Ironing Out the Details: A Review of Iron Deficiency Anemia and Safety Update for Iron Replacement Products

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Disclosure

• I do not have (nor does any immediate family member have) a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation.

• There was no financial support obtained for this CPE activity.
Objectives

• Compare and contrast different laboratory values used in the diagnosis of iron deficiency anemia

• Describe unique characteristics of different oral and parenteral iron replacement products

• Integrate safety information pertaining to administration of iron replacement products into patient care
Epidemiology

• Iron deficiency affects 2 billion people worldwide
  – Recent prevention efforts have recently decreased global rates of deficiency
  – Prevalence is now highest in Central and West Africa and South Asia
• Iron deficiency is the most common cause of anemia worldwide
Risk Factors

• Insufficient dietary intake
• Blood loss due to worm colonization
• Vegetarian diet
• Chronic blood loss
• Malabsorptive disorders (short bowel syndrome, inflammatory bowel disease)
• Reduced iron intake from prolonged breastfeeding and/or excessive cow’s milk intake
• Heavy menstrual bleeding in adolescent females
## Risk Factors

### Table 1. Causes of Iron Deficiency.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physiologic</strong></td>
<td></td>
</tr>
<tr>
<td>Increased demand</td>
<td>Infancy, rapid growth (adolescence), menstrual blood loss, pregnancy (second and third trimesters), blood donation</td>
</tr>
<tr>
<td><strong>Environmental</strong></td>
<td>Insufficient intake, resulting from poverty, malnutrition, diet (e.g., vegetarian, vegan, iron-poor)</td>
</tr>
<tr>
<td><strong>Pathologic</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased absorption</td>
<td>Gastrectomy, duodenal bypass, bariatric surgery, <em>Helicobacter pylori</em> infection, celiac sprue, atrophic gastritis, inflammatory bowel diseases (e.g., ulcerative colitis, Crohn’s disease)*</td>
</tr>
<tr>
<td>Chronic blood loss</td>
<td>Gastrointestinal tract, including esophagitis, erosive gastritis, peptic ulcer, diverticulitis, benign tumors, intestinal cancer, inflammatory bowel diseases, angiodysplasia, hemorrhoids, hookworm infestation, obscure source</td>
</tr>
<tr>
<td></td>
<td>Genitourinary system, including heavy menses, menorrhagia, intravascular hemolysis (e.g., paroxysmal nocturnal hemoglobinuria, autoimmune hemolytic anemia with cold antibodies, march hemoglobinuria, damaged heart valves, microangiopathic hemolysis)</td>
</tr>
<tr>
<td></td>
<td>Systemic bleeding, including hemorrhagic telangiectasia, chronic schistosomiasis, Munchausen’s syndrome (e.g., self-induced hemorrhages)</td>
</tr>
<tr>
<td><strong>Drug-related</strong></td>
<td>Glucocorticoids, salicylates, NSAIDs, proton-pump inhibitors</td>
</tr>
<tr>
<td><strong>Genetic</strong></td>
<td>Iron-refractory iron-deficiency anemia</td>
</tr>
<tr>
<td><strong>Iron-restricted erythropoietic</strong></td>
<td>Treatment with erythropoiesis-stimulating agents, anemia of chronic disease, chronic kidney disease*</td>
</tr>
</tbody>
</table>

* Inflammatory conditions may be associated with iron deficiency. NSAIDs denotes nonsteroidal antiinflammatory drugs.
Definitions

• Anemia: Hemoglobin values that are more than 2 standard deviations below the mean
  – Men: Hgb < 13.4 g/dL, Women: Hgb < 12 g/dL

• Iron deficiency: reduction in iron stores
  – Reflected by a low ferritin
  – Anemia not necessarily present (Hgb still normal)

• Iron Deficiency Anemia = depleted iron stores result in low Hgb/Hct

Laboratory Parameters

- Complete Blood Count (CBC)
  - Hemoglobin (Hgb or Hb)
  - Hematocrit (Hct)
  - Red Blood Cell Count (RBC)

- Red Blood Cell Indices
  - Mean Corpuscular/Cell Volume (MCV)
  - MCH
  - MCHC
  - Red Cell Distribution Width (RDW)

- Iron Studies
  - Ferritin
  - Transferrin
  - Iron
  - Total Iron Binding Capacity (TIBC)
  - Transferrin Saturation (% Sat)
CBC

- Dependent on RBC mass and plasma volume
  - Values decrease when plasma volume increases (dilution)
  - Values increase when plasma volume decreases (hemoconcentration)
Red Blood Cell Count (RBC)

• The number of red corpuscles in a given amount of blood

• Normal Values
  – Adult Men: $4.5-5.9 \times 10^6 \text{ cells/} \mu\text{L}$ or $4.5-5.9 \times 10^{12} \text{ cells/L}$
  – Adult Women: $4.1-5.1 \times 10^6 \text{ cells/} \mu\text{L}$ or $4.1-5.1 \times 10^{12} \text{ cells/L}$
Hemoglobin (Hgb)

• A protein found in blood cells that carries oxygen to tissues

• Laboratory Value
  – The amount of the protein found in a given volume of whole blood (usually 100 mL)
  – Provides an indication of the oxygen transport capacity of the blood

• Normal Values
  – Men: 14-17.5 g/dL
  – Women: 12.3-15.3 g/dL
Hematocrit (Hct)

• The percentage volume of blood that is composed of erythrocytes
• Also known as the packed cell volume
• Generally three times the value of Hgb
• Normal Values
  – Men: 42-50%
  – Women: 36-45%

Mean Corpuscular/Cell Volume (MCV)

• Measure of the average red blood cell volume

• Calculation: \( MCV = \frac{Hct}{RBC} \)

• Determines the type of anemia
  
  – Macrocytic (MCV > 100 fL/cell)
    
    – Causes: Vitamin B12 deficiency, folate deficiency, increase in peripheral reticulocytes, cold agglutinins
  
