Abstracts

Thirty Second Annual Symposium on Etiology, Pathogenesis, and Treatment of Parkinson Disease and Other Movement Disorders

Presented by the Parkinson Study Group, Huntington Study Group, Dystonia Study Group, Cooperative Ataxia Group, and Tremor Research Group

Saturday, April 6, 2019
Sheraton Grand at Wild Horse Pass, Phoenix, Arizona
8:00 a.m. to 1:30 p.m.

The symposium will consist of current issues in Parkinson disease and other movement disorders. There will be peer-reviewed platform and poster presentations designed to communicate recent research advances, including new pharmacological and non-pharmacological treatment options in the field of Parkinson disease, Huntington disease, ataxia, dystonia, Tourette’s syndrome, and tremor. This program is in honor of the late Clifford W. Shults, MD and hosted by the PSG Executive and Symposia Committees.

8:00-8:10 AM
Introduction and acknowledgements: Jeff Bronstein, MD, PhD, Chair, PSG Symposia Committee.

PLATFORM ABSTRACT PRESENTATIONS: This segment of the program consists of two 10-minute platform presentations with five minutes for questions and answers by the audience.

8:10-8:25 AM
Presentation: Efficacy and Safety of Apomorphine Sublingual Film for the Treatment of “OFF” Episodes in Patients with Parkinson’s Disease: A Phase 3, Double-Blind, Placebo-Controlled Trial

Objective: This phase 3, double-blind, placebo-controlled study evaluated the efficacy and safety of apomorphine sublingual film (APL-130277; APL) as an acute, intermittent therapy for “OFF” episodes in patients with Parkinson’s Disease (PD).

Background: A previous phase 2 study suggested that APL is efficacious for treatment of individual “OFF” episodes.

Methods: Adult patients with PD and ≥1 “OFF” episode per day while on stable doses of levodopa/adjunctive PD medications receiving increasing doses of APL (10–35 mg) in an open-label titration phase until a self-rated FULL “ON” response at week 12. The key secondary endpoint was the percentage of patients with a self-rated FULL “ON” response within 30 minutes postdose at week 12 was significantly higher for APL versus placebo (35% vs 16%; P=0.0426). The most common APL-associated, treatment-emergent adverse events (TEAEs) were nausea (28%), somnolence (15%), and dizziness (9%); the most common oral TEAE was oral mucosal erythema (7%); most TEAEs were mild and reversible upon treatment discontinuation.

Conclusion: APL was an efficacious and well-tolerated treatment for the acute, intermittent management of “OFF” episodes associated with PD.

8:25-8:40 AM
Presentation: Are Lewy bodies associated with sympathetic pathology in dementia subjects?
D.R. Shprecher, M. Callan, B. Cutler, G. Serrano, C.H. Adler, H.A. Shill, J. N. Caviness, M. N. Sabbagh, C. M. Belden, E. Driver-Dunckley, S. H. Mehta, L. I. Sue, K. J. Davis, E. Zamrini, T. G. Beach, C. Roberts Center, Banner Sun Health Research Institute, Sun City, AZ, USA; 2Civin Laboratory for Neuropathology, Banner Sun Health Research Institute, Sun City, AZ, USA; 3Department of Neurology, Mayo Clinic College of Medicine, Scottsdale, AZ, USA; 4Barrow Neurological Institute, Phoenix, AZ, USA; University of Arizona College of Medicine-Phoenix.

Objective: Determine if Alzheimer subjects with Lewy bodies show sympathetic cardiac denervation.

Background: Comorbid Lewy body (LB) pathology is very common in Alzheimer disease (AD), and may confound clinical trial design—yet there is no in-vivo test to identify it. Tissue studies have shown cardiac sympathetic denervation in Parkinson disease and dementia with Lewy bodies, but have not been explored in mixed AD/LB cases.

Methods: We analyzed 30 cases with autopsy-confirmed AD/DLB, 30 AD/LB not meeting DLB criteria, 30 AD-no LB, 30 incidental Lewy body disease (ILBD) and 22 controls without LB. Using tyrosine hydroxylase (TH) staining of epicardial and myocardial tissue, we tested the hypothesis that AD/LB will be distinguishable from AD without LB by the loss of cardiac noradrenergic nerve fibers, supporting the feasibility of clinically separating these conditions using cardiac nuclear imaging. Staining was graded on a 0–3 point Likert scale, (0=absent, 1=sparse, 2=moderate, 3= numerous).

1.46 with APL and –3.5 ± 1.29 with placebo (difference, −7.6 points; P=0.0002). Separation from placebo was seen as early as 15 minutes and persisted up to the 90-minute timepoint. The self-rated FULL “ON” response rate within 30 minutes postdose at week 12 was significantly higher for APL versus placebo (35% vs 16%; P=0.0426). The most common APL-associated, treatment-emergent adverse events (TEAEs) were nausea (28%), somnolence (15%), and dizziness (9%); the most common oral TEAE was oral mucosal erythema (7%); most TEAEs were mild and reversible upon treatment discontinuation.

Conclusion: APL was an efficacious and well-tolerated treatment for the acute, intermittent management of “OFF” episodes associated with PD.
Results: Kruskal-Wallis analysis of variance between groups indicated a significant difference (p = 0.008) between the groups (medians: control 2.5; ILBD 1.5; AD-DBL 1.0; PD 1.0; AD-LB 3.0; AD-no LB 2.0), and subsequent pair-wise Mann-Whitney analysis showed that PD (p = 0.014) and DBL (p = 0.008) subjects have significantly reduced TH fiber density as compared to controls. The TH density in ILBD hearts was midway between the control and PD or DBL groups but the difference was too small for this to reach significance (p = 0.16).

Conclusion: The clear separation of DBL from controls based on cardiac TH fiber density is the first report of a statistically significant difference between these groups. Our data therefore strengthen the rationale for using cardiac nuclear imaging with a nonadrenergic nuclear imaging ligand, metaiodobenzylguanidine (MIBG) to separate DBL from AD with DBL, an important concept as most cases of AD/DBL are not recognized as such during life. Our results indicate that MIBG would not be likely to clinically separate the AD/LB from AD subjects without LB.

KEYNOTE PRESENTATIONS: The theme for the next segment of the program is Advancing Clinical Trials in PD and Neurodegenerative Disorders. This segment consists of four (4) major talks with ample time for questions from the audience.

8:40-9:15 AM
Presentation: The rationale for targeting LRRK2 and GBA
Andrew West, PhD, Professor, Duke Center for Neurodegeneration Research, Departments of Pharmacology and Cancer Biology and Neurology, Durham, NC.

9:35-10:30 AM
Presentation: Parkinson Phenotype of Patients with LRRK2 and GBA mutations.
Susan Bressman, MD, Professor and Chair, Mount Sinai Beth Israel, New York, NY.

10:30-12:00 PM
Formal Poster Session: This session consists of presentation of posters by the presenting author with audience participation. A variety of current topics and late-breaking research on movement disorders are presented. Two short poster highlights kick-off the poster session (5 min).

Poster Highlight: Safety and Efficacy of VY-AADC01 for Medication Refractory Parkinson’s Disease in an On-going Phase Ib study, Chad Christine, presenting author.

Poster Highlight: Preliminary findings of the use of cannabis in Parkinson disease, Maureen Leehey, presenting author.

12:00-12:55 PM
Presentation: The Current Status of Clinical Trials Targeting Patients with LRRK2 and GBA mutations.
Brian Fiske, PhD, Senior Vice President, Research Programs, The Michael J. Fox Foundation for Parkinson’s Research, New York, NY.

12:55-1:25 PM
Presentation: Patient Perspectives on Living with an Inherited Form of Parkinson Disease.
Mr. Ofer Nemirowsky, Patient Advocate

CLOSING REMARKS. Jeff Bronstein, MD, PhD, Chair, PSG Symposia Committee.

POSTER 1
Symptom Improvements with Once-Daily Opicapone in Patients with Parkinson’s Disease and Motor Fluctuations: Results from a Phase 3, Randomized Clinical Trial (BIPARK-1)
M. Lew,1 K.A. Hauser,2 J. Ferreira,2 W. Poewe,4 O. Rascol,5 K. Olson,6 K. Farahmand,7 S. Siegert,6 J.F. Rocha,7 P. Soares-da-Silva,7,8 G.S. Liang,5, 6University of South Florida, Tampa, FL, USA; 2University College London, London, United Kingdom; 3Medical University of Innsbruck, Innsbruck, Austria; 4Medical University of Innsbruck, Innsbruck, Austria; 5Medical University of Innsbruck, Innsbruck, Austria; 6University Porto, Porto, Portugal; 7University Porto, Porto, Portugal.

