

Time to Hang the White Coats in the Closet?

BY DOUG BRUNK

SAN DIEGO — It may be time for North Americans to follow the British in their 2007 ban on white lab coats in the health care setting.

Researchers at Virginia Commonwealth University in Richmond used pigskin as an in vitro model to demonstrate that large inoculums of methicillin-resistant *Staphylococcus aureus* (MRSA),

vancomycin-resistant enterococci (VRE), and pan-resistant *Acinetobacter* (PRA) bacteria could be transferred from a white cotton lab coat to pigskin 1 minute, 5 minutes, and 30 minutes after inoculation.

“Previous research has indicated that you could isolate organisms from materials such as hospital curtains, neckties, and lab coats, but we wanted to find out if you could take the inoculum from the cloth of a lab coat, transfer it to skin, and

isolate the inoculum from the skin,” Dawn L. Butler said in an interview during a poster session at the annual meeting of the Society for Healthcare Epidemiology of America. “We did.”

Ms. Butler, a second-year medical student at the university, and her associates diluted MRSA, VRE, and PRA and inoculated them onto swatches of one clean, cotton medical lab coat. Next, they rubbed sanitized pieces of pigskin across the in-

oculated swatches, and a touch prep of the pigskin onto selective media was performed to determine if the inoculated organism could be isolated from the pigskin.

These steps were performed for each of the three study isolates at 1 minute, 5 minutes, and 30 minutes. Selective media were used to prevent growth of contaminants, followed by incubation of the cloth swatches for 24 hours in thioglycolate broth to verify the viability of organisms.

All of the swatches had grown organisms on respective selective media at 24 hours, confirming organism viability on the cotton lab coat.

“Everybody criticizes the British for banning white lab coats in the health care setting, saying that nobody’s ever shown that lab coats can transmit an infection,” Dr. Michael Edmond, chair of the division of infectious diseases at VCU, said



It’s possible to ‘take the inoculum from the cloth of a lab coat, transfer it to skin, and isolate [it] from the skin.’

MS. BUTLER

at the meeting. “This shows that it’s biologically plausible, because in the laboratory we did transmit the organism from the coat to the skin.”

In a related poster, 141 physicians from nine VCU departments were surveyed about their attitudes regarding white lab coats. Most of the respondents (90%) were aged 29-39 years. Slightly more than half were men (52%) and the majority were medical residents (42%), followed by interns (35%), attending physicians (17%), and fellows (6%), reported Dr. J. Daniel Markley Jr., a second-year internal medicine resident at the university.

Previous studies have shown that nosocomial pathogens can persist on fabric for months, but when the survey participants were asked how long a microbe can survive on fabric, 2% said hours, 49% said days, 28% said weeks, 18% said months, and 3% said years.

While 90% of respondents reported wearing their white coats daily or most days of the week, 62% said that they wait 2 weeks or longer to launder them.

Nearly half of respondents (49%) believed that patient perception of physicians would be adversely affected if white coats were discontinued, yet 74% believed that banning white coats could have a significant effect on hospital-acquired infection.

Dr. Markley also reported that 87% of male physicians would stop wearing ties if recommended and 42% of respondents would stop wearing a watch, but only 48% would comply with a “bare below the elbow” policy. They wouldn’t want to wear a lab coat with short sleeves “because they don’t want to be viewed as a dentist,” Dr. Markley said.

The researchers had no conflicts of interest to disclose.

Reference: 1. Van Wyck DB, Roppolo M, Martinez CO, Mazzy RM, McMurray S, for the United States Iron Sucrose (Venofer®) Clinical Trials Group. A randomized, controlled trial comparing IV iron sucrose to oral iron in anemic patients with nondialysis-dependent CKD. *Kidney Int*. 2005;68:2946-2956. 2. Data on file. American Regent, Inc., Shirley, NY.