  – Normocytic (MCV 80-100 fL/cell) *normal range*
  
  – Microcytic (MCV < 80 fL/cell)

  • Causes: Iron deficiency anemia, \( \beta \)-thassemia
Mean Corpuscular/Cell Hemoglobin (MCH)

- Measure of the concentration of hemoglobin in a given volume of packed red blood cells

- Calculation: $MCH = \frac{Hgb}{RBC}$

- Normal range: 320-360 g/L

- Describes the color of the red blood cells
  - Low MCH = Hypochromic (pale)
Mean Cell Hemoglobin Concentration (MCHC)

• Calculation: MCHC = \( \frac{Hgb}{Hct} \)

• Normal Value: 33 g/dL

• Iron deficiency is the only anemia in which the MCHC is routinely low
  – Other disorders of hemoglobin synthesis will cause MCHC to be low
Red Cell Distribution Width (RDW)

- Measure of the variation of red blood cell width
- Coefficient of variation of the MCV

Calculation: \[ RDW = \frac{\text{Standard deviation of MCV}}{\text{Mean value of MCV}} \times 100 \]

- Normal range: 11-14%

- Helps determine if anemia is from a single or mixed cause
  - Elevated level=anisocytosis (variation in red cell size)
Serum Ferritin

• Iron-protein complex found in macrophages
  – Some found in serum
• Measure of iron stores in the body
• Normal range: >10-20 μg/L
• Acute phase reactant
Serum Transferrin and Iron

• Transferrin
  – Iron-protein complex responsible for iron transport
  – Reflects total iron binding capacity
  – Normal Range: 200-400 mg/dL

• Iron
  – Measures iron bound to transferrin
  – Normal range: 50-150 μg/dL
Total Iron Binding Capacity (TIBC)

- Measure of the iron binding capacity of transferrin
- Increased in IDA due to a compensatory increase in transferrin synthesis
- Normal Range: 250-410 μg/dL
Transferrin Saturation (% Sat)

- Calculation: \[ \% \text{ Saturation} = \frac{\text{Serum Iron}}{\text{TIBC}} \]

- Iron deficient erythropoiesis exists if % Saturation is <15%

- Decreases in IDA because TIBC is increased

Is this Iron Deficiency Anemia?

- 42 year old female with crohn’s disease, parenteral nutrition dependent, receives minimal oral intake
- CBC: RBC = 3.8 x 10^6 cells/μL; Hgb: 9.4 g/dL; Hct: 31%
- Cell Indices: MCV=70 fL/cell; MCH: 237 g/L; MCHC=30 g/dL; RDW: 15%
- Iron Studies: Ferritin: 9 μg/L; Transferrin: 415 mg/dL; Iron: 40 μg/dL; TIBC: 440 μg/dL; % Sat: 9%
### Table 2
Laboratory tests in microcytic anemias

<table>
<thead>
<tr>
<th>Test</th>
<th>Iron Deficiency Anemia</th>
<th>Anemia of Inflammation</th>
<th>α- or β-Thalassemia Trait</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCV</td>
<td>↓</td>
<td>nl or ↓ (70)</td>
<td>↓ ↓ (65–75)</td>
</tr>
<tr>
<td>RDW</td>
<td>↑↑</td>
<td>nl or sl ↑</td>
<td>nl or sl ↑</td>
</tr>
<tr>
<td>RBC</td>
<td>↓</td>
<td>↓</td>
<td>↑ or nl</td>
</tr>
<tr>
<td>Serum iron</td>
<td>↓</td>
<td>↓</td>
<td>nl or ↑</td>
</tr>
<tr>
<td>TIBC</td>
<td>↑</td>
<td>nl or ↓</td>
<td>nl or ↓</td>
</tr>
<tr>
<td>Transferrin saturation</td>
<td>↓</td>
<td>↓</td>
<td>nl</td>
</tr>
<tr>
<td>Ferritin</td>
<td>↓ ↓</td>
<td>nl or ↑</td>
<td>nl or ↑</td>
</tr>
<tr>
<td>Soluble transferrin receptor</td>
<td>↑</td>
<td>nl</td>
<td>↑</td>
</tr>
</tbody>
</table>
Oral Iron Replacement Therapies
Enteral Iron

- Absorbed from diet in the duodenum and proximal jejunum
  - Reduced to ferrous form by duodenal cytochrome b
  - Ferrous form of iron transported into the enterocyte by divalent metal transporter 1
  - Ferrous iron can then be stored as ferritin or is shunted to ferroportin, which converts it into ferric iron,
  - Ferric iron immediately binds to transferrin and is transported to the bone marrow for hemoglobin synthesis
Drug-Food Interactions With Iron

• Enhances iron absorption:
  – Vitamin C

• Decreases iron absorption:
  – Taking iron supplement with meat
    • Saturable enterocyte absorption
  – Calcium
  – Fiber
  – Tea/coffee
Oral Iron Therapies

<table>
<thead>
<tr>
<th>Iron Supplement</th>
<th>Elemental Iron Content</th>
<th>Iron Salt Content</th>
<th>% Elemental Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous Fumarate</td>
<td>106 mg</td>
<td>324 mg</td>
<td>33</td>
</tr>
<tr>
<td>Ferrous Sulfate</td>
<td>65 mg</td>
<td>325 mg</td>
<td>20</td>
</tr>
<tr>
<td>Ferrous Gluconate</td>
<td>37.5 mg</td>
<td>324 mg</td>
<td>11.6</td>
</tr>
</tbody>
</table>

- Multiple products of various iron content exist
- These preparations are equally bioequivalent
- Recommended dose:
  - Adult: 100-200 mg/day in 2-3 divided doses
  - Pediatric: 3-6 mg/kg/day in 3 divided doses

Multivitamins With Iron

- **Poly-vi-sol®** with iron: 1 mL = 10 mg iron
- **Flinstones™** with iron: 1 tablet = 18 mg iron
- **One-a-Day® Women’s**: 1 tablet = 18 mg iron
- **One-a-Day® Men’s**: 1 tablet = none
- **Centrum® Silver**: 1 tablet = none
Common Adverse Effects