Objective: To evaluate the efficacy of once-daily opicapone by baseline characteristics in adults with Parkinson’s disease (PD) and motor fluctuations.

Background: Catechol-O-methyltransferase inhibitors (COMT-I) were developed to prolong the clinical actions of levodopa in PD patients. Opicapone, a novel and highly selective COMT-I, is being developed in the U.S. as an adjunct to levodopa in adults with PD and motor fluctuations. The efficacy of once-daily opicapone was demonstrated in two international phase 3 studies, BIPARK-1 (NCT01568073) and BIPARK-2 (NCT01227655).

Methods: In BIPARK-1, 590 participants received 14-15 weeks of double-blind treatment with opicapone (5mg, 25mg, 50mg), entacapone (200mg), or placebo as an adjunct to their current levodopa regimen. The primary endpoint was the change from baseline in absolute OFF-time.

Results: Overall, 407 subjects were included in the full analysis set for efficacy analyses (5mg = 119, 25mg = 116, 50mg = 115, entacapone = 120, placebo = 120). A statistically significant decrease (improvement) in absolute OFF-time from baseline to Week 14/15 was observed with opicapone 50mg versus placebo (least squares mean change ± standard error, hours): 50mg, −1.99 ± 0.23; placebo, −1.08 ± 0.22; p=0.003. In the subgroup analyses, concurrent PD therapies did not have a significant interaction with treatment effect. Subgroup sizes and least squares mean changes in absolute OFF-time (± standard error, hours) were as follows: with DA (50mg [n=79], −1.87 ± 0.28; placebo [n=88], −0.97 ± 0.26); without DA (50mg [n=36], −2.05 ± 0.40; placebo [n=32], −0.76 ± 0.42); with DA+MAOBI (50mg [n=20], −1.43 ± 0.53; placebo [n=21], −0.92 ± 0.52); without DA+MAOBI (50mg [n=95], −2.07 ± 0.26; placebo [n=99], −0.95 ± 0.24).

Conclusion: Overall, once-daily opicapone 50mg was effective in reducing absolute OFF-time compared to placebo in PD patients taking levodopa. Similar improvement was observed in patients also taking concurrent DAs with or without MAOBI.

POSTER 2
BIPARK-2 Results: Efficacy of Once-Daily Opicapone for the Treatment of Patients with Parkinson’s Disease and Motor Fluctuations
R.A. Hauser,1 M. Lew,2 A.J. Lees,3 W. Poewe,4 O. Rascol,5 K. Olson,6 K. Farahmand,7 S. Siegert,6 J.F. Rocha,7 P. Soares-da-Silva,7,8 G.S. Liang,5, 6University of South Florida, Tampa, FL, USA; 2University of Southern California, Los Angeles, CA, USA; 3University College London, London, United Kingdom; 4Medical University of Innsbruck, Innsbruck, Austria; 5Medical University of Innsbruck, Innsbruck, Austria; 6University Porto, Porto, Portugal; 7University Porto, Porto, Portugal.

Objective: To evaluate the efficacy of once-daily opicapone by baseline characteristics in adults with Parkinson’s disease (PD) and motor fluctuations.

Background: Catechol-O-methyltransferase inhibitors (COMT-I) were developed to prolong the clinical actions of levodopa in PD patients. Opicapone, a novel and highly selective COMT-I, is being developed in the U.S. as an adjunct to levodopa in adults with PD and motor fluctuations. The efficacy of once-daily opicapone was demonstrated in two international phase 3 studies, BIPARK-1 (NCT01568073) and BIPARK-2 (NCT01227655).

Methods: In BIPARK-2, 407 participants received 14-15 weeks of double-blind treatment with opicapone (25mg, 50mg) or placebo, The primary endpoint was the change from baseline in absolute OFF-time.

Results: For the targeted opicapone dose (50mg) are presented. Results: 590 subjects were included in the full analysis set for efficacy analyses. (5mg=119, 25mg=116, 50mg=115, entacapone=120, placebo=120). A statistically significant decrease (improvement) in absolute OFF-time from baseline to Week 14/15 was observed with opicapone 50mg versus placebo (least squares mean change ± standard error, hours): 50mg, −1.99 ± 0.23; placebo, −1.08 ± 0.22; p=0.003. In the subgroup analyses, concurrent use of other PD therapies at baseline, including dopamine agonists (DA) and DA plus monoamine oxidase-B inhibitors (DA+MAOBI). Results for the targeted opicapone dose (50mg) are presented.

Results: In BIPARK-2, 407 participants received 14-15 weeks of double-blind treatment with opicapone (5mg, 25mg, 50mg), entacapone (200mg), or placebo as an adjunct to their current levodopa regimen. The primary endpoint was the change from baseline in absolute OFF-time.

Exploratory subgroup analyses were conducted in participants based on concurrent use of other PD therapies at baseline, including dopamine agonists (DA) and DA plus monoamine oxidase-B inhibitors (DA+MAOBI). Results for the targeted opicapone dose (50mg) are presented.

Results: 590 subjects were included in the full analysis set for efficacy analyses (5mg=119, 25mg=116, 50mg=115, entacapone=120, placebo=120). A statistically significant decrease (improvement) in absolute OFF-time from baseline to Week 14/15 was observed with opicapone 50mg versus placebo (least squares mean change ± standard error, hours): 50mg, −1.99 ± 0.23; placebo, −1.08 ± 0.22; p=0.003. In the subgroup analyses, concurrent PD therapies did not have a significant interaction with treatment effect. Subgroup sizes and least squares mean changes in absolute OFF-time (± standard error, hours) were as follows: with DA (50mg [n=79], −1.87 ± 0.28; placebo [n=88], −0.97 ± 0.26); without DA (50mg [n=36], −2.05 ± 0.40; placebo [n=32], −0.76 ± 0.42); with DA+MAOBI (50mg [n=20], −1.43 ± 0.53; placebo [n=21], −0.92 ± 0.52); without DA+MAOBI (50mg [n=95], −2.07 ± 0.26; placebo [n=99], −0.95 ± 0.24).

Conclusion: Overall, once-daily opicapone 50mg was effective in reducing absolute OFF-time compared to placebo in PD patients taking levo-dopa. Similar improvement was observed in patients also taking concurrent DAs with or without MAOBI.

Movement Disorders, Vol. 34, Suppl. 1, 2019
not have a significant interaction with treatment effect. Least squares mean changes in absolute OFF-time (± standard error, hours) were as follows: with DA (50mg, \(−2.01±0.28\); placebo, \(−1.14±0.28\)) without DA (50mg, \(−1.94±0.39\); placebo, \(−0.93±0.43\)), with MAOBI (50mg, \(−1.66±0.48\); placebo, \(−0.27±0.52\)), without MAOBI (50mg, \(−2.12±0.26\); placebo, \(−1.33±0.27\)), with DA+MAOBI (50mg, \(−1.27±0.61\); placebo, \(+0.05±0.64\)) without DA +MAOBI (50mg, \(−2.11±0.25\); placebo, \(−1.27±0.26\)).

Conclusions: Overall, once-daily opicapone 50 mg was effective in reducing absolute OFF-time compared to placebo in PD patients taking levodopa, with similar improvement observed in patients who were also taking concurrent DAs with or without MAOBIs.

**POSTER 3**

Safety results of a 12-month, dose-level blinded study of CVT-301 (levodopa inhalation powder) in patients with Parkinson’s disease

R. A. Hauser,1 C. H. Waters,2 M. Lew,3 E. S. Farbman,4 M. Klingler,5 C. Oh1 1National Parkinson Foundation Center of Excellence, University of South Florida, Tampa, FL; 2Columbia University Medical Center, New York, NY; 3Keck/University of Southern California School of Medicine, Los Angeles, CA; 4Roseman University, Las Vegas, NV; 5Acorda Therapeutics, Inc., 420 Saw Mill River Road, Ardsley, NY.