Venofer®

iron sucrose injection, USP

Brief Summary (See Package Insert For Full Prescribing Information)

Therapeutic Class: Hematinic

CLINICAL INDICATIONS AND USAGE

Venofer® (iron sucrose injection, USP) is indicated in the treatment of iron deficiency anemia in the following patients:

- non-dialysis dependent chronic kidney disease (NDD-CKD) patients receiving an erythropoietin
- non-dialysis dependent chronic kidney disease (NDD-CKD) patients not receiving an erythropoietin

CONTRAINDICATIONS

The use of Venofer® is contraindicated in patients with evidence of iron overload, in patients with known hypersensitivity to Venofer® or any of its inactive components, and in patients with anemia not caused by iron deficiency.

WARNINGS

Hypersensitivity reactions have been reported with injectable iron products. See PRECAUTIONS and ADVERSE REACTIONS.

PRECAUTIONS

General: Because body iron excretion is limited and excess tissue iron can be hazardous, caution should be exercised to withhold iron administration in the presence of evidence of tissue iron overload. Patients receiving Venofer® require periodic monitoring of hematologic and hematimetric parameters (hemoglobin, hematocrit, serum ferritin and transferrin saturation). Iron therapy should be withheld in patients with evidence of iron overload. Transferrin saturation values increase rapidly after IV administration of iron sucrose; thus, serum iron values may be reliably obtained 48 hours after IV dosing. See DOSAGE AND ADMINISTRATION and OVERDOSAGE.

Hypersensitivity Reactions: Serious hypersensitivity reactions have been reported in patients receiving Venofer®. No life-threatening hypersensitivity reactions were observed in the clinical studies. Several cases of mild or moderate hypersensitivity reactions were observed in these studies. There are post-marketing spontaneous reports of life-threatening hypersensitivity reactions in patients receiving Venofer®. See ADVERSE REACTIONS.

Hypotension: Hypotension has been reported frequently in hemodialysis dependent chronic kidney disease patients receiving intravenous iron. Hypotension also has been reported in non-dialysis dependent and peritoneal dialysis dependent chronic kidney disease patients receiving intravenous iron. Hypotension following administration of Venofer® may be related to rate of administration and total dose administered. Caution should be taken to administer Venofer® according to recommended guidelines. See DOSAGE AND ADMINISTRATION.

Carcinogenesis, Mutagenesis, and Impairment of Fertility:

No long-term studies in animals have been performed to evaluate the carcinogenic potential of Venofer®.

Venofer® was not genotoxic in the Ames test, the mouse lymphoma cell (L5178Y/TK+/-) forward mutation test, the human lymphocyte chromosome aberration test, or the mouse micronucleus test.

Venofer® at IV doses up to 15 mg iron/kg/day (about 1.2 times the recommended maximum human dose on a body surface area basis) was found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy Category B: Teratology studies have been performed in rats at IV doses up to 13 mg iron/kg/day (about 0.5 times the recommended maximum human dose on a body surface area basis) and rabbits at IV doses up to 13 mg iron/kg/day (about 1 times the recommended maximum human dose on a body surface area basis) and have revealed no evidence of impaired fertility or harm to the fetus due to Venofer®. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Venofer® is excreted in milk of rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Venofer® is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of Venofer® in pediatric patients have not been established. In a country where Venofer® is available for use in children, at a single site, five premature infants (weight less than 1,250 g) developed necrotizing enterocolitis and two of the five expired during or following a period when they received Venofer®, several other medications and erythropoietin. Necrotizing enterocolitis may be a complication of prematurity in very low birth weight infants. No causal relationship to Venofer® or any other drugs could be established.

Geriatric Use: The five pivotal clinical trials did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger subjects. No overall differences in safety were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Adverse Events observed in all treated populations

The frequency of adverse events associated with the use of Venofer® has been documented in six randomized clinical trials involving 231 hemodialysis dependent, 139 non-dialysis dependent and 75 peritoneal dialysis dependent-CKD patients; and in two post-marketing safety studies involving 1,051 hemodialysis dependent-CKD patients for a total of 1,496 patients. In addition, over 2,000 patients treated with Venofer® have been reported in the medical literature.

