Physician Reaction to Spontaneous Rises in Transferrin Saturation and Serum Ferritin Levels in End-Stage Renal Disease Patients

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Introduction

- Ferric citrate is an oral phosphate binder in clinical development for treatment of hyperphosphatemia in end-stage renal disease (ESRD) patients.
  - Phase 2 studies demonstrated statistically and clinically significant reductions in serum phosphorus and modest increases in transferrin saturation (TSAT) and serum ferritin.[1,2]
- TSAT and serum ferritin potentially impact the need for erythropoiesis-stimulating agents (ESAs) and intravenous (IV) iron.
- ***Using electronic medical records of hemodialysis (HD) patients within a large US dialysis organization, we examined ESA and iron prescribing behavior in response to non-treatment related increases in TSAT and serum ferritin similar to those measured in ferric citrate clinical trials.***

Methods

- This was a retrospective 2-year study (6/1/2008-5/31/2010) of adult (>18 years) prevalent ESRD patients (≥120 days) receiving phosphate binder therapy and experiencing non-treatment related, concurrent qualifying increases in TSAT and serum ferritin.
- Qualifying increases were considered equivalent to those in the ferric citrate clinical studies if:
  - Serum ferritin increased ≥ 15% but ≤ 25%
  - TSAT increased ≥ 10%
  - The index date of iron storage increase was defined as the date of the earlier rise (TSAT or serum ferritin).
- Study endpoints were the mean dose change in ESA (epoetin alfa) and IV iron (iron sucrose) occurring in the 2 months after concurrent, qualifying TSAT and serum ferritin increases (baseline).

Results

Patient Demographics

General	N	Mean (SD)
Age in years	1983	63.2 (14.5)
Vintage in years	1940	5.3 (3.5)
Male	1128	56.9%
Race	**n**	**%**
White	819	41.3
Black	755	38.1
Hispanic	237	12.0
Asian	70	3.5
American Indian or Alaskan Native	27	1.4
Native Hawaiian or Pacific Islander	10	0.5
Primary insurer	**n**	**%**
Medicare	1586	80.0
Other	221	11.1
Medicaid	137	6.9
Veterans Administration	29	1.5
No Insurance	10	0.5
Primary cause ESRD	**n**	**%**
Diabetic kidney disease	906	45.7
Hypertensive	564	28.4
Other	468	23.6
Polycystic	45	2.3

Patient Disposition

DaVita HD patient database ~130,000 patient records

↓

32,829 TSAT records / 4,656 ferritin records

↓

2,088 records ≤15 days apart

↓

1,983 unique HD patients

Patient Distribution for ESA and Iron Dosing at Baseline [n (%)]

Baseline iron dose group (mg)	Baseline ESA dose group (units) Lowest 1 -< 2000	Low 2000 - <4500	Moderate 4500- <9000	High ≥ 9000	All
0 to < 16	221 (10.84)	235 (11.53)	150 (7.36)	92 (4.51)	698 (34.26)
16 to < 32	197 (9.67)	243 (11.92)	196 (9.62)	137 (6.72)	773 (37.94)
≥ 32	51 (2.50)	123 (6.03)	148 (7.26)	244 (11.98)	566 (27.78)
All	469 (23.02)	601 (29.50)	494 (24.25)	473 (23.22)	2037 (100)

Absolute Changes from Baseline in ESA and Iron Dosing [mean (standard deviation)]

Baseline iron dose group (mg)		Baseline ESA dose group (units) Lowest 1 -< 2000	Low 2000 - <4500	Moderate 4500- <9000	High ≥ 9000	All
0 to < 16						
	ESA	+772.1 (1,484.0)	+660.5 (2,456.6)	+51.8 (2,662.9)	-888.2 (4,811.6)	+360.9 (2,751.4)
	Iron	-0.92 (5.75)	-0.98 (4.66)	-0.07 (6.68)	-0.23 (8.81)	-0.67 (6.13)
16 to < 32						
	ESA	+542.0 (1,485.4)	-51.0 (1,884.7)	-1,081.8 (2,675.0)	-1,328.6 (4,079.2)	-387.7 (2,635.9)
	Iron	-4.23 (8.53)	-3.76 (9.50)	-3.38 (8.78)	-4.54 (11.01)	-3.92 (9.37)
≥ 32						
	ESA	+226.7 (1,197.6)	-274.0 (1,659.6)	-1,332.8 (3,174.6)	-3,080.7 (5,583.8)	-1,715.7 (4,288.3)
	Iron	-15.19 (16.05)	-13.16 (17.93)	-11.32 (17.36)	-17.33 (22.05)	-14.66 (19.65)
All						
	ESA	+616.1 (1,463.9)	+181.6 (2,121.5)	-812.8 (2,883.7)	-2,146.7 (5,124.8)	-500.2 (3,316.5)
	Iron	-3.87 (9.57)	-4.60 (11.43)	-4.75 (12.42)	-10.30 (18.85)	-5.79 (13.62)

- **Study limitations**
  - Retrospective, observational study
  - Simultaneous elevations in TSAT and serum ferritin were examined to minimize the possibility that some ferritin elevations were due to inflammatory response; however, patients with only moderate changes in these values were included.[3]

Summary

- Physicians may respond to non-treatment related rises in TSAT and serum ferritin by reducing ESA and iron doses, particularly in patients with high baseline use.
- A mean decrease in ESA dose of 500.2 units was measured for all patients, while a reduction of 3,080.7 units was measured for patients with highest baseline ESA and iron doses.
- A mean decrease in iron dose of 5.79 mg was measured for all patients, while a 17.3 mg mean decrease was observed for patients with the highest baseline ESA and iron doses.
- If approved for use as a phosphate binder, ferric citrate may reduce ESA and iron usage by HD patients and have incremental economic value within the Medicare bundle reimbursement plan.[4]

References

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