• Nausea
• Vomiting
• Stomach pain
• Constipation
• Darkening of stools
• Contact dermatitis
Intravenous Iron Replacement Therapies
## Indications for Intravenous Iron

### Table 3. Indications for Parenteral Iron Therapy.

<table>
<thead>
<tr>
<th>Established indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure of oral therapy</td>
</tr>
<tr>
<td>Iron intolerance or with low iron levels that are refractory to treatment (e.g.,</td>
</tr>
<tr>
<td>after gastrectomy or duodenal bypass, with <em>Helicobacter pylori</em> infection,</td>
</tr>
<tr>
<td>or with celiac disease, atrophic gastritis, inflammatory bowel disease, or</td>
</tr>
<tr>
<td>genetically induced IRIDA*</td>
</tr>
<tr>
<td>Need for quick recovery (e.g., with severe iron deficiency in the second or third</td>
</tr>
<tr>
<td>trimester of pregnancy or with chronic bleeding that is not manageable with oral iron,</td>
</tr>
<tr>
<td>as may occur in patients with congenital coagulation disorders)</td>
</tr>
<tr>
<td>Substitution for blood transfusions when not accepted by patient for religious</td>
</tr>
<tr>
<td>reasons</td>
</tr>
<tr>
<td>Use of erythropoiesis-stimulating agents in chronic kidney disease</td>
</tr>
</tbody>
</table>

**Potential indication**

| Anemia of chronic kidney disease (without treatment of erythropoiesis-stimulating      |
| agents)                                                                               |
| Persistent anemia after use of erythropoiesis-stimulating agents in patients           |
| with cancer who are receiving chemotherapy                                            |
| Anemia of chronic disease unresponsive to treatment with erythropoiesis-stimulating   |
| agents alone                                                                            |

**Potential indication with insufficient supporting data**

| Iron deficiency in heart failure                                                     |
| Transfusion-sparing strategy in surgical patients                                    |
Intravenous Iron

- All products are colloids of spherical iron-carbohydrate nanoparticles
  - Core of each particle: iron-oxyhydroxide gel
  - A carbohydrate shell is required to stabilize the core, slow down the release of bioactive iron, and maintain a colloidal suspension
- Products differ in the size of the core and the type and density of the surrounding carbohydrate
Mechanism of Action

- When administered:
  - The iron carbohydrate complex is phagocytized by macrophages
  - Iron is released from the complex and then assimilated into ferritin or released into extracellular transferrin
Intravenous Iron Options

• First Generation
  – Iron Dextran (High Molecular Weight)

• Second Generation
  – Iron Dextran (Low Molecular Weight)
  – Sodium Ferric Gluconate
  – Iron Sucrose

• Third Generation
  – Ferrumoxytol
  – Ferric Carboxymaltose
# Comparison of IV Iron Products

<table>
<thead>
<tr>
<th>Iron Product</th>
<th>Carbohydrate</th>
<th>Side (Daltons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Molecular Weight Iron Dextran*</td>
<td>Dextran polysaccharides</td>
<td>400,000</td>
</tr>
<tr>
<td>Low Molecular Weight Iron Dextran</td>
<td>Dextran polysaccharides</td>
<td>150,000-165,000</td>
</tr>
<tr>
<td>Sodium Ferric Gluconate</td>
<td>Gluconate</td>
<td>289,000-444,000</td>
</tr>
<tr>
<td>Iron Sucrose</td>
<td>Sucrose</td>
<td>34,000-60,000</td>
</tr>
<tr>
<td>Ferrumoxytol</td>
<td>Polyglucose sorbitol carboxymethylether</td>
<td>750,000</td>
</tr>
<tr>
<td>Ferric Carboxymaltose</td>
<td>Carboxymaltose</td>
<td>150,000</td>
</tr>
</tbody>
</table>

*High Molecular Weight Iron Dextran is now discontinued in the United States
Iron Dextran

• FDA Approved Indication: Iron deficiency anemia in which oral therapy is unsatisfactory or impossible
• FDA approved for ages 4 months or older
• Black Box warning for hypersensitivity reactions
  – Mandates a test dose be given
BOXED WARNING

WARNING: RISK FOR ANAPHYLACTIC-TYPE REACTIONS

Anaphylactic-type reactions, including fatalities, have followed the parenteral administration of iron dextran injection.

- Have resuscitation equipment and personnel trained in the detection and treatment of anaphylactic-type reactions readily available during INFeD administration.

Administer a test INFeD dose prior to the first therapeutic dose. If no signs or symptoms of anaphylactic-type reactions follow the test dose, administer the full therapeutic INFeD dose.

- During all INFeD administrations, observe for signs or symptoms of anaphylactic-type reactions. Fatal reactions have followed the test dose of iron dextran injection. Fatal reactions have also occurred in situations where the test dose was tolerated.

- Use INFeD only in patients in whom clinical and laboratory investigations have established an iron deficient state not amenable to oral iron therapy.

