Inova™

Parkinson's and Movement Disorders Center

2025 Health Care Professionals Conference

Inova Conference Center, 2nd floor
8100 Innovation Park Drive
Fairfax, VA 22037

Friday,
March 21, 2025

Speaker:

Hannah Irving MD

Movement Disorders Specialist

Inova Parkinson’s and Movement Disorders Center (IPMDC)

Disclosures

Nothing to disclose.

What is a Movement Disorders Specialist (MDS)?

Doctor - MDS vs Neurologist vs PCP

- Fellowship training
- An expert general neurologist ≠ a Movement Disorders Specialist

A Great Team!

Inova™ Parkinson's and Movement Disorders Center

Movement Disorders Specialists

Drew Falconer, MD
Medical Director, IPMDC

Sean Rogers, MD, PhD
Medical Director,
Memory Disorders

Kyla Newman
Physician associate

Sonia Gow
Program and
Community
Care Manager

David Whitney, MD

Hannah Irving, MD

Abigail Lawler, MD

Mick Reedy, MD

Jenn Pauldurai, MD
Cognitive and behavioral
neurologist

Inova™

Neurosciences

Parkinson's and Movement Disorders Center (IPMDC)

Alexandria
1500 N. Beauregard St.
#300
Alexandria, VA 22311

Gainesville
7051 Heathcote Village Way
#230
Gainesville, VA 20155

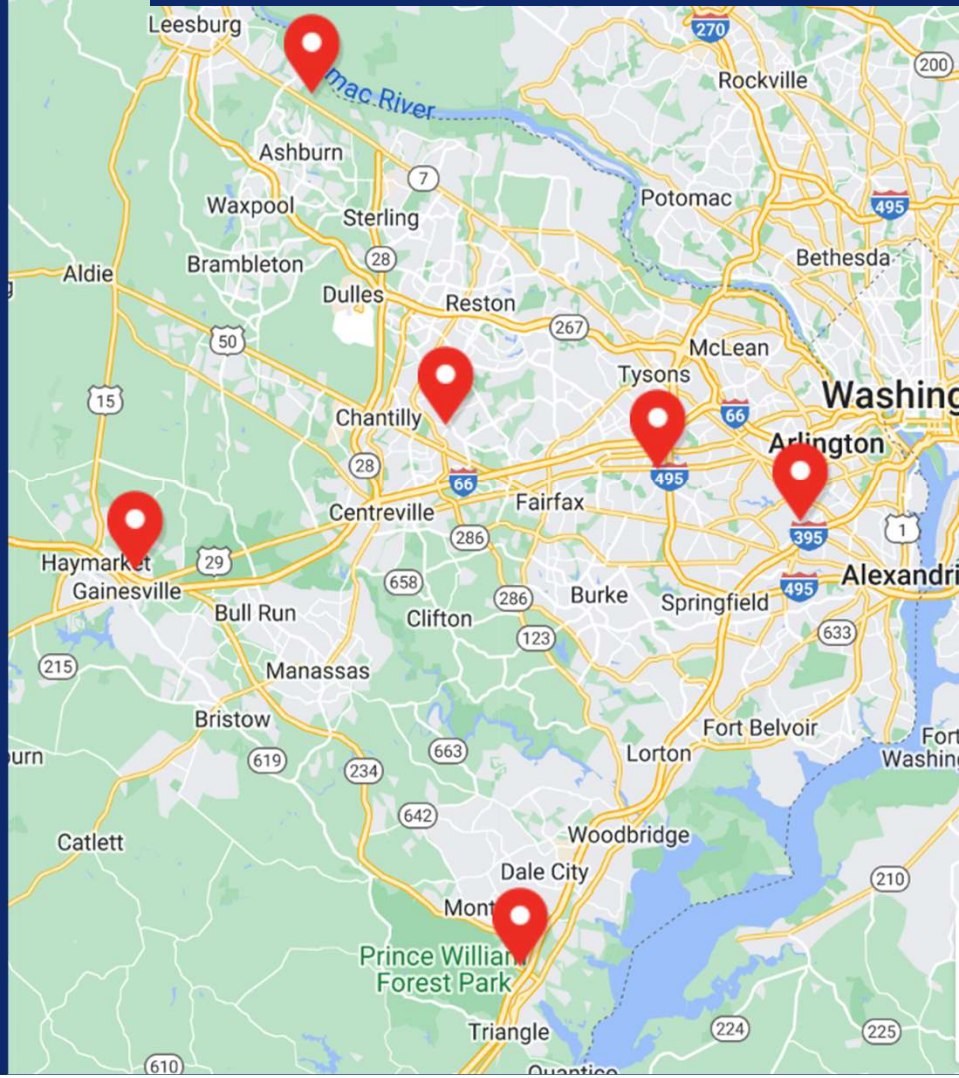
Fairfax
8081 Innovation Park Dr.
#900
Fairfax, VA 22031

Leesburg
44055 Riverside Parkway
#242,
Leesburg, VA 20176

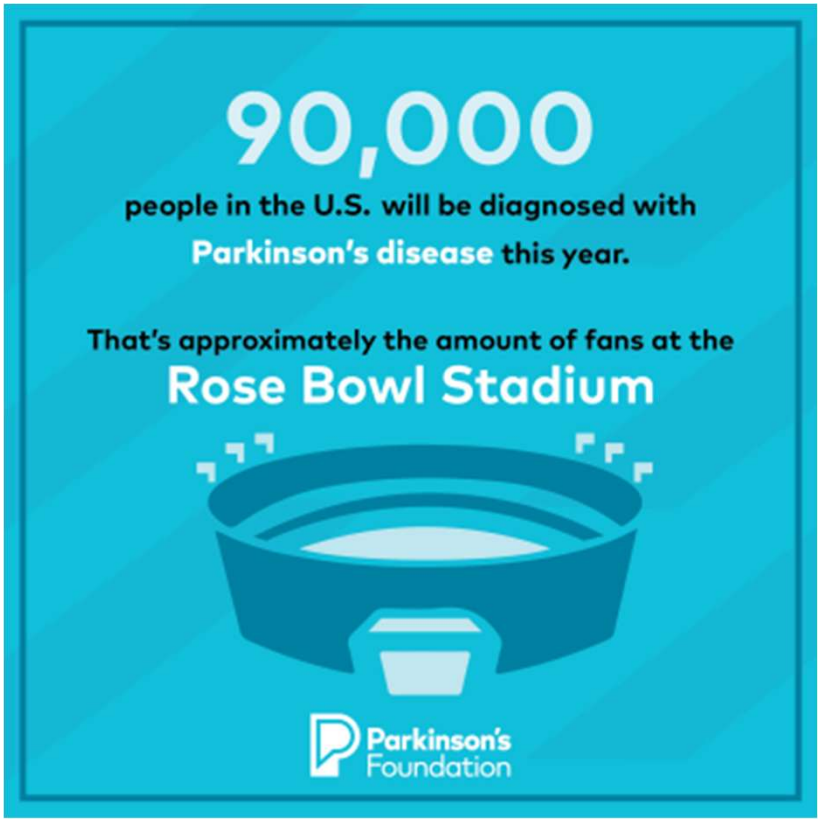
Fair Oaks
3580 Joseph Siewick Dr.
#206
Fairfax, VA 22033