Objective: We present safety results of a 12-month extension study of a phase 3 trial (SPAN-PD284) of Inbrija (CVT-301), a levodopa inhalation powder developed for intermittent treatment of OFF symptoms in patients on a carbidopa/levodopa regimen.

Background: A 12-month, open-label, randomized, controlled study showed that patients with Parkinson’s disease (PD) treated with the adjunctive CVT-301 84 mg presented no clinically significant difference in pulmonary function vs. an observational cohort (Obs). Mean change from baseline at 12 months for forced expiratory volume in 1 second (FEV1) was \(−0.117\) L (Obs) and \(−0.105\) L (CVT-301); for forced vital capacity (FVC): \(−0.125\) L (Obs) and \(−0.155\) L (CVT-301); and for diffusion capacity of the lungs for carbon monoxide (DLCO): \(0.72\) mL/min/mmHg (Obs) and \(0.38\) mL/min/mmHg (CVT-301).

Design/Methods: Patients from previous CVT-301 studies, and eligible CVT-301-naïve patients, were enrolled. Patients maintained their oral carbidopa/levodopa regimen. All patients were on active CVT-301 treatment but were blinded to dose (60mg or 84mg N=325). Study visits occurred every 3 months. Pulmonary function was assessed by spirometry. Other safety assessments included in-clinic occurrence and severity of dyskinesia and dyskinesia assessment scales.

Results: Average number of CVT-301 doses was 1.94/day. 28 patients (8.6%) withdrew due to AEs. Overall most frequent AEs (≥5%) were cough (15.4%), fall (13.1%), upper respiratory tract infection (7.1%), and dyskinesia (5.1%). Severe AEs (≥1) were cough (1.9%) and dyskinesia (0.6%). There were no serious AEs of cough and 7 patients discontinued due to cough. In-clinic dyskinesia was recorded in 11.2% of patients (month 0) and 13.8% (month 12); most were mild; none rated severe. Overall FEV1 12-month mean change from baseline was \(−0.092\) L, for FVC the change was \(−0.097\) L, and for DLCO the change was \(−0.922\) mL/min/mmHg.

Conclusions: CVT-301 was well tolerated. The observed 12-month decline in pulmonary function was generally consistent with that reported in PD patients in the previous long-term safety study.

**POSTER 4**

Examining Parkinson’s Disease Psychosis Treatment Outcomes in the Real World: Interim Year 1 Findings from the INSYTE Observational Study

J.G. Goldman,1,2 S.H. Fox,3 S. Isaacs,4,5 D. Fredericks,6 J. Trotter,7 K. Healy,7 N.J. Larsen,9 A. Ryan,8 A. Shim,6 1Parkinson’s Disease & Movement Disorders, Shirley Ryan Abilitylab, Chicago, Illinois, USA; 2Northwestern University Feinberg School of Medicine, Chicago, IL, USA; 3Toronto Western Hospital, Toronto, Ontario, Canada; 4Parkinson’s Disease and Movement Disorders Center of Boca Raton, Boca Raton, Florida, USA; 5Florida International University Herbert Wertheim College of Medicine, Boca Raton, FL, USA; 6ACADIA Pharmaceuticals Inc., San Diego, California, USA; 7Worldwide Clinical Trials, Morrisville, North Carolina, USA.

Background: Approximately half of Parkinson’s disease patients experience psychotic symptoms during the course of the disease, but longitudinal studies have not evaluated treatment modalities and outcomes in actual medical practice, and minimal data are available on antipsychotic (AP) therapy in Parkinson’s disease (PD).

Objective: INSYTE is an ongoing prospective, observational study of PDP management and treatment outcomes, with the primary objective of examining the safety and efficacy of APs and other treatment approaches in the management of PDP, and how treatment decisions affect quality of life and patient and caregiver burden.

Methods: INSYTE is enrolling up to 750 patients and their caregivers from up to 100 sites in the United States. Participating patients will have a diagnosis of PDP prior to enrollment. INSYTE employs validated assessment instruments but does not impose a predefined visit schedule, medical tests, laboratory tests, procedures, or interventions. Data will be compiled for up to three years from enrollment.

Results: Baseline findings from 334 enrolled participants indicate that most are white (95%), male (63%), retired (76%), married (75%), and live in a private residence (92%). Average age is 74.7 years. Most patients (86%) have a caregiver. Mean durations since PD and PDP diagnosis were 8.8 and 2.6 years, respectively. At baseline, 12% had no cognitive impairment, 50% had slight or mild impairment, and 38% had moderate or severe impairment. At enrollment, 33% of patients were using an AP. Of those, 82% were on monotherapy (primarily pimavanserin [50%] or quetiapine [25%]). Pimavanserin+quetiapine was the most frequently employed combination AP therapy (15%).

Conclusion: INSYTE is the largest observational study to date to explore PDP treatments and patient outcomes in a real-world setting. Results will better inform the scientific community on current practices and potentially support updates to treatment guidelines and standards of care for management of PDP. Previously presented at the 2019 Annual Meeting of the American Association for Geriatric Psychiatry; Mar 01–04, 2019; Atlanta, Georgia, USA.

FUNDING: The INSYTE Observational Study is funded by ACADIA Pharmaceuticals, Inc.

**POSTER 5**

Prevalence and Patterns of Rest and Action Tremor in Drug-naive Parkinson’s Disease

D. K. Gupta,1 J. T. Boyd,1 S. Kuo.2 1Binter Center for Parkinson’s Disease and Movement Disorders, University of Vermont Medical Center, Burlington, Vermont, USA; 2Center for Parkinson’s Disease and Movement Disorders, The Neurological Institute of New York, Columbia University Medical Center, New York City, New York, USA.

Objective: We aimed to describe the prevalence and patterns of rest and action tremor in a large, prospective cohort of PD patients.

Background: Rest tremor (RT) is a cardinal and most visible symptoms of PD. However, there is a surprising lack of data its prevalence in PD. The relationship of RT with action tremor (AT) in PD is also remains poorly described.

Methods: Baseline data of PD patients (n = 418) from the Parkinson Progression Marker Initiative (PPMI) study, were accessed as of September 1, 2019. RT, postural tremor, and kinetic tremor were captured by value of >= 1 on items 3.17, 3.15, and 3.16, respectively, in part III (motor) of the MDS-UPDRS scale. AT was defined by presence of both postural AND kinetic tremor. RT severity was captured by adding five sub-items of RT (3.17) and then multiplying the sum with constancy of RT (3.18).

Results:

- Nearly 88% of patients had at least one type of tremor, compared to 27% of patients with all three types of tremor.
- RT was the most common (~ 69%), followed by postural tremor (~ 63%), and kinetic tremor (~ 51%).
- AT was present in 37% (156/423) patients, among which 74% also had RT.
- Among patients with RT (290/423), 40% had AT. In contrast, among patients with no RT (156/423), 30% had AT.
- Among patients with RT (290/423), those with AT had significantly (p = 0.000) higher RT severity (5.7 ± 5.4) versus those without AT (3.9 ± 3.3).

Conclusions: AT is present in 40% of PD patients with RT, compared to 30% of PD patients without RT. The severity of RT is greater in PD patients with AT versus those without AT. These results suggest that there may be cross-interactions between basal ganglia and cerebellothalamic circuitry in mediating RT and AT, respectively, in PD.
POSTER 6

Improving Clinical Trials Through The Science of Patient Engagement
K. Schroeder,1 M. Feeney,1 C. Evers,1 C. Gallagher,1 V. Todaro.1 1Parkinson’s Foundation, New York, NY, USA.

Background: Patient engagement is the inclusion of patients as equal partners in research decision making, at each step from determining therapeutic targets to disseminating study results. Although patient engagement is a rapidly expanding field, rigorous methodology and metrics are not established. To fill this gap, the Parkinson’s Foundation is developing an evidenced-based, standardized approach to patient engagement.

Objective: To make Parkinson’s disease research more efficient and effective by developing and implementing the science of patient engagement in research.

Methods: A landscape review of patient engagement was conducted. Gaps in methodologies, metrics, tools and best practices were identified. Four gaps were selected as priorities to address:

- Poorly-defined metrics for the quality, quantity and impact of patient engagement.
- Few standardized tools.
- Lack of clarity of the role of patient advocacy groups.
- No models for partnerships between international patient organizations.

A strategic plan was created to address these gaps and establish a basis for the science of patient engagement.

