



## Early Parkinson's Disease Trials

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# Agenda

- Commonly used PD medications & How They Work
- Surgical Treatments
- What is your role in management of PD? Diet and Exercise
- What's new in Surgical and Treatment for PD?
- Research as an Option

# Introduction

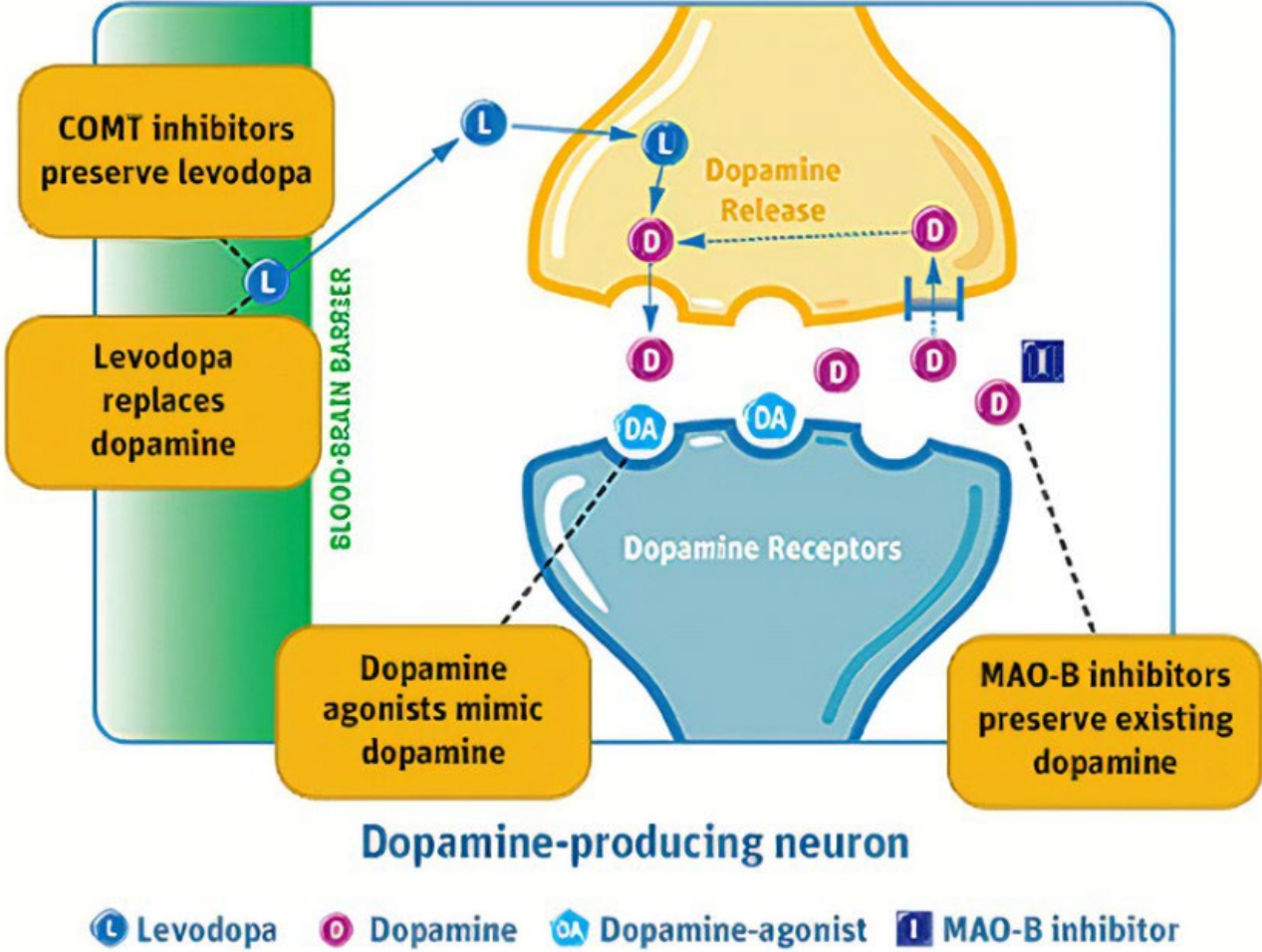
Around the world, more than 6 million people live with Parkinson's

Monitored based on motor symptoms

Urinary symptoms often go unreported as they are not motor

<b>Motor symptoms of PD</b>	<b>Non-motor symptoms</b>
Resting tremor	Constipation
Rigidity	Autonomic dysfunction
Bradykinesia	Impaired olfaction
Postural instability	Dementia
Festinating gait	Depression
Micrographia	Sleep disorders
Masked facies	Impulse control disorders
Retropulsion	Psychosis
Hypophonic speech	