Dumfries
3800 Fettler Park
#312
Dumfries, VA 22025

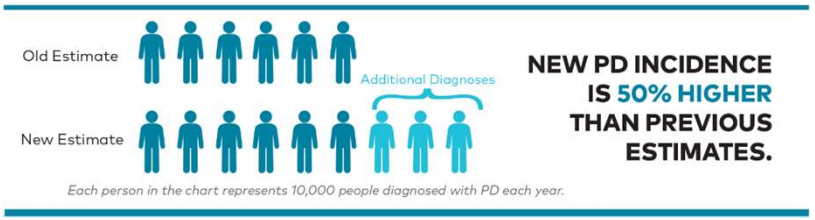
To schedule an appointment please call
571.472.4200

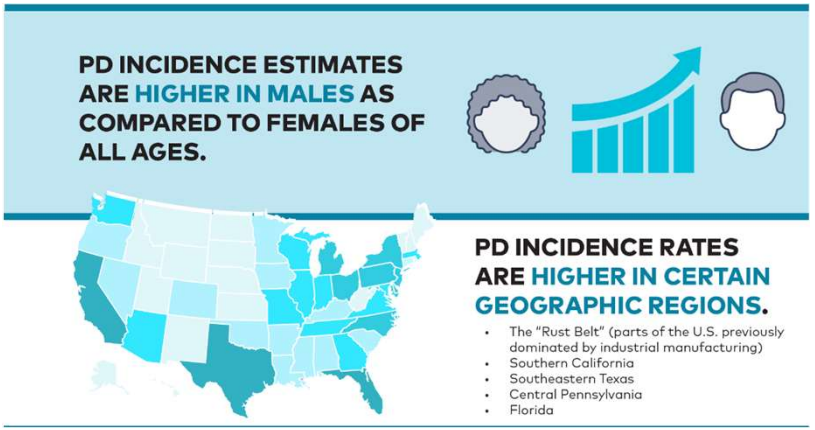


Numbers are going up



Numbers are going up



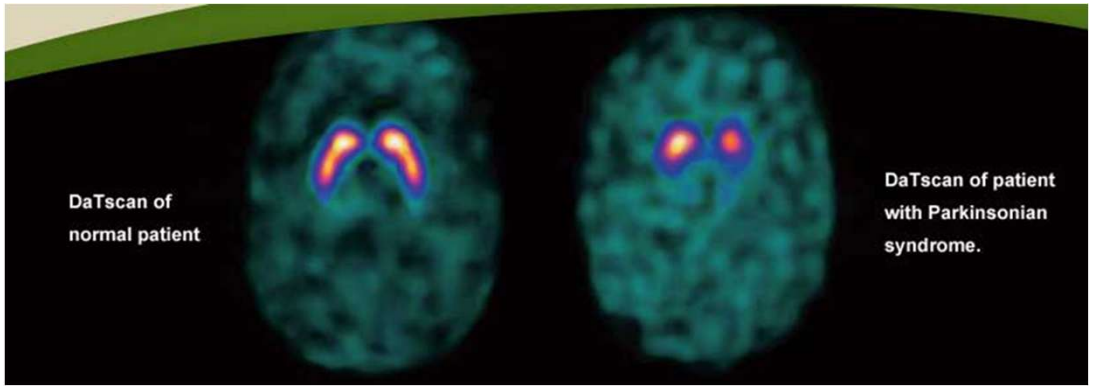


DaTscan

Dopamine Active Transporter

PET scan of brain highlighting dopamine transport system.

FDA approved since 2010, covered by most insurers.



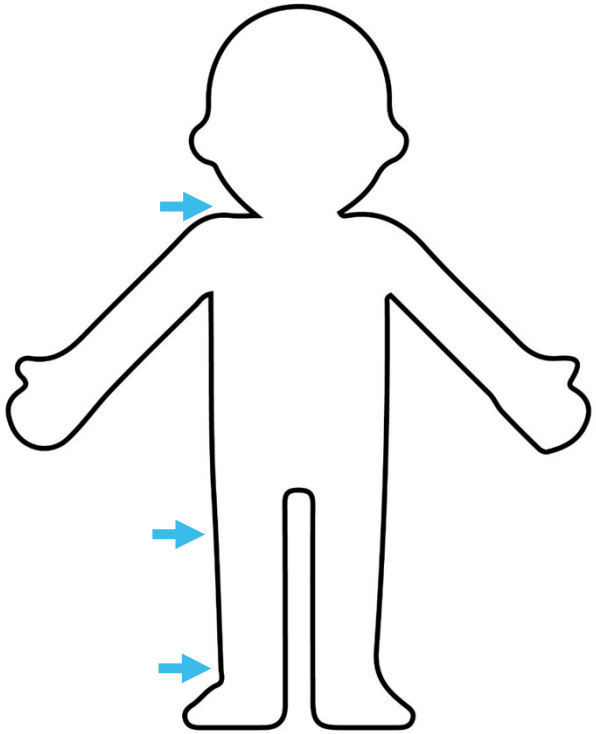
http://www.kernradiology.com/images/DaTscan_07.jpg

Syn-One skin biopsy

Checks for the deposit of phosphorylated alpha-synuclein in the skin

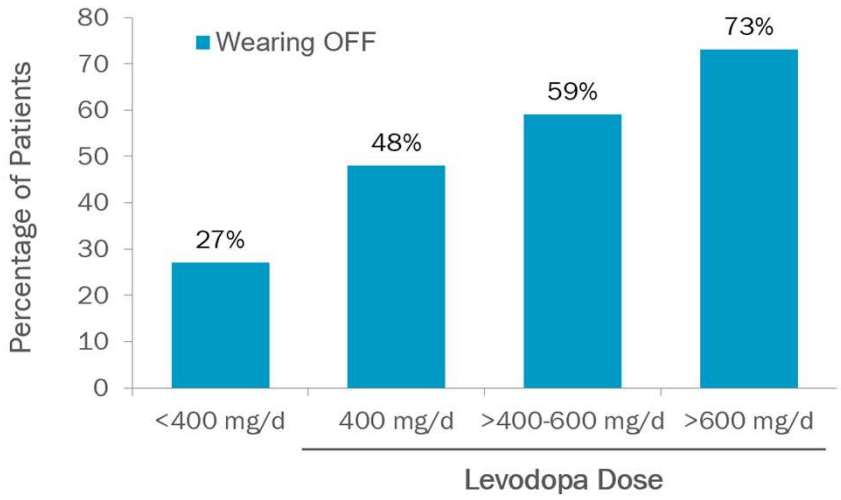
FDA approved to assist with a diagnosis of Parkinsonism.

