MALATTIA DI PARKINSON: NUOVI APPROCCI TERAPEUTICI

NAPOLI, 13 DICEMBRE 2019

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Centro per le Malattie Neurodegenerative
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Perchè abbiamo bisogno di nuovi farmaci

- Nonostante i trattamenti disponibili, incompleto controllo degli OFF
- Discinesie
- Problemi psichiatrici
- Freezing della marcia
- Deterioramento cognitivo
- Mancanza di farmaci che bloccano o rallentano la progressione della malattia

Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial

Jeffrey Cummings, Stuart Isaacson, Roger Mills, Hilde Williams, Kathy Chi-Burris, Anne Corbett, Rohit Dhall, Clive Ballard

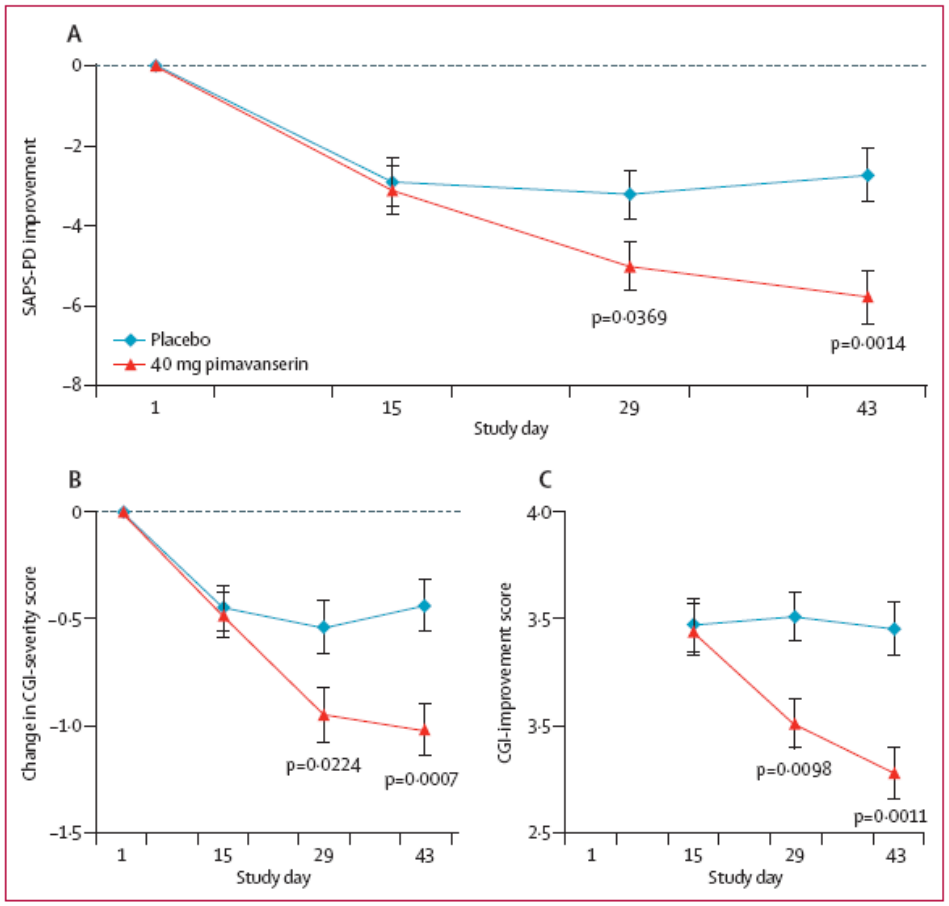


Figure 2: **Treatment effects on psychosis severity reduction in the 6 week study period in the full analysis set**
The full analysis set includes all patients who received ≥1 dose and had a SAPS assessment at baseline and at least one afterwards. Datapoints show least squares means (standard error). (A) SAPS-PD improvement. (B) Change in CGI-severity score. (C) CGI-improvement scores. SAPS=scale for assessment of positive symptoms. CGI=clinical global impression.

Pimavanserin Acadia approved by FDA

New Drugs

- Dopamine-Agonists
  - **Tavapadon** (CVL-751-PD-003)
    - potent, orally-administered, selective partial agonist of the dopamine D1 and D5 receptors

New Dopamine Agonist: Lu AF28996 /Lu AA40326 LUNDBECK

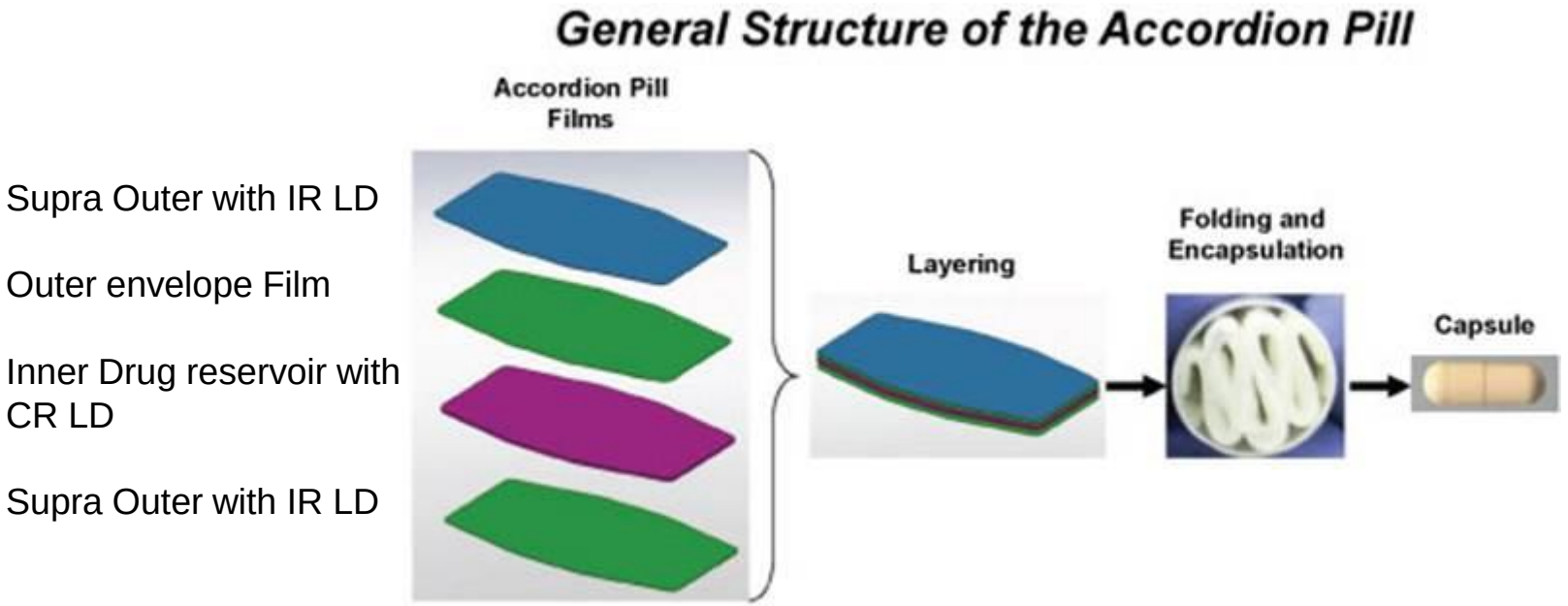
- Lu AF28996 is an orally administered compound in development for the treatment of Parkinson's disease, with primary focus on patients with motor fluctuations

- Lu AF28996 acts as a DA agonist at all receptor subtypes (D1 to D5).

New Levodopa formulations

Accordion Pill ™ INTEC PHARMA

- È un sistema di “advanced oral drug delivery dosage” basata sulle proprietà tecnologiche di rilascio combinato della LD



Accordion Pill ™

Phase III double blind double dummy placebo controlled study to demonstrate superiority of accordion pill versus standard levodopa in PD patients with fluctuations.

Not superior to standard levodopa. The design of the AP-CD/LD trial inflated the benefit of the Sinemet arm, as it allowed for higher doses of the comparator drug.

New Drugs: l-dopa

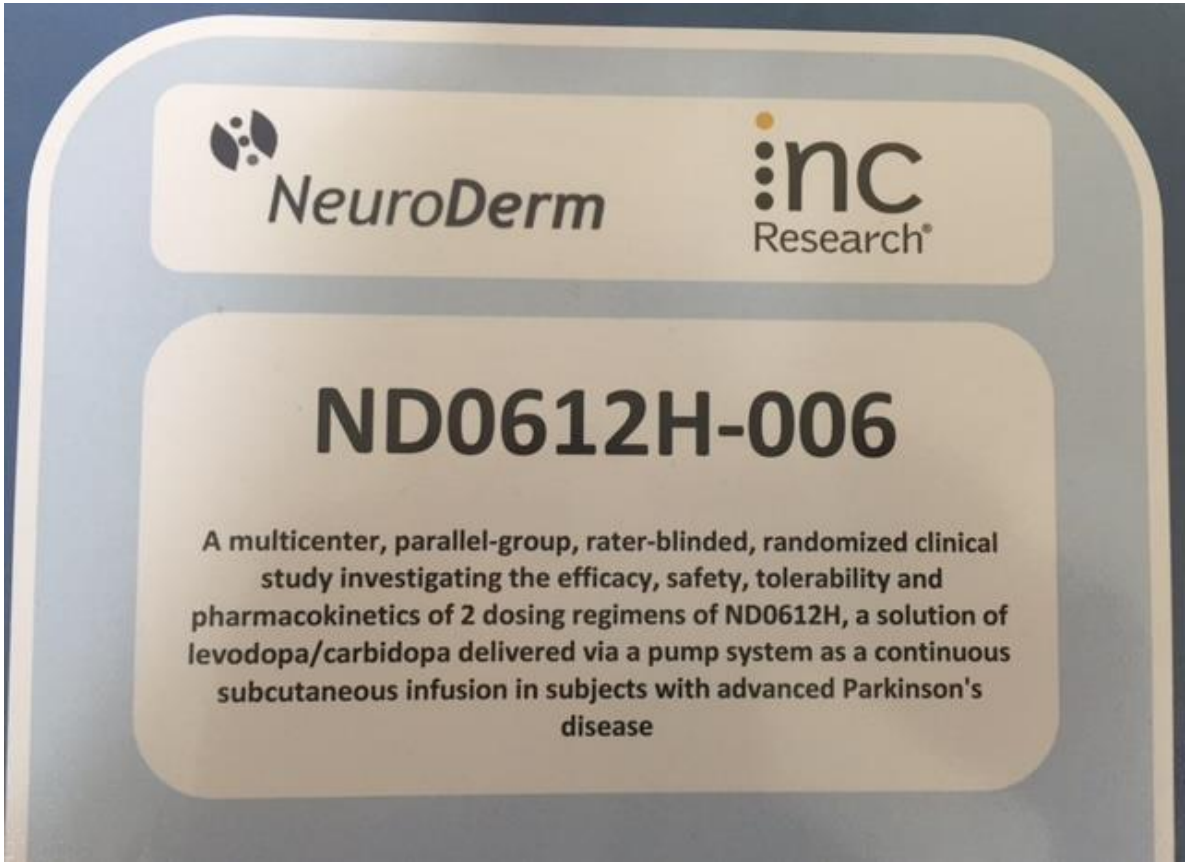
IPX066

PK Characteristics	• RYTARY provides both an initial and extended levodopa plasma concentrations after a single dose.