Results: The Parkinson’s Foundation launched one project to better define metrics in patient engagement. A standardized tool for patient engagement which the Foundation took a leadership role in developing is in beta testing. Another project is underway to address the lack of clarity of the role of patient advocacy groups. A collaboration with Parkinson’s UK on patient engagement in research established a model for partnerships between international organizations. Evaluation of these initiatives is ongoing. Based on impact, initiatives maybe replicated and scaled.

Conclusions: The Parkinson’s Foundation has built on its track record of leadership in the field.

POSTER 7

Long-term Yearly Trends of PEG Tube Placement in Neuromuscular Disorders

Background: Aspiration pneumonia is a leading cause of death in Parkinson’s disease (PD). Although percutaneous endoscopic gastrostomy (PEG) has its proven value in ALS, the evidence does not support its use in Alzheimer’s disease (AD), and is insufficient in PD. However, evidence shows that PEG does not prevent aspiration with patients with dysphagia.

Objective: We sought to determine the incidence of PEG placement in PD, AD, or ALS population, describe yearly trends from 1990 to 2010, and analyze its association with length of stay and discharge destination.

Methods: Secondary analysis of a national database from 1990 to 2010 was conducted using International Classification of Diseases, 9th revision, Clinical Modification codes for PD, AD, and ALS, and procedure codes for PEG. Descriptive analysis was performed for all years using binomial regression model to determine the trend of PEG placement over the 21 years. The median length of stay and discharge destinations were compared.

Results: PEG tube placement was, on average, 3.5% lower per year (P < .001) in PD, 6.7% lower per year (P < .001) in AD, and 0.3% lower per year (P = .007) in ALS. Median length of stay increased 3 to 6 days in all patients with PEG placement. Odds of being discharged to a long-term or short-term facility more than doubled with PEG (OR 2.7, 95% CI 2.6-2.7 in AD, and OR 4.8, CI 4.6-4.9 in PD). But it halved in ALS patients (OR 0.5, CI 0.4-0.5).

Conclusion: Our results show that the rate of PEG placement in ALS was unchanged, while the rates among PD and AD patients have declined. However, thousands of PD and AD patients still undergo PEG placement each year despite limited evidence to support its use. Further research is necessary to understand the effects of PEG on outcome, physician practices and patient expectations in advanced PD.

POSTER 8

Prevalence of REM Sleep Behavior Disorder in Sun City, Arizona
D.R. Shreprecher,1 G.E.Serrano,2 N. Zhang, MS,3 A. Intoria,2 K. J. Davis,2 M. Glass,2 J. Curry,2 J. Walker,2 B. Cutler,2 M. Callan,3 A. Garcia,3 L. I. Sue,3 T. G. Beach,3 Cleo Roberts Center, Banner Sun Health Research Institute, Sun City, AZ, USA; 2Civin Laboratory for Neuropathology, Banner Sun Health Research Institute, Sun City, AZ, USA; 3Department of Biostatistics, Mayo Clinic College of Medicine, Scottsdale, AZ, USA.

Objective: Determine prevalence of REM Sleep Behavior Disorder (RBD) in Sun City, Arizona

Background: RBD is the strongest known clinical risk factor for Parkinson disease (PD) and related disorders, however prevalence data necessary to guide design of PD prevention trials are limited.

Methods: We designed a survey using the RBD single item question (RBD1Q) for probable RBD (pRBD), “have you ever been told, or suspected yourself, that you act out your dreams while asleep (for example, punching; flailing your arms; making running movements; shouting out loud; knocking things over; jumping out of bed)?” and the Innsbruck RBD Inventory for high-likelihood RBD (HL-RBD). Four out of 5 “yes” responses to these more specific questions have been shown to increase specificity of RBD1Q in a community-based sample. Attempts by telephone and mail were made to administer it to 1000 individuals in the Sun City, Arizona zip code. Individuals answering “yes” to 4/5 Inventory questions were considered to have HL-RBD.

Results: Of 3,000 individuals contacted, there were 484 respondents (response rate 16%), who were 96.7% Caucasian, mean age 78 (SD 8.5). Of these, 48 (9.9%) endorsed pRBD by RBD1Q, 7 with history of PD or other potential cause of RBD. 16 (4%) had HL-pRBD, 3 with history of potential secondary cause.

Conclusions: Previous research suggests that 66% of HL-pRBD respondents will have polysomnogram confirmed RBD. Recognizing potential limitation of respondent bias, prevalence of idiopathic cases was 8.5% pRBD and 2.8% HL-RBD in our retirement community with a mean age 78.

POSTER 9

Are Lewy bodies associated with sympathetic pathology in dementia subjects?
D. R. Shreprecher,1 Michael Callan,2 Brett, Cutler,4 Geidy Serrano, PhD,2 Charles H. Adler, MD PhD,3 Holly A. Shill, MD,4 John N. Caviness, MD,3 Marwan N. Sabbagh, MD,3 Christine M. Belden, PsyD,4 Erika Driver-Dunkley,4 Shyamal H. Mehta, MD PhD,3 Lucia I. Sue, BS,2 Kathryn Davis, BA, Edward Zanrini, MD,4 Thomas G. Beach,2 Cleo Roberts Center, Banner Sun Health Research Institute, Sun City, AZ, USA; 2Civin Laboratory for Neuropathology, Banner Sun Health Research Institute, Sun City, AZ, USA; 3Department of Neurology, Mayo Clinic College of Medicine, Scottsdale, AZ, USA; 4Barrow Neurological Institute, Phoenix, AZ, USA; University of Arizona College of Medicine-Phoenix, USA.

Objective: Determine if Alzheimer subjects with Lewy bodies show sympathetic cardiac denervation.

Background: Comorbid Lewy body (LB) pathology is very common in Alzheimer disease (AD), and may confound clinical trial design; yet there is no in-vivo test to identify it. Tissue studies have shown cardiac sympathetic denervation in Parkinson disease and dementia with Lewy bodies, but have not been explored in mixed AD/LB cases.

Methods: We analyzed 30 cases with autopsy-confirmed AD/LDB, 30 AD-no LB not meeting DLB criteria, rigidopathology and motor criteria. 30 incidential Lewy body disease (ILBD) and 22 controls without LB. Using tyrosine hydroxylase (TH) staining of epicardial and myocardial tissue, we tested the hypothesis that AD/LB will be distinguishable from AD without LB by the loss of tyrosine hydroxylase. Another project is underway to address the lack of clarity of the role of patient advocacy groups. A collaboration with Parkinson’s UK on patient engagement in research established a model for partnerships between international organizations. Evaluation of these initiatives is ongoing. Based on impact, initiatives maybe replicated and scaled.

Results: Previous research suggests that 66% of HL-pRBD respondents will have polysomnogram confirmed RBD. Recognizing potential limitation of respondent bias, prevalence of idiopathic cases was 8.5% pRBD and 2.8% HL-RBD in our retirement community with a mean age 78.

Conclusions: Previous research suggests that 66% of HL-pRBD respondents will have polysomnogram confirmed RBD. Recognizing potential limitation of respondent bias, prevalence of idiopathic cases was 8.5% pRBD and 2.8% HL-RBD in our retirement community with a mean age 78.

Conclusion: Our results show that the rate of PEG placement in ALS was unchanged, while the rates among PD and AD patients have declined. However, thousands of PD and AD patients still undergo PEG placement each year despite limited evidence to support its use. Further research is necessary to understand the effects of PEG on outcome, physician practices and patient expectations in advanced PD.

Are Lewy bodies associated with sympathetic pathology in dementia subjects?

Prevalence of REM Sleep Behavior Disorder in Sun City, Arizona

Are Lewy bodies associated with sympathetic pathology in dementia subjects?
between the control and PD or DLB groups but the difference was too small for this to reach significance (p = 0.16). 

Conclusions: The clear separation of DLB from controls based on cardiac TH fiber density is the first report of a statistically significant difference between these groups. Our data therefore strengthen the rationale for using cardiac nuclear imaging with a noradrenergic nuclear imaging ligand, meta-iodobenzylguanidine (MIBG) to separate DLB from AD with DLB, an important concept as most cases of AD/LBD are not recognized as such during life. Our results indicate that MIBG would not be likely to clinically separate the AD/LBD from AD subjects without LB.