Treatment-emergent adverse events reported by ≥ 2% of treated patients with NDD-CKD in the randomized clinical trials, whether or not related to Venofer® administration, are listed by indication in Table 2.

Treatment-emergent adverse events reported in ≥ 2% of patients by dose group are shown in Table 3.

Table 2. Most Common Treatment-Emergent Adverse Events Reported in ≥ 2% of Patients with NDD-CKD by Clinical Indication (Multidose Safety Population)

Adverse Events (Preferred Term)	NDD-CKD	
	Venofer® (N=139)	Oral Iron (N=139)
	%	%
Subjects with any adverse event	76.3	73.4
Ear and Labyrinth Disorders		
Ear Pain	2.2	0.7
Eye Disorders		
Conjunctivitis	0	0
Gastrointestinal Disorders		
Abdominal pain NOS*	1.4	2.9
Constipation	4.3	12.9
Diarrhea NOS	7.2	10.1
Dysgeusia	7.9	0
Nausea	8.6	12.2
Vomiting NOS	5.0	8.6
General Disorders and Administration Site Conditions		
Asthenia	0.7	2.2
Chest pain	1.4	0
Edema NOS	6.5	6.5
Fatigue	3.6	5.8
Feeling abnormal	0	0
Infusion site burning	3.6	0
Injection site extravasation	2.2	0
Injection site pain	2.2	0
Peripheral edema	7.2	5.0
Pyrexia	0.7	0.7
Infections and Infestations		
Catheter site infection	0	0
Nasopharyngitis	0.7	2.2
Peritoneal infection	0	0
Sinusitis NOS	0.7	0.7
Upper respiratory tract infection NOS	0.7	1.4
Urinary tract infection NOS	0.7	5.0
Injury, Poisoning and Procedural Complications		
Graft complication	1.4	0
Investigations		
Cardiac murmur NOS	2.2	2.2
Fecal occult blood positive	1.4	3.6
Metabolism and Nutrition Disorders		
Fluid overload	1.4	0.7
Gout	2.9	1.4
Hyperglycemia NOS	2.9	0
Hypoglycemia NOS	0.7	0.7
Musculoskeletal and Connective Tissue Disorders		
Arthralgia	1.4	2.2
Arthritis NOS	0	0

Table 3. Most Common Treatment-Emergent Adverse Events Reported in ≥ 2% of Patients with NDD-CKD by Dose Group (Multidose Safety Population)

Adverse Events (Preferred Term)	NDD-CKD		
	200 mg (N=109)	500 mg (N=30)	%
Subjects with any adverse event	75.2	80.0	
Ear and Labyrinth Disorders			
Ear Pain	0.9	6.7	
Eye Disorders			
Conjunctivitis	0	0	
Gastrointestinal Disorders			
Abdominal pain NOS*	1.8	0	
Constipation	3.7	6.7	
Diarrhea NOS	6.4	10.0	
Dysgeusia	9.2	3.3	
Nausea	9.2	6.7	
Vomiting NOS	5.5	3.3	
General Disorders and Administration Site Conditions			
Asthenia	0.9	0	
Chest pain	0.9	3.3	
Edema NOS	7.3	3.3	
Fatigue	4.6	0	
Feeling abnormal	0	0	
Infusion site burning	3.7	3.3	
Injection site pain	2.8	0	
Peripheral edema	5.5	13.3	
Pyrexia	0.9	0	
Infections and Infestations			
Catheter site infection	0	0	
Nasopharyngitis	0.9	0	
Peritoneal infection	0	0	
Sinusitis NOS	0	3.3	
Upper respiratory tract infection NOS	0.9	0	
Injury, Poisoning and Procedural Complications			
Graft complication	1.8	0	
Investigations			
Cardiac murmur NOS	2.8	0	
Fecal occult blood positive	1.8	0	
Metabolism and Nutrition Disorders			
Fluid overload	1.8	0	
Gout	1.8	6.7	
Hyperglycemia NOS	3.7	0	
Hypoglycemia NOS	0.9	0	
Musculoskeletal and Connective Tissue Disorders			
Arthralgia	0.9	3.3	
Back pain	1.8	3.3	
Muscle cramp	0	3.3	
Myalgia	2.8	6.7	