IPX203

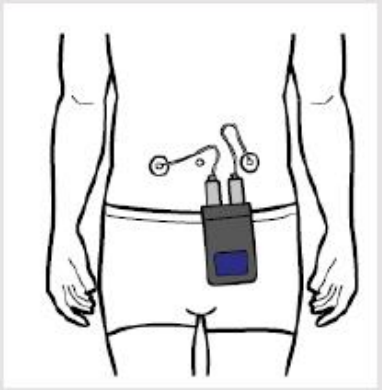
Phase III: STUDIO RANDOMIZZATO CONTROLLATO PER CONFRONTARE LA SICUREZZA E L'EFFICACIA DI IPX203 CON CARBIDOPA-LEVODOPA A RILASCIO IMMEDIATO IN PAZIENTI AFFETTI DA MALATTIA DI PARKINSON CON FLUTTUAZIONI MOTORIE

Levodopa subcutaneous infusion



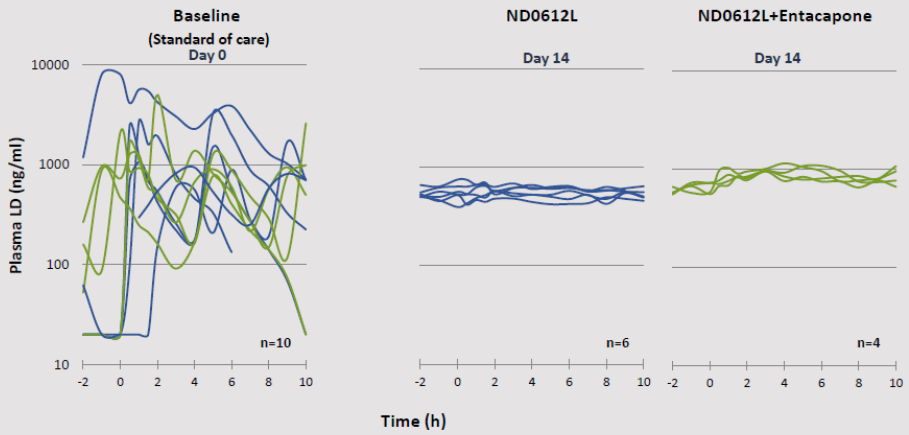
L-dopa subcutaneous infusion phase II

- ✓ ND0612 is a proprietary liquid formulation of LD/CD 60/7.5 mg/mL
- ✓ ND0612 enables for the first time subcutaneous administration of LD/CD
- ✓ Until now poor levodopa solubility has precluded this approach
- ✓ ND0612 is a delivered by a pump system
- ✓ Subcutaneous infusion of LD has the potential to provide a more convenient and better tolerated route of continuous levodopa delivery



Phase II – second period pharmacokinetics
ND0612L stabilizes LD plasma concentration

An average steady plasma levodopa concentration of 550ng/ml was maintained with ND0612L alone, and 800ng/ml when combined with oral entacapone

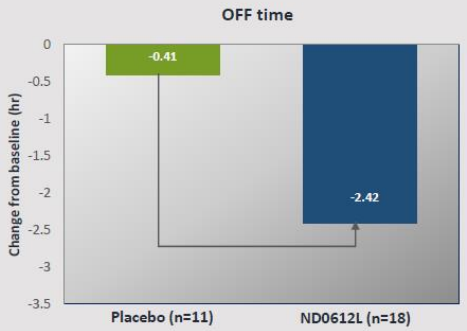


ND0612L transforms levodopa PK in PD patients

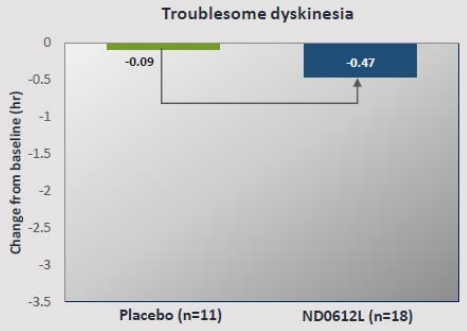
ND0612L reduces OFF time w/o increasing dyskinesia (in clinic)

Improves motor fluctuations without "paying the penalty" of troublesome dyskinesia

- Early onset of treatment effect observed



2 Hours reduction in OFF time
41% vs. 9% in the placebo



Reduction in troublesome dyskinesia

Courtesy of Prof. Stocchi

Levodopa subcutaneous infusion

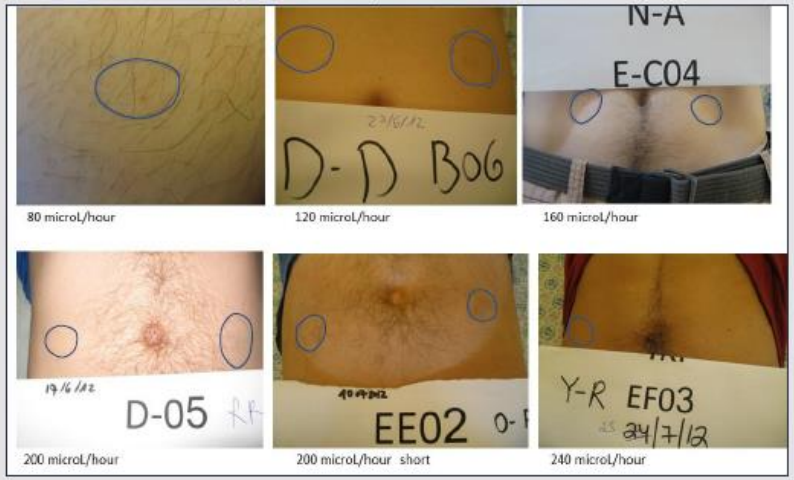
Good safety profile

No systemic or local irritation , all patients elected to continue to the open label extension phase

In volunteers and PD patients so far:

- Draize score slightly elevated, slight pruritus, similar in both groups, normalized at week 3
- SC nodules (0.5-1cm) resolving spontaneously
- No particular systemic AE
- No patient discontinued early
- Local safety – similar to Phase I in healthy subjects

Skin local safety in healthy volunteers - no local irritation

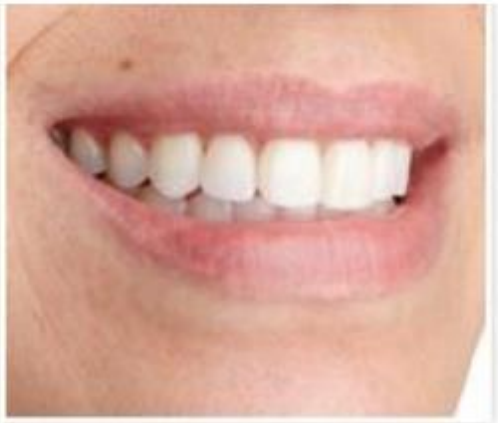


Transient and reversible local minor reaction

Levodopa oral infusion

ITM hearing device inserted in-the-mouth

Custom fits around the upper back teeth



ITM is nearly invisible when worn

SynAgile Solution: DopaFuse™

synAgile

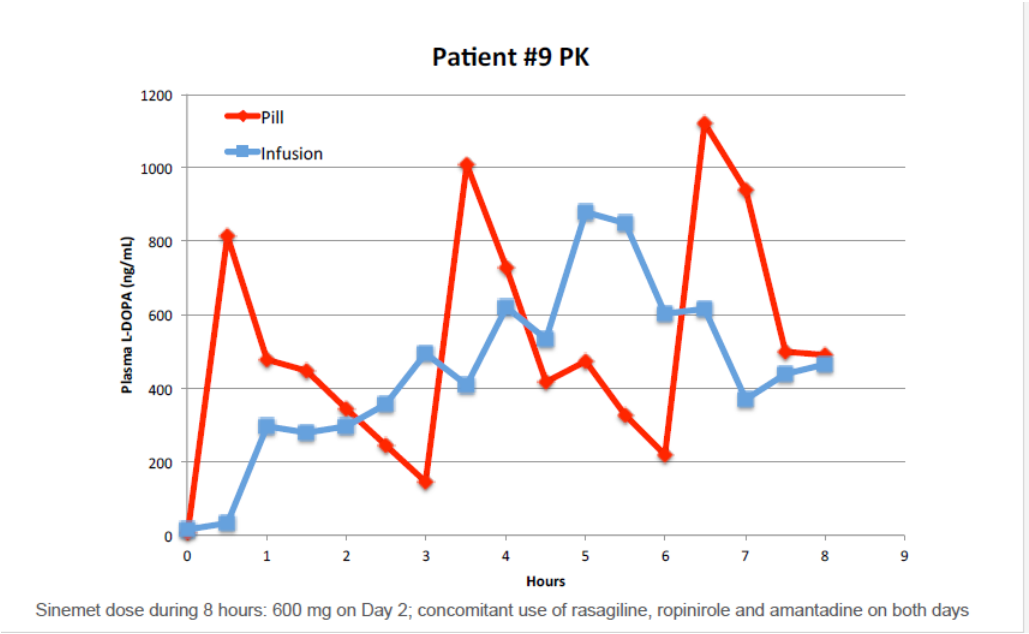
- Continuous intra-oral infusion of concentrated L-DOPA/carbidopa suspension
- Approved APIs and route of administration
- Miniature drug delivery device resides in the mouth
  - Simple, passive, mechanical technology – no chemistry or electronics
  - Drug delivery at constant, factory-set infusion rates

Movement Disorders

Continuous vs Intermittent Oral Administration of Levodopa in PD Patients With Motor Fluctuations – A PK, Safety, and Efficacy Study

Olanow CW[1-3], TortiM[4], Kieburtz K[1,5], Leinonen M[1], Vacca L[4], Grassini P[4], Heller A[6], Heller E[6], Stocchi F[4].

