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FDA Perspective on Gadolinium Retention

Conflicts of Interest

U.S. FOOD & DRUG ADMINISTRATION

No conflicts of interest reported.

FDA Perspective

U.S. FOOD & DRUG ADMINISTRATION

https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/MedicalImagingDrugsAdvisoryCommittee/ucm553470.htm
https://www.fda.gov/Drugs/DrugSafety/ucm589213.htm

- GBCAs contain a “heavy metal” called gadolinium. Small amounts can stay in your body including the brain, bones, skin and other parts of your body for a long time (several months to years).
- No known harmful effects in patients with normal kidneys. More studies underway.
- Gadolinium retained more after Omniscan or Optimark than after Eovist, Magnevist, or MultiHance. Gadolinium retained least after Dotarem, Gadavist, or ProHance.
- Some people can feel pains, tiredness, and skin, muscle or bone ailments for a long time. These conditions have not been directly linked to GBCAs.
- People who get many doses, women who are pregnant, and young children may be at increased risk. Consider retention characteristics when choosing GBCAs for these patients. Minimize repetitive and closely spaced administrations.

Selected reports of positive safety signals that underlie need for further study

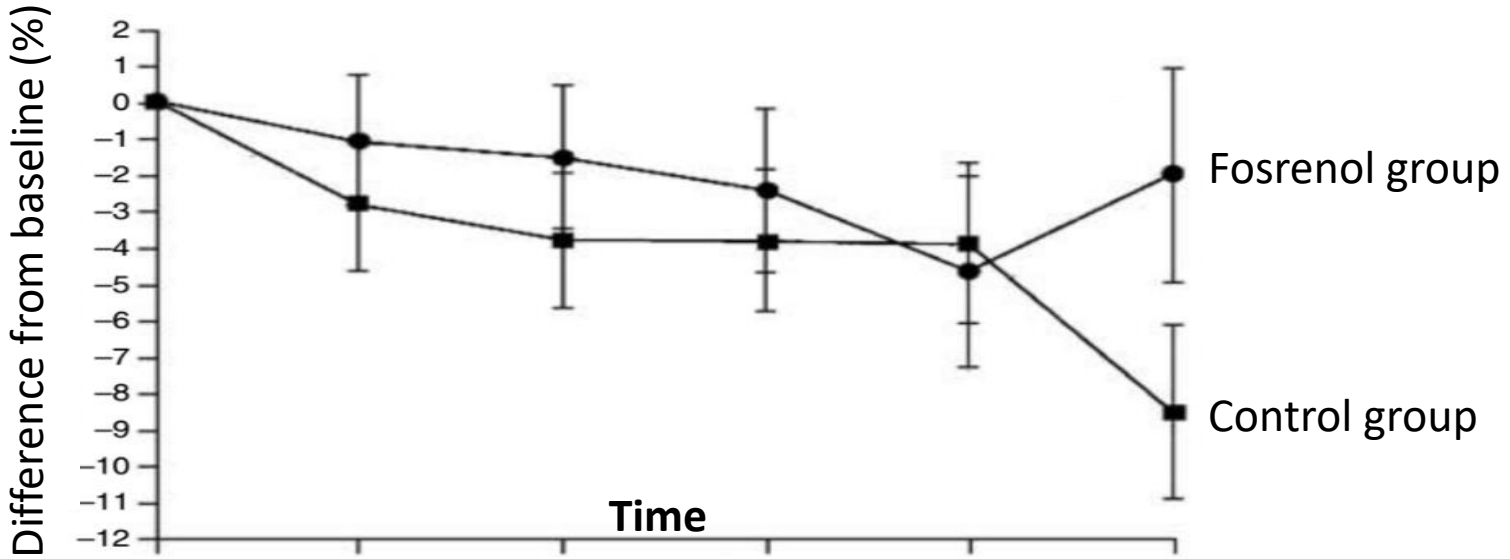
--	Lanthanides in animals	Lanthanides in humans	GBCA in animals	GBCA in humans
Brain	**He 2008**	**Sun 2017**	**Khairinisa 2017**	**Forslin 2017**
Body	**Haley 1963**	**Shelly 1958**	**Idee 2014**	**Roberts 2016**

Approach to safety evidence generation

Classification	Type of data source	Example	Status
Descriptive	Spontaneous adverse event reporting	FAERS, manufacturer databases	Ongoing
	Publications	Scientific literature: case reports, cases series	Ongoing
		Non-peer-reviewed sources	Ongoing
	Enhanced pharmacovigilance	Standardized data collection, development of case definition	Protocol development
Analytical	Administrative databases	Mother-baby linkages	Ongoing
	Epidemiologic / observational	Cohort prospective and retrospective	Ongoing
	Immunological	Harnessing preclinical advances for biomarkers / identification of vulnerable patients	Early development
	Prospective controlled (primarily to exclude clinically meaningful magnitude of neurobehavioral harm)	Developmental and juvenile animal studies (mice and non-human primates)	Protocol development
		Matched control or randomized safety trial in neurologically normal adults	Protocol development

Fosrenol precedent: How was safety evaluated after concern for brain retention with another lanthanide drug?

Change over 24 months in neuropsychological testing was compared between patients randomized to lanthanum carbonate (Fosrenol) vs. standard care (control).
Rates of decline were similar across all domains of the Cognitive Drug Research battery (Digit Vigilance Task shown)



	Baseline	Visit 9	Visit 12	Visit 15	Visit 18	Final
Month	0	3.5	6	12	18	24
Lanthanum carbonate (*n*)	174	153	121	89	63	47
Standard therapy (*n*)	178	153	143	121	93	77

Altmann 2007