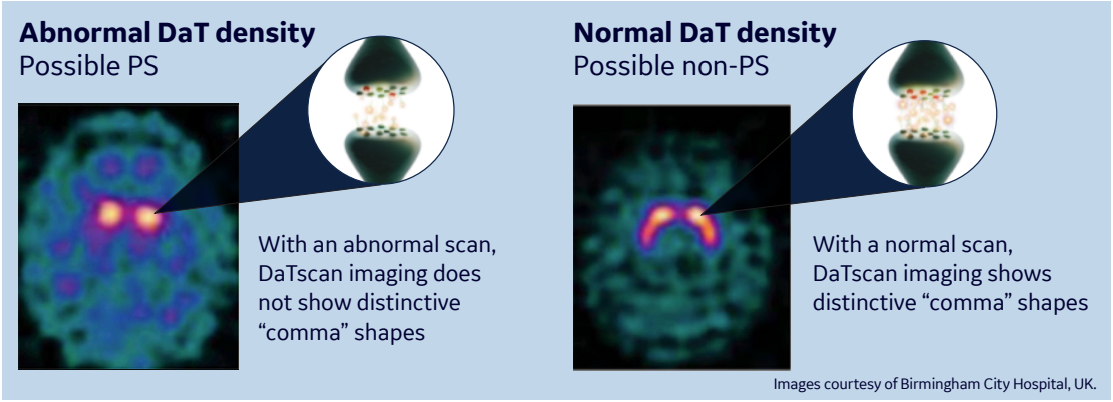
GE Healthcare

DaTscan™ (Ioflupane I 123 Injection) imaging may help clarify diagnoses

Two principal, multicenter clinical trial studies that examined the role of [^{123}I]FP-CIT, DaTscan (I 123 Ioflupane) SPECT, in clinical practice accompanied the NDA for DaTscan[1]

Study 1 reported on [^{123}I]FP-CIT, DaTscan (I 123 Ioflupane) SPECT in patients with early suspected parkinsonism, comparing baseline scan results to the consensus clinical diagnosis established three years later[1]

- Study 1 included 99 patients with early signs and/or symptoms of PS[1]
  - Patients with early features of parkinsonism; patients with features suggestive of MSA or PSP were excluded
  - Baseline clinical diagnoses consisted of probable PD (44%), possible PD (31%), "benign" PD (6%), possible ET (11%), and other diagnoses (7%)
- Clinical diagnosis at 36 months was established by the consensus of two movement disorder specialists who were blind to SPECT findings and working site diagnosis[2]
- For almost all subjects, SPECT imaging results remained the same throughout the study*[2]
- The inter-reader agreement of the visual interpretation of scans (normal vs abnormal) was very high at all time points. Both positive and negative percent agreement between clinical diagnosis and imaging increased from baseline to 36 months, suggesting that clinical diagnosis tended to move toward agreement with the imaging result as more clinical information became available[2]



Images courtesy of Birmingham City Hospital, UK.

*Imaging results changed from normal at baseline to abnormal at 36 months in one subject with a consensus clinical diagnosis at 36 months of possible Parkinson's disease (PD). In another subject, the initial SPECT finding of abnormal at baseline was changed to normal at 36 months with a consensus clinical diagnosis at 36 months of probable PD.

MSA, multiple system atrophy; **NDA,** new drug application; **PS,** parkinsonian syndrome; **PSP,** progressive supranuclear palsy; **SPECT,** single-photon emission computed tomography.

Product Indication and Use: DaTscan™ (Ioflupane I 123 Injection) is a radiopharmaceutical indicated for striatal dopamine transporter visualization using single-photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndromes (PSs). In these patients, DaTscan may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson's disease [PD], multiple system atrophy [MSA], and progressive supranuclear palsy [PSP]). DaTscan is an adjunct to other diagnostic evaluations.

DaTscan was not designed to distinguish among PD, MSA, and PSP. The effectiveness of DaTscan as a screening or confirmatory test and for monitoring disease progression or response to therapy has not been established.

Please see Important Safety Information on back page, and enclosed full Prescribing Information.

