Iron Isomaltoside Use in Non-Dialysis Chronic Kidney Disease and Independent Dialysis Patients at Vancouver General Hospital

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Background

- Iron deficiency anemia requiring iron supplementation is a common condition in chronic kidney disease (CKD)
  - Oral iron is limited by issues with tolerance, adherence and efficacy
  - IV iron formulations include: iron sucrose, sodium ferric gluconate and **iron isomaltoside (Monoferric©)**
- Iron isomaltoside is a new IV iron option in Canada
  - Low content of labile and free iron reduces immunogenic potential, allowing for larger single doses to be given over a shorter period of time
  - Benefits include: shorter time to reach iron repletion dose, larger single dose, fewer infusion clinic visits, preservation of peripheral vasculature for potential fistula formation
  - Infusion rate: 15 mL/hr x 20 min, then 120 mL/hr
    - Slower than monograph to reduce risk of Fishbane reactions (flushing, tightness or pain in back/chest)
  - Monitoring: vital signs pre-infusion, 20 minutes into infusion, and 30 minutes post-infusion

Objectives

- To evaluate the efficacy and safety of iron isomaltoside in non-dialysis CKD (ND-CKD) and independent dialysis (PD and HHD) patients
- Primary Endpoints: changes in hemoglobin, ferritin, TSAT
- Secondary Endpoints: changes in doses of erythropoiesis-stimulating agents (ESAs) and oral iron; adverse events

Methods

- **Retrospective chart review:** Nov 2019-Aug 2021
- **Inclusion**:
  - VGH Independent dialysis (PD, HHD) or ND-CKD patients
  - Minimum of one dose of iron isomaltoside administered
- **Data collection**: PROMIS database; patient charts
- **Statistics**:
  - Descriptive statistics
  - Paired 2-tailed t-test; $p<0.05$ considered significant

Inclusion Flow Diagram

63 patients ordered iron isomaltoside

11 patients **excluded** as never received dose
- 4 – workload issues for scheduling dose
- 2 – refused to go to hospital
- 1 – repeat iron studies normal, dose cancelled
- 1 – missed appointment
- 1 – transferred to St. Paul's Hospital, received dose there
- 1 – transferred to in-center hemodialysis
- 1 – order missed

52 patients **received** iron isomaltoside (**54 courses** total)

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Results

Baseline Characteristic	**N=52 patients**
Male, n (%)	30 (57.6)
Age (years), mean (SD)	70.4 (14.4)
Weight (kg), mean (SD)	74.6 (17.5)
Allergies (no.), median (range)	1 (0-2)
Renal Status, n (%)	
Non-Dialysis CKD	40 (76.9)
Peritoneal Dialysis	11 (21.2)
Home Hemodialysis	1 (1.9)
ESA Use Prior to Iron Isomaltoside, n (%)	27 (51.9)
Darbepoetin (Aranesp®), n (% of ESA users)	25 (92.6)
Epoetin alfa (Eprex®), n (% of ESA users)	2 (7.4)
Oral Iron Use Prior to Iron Isomaltoside, n (%)	31 (59.6
Ferrous fumarate, n (% of iron users)	26 (83.9)
Ferrous sulfate, n (% of iron users)	1 (3.2)
Iron polysaccharide (Feramax®), n (% of iron users)	2 (6.5)
Ferrous gluconate, n (% of iron users)	2 (6.5)
Iron Isomaltoside Dosage, n (%)	**N=54 courses**
500 mg x 1	14 (25.9)
1000 mg x 1	38 (70.4)
500 mg weekly x 2	1 (1.9)
1000 mg weekly x 2	1 (1.9)