- Patients with a history of drug allergy or multiple drug allergies may be at increased risk of anaphylactic-type reactions to INFeD.
Test Dose

• Assesses tolerance of patient to the medication

• Pediatrics:
  – Infants <10 kg: 10 mg
  – Children 10-20 kg: 15 mg
  – Children >20 kg: 25 mg

• Adults: 25 mg x 1 dose

• Monitor for 1 hour after administration
  – If tolerated, can give remainder of doses after

• Have medications for reactions pre-ordered PRN
  – Diphenhydramine, hydrocortisone, epinephrine

• May cause false reassurance
Dosing: Iron Deficit Calculation

- Iron Deficit (mg) =
  \[0.3 \times \text{weight in lbs} \times [100 - \left(\frac{\text{Actual Hgb}}{\text{Goal Hgb}}\right) \times 100]\]
  - Goal Hgb = 14.8 g/dL
  - If <15 kg, goal is adjusted to 12 g/dL
- Iron Deficit (mg) = 50 \times [0.442 (\text{Goal Hg} - \text{Actual Hgb}) \times \text{LBW} + (0.26 \times \text{LBW})]
  - LBW=lean body weight
  - For patients weighing 5-15 kg, use actual body weight
Iron Dextran: Intramuscular Administration

• Z-track Technique
  – IM injection into buttocks (rotate daily)
  – Dosing:
    • Infants <5 kg: 25 mg
    • Children 5-10 kg: 50 mg
    • Children >10 kg, Adolescents, and Adults: 100 mg
    • Maximum: 100 mg (2 mL) per dose
    • Continue repletion until iron deficit given
  – Not recommended due to side effects (discomfort, tissue damage, skin discoloration)

Iron Dextran: Intravenous Administration

• Pediatric and Adult Dosing
  – Up to 100 mg maximum per dose until iron deficit completed
  – Administered no faster than 50 mg/min
  – Dilution not recommended for this dosing regimen
Iron Dextran: Total Dose Infusion

• After test dose/monitoring, the remainder of the iron deficit is given to the patient.

• Total replacement dose can be diluted in 250-1000 mL of normal saline.
  – Dilution in 5% dextrose can cause an increased incidence of pain and phlebitis.
  – Infused over 4 to 6 hours (dependent on dose).

Sodium Ferric Gluconate

• FDA approved for patients with chronic kidney disease receiving hemodialysis who are receiving supplemental epoetin therapy
• FDA approved for ages 6 and older
• No black box warning
• No test dose required
Dosing and Administration: Sodium Ferric Gluconate

• Adult
  – 125 mg elemental iron/dose x 8 doses (total: 1000 mg elemental iron)
  – Can be diluted in 100 mL of normal saline or can be given undiluted (maximum rate: 12.5 mg/min)
  – Infused slowly over 1 hour during dialysis

• Pediatric
  – 1.5 mg/kg elemental iron (maximum: 125 mg) x 8 doses
  – Dilute in 25 mL of normal saline (giving undiluted not recommended)
  – Infused slowly over 1 hour during dialysis
Iron Sucrose

• FDA approved for patients with anemia and chronic kidney disease
• FDA approved for ages 2 and older
• No black box warning
• No test dose required
<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing</th>
<th>Dilution and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis (HD) Dependent Chronic Kidney Disease (CKD)</td>
<td>100 mg x 10 doses during consecutive HD sessions</td>
<td>Give undiluted as slow intravenous injection over 2-5 minutes or dilute in no more than 100 mL of normal saline and give over at least 15 minutes</td>
</tr>
<tr>
<td>Non-Dialysis Dependent Chronic Kidney Disease</td>
<td>200 mg x 5 doses over 14 days</td>
<td>Give undiluted as slow intravenous injection over 2-5 minutes or dilute in no more than 100 mL of normal saline and give over at least 15 minutes</td>
</tr>
</tbody>
</table>
| Peritoneal Dialysis Dependent Chronic Kidney Disease | Day 1 and 14: 300 mg  
Day 28: 400 mg | 300 mg doses: Dilute in no more than 250 mL normal saline and give over 1.5 hours  
400 mg dose: Dilute in no more than 250 mL of normal saline and give over 2.5 hours |
# Pediatric Dosing: Iron Sucrose

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing</th>
<th>Dilution and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis (HD) Dependent Chronic Kidney Disease (CKD)</td>
<td>0.5 mg/kg (maximum dose: 100 mg) every 2 weeks for 12 weeks</td>
<td>Give undiluted as slow intravenous injection over 5 minutes or dilute in 25 mL of normal saline and give over at least 5-60 minutes</td>
</tr>
<tr>
<td>Non-Dialysis Dependent and Peritoneal Dialysis Dependent Chronic Kidney Disease</td>
<td>0.5 mg/kg (maximum dose: 100 mg) every 4 weeks for 12 weeks</td>
<td>Give undiluted as slow intravenous injection over 5 minutes or dilute in 25 mL of normal saline and give over at least 5-60 minutes</td>
</tr>
</tbody>
</table>
Ferumoxytol

- FDA Approved Indication: treatment of iron deficiency anemia in adult patients with CKD
- FDA approved for adults only
- Black Box Warning
- Test dose not required
Dosing and Administration

• Adult
  – 510 mg elemental iron x 1 dose, followed by 510 mg elemental iron x 1 dose 3 to 8 days later
  – Infuse in 50-200 mL of normal saline or 5% dextrose over at least 15 minutes

• Pediatric
  – 5.8-12 mg/kg elemental iron/dose
  – Given over 15-60 minutes

Ann Pharmacotherapy 2011; 45: e63.
Efficacy and safety of IV ferumoxytol for adults with iron deficiency anemia previously unresponsive to or unable to tolerate oral iron

Saroj Vadhan-Raj,1 William Strauss,2* David Ford,3 Kristine Bernard,2 Ralph Boccia,4 Joe Li,2 and Lee F. Allen2

• Randomized, double blind, placebo controlled, multicenter, multinational, phase III trial

• Screening period of up to 2 weeks followed by a five week treatment period

  – Day 1 visit (dose 1 given), Week 1 visit (dose 2 given; 2-8 days post dose 1), then weekly through week 5

  – Patients stratified in a 3:1 ratio to ferumoxytol:placebo

  – Study dose: 510 mg elemental iron per dose
Inclusion Criteria

• >18 years old
• Iron Deficiency Anemia
  – Hgb <10 g/dL
  – % Sat <20%
  – History of unsatisfactory oral iron therapy or unable to use oral iron

Exclusion Criteria

• History of allergy to IV iron
• Hgb < 7 g/dL
• Serum ferritin >600 mg/mL
• Known non-iron cause of anemia
• Active infection
• Hematologic malignancy
• Receiving dialysis or had a GFR <30 mL/min/1.73 m²
Efficacy and safety of IV ferumoxytol for adults with iron deficiency anemia previously unresponsive to or unable to tolerate oral iron

