

Overview of Parkinson's disease Research at University of Colorado



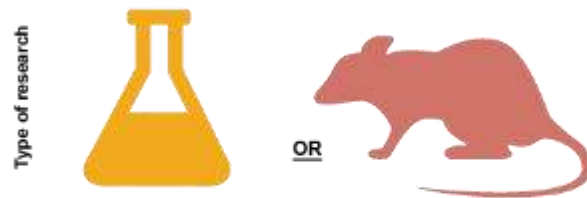
Brian D. Berman, MD, MS
May 12, 2018



University of Colorado
Movement Disorders Center

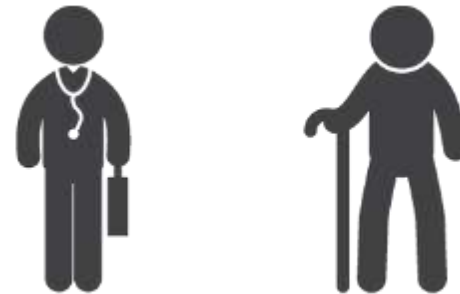
Terminology

- **Basic science** – pure/fundamental scientific research that is typically conducted “benchtop” or in a lab and aims to improve understanding of disease.

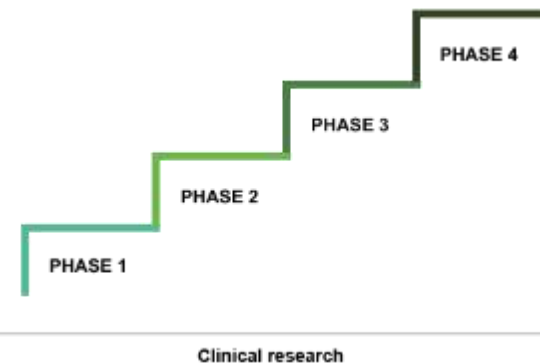


Laboratory research

- **Clinical research** – the study of health and illness in people.



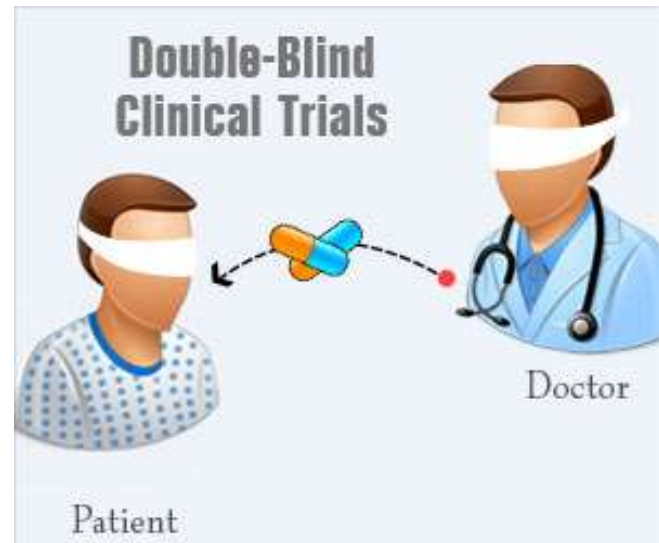
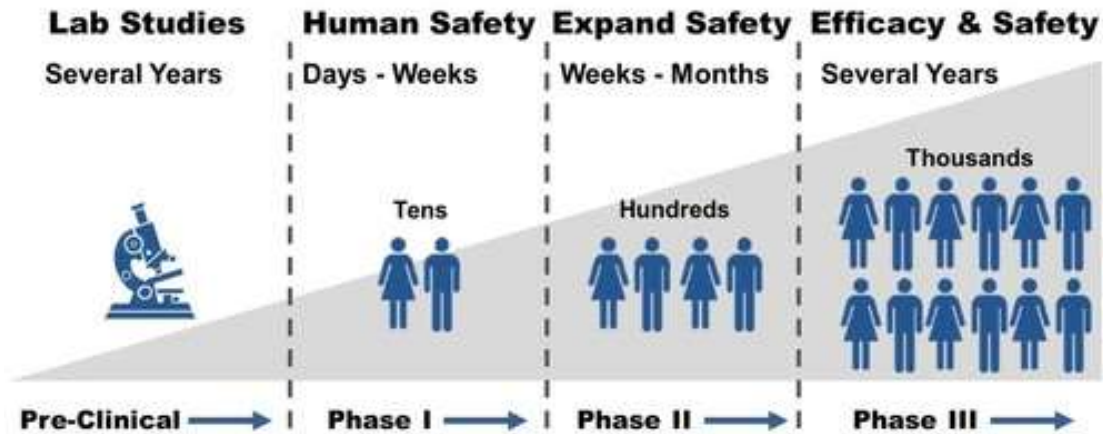
Human research with medical supervision



- **Clinical trials** – clinical research that aims to determine the safety and effectiveness (efficacy) of medications, devices, diagnostic products and treatment regimens intended for human use.

