SUPPLEMENTARY MATERIAL

TITLE

A Multicenter Single-Arm Study of Switching to Ferric Citrate Hydrate for Iron Deficiency Anemia in Patients Intolerant to Oral Iron: RIO-SWITCH

AUTHORS

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Table S1. Questionnaire to evaluate the degree of nausea and vomiting and interference with daily life during the previous treatment

Items
Continuation of treatment and degree of interference with daily life • Whether the patient takes oral iron preparation currently • If not currently taking an oral iron preparation, when was the last time they took one (e.g., about a month ago for about a week)
Degree of the interference with daily life • Degree of interference with daily life due to taking oral iron preparations (4-grade evaluation) • Degree of difficulty due to taking oral iron preparations (4-grade evaluation)
Degree of nausea, vomiting, and their interference with daily life • Score of the most severe nausea and vomiting during treatment on a scale of 0 to 10 (11-grade evaluation) and the number of times per day the patient was vomiting when it was most severe • Degree of interference with daily life caused by nausea and/or vomiting (5-grade evaluation) • Specific interferences with daily life caused by nausea and/or vomiting   ○ Examples of choices: poor appetite, difficulty concentrating on work, difficulty concentrating on housework; multiple choices were allowed • Degree of interference with appetite caused by nausea and/or vomiting (3-grade evaluation)

Notes: The questionnaire was prepared in Japanese and translated into English for inclusion in this manuscript.

Table S2. Questionnaire to evaluate the degree of nausea and vomiting and interference with daily life during the ferric citrate hydrate treatment

Items
Overall evaluation of treatment with ferric citrate hydrate • Overall evaluation of treatment with ferric citrate hydrate compared with previous oral iron preparation (5-grade evaluation)   ○ Example of indicators: effectiveness and adverse events
Degree of the interference with daily life • Degree of interference in daily life due to taking ferric citrate hydrate (4-grade evaluation) • Degree of difficulty due to taking ferric citrate hydrate (4-grade evaluation)
Degree of nausea, vomiting, and their interference with daily life • Score of the most severe nausea and vomiting during treatment on a scale of 0 to 10 (11-grade evaluation) and the number of times per day the patient was vomiting when it was most severe • Degree of interference with daily life caused by nausea and/or vomiting (5-grade evaluation) • Specific interferences with daily life caused by nausea and/or vomiting   ○ Examples of choices: poor appetite, difficulty concentrating on work, difficulty concentrating on housework; multiple choices were allowed • Degree of interference with appetite caused by nausea and/or vomiting (3-grade evaluation)

Notes: The questionnaire was prepared in Japanese and translated into English for inclusion in this manuscript.

Table S3. Medication compliance rate classified by previous oral iron preparation.

Medication compliance, %	**Oral iron preparations prior to study participation**			
	Sodium ferrous citrate (*n* = 22[a])	**Dried ferrous sulfate (*n* = 5[b])**	**Soluble ferric pyrophosphate (*n* = 2[c])**	**Ferrous fumarate (*n* = 1[c])**
Until Week 4 (*n* = 24)	94.91 ± 8.24	92.48 ± 7.93	92.86 ± 10.10	82.93
Week 4 to Week 8 (*n* = 6)	91.43 ± 8.64	100.00	NA	NA
Until the end of treatment (*n* = 30)	94.68 ± 8.17	93.19 ± 8.13	92.86 ± 10.10	82.93

Notes: Data are mean ± standard deviation. The medication compliance was defined as the percentage of days a patient received the study treatment during the study treatment period.

[a]For 17 patients with a hemoglobin level ≥ 11.0 g/dL at Week 4, the study period was from baseline to the day before Week 4. For the five patients with a hemoglobin level < 11.0 g/dL at Week 4, the study period was from baseline to the day before Week 8.

[b]For four patients with a hemoglobin level ≥ 11.0 g/dL at Week 4, the study period was from baseline to the day before Week 4. For the one patient with a hemoglobin level < 11.0 g/dL at Week 4, the study period was from baseline to the day before Week 8.

[c]The study period was from baseline to the day before Week 4 because all patients had a hemoglobin level ≥ 11.0 g/dL at Week 4.

NA, not applicable.

Table S4. Summary of adverse events

Adverse event	No. events	No. patients (%) *n* = 30
Nausea	3	3 (10.0)
Abdominal discomfort	2	2 (6.7)
Constipation	2	2 (6.7)
Nasopharyngitis	2	2 (6.7)
Abdominal distention	1	1 (3.3)
Diarrhea	1	1 (3.3)
Headache	1	1 (3.3)
Insomnia	1	1 (3.3)
Loose stools	1	1 (3.3)
Menopausal symptoms	1	1 (3.3)
Neck pain	1	1 (3.3)
Vomiting	1	1 (3.3)

Table S5. Summary of adverse drug reactions

Adverse drug reaction	No. events	No. patients (%) ***n* = 30**
Nausea	3	3 (10.0)
Abdominal discomfort	2	2 (6.7)
Constipation	2	2 (6.7)
Abdominal distention	1	1 (3.3)
Diarrhea	1	1 (3.3)

