

On-line Table 1: The characteristics of 8 ferumoxytol studies at our institution

IRB No.	Objective	Patients, No. ^a	Pathologies	Fe Injections and Total Doses	Reference
8097	Ferumoxytol MRI enhancement time course in brain tumors	13	Primary BT (12), metastasis (1)	1 mg/kg, 3 mg/kg; Total: 4 mg/kg	Neuwelt et al ^{8,9}
2753	Vascular cerebral imaging with ferumoxytol throughout standard GBM radio/chemotherapy	12	GBM (12)	2 mg/kg; Total: 2 mg/kg	Varallyay et al, ⁵ Gahramanov et al, ^{33,35} Hamilton et al, ³⁶ Nasser et al ³⁷
2864	Permeability and perfusion MRI in brain tumors using ferumoxytol and gadolinium in 3T and 7T magnets	20	High-grade BT (17), low-grade BT (2), meningioma (1)	1 mg/kg, 3 mg/kg; Total: 4 mg/kg	Gahramanov et al, ^{33,35} Hamilton et al, ³⁶ Nasser et al ³⁷
1562 ^b	Ferumoxytol vs gadolinium imaging in various CNS pathologies	156	Meningioma (12), primary BT (74), metastasis (20), vascular (18), demyelination (10), spine (4), other (18)	75 mg, 150 mg, 285 mg; Total: 510 mg	Varallyay et al, ⁵ Gahramanov et al, ^{33,35} Hamilton et al, ^{36,41} Nasser et al, ³⁷ Dósa et al, ^{38,39} Farrell et al ⁴⁰
3678	Changes in brain tumor vascularity after antiangiogenic therapy versus steroid therapy	5	GBM (5)	2 mg/kg; Total: 2 mg/kg	Gahramanov et al ³³
5405	Vascular properties of pediatric brain tumors using ferumoxytol	12	High-grade BT (8), low-grade BT (4)	1 mg/kg, 1–3 mg/kg; Total: 2–4 mg/kg	Thompson et al ⁴²
813	Ferumoxytol and gadolinium imaging of brain tumors in a single imaging session	123	Primary BT (105), CNS lymphoma (5), metastasis (13)	1 mg/kg, 3 mg/kg; Total: 4 mg/kg	Nasser et al, ³⁷ Dósa et al, ³⁸ Hamilton et al ⁴¹
9846 ^b	Steady-state blood volume imaging throughout GBM treatment	9	GBM (7), other (2)	1 mg/kg, 2 mg/kg, 4 mg/kg; Total: 7 mg/kg ^c	

Note:—BT indicates brain tumor; IRB, institutional review board; GBM, glioblastoma.

^a Patients may have participated in more than 1 protocol.

^b Total dose 7 mg/kg, but not exceeding 510 mg total.

On-line Table 2: Organ systems potentially affected by ferumoxytol-related AEs and their severity-based classification using FDA and CTCAE guidelines

FDA	Adverse Events			Serious Adverse Events	
	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grade 4 (Anaphylaxis)	Grade 5 (Death)
CTCAE					
Organ system					
Cardiac	Hypertension	Chest tightness, tachycardia	Hypotension ^a	Shock	Cardiac arrest
Skin	Injection site pain, itching erythema; asymptomatic transient flush, rash, macular/papular eruption; mild or localized pruritus, hyperpigmentation	Injection site pain or swelling with inflammation or phlebitis; symptomatic flush, urticaria, macular/papular eruptions covering <50% BSA; generalized pruritus, hyperpigmentation	Injection site ulceration/necrosis; intense, widespread pruritus interfering with ADL; severe, generalized macular/papular/vesicular eruption covering >50% BSA	Generalized exfoliative, ulcerative, or bullous dermatitis	
Gastrointestinal	Constipation, diarrhea, GERD, nausea, vomiting, taste alteration	Constipation (treatment indicated), diarrhea or vomiting (IV fluids indicated)			
Musculoskeletal	Pain (treatment required)				
Neurology	Transient myalgia, arthralgia ^b	Pain (treatment required)	Loss of consciousness		
Constitutional	Transient headache ^c	Headache (treatment required)			
Ocular/Visual	Fatigue				
Respiratory	Red eye				
	Cough	Cough (narcotic medication needed), dyspnea, wheezing	Stridor, symptomatic bronchospasm	Life-threatening bronchospasm	Death
Vascular	Asymptomatic vein injury	Symptomatic vein injury	Vein injury, repair or revision indicated		

Note:—ADL indicates activities of daily living; BSA, body surface area; GERD, gastroesophageal reflux disease.

^a Systolic blood pressure of less than 90 mmHg or greater than 30% decrease from that patient's baseline.

^b Myalgias and arthralgias (eg, back pain, chest discomfort) are called Fishbane reactions. These are transient, mild infusion reactions (not HSR) and usually they do not require any treatment.