Terminology

Phases of a Clinical Trial



Clinical Research at the University of Colorado

- Pharmacological and surgical clinical trials that aim to find novel ways to slow, stop or reverse the progression of PD.
- Investigations and clinical trials that aim to find better treatments for motor & non-motor symptoms.
- Clinical research into non-pharmacological, supportive-based and complementary approaches to treatment of patients and caregivers.

Neuroprotection



Nilotinib in PD

OPEN

The c-Abl inhibitor, Nilotinib, protects dopaminergic neurons in a preclinical animal model of Parkinson's disease

SUBJECT AREAS:
PARKINSON'S DISEASE
NEUROLOGY
NEURODEGENERATIVE DISEASES

Senthilkumar S. Karuppagounder^{1,2,6}, Sourav Brahmachari^{1,2,6}, Yunjong Lee^{1,2,3,6}, Valina L. Dawson^{1,2,3,5,6}, Ted M. Dawson^{1,2,4,5,6*} & Han Seok Ko^{1,2,7*}

Human Molecular Genetics, 2013, Vol. 22, No. 16 3315–3328
doi:10.1093/hmg/ddt192
Advance Access published on May 10, 2013

Nilotinib reverses loss of dopamine neurons and improves motor function in a mouse model of Parkinson's disease
of α -syn
Research Report

Michaeline L. Ho

Journal of Parkinson's Disease 6 (2016) 503–517
DOI 10.3233/JPD-160867
IOS Press

503

Nilotinib Effects in Parkinson's Disease and Dementia with Lewy Bodies



A Randomized, Double-Blind, Placebo-Controlled, Phase IIa, multicenter study of Nilotinib in PD



- Two-Cohort Study:
 - Moderate to advanced PD (N=75, 6 months)
 - Early/de novo PD (N=60, 12 months)
- Two doses (150mg and 300mg) vs placebo
- Goal to determine safety, tolerability, clinical and biological activity of Nilotinib in PD

A Multicenter, Randomized, Double-Blind, Placebo-
Controlled Study, with an Active-Treatment Dose-
Blinded Period to Evaluate the Safety,
Pharmacokinetics, and Pharmacodynamics of
BIIB054 in Subjects with Parkinson's Disease



Spark

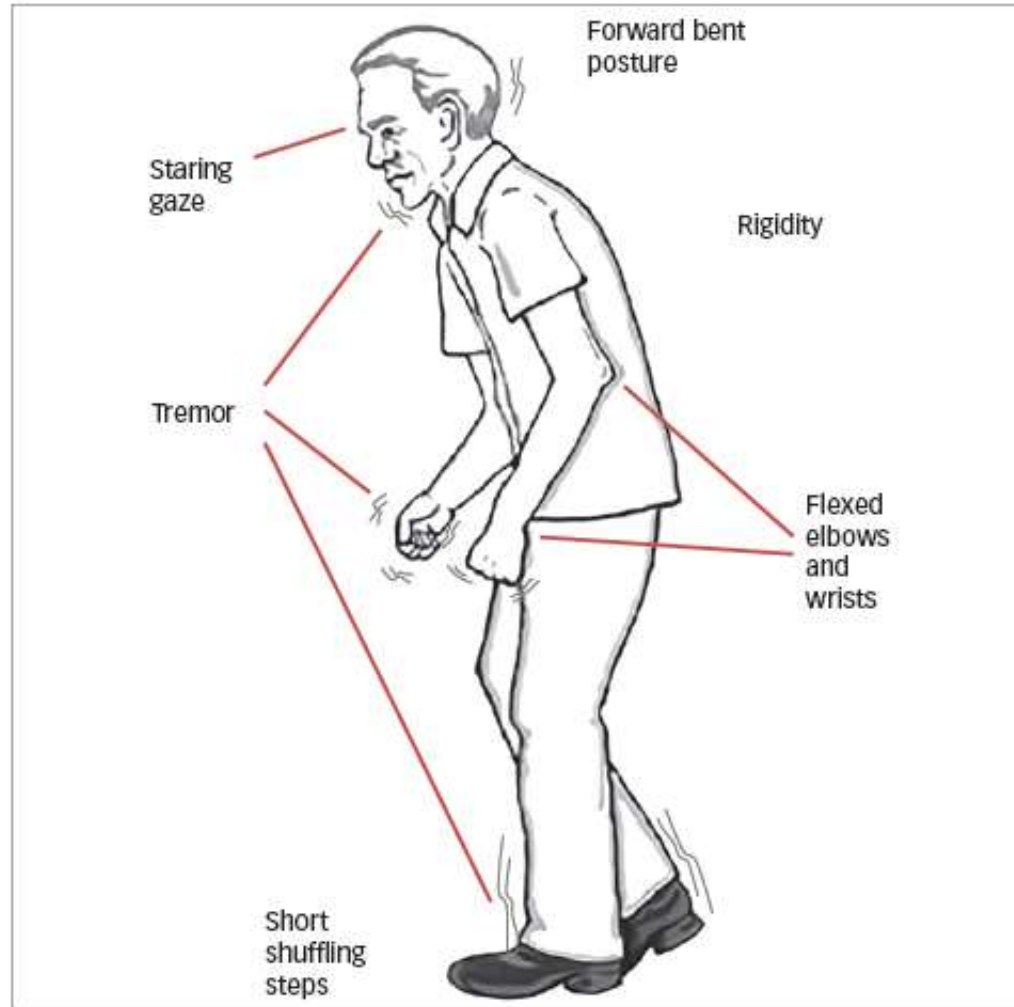
- BIIB054 is a human monoclonal antibody that selectively targets pathologic, aggregated α -synuclein but spares physiological α -synuclein
- Goal is to reduce the build up of pathologic, aggregated α -synuclein & prevent its spread
- Phase 2 multicenter clinical trial in de novo PD to test if tolerated and determine optimal dose for both safety and potential efficacy
 - Screening (40-80 years old, Dx with PD w/in 3 yrs)
 - 48 week treatment period
 - 12 week follow-up period
 - Evaluations include MRI, DaT SPECT, LPs