# How PD Medications Work



# Oral Treatment of Motor Symptoms

## Several Researched at EvergreenHealth

- Carbidopa/Levodopa
    - Immediate Release (Sinemet)
    - Extended Release (Sinemet CR)
    - Rytary (IR + ER)
    - Intestinal Gel (Duopa)
  - Dopamine Agonists
    - Pramipexole (Mirapex)
    - Ropinirole (Requip)
    - Rotigotine (Neupro patch)
    - Apomorphine (Apokyn injection),  
Apomorphine (Kynmobi, Sublingual film)
  - MAO-B inhibitors
    - Selegiline (Eldepryl)
    - Rasagiline (Azilect)
    - Safinamide (Xadago)
  - COMT inhibitors
    - Entacapone (Comtan)
    - C/L/Entacapone (Stalevo)
    - Tolcapone (Tasmar)
    - Opicapone (Ongentys)
- ### Amantadine
- Amantadine
  - Amantadine ER (Gocovri)
  - Adenosine A2 Antagonist
    - Nourianz

## Recently approved drug: Sublingual Apomorphine, a novel dopamine agonist

- Fast-acting ,on- demand treatment of 'OFF' episodes.
- Treats acute, intermittent 'OFF' episodes
- Half life≈ 3 h, store 20-25C
- Side effects: N/V, Sleepiness, Dizziness, mouth sores, falls, hallucinations, compulsive behavior, fever, priapism
- 10mg , 15mg, 20mg,25mg, 30mg SubL film ,2 hrs apart, up to 5 times a day.
- Must be whole! 'Do not's: Cut, chew, swallow
- Drug interaction: 5HT3 antagonist, can cause low BP and black outs.



# Opicapone, highly selective COMT inhibitor

- Adjunctive treatment to Levodopa/Carbidopa to treat 'OFF' episodes
- Half-life  $\approx$ 3.2 hrs.,
- 50mg hard capsules, once daily at bedtime,
- 'Do not's : Don't eat 1 hour before and after.
- Contraindication: Drug interaction with Non-selective MAOI, Pheochromocytoma
- Side effects: Somnolence, syncope/hypotension, dyskinesia, hallucinations, compulsive DO, hyperpyrexia
- Serious AEs: Dyskinesia, high Creatinine levels, etc.

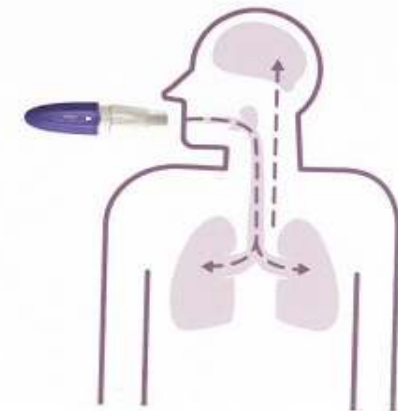
# INBRIJA: Levodopa Inhalation Powder (ACORDA)

- The U.S. Food and Drug Administration has approved a new treatment for intermittent treatment of “off” periods in people with Parkinson’s disease treated with carbidopa/levodopa.
- FDA approved December 27, 2018
- Trade name: Inbrija®
- Rescue therapy for OFF periods
- 1 dose= 2 caps= 84 mg total
- Maximum 1 dose/OFF period up to 5 doses/day
- SE: cough, URI, nausea, sputum discoloration, dyskinesia
- Lewitt et al. *Mov Disord* '16



## The Pulmonary Route

INBRIJA offers systemic delivery via the pulmonary route. Pulmonary absorption bypasses GI challenges that can contribute to variable absorption of levodopa and the occurrence of OFF periods.<sup>1,2</sup>

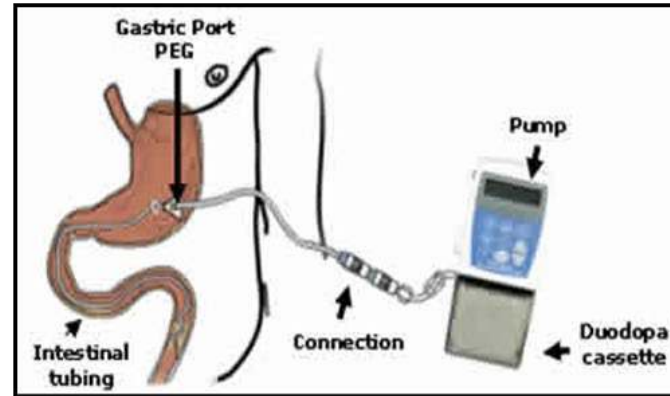


# Recently Approved Drug: Duopa

LCIG is delivered to the upper intestine by a catheter inserted via percutaneous endoscopic gastrostomy - with jejunal extension tube (PEG-J) for long-term treatment.