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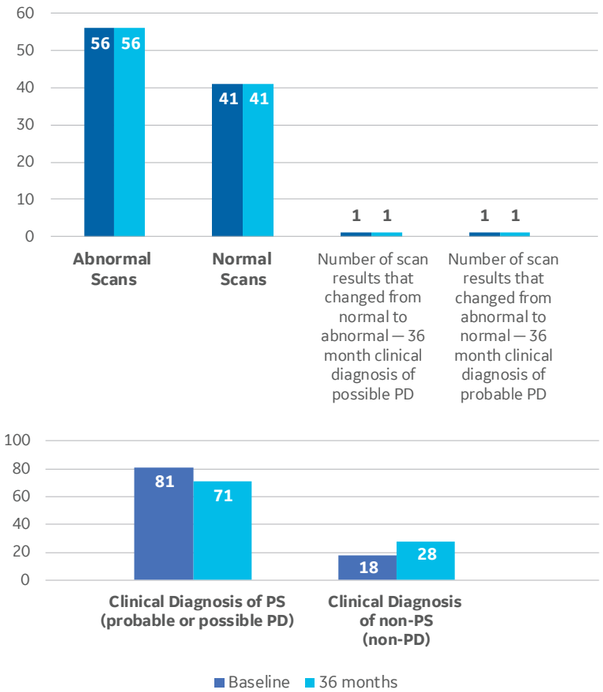
Study 1 (Cont'd)

99 subjects, 30 to 90 years of age with UPDRS scores ≤16, completed both the imaging and consensus clinical diagnosis at 36 months[2]

Images were evaluated by three independent nuclear medicine physicians who were blind to clinical information



Clinical diagnosis was performed by two movement disorder specialists who were blind to SPECT findings and the working site diagnosis

Adapted from Hauser and Grosset, 2011.

- AEs were recorded from the first [^{123}I]FP-CIT administration until the 36-month telephone follow-up with a total of 405 scans performed
- Among the 179 subjects in the safety population, 122 experienced a total of 400 AEs during the 36-month period
  - 376 AEs (94%) were deemed by the investigator to be unrelated to [^{123}I]FP-CIT
  - During the 36-month study period, a total of 4 subjects died and 32 subjects (18%) experienced 71 nonfatal serious AEs (SAEs), none of which were deemed to be related to [^{123}I]FP-CIT
- The most frequently reported AE was headache (15% of subjects)
- Only 24 AEs (6.0%) reported by 13 subjects were considered as having reasonable relationship to [^{123}I]FP-CIT, most of which were mild in intensity (14, 3.5%)
  - Headache (n = 5, 3%)
  - Nausea (n = 3, 2%)
  - Injection-site hematoma, dizziness, and dysgeusia (n = 2, 1%)

AEs, adverse events; **MSA,** multiple system atrophy; **PD,** Parkinson's disease; **PS,** parkinsonian syndrome; **PSP,** progressive supranuclear palsy; **SPECT,** single-photon emission computed tomography; **UPDRS,** Unified Parkinson's Disease Rating Scale.

Study 2 was a trial of DaTscan SPECT in patients with established diagnoses of parkinsonian syndrome (PS) or essential tremor (ET). Subjects' images were evaluated by blinded reading panel of four experienced nuclear medicine physicians and a neurologist with limited experience assessing [^{123}I]FP-CIT, DaTscan (I 123 Ioflupane) SPECT scans. Readers rated the images of each case as normal or abnormal[2]

- Study 2 consisted of 185 patients with established diagnoses of PS or ET
- Clinical diagnoses consisted of:
  - 158 patients with a PS (PD [130], MSA [18], and PSP [10])
  - 27 patients with ET

Positive and negative percent agreements for Study 2[1]

Study 2 (patients with established diagnoses of PS or ET, n = 185)

	Positive percent agreement (95 % CI) (% patients with an abnormal DaTscan image among patients with PS)	Negative percent agreement (95 % CI) (% patients with a normal DaTscan image among patients with non-PS)
	n = 158	n = 27
Reader A	93 (88, 97)	96 (81, 100)
Reader B	97 (93, 99)	74 (54, 89)
Reader C	96 (92, 99)	85 (66, 96)
Reader D	92 (87, 96)	93 (76, 99)
Reader E	94 (90, 97)	93 (76, 99)

The effectiveness of DaTscan as a screening or confirmatory test and for monitoring disease progression or response to therapy has not been established.