Saroj Vadhan-Raj,1 William Strauss,2* David Ford,3 Kristine Bernard,2 Ralph Boccia,4 Joe Li,2 and Lee F. Allen2

• Patients randomized: 812 patients
• Intent-to-treat/safety population: 808 patients
  – Ferumoxytol group: 608 patients
  – Placebo group: 200 patients
• No difference in baseline characteristics
Efficacy and safety of IV ferumoxytol for adults with iron deficiency anemia previously unresponsive to or unable to tolerate oral iron

Saroj Vadhan-Raj,1 William Strauss,2* David Ford,3 Kristine Bernard,2 Ralph Boccia,4 Joe Li,2 and Lee F. Allen2

TABLE 1. Summary of Primary and Secondary Efficacy Endpoints (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Efficacy endpoint</th>
<th>Treatment groups</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ferumoxytol (n = 608)</td>
<td>Placebo (n = 200)</td>
</tr>
<tr>
<td>Primary:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients with ≥2.0 g/dL Hgb increase at any time from Baseline to Week 5, n (%)</td>
<td>493 (81.1)</td>
<td>11 (5.5)</td>
</tr>
<tr>
<td>Secondary:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) change in Hgb (g/dL) from Baseline to Week 5</td>
<td>2.6 (1.5)</td>
<td>0.1 (0.9)</td>
</tr>
<tr>
<td>Proportion of patients with Hgb level ≥12.0 g/dL at any time from Baseline to Week 5, n (%)</td>
<td>307 (50.5)</td>
<td>6 (3.0)</td>
</tr>
<tr>
<td>Mean (SD) change in TSAT (%) from Baseline to Week 5</td>
<td>11.4 (15.1)</td>
<td>0.4 (5.8)</td>
</tr>
<tr>
<td>Mean (SD) change in FACIT-Fatigue score from Baseline to Week 5</td>
<td>11.7 (11.7)</td>
<td>6.8 (9.5)</td>
</tr>
<tr>
<td>Mean time (days) to Hgb increase of ≥2.0 g/dL or to an Hgb level of ≥12.0 g/dL from Baseline</td>
<td>23.5</td>
<td>42.5</td>
</tr>
</tbody>
</table>

*a P value for the treatment difference was from the Cochran-Mantel-Haenszel test, adjusted for Baseline Hgb level and underlying condition.

*b P value was derived from the least-squares mean and an analysis of covariance model, adjusted for Baseline Hgb and underlying condition.

*c P value was derived from log-rank statistic comparing homogeneity of survival curves between treatment groups.

FACIT, Functional Assessment of Chronic Illness Therapy; Hgb, hemoglobin; SD, standard deviation; TSAT, transferrin saturation.
Efficacy and safety of IV ferumoxytol for adults with iron deficiency anemia previously unresponsive to or unable to tolerate oral iron

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TABLE II. Summary of TEAEs by Treatment Group (Safety Population)

<table>
<thead>
<tr>
<th>AE category</th>
<th>Ferumoxytol (n = 608)</th>
<th>Placebo (n = 200)</th>
<th>Total (N = 808)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All TEAEs</td>
<td>718</td>
<td>299 (49.2)</td>
<td>206</td>
</tr>
<tr>
<td>Treatment-related AEs</td>
<td>176</td>
<td>89 (14.6)</td>
<td>25</td>
</tr>
<tr>
<td>SAEs</td>
<td>23</td>
<td>16 (2.6)</td>
<td>6</td>
</tr>
<tr>
<td>Treatment-related SAEs</td>
<td>4</td>
<td>4 (0.7)</td>
<td>0</td>
</tr>
<tr>
<td>Protocol-defined AEs of special interesta</td>
<td>26</td>
<td>22 (3.6)</td>
<td>2</td>
</tr>
<tr>
<td>Cardiovascular AE composite endpoint</td>
<td>6</td>
<td>5 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>AEs resulting in temporary discontinuation of study drug</td>
<td>4</td>
<td>3 (0.5)</td>
<td>0</td>
</tr>
<tr>
<td>AEs resulting in permanent discontinuation of study drug</td>
<td>17</td>
<td>12 (2.0)</td>
<td>2</td>
</tr>
<tr>
<td>AEs resulting in study discontinuation</td>
<td>5</td>
<td>3 (0.5)</td>
<td>3</td>
</tr>
<tr>
<td>Deathc</td>
<td>2</td>
<td>2 (0.3)</td>
<td>1</td>
</tr>
<tr>
<td>Treatment-emergent AEs reported in ≥2% of patients</td>
<td>41</td>
<td>35 (5.8)</td>
<td>13</td>
</tr>
<tr>
<td>Headache</td>
<td>32</td>
<td>28 (4.6)</td>
<td>5</td>
</tr>
<tr>
<td>Nausea</td>
<td>28</td>
<td>24 (3.9)</td>
<td>7</td>
</tr>
<tr>
<td>Dizziness</td>
<td>20</td>
<td>17 (2.8)</td>
<td>6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>19</td>
<td>17 (2.8)</td>
<td>7</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>17</td>
<td>16 (2.6)</td>
<td>4</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>15</td>
<td>13 (2.1)</td>
<td>2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>16</td>
<td>12 (2.0)</td>
<td>3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12</td>
<td>12 (2.0)</td>
<td>0</td>
</tr>
<tr>
<td>Rash</td>
<td>11</td>
<td>11 (1.8)</td>
<td>7</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>11</td>
<td>9 (1.5)</td>
<td>5</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>10</td>
<td>10 (1.6)</td>
<td>7</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>4</td>
<td>4 (0.7)</td>
<td>4</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Adverse effects of special interest: moderate to severe signs of hypotension or hypersensitivity associated with IV iron use
• Conclusions