Phenylbutyrate in PD

- PD gene PANK7 encodes the protein DJ-1
- Increasing DJ-1 expression may clear α -synuclein and block its toxic effects
- Phenylbutyrate shown to increase DJ-1 expression
- Study now to see if phenylbutyrate can clear alpha-synuclein from the brain and slow PD (enrolling 2019).

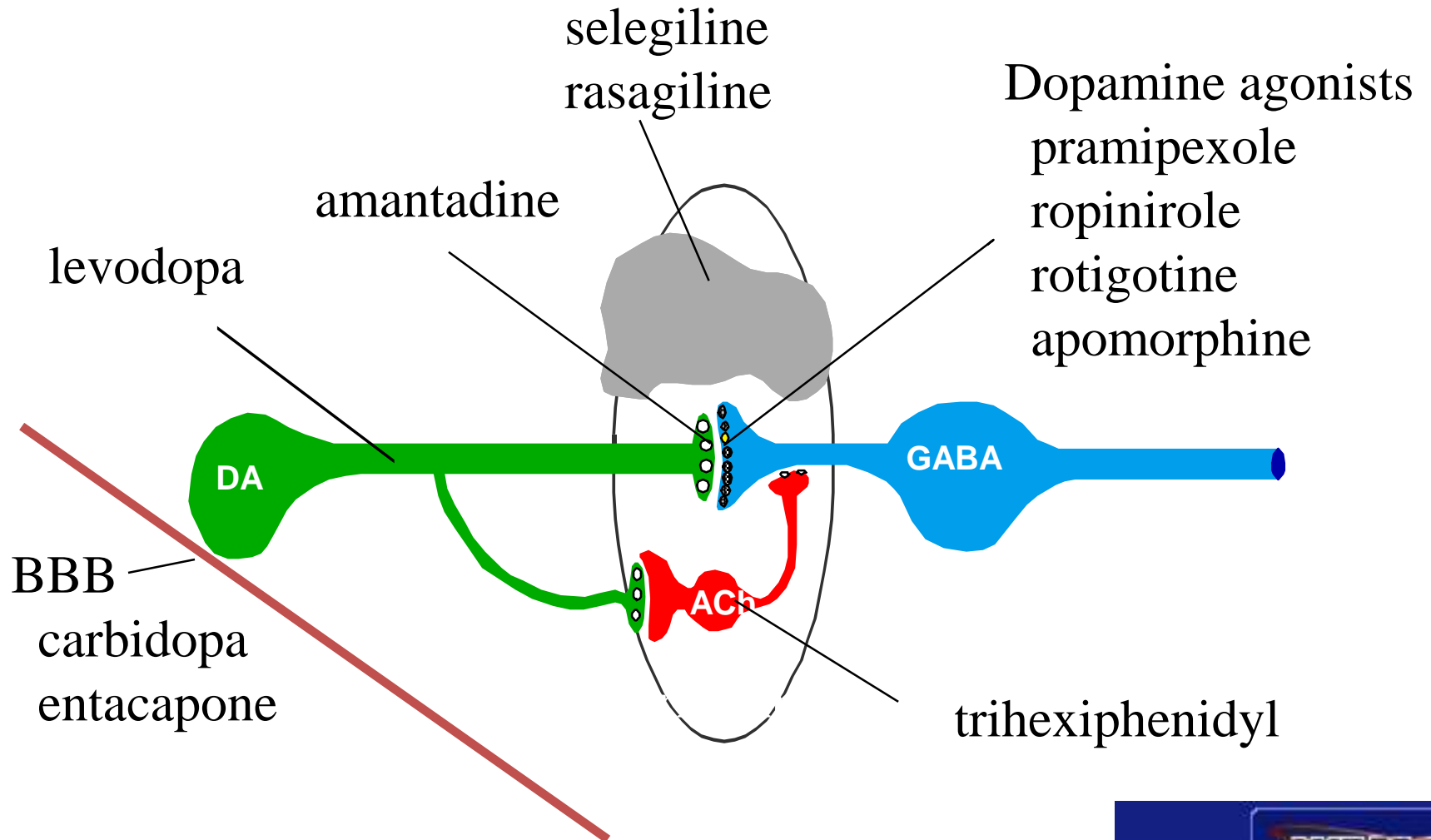


Motor symptom treatment



Adapted from information presented in Rodriguez-Oroz et al., 2009.⁴

Mainstay: dopaminergic therapy



A Proof of Concept Study to Investigate the Effect of IPT803 Adjunct Treatment in Patients with Parkinson's Disease