- **Objectives:**
  - To assess the plasma pharmacokinetics of continuous intra-oral infusion of LD/CD vs. intermittent administration of standard oral LD/CD
  - To assess the safety and tolerability of continuous intra-oral infusion of LD/CD
  - To assess the effect on PD motor function of continuous intra-oral infusion of LD/CD vs. intermittent administration of standard oral LD/CD
- **Study Design:** 18 PD subjects with motor fluctuations on stable doses of levodopa +/- other dopaminergic therapy who meet entry criteria and sign an IRB-approved informed consent will participate in this study.



Continuous oral delivery of l-dopa/carbidopa was associated with less plasma variability and reduced off time in comparison to standard intermittent oral l-dopa/carbidopa therapy

Courtesy of Prof. Stocchi

RESEARCH ARTICLE

A Randomized Trial of Inhaled Levodopa (CVT-301) for Motor Fluctuations in Parkinson's Disease

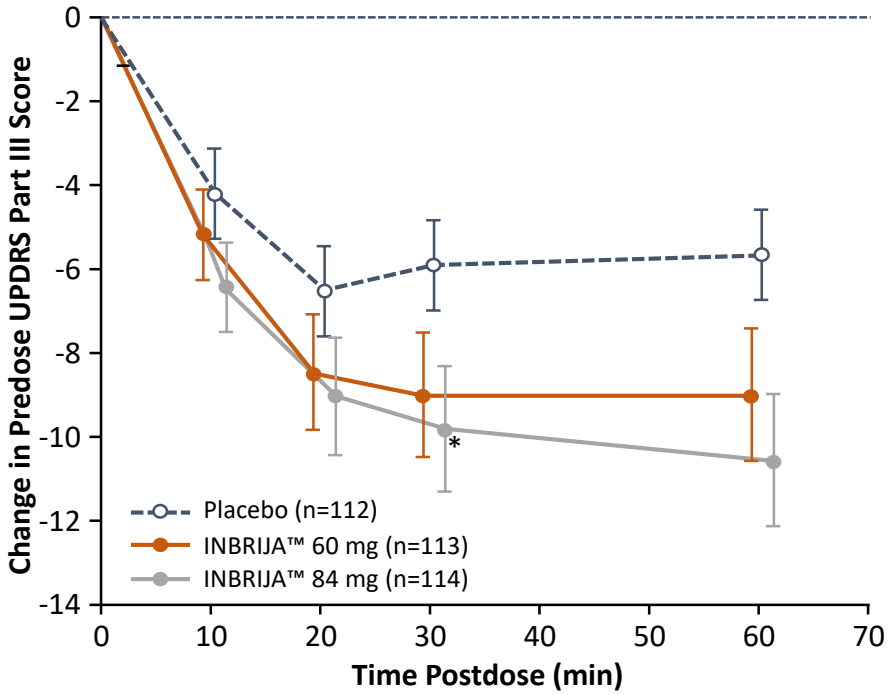
Peter A. LeWitt, MD, MMSc,[1*] Robert A. Hauser, MD, MBA,[2] Donald G. Grosset, MD,[3] Fabrizio Stocchi, MD,[4] Marie-Helene Saint-Hilaire, MD,[5] Aaron Ellenbogen, DO, MPH,[6] Mika Leinonen, MSc,[7] Neil B. Hampson, MD,[8] Tia DeFeo-Fraulini, MS,[9] Martin I. Freed, MD, FACP,[9] and Karl D. Kieburtz, MD, MPH[10]

Inhaled Levodopa

- The CVT 301 study included 86 patients with PD who experienced at least two hours of "off" time per day. They were randomly assigned to either CVT-301 or placebo in addition to their oral LD regimen. Each participant was told to self-administer the drug as needed for "off" states up to three times per day over a four-week period. During the first two weeks, participants took 35mg of inhaled LD with each administration. This was increased to 50mg for weeks three and four.

CVT 301

- Phase 3 randomized, double-blind, placebo-controlled trial in 351 patients with PD experiencing motor fluctuations while on a levodopa plus a dopa-decarboxylase inhibitor regimen[a]
- LS mean change in UPDRS Part III score from predose to 30 minutes postdose at Week 12 was -9.8 for INBRIJA™ 84 mg vs -5.9 for placebo (*P*=0.0088)
- At Week 12, the percentage of **patients maintaining** an "ON" state through 60 minutes with INBRIJA™ 84 mg was 58% vs 36% with placebo (*P*=0.0027)

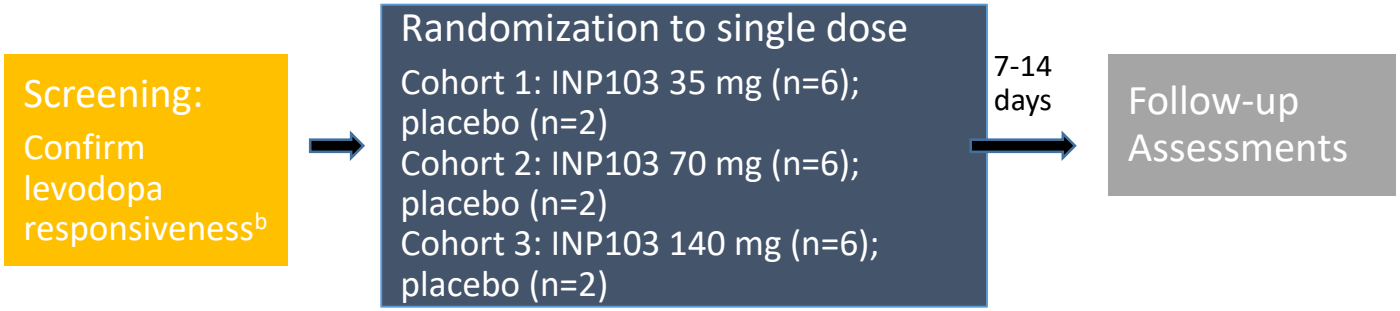


[a]Daily "OFF" periods of ≥2 hours and showed an improvement of ≥25% in the UPDRS motor score from "OFF" to "ON" state after use of an oral levodopa plus a dopa-decarboxylase inhibitor combination. Patients were randomized to receive placebo, INBRIJA™ 60 mg, or INBRIJA™ 84 mg, self-administered on an as-needed basis (up to 5 times per day). The total patient population had a mean disease duration of 8.3 years, mean total of 5.4-5.6 "OFF" hours per day, and 63-66% of patients had a modified Hoehn and Yahr score <2.5.

LeWitt PA, et al. *Lancet Neurol*. 2019;18:145-154.

Intranasal Levodopa

- INP103/POD® Levodopa is a drug device combination that delivers levodopa to the highly vascularized upper nasal cavity
  - Targeting upper nasal cavity minimizes the amount of drug dripping out of the nose or running into the pharynx after administration
- A randomized, double-blind, placebo-controlled phase 2a study is evaluating INP103 in 24 patients with idiopathic PD and "OFF" episodes while on stable levodopa



- Primary endpoint: safety and tolerability of single-dose INP103 in patients with PD during an "OFF" episode
  - All PD medications stopped at 22:00 the evening before dosing
  - When morning "OFF" confirmed, benserazide 25 mg administered
  - 60 minutes later, INP103 or placebo administered

