2334 A Single Infusion of Iron Isomaltoside 1000 Allows a More Rapid Hemoglobin Increment Than Multiple Doses of Iron Sucrose with a Similar Safety Profile in Patients with Iron Deficiency Anemia

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Introduction: Iron deficiency anemia (IDA) is prevalent and associated with reduced quality of life (QoL) and worsened disease outcomes. Oral iron administration remains the front line standard but its use is associated with an unacceptably high incidence of gastrointestinal side effects and low adherence. Further, in many conditions associated with blood loss, iron losses may exceed the capacity for oral iron absorption. Use of intravenous (IV) iron, especially if given in a single dose, may result in better compliance, fewer visits to the medical practitioner, and overall improvement in QoL. To date, no product has been licensed in the USA for single visit complete replacement dosing. To address this issue, this trial compared the safety and efficacy of iron isomaltoside 1000 with the most commonly prescribed IV formulation, iron sucrose, in patients intolerant of, or unresponsive to oral iron or likely to receive a blood transfusion.

Methods: This was a randomized, open-label, comparative, multi-center trial conducted in the USA. Patients with IDA were randomized 2:1 to either iron isomaltoside administered as a single dose of 1000 mg infused over 20 min at baseline or iron sucrose administered as 200 mg IV injections according to label and repeated up to 5 times. The primary endpoints were adjudicated serious or severe hypersensitivity events starting on or after the first dose of treatment (if the upper bound of the 95 % CI was <3 %, the safety objective was met) and change in hemoglobin (Hb) from baseline to week 8.

Results: A total of 1512 patients were enrolled of whom 26 % had gastrointestinal and 50 % gynecologic blood loss. The mean (standard deviation [SD]) age was 44 (15) years. The mean (SD) cumulative dose of iron was 975 (145) mg and 905 (217) mg in the iron isomaltoside and iron sucrose group, respectively. All required 1 visit for iron correction with iron isomaltoside and 4 to 5 visits for iron sucrose.

The frequency of subjects with serious or severe hypersensitivity reactions was 0.3% in the iron isomaltoside group versus 0.4 % in the iron sucrose group (95% CI: 0.88 for iron isomaltoside and 1.45 for iron sucrose), meeting the primary safety endpoint.

The treatment groups had statistically similar adverse drug reactions (ADRs), 12.5 % in the iron isomaltoside group and 12.8 % in the iron sucrose group. Only 0.2 % of patients in iron isomaltoside group and 0.4 % in iron sucrose group experienced serious ADRs. There were no related fatalities. The frequency of composite cardiovascular safety endpoint was 0.8 % in the iron isomaltoside group and 1.2 % in the iron sucrose group ($p = 0.57$). The frequency of hypophosphatemia (*s*-phosphate <2 mg/dL) was low and similar in the 2 groups (3.9 % in the iron isomaltoside and 2.3 % in the iron sucrose group). No patients had *s*-phosphate <1 mg/dL.

The primary efficacy endpoint of non-inferiority in Hb change from baseline to week 8 was met. Iron isomaltoside lead to a significantly more rapid and increased Hb response in the first 2 weeks. This was reflected in both Hb change from baseline and proportion of responders with Hb increases ≥2 g/dL. Hb increased with least square means of 0.70 and 0.44 g/dL at week 1 ($p <0.0001$) and 1.48 and 1.19 g/dL at week 2 ($p <0.0001$) for iron isomaltoside and iron sucrose respectively, and the proportion of responders were 5.3 and 2.5 % at week 1 ($p = 0.0077$) and 32.6 and 20.8 % at week 2 ($p <0.0001$) for iron isomaltoside and iron sucrose respectively. Larger improvement in Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scores were observed with iron isomaltoside at week 1 ($p = 0.04$). A faster and greater response with iron isomaltoside was also observed for *s*-ferritin and transferrin saturation.

Conclusion: Iron isomaltoside 1000 administered as 1000 mg in a single visit resulted in a faster and more pronounced hematological response and improvement in fatigue compared to iron sucrose which requires multiple visits. The safety profile was similar with a low frequency of hypersensitivity reactions, cardiovascular events, and serious ADRs. The frequency of hypophosphatemia was low in both treatment groups and no patients had *s*-phosphate <1 mg/dL.

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