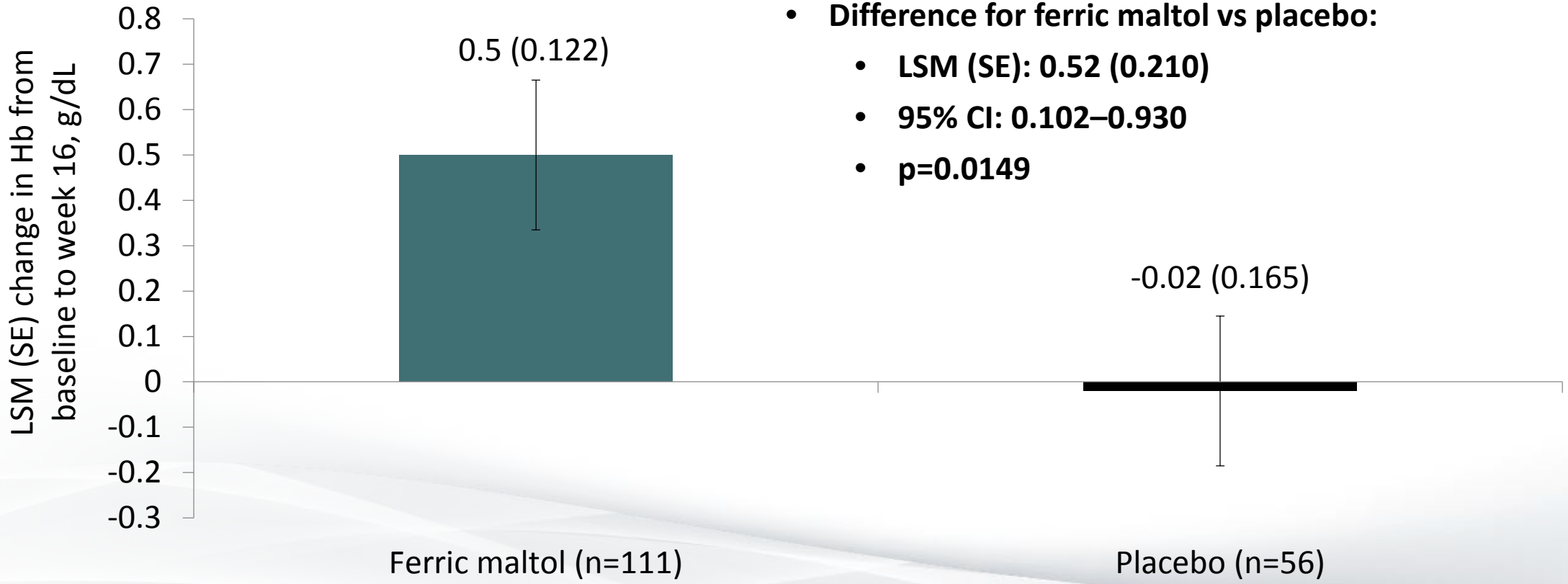
AE, adverse event; BID, twice daily; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; SAE, serious adverse event; TSAT, transferrin saturation.

Patient demographics and baseline disease characteristics (ITT population)

Demographic, n (%)		Ferric maltol (n=111)	Placebo (n=56)	Total (N=167)
Age, years	Mean (SD)	68.5 (12.4)	65.2 (12.8)	67.4 (12.6)
Sex, n (%)	Female	78 (70.3)	39 (69.6)	117 (70.1)
	Male	33 (29.7)	17 (30.4)	50 (29.9)
Race, n (%)	Asian	2 (1.8)	0	2 (1.2)
	American Indian	1 (0.9)	0	1 (0.6)
	African American	23 (20.7)	12 (21.4)	35 (21.0)
	White	81 (73.0)	42 (75.0)	123 (73.7)
	Other	4 (3.6)	2 (3.6)	6 (3.6)
Hb, g/dL	Mean (SD)	10.06 (0.769)	10.03 (0.817)	10.05 (0.783)
	<9.5, n (%)	21 (18.9)	11 (19.6)	32 (19.2)
	≥9.5, n (%)	90 (81.1)	45 (80.4)	135 (80.8)
eGFR, mL/min/1.73 m^2	Mean (SD)	31.9 (11.53)	29.7 (10.56)	31.1 (11.23)
	≤30, n (%)	59 (53.2)	30 (53.6)	89 (53.3)
	>30, n (%)	52 (46.8)	26 (46.4)	78 (46.7)

eGFR, estimated glomerular filtration rate; Hb, hemoglobin; ITT, intent-to-treat.