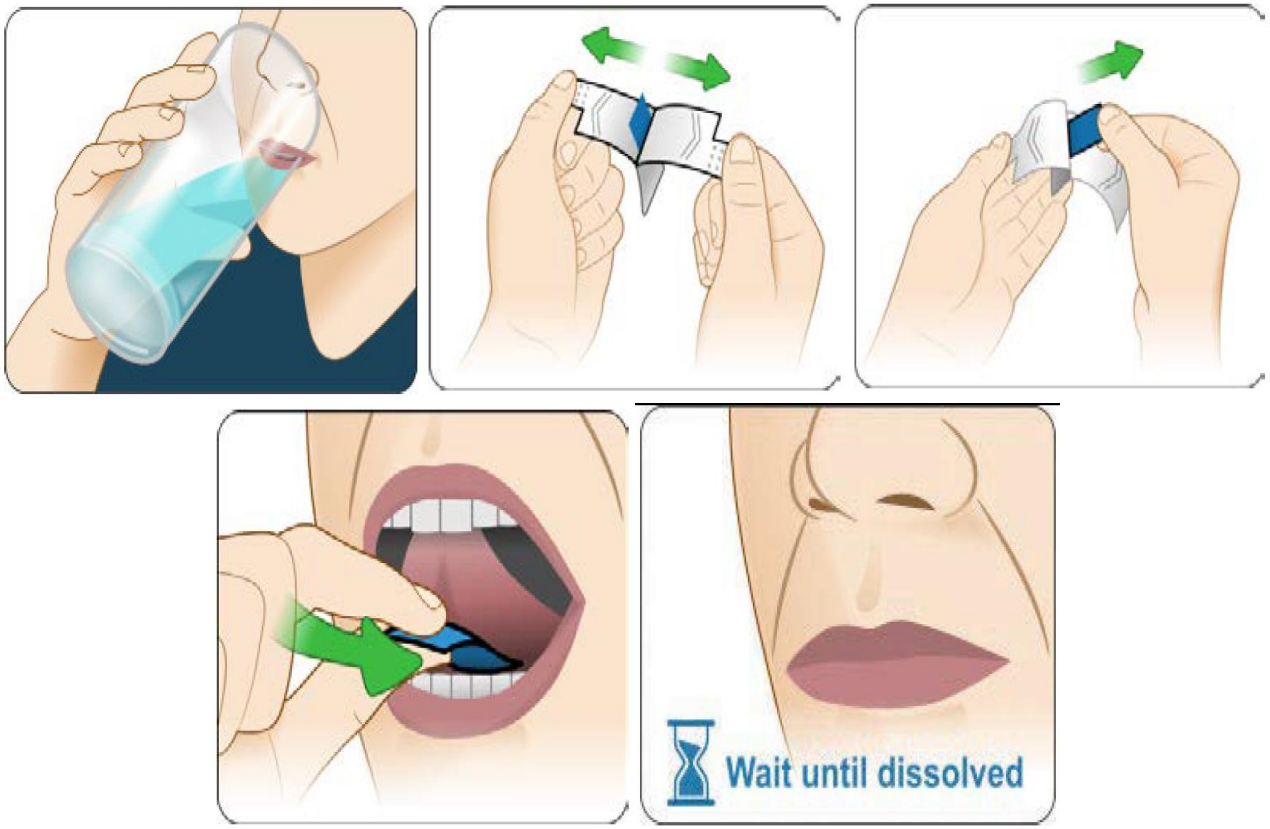
[a]Patients must be modified Hoehn and Yahr stage 1-3 when "ON."
[b]Patients must demonstrate 30% DA responsiveness by UPDRS Part III Motor Examination Score to their usual anti-"OFF" medication during the screening period.

Shrewsbury SA, et al. Presented at: World Congress on Parkinson's Disease and Related Disorders; August 19-22, 2018; Lyon, France.

APOMORPHINE -APL-130277 SUNOVION

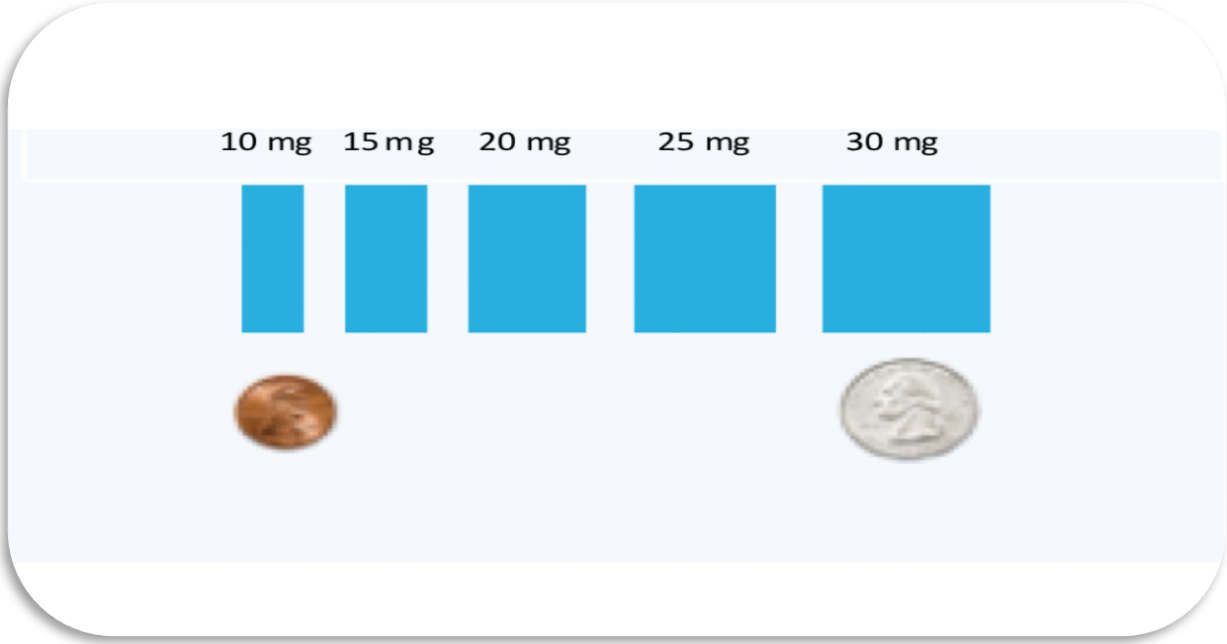
- Sublingual apomorphine strip
- Thin film bi-layer
  - First layer contains apomorphine - designed for rapid diffusion and absorption
  - Second layer contains a buffer - designed to neutralize acid generation and prevent skin/ mucosal lesions and irritation

Apomorphine Sublingual Film



Data on file, Sunovion Pharmaceuticals Inc.

APL-130277 Sublingual Apomorphine



As fast as 10 sec, with no lag !

Apomorphine Hydrochloride

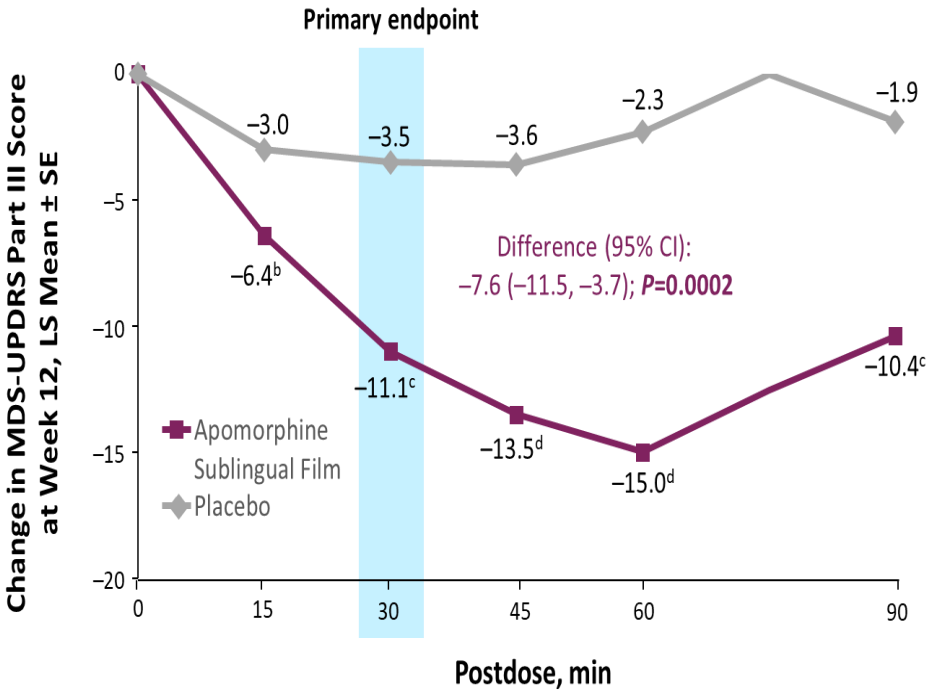
Buffer, pH modifier

CYNAPSUS

- Apomorphine dose is compatible with thin-film technology
- API in very rapid dissolving form (milled or amorphous)
- API + buffer react in-situ to form “free-base”
- Free base has highest absorption rate, best bioavailability

Apomorphine Sublingual Film – Efficacy

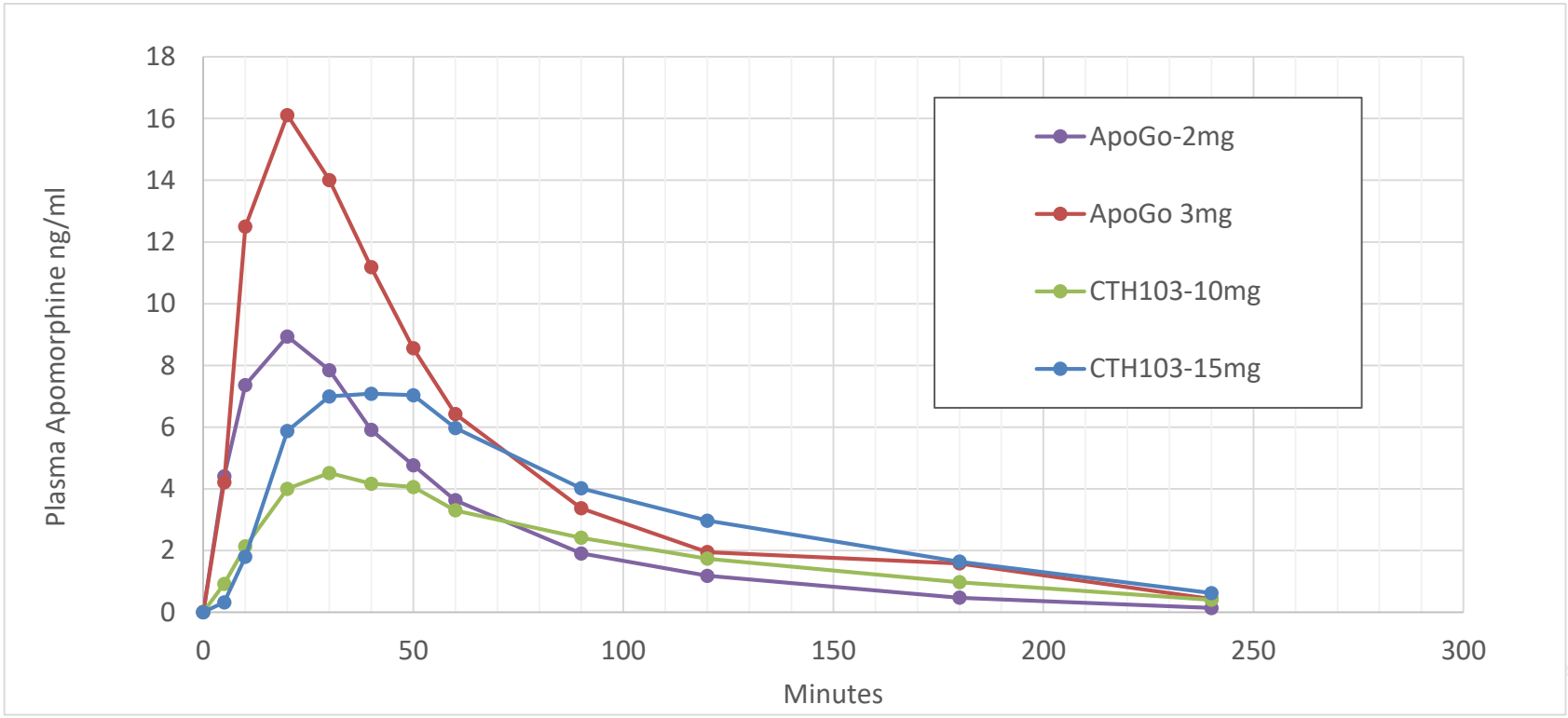
- Phase 3 randomized, double-blind, placebo-controlled trial in 109 patients with idiopathic PD and "OFF" episodes[a]
- LS mean change in MDS-UPDRS Part III score from predose to 30 minutes postdose at Week 12 (primary endpoint) was –11.1 for apomorphine sublingual film and –3.5 for placebo (*P*<0.0002)
- Significantly more patients receiving apomorphine sublingual film achieved a self-rated FULL "ON" response within 30 minutes postdose compared with placebo at Week 12 (35% vs 16%; *P*=0.0426; key secondary endpoint)