POTENTIAL DIAGNOSIS	ASSESSMENT	STAIN
Synucleinopathy	Phosphorylated alpha-synuclein	P-SYN
Small fiber neuropathy	Reduced IENFD	Protein Gene Product 9.5 (PGP 9.5)
Amyloidosis	Amyloid deposition	Congo Red
Skin morphology	Dermatologic abnormality	Hematoxylin & Eosin (H&E)



Off time is the enemy

- Prevalence of ~25–50% within a period of 2–6 years of initiating carbidopa/levodopa treatment[1,2]
- In a single-visit pilot study of 151 patients with PD on stable doses of levodopa for ≥4 weeks, 64% reported experiencing motor fluctuations[3]



Online survey of 3,000+

70% reported 2+ Off episodes a day.

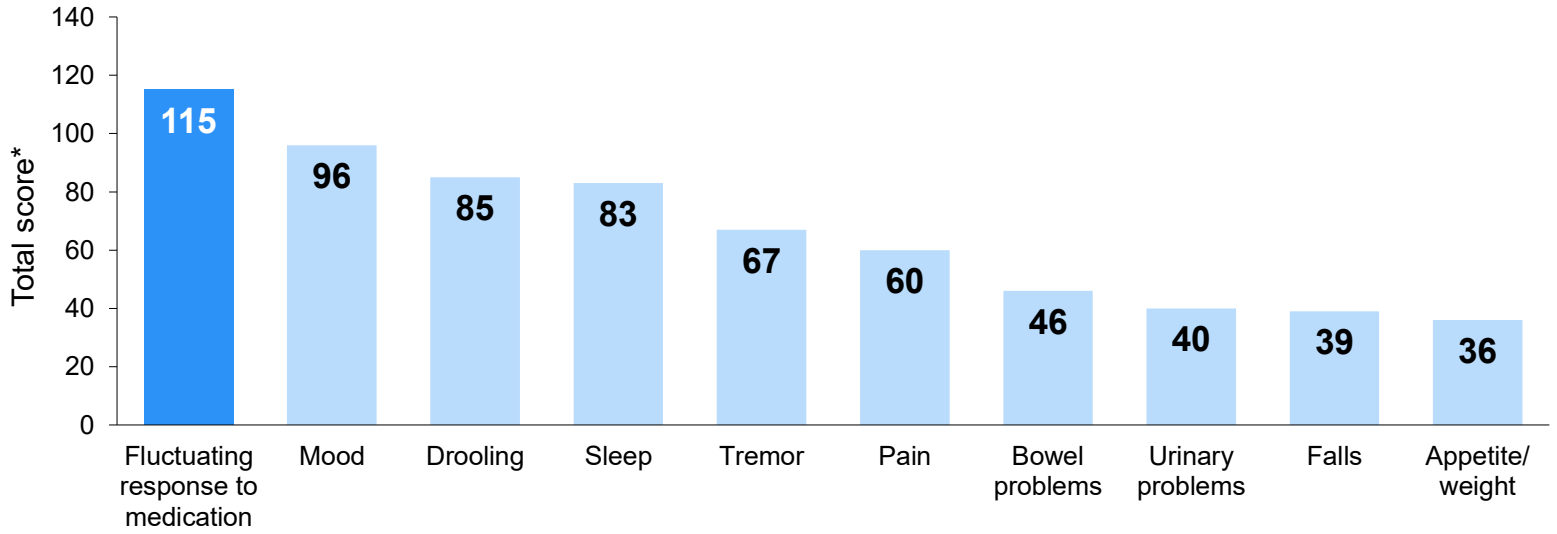
65% reported 2 or more hours a day

50% – moderate/severe, affected daily activities

1.Chou KL, et al. *Parkinsonism Relat Disord*. 2018;51:9-16. **2.** Ahlskog JE, et al. *Mov Disord*. 2001;16:448-458. **3.** Stocchi F, et al. *Eur J Neurol*. 2019;26:821-826.
Mantri S, Lepore M, Edison B, Daeschler M, Kopil CM, Marras C, Chahine LM. The Experience of OFF Periods in Parkinson's Disease: Descriptions, Triggers, and Alleviating Factors. J Patient Cent Res Rev. 2021 Jul 19;8(3):232-238. doi: 10.17294/2330-0698.1836. PMID: 34322575;
Stamford et al. Off-Park Survery Steering Group. J Parkinsons Dis 2015;5(3)533-539.

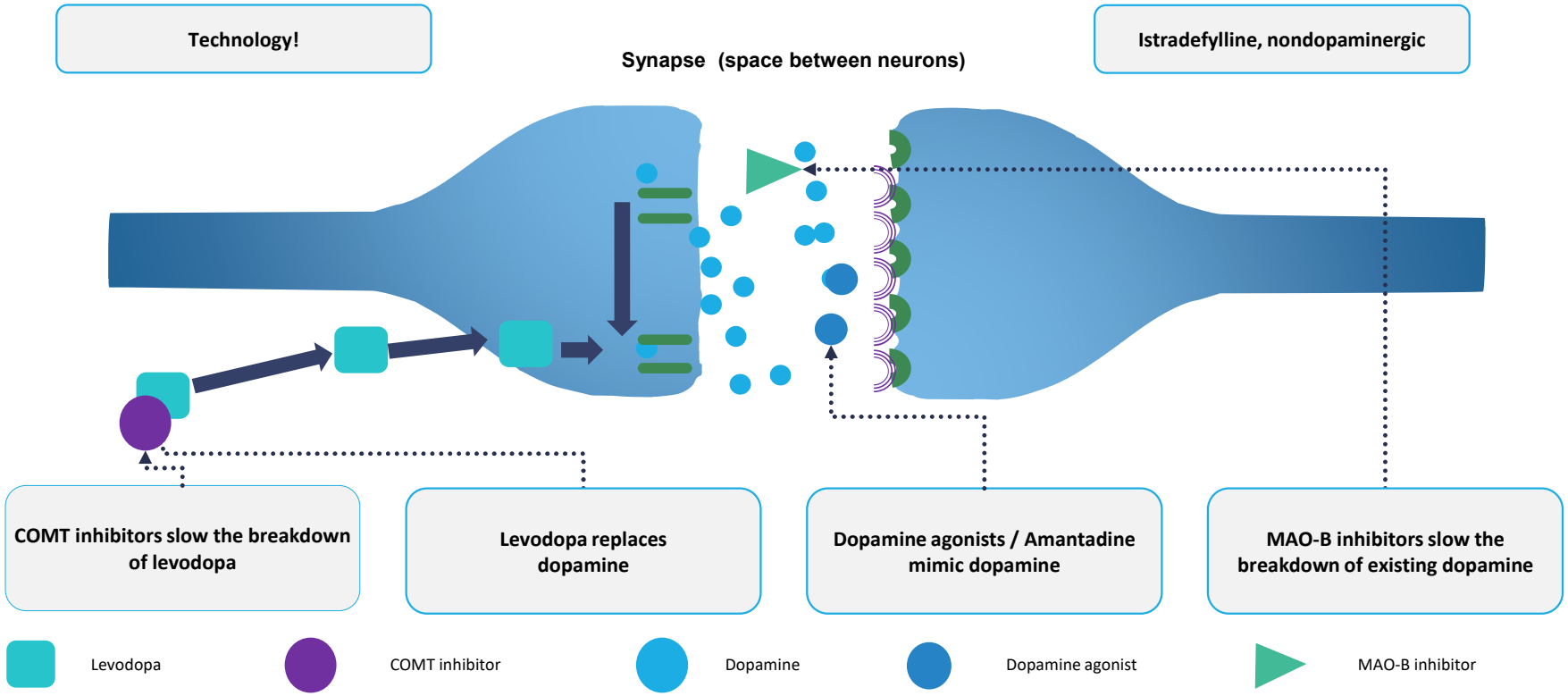
Not just off time, but fluctuations

Ranking of most bothersome PD-related symptoms experienced by patients with more than 6 years disease duration (N=173)