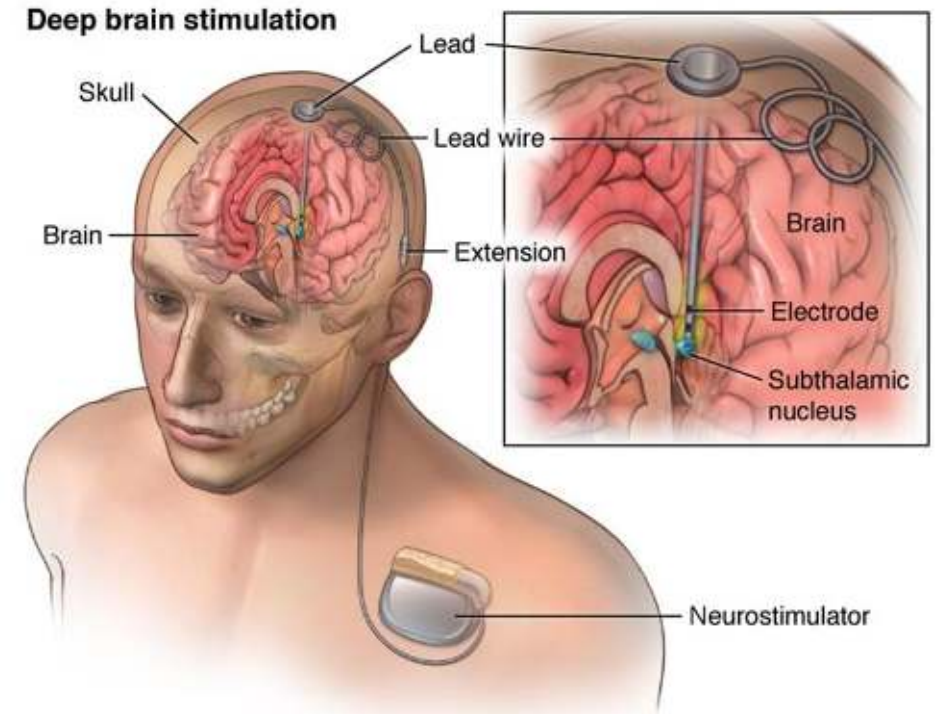
The levodopa-carbidopa intestinal gel infusion system consists of a suspension which is dispensed in medication cassette reservoirs designed to be connected to a portable pump.

The contents of the medication cassette reservoir are delivered over a 16-hour period, administered as one morning bolus dose, continuous hourly infusions and intermittent extra bolus doses when needed (maximum of 5 boluses per day).



# Deep Brain Stimulation

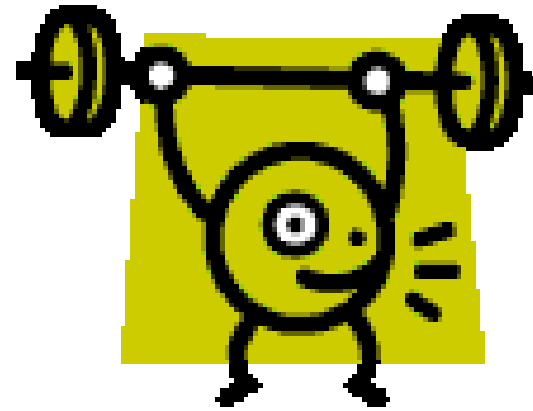
- DBS is an effective treatment for the motor symptoms in PD.
- One study reported less nighttime urination in patients who had DBS.
- Other studies reported DBS had no significant effect on urinary symptoms.
- Larger studies are needed to indicate improvements in patients with PD and urologic quality of life.
- Upcoming Trial: Vercise Observational



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# Approach to PD

- Find a team you trust
  - Neurologist, Nurse, Physical/Occupational/Speech Therapists, Psychologist
- Education
- EXERCISE
- Gratitude
- Participate in Research



# Diet recommendations

## HEALTHY EATING PLATE

**HEALTHY OILS**

Use healthy oils (like olive and canola oil) for cooking, on salad, and at the table. Limit butter. Avoid trans fat.

**WATER**

Drink water, tea, or coffee (with little or no sugar). Limit milk/dairy (1-2 servings/day) and juice (1 small glass/day). Avoid sugary drinks.

**VEGETABLES**

The more veggies – and the greater the variety – the better. Potatoes and French fries don't count.

**WHOLE GRAINS**

Eat a variety of whole grains (like whole-wheat bread, whole-grain pasta, and brown rice). Limit refined grains (like white rice and white bread).