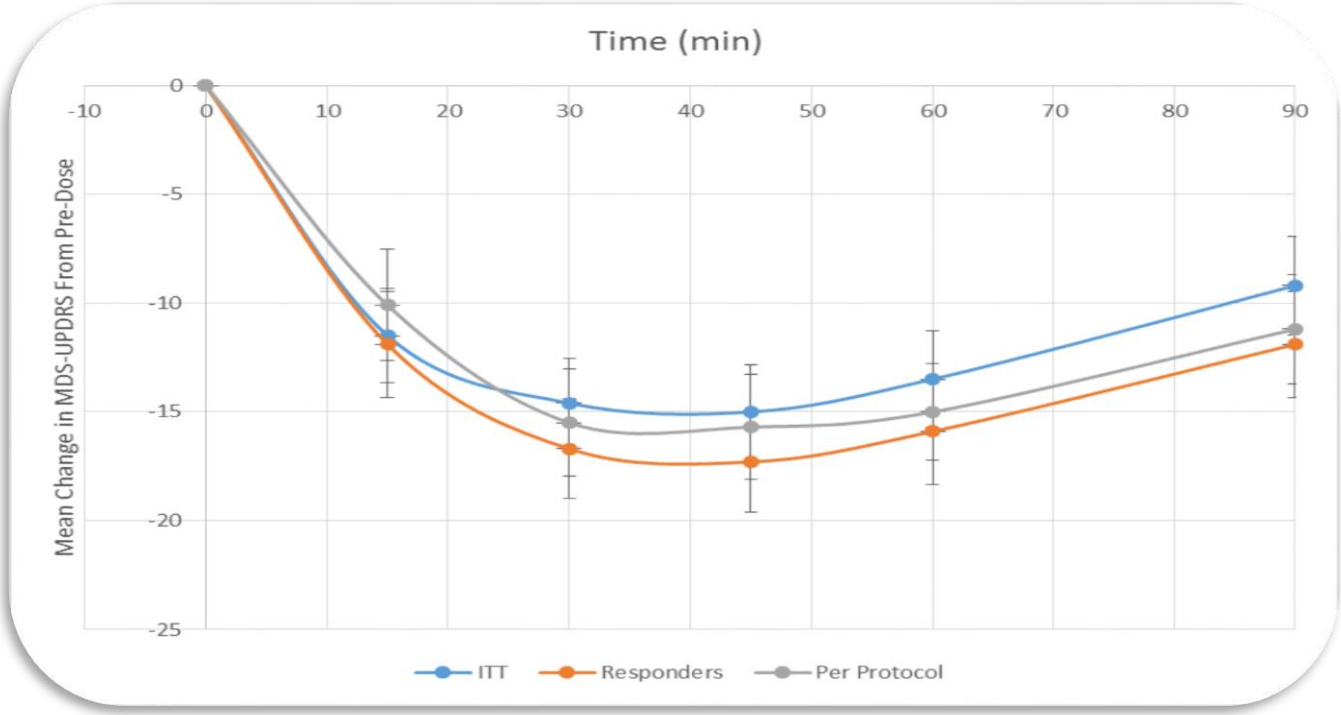
[a]Patients had a modified Hoehn and Yahr stage of 1-3 when "ON," ≥1 "OFF" episode per day, and ≥2 hours total daily "OFF" time; [b]*P*<0.05. [c]*P*<0.001. [d]*P*<0.0001.

Factor SA, et al. Presented at: International Congress of Parkinson's Disease and Movement Disorders (MDS), October 5-9, 2018; Hong Kong. Poster 247.

Apokyne VS APL-130277 - PK



Mean Change in UPDRS-III Score



Adenosine A2A receptors antagonists

- Adenosine A2A receptors are predominantly expressed in the GABAergic striato-external pallidal output neurons.
- Adenosine A2A receptor activation increases the excitability of the GABAergic striato-external pallidal output neurons via adenosine A2A receptors in the striatum and external globus pallidus.
- Thus, blockade of adenosine A2A receptors would result in a decrease in excessive activation of the striato-external pallidal output pathway, restore the balance in the basal ganglia thalamocortical circuit and provide an alternative, nondopaminergic approach to symptomatic relief of PD.

Istradefylline: selective A2A adenosine receptor antagonist

Movement Disorders
Vol. 25, No. 10, 2010, pp. 1437–1443

Clinical Efficacy of Istradefylline (KW-6002) in Parkinson's Disease: A Randomized, Controlled Study

Yoshikuni Mizuno, MD,[1]* Kazuko Hasegawa, MD,[2] Tomoyoshi Kondo, MD,[3] Sadako Kuno, MD,[4] and Mitsutoshi Yamamoto, MD[5]; The Japanese Istradefylline Study Group

- A total of 363 subjects were randomly assigned to receive 20 mg/day (n=119) or 40 mg/day istradefylline (n=125), or placebo (n=119). The primary outcome variable was the change from baseline at endpoint in daily OFF time based on patients' ON/OFF diaries.

A Randomized Trial of a Low-Dose Rasagiline and Pramipexole Combination (P2B001) in Early Parkinson's Disease

C. Warren Olanow, MD,[1,2*] Karl Kieburtz, MD,[1,3]
Mika Leinonen, MSc,[1,4] Lawrence Elmer, MD,[5]
Nir Giladi, MD,[6] Robert A. Hauser, MD,[7]
Olga S. Klepiskaya, MD,[8] David L. Kreitzman, MD,[9]
Mark F. Lew, MD,[10] David S. Russell, MD,[11]
Shaul Kadosh, MSc,[12] Pninit Litman, PhD,[13]
Hadas Friedman, MSc,[13] Nurit Linvah, PhD,[13] and
for the P2B Study Group[1]

- Novel slow release, low dose of Rasagiline and Pramipexole, taken once-daily
- Preclinical studies demonstrated that this combination provides sinergistic effects in MTPP-treated rodents with respect on motor benefit and striatal dopamine levels
- The slow release formulation showed enhanced motor benefit compared to the same doses of the IR of both drugs

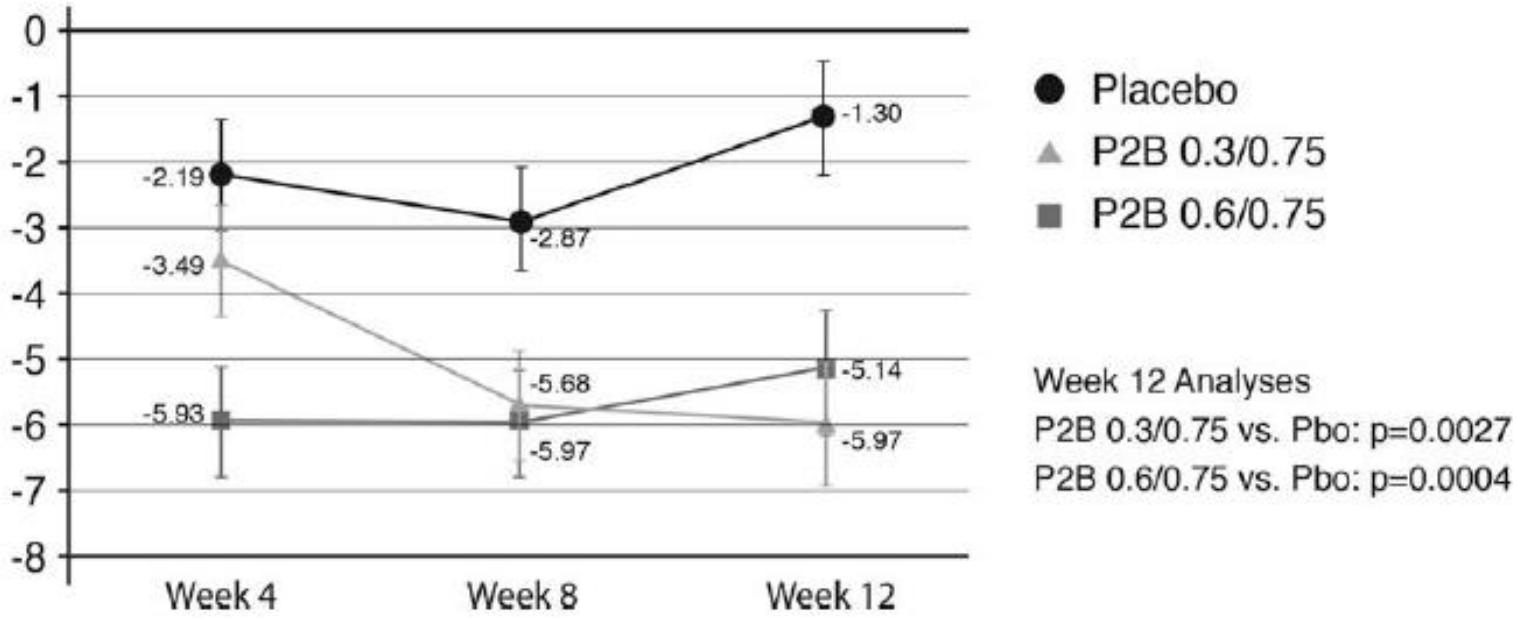
12 week, Prospective, placebo-controlled, double blind study testing two doses of P2B001 in untreated PD patients