^c A transient, mild headache can be a normal reaction to iron infusion.

On-line Table 3: Symptom- and severity-based management of ferumoxytol related hypersensitivity reactions during MR imaging^a

Severity	Sign/Symptom	Management	Medications
Potentially life-threatening HSR	Cardiorespiratory arrest Anaphylaxis, shock	1. Stop iron infusion; 2. Remove patient from MRI; 3. Call fast response team; 4. Start ACLS if necessary; 5. Monitor patient; 6. Medications; 7. Transfer to ICU	Start: ACLS Adrenaline (0.1 mg 1/10,000 solution over 5 minutes IV or 0.3–0.5 mg 1/1000 solution IM), elevate the lower extremities, O ₂ face mask (6–8 L/min), nebulized β_2 agonist (eg, salbutamol solution 2.5 mg/3 mL or 5 mg/3 mL), rapid volume load (eg, 1–2 L saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV) Adrenaline (0.1 mg 1/10,000 solution over 5 minutes IV or 0.3–0.5 mg 1/1000 solution IM), elevate the lower extremities, repeat BP measurement, O ₂ face mask (6–8 L/min), rapid volume load (eg, 1–2 L saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV) Adrenaline (0.1 mg 1/10,000 solution over 5 minutes IV or 0.3–0.5 mg 1/1000 solution IM), O ₂ face mask (6–8 L/min), nebulized β_2 agonist (eg, salbutamol solution 2.5 mg/3 mL or 5 mg/3 mL), rapid volume load (eg, 1–2 L saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV)
Mild or moderate HSR	Hypotension (decrease $\geq$ 30% of SBP, or SBP drops under 90 mmHg, with repeated BP measurement) Stridor, symptomatic bronchospasm (cyanosis) Hypertension (may be anxiety related) Hypotension (decrease $<$ 30% of SBP, 5%–10% difference can be normal or measurement error) Chest tightness, tachycardia Asymptomatic flush, rash, erythema, eruptions, edema Symptomatic flush, rash, erythema, eruptions, edema	1. Stop iron infusion; 2. Remove patient from MRI if needed; 3. Call physician; 4. Monitor patient; 5. Medications; 6. Observation for 1–4 hours	No therapy. Antihypertensive treatment if SBP $\geq$ 180 mmHg or DBP $\geq$ 120 mmHg (eg, captopril 6.25–12.5 mg orally), repeat BP measurement Wait for at least 15 minutes, elevate the lower extremities, repeat BP measurement: if improving, consider continuing the imaging (restart iron infusion at 25%–50% reduced rate); if not better, isotonic fluid load (eg, 500 mL saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV) Isotonic fluid load (eg, 500 mL saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV) Wait for at least 15 minutes: if improving, consider continuing the imaging (restart iron infusion at 25%–50% reduced rate); if not better, isotonic fluid load (eg, 500 mL saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV) Isotonic fluid load (eg, 500 mL saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV)

Continued on next page

On-line Table 3: Continued

Severity	Sign/Symptom	Management	Medications
	Cough-mild		Wait for at least 15 minutes: if improving, consider continuing the imaging (restart iron infusion at 25%–50% reduced rate); if not better, isotonic fluid load (eg, 500 mL saline), IV corticosteroid (eg, 100–500 mg hydrocortisone IV)
	Dyspnea, wheezing, severe cough, shortness of breath		O ₂ face mask (l–2 L/min), isotonic fluid load (eg, 500 mL saline), nebulized β_2 agonist (eg, salbutamol solution 2.5 mg/3 mL or 5 mg/3 mL), IV corticosteroid (eg, 100–500 mg hydrocortisone IV)
	Nausea, vomiting		Antiemetic treatment (eg, prochlorperazine 5–10 mg orally, 2.5–10 mg IV)
	Dizziness		Wait for at least 15 minutes: if improving, consider continuing the imaging (restart iron infusion at 25%–50% reduced rate); if not better, isotonic fluid load (eg, 500 mL saline)
Other reactions	Back pain, myalgia, arthralgia, muscle spasm (Fishbane reaction) Headache	1. Stop iron infusion; 2. Remove patient from MRI if needed; 3. Monitor patient; 4. Medications if needed	No therapy needed
	Dysgeusia (taste alteration)		No therapy or NSAID (eg, ketorolac 20 mg orally, 30 mg IV) No therapy needed

Note:—ACLS indicates advanced cardiac life support; BP, blood pressure; DBP, diastolic blood pressure; IM, intramuscularly; NSAID, nonsteroidal anti-inflammatory drug; SBP, systolic blood pressure.

^a Recommendations based on Rampton et al.³² UpToDate data base,⁴³ and American College of Radiology Manual on Contrast Media, Version 10.2.⁴⁴