POSTER 10

Levodopa Responsive Parkinsonism and Motor Neuron Disease: A Common Cause?
B. Barton. Rush University Medical Center, Chicago, IL, USA and Jesse Brown VA Medical Center, Chicago, IL, USA.

Objective: Explore possible links between degenerative parkinsonism and motor neuron disease

Background: A 54-year-old man presenting with slowly progressive right hand tremor and right leg stiffness of four years duration was diagnosed with Parkinson’s disease. Exam showed asymmetric mild-moderate bradykinesia, rigidity, and intermittent rest tremor. He had a history of transient delusional disorder but was never treated with antipsychotics. Treatment with levodopa was well tolerated and led to sustained, marked improvement of motor symptoms. Over the course of 2 years he developed motor fluctuations, with levodopa response shortening to 3 hours, and mild dyskinesia in the legs. He then noted more rapid deterioration with greater difficulty walking, more muscle spasms and stiffness, weight loss, and progressive shortness of breath, all of which didn’t respond well to adjustments in levodopa. He was admitted for respiratory insufficiency and detailed exam revealed muscle fasciculations and new weakness. Limited EMG demonstrated multifocal denervation, which, after exclusion of other causes, was felt to represent ALS.

Methods: Case Report and Review of Literature

Results: Simultaneous clinical diagnosis of levodopa-responsive parkinsonism and ALS is rare. Environmental/genetic factors can give risk to both, but this is in typically isolated populations (Guam, Japan). Some proteinopathies/mutations are found in both ALS and degenerative parkinsonism (C9orf72, DJ-1, VCP, optineurin, SOD1). Rare cases of this “Brait-Fahn-Schwarz disease” have been described (levodopa responsive parkinsonism and subsequent ALS syndrome) and appear to be of heterogeneous causes.

POSTER 11

Dopamine transporter (DAT) imaging to enrich for Parkinson’s disease during screening of recently diagnosed candidates for the SURE-PD3 phase 3 clinical trial
G. F. Crotty,1 E.A. Macklin,2 Ken Marek,3 A. Ascherio,4 M. A Schwarzschild.1 1Department of Neurology, Massachusetts General Hospital, Boston, MA, USA; 2Department of Medicine, Massachusetts General Hospital, Boston, MA, USA; 3Institute for Neurodegenerative Disorders, New Haven, CT, USA; 4Department of Epidemiology, Harvard T. H. School Chan School of Public Health, Boston, MA, USA.

Objective: To compare patients with clinically defined early PD with and without evidence of dopaminergic deficit by DAT imaging during screening for the SURE-PD3 trial.

Background: In the SURE-PD3 trial, DAT imaging was the final stage of a three-stage screening process. DAT imaging was used to enrich the trial cohort for patients with defined PD by excluding individuals classified as SWEDDs (scans without evidence of dopaminergic deficit).

Methods: DAT imaging was carried out at 57 study sites on participants who had passed initial screening for lower serum urate, clinically defined de novo PD and various medical exclusions. Evidence of dopaminergic deficit was centrally assessed based on visual interpretation by 2 to 4 nuclear medicine specialists. Specific binding ratios (SBRs) of striatal regions were calculated using a standardized software analysis platform.

Results: 336 subjects underwent DAT imaging. Thirty (9%) were negative for dopaminergic deficit. SBRs were higher in SWEDDs compared to non-SWEDDs. The mean age and duration of PD symptoms were similar between groups. Regarding features of parkinsonism, rigidity was less prevalent in SWEDDs. Tremor, bradykinesia and postural instability were similar between groups. In SWEDDs, the MDS-UPDRS Part 1 score and the Neuro-QoL sleep disturbance score were higher (i.e. worse) and the MDS-UPDRS Part 3 score and Neuro-QoL Cognitive function were lower (i.e. better) than in non-SWEDDs. Mean serum urate in SWEDDs was 4.5 ± 0.9 mg/dL vs. 4.5 ± 0.8 mg/dL in non-SWEDDs (p=0.8).

Conclusion: SWEDDs had similar demographics and overall parkinsonian features to non-SWEDDs. Our results support use of DAT imaging in PD clinical trials. By removing SWEDDs, we enriched the study population and likely improved power to detect an effect of urate elevation. Interestingly, some non-motor symptoms were more prevalent in SWEDDs than in non-SWEDDs. Further investigation on this finding is warranted.

POSTER 12

A Phase 3 study of isradipine as a disease modifying agent in patients with early Parkinson’s disease (STEAZY-PD III)
Parkinson Study Group (T. Simuni)* Northwestern University Medical School, Department of Neurology, Chicago, IL, USA.

Objective: To assess the efficacy of isradipine, a dihydropyridine calcium channel antagonist to slow the progression of Parkinson’s disease (PD).

Background: STEADY-PD III is an NINDS funded Phase 3, parallel group, international, multicenter, double blind study evaluating the efficacy of isradipine 10mg daily as a disease-modifying agent in early PD. The study is being conducted at 54 Parkinson Study Group sites in US and Canada.

Methods: The study recruited 336 participants with de novo PD not requiring symptomatic therapy and followed them prospectively for 36 months. The primary outcome is the change from baseline to the Unified Parkinson Disease Rating Scale (UPDRS) Part I-II score as measured in the ON state at month 36, in the active arm compared to the placebo arm. Secondary outcome measures include: 1) Time to initiation and utilization of dopaminergic therapy; 2) Time to onset of motor complications; 3) Change in UPDRS in the OFF state, 4) Change in non-motor disability and other PD motor and non-motor outcome measures.

Results: Enrollment was started in November 2014 and was completed in 12 months, 6 months ahead of schedule including 10% minority recruitment. At baseline the cohort was age 62 (SD=9), 68% male, and 0.9 (SD=0.7) years from PD diagnosis. The last participant completed the study in December 2018. Study retention rate is 95%, 297 have initiated PD symptomatic therapy. Data lock is scheduled for January 2019 and final data analysis will be available February 2019.

Conclusion: STEADY-PD III final results will be presented at the American Academy of Neurology May 2019 meeting. The study has a number of unique design features, including the longest duration disease modifying interventional study (3-year) in de novo population and assessment of the primary outcome in the medications ON state. Retention and completion rates have been higher than expected.

Study supported by the NINDS U01NS080818 and U01NS080840*
A full listing of the PSG authors of this report will be detailed at the poster presentation.

POSTER 13

NILO-PD: A Phase 2a Study Of Nilotinib In Patients With Advanced Parkinson’s Disease: Study Design And Status Update
NILO-PD Steering Committee (authorship); T. Simuni,1 B. Fiske,2 K. Merchant,3 C. S. Coffey,4 H. Matthews,5 R. K.Wyse,6 P. Brundin,6 D. K. Simon,7 M. Schwarzschild,8 D. Weiner,9 J. Adams,10 C. Venuto,10 L. Trusso10 , L. Baker,10 M. Kostrzebski,10 T. Ward,1 Gary Rafaloff11 On behalf of the NILO-PD PSG Investigators 1Northwestern University, Chicago, IL, USA; 2Michael J. Fox Foundation, New York, NY, USA; 3TransThera Consulting Co., Portland, OR, USA; 4University of Iowa, Iowa City IA, USA; 5The Cure Parkinson’s Trust, United Kingdom; 6Van Andel Research Institute, Grand Rapids, MI, USA; 7Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA; 8Massachusetts General Hospital, Boston, MA, USA; 9Consultant, Austin, TX, USA; 10University of Rochester, Rochester, NY, USA; 11Patient Research Advocate, Marlboro, NJ, USA.

Objective: To assess the safety and tolerability of nilotinib (150-300 mg once daily) in moderate/advanced Parkinson’s disease (PD).

Background: Nilotinib is approved by the FDA for chronic myeloid leukaemia but not for PD. Several cell and animal model studies suggest that nilotinib may reduce alpha-synuclein pathology in PD. A small open-label clinical
study tested the safety/tolerability of nilotinib in PD for the first time and reported that there were positive, though exploratory, signs of clinical benefits.

Methods: NILO-PD is a Phase 2 randomized, double-blind, placebo-controlled, parallel group study. The study enrolled 76 participants with moderate to advanced PD in Cohort 1. The participants were randomized 1:1:1 to a once daily dose of nilotinib or placebo (150 mg: 300 mg: placebo) for 6 months. The primary outcome is safety and tolerability. Secondary and exploratory outcomes include assessment of symptomatic effects of nilotinib, impact of nilotinib on progression of PD disability (MDS-UPDRS OFF/ON), the cognitive function (DRS-2), quality of life, pharmacokinetics, and a battery of serum and spinal fluid biomarkers.