– IV ferumoxytol was effective in increasing hemoglobin levels by >2 mg/dL with two 510 mg doses

– Authors concluded that the medication was well tolerated

• 49.2% of patients that received ferumoxytol had a treatment related adverse event

• Most were mild to moderate in intensity

• 3.6% of patients that received ferumoxytol experienced moderate to severe hypotension or hypersensitivity
Adverse effects of special interest: moderate to severe hypotension requiring medical intervention/hospitalization, acute decreases in systolic blood pressure from baseline >30% during the 60 minute observation period, symptomatic hypotension, systemic allergic reactions (anaphylaxis), and milder symptoms of hypersensitivity.
FDA Drug Safety Communication: FDA strengthens warnings and changes prescribing instructions to decrease the risk of serious allergic reactions with anemia drug Feraheme (ferumoxytol)

[3-30-2015]

Safety Announcement

The U.S. Food and Drug Administration (FDA) is strengthening an existing warning that serious, potentially fatal allergic reactions can occur with the anemia drug Feraheme (ferumoxytol). We have changed the prescribing instructions and approved a Boxed Warning, FDA's strongest type of warning, regarding these serious risks. Also added is a new Contraindication—a strong recommendation against use of Feraheme in
Black Box Warning

WARNING: RISK FOR SERIOUS HYPERSENSITIVITY/ANAPHYLAXIS REACTIONS
See full prescribing information for complete boxed warning.

Fatal and serious hypersensitivity reactions including anaphylaxis have occurred in patients receiving Feraheme. Initial symptoms may include hypotension, syncope, unresponsiveness, cardiac/cardiorespiratory arrest.

- Only administer Feraheme when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions. (5.1)
- Observe for signs or symptoms of hypersensitivity reactions during and for at least 30 minutes following Feraheme infusion including monitoring of blood pressure and pulse during and after Feraheme administration. (5.1)
- Hypersensitivity reactions have occurred in patients in whom a previous Feraheme dose was tolerated. (5.1)
Monitoring: Ferumoxytol

• Monitor for at least 30 minutes after infusion and until clinically stable
  • Pediatric patients monitored for 1 hour after infusion
• Hypersensitivity reactions have occurred in patients that previously tolerated the medication
New Uses for Ferumoxytol

• Takes advantage of properties of the drug:
  – Ultrasmall, superparamagnetic iron oxide agent
  – $T_1$ shortening effects
  – Long blood-pool residence time
  – Clearance through the reticuloendothelial system
  – Does not include gadolinium

• Uses:
  – Vascular and nodal metastasis contrast agent
  – Macrophage cell labeling (research)

• Most published studies are in adults, but it has been used safely in pediatrics (CMH will publish this summer)
Safety and Technique of Ferumoxytol Administration for MRI

Shreyas S. Vasanawala,¹* Kim-Lien Nguyen,² Michael D. Hope,³ Mellena D. Bridges,⁴ Thomas A. Hope,³ Scott B. Reeder,⁵ and Mustafa R. Bashir⁶

FIG. 1. Representative applications include detailed cardiovascular imaging (top) and assessment of tumor perfusion through pre-(bottom left) and postcontrast (bottom right) imaging in a patient with a single kidney nearly replaced by metastasis.
Ferric Carboxymaltose

- FDA Approved Indications: Iron deficiency anemia in patients who do not tolerate oral iron; Anemia of Non-Dialysis Dependent CKD
- FDA approved for adults only
- No Black Box Warning
- Test dose not required
Dosing: Ferric Carboxymaltose

• Adult
  – Less than 50 kg: 15 mg/kg elemental iron on day 1; repeat dose 7 days later
    • Maximum: 1500 mg elemental iron per course
  – Greater than or equal to 50 kg: 750 mg on day 1; repeat dose 7 days later
    • Maximum: 1500 mg elemental iron per course
Administration: Ferrous Carboxymaltose

• IV Push
  – Give undiluted at ~100 mg/minute

• IV infusion
  – Dilute to $\geq 2 \text{ mg/mL}$ over at least 15 minutes
Monitoring: Ferric Carboxymaltose

- Monitor for at least 30 minutes after infusion and until clinically stable.
Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial

• Randomized, open-label, active-controlled, multicenter, non-inferiority trial

• Patients allocated in 1:1 fashion to ferric carboxymaltose or iron sucrose

• Ferric carboxymaltose: 15 mg/kg elemental iron (maximum dose: 750 mg)
  – Given as an undiluted IV push (rate=100 mg/min) on days 0 and 7 (maximum total dose = 1500 mg)

• Iron sucrose: 200 mg elemental iron
  – Given as undiluted IV push over 2-5 minutes on Days 0, 7, and 14, with two additional doses given between days 7 and 14 (total dose = 1000 mg)
Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial

- **Eligibility Criteria**

  - > 18 years old
  - Hemoglobin value ≤11.5 g/dL
  - Screening visit ferritin <100 mg/mL or ferritin <300 ng/mL when transferrin saturation was ≤ 30%
  - Chronically impaired renal function, defined as:
    - GFR <60 mL/min/1.73 m² (MDRD) or
    - Two consecutive measurements of a GFR <60 mL/min/1.73 m² during the screening period and documented kidney damage
  - Stable erythropoiesis stimulating agent dose (if using)
Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial

Table 2. Mean change in hemoglobin from the baseline to the highest value between baseline and Day 56 or time of intervention (modified intent-to-treat population)