Politis M, et al. *Mov Disord*. 2010; 25(11): 16466-1651

Different avenues of treatment



COMT = catechol-*O*-methyltransferase.
MAO-B = monoamine oxidase-B.

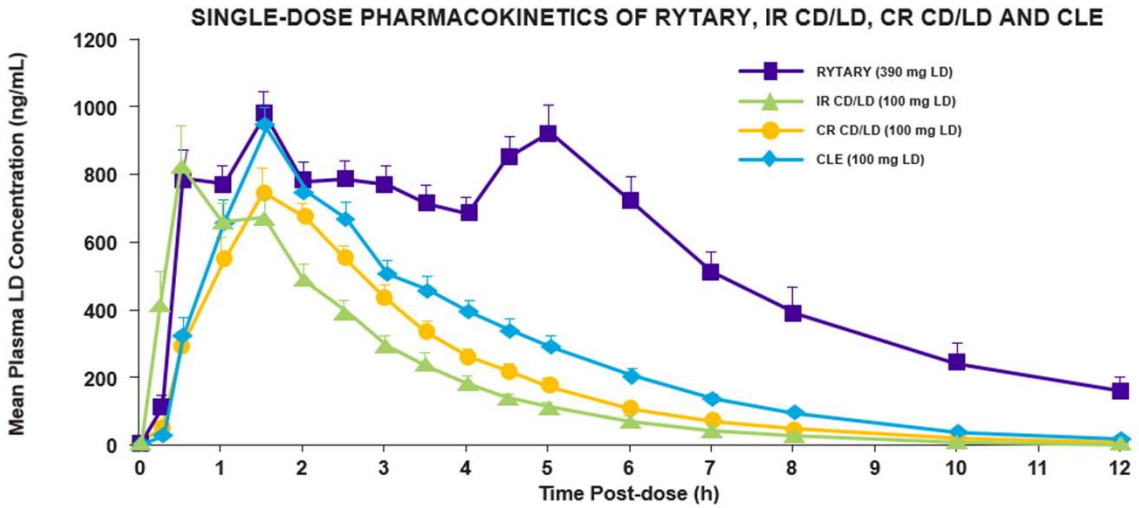
Kalia LV et al. *Lancet.* 2015;386:896–912

Longer lasting carbidopa/levodopa 2015

Rytary™ (carbidopa/levodopa)

RYTARY®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
23.75 mg/95 mg • 36.25 mg/145 mg
48.75 mg/195 mg • 61.25 mg/245 mg

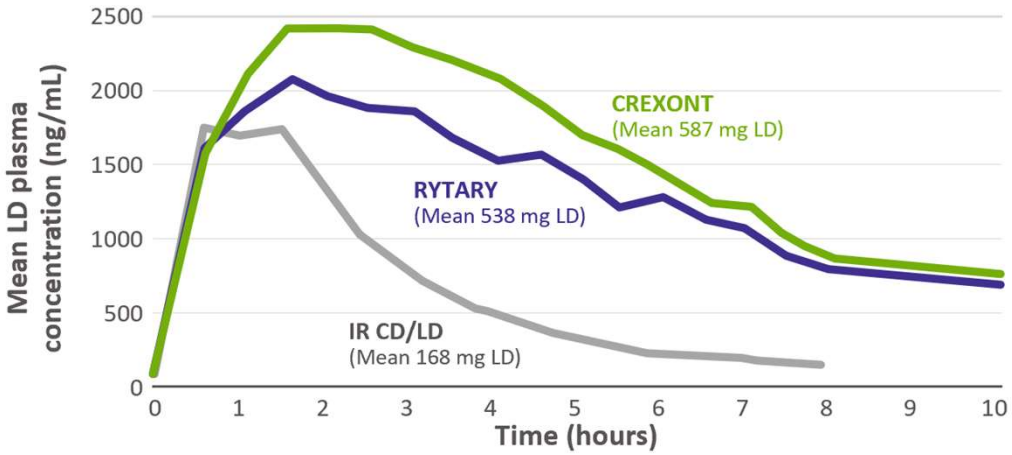
- History of evolution of levodopa delivery -------->
- Equivalent dose of Rytary on average 1.2 more hours of "on time" compared to IR.



Longer lasting carbidopa/levodopa 2024

Crexont ™ (carbidopa/levodopa)

- Capsule/bead formula.
- Adhesive polymer.
- 4.8 hrs above 50% Cmax, 3x daily (avg)
- 1.6 hr longer on time per dose (avg)

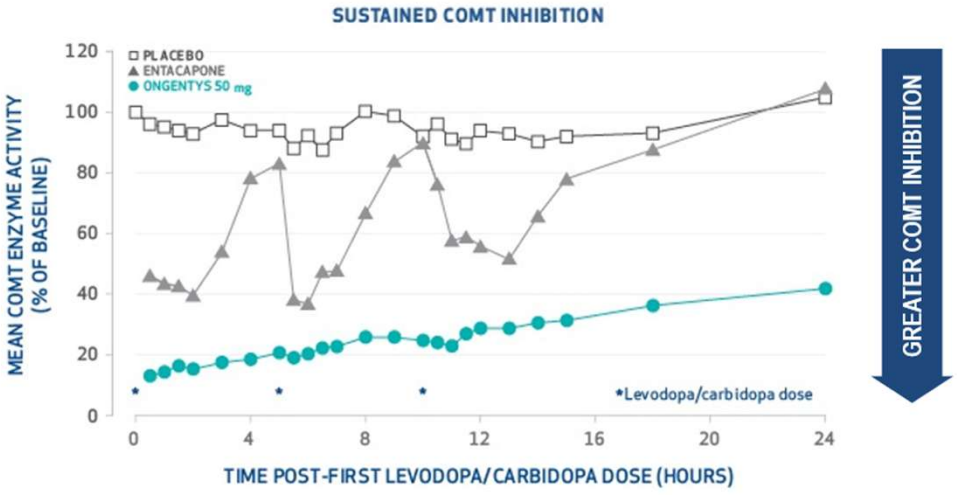


1. Hauser RA et al. *JAMA Neurol.* 2023;80(10):1062-1069.

Maximizing levodopa

Ongentys™ (opicapone)