**FRUITS**

Eat plenty of fruits of all colors.

**HEALTHY PROTEIN**

Choose fish, poultry, beans, and nuts; limit red meat and cheese; avoid bacon, cold cuts, and other processed meats.

**STAY ACTIVE!**

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The Nutrition Source  
[www.hsph.harvard.edu/nutritionsource](http://www.hsph.harvard.edu/nutritionsource)

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# Approach to PD



## Find a team you trust

Neurologist, Nurse,  
Physical/Occupational/Speech  
Therapists, Psychologist



## Education



## EXERCISE



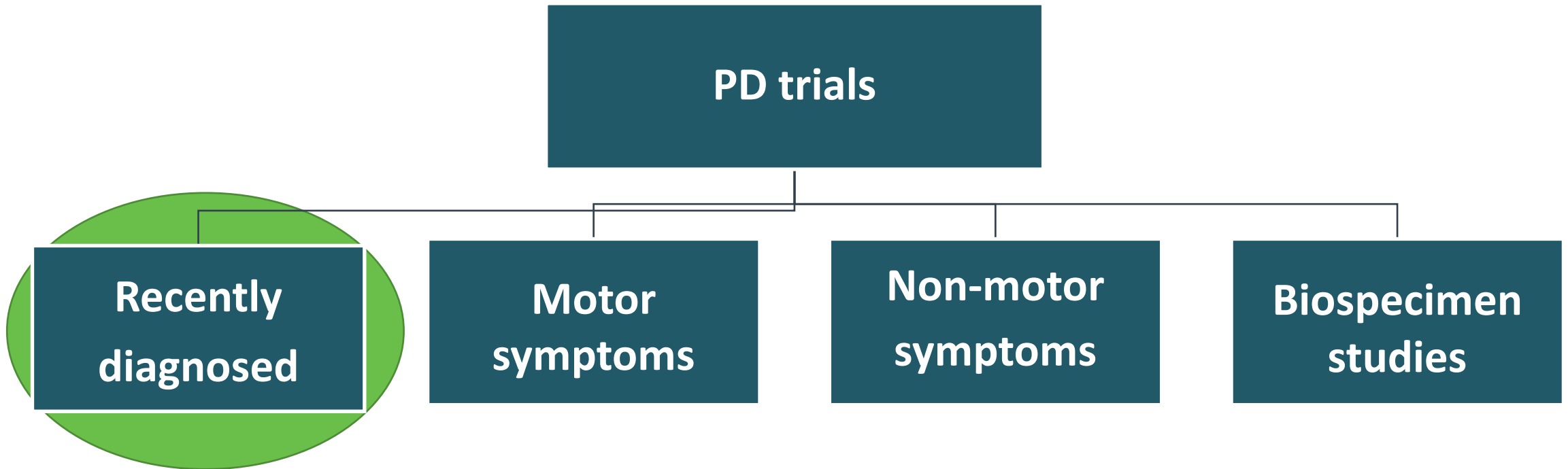
## Gratitude



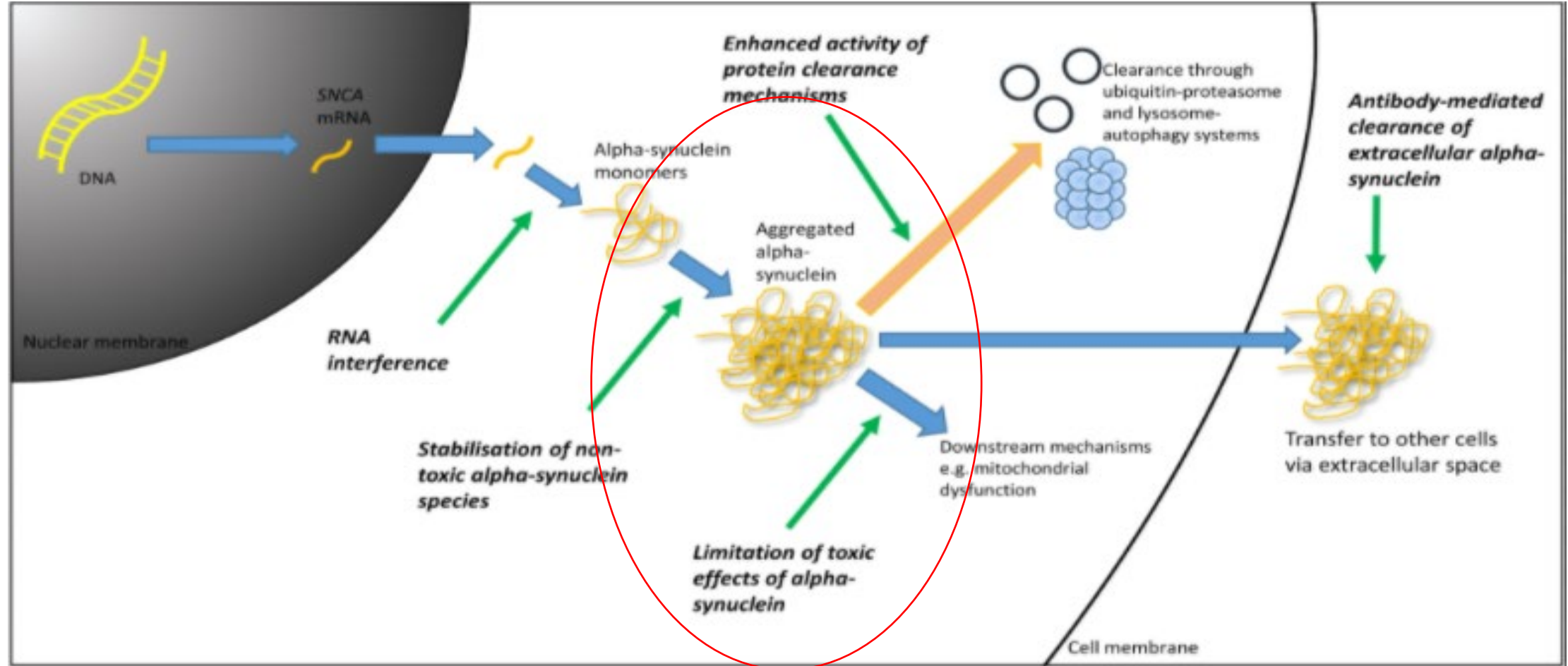
## Participate in Research

# Parkinson's disease trials breakdown

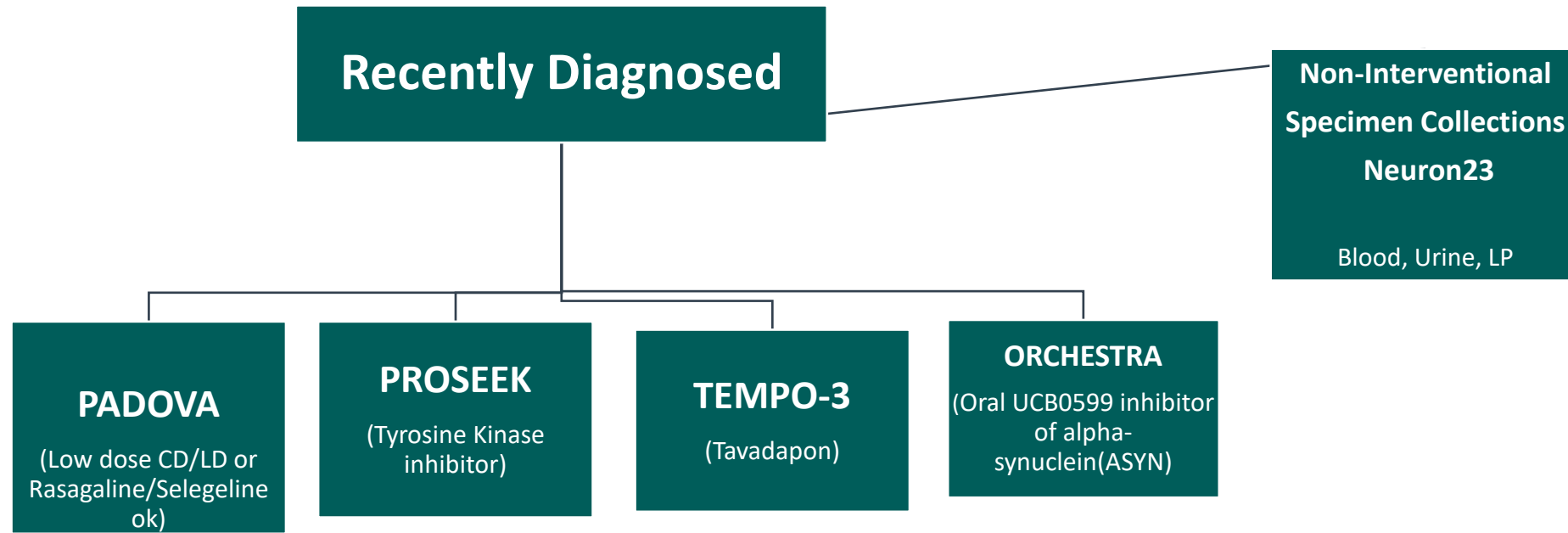
Vision: A trial for Every Patient<sup>®</sup>