<table>
<thead>
<tr>
<th></th>
<th>FCM (n = 1249)</th>
<th>Iron sucrose (n = 1244)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Highest</td>
</tr>
<tr>
<td>Overall, mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Hb, mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥9.0 g/dL</td>
<td>10.31 (0.831)</td>
<td>11.44 (1.185)</td>
</tr>
<tr>
<td>Baseline Hb, mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤9.0 g/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.1–10.0 g/dL</td>
<td>8.43 (0.518)</td>
<td>10.13 (1.678)</td>
</tr>
<tr>
<td>≥10.1 g/dL</td>
<td>9.60 (0.289)</td>
<td>10.89 (1.126)</td>
</tr>
<tr>
<td>ESA use, mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.32 (0.823)</td>
<td>11.43 (1.147)</td>
</tr>
<tr>
<td>Yes</td>
<td>10.27 (0.868)</td>
<td>11.47 (1.350)</td>
</tr>
<tr>
<td>CKD stage, mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10.41 (0.783)</td>
<td>12.04 (1.269)</td>
</tr>
<tr>
<td>3–4</td>
<td>10.33 (0.822)</td>
<td>11.45 (1.149)</td>
</tr>
<tr>
<td>5</td>
<td>10.02 (0.924)</td>
<td>10.78 (1.265)</td>
</tr>
</tbody>
</table>
Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial

Table 4. Components of the primary composite safety endpoint (safety population)

<table>
<thead>
<tr>
<th>Study group</th>
<th>FCM (n = 1276) n (%)</th>
<th>Iron sucrose (n = 1285) n (%)</th>
<th>Difference (95% CI)(^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any composite safety endpoint component</td>
<td>175 (13.71%)</td>
<td>156 (12.14%)</td>
<td>1.57% (−1.10 to 4.25%)</td>
</tr>
<tr>
<td>Death due to any cause</td>
<td>15 (1.18%)</td>
<td>18 (1.40%)</td>
<td>−0.23% (−1.18 to 0.73%)</td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>8 (0.63%)</td>
<td>14 (1.09%)</td>
<td>−0.46% (−1.25 to 0.33%)</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>3 (0.24%)</td>
<td>3 (0.23%)</td>
<td>0.00% (−0.45 to 0.45%)</td>
</tr>
<tr>
<td>Unstable angina requiring hospitalization</td>
<td>11 (0.86%)</td>
<td>3 (0.23%)</td>
<td>0.63% (−0.02 to 1.28%)</td>
</tr>
<tr>
<td>CHF requiring hosp./medical intervention</td>
<td>38 (2.98%)</td>
<td>34 (2.65%)</td>
<td>0.33% (−1.03 to 1.69%)</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>18 (1.41%)</td>
<td>13 (1.01%)</td>
<td>0.40% (−0.53 to 1.32%)</td>
</tr>
<tr>
<td>Protocol-defined hypertensive events(^{b})</td>
<td>95 (7.45%)</td>
<td>56 (4.36%)</td>
<td>3.09% (1.19 to 4.99%)</td>
</tr>
<tr>
<td>Protocol-defined hypotensive events(^{c})</td>
<td>23 (1.80%)</td>
<td>41 (3.19%)</td>
<td>−1.39% (−2.67 to −0.10%)</td>
</tr>
<tr>
<td>Composite endpoint excluding hypertensive/hypotensive events</td>
<td>70 (5.49%)</td>
<td>69 (5.37%)</td>
<td>0.12% (−1.72 to 1.95%)</td>
</tr>
<tr>
<td>Death, myocardial infarction, or stroke</td>
<td>24 (1.88%)</td>
<td>35 (2.72%)</td>
<td>−0.84% (−2.08 to 0.40%)</td>
</tr>
</tbody>
</table>

CI, confidence interval; CHF, congestive heart failure; FCM, ferric carboxymaltose.

\(^{a}\)Confidence interval constructed with the normal approximation to the binomial with Wald continuity correction.

\(^{b}\)During the observation period immediately following study drug administration, hypertension was defined as an increase in systolic blood pressure >20 mm Hg that resulted in a value of >180 mm Hg or an increase in diastolic blood pressure >15 mm Hg that resulted in a value of >105 mm Hg.

\(^{c}\)During the observation period immediately following study drug administration, hypotension was defined as a decrease in systolic blood pressure >20 mm Hg that resulted in a value of <90 mm Hg or a decrease in diastolic blood pressure >15 mm Hg that resulted in a value of <50 mmHg.
Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial

• Conclusions:
  – Ferric carboxymaltose was non-inferior to iron sucrose
    • Authors concluded that ferric carboxymaltose was statistically superior to iron sucrose for increase in hemoglobin
  – Clinical significance of 1.13 vs. 0.92 g/dL?
    • Ferric carboxymaltose allows more iron to be administered safely in fewer infusions and over a shorter period of time than iron sucrose
      – Total amount of iron administered different between study groups
  • Generally well tolerated
Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron

Jacquelyn M. Powers, MD, MS\textsuperscript{1,2,3}, Mark Shamoun, MD\textsuperscript{4,5}, Timothy L. McCavit, MD, MS\textsuperscript{6,7}, Leah Adix, CCRP\textsuperscript{5}, and George R. Buchanan, MD\textsuperscript{4,5,8}

- Retrospective, single center, cohort study
- Patients with iron deficiency anemia who received ferric carboxymaltose between June 1, 2014 and June 10, 2015 were included
  - Patients without anemia who received ferric carboxymaltose were excluded
Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron

Jacquelyn M. Powers, MD, MS\textsuperscript{1,2,3}, Mark Shamoun, MD\textsuperscript{4,5}, Timothy L. McCavit, MD, MS\textsuperscript{6,7}, Leah Adix, CCRP\textsuperscript{5}, and George R. Buchanan, MD\textsuperscript{4,5,8}

- **Dosing:** 15 mg/kg (maximum: 750 mg/dose)
  - >50 kg: 2 doses given at least 7 days apart (maximum total dose: 1500 mg)
  - <50 kg: decision to give 1 or 2 doses was left to the hematologist; if 2\textsuperscript{nd} dose given, given 7 days apart

- **Administered over 15 minutes**
Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron

Jacquelyn M. Powers, MD, MS1,2,3, Mark Shamoun, MD4,5, Timothy L. McCavit, MD, MS6,7, Leah Adix, CCRP8, and George R. Buchanan, MD4,5,8