- IPT803 mechanism of action is still under investigation, but it is believed to act through dopamine and endorphin pathways.
- Study also aims to understand what patient characteristics are related to treatment efficacy
- 12-week study (subgroup will participate in fMRI study)
 - Age >30, H&Y <3
 - Stable medications

Neurologic Music Therapy for fine motor problems



Randomized
Controlled
Trial

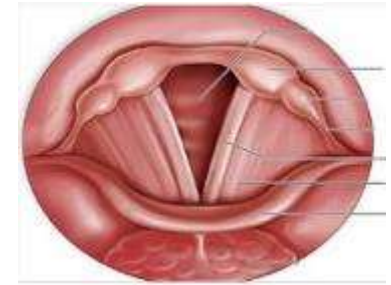


Neurologic Music Therapy



Occupational Therapy

Treatment of the **voice impairment** with collagen injections in vocal folds (VoCAL-PD)



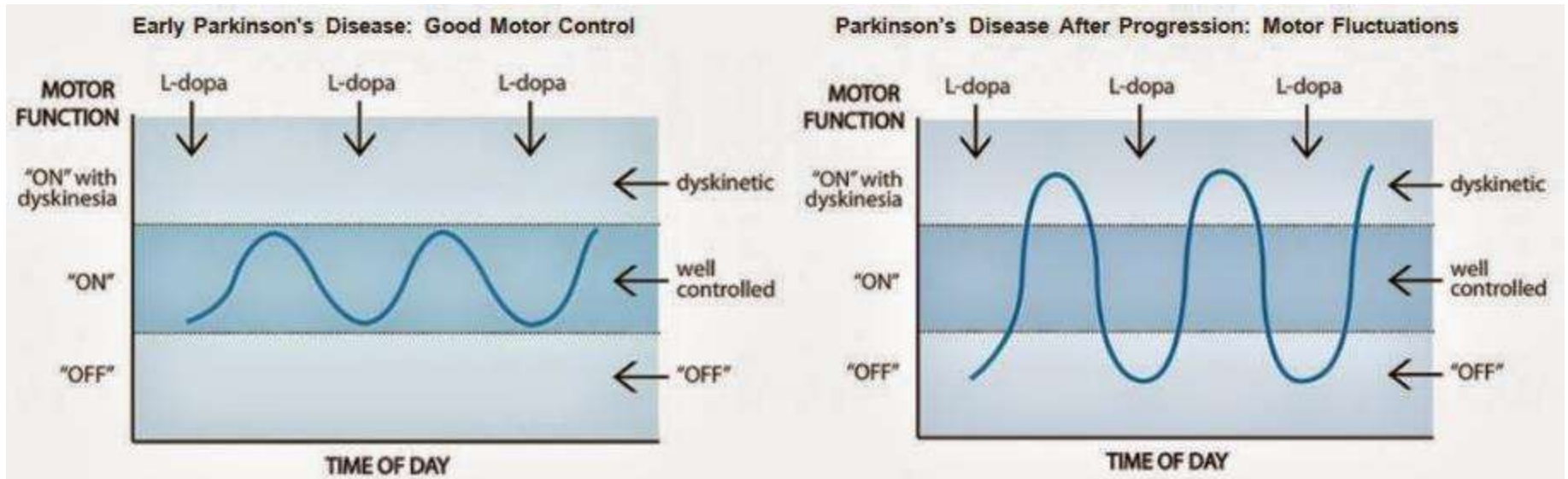
- More than 90% of PD patients have voice and speech impairments
- Current treatment options only speech therapy, Lee Silverman Voice treatment (LSVT), etc.
- Vocal fold augmentation with collagen injections is being used safely for many disorders of vocal folds
- The goal of this study is to objectively analyze effect of injections in PD

A randomized, double blind, placebo-controlled paralleled study of tolerability and efficacy of Cannabidiol (CBD) on motor symptoms in Parkinson's disease

- Cannabidiol (CBD) is a component of cannabis
 - Does not cause “high”
 - May help motor symptoms in PD and be neuroprotective
- Study evaluates the effect of CBD on all aspects of PD
- Study lasts ~3 weeks