- 1x daily peripheral COMT inhibitor
- Significant boost in levodopa availability.
- 1.95 improvement in off time, Δ1.01hr

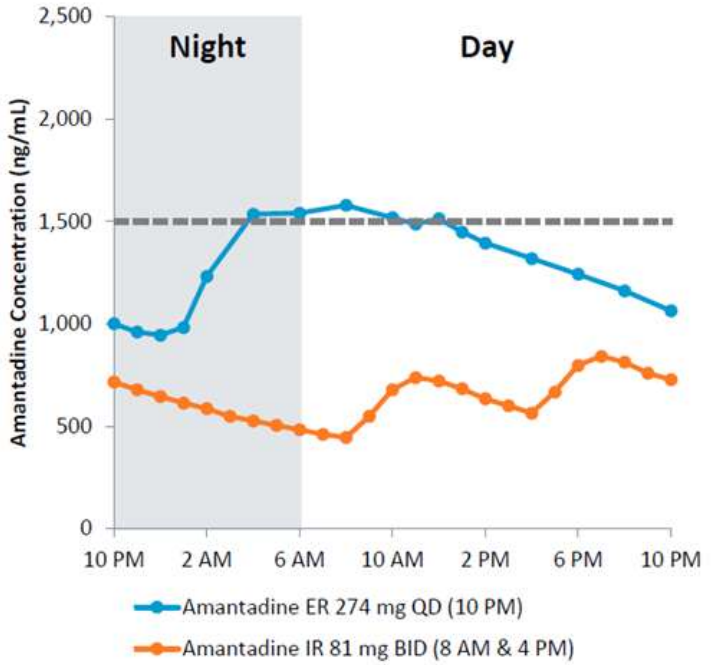


Amantadine, off time + dyskinesia control

GOCOVRI® (amantadine) extended release capsules

Gocovri™ (amantadine ER)
Supernus

- 1x daily delayed release, extended release.
- Dyskinesia AND Off Time
- 41% reduction in dyskinesia, 21% reduction in off time (avg) – 45% more good ON time daily.



Non-dopaminergic approach

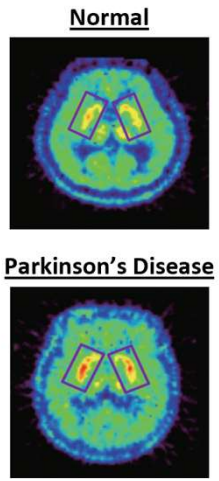
Nourianz™ (istradefylline)

NOURIANZ™ (istradefylline) tablets 20 mg | 40 mg

Indicated as adjunctive treatment to levodopa in adult patients with Parkinson's disease (PD) experiencing wearing off phenomena.

- Indirect pathway – adenosine A2a receptor antagonist
- Addition reduced levodopa dose escalation over 37 weeks[1] and 72 months[2]
- Effective in tremor dominant and postural instability and gait difficulty subtypes (*post hoc*)[3].

A_{2a} Receptor PET imaging[1]



Increase in A_{2a} Receptors with PD progression[1]

1.Hatano T et al. Impact of Istradefylline on Levodopa Dose Escalation in Parkinson's Disease: ISTRA ADJUST PD Study, a Multicenter, Open-Label, Randomized, Parallel-Group Controlled Study. Neurol Ther. 2024 Apr;13(2):323-338.
2.Hattori N et al. Real-world evidence on levodopa dose escalation in patients with Parkinson's disease treated with istradefylline. PLoS One. 2023 Dec 22;18(12):e0269969
3.Torres-Yaghi et al. Istradefylline effects on tremor dominance (TD) and postural instability and gait difficulty (PIGD). Clin Park Relat Disord. 2023 Oct 14;9:100224.

Rescue option #1 - Apokyn

Apokyn™ (apomorphine injection)

Supernus

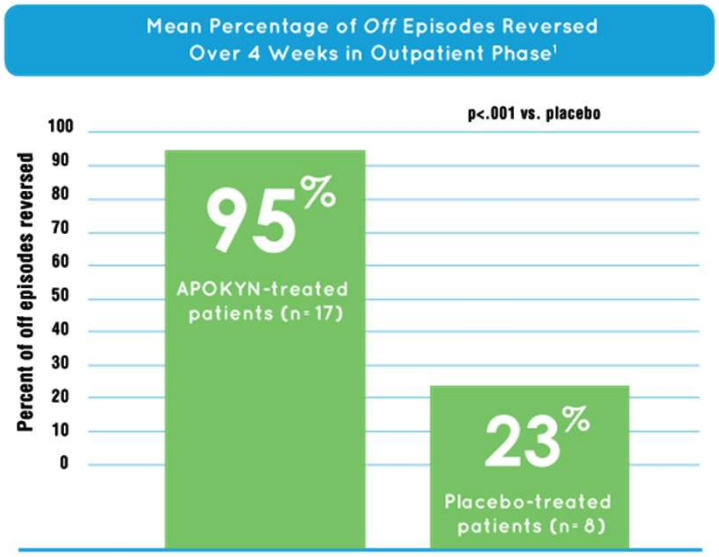
Rapid onset Dopamine Agonist via injection

For different types of OFF episodes:

- Rapid off, wearing off
- Dose failure / unexpected off
- Delayed on
- First AM symptoms or exercise intolerance

Achieve ON within 10-20 minutes

APOKYN® apomorphine hydrochloride injection Be on. Live life.



Rescue option #2 - Inbrija

Inbrija™ (levodopa inhalation powder)

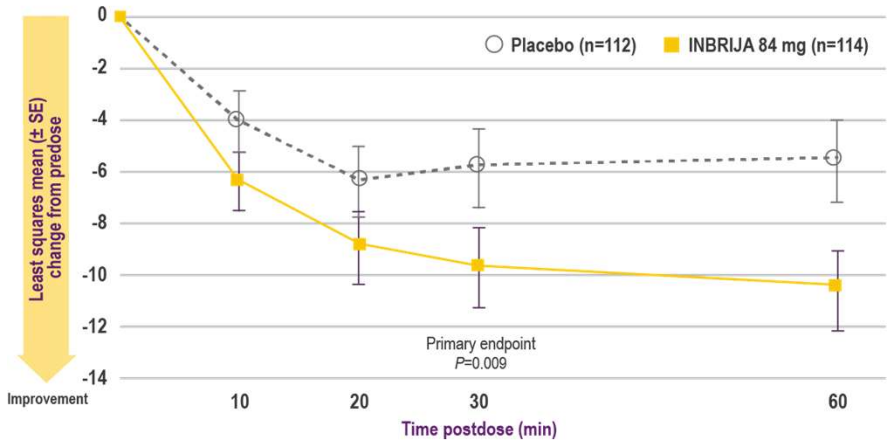
Rapid onset levodopa through inhaler

For different types of OFF episodes:

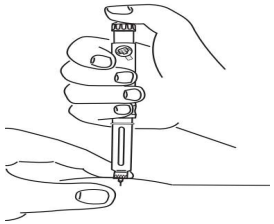
- Rapid off, wearing off
- Dose failure / unexpected off
- Delayed on
- First AM symptoms or exercise intolerance

Achieve ON within 10 minutes, can take up to 5x daily

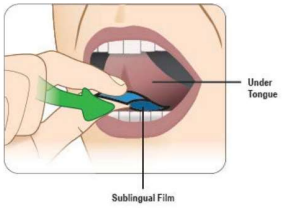
UPDRS Part III Score Change From 0-60 Minutes Postdose at Week 12

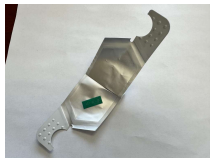


As needed / on demand

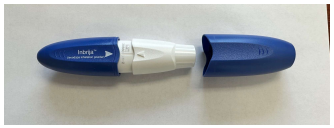


20 minutes post-dose: –23.9 vs –0.1 (*P*<0.001)[1]





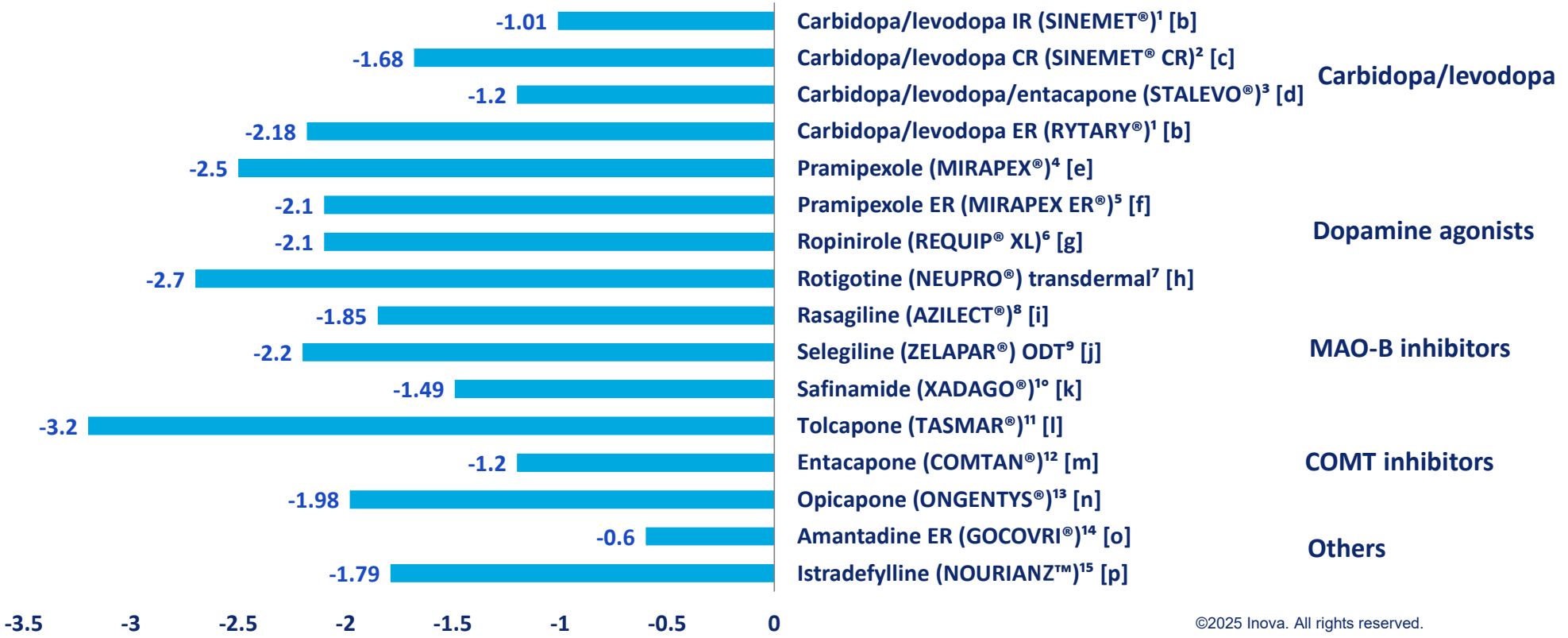
30 minutes post-dose: –11.1 vs –3.5 (*P*=0.0002)[2]



30 minutes post-dose: –9.8 vs –5.9 (*P*=0.0088)[3]

1. Dewey RB, Hutton JT, LeWitt PA, Factor SA. A randomized, double-blind, placebo-controlled trial of subcutaneously injected apomorphine for parkinsonian off-state events. Arch Neurol. 2001;58(9):1385–1392. **2.** Olanow CW, et al. Lancet Neurol. 2020;19:135-144.
3. LeWitt PA et al; SPAN-PD Study Investigators. Safety and efficacy of CVT-301 (levodopa inhalation powder) on motor function during off periods in patients with Parkinson's disease: a randomized, double-blind, placebo-controlled phase 3 trial. Lancet Neurol. 2019 Feb;18(2):145-154. doi: 10.1016/S1474-4422(18)30405-8.

Summary of OFF time reduction



Isaacson SH, Pagan FL, Lew MF, Pahwa R. Should "on-demand" treatments for Parkinson's disease OFF episodes be used earlier? Clin Park Relat Disord. 2022 Aug 12;7:100161. doi: 10.1016/j.prdoa.2022.100161. PMID: 36033905

Technology – Foslevodopa Pump

Vyalev™ (foscarbidopa/foslevodopa)
Abbvie

- 24 hour subq foslevodopa pump
- 2.72 hr increased ON time
- 83% waking in the ON state, reduced sleep disturbance (36%)
- Replaces oral levodopa
- Currently available non-Medicare – Medicare later this year.

Pahwa R, Soileau MJ, Standaert DG, et al. Rapid onset of good ON-time and improvement in motor-state stability in aPD patients after treatment with continuous subcutaneous foslevodopa/foscarbidopa. Poster presented at: The International Congress of Parkinson's Disease and Movement Disorders (MDS); September 15-18, 2022; Madrid, Spain.