Primary endpoint: change in Hb concentration from baseline to week 16 (ITT population)



- **Difference for ferric maltol vs placebo:**
  - **LSM (SE): 0.52 (0.210)**
  - **95% CI: 0.102–0.930**
  - **p=0.0149**

CI, confidence interval; Hb, hemoglobin; ITT, intent-to-treat; LSM, least-squares mean; SE, standard error.

Secondary efficacy analyses (ITT population)

	Ferric maltol	Placebo	Ferric maltol vs placebo	p value
Hb levels at week 16, % patients			Adjusted odds ratio (95% CI)	
≥1 g/dL change from baseline	19.8	8.9	2.48 (0.86–7.14)	0.0923
≥2 g/dL change from baseline	6.3	0.0	NC*	NC*
≥11 g/dL	26.0	17.5	2.60 (1.02–6.60)	**0.0442**
Iron parameters: changes from baseline to week 16			LSM difference (SE) (95% CI)	
Ferritin, µg/dL	25.49 (5.400)	–8.25 (7.614)	33.73 (9.354) (15.264–52.205)	**0.0004**
TSAT, %	3.78 (0.638)	–0.69 (0.900)	4.47 (1.106) (2.286–6.653)	**<0.0001**
Serum iron, µmol/L	1.58 (0.350)	–0.21 (0.494)	1.79 (0.606) (0.591–2.985)	**0.0037**

*As the placebo group had no patients who met the criteria, the odds ratio was not calculated.

CI, confidence interval; Hb, hemoglobin; ITT, intent-to-treat; LSM, least-squares mean; NC, not calculated; SE, standard error; TSAT, transferrin saturation.

Adverse events (safety population)

- A higher proportion of patients on ferric maltol vs placebo completed 16 weeks of treatment:
  - Ferric maltol 81% (n=90/111)
  - Placebo 70% (n=39/56)

		Ferric maltol (n=111)	Placebo (n=56)
Patients with treatment-emergent adverse events (TEAEs)		% patients	% patients
Any TEAE	(deemed related to study drug)	67.6 (18.9)	75.0 (10.7)
Serious TEAE	(deemed related to study drug)	20.7 (0)	21.4 (0)
TEAE resulting in death	(deemed related to study drug)	0.9 (0)	1.8 (0)
TEAE resulting in treatment withdrawal	(deemed related to study drug)	6.3 (2)	8.9 (2)

Adverse events (safety population)

	Ferric maltol (n=111)	Placebo (n=56)
Adverse events affecting ≥5% of patients	% patients	% patients
Gastrointestinal disorders	40.5	30.4
Diarrhea	9.0	8.9
Nausea	8.1	8.9
Constipation	8.1	3.6
Feces discolored	7.2	1.8
Metabolism and nutrition disorders	18.9	23.2
Hyperkalemia	3.6	12.5
Infections and infestations	15.3	23.2
Urinary tract infection	6.3	8.9
Renal and urinary disorders	9.0	10.7
Acute kidney injury	4.5	7.1
Blood and lymphatic system disorders	4.5	16.1
Anemia	3.6	10.7

Conclusion

- Oral ferric maltol resulted in statistically significant and clinically meaningful increases in hemoglobin concentration, and in all iron parameters, from baseline to week 16 vs placebo, supporting the efficacy of oral ferric maltol in treating IDA in patients with stage 3 or 4 CKD
- Ferric maltol was generally well tolerated with a lower rate of discontinuation due to AEs than placebo. Only minor differences were noted in the safety profile and overall GI AEs vs placebo

AEs, adverse events; CKD, chronic kidney disease; GI, gastrointestinal; IDA, iron-deficiency anemia.

Acknowledgments

- The AEGIS-CKD trial was sponsored by Shield TX (UK) Ltd, Gateshead Quays, UK
- The authors wish to thank Succinct Medical Communications for editorial and studio assistance in the preparation of this presentation