Motor fluctuation treatment

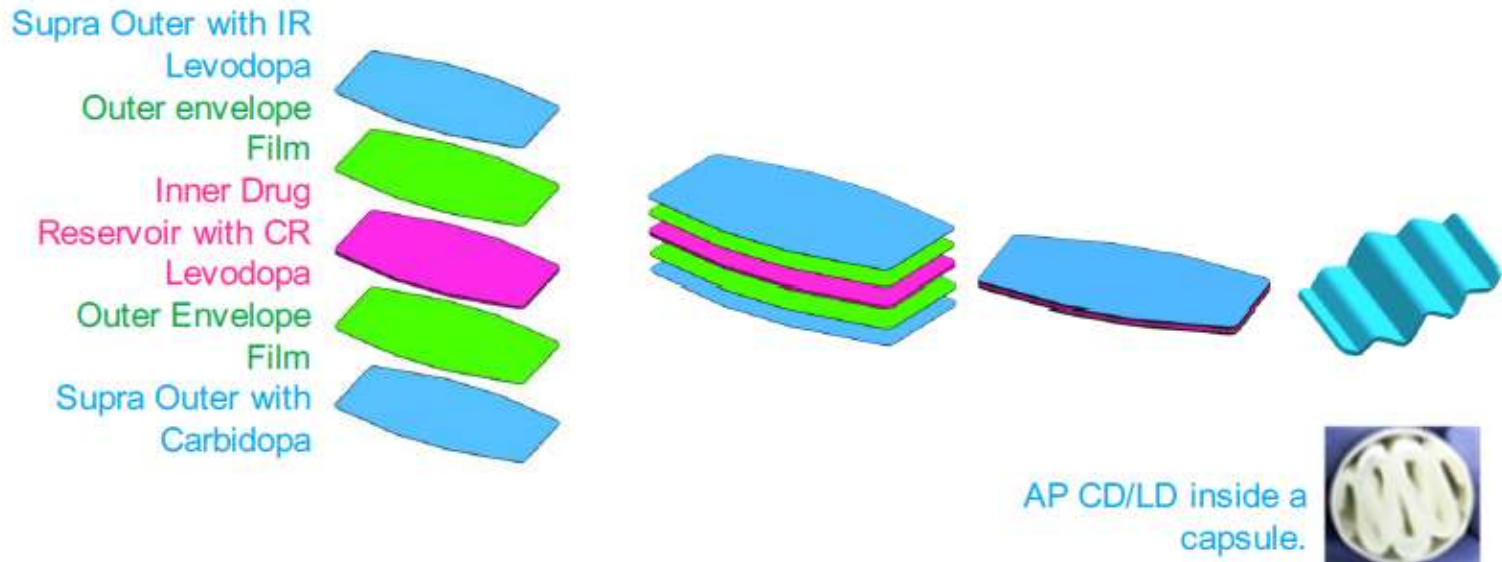


Cynapsus CTH-301 Trial

- Investigating the safety and effectiveness of an oral, sublingual therapy of Apomorphine for patients with PD who are experiencing motor fluctuations (known as OFF episodes)
- 13 visits over about 231 days
- Major Inclusion Criteria:
 - Response and stable dosing to L-Dopa
 - At least 2 hours or more of OFF time



Accordion pill for fluctuating PD patients



- Study of Intec Accordion CL formulation gastroretentive platform.
- Active control (immediate release carbidopa/levodopa)
- Inclusion: At least 2.5 hours or more of OFF time

Sub-cutaneous infusion of carbidopa/ levodopa (Neuroderm) for patients with PD

- Aim to treat unreliable effect of levodopa with early wearing off.
- Constant infusion of liquid CD/LD under the skin
 - Very small (insulin-like) needle and small pump
 - Constant infusion provides smooth, steady effect
- Inclusion: At least 2 hours or more of OFF time

