Sustained Improvements in Fatigue and Quality of Life in Patients with Iron Deficiency Anemia Due to Gastrointestinal Disorders Following a Single Course of Ferumoxytol

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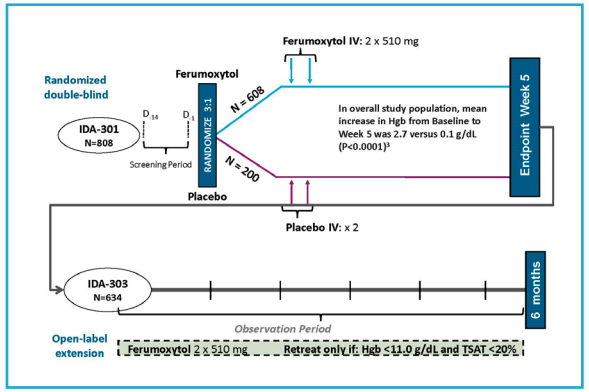
Background

- Iron deficiency anemia (IDA) is common in patients with gastrointestinal (GI) disease, as a result of chronic blood loss, malnutrition, or malabsorption of iron, often coexisting with impaired utilization of endogenous iron in patients with chronic inflammation, such as inflammatory bowel disease (IBD) [1,2]
- Oral iron is often first-line treatment, but many patients do not tolerate it, or do not adequately respond; many live with chronic anemia and its related negative effects[2]
- A Phase 3 double-blind, placebo-controlled trial (NCT01114139) previously found that patients unsuccessfully treated with oral iron, including those with underlying GI diseases, had very poor baseline HRQOL scores associated with fatigue, and that IV iron treatment resulted in significant, clinically meaningful improvement[2,3]
- To explore the durability of this treatment effect, this subgroup analysis reports on the impact on patient-reported outcomes (PRO) of a single course of IV ferumoxytol, received during the double-blind trial, over the subsequent 6-month extension study (NCT01114217)[4] in patients with IDA due to GI disorders

Methods

- 6-month, Phase 3, open-label extension study (IDA 303, NCT01114217)[4]
- The study enrolled patients who had completed a randomized, placebo-controlled, double-blinded, Phase 3 study (IDA 301, NCT01114139)[3]
- Enrolled patients were evaluated for IDA monthly throughout the 6-month observation period
- Those with persistent or recurrent IDA at any evaluation visit (defined as Hgb <11.0 g/dL and TSAT <20%) received a course of ferumoxytol (2 x 510 mg, 3 to 8 days apart)
- The same validated PRO instruments were administered in this extension study as in the preceding double-blind trial:
  - Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-Fatigue), assessed monthly
  - Linear Analogue Scale Assessment (LASA) of Energy, Activities of Daily Living (ADL), and HRQOL, assessed at Months 4 and 7
- This analysis reports results for the subgroup of patients who did not meet the protocol-specified retreatment criteria and therefore did not receive any additional doses of ferumoxytol during the entire 6-month period of the extension study

Figure 1. Overall Study Design



Results

- The extension study enrolled 78.5% of patients from the previous Phase 3 study (163/200 placebo, 471/608 ferumoxytol)
- The most common primary underlying conditions were abnormal uterine bleeding (41.8%), GI disorder (33.0%), and cancer (3.5%)

Table 1. Baseline Demographics: GI Patients, No Retreatment Group

Baseline Demographics	GI Patients, No Retreatment (N=94)
Sex female, n (%)	78 (83)
Race, n (%)	
White	71 (76)
Black or African American	9 (10)
Asian	13 (14)
Other or Unknown	1 (1)
Hgb, g/dL, mean (SD)	8.9 (0.8)
Age, years, mean (SD)	46.1 (13.9)
Weight, Kg, mean (SD)	78 (23.5)

- Most patients who had received a dose of ferumoxytol in the double-blind trial did not meet the criteria for retreatment during the extension study, and did not receive any further doses (285/471; 61% Overall) including 67.6% (94/139) of those with IDA due to GI disorders
- GI patients' mean Hgb had increased from 8.9±0.8 g/dL at Baseline to 12.3±0.9 at Week 5 of the double-blind trial and remained above 12.0 throughout the 6-month extension study visits (Month 7 Hgb 12.5±1.1) despite receiving no further ferumoxytol
- At Baseline of the double-blind trial, FACIT-Fatigue scores were lower for the overall study population (24.3±12.3), and for the GI subgroup (22.6±11.8) than general (non-anemic) US population norms (43.6), and comparable to anemic cancer patients receiving chemotherapy (23.9)[5]