Primary Endpoints

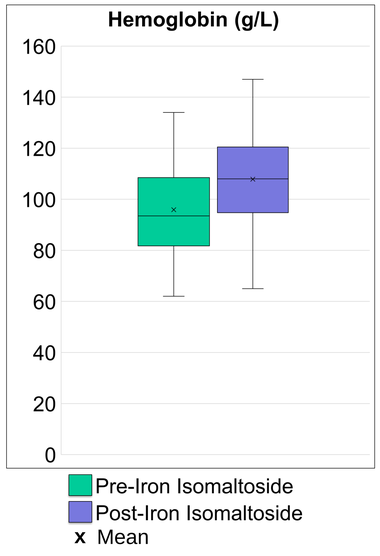
Parameter	Pre-Iron Isomaltoside	Post-Iron Isomaltoside	Difference	P-Value	Median Time to Repeat Lab (range)
Hemoglobin (g/L), mean (SD) [n=50 IV iron courses]	95.9 (16.9)	107.8 (18.0)	+12.0	<0.0001	73 days (9-137 days)
Ferritin (mcg/L), mean (SD) [n=43 IV iron courses]	166.1 (135.7)	422.7 (311.9)	+256.6	<0.0001	70 days (9-138 days)
TSAT, mean (SD) [n=44 IV iron courses]	0.14 (0.05)	0.23 (0.07)	+0.09	<0.0001	72 days (9-138 days)

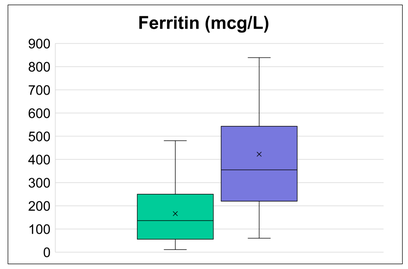
Secondary Endpoints

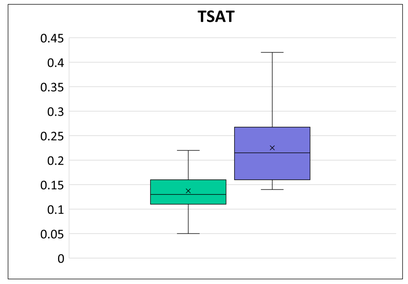
Drug	Pre-Iron Isomaltoside	Post-Iron Isomaltoside	P-Value
Darbepoetin (mcg/week), mean (SD) [n=14 IV iron courses]	36.6 (31.7)	30.2 (22.2)	0.08
Epoetin alfa (units/week), mean (SD) [n=3 IV iron courses]	9000 (5,567.8)	8000 (2,000.0)	0.68
Oral Iron (mg/day), mean (SD) [n=35 IV iron courses]	164.2 (107.8)	149.9 (126.3)	0.32

Adverse Event	N=54 Iron Isomaltoside Courses [a,b]
No adverse events noted by nurse	46 (85.2%)
Dizziness	2 (3.7%)
Drowsiness	1 (1.9%)
Headache	1 (1.9%)
Hypotension (>30% or >20 mm Hg drop in baseline systolic BP)	1 (1.9%) [c]
Paresthesia	1 (1.9%)
Stomach upset	1 (1.9%)
Anaphylaxis	0
Fishbane reaction	0

[a] 2 patients received 2 doses of iron isomaltoside 8 months apart (neither displayed adverse events in either course)
[b] 7 events occurred in 6 patients (1 patient experienced both drowsiness [had been ongoing for 1 week] and dizziness)
[c] 1 patient developed asymptomatic hypotension and was discharged home without treatment







Strengths

- First Canadian study to evaluate IV iron isomaltoside in ND-CKD and independent dialysis patients
- Clear chart documentation of adverse events by nurses for all patients during infusions
  - Nurses explicitly noted if patient had no signs or symptoms of adverse reactions to iron isomaltoside

Limitations

- Retrospective design
- Small sample size
- Use of surrogate outcomes
- Variable timing and completeness of follow-up labs
- Short-term follow-up

Conclusions

- Single doses of iron isomaltoside resulted in statistically significant increases in hemoglobin, ferritin, and TSAT
- Iron isomaltoside was generally well tolerated:
  - 6 (11.5%) patients experienced at least 1 adverse event
  - No interventions required for any adverse event
- BC Renal Agency approval criteria for iron isomaltoside:
  - Intolerance or poor response to oral iron *AND*
  - Hemoglobin <110 g/L *AND* TSAT <20% *AND*
  - Total dose exceeds 300 mg IV iron