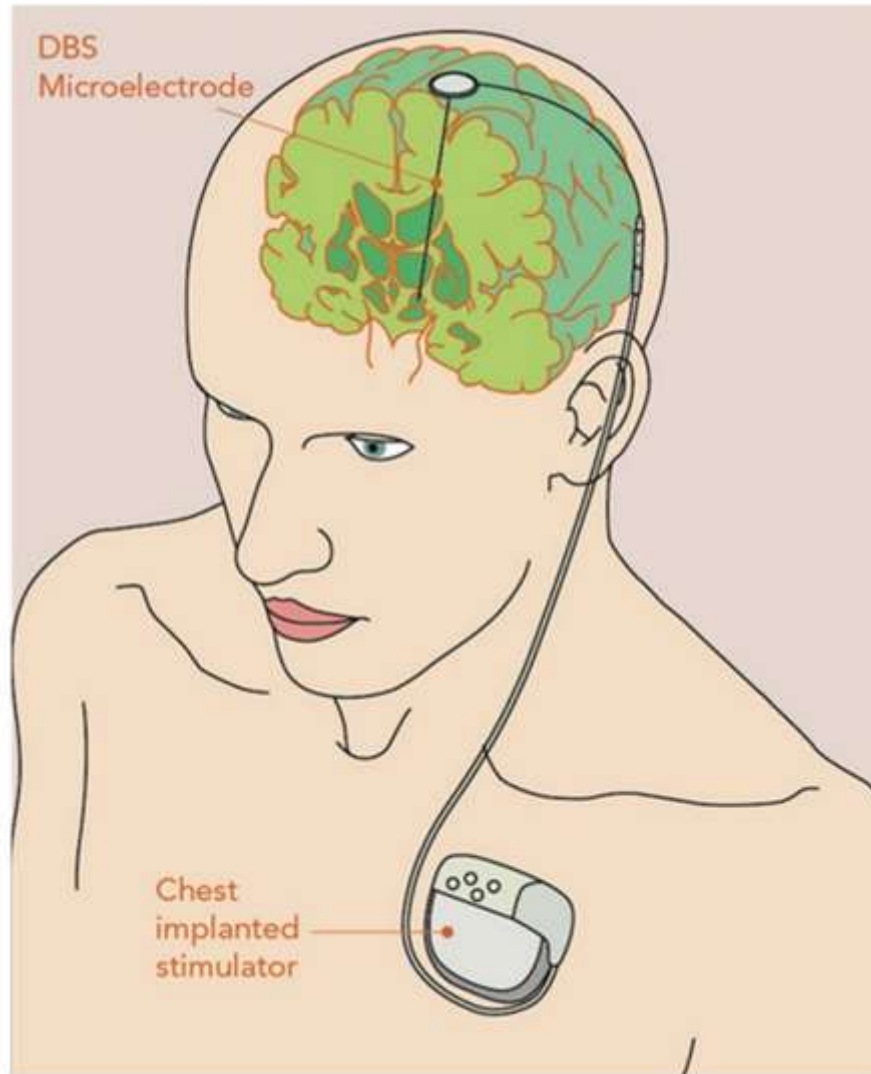


Open-Label Study of Apomorphine by Continuous Subcutaneous Infusion in Advanced PD



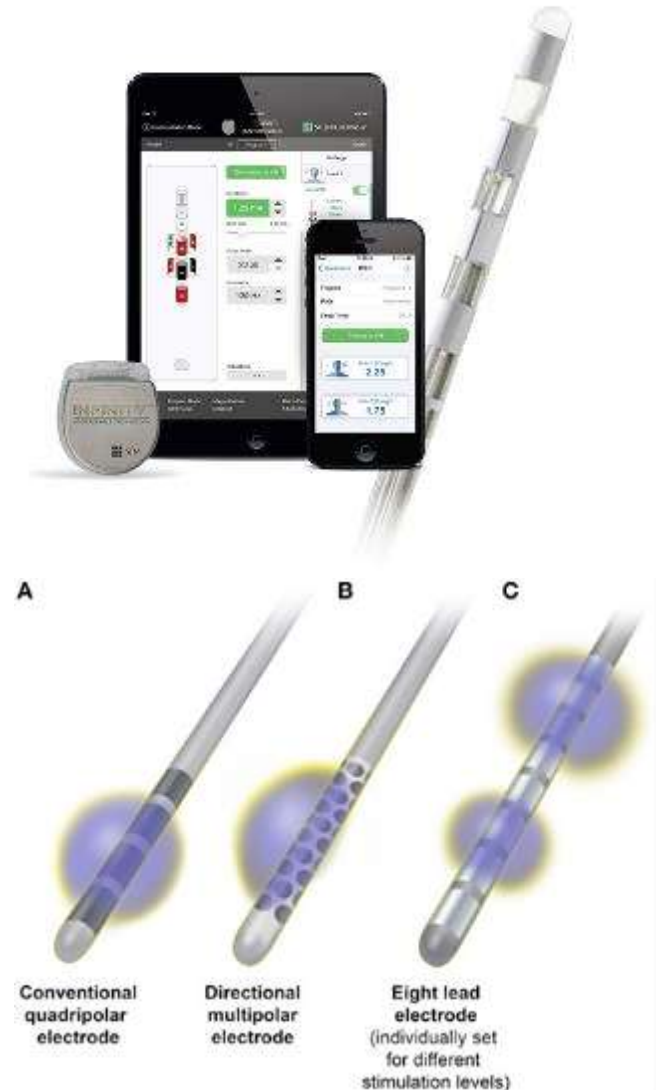
- Dopamine agonist
 - Not related to morphine
- Approved & used in UK and other European countries
- Only available in US through research study
 - 1 year open label study, then can continue
- Inclusion: At least 2.5 hours OFF time

Surgical treatment



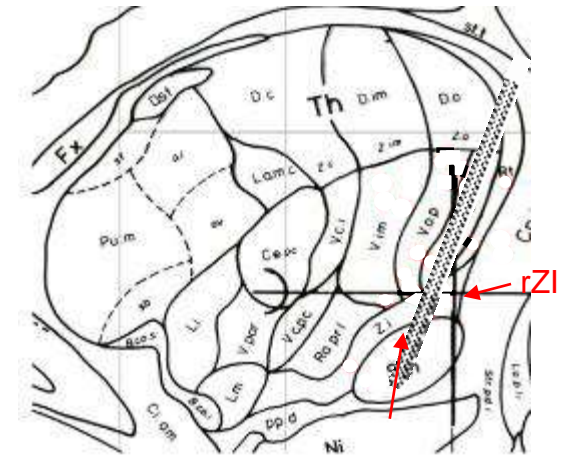
Infinity Deep Brain Stimulation System PROGRESS

- Long – term follow up of the performance of newest implanted DBS system.
- Demonstrate superiority of directional (steerable) DBS lead
- Patients, who need DBS are implanted with this system and followed long term



Novel Targets for DBS

- Adverse effects can occur with STN DBS (Dyskinesias, ataxia, behavioral & mood problems).
- Stimulation of zona incerta (ZI) may be more effective than traditional targets.
- Study aims to determine effect of combined ZI and STN compared to standard STN.
- *Does not require any change to standard STN DBS procedure with exception that one contact will be placed in the ZI.