# Alpha synuclein pathway for Early Diagnosed PD



# Trials under way for Recently Diagnosed (within 2-3 years)



**Soon coming** — Genetic Targets for LRRK2 (with and without)

# BN42358 - PADOVA

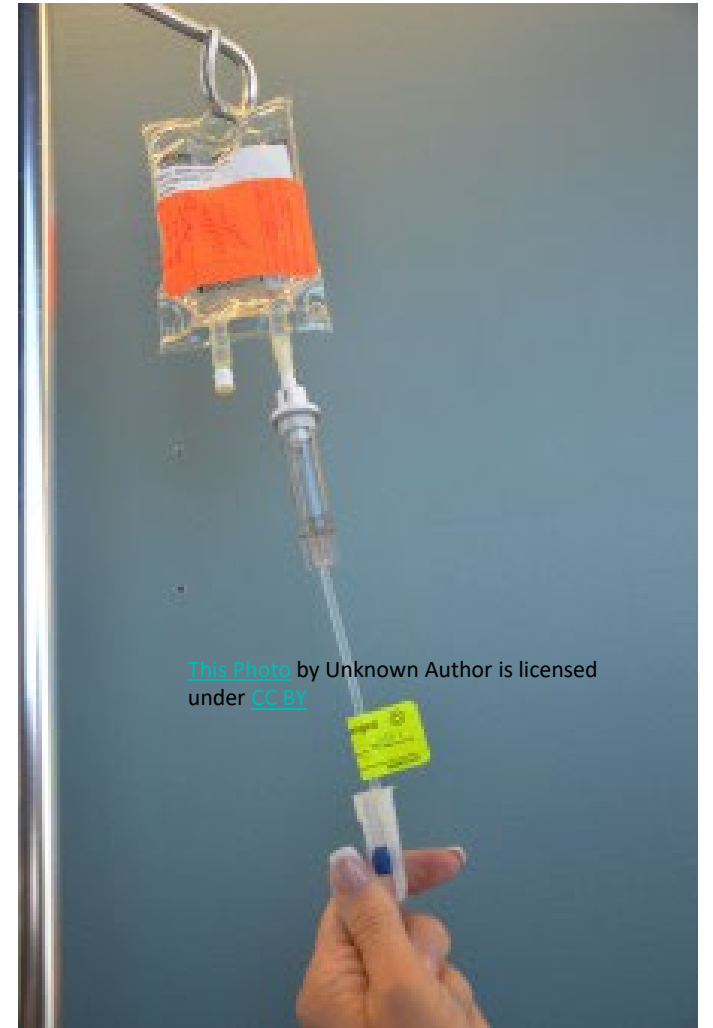
**Drug name:** PRASINEZUMAB

**Mechanism of action:** Evidence suggests that prasinezumab, a monoclonal antibody designed to preferentially bind to aggregated forms of alpha-synuclein, has the potential to slow or halt the progression of PD by preventing cell-to-cell transmission of pathogenic forms of alpha-synuclein

**Phase:** 2b

**# of Visits:** 20

**Study Duration:** 76 weeks



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# CLR\_18\_06 – PROSEEK

**Drug name:** K0706

**Mechanism of action:** K0706 is a novel BCR-ABL tyrosine kinase inhibitor. Generally, cellular tyrosine kinase has multiple roles in maintenance of neuronal health and function, but its over-activation has been shown to play a role in the pathophysiology of multiple neurodegenerative disease.

**Phase:** 2

**# of Visits:** 12

**Study Duration:** 40 weeks



# PD0053 – ORCHESTRA

**Drug name:** UBC0599

**Mechanism of action:** UCB0599 acts at an early-stage of ASYN aggregation by inhibiting the initial nucleation event or seed formation by inhibiting misfolding; therefore, it may halt the progression of PD vs only treating the symptoms.

**Phase:** 2A

**# of Visits:** 10 clinic + 6 remote/home

**Study Duration:** 18 weeks during treatment; 21 weeks total



# 283PD201 – LUMA – **Soon Enrolling**

**Drug name:** BIIB122

**Mechanism of action:** BIIB122 is a selective, orally bioavailable, central nervous system-penetrant, reversible inhibitor of LRRK2. Inhibition of LRRK2 kinase, a genetically validated target, is expected to improve lysosomal function in patients with PD who do (LRRK2-PD) and do not have pathogenic LRRK2 variants.