Results: The study is conducted at 25 Parkinson Study Group (PSG) sites in US. Recruitment started in November 2017 and was completed in December 2018. 125 participants were screened and 76 randomized (39.2% screened failure). Baseline characteristics of study participants are summarized by mean (standard deviation) unless otherwise noted: 64.6 (7.5) years of age, 31.6% female, 54.7 (8.0) years at diagnosis, 9.9 (4.7) years of disease duration, 66.4 (19.5) MDS-UPDRS OFF score, 48.3 (16.1) MDS-UPDRS ON score, 27.1 (2.2) MOCA score. The study is scheduled to complete subjects’ ascertainment in September 2019 and primary outcome results are expected by December 2019.

Conclusion: This study will provide further information on safety/ tolerability, dose selection and biomarkers profile of nilotinib as a potential novel symptomatic and disease-modifying therapy for PD, and determine if it is warranted to proceed with future studies in PD de novo population.

POSTER 14

Treatment of Anxiety in Parkinson’s Disease: A Systematic Literature Review

J.J. Chen, 1 H. Hua. 2

1Loma Linda University, Loma Linda, CA, USA; 2Marshall B. Ketchum University, Fullerton, CA, USA.

Objective: To conduct a systematic literature review evaluating efficacy and tolerability of interventions for management of anxiety symptoms in patients with Parkinson’s Disease (PD).

Background: Symptoms of anxiety are common in patients with PD. However, a systematic literature review of interventions for this condition has not been previously published.

Methods: A systematic literature search was performed to identify controlled trials of interventions for management of anxiety symptoms in PD. Searches were performed in PubMed, Cochrane Library, and EMBASE (1947 to December 2018) with no language restrictions. Eligible studies were randomized, blinded, and placebo- or comparator-controlled. Study methodology, patient- and treatment-level data were independently extracted, verified, and summarized using descriptive statistics. The studies underwent quality assessment for risk of bias based on Cochrane metrics. Documentation of the inclusion and exclusion process is presented in the Preferred Reporting Items of Systematic Reviews and Meta-Analyses format.

Results: 310 potentially relevant articles were identified and seven randomized clinical trials (RCTs) met inclusion criteria for data extraction and synthesis. Of the seven RCTs (total n=165 subjects), four (n=137) involved cognitive-behavioral therapies (CBT), two (n=28) pharmacologic therapies (bromazepam, levodopa), and one (n=14) acoustic therapy. In two of the four CBT studies, anxiety symptoms significantly improved and CBT was well tolerated. Of the pharmacologic interventions, bromazepam significantly improved anxiety symptoms but sedation and dizziness were common. Acoustic therapy was not associated with symptom improvement. Quality assessment indicates the CBT results are subject to high risk of bias due to performance bias (eg, blinding methods).

Conclusions: Preliminary evidence suggests that non-pharmacologic therapies (e.g., CBT) may be efficacious in improving anxiety symptoms in patients with PD. Evidence for pharmacologic interventions is extant and insufficient. Additional randomized controlled trials are warranted for both CBT and pharmacologic interventions for management of anxiety in patients with PD.

POSTER 15

A Virtual Cohort Study of LRRK2 G2019S Carriers: A Novel Model for Long-Term Observation

R.B. Schneider, 1 T.L. Myers, 1 R.N. Alcalay, 2 E.R. Dorsey, 1 R. Holloway. 3

1University of Rochester, Rochester, NY, USA; 2Columbia University, NY, USA.

Objective: In anticipation of precision medicine clinical trials, we will establish the feasibility of engaging, following, and prospectively characterizing a nationwide cohort of 23andMe-identified LRRK2 G2019S carriers with and without manifest motor Parkinson’s disease (PD).

Background: LRRK2 is a promising target for the development of disease-modifying therapeutics for PD, but enrollment of carriers into trials using current recruitment strategies may be challenging. Collaboration with 23andMe, the direct-to-consumer personal genomics company that has genotyped over 3 million individuals, will allow us to move beyond traditional site-based recruitment to reach a larger number of individuals. Virtual studies use technology to conduct remote assessments and may improve efficiency, reduce costs, and reduce barriers to participation. The characterization and engagement of a large, geographically-dispersed cohort could address critical gaps in knowledge regarding LRRK2 that will inform the design of trials.

Methods: We will enroll 300 23andMe-identified LRRK2 G2019S carriers (250 without PD, 50 with PD) in this 36-month virtual, prospective, observational study. Participants will complete annual virtual research visits conducted by a centralized research team. Assessments will include standard patient-reported outcome measures and clinician-reported outcome measures (modified for remote assessment). Study progress will be overseen by a Steering Committee that features individuals with PD and carriers of LRRK2 G2019S.

Results: Enrollment will begin during the first quarter of 2019. We will 1) assess our ability to recruit and retain a national cohort into a 36-month virtual study, 2) prospectively characterize the cohort and compare its demographics and disease characteristics to those of traditionally-established LRRK2 G2019S cohorts, and 3) assess the value of this model in creating a clinical trial-ready cohort.

Conclusions: We will use novel research methods to prospectively characterize and engage a large cohort of LRRK2 G2019S carriers. This study is funded under the University of Rochester Udall Center (NINDS P50NS108676).

POSTER 16

Intensity-based exercise groupings in Parkinson’s Disease: Analysis from the Parkinson’s Foundation Quality Improvement Initiative (PF-QII)

D. Larson, 1 M. Rafferty, 1, 2 A. Roberts, 3 S. Wu, 1 H. Gao, 3 T. Simuni. 1

1Northwestern University Feinberg School of Medicine, Chicago, IL, USA; 2Shirley Ryan Ability Lab, Chicago, IL, USA; 3University of Florida, Gainesville, FL, USA.

Objective: To describe duration and intensity-based exercise groups in individuals with Parkinson’s Disease (PD).

Background: Evidence suggests that regular exercise slows functional decline in individuals with PD. There are limited data characterizing the impact of exercise intensity. The PF-QII dataset’s recent inclusion of exercise duration and intensity data enables further exploration.

Methods: All individuals with PD enrolled in the PF-QII registry with at least one New Data Collection Form were used to identify participants’ exercise characteristics. Participants were first grouped by exercise duration (hrs/wk, <2.5hrs/wk, ≥2.5hrs/wk). A second grouping used K-means clustering with individuals’ self-reported exercise intensity. Analysis of variance and Chi-squared tests were used to compare participants’ characteristics across groups.

Results: A total of 5,203 participants were included in analysis. The K-means cluster analysis identified four distinct intensity-based groups: Almost-none, Light-dominant, Moderate-dominant, and Vigorous-dominant. Light-dominant participants had greater exercise duration (24±10 hrs/wk) compared to Moderate- and Vigorous-dominant (both 8±4 hrs/wk). Participants in both Vigorous-dominant and Duration Category ≥2.5hrs/wk were more likely to be male, younger, better educated, and newly diagnosed, with fewer comorbidities, and better disease status (p<0.0001). After controlling for age, Hoehn &Yahr stage, years since diagnosis, and cognitive status, both duration and intensity groupings showed a significant correlation of improved scores on The Modified Caregiver Strain Index (MCSI) and Parkinson’s Disease Questionnaire (PDQ-39) in high exercise groups compared to low exercise groups (p<0.05). No significant correlation was found between exercise grouping and hospitalization/ER visits, fall frequency, motor fluctuations, or dyskinesias.

Conclusion: Grouping exercisers with PD by intensity in addition to duration of exercise provides valuable insight into the differences between exercise categories. Next steps include longitudinal analyses of change in outcomes related to exercise intensity group.
POSTER 17
Capturing Parkinson’s disease heterogeneity with quantitative mobility measures
E. Hill,1 I. Alfradique-Dunham,1 C. G. Mangleburg,1 B. Ripperger,1 A. Stillwell,1 S. Rao,1 H. Saade,1 A. Tarakad,1 J. Jimenez-Shahed,1 J. Jankovic,1 R. Dawe,2 A. Buchman,2 J. M. Shulman,1 1Baylor College of Medicine, Houston, TX, USA; 2Vanderbilt University Medical Center, Nashville, TN, USA; 3Henry Ford Hospital and Department of Neurology, Wayne State University School of Medicine, Detroit, MI, USA; 4Vanderbilt University Medical Center, Nashville, TN, USA; 5Neurocrine Biosciences, Inc., San Diego, CA, USA; 6BIAL-Portela & Ca SA, Sao Mamede do Coronado, Portugal; 7University Porto, Porto, Portugal.