- Two dosages/matching placebo:

  PPX 0.3 mg + RAS 0.75 mg (P2B001 0.3/0.75 mg)

  PPX 0.6 + RAS 0.75 mg (P2B001 0.6/0.75 mg)
- Primary Endpoint: Change in Total UPDRS I-III between baseline and final visit
- Secondary Endpoints: Change in PDQ 39, UPDRS II and III subscores, responders analysis (i.e. improvement of $\geq$4 point in Total UPDRS) for each dosage between baseline and final visit
- 149 subjects enrolled, 136 completed the study

Results of P2B001 study:



- Mean change ± standard deviation from baseline in total UPDRS score at each visit

Treatment of Dyskinesia

Metabotropic glutamate receptor antagonists

- L-Dopa-induced dyskinesias (LID) are consistently associated with abnormal glutamate transmission in the basal ganglia in rodent and primate models of PD and LID. Extracellular glutamate levels are markedly increased in the basal ganglia of dopamine-lesioned rats receiving L-Dopa. The putative sources of this glutamate are neurons extending to the striatum from the cortex.
- There are two subtypes of glutamate receptor: **ionotropic** and **metabotropic.**

Glutamate Receptor Modulator: PXT002331
PREXTON - LUNDBECK

- mGluR4 receptors are localized presynaptically on the striato-pallidal meurons and on the subthalamo-nigral projections
- mGluR4 activation decreases GABAergic and glutamatergic transmission and by restoring the equilibrium between the direct and indirect pathways, may improve motor function in PD
- PXT002331 is the first MgluR4 positive Allosteric Modulator, a new class of drugs, being developed for PD

Glutamate Receptor Modulator

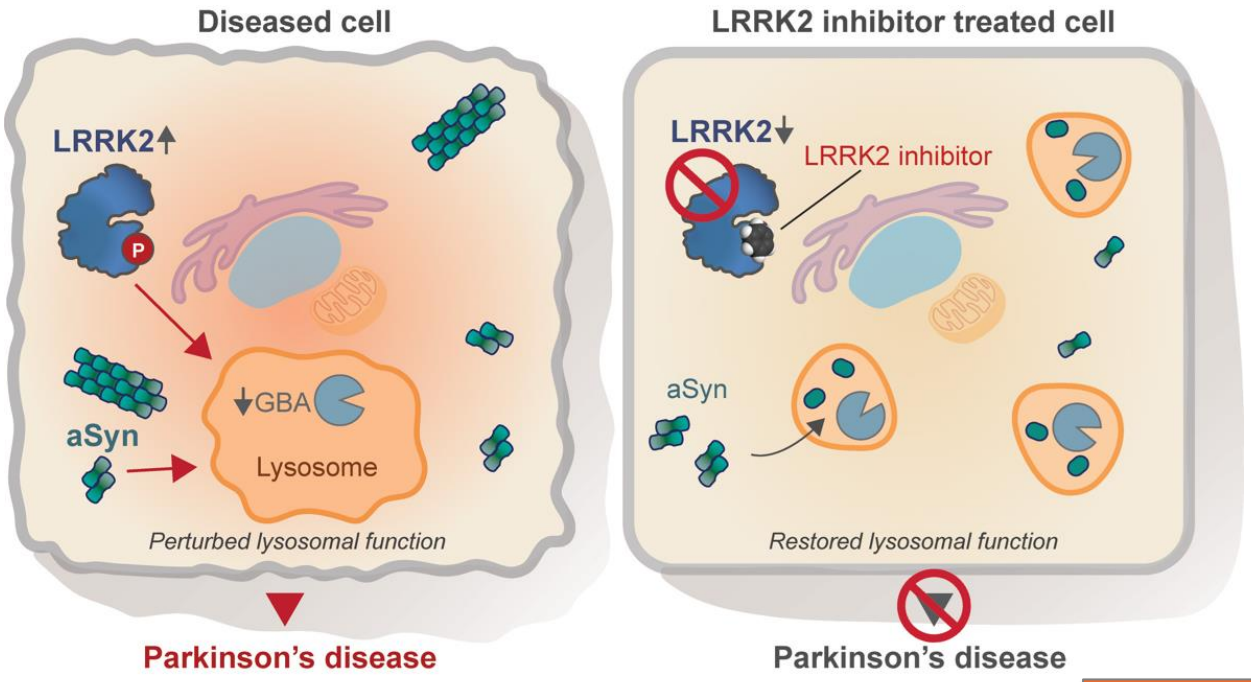
- Several studies in MPTP primates have demonstrated the efficacy of PXT002331 in the treatment of motor fluctuations and induced dyskinesias, without inducing any apparent change in behaviour, or any cognitive impairment or dyskinesia.
- **A Multi-center, Double-Blind, Randomized, Placebo-Controlled, Parallel-arm phase IIa trial to Evaluate the Efficacy, Safety and Tolerability of 28-Day Oral Treatment with PXT002331 in Reducing Motor Complications of Levodopa Therapy in Parkinson's Disease Patients Experiencing End-of-Dose Wearing Off and Levodopa-Induced Dyskinesia.**

New Drugs

- Drug-induced dyskinesia
  - **Buspirone + Zolmitriptan** (Contera Pharma)
    - Agonista recettori Serotoninergici 1A, 1B, 1D
  - **Foliglurax PXT002331** (Lundbeck)
    - MGluR4 PAM: L'attivazione di mGluR4 riduce la trasmissione GABAergica e glutamatergica

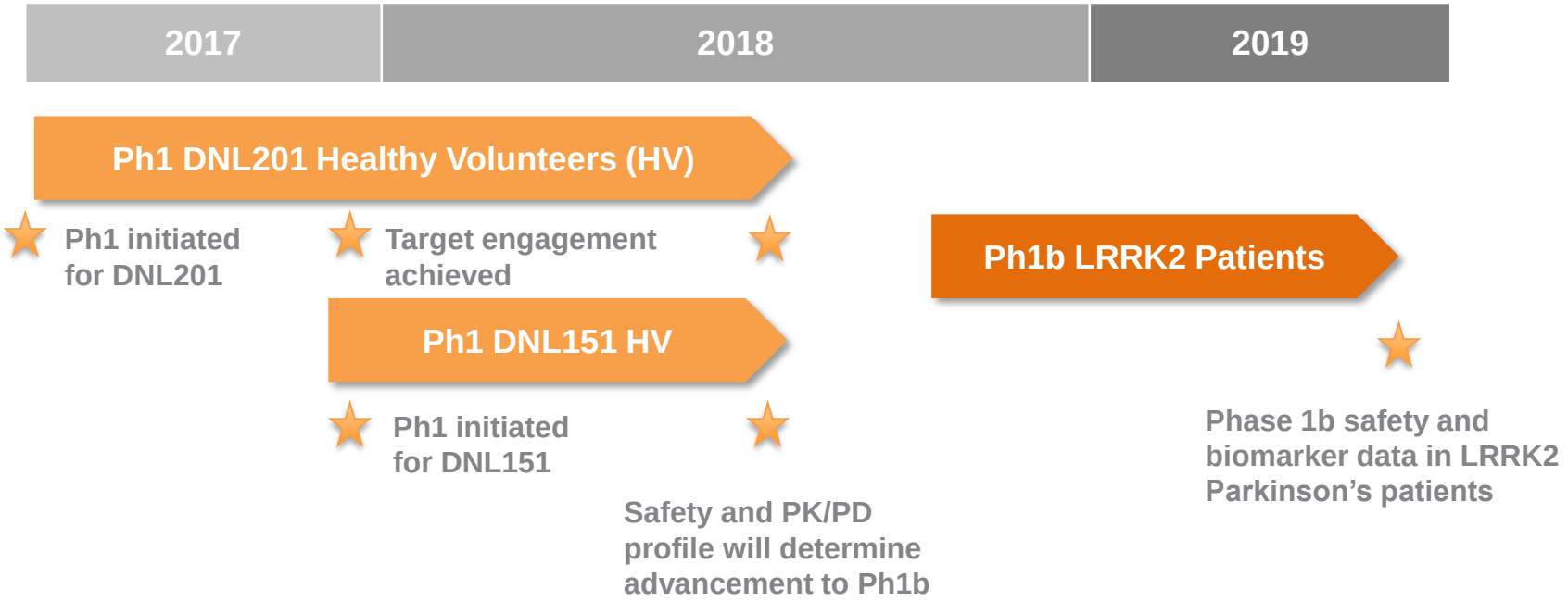
LRRK2 HYPERACTIVITY DRIVES LYSOSOMAL DYSFUNCTION AND PD

- Increased LRRK2 kinase activity impairs lysosomal function and drives familial PD
- LRRK2 inhibition can restore normal lysosomal function and reduce toxicity in PD models