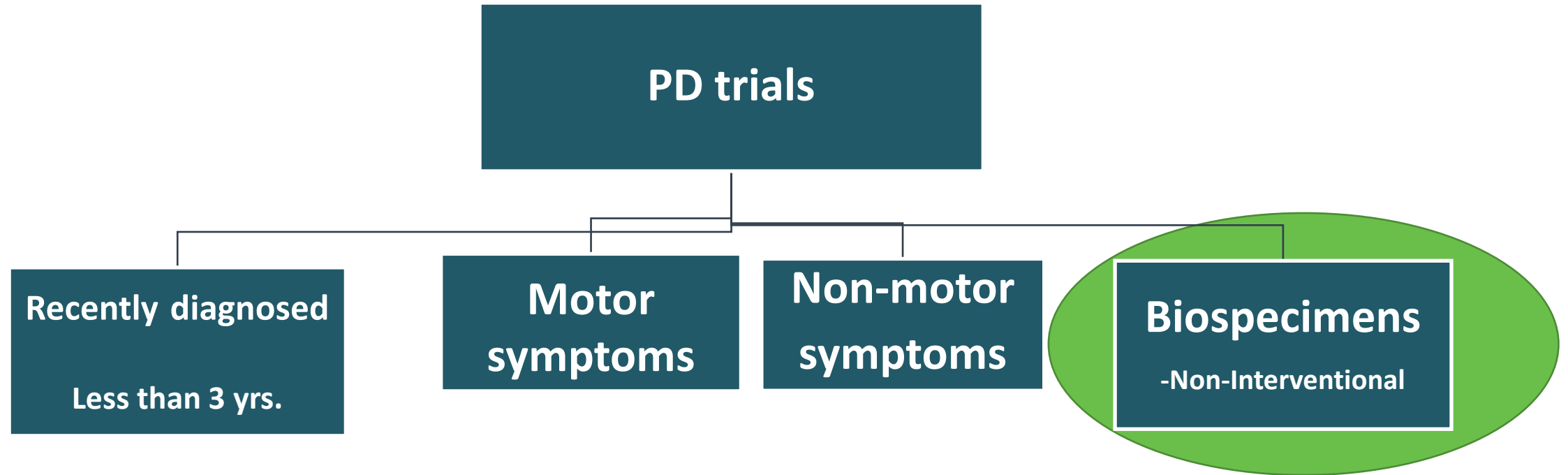
**Phase:** 2b

**# of Visits:** 19

**Study Duration:** 144 weeks



# Parkinson's disease trials breakdown



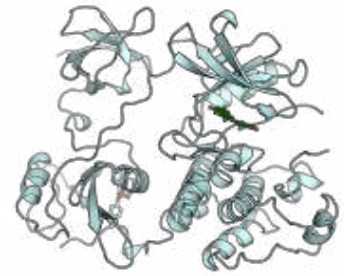
# Biospecimen Trials

- **Neuron-23:** Spinal fluid and blood samples on people with Parkinson's
- **Synuclein-One:** Skin Biopsy for **Healthy Controls**. One time visit. Control volunteers also needed (great for caregivers to participate).



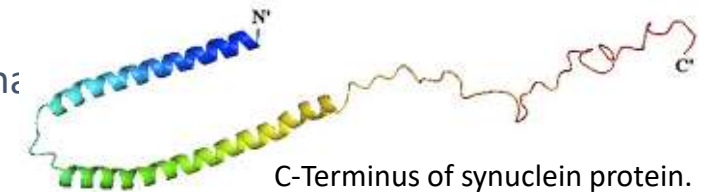
# At a Glance – Early PD Trials

**ProSeek:** 40 wk. double blind oral treatment plus open label for 3 years; LP can be waived by skin biopsy required.



Tyrosine Kinase

**Padova:** 76 wk. double blind IV drug treatment plus Open Label; Dx < 3 yrs.; LP optional



C-Terminus of synuclein protein.

**TEMPO-2:** 27 wk. double blind oral treatment plus Open Label. Symptom Management Study.

**Orchestra:** 78 wk. treatment; Alpha synuclein; double blind; some home nurse visits ; LP optional

**Neuron-23 Biorepository:** Blood, urine, and lumbar punctures for patients diagnosed within 3 years with PD.

**PLUS,** 2 new trials with oral drug that targets LRRK2 gene in patients with PD.

# A Trial for Every Patient

## Hence, if you are Diagnosed with PD within last—

- 2 years, LRRK2 status unknown, and no other PD meds, we may discuss –
  - Neuroprotection (Orchestra study; LRRK2 +/- study, soon coming)
  - Specimen Collections
  
- 3 years, on MAO-B inhibitor monotherapy, we may discuss –
  - Symptom Management (Tempo-2)
  - Neuroprotection Studies (Padova and ProSeek studies)
  - Specimen Collections
  
- 3 years, on MAO-B inhibitors **OR** Levodopa/Carbidopa, we may discuss –
  - Neuroprotection (Padova)
  - Specimen Collections
  
- 5 years, on MAO-B inhibitors **and** Levodopa/Carbidopa, we may discuss –
  - Neuroprotection (Luma)



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## MJ Fox Grant awarded to EvergreenHealth for survey regarding PD Research.