Table II. Laboratory test results before and after FCM infusion in patients with IDA

<table>
<thead>
<tr>
<th>Variables</th>
<th>Preinfusion, median (range)</th>
<th>Postinfusion, median (range)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hgb concentration, g/dL</td>
<td>9.1 (5.5-12.2)</td>
<td>12.3 (8.8-16)</td>
</tr>
<tr>
<td>Combined results</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Heavy menstrual bleeding</td>
<td>8.9 (6.6-11.3)</td>
<td>12.5 (10.4-16)</td>
</tr>
<tr>
<td>Nutritional</td>
<td>9.6 (6.4-11.5)</td>
<td>12.2 (10.5-13.6)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>9.3 (5.5-12.2)</td>
<td>11.0 (8.8-14.1)</td>
</tr>
<tr>
<td>Mean corpuscular volume, fl</td>
<td>69.1 (49.5-92.4)</td>
<td>79.1 (64.9-91.8)</td>
</tr>
<tr>
<td>Serum ferritin level, ng/mL</td>
<td>3.4 (1-35)</td>
<td>114.7 (2.3-407.5)</td>
</tr>
</tbody>
</table>

*Follow-up laboratory testing was done at 4-12 weeks postinfusion.

Table III. Hematologic response following 1 dose vs 2 doses of FCM in patients with IDA

<table>
<thead>
<tr>
<th>Variables</th>
<th>One dose (n = 25)</th>
<th>Two doses (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median</td>
<td>3.2</td>
<td>9.4</td>
</tr>
<tr>
<td>Hgb concentration, g/dL, median (range)</td>
<td>9.3 (5.5-12.2)</td>
<td>8.7 (5.9-11.1)</td>
</tr>
<tr>
<td>Baseline</td>
<td>12.2 (8.8-14)</td>
<td>12.7 (10-16)</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum ferritin, ng/mL, median (range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline; 1 dose (n = 24), 2 doses</td>
<td>4.4 (1-18.2)</td>
<td>3.1 (1.4-35)</td>
</tr>
<tr>
<td>Follow-up; 1 dose (n = 20), 2 doses</td>
<td>68.7 (3.6-374)</td>
<td>217.2 (2.3-407.5)</td>
</tr>
<tr>
<td>Complete response, %</td>
<td>72%</td>
<td>63%</td>
</tr>
<tr>
<td>Partial response, %</td>
<td>28%</td>
<td>33%</td>
</tr>
<tr>
<td>No response, %</td>
<td>0%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Follow-up laboratory testing was done at 4-12 weeks postinfusion.
Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron

Jacquelyn M. Powers, MD, MS1,2,3, Mark Shamoun, MD4,5, Timothy L. McCavit, MD, MS6,7, Leah Adix, CCRP5, and George R. Buchanan, MD4,5,8

- 84% of patients had no adverse event
- 7 Children reported an adverse effect during or immediately after their infusions:

Table IV. Summary of adverse events

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Age</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>17 y</td>
<td>Oxygen, diphenhydramine, albuterol, and IV hydrocortisone</td>
<td>Infusion stopped; resolution within 5 minutes and monitored for 1 hr before discharge to home</td>
</tr>
<tr>
<td>Tingling</td>
<td>17 y</td>
<td>Warm pack placed; resolved with completion of infusion</td>
<td>Resolved with completion of infusion; received 2 doses</td>
</tr>
<tr>
<td>Extravasation</td>
<td></td>
<td>Subsequent referral to plastic surgery for consideration of laser therapy</td>
<td>Localized, painless iron staining of skin; received 2 doses (occurred with second dose)</td>
</tr>
<tr>
<td>Urticaria/pruritis</td>
<td>15 y</td>
<td>IV diphenhydramine</td>
<td>Received one-half of infusion</td>
</tr>
<tr>
<td></td>
<td>12 y</td>
<td>IV diphenhydramine</td>
<td>No further doses of FCM</td>
</tr>
<tr>
<td></td>
<td>16 y</td>
<td>Oral diphenhydramine and hydrocortisone</td>
<td>No further doses of FCM</td>
</tr>
<tr>
<td></td>
<td>16 y</td>
<td>Oral diphenhydramine, topical hydrocortisone cream</td>
<td>Occurred after the second FCM dose</td>
</tr>
</tbody>
</table>
Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron

Jacquelyn M. Powers, MD, MS¹,²,³, Mark Shamoun, MD⁴,⁵, Timothy L. McCavit, MD, MS⁶,⁷, Leah Adix, CCRP⁸, and George R. Buchanan, MD⁴,⁵,⁸

• Conclusion:
  – Ferric carboxymaltose was effective in increasing hemoglobin in adult and pediatric patients
  – Ferric carboxymaltose was generally well tolerated
Contraindications to Iron Replacement Therapy

• Bacterial infection

• History of hypersensitivity reactions to product
  – No/low cross sensitivity between products

• Recent blood transfusion
Common Adverse Effects

• Transient adverse effects: nausea, vomiting, pruritus, headache, flushing

• Usually resolve within 48 hours: arthralgia, myalgia, back and chest pain

• Rare but serious: Hypersensitivity

• IM administration: permanent dying of skin
Monitoring

• If infusion reaction occurs, can slow infusion rate or give supportive medications and monitor for improvement

• Hypersensitivity reactions
  – Monitor at least 30-60 minutes after infusion

• Iron overload
  – Monitor ferritin 1 week after dose and every three months

NEJM 2015; 372: 1832-43.
The Future

• Iron Isomaltoside
  – Not FDA approved (available in Europe)
  – Allows for total dose infusion

• Serum hepcidin levels
Ironing Out the Details: A Review of Iron Deficiency Anemia and Safety Update for Iron Replacement Products

Kyle Hampson, Pharm.D., CNSC
Clinical Pharmacy Specialist, Nutrition Support and Intestinal Rehabilitation
Children’s Mercy Hospitals and Clinics
Kansas City, Missouri