(Table 2 continued)

Adverse Events (Preferred Term)	NDD-CKD	
	Venofer® (N=139)	Oral Iron (N=139)
	%	%
Musculoskeletal and Connective Tissue Disorders		
Back pain	2.2	3.6
Muscle cramp	0.7	0.7
Myalgia	3.6	0
Pain in extremity	4.3	0
Nervous System Disorders		
Dizziness	6.5	1.4
Headache	2.9	0.7
Hypoesthesia	0.7	0.7
Respiratory, Thoracic and Mediastinal Disorders		
Cough	2.2	0.7
Dyspnea	3.6	0.7
Dyspnea exacerbated	2.2	0.7
Nasal congestion	1.4	2.2
Pharyngitis	0	0
Rhinitis allergic NOS	0.7	2.2
Skin and Subcutaneous Tissue Disorders		
Pruritus	2.2	4.3
Rash NOS	1.4	2.2
Vascular Disorders		
Hypertension NOS	6.5	4.3
Hypotension NOS	2.2	0.7

*NOS—Not otherwise specified

(Table 3 continued)

Adverse Events (Preferred Term)	NDD-CKD	
	200 mg (N=109)	500 mg (N=30)
	%	%
Musculoskeletal and Connective Tissue Disorders		
Pain in extremity	4.6	3.3
Nervous System Disorders		
Dizziness	5.5	10.0
Headache	3.7	0
Respiratory, Thoracic and Mediastinal Disorders		
Cough	0.9	6.7
Dyspnea	1.8	10.0
Pharyngitis	0	0
Skin and Subcutaneous Tissue Disorders		
Pruritus	0.9	6.7
Vascular Disorders		
Hypertension NOS	6.4	6.7
Hypotension NOS	0.9	6.7

*NOS—Not otherwise specified

Drug related adverse events reported by ≥ 2% of Venofer® (iron sucrose injection, USP) treated patients are shown by dose group in Table 4.

Table 4. Most Common Adverse Events Related to Study Drug Reported in ≥ 2% of Patients with NDD-CKD by Dose Group (Multidose Safety Population)

Adverse Events (Preferred Term)	NDD-CKD	
	200 mg (N=109)	500 mg (N=30)
	%	%
Subjects with any adverse event	23.9	20.0
Gastrointestinal Disorders		
Diarrhea NOS*	0	0
Dysgeusia	7.3	3.3
Nausea	2.8	0
General Disorders and Administration Site Conditions		
Infusion site burning	3.7	0
Injection site pain	2.8	0
Peripheral edema	1.8	6.7
Nervous System Disorders		
Dizziness	2.8	6.7
Headache	2.8	0
Vascular Disorders		
Hypotension NOS	0	6.7

*NOS—Not otherwise specified

Adverse Events Observed in Non-Dialysis Dependent Chronic Kidney Disease (NDD-CKD) Patients

In the pivotal study of 182 NDD-CKD patients, 91 were exposed to Venofer®. Adverse events, whether or not related to Venofer®, reported by ≥ 5% of the Venofer® exposed patients were as follows: dysgeusia (7.7%), peripheral edema (7.7%), diarrhea (6.5%), constipation (6.5%), nausea (6.5%), dizziness (6.5%), and hypertension (6.5%). One serious related adverse reaction was reported (hypotension and shortness of breath not requiring hospitalization in a Venofer® patient). Two patients experienced possible hypersensitivity/allergic reactions (local edema/hypotension) during the study. Of the 5 patients who prematurely discontinued the treatment phase of the study due to adverse events (2 oral iron group and 3 Venofer® group), three Venofer® patients had events that were considered drug-related (hypotension, dyspnea and nausea).

Hypersensitivity Reactions: See WARNINGS and PRECAUTIONS.