Grant seeks to understand barriers to recruitment and participation on Parkinson's Disease studies.

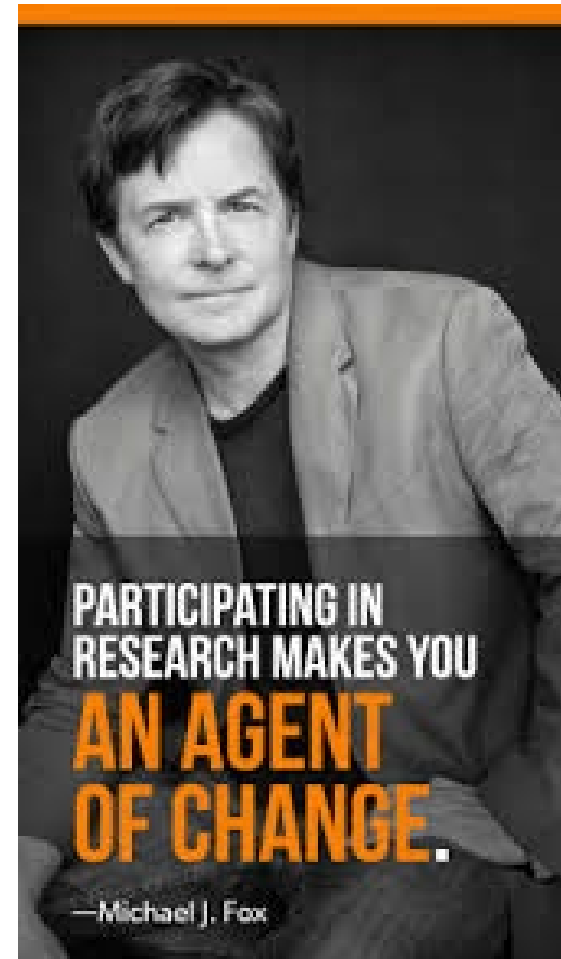
- 15 minutes at a computer to seek opinion on Clinical Trials.
- Patients and Caregivers can participate

How do you get involved?

**425-899-5385**

[EvergreenResearch@EvergreeHealth.com](mailto:EvergreenResearch@EvergreeHealth.com)

Research Website: [www.evergreenhealth.com/clinical-trials](http://www.evergreenhealth.com/clinical-trials)



## Clinical Trials

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## Find a Clinical Trial

EvergreenHealth believes that clinical research is integral to the advancement of medicine. In addition to providing patients with the best possible care, our research program is on the forefront of investigating new treatments. You can look for a clinical trial by using the search bar, or by clicking on the listings below.

Search

Clinical Trial Categories

Locations

Alzheimer's Disease	2 Trials
COVID-19	3 Trials
Hepatology	1 Trial
Huntington's Disease	2 Trials
Infectious Disease	1 Trial
Lung Cancer	1 Trial
Multiple Sclerosis	6 Trials
Neurogenic Orthostatic Hypotension (NOH)	1 Trial
Pain Management	2 Trials
Parkinson's Disease	22 Trials
Pulmonary	2 Trials

# Contact us directly through website

**Contact Us**

Call us at **425-899-5385** or use our online information request form.

**Online Form**

**Clinical Trials**

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## Clinical Trials Information Request

We would be happy to answer your questions and provide information about our research programs at EvergreenHealth.

If you have a time sensitive question, please call our Research main line at (425) 899-5385 during business hours to speak with staff.

Required fields are marked with \*

Name

First Name\*

Last Name\*

Daytime Phone\*

999-999-9999

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Email Address\*

I am interested in:

- Cancer Trials
- Cardiovascular Trials
- Multiple Sclerosis Trials
- Parkinson's Trials
- Orthopedic Trials
- Other

Specific Comments/Questions/Requests:

What other trials would you like to know more about at Evergreen Health?

Would you like to receive research study emails from us?\*

Yes  No

How would you prefer to be contacted?\*

Phone  Email

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# RESEARCH IS PART OF THE CONTINUUM OF CARE AT EVERGREENHEALTH PATIENT CENTRIC APPROACH

## You are not alone: Your PD management team



**The most important team member is YOU!**

## Questions?

**Research Main Line: 425-899-5385**

**To hear more about us, visit:**

**[www.evergreenhealth.com/clinical-trials](http://www.evergreenhealth.com/clinical-trials)**