Objective: To evaluate clinic-based, quantitative mobility measures using a wearable sensor in comparison with the standard clinic assessment for characterization of Parkinson’s disease (PD) heterogeneity, including motor subtypes, cognition, and disability.

Background: There is substantial heterogeneity in PD motor and non-motor features. At least two major subtypes have been recognized, tremor dominant (TD) and postural instability gait disorder (PIGD), with potential implications for progression and overall disability. Compared to standard clinical rating scales, instrumented motor testing may offer more sensitive and robust characterization of PD motor and non-motor features.

Methods: During routine clinic visits, subjects with PD completed a 10-minute motor protocol, including a 32-foot walk, Timed Up and Go (TUG) with turn, and standing posture task, while wearing a sensor device (DynaPort Hybrid, McRoberts BV). 12 previously-validated mobility measures were computed. Regression analyses evaluated each metric in relation to (i) motor MDS-UPDRS, (ii) motor subtype (TD vs. PIGD), (iii) cognition (Montreal Cognitive Assessment, MoCA), and (iv) disability (Patient-Reported Outcomes Measurement Information System-29). All primary analyses included age, gender, and disease duration as covariates, and we secondarily adjusted for MDS-UPDRS.

Results: In 200 subjects with PD (63% male, age 65±9, 68% H&Y stage 2, MoCA 25±3), 6 out of 12 mobility measures were not associated with motor MDS-UPDRS, revealing independent features of motor performance measured by the device. Measures of gait (speed, cadence, step regularity), transitions in the TUG (stand to sit and sit to stand), and turn (yaw) were significantly associated with PD motor subtype, cognition, and disability (all anti-correlated, p<0.05). All associations were robust to adjustment for motor MDS-UPDRS.

Conclusion: Quantitative mobility measures correlate with indices of PD motor and non-motor heterogeneity. Moreover, these metrics capture relevant features of motor performance beyond those obtained using the MDS-UPDRS. Clinic-based, wearable sensors show promise for enhanced phenotyping and dissection of PD heterogeneity.

POSTER 18
Pharmacokinetics of Opicapone and Effect on COMT and Levodopa Pharmacokinetics in Patients with Parkinson’s Disease
G. Loewen,1 P. LeWitt,2 C.W. Olano,2 K.D. Kieburz,4 G.S. Liang,1 R. Jimenez,1 K. Olson,1 E. Roberts,1 1Neurocrine Biosciences, Inc., San Diego, CA, USA; 2Henry Ford Hospital and Department of Neurology, Wayne State University School of Medicine, West Bloomfield, MI, USA; 3Mount Sinai School of Medicine, New York, NY, USA; 4University of Rochester Medical Center, Rochester, NY, USA.

Objective: To evaluate the pharmacokinetics and pharmacodynamics of opicapone in Parkinson’s disease (PD).

Background: Opicapone is a novel, highly-selective, peripheral COMT inhibitor under development in the U.S. as an adjunct to levodopa for PD with motor fluctuations. The efficacy of opicapone has been evaluated in two international Phase 3 studies (BIPARK-1 [NCT01568073], BIPARK-2 [NCT01227655]).

Methods: Participants received double-blind (DB) treatment with opicapone (5mg [BIPARK-1 only], 25mg, 50mg), entacapone (200mg [BIPARK-1 only], or placebo for 14-15 weeks added to levodopa. Participants completing DB treatment were eligible to enroll in the 1-year open-label (OL) phase of each study. Efficacy analyses included mean changes from baseline in absolute ON-time without troublesome dyskinesia (defined as either no dyskinesia or non-troublesome dyskinesia). Results for the 50mg opicapone dose are presented, along with dyskinesia as a treatment-emergent adverse event (TEAE).

Results: BIPARK-1 (opicapone at 5mg=119, 25mg=116, 50mg=115; entacapone=120; placebo=33), a significant increase from baseline to Week 14/15 in absolute ON-time without troublesome dyskinesia was found for opicapone 50mg versus placebo (least-squares mean change [±standard error], hours): 50mg, 1.9±0.2; placebo, 0.9±0.2; P=0.002. Similar results arose from BIPARK-2 (25mg=125, 50mg=147, placebo=135) 50mg, 1.7±0.3; placebo, 0.9±0.3; P=0.025. Improvements in ON-time without troublesome dyskinesia were sustained in long-term extension studies, with mean changes from DB baseline to OL endpoint (±standard deviation) in all opicapone-treated participants of 2.0±2.6 hours for BIPARK-1 (N=494) and 1.8±3.2 hours for BIPARK-2 (N=339). In the pooled DB safety population (N=631), a TEAE of dyskinesia was reported in 17.4% of all opicapone-treated (versus 6.2% for placebo). Few subjects had dyskinesia TEAE leading to discontinuation (opicapone, 1.9%; placebo, 0.4% or serious dyskinesia (opicapone, 0.3%, placebo, 0%).

Conclusions: Once-daily opicapone increased ON-time without troublesome dyskinesia in PD patients with motor fluctuations.

POSTER 19
Once-Daily Opicapone Increases ON-Time in Patients with Parkinson’s Disease: Results from Two Phase 3 Studies
P.A. LeWitt,1 D.O. Claassen,2 K. Olson,3 K. Farahmand,3 S. Siegert,3 M. Alraii,3 J.F. Rocha,3 P. Soares-da-Silva,3 G.S. Liang,1 1Henry Ford Hospital and Department of Neurology, Wayne State University School of Medicine, West Bloomfield, MI, USA; 2U.S. for PD as an adjunct to levodopa-related motor fluctuations. Opicapone is a novel, highly-selective, peripheral COMT inhibitor being developed in the U.S. to prolong the clinical actions of levodopa. Opicapone is a catechol-O-methyltransferase (COMT) inhibitor being developed in the U.S. to prolong the clinical actions of levodopa. Opicapone is a novel, highly-selective, peripheral COMT inhibitor being developed in the U.S. to prolong the clinical actions of levodopa. Opicapone is a novel, highly-selective, peripheral COMT inhibitor being developed in the U.S. to prolong the clinical actions of levodopa. Opicapone is a novel, highly-selective, peripheral COMT inhibitor being developed in the U.S. to prolong the clinical actions of levodopa.

Objective: To evaluate once-daily opicapone in Parkinson’s disease (PD).

Background: Catechol-O-methyltransferase (COMT) inhibitors were developed to prolong the clinical actions of levodopa. Opicapone is a novel, highly-selective, peripheral COMT inhibitor under development in the U.S. as an adjunct to levodopa for PD with motor fluctuations. The efficacy of opicapone has been evaluated in two international Phase 3 studies (BIPARK-1 [NCT01568073], BIPARK-2 [NCT01227655]).

Methods: Participants received double-blind (DB) treatment with opicapone (5mg [BIPARK-1 only], 25mg, 50mg), entacapone (200mg [BIPARK-1 only], or placebo for 14-15 weeks added to levodopa. Participants completing DB treatment were eligible to enroll in the 1-year open-label (OL) phase of each study. Efficacy analyses included mean changes from baseline in absolute ON-time without troublesome dyskinesia (defined as either no dyskinesia or non-troublesome dyskinesia). Results for the 50mg opicapone dose are presented, along with dyskinesia as a treatment-emergent adverse event (TEAE).

Results: BIPARK-1 (opicapone at 5mg=119, 25mg=116, 50mg=115; entacapone=120, placebo=33), a significant increase from baseline to Week 14/15 in absolute ON-time without troublesome dyskinesia was found for opicapone 50mg versus placebo (least-squares mean change [±standard error], hours): 50mg, 1.9±0.2; placebo, 0.9±0.2; P=0.002. Similar results arose from BIPARK-2 (25mg=125, 50mg=147, placebo=135) 50mg, 1.7±0.3; placebo, 0.9±0.3; P=0.025. Improvements in ON-time without troublesome dyskinesia were sustained in long-term extension studies, with mean changes from DB baseline to OL endpoint (±standard deviation) in all opicapone-treated participants of 2.0±2.6 hours for BIPARK-1 (N=494) and 1.8±3.2 hours for BIPARK-2 (N=339). In the pooled DB safety population (N=631), a TEAE of dyskinesia was reported in 17.4% of all opicapone-treated (versus 6.2% for placebo). Few subjects had dyskinesia TEAE leading to discontinuation (opicapone, 1.9%; placebo, 0.4% or serious dyskinesia (opicapone, 0.3%, placebo, 0%).