LRRK2 Inhibitor

DENALI LRRK2 CLINICAL PROGRAM SUMMARY

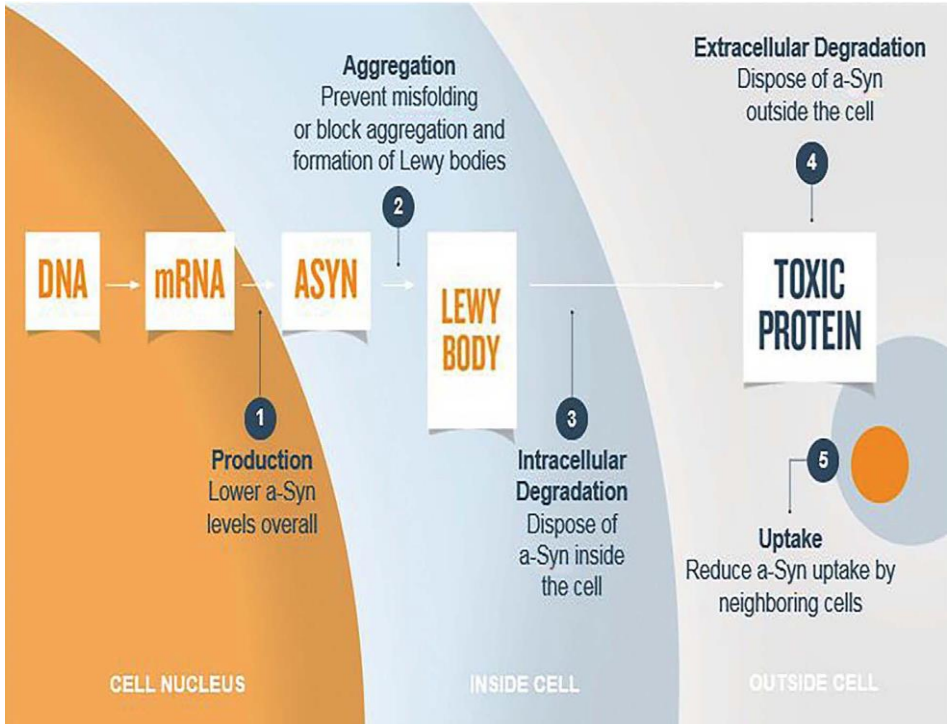


- DNL201 and DNL151 are CNS-penetrant, reversible, small molecule inhibitors of LRRK2 kinase
- Phase 1 evaluation of safety, PK and pharmacodynamics are ongoing

LRRK2 Inhibitor

Potential therapeutic targets for Synucleinopathies

Parkinson's disease (PD), Dementia with Lewy bodies (DLB) and Multiple System Atrophy (MSA)



1 Reducing alpha-syn production

2 Inhibiting alpha-syn aggregation

3 Promoting degradation of intracellular alpha-syn aggregates

4 Increase extracellular alpha-syn degradation: active and passive immunotherapies

(Brundin P et al, Exp Neurol 2017)

Therapeutic approaches to target alpha-synuclein pathology

1 Reducing alpha-synuclein production

Beta-2AR agonists (currently approved for asthma)?
Preclinical studies: clenbuterol lowered a-syn expression by over 35%, in dose-dependent manner
Epidemiological studies (Norway): treatment with beta-2AR agonist salbutamol was associated with lower risk of PD and conversely beta-2AR antagonist propanolol was associated with an increased PD risk (Mittal 2017)

The β2-adrenoreceptor (β2AR) is a regulator of the α-synuclein gene (SNCA)
Beta-2AR agonists should be tested as potential disease-modifying agents in PD

2 Inhibiting alpha-synuclein aggregation

Intrabodies:
- small antibody fragments (140-250 amino acids) that target antigens intracellularly
- can bind a-syn monomers and prevent them from oligomerizing
- unlike immunotherapies, intrabodies require direct CNS delivery using viral vectors

NPT200-11 (Neuropore therapies in partnership with UCB Pharma): no ongoing trials, only one phase 1 completed in HS

Therapeutic approaches to target alpha-synuclein pathology

3 Promoting degradation of intracellular alpha-synuclein aggregates

Enhancement of autophagic processes → increased clearance of pathological a-syn

Nilotinib: approved for Chronic Myelogenous Leukemia
was shown to attenuate a-syn levels in A53T transgenic mice and protect substantia nigra dopamine neurons from toxicity in a model with a-syn overexpression (Hebron 2013)

Drugs used in oncology are limited in their therapeutic potential for CNS disorders because of pharmacokinetics (poor absorption across the BBB) and small therapeutic window for chronic usage such required in PD
A recent small, open-label study in PDD and DLB patients tested nilotinib at doses much lower than those used against cancer (Pagan et al., J Parkinson Dis 2016)

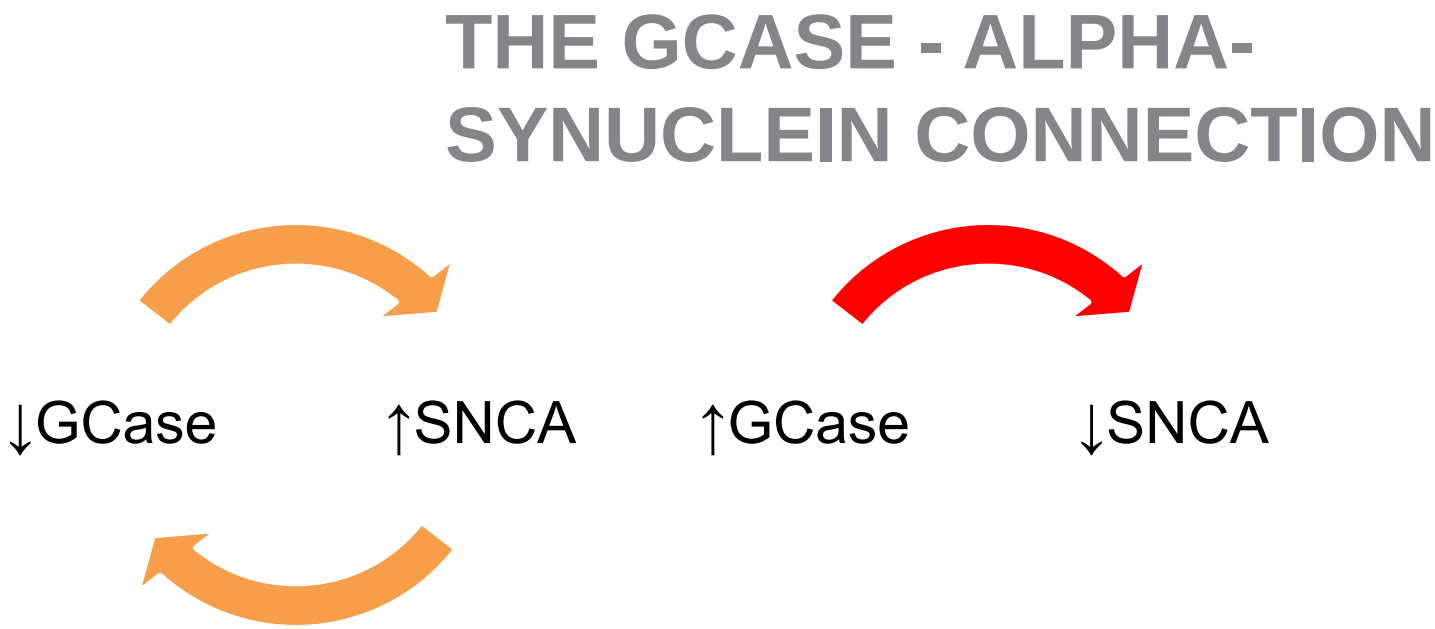
Nilotinib Effects in Parkinson's Disease and Dementia with Lewy Bodies

Primary outcomes: safety and tolerability. Clinical outcomes were exploratory.
12 subjects randomized into Nilotinib 150 mg (n = 5) or 300 mg (n = 7), orally every day for 24 weeks.
Nilotinib appear to be safe and tolerated, is detectable in the cerebrospinal fluid (CSF)
Motor and cognitive outcomes suggest a possible beneficial effect on clinical outcomes.

Therapeutic approaches to target alpha-synuclein pathology

3 Promoting degradation of intracellular alpha-synuclein aggregates

Action on Lysosomal enzyme β-glucocerebrosidase (GBA)
GBA enzyme function represents an interesting pharmacological target for PD:
preclinical studies suggest that increasing GBA enzyme activity can reduce alpha-synuclein levels



Schapira Lancet 2014

Therapeutic approaches to target alpha-synuclein pathology

Promoting degradation of intracellular alpha-synuclein aggregates

MOVES-PD:
A Global Study to Assess the Drug Dynamics, Efficacy, and Safety of GZ/SAR402671 in Parkinson's Disease Patients Carrying a Glucocerebrosidase (GBA) Gene Mutation (NCT02906020)
Phase 2 (Genzyme/Sanofi)
GZ/SAR402671 inhibits the production of glycosphingolipids (substrate for GCase)

Ambroxol: approved mucolytic, acts as a chaperone and improves lysosomal function in cells with GBA mutations in vitro.
There are currently two separate phase 2 trials ongoing that are testing safety, tolerability and efficacy of Ambroxol in PD:

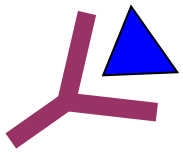
NCT02941822
Ambroxol in Disease Modification in Parkinson Disease (AiM-PD)
20 patients (10 GBA-positive & 10 GBA-negative status)
Active not recruiting

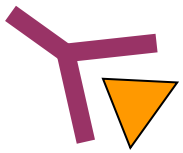
NCT02914366
Ambroxol as a Treatment for Parkinson's Disease Dementia
Last update 2017

Therapeutic approaches to target alpha-synuclein pathology: increase extracellular degradation

Tailored Antibodies

Original





Mimotope / AFFITOPE®

Active immunotherapy

AFFITOPE

PD01A and PD03A s.c

Phase 1 studies (AFF008, AFF008E, AFF008A, AFF008AA: PD01A low dose -15- vs high dose -75) completed in PD patients and small numbers of MSA subjects (AFF009-AFF011)

AFFITOPEs: short immunogenic peptides (B response) containing a sequence too short to induce T cell reponse but able to mimic original epitope and designed to prevent cross-reactivity of the induced antibodies with the other synuclein family members such as bSyn