Figure 2 Monthly Hgb Levels and FACIT-Fatigue Scores Following a Single Course of Ferumoxytol Therapy in GI Patients

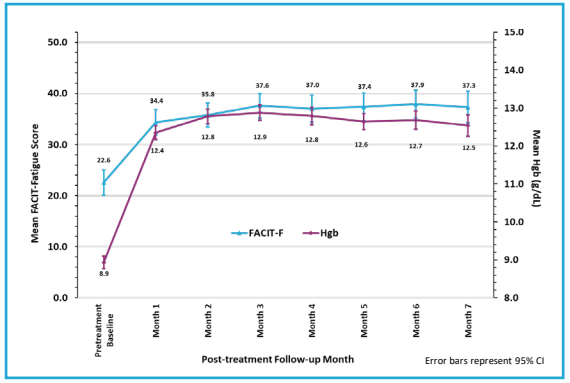


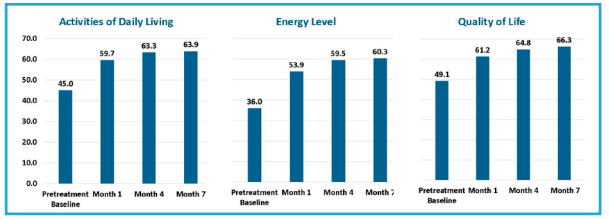
Table 2. Changes from Baseline in Patient Reported Outcomes Following a Single Course of Ferumoxytol Therapy in GI Patients

Instrument	GI Baseline	GI Change from Pretreatment Baseline		MID[6,7]
	Pretreatment Mean (SD)	Month 4 Mean (95% CI)	Month 7 Mean (95% CI)	
LASA-Energy	36.0 (21.9)	18.5 (12.8, 24.6)	16.2 (10.4, 22.1)	9.61
LASA-Activity	45.0 (22.3)	13.2 (7.3, 19.2)	13.4 (7.5, 19.3)	8.74
LASA-QOL	49.1 (21.6)	11.6 (6.4,16.9)	12.0 (6.7, 17.2)	9.81
FACIT-Fatigue	22.6 (11.8)	11.3 (8.7, 14.0)	9.8 (7.0, 12.5)	3.0

MID = Minimum Important Difference. SD= standard deviation. CI = Confidence interval
Change from Baseline uses an imputed value of 0 for missing values at post-baseline visits.
The 95% CI is from the paired t-test.

- By Week 5 following ferumoxytol treatment, FACIT-Fatigue scores had increased significantly (Overall 36.1±11.2; GI 34.3±12.0), approaching general population norms. This improvement was sustained over the following 6 months (Month 7 score Overall 38.8±11.5; GI 37.3±12.0)

Figure 3. LASA-Activity, -Energy, and -QOL Scores Following a Single Course of Ferumoxytol Therapy in GI Patients



- Similarly, the significant improvements in LASA Activity, Energy, and QOL scores that were observed in the double-blind trial were also maintained over the following 6 months

Conclusions

- These data suggest that ferumoxytol may provide important clinical benefits to IDA patients with a history of unsatisfactory oral iron therapy; these benefits include reductions in fatigue, increased energy and ability to perform activities of daily living, and improved HRQOL
- This is important especially in light of the poor baseline energy and HRQOL scores of patients with IDA due to GI disorders and a history of unsatisfactory oral iron therapy or in whom oral iron could not be used
- This study found that for the majority of patients with IDA due to GI disorders, significant improvements in fatigue and energy domains, greater than the previously reported Minimal Clinically Important Differences (MID), were achieved and sustained for 6 months following a single course of ferumoxytol

References

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Disclosures

Sadiq: AMAG Pharmaceuticals, Inc.: Employment, Equity Ownership. Yu: AMAG Pharmaceuticals, Inc.: Employment. Dahl: AMAG Pharmaceuticals, Inc., Equity Ownership

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