Hauser RA, Bergmans B, Malaty I, et al. Effects of continuous subcutaneous infusion of foslevodopa/foscarbidopa on sleep dysfunction in people with Parkinson's. Poster presented at: The American Academy of Neurology 76th Annual Meeting (AAN); April 13-18, 2024; Denver, CO

Technology – Apomorphine Pump

Onapgo™ (apomorphine infusion)
Supernus

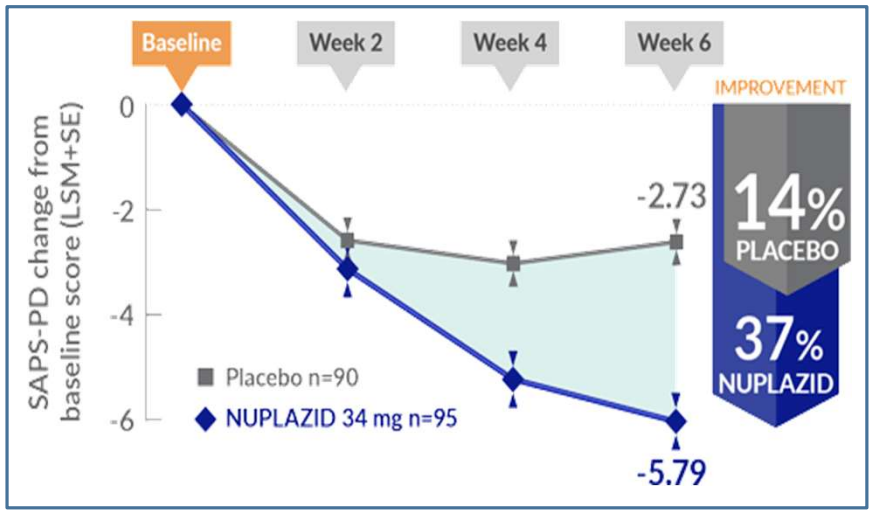
- Add on subq pump during waking hours
- 2.8+ hr increased ON time
- Added in addition to foundational oral therapies
- Coming April/May 2025

Hallucinations and Psychosis

Nuplazid™ (Pimavanserin)
Acadia

NUPLAZID™
(pimavanserin) tablets

- First antipsychotic medication specifically designed for hallucinations and 'psychosis' associated with Parkinson's Dementia and Lewy Body Dementia.
- Serotonin Agonist with no impact on dopamine receptors
- + SAPS-PD improvement with no change in UPDRS
- More effective when prescribed sooner, when hallucinations are beginning.



Hacksell, Uli et al. "On the Discovery and Development of Pimavanserin: A Novel Drug Candidate for Parkinson's Psychosis." *Neurochemical Research*39.10 (2014): 2008–2017. *PMC*. Web. 4 June 2015.

Inova™

CREXONT® (carbidopa and levodopa) EXTENDED-RELEASE CAPSULES 35mg/140mg · 52.5mg/210mg 70mg/280mg · 87.5mg/350mg

RYTARY® (carbidopa and levodopa) EXTENDED-RELEASE CAPSULES

New toolbox and growing

Dhivy™ (carbidopa/levodopa)

VYALEV™ 240 mg/mL+12 mg/mL solution for infusion fosLevodopa/fosCarbidopa

ONAPGO™ (apomorphine HCl) injection, for subcutaneous use • 4.9 mg/mL

APOKYN® Be on. Live life. apomorphine hydrochloride injection

Inbrija™ (levodopa inhalation powder) 42 mg capsules

Ongentys® (opicapone) capsules

Parkinson's and Movement Disorders Center

GOCOVRI® (amantadine) extended release capsules

Dopamine Agonist

Carbidopa/Levodopa formulation

MAOB inhibitor

NOURIANZ™ (istradefylline) tablets 20 mg | 40 mg

COMT inhibitor

Neupro® (Rotigotine Transdermal System)

NUPLAZID™ (pimavanserin) tablets

A2a agonists

Amantadine derivatives

NUEDEXTA® (dextromethorphan HBr and quinidine sulfate) capsules 20 mg 10 mg

Rescue Therapies

Symptom specific therapies

Mirapex® pramipexole dihydrochloride

XADAGO® (safinamide) tablets

Osmolex ER™ (amantadine) Extended-release Tablets

AZILECT® Once-Daily (rasagiline tablets)

Stalevo® (levodopa, carbidopa and entacapone) tablets

Northera™ (droxidopa) Capsules 100 mg • 200 mg • 300 mg

REQUIP® ropinirole HCl

PARCOPA® (carbidopa and levodopa orally disintegrating tablets)

COMTan® (entacapone) tablets

Timing of Medications

- Very little flexibility in scheduling.
- 4 hours means 4 hours apart.
- Look for lower limit of the window (i.e., No closer than 4 hours apart)

- Timing of protein and meals with meds
- Space tube feedings away from meds

Contraindicated medications

Additional information at: www.ipmdc.org/hospital

AVOID:

- **haloperidol (Haldol™)** and most neuroleptics
- prochlorperazine (Compazine), metoclopramide (Reglan), promethazine (Phenergan) droperidol (Inapsine)
- Selective MAO B inhibitors, such as rasagiline (Azilect), selegiline (l-deprenyl, Eldepryl), and selegiline HCL oral disintegrating (Zelapar) are contraindicated with commonly prescribed medications such as meperidine (Demerol) and tramadol (Rybix, Ryzolt, Ultram)

CONSIDERED SAFE:

- pimavanserin (Nuplazid)
  quetiapine (Seroquel)
  clozapine (Clozaril)
- trimethobenzamide (Tigan)
  ondansetron (Zofran)
- To avoid potential interactions, it may be appropriate to hold the MAO B inhibitor for 2 weeks prior to surgery and resume when pain is under control. If surgery is imminent, please use alternative medications for pain and check with the pharmacy or our neurologists for other potential drug interactions.

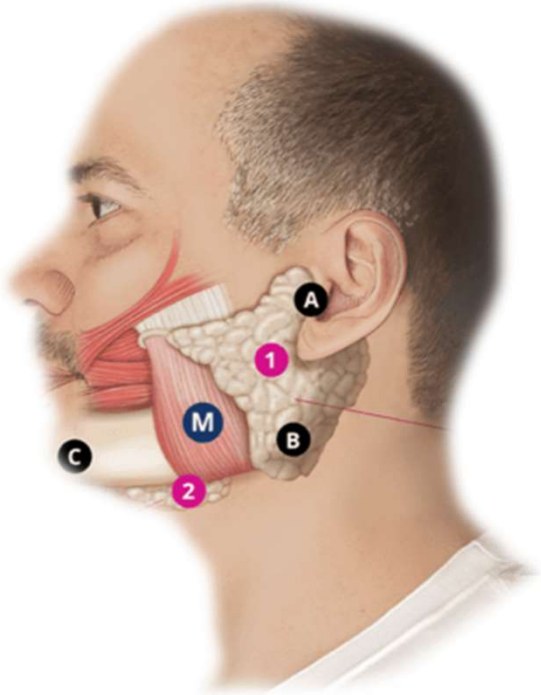
Botulinum Toxin for Chronic Drooling (Sialorrhea)

Botox ® - Abbvie

BOTOX® onabotulinumtoxinA injection

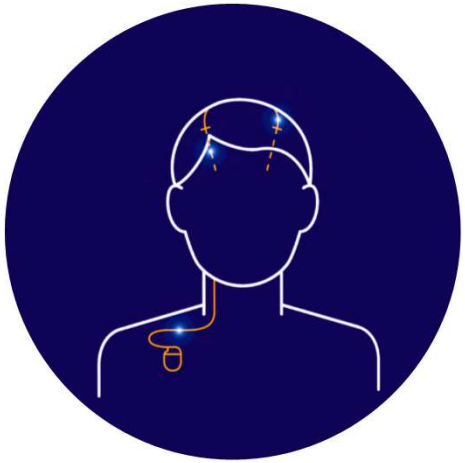
Xeomin® - Merz

XEOMIN® incobotulinumtoxinA



Technology – Deep Brain Stimulation

Three companies, different perks



- Recent onset motor complications – 2+ more ON time
- Longer term motor complications – 5+ more ON time
- Significant quality of life improvement and medication reduction

1.Schuepbach WMM, Rau J, Knudsen K, et al: Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. February 14, 2013;368:610-22 7.
2. Weaver FM, Follett K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson disease: a randomized controlled trial. JAMA. 2009;301(1):63-73.