Non-motor symptoms



Study of thinking, memory, and everyday functioning in PD

- Study to develop a performance-based test of thinking ability and compare with other standard cognitive tests
- 1 visit lasting 3-4 hours that includes questionnaires and neuropsychological tests.
- A second visit lasting 30-45 minutes that includes repeating a test of everyday functioning
- Inclusion: PD with normal cognition or mild cognitive impairment.



Dementia Biomarker

- Biomarkers are tests that can be used to diagnose, measure treatment responses, or follow progression.
- We aim to see if patterns of brain activity may help us to diagnose dementia in PD earlier, allow better monitoring of treatments or find new treatment targets.
- Would involve 1-2 visits for cognitive testing and brain scans.



PD Dementia treatment

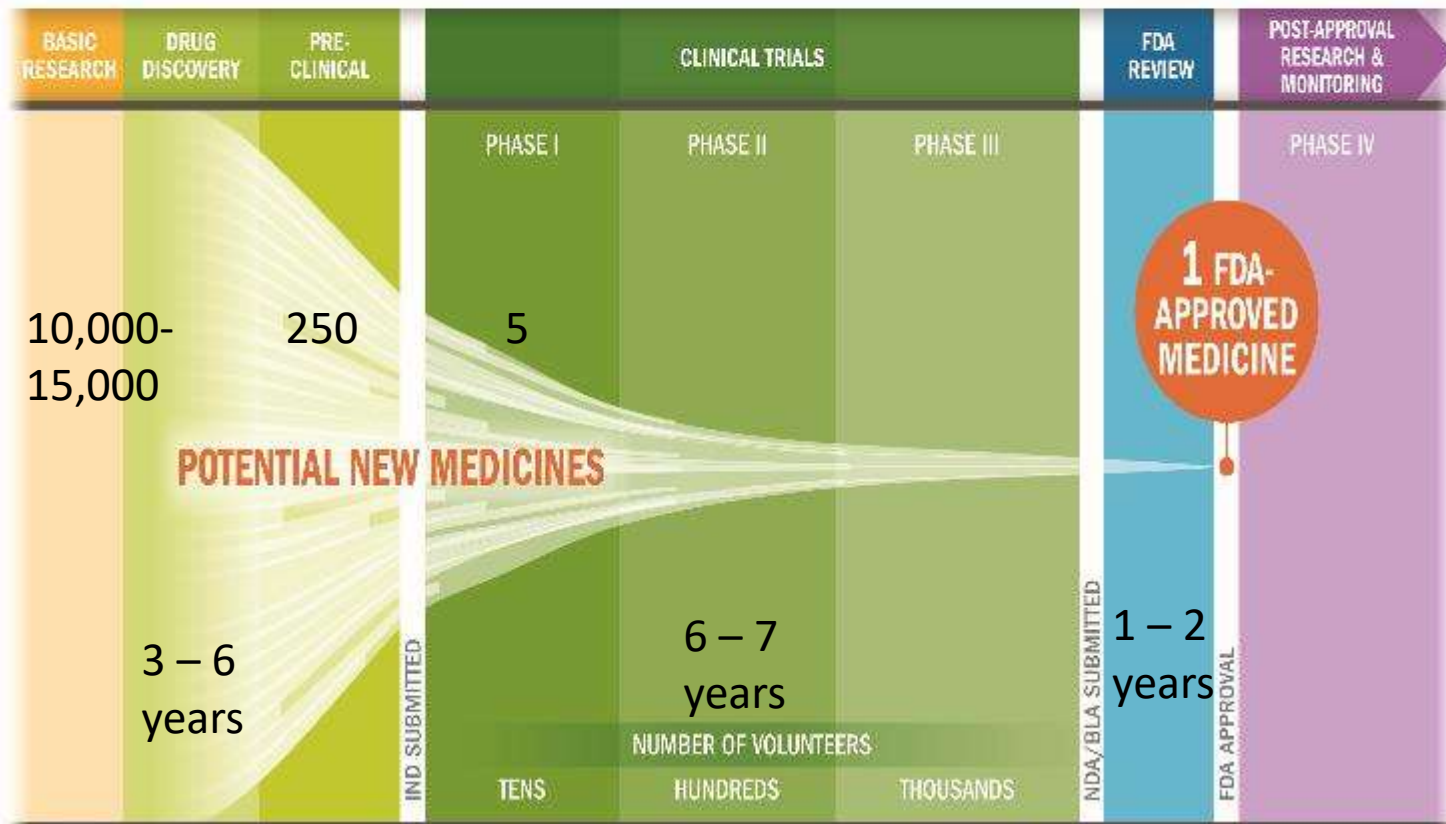
- Cognitive impairment in PD is common and there are only limited treatment options.
- Some of the cognitive symptoms are likely related to the dopamine insufficiency.
- There is a brand new type of medication that can improve the effect of dopamine in the brain and may improve memory and cognition.
- Phase II 12-week trial of LY3154207 in Mild-to-Moderate Parkinson Disease Dementia



Why Participate?