- AEs reported in more than 1% of the 189 subjects who underwent [^{123}I]FP-CIT SPECT scan:
  - Headache (n = 15, 7.9%)
  - Flu-like symptoms (n = 4, 2%)
  - Injection-site bleeding (n = 4, 2%)
  - Vertigo (n = 4, 2%)
  - Paresthesia (n = 3, 1.5%)
- Of the 65 AEs reported in 36 subjects, fewer than half (n = 30) were thought to be probably or possibly related to [^{123}I]FP-CIT
- There was one report of a serious AE, consisting of extrapyramidal symptoms that the investigator judged to be unrelated to [^{123}I]FP-CIT

AEs, adverse events; **CI,** confidence interval; **PD,** Parkinson's disease; **SPECT,** single-photon emission computed tomography.

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PRODUCT INDICATION AND USE

DaTscan™ (Ioflupane I 123 Injection) is a radiopharmaceutical indicated for striatal dopamine transporter visualization using single-photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndromes (PSs). In these patients, DaTscan may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson's disease [PD], multiple system atrophy [MSA], and progressive supranuclear palsy [PSP]). DaTscan is an adjunct to other diagnostic evaluations.

DaTscan was not designed to distinguish among PD, MSA, and PSP. The effectiveness of DaTscan as a screening or confirmatory test and for monitoring disease progression or response to therapy has not been established.

Important Safety Information About DaTscan

CONTRAINDICATIONS

- DaTscan is contraindicated in patients with known hypersensitivity to the active substance, any of the excipients, or iodine

WARNINGS AND PRECAUTIONS

- **Hypersensitivity Reactions:** Hypersensitivity reactions, generally consisting of skin erythema and pruritus, have been reported following DaTscan administration
- **Thyroid Accumulation:** The DaTscan injection may contain up to 6% of free iodide (iodine 123 or I-123). To decrease thyroid accumulation of I-123, block the thyroid gland at least one hour before administration of DaTscan; failure to do so may increase the long-term risk for thyroid neoplasia

ADVERSE REACTIONS

- In clinical trials, headache, nausea, vertigo, dry mouth, or dizziness of mild to moderate severity were reported. In postmarketing experience, hypersensitivity reactions and injection-site pain have been reported

DRUG INTERACTIONS

- Drugs that bind to the dopamine transporter with high affinity may interfere with the DaTscan image. The impact of dopamine agonists and antagonists on DaTscan imaging results has not been established

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Radioactive iodine products cross the placenta and can permanently impair fetal thyroid function. Administration of a thyroid blocking agent is recommended before the use of DaTscan in a pregnant woman. All radiopharmaceuticals have potential to cause fetal harm. There are no available data on DaTscan use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Advise pregnant woman of the potential risks of fetal exposure to radiation with the administration of DaTscan
- **Lactation:** Iodine 123 (I 123), the radionuclide in DaTscan, is present in human milk. There is no information on the effects on breastfed infants or on milk. Advise a lactating woman to interrupt breastfeeding and pump and discard breast milk for at least 6 days after DaTscan administration to minimize radiation exposure to a breastfeeding infant
- **Pediatric Use:** The safety and efficacy of DaTscan have not been established in pediatric patients
- **Geriatric Use:** There were no differences in responses between elderly patients and younger patients that would require a dose adjustment
- **Renal and Hepatic Impairment:** The effect of renal or hepatic impairment on DaTscan imaging has not been established. The kidney excretes DaTscan; patients with severe renal impairment may have increased radiation exposure and altered DaTscan images

OVERDOSAGE

- It is unknown whether or not ioflupane is dialyzable. The major risks of overdosage relate to increased radiation exposure and long-term risk for neoplasia. In case of radioactivity overdosage, frequent urination and defecation should be encouraged to minimize radiation exposure to the patient

PROCEDURE — Radiation Safety

- DaTscan emits radiation and must be handled with safety measures to minimize radiation exposure to clinical personnel and patients

Prior to DaTscan administration, please read the enclosed full Prescribing Information for additional Important Safety Information.

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 800 654 0118 (option 2, then option 1) or the FDA at 800 FDA 1088 or www.fda.gov/medwatch.

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References: 1. DaTscan [prescribing information]. Arlington Heights, IL: GE Healthcare; 2020. **2.** Hauser RA, Grosset DG. $^{[123]}$FP-CIT (DaTscan) SPECT brain imaging in patients with suspected parkinsonian syndromes. *J Neuroimaging*. 2012;22:225-230.

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