

## **SUPPLEMENTARY METHODS**

### **Inclusion and Exclusion Criteria**

The inclusion criteria for this trial are as follows:

- Men and non-lactating women with negative serum pregnancy test (for women of child-bearing potential) at Screening
- Age >18 years
- CKD with eGFR <60 mL/min at Screening using the 4-variable Modification of Diet in Renal Disease (MDRD) equation (with a limit of up to 20% of the target randomization of 230 subjects with eGFR <15 mL/min)
- Patients who were intolerant of or have had an inadequate therapeutic response to oral iron supplements (in the opinion of the investigator)
- Hgb  $\geq$  9.0 g/dL and  $\leq$ 11.5 g/dL at Screening
- Serum ferritin  $\leq$ 200 ng/mL and TSAT  $\leq$ 25% at Screening
- Serum iPTH  $\leq$ 600 pg/mL at Screening
- Must consume a minimum of 2 meals per day
- Willing and able to give written informed consent

The exclusion criteria for this trial are as follows:

- Serum phosphate <3.5 mg/dL at Screening
- Liver enzymes (ALT/AST) >X3 times upper limit of normal at Screening
- Symptomatic gastrointestinal bleeding or inflammatory bowel disease within 12 weeks prior to Screening
- Evidence of acute kidney injury or requirement for dialysis within 12 weeks prior to Screening
- Scheduled kidney transplant or initiation of dialysis planned within 24 weeks of Screening
- IV iron administered within 4 weeks prior to Screening
- Erythropoiesis-stimulating agent (ESA) administered within 4 weeks prior to Screening
- Blood transfusion within 4 weeks prior to Screening
- Receipt of any investigational drug within 4 weeks prior to Screening
- Active infection requiring antibiotics at Screening
- Cause of anemia other than iron deficiency or chronic kidney disease
- Malignancy (except non-melanoma skin cancer or disease-free for  $\geq$ 2 years after curative therapy)
- History of hemochromatosis
- Active drug or alcohol dependence or abuse (excluding tobacco use or medicinal marijuana) within the 12 months prior to Screening or evidence of such abuse (in the opinion of the PI)

- Subjects with known allergic reaction to previous oral iron therapy
- Previous intolerance to oral ferric citrate
- Psychiatric disorder that interferes with the subject's ability to comply with the study protocol
- Planned surgery or hospitalization (anticipated to last >72 hours) during the randomized period of the trial other than dialysis access related surgery.
- Any other medical condition that, in the opinion of the PI, renders the subject unable to or unlikely to complete the trial or that would interfere with optimal participation in the trial or produce significant risk to the subject
- Inability to cooperate with study personnel

**Supplementary Table S1.** Serious Adverse Events During the Randomized Period  
(Safety Population)

<b>System Organ Class Preferred Term, n (%)</b>	<b>Ferric Citrate (N=117)</b>	<b>Placebo (N=116)</b>
At least 1 SAE	14 (12.0)	13 (11.2)
Blood and Lymphatic System Disorders	1 (0.9)	1 (0.9)
Iron deficiency anemia	1 (0.9)	0
Anemia	0	1 (0.9)
Cardiac Disorders	3 (2.6)	3 (2.6)
Cardiac arrest	1 (0.9)	0
Cardio-respiratory arrest	1 (0.9)	0
Sick sinus syndrome	1 (0.9)	0
Cardiac failure congestive	0	2 (1.7)
Acute myocardial infarction	0	1 (0.9)
Cardiac failure acute	0	1 (0.9)
Gastrointestinal disorders	2 (1.7)	1 (0.9)
Colitis ischaemic	1 (0.9)	0
Dysphagia	1 (0.9)	0
Vomiting	0	1 (0.9)
General Disorders and Administration Site Conditions	0	1 (0.9)
Necrosis	0	1 (0.9)
Hepatobiliary Disorders	0	1 (0.9)
Cholangitis acute	0	1 (0.9)
Infections and Infestations	4 (3.4)	6 (5.2)
Pneumonia	2 (1.7)	1 (0.9)
Clostridium difficile colitis	1 (0.9)	1 (0.9)
Sepsis	1 (0.9)	1 (0.9)
Abscess limb	1 (0.9)	0
Diverticulitis	1 (0.9)	0
Septic shock	1 (0.9)	0
Urinary tract infection fungal	1 (0.9)	0
Cellulitis	0	2 (1.7)
Osteomyelitis	0	1 (0.9)
Pyelonephritis acute	0	1 (0.9)
Injury, Poisoning, and Procedural Complications	3 (2.6)	0
Abdominal wound dehiscence	1 (0.9)	0
Procedural haemorrhage	1 (0.9)	0
Procedural nausea	1 (0.9)	0
Procedural vomiting	1 (0.9)	0
Investigations	1 (0.9)	0
Blood glucose increased	1 (0.9)	0
Metabolism and Nutrition Disorders	3 (2.6)	2 (1.7)
Hyperglycaemia	2 (1.7)	0
Diabetic ketoacidosis	1 (0.9)	0
Fluid overload	1 (0.9)	0
Hypoglycaemia	1 (0.9)	0