DBS Indications

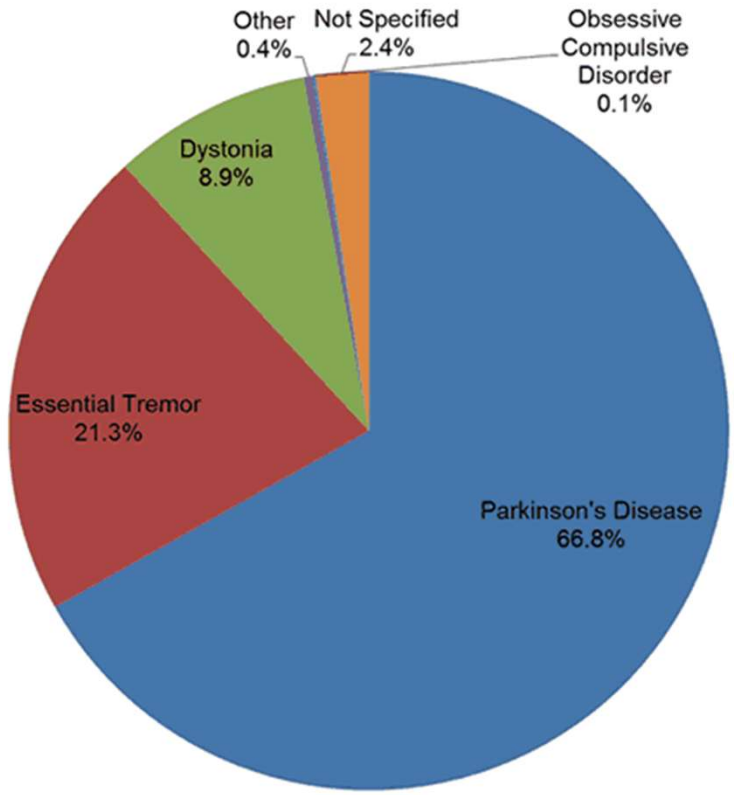
FDA indicated for:

- Parkinson's Disease
- Essential Tremor
- Dystonia

FDA approval:

- Essential tremor - 1997
- Parkinson's disease - 2002
- Dystonia - 2003

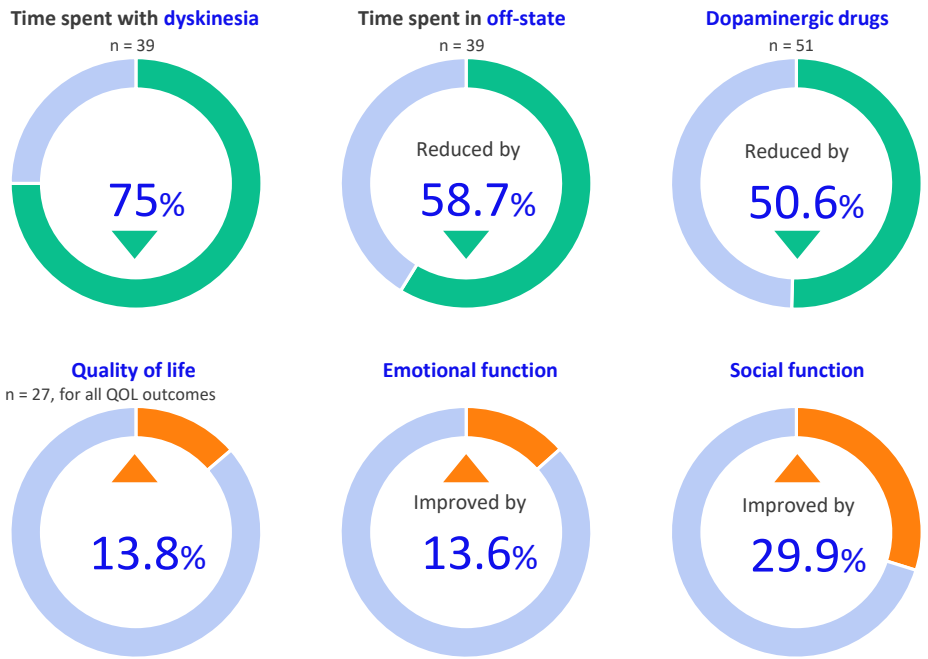
Covered by all insurance providers.



Implantable Systems Performance Registry (ISPR) for deep brain stimulation systems. July 2009 -July 31, 2013.

Long term effects of deep brain stimulation in PD

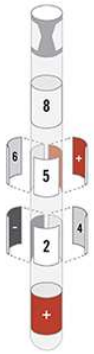
- 15 years and beyond after surgery:



Bove F, Mulas D, Cavallieri F, et al. Long-term Outcomes (15 Years) After Subthalamic Nucleus Deep Brain Stimulation in Patients With Parkinson Disease. Neurology. 2021 Jun 2:10.

An expanding field – pick your fit

- Directional stimulation.
- Remote programming.
- Improved technology and wireless.
- Smaller technology, thinner.
- Longer battery life and rechargeable systems.
- Variety of rechargeable systems.



Technology – Focused Ultrasound

Nonsurgical Lesioning – sustained efficacy?

- Only for tremor
- Outcomes over 16 months:
  - Immediate tremor improvement – 96%
  - Sustained improvement 63%
  - Complete tremor recurrence – 17%

1. Maragkos GA, Kosyakovsky J, Zhao P, Kearns KN, Rush-Evans S, Moosa S, Elias WJ. Patient-Reported Outcomes After Focused Ultrasound Thalamotomy for Tremor-Predominant Parkinson's Disease. Neurosurgery. 2023 Oct 1;93(4):884-891.

To the future!

Nonsurgical Lesioning

- New inhibitors, oral therapies
- Pump-based and sub-cutaneous formulations
- Improved technology
- Targeted protein therapy
- Cure

Inova™ Parkinson's and Movement Disorders Center

Contact Us!

To schedule an appointment please call **571.472.4200**

Sonia Gow
Program and Community Care Manager
Inova Parkinson's & Movement Disorders Center
Sonia.Gow@inova.org | (703) 375-9987

www.inova.org/move - clinical

www.ipmdc.org – programs and resources

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