Active Immunization Therapies for Parkinson's Disease and Multiple System Atrophy

Therapy	Indication	Intervention	Identifier	Title	Phase	Sponsor
Active immunization	PD	PD01A	NCT01568099	Tolerability and Safety of Subcutaneous Administration of Two Doses of AFFITOPE® PD01A in Early Parkinson's Disease	Phase I	AFFiRiS
	PD	PD01A	NCT02216188	Follow-up Study to Assess One Boost Immunization With AFFITOPE® PD01A With Regard to Safety and Clinical Activity	Phase I	AFFiRiS
	PD	PD01A	NCT01885494	AFF008E: Observational Phase 1b Follow-up Extension Study for Patients With Parkinson's Disease After Immunization With AFFITOPE® PD01A	Phase Ib	AFFiRiS
	PD	PD03A	NCT02267434	Study Assessing Tolerability and Safety of AFFITOPE® PD03A in Patients With Early Parkinson's Disease (AFF011)	Phase I	AFFiRiS
	MSA	PD01A; PD03A	NCT02270489	Study Assessing Safety and Therapeutic Activity of AFFITOPE® PD01A and PD03A in Patients With Early MSA	Phase I	AFFiRiS

Summary of phase I clinical studies on PD and MSA patients, now completed

Objectives were safety, tolerability and immunogenicity.
Studies were not designed to assess clinical efficacy, moreover lack of double blind design: no peer reviewed publication available, data published only by means of Affiris announces

According to presented data:
Immune response in 86% of vaccinated PD patients, with specific antibodies generated in the 63% of responders.
No long-term safety concerns (up to 48 months)
Clinical efficacy needs to be confirmed in phase 2 studies

Schneeberger, MDS 2015

Therapeutic approaches to target alpha-synuclein pathology: increase extracellular degradation

Passive immunotherapy: monoclonal antibodies against a-syn

PRX002 (Prothena) **target: C-terminus domain**
Phase 1 study completed in PD patients, results published;
Phase 2 ongoing

BIIB054 (Biogen) **target: N-terminus domain**
Phase 1 study completed in PD patients, results published;
Phase 2 ongoing

MEDI1341 (AstraZeneca)
a-syn antibody for PD
Phase 1 study ongoing in HS (NCT03272165)
Estimated completion July 2020

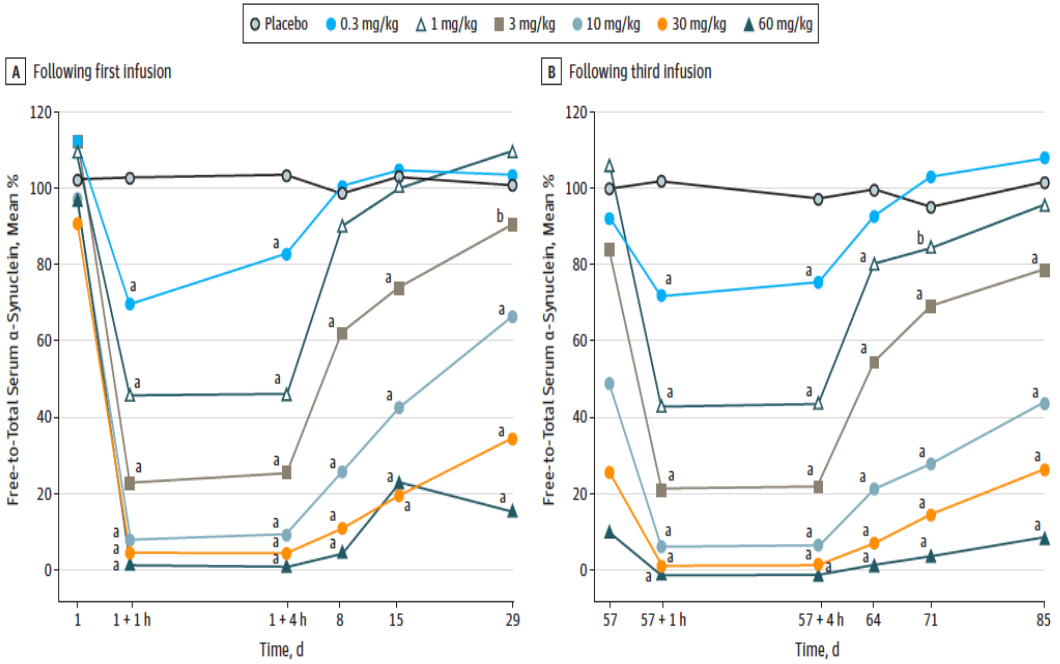
JAMA Neurology | Original Investigation

Safety and Tolerability of Multiple Ascending Doses of PRX002/RG7935, an Anti-α-Synuclein Monoclonal Antibody, in Patients With Parkinson Disease

A Randomized Clinical Trial

Single and multiple doses: generally safe and well tolerated

A dose-dependent increase of PRX002 in CSF was reported, reaching concentrations that may be expected to engage extracellular aggregated α-syn in the brain



(Jankovic J, 2018)

Phase 2: ongoing….
A Study to Evaluate the Efficacy of Prasinezumab (RO7046015/PRX002) in Participants With Early Parkinson's Disease (PASADENA)

Multicenter, randomized, double-blind, placebo-controlled study

Intravenous infusion every 4 weeks
Prasinezumab (RO7046015/PRX002)
3500/4500 mg or 1500 mg versus placebo

Part 1: 52-week, double-blind, placebo-controlled treatment period
Part 2: all-participants-on-treatment blinded dose extension for additional 52 weeks

Participants: early Parkinson's Disease (PD) untreated or treated with monoamine oxidase B (MAO-B) inhibitors since baseline.
Estimated completion date: february 2021
Primary outcome: MDS UPDRS I-II-III

prothena

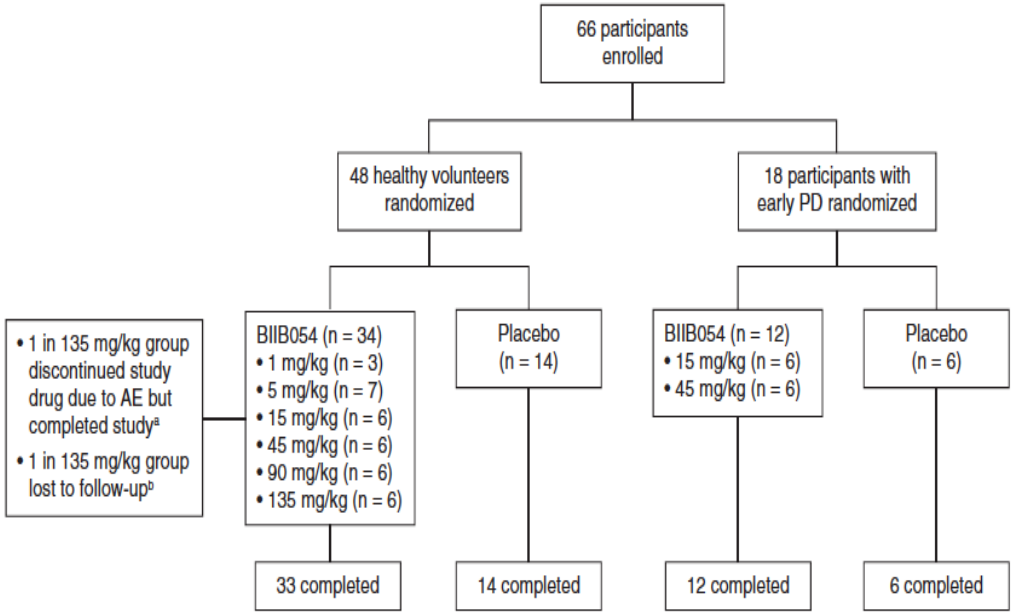
Roche

RESEARCH ARTICLE

Randomized Phase I Clinical Trial of Anti–α-Synuclein Antibody BIIB054

BIIB054: monoclonal human antibody targeting the N-terminal region of aggregated forms of α-synuclein (aa 4-10);

BIIB054 aims to slow the deposition of α-syn in early stage PD-patients
Results of the **Phase 1 single dose study in PD** patients: favorable PK, safety and tolerability profiles



(Brys, MDS 2019)

Phase 2 ongoing trial

Evaluating the Safety, Pharmacokinetics, and Pharmacodynamics of BIIB054 in Participants With Parkinson's Disease (SPARK)
NCT03318523

Active not Recruiting
Estimated completion June 2021
Iv infusion every 4 weeks
BIIB054 250-1250-3500 mg vs placebo

Primary endpoints: to test safety of BIIB054
Secondary endpoints: to evaluate pharmacodynamic, pharmacokinetic and immunogenicity of BIIB054

Inclusion criteria

- Diagnosis of PD within a maximum of 3 years prior to screening;
- Modified H&Y Stage <= 2.5
- No known or suspected causes of parkinsonism;
- Patient has not received any treatment for PD at last 12 weeks before; has received PD medications for a maximum of 30 days;
- DaT/SPECT consistent with parkinsonism
- MoCA score > 23

SPECTRAMAX LIGHT THERAPY DEVICE

Double-blind controlled trial of Spectramax™ light therapy for the treatment of Parkinson's disease patients on stable dopaminergic therapy

To evaluate the safety and effectiveness of Spectramax specialized bandwidth light therapy (LT) as adjunctive treatment in Parkinson's disease (PD).

Spectramax LT (950 lux blue/green LED light, λ = 460 - 570 nm) or control LT with a bandwidth that was not thought to be biologically active (100 lux white LED light, λ = 415 - 780 nm), for 60 minutes each evening for 6 months.

92 subjects (45 active, 47 sham) were enrolled at 3 centers in the US and Europe. Conclusion: Once-daily Spectramax LT is associated with a trend in improving PD symptom severity, and significantly improved non-motor symptoms and quality of life. LT was well-tolerated. Larger double-blind studies are warranted to further study the effectiveness of LT in PD.

Videnovic A. et al. 2018