Figure S1. Flowchart of questions in the patient diary

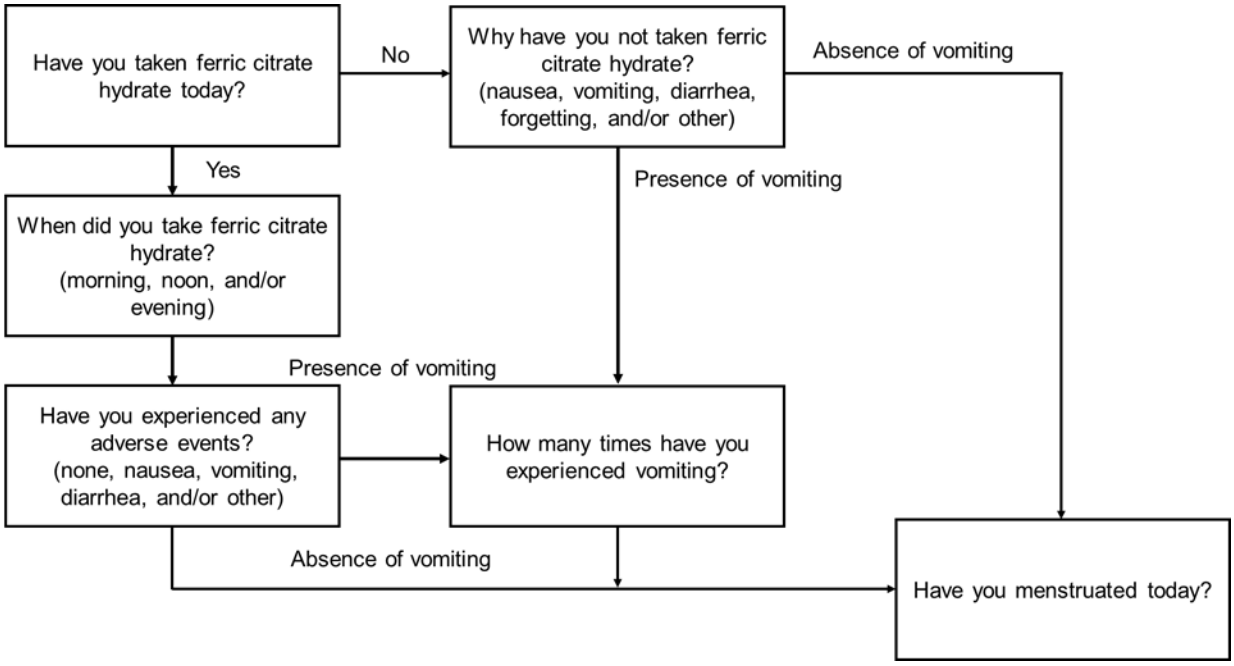
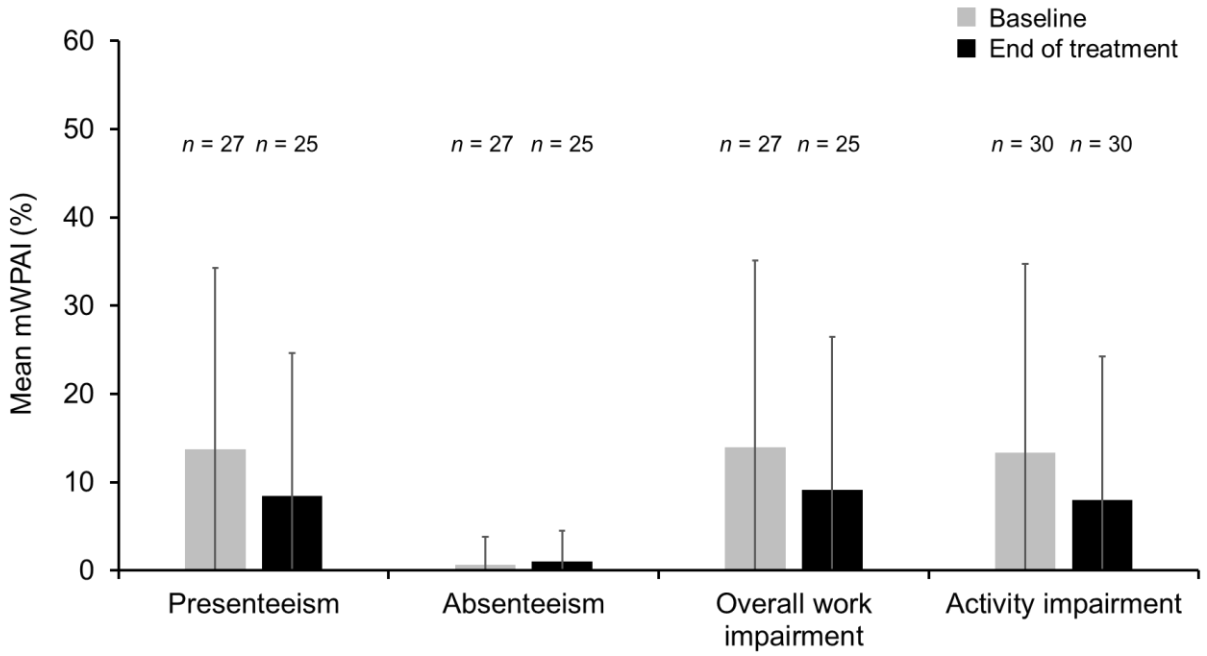


Figure S2. Impact of nausea and vomiting on work productivity and activity impairment

(A) mWPAI-GH scores in all patients



(B) mWPAI-GH scores in patients with presenteeism score > 0 at baseline