<b>System Organ Class Preferred Term, n (%)</b>	<b>Ferric Citrate (N=117)</b>	<b>Placebo (N=116)</b>
Gout	0	1 (0.9)
Hyperkalaemia	0	1 (0.9)
Musculoskeletal and Connective Tissue Disorders	1 (0.9)	0
Back pain	1 (0.9)	0
Nervous System Disorders	4 (3.4)	0
Metabolic encephalopathy	2 (1.7)	0
Status epilepticus	1 (0.9)	0
Syncope	1 (0.9)	0
Renal and Urinary Disorders	4 (3.4)	5 (4.3)
Renal failure acute	3 (2.6)	2 (1.7)
Renal failure chronic	1 (0.9)	2 (1.7)
Hydronephrosis	0	1 (0.9)
Renal impairment	0	1 (0.9)
Urinary retention	0	1 (0.9)
Respiratory, Thoracic and Mediastinal Disorders	4 (3.4)	2 (1.7)
Acute respiratory failure	3 (2.6)	1 (0.9)
Chronic respiratory failure	1 (0.9)	0
Pneumonia aspiration	1 (0.9)	0
Pulmonary fibrosis	1 (0.9)	0
Chronic obstructive pulmonary disease	0	1 (0.9)
Hypoxia	0	1 (0.9)
Surgical and Medical Procedures	1 (0.9)	0
Toe amputation	1 (0.9)	0
Vascular Disorders	1 (0.9)	0
Hypertension	1 (0.9)	0

**Supplementary Table S2.** Summary of Suspected Study Drug-related Treatment-emergent Adverse Events During the Randomized Period (Safety Population)

<b>System Organ Class, Preferred Term, n (%)</b>	<b>Ferric citrate (N=117)</b>	<b>Placebo (N=116)</b>
At least 1 study drug-related TEAE	35 (29.9)	26 (22.4)
Gastrointestinal Disorders	30 (25.6)	22 (19.0)
Faeces discoloured	14 (12.0)	0
Diarrhoea	12 (10.3)	12 (10.3)
Constipation	12 (10.3)	10 (8.6)
Nausea	3 (2.6)	1 (0.9)
Abdominal discomfort	2 (1.7)	0
Abdominal pain	2 (1.7)	0
Flatulence	1 (0.9)	2 (1.7)
Vomiting	1 (0.9)	1 (0.9)
Dyspepsia	1 (0.9)	0
Abdominal pain upper	0	1 (0.9)
Gastroesophageal reflux disease	0	1 (0.9)
General Disorders and Administration Site Conditions	1 (0.9)	1 (0.9)
Oedema peripheral	1 (0.9)	0
Fatigue	0	1 (0.9)
Investigations	1 (0.9)	0
Hepatic enzyme increased	1 (0.9)	0
Metabolism and Nutrition Disorders	1 (0.9)	3 (2.6)
Hypophosphataemia	1 (0.9)	2 (1.7)
Fluid retention	0	1 (0.9)
Nervous System Disorder	1 (0.9)	2 (1.7)
Headache	1 (0.9)	2 (1.7)
Skin and Subcutaneous Tissue Disorders	1 (0.9)	1 (0.9)
Rash	1 (0.9)	1 (0.9)
Vascular disorders	1 (0.9)	0
Hypertension	1 (0.9)	0

Denominators for percentages are N, the total number of subjects per group. At each level of subject summarization, a subject will be counted only once if the subject reports 1 or more events. Only TEAEs that started prior to or on the Week 16 visit date are summarized. TEAE=treatment-emergent adverse event.