THE BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS

From drug discovery through FDA approval, developing a new medicine takes at least 10 years on average and costs an average of \$2.6 billion.* Less than 12% of the candidate medicines that make it into Phase I clinical trials will be approved by the FDA.



Why Participate?

- All of your
– ↓ male
– Now 75%
 - 90% of cli
– This me
expensiv
 - People in
– Close ok
– Placebo
– Gives ar
 - It is a unic
- al trials
- n, more
- munity



Your Research About Research

- Sponsor?
- Privacy protected?
- Inclusion/Exclusion criteria?
- Time and commitment?
- Chances of being in “control” or “placebo” group?
- Will the treatment harm me? What are the risks?
 - Closely monitored by IRB, FDA
- What are the potential benefits?

Research Resources



University of Colorado
Movement Disorders Center
www.ucdenvermovement.org



Learn about Parkinson's clinical trials

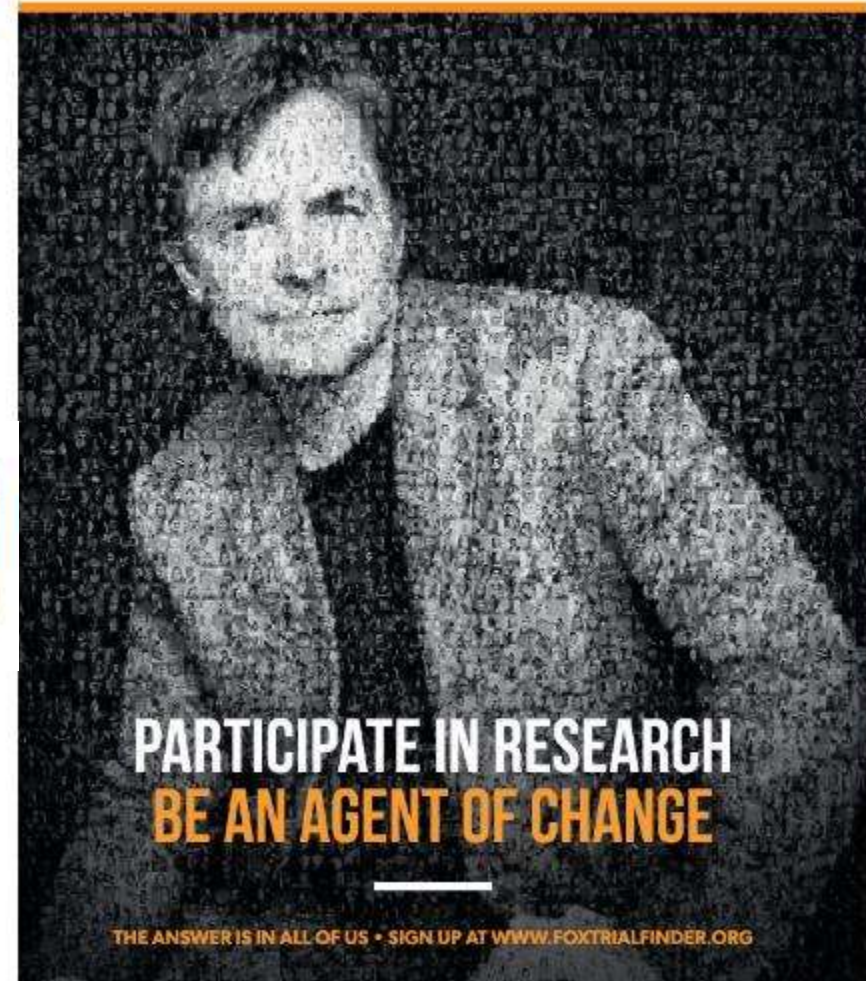
PDtrials
WWW.PDTRIALS.ORG



ClinicalTrials.gov

A service of the U.S. National Institutes of Health

FOX  TRIAL FINDER
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH



PARTICIPATE IN RESEARCH
BE AN AGENT OF CHANGE

THE ANSWER IS IN ALL OF US • SIGN UP AT WWW.FOXTRIALFINDER.ORG



University of Colorado Movement Disorders Center



Lauren
Seeberger,
MD



Maureen
Leehey,
MD



Brian
Berman, MD
MS



Drew Kern,
MD MS



Olga
Klepitskaya, MD



Benzi Kluger,
MD



Heather
Baer, MD



Abbie
Collins, MD

MDC Mission

- Excellence in clinical care
- Patient and physician outreach
- Train the clinicians and scientists of tomorrow
- Make advances in clinical and basic research



Christen
Epstein,
FNP



Jessica Barr,
PAC

To Schedule an Appointment:

720.848.2080 (Aurora)
720.848.2100 (Lone Tree)
303.544.3900 (Boulder)

DBS Referral:

720.848.0015 (Fax relevant notes)

Research Recruitment line: 303-724-4644