Conclusions: Once-daily opicapone increased ON-time without troublesome dyskinesia in PD patients with motor fluctuations.

POSTER 20
Inhaled levodopa (CVT-301) for treatment of OFF periods in Parkinson’s disease: efficacy as assessed by 39-item Parkinson’s Disease Quality of Life (QoL) Questionnaire
P. LeWitt,1 R. A. Hauser,2 C. Oh,3 J. Qian,3 C. Kenney 3, I. Abeynayake1 1Henry Ford Hospital and Wayne State University School of Medicine, Bloomfield, MI; 2University of South Florida, Tampa, FL; 3Acorda Therapeutics, Inc., Ardsley, NY.

Objective: To evaluate the pharmacokinetics and pharmacodynamics of opicapone in Parkinson’s disease (PD).

Background: Opicapone is a novel, highly-selectively acting, highly-selective catechol-O-methyltransferase (COMT) inhibitor being developed in the U.S. for PD as an adjunct to levodopa-related motor fluctuations.

Methods: Patients with stable PD were administered once-daily opicapone (opicapone, 1.9%; placebo, 0.4%) or serious dyskinesia (opicapone, 0.3%, placebo, 0%).

Conclusions: Once-daily opicapone 50mg resulted in substantial and prolonged COMT inhibition, which increased systemic exposure to levodopa and led to both decreased peak-to-trough fluctuations in levodopa concentrations and to higher trough levodopa concentrations.
POSTER 21

Brainstem Modulation Therapy for the Management of Parkinson’s Disease: Results from a Single-Site Randomized Controlled Trial

K. Ade,1 D. Wilkinson,2 A. Podlewski,3 S. E. Banducci,4 T. Pellat-Higgins,2 M. Bodani,2 M. Sakel FRCP,1 L. Smith,1 P. LeWitt6 Scion NeuroStim, LLC, Raleigh, North Carolina, USA; 2School of Psychology, University of Kent, Canterbury, UK; 3Centre for Health Services Studies, University of Kent, Canterbury, UK; 4Neuropsychiatry Service, Kent & Medway NHS and Social Care Partnership Trust, UK; 5East Kent Neuro-Rehabilitation Service, East Kent Hospitals University NHS Foundation Trust, Canterbury, UK; 6Parkinson’s Disease & Movement Disorders Program, Henry Ford Hospital and Wayne State University School of Medicine, West Bloomfield, MI, USA.

Objective: To evaluate the feasibility and efficacy of a caloric vestibular stimulation (CVS)-mediated brainstem modulation device for the treatment of motor and non-motor symptoms in Parkinson’s disease (PD).

Background: A recent case study showed that repeated sessions of CVS using a solid-state ThermoNeuroModulation (TNM™) device, developed by Scion NeuroStim, LLC, relieved motor and non-motor symptoms associated with PD. Here, we sought to confirm these results in a prospective, double-blind, randomized, placebo treatment-controlled study. The TNM device delivers CVS via continually-varying thermal waveforms through aluminum ear-probes mounted on a wearable headset. Unlike conventional and water irrigators, treatments can easily be self-administered at home with few side effects and with a high degree of dose control.

Methods: 33 PD subjects receiving stable anti-Parkinsonian therapy completed an active (n=16) or placebo (n=17) treatment period. Subjects self-administered daily treatments as needed up to 5 times/day. PDQ-39 and PGIC were completed at baseline, 4, 8, and 12 weeks. A post-hoc analysis using an anchor-based approach examined the change in PDQ-39 domains (mobility and activities of daily living [ADL]). The PGIC (scored from 1 ["much improved"] to 7 ["much worse"]) was used as anchor for the 12-week study period.

Results: Improvement in PDQ-39 ADL and mobility was linked to the minimum improvement in PGIC ("a little improved") with estimated changes of -1.979(95%CI -0.01) for ADL, and -1.335(95%CI -0.01) for mobility scores when the 3 treatment arms were pooled. Estimated treatment differences vs placebo for the CVT-301 84-mg dose were −2.08, for ADL, and −2.19 for mobility. For both doses, treatment differences in ADL and mobility were above the estimates correlating with minimum improvement in PGIC.

Conclusions: Patients treated with CVT-301 showed more improvement in ADL and mobility as assessed by PDQ-39 which correlated with improvement in PGIC as compared with placebo-treated patients at 12 weeks. Maintaining independence in ADL helps optimize QoL for PD patients.

POSTER 22

Safety and Tolerability of Opicapone in Patients with Parkinson’s Disease and Motor Fluctuations: Pooled Analysis of Two Phase 3 Studies

D. Kremens,1 W. Poewe,2 O. Rascol,3 K. Olson,4 K. Farahmand,4 S. Siegert,1 C. McMicken,5 J.F. Rocha,1 P. Soares-da-Silva,1 G.X. Liang4 Thomas Jefferson University, Philadelphia, PA, USA; 2Medical University of Innsbruck, Innsbruck, Austria; 3Toulouse University Hospital, Toulouse, France; 4Neurocrine Biosciences, Inc., San Diego, CA, USA; 5BIAL-Portela & Ca SA, Sao Mamede do Corumao, Portugal; 6University Porto, Porto, Portugal.

Objective: To evaluate the adverse event profile of once-daily opicapone in adults with Parkinson’s disease (PD) and motor fluctuations.

Background: Cathecol-O-methyltransferase inhibitors (COMT-I) were developed to prolong the clinical actions of levodopa in PD patients. Opicapone is a novel, peripherally-acting, highly-selective COMT-I that is being developed in the U.S. as an adjunct to levodopa in adults with PD and motor fluctuations. In two international, double-blind, placebo-controlled phase 3 studies (BIPARK-1[NCT01568073], BIPARK-2 [NCT01227655]), participants received once-daily opicapone (5mg [BIPARK-1 only], 25mg, 50mg), entacapone (BIPARK-1 only), or placebo for 14-15 weeks in addition to levodopa.

Methods: Preliminary analyses are presented using pooled data from BIPARK-1 and BIPARK-2. Participants who received entacapone or opicapone 5mg were not included in the pooled analysis. Assessments included treatment-emergent adverse events (TEAEs), TEAEs of special interest, laboratory, vital sign, and electrocardiogram (ECG) evaluations.

Results: The pooled analysis included 766 participants (placebo=257, 25mg=244, 50mg=265). Demographics and baseline characteristics were generally similar across treatment groups. No apparent dose-related effect was found for TEAE occurrence (placebo=57.2%, 25mg=62.3%, 50mg=64.2%), serious TEAEs (placebo=4.3%, 25mg=2.0%, 50mg=4.9%), or TEAEs leading to discontinuation (placebo=7.4%, 25mg=5.7%, 50mg=9.1%). Dyskinesia was the most common TEAE in all treatment groups (placebo=6.2%, 25mg=16.0%, 50mg=20.4%), but few participants had dyskinesia leading to discontinuation (placebo=0.4%, 25mg=0.8%, 50mg=3.0%) or serious dyskinesia (placebo=0%, 25mg=0.4%, 50mg=0.4%). None of the following were reported in opicapone-treated participants: serious/severe diarrhea, myocardial ischemia, or melanoma. No severe or serious hepatobiliary TEAEs were reported except for 1 case of acute cholecystitis (50mg); 2 subjects (25mg) reported urine discoloration. There were no clinically relevant differences between opicapone and placebo in laboratory parameters, vital signs, or ECGs.

Conclusions: Adding opicapone up to 50mg once daily to levodopa was generally well tolerated. TEAEs reported with other COMT-I, such as hepatic injury and serious/severe diarrhea, were not observed. Final analyses will be presented at the meeting.

POSTER 23

Design of a novel pilot trial of Transauricular Vagal Nerve Stimulation in Parkinson’s Disease

C