In clinical studies, several patients experienced hypersensitivity reactions presenting with wheezing, dyspnea, hypotension, rashes, or pruritus. Serious episodes of hypotension occurred in 2 patients treated with Venofer® at a dose of 500 mg.

The post-marketing spontaneous reporting system includes reports of patients who experienced serious or life-threatening reactions (anaphylactic shock, loss of consciousness or collapse, bronchospasm with dyspnea, or convulsion) associated with Venofer® administration.

OVERDOSAGE

Dosages of Venofer® (iron sucrose injection, USP) in excess of iron needs may lead to accumulation of iron in storage sites leading to hemosiderosis. Periodic monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognizing iron accumulation. Venofer® should not be administered to patients with iron overload and should be discontinued when serum ferritin levels equal or exceed established guidelines [1]. Particular caution should be exercised to avoid iron overload where anemia unresponsive to treatment has been incorrectly diagnosed as iron deficiency anemia.

Symptoms associated with overdosage or infusing Venofer® too rapidly included hypotension, dyspnea, headache, vomiting, nausea, dizziness, joint aches, paresthesia, abdominal and muscle pain, edema, and cardiovascular collapse. Most symptoms have been successfully treated with IV fluids, hydrocortisone, and/or antihistamines. Infusing the solution as recommended or at a slower rate may also alleviate symptoms.

Preclinical Data:

Single IV doses of Venofer® at 150 mg iron/kg in mice (about 3 times the recommended maximum human dose on a body surface area basis) and 100 mg iron/kg in rats (about 8 times the recommended maximum human dose on a body surface area basis) were lethal.

The symptoms of acute toxicity were sedation, hypomotility, pale eyes, and bleeding in the gastrointestinal tract and lungs.

DOSAGE AND ADMINISTRATION

The dosage of Venofer® is expressed in terms of mg of elemental iron. Each mL contains 200 mg of elemental iron.

Most CKD patients will require a minimum cumulative replacement dose of 1,000 mg of elemental iron, administered over sequential sessions, to achieve a favorable hemoglobin response and to replenish iron stores (ferritin, TSAT).

Administration: Venofer® must only be administered intravenously either by slow injection or by infusion.

Recommended Adult Dosage:

Non-Dialysis Dependent Chronic Kidney Disease Patients (NDD-CKD): Venofer® is administered as a total cumulative dose of 1,000 mg over a 14 day period as a 200 mg slow IV injection (indicated over 2 to 5 minutes on 5 different occasions within the 14 day period). There is limited experience with administration of an infusion of 500 mg of Venofer®, diluted in a maximum of 250 mL of 0.9% NaCl, over a period of 0.5-4 hours day 1 and day 14; hypotension occurred in 2 of 30 patients treated. (See CLINICAL TRIALS, Study D: Non-Dialysis Dependent Chronic Kidney Disease (NDD-CKD) Patients and ADVERSE REACTIONS, Adverse Events Observed in Non-Dialysis Dependent Chronic Kidney Disease (NDD-CKD) Patients sections.)

HOW SUPPLIED

Venofer® is supplied in 5 mL and 10 mL single dose vials. Each 5 mL vial contains 100 mg elemental iron (20 mg/mL) and each 10 mL vial contains 200 mg elemental iron (20 mg/mL). Contains no preservatives. Store in original carton at 25°C (77°F). Excursions permitted to 15°-30°C (59°-86°F). [See the USP controlled room temperature]. Do not freeze.

Sterile
NDC-0517-2340-01 100 mg/5 mL Single Dose Vial Individually Boxed
NDC-0517-2340-10 100 mg/5 mL Single Dose Vial Packages of 10
NDC-0517-2340-25 100 mg/5 mL Single Dose Vial Packages of 25
NDC-0517-2310-01 200 mg/10 mL Single Dose Vial Individually Boxed
NDC-0517-2310-05 200 mg/10 mL Single Dose Vial Packages of 5
NDC-0517-2310-10 200 mg/10 mL Single Dose Vial Packages of 10

Rx Only

REFERENCE: [1] National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease, 2000. *Am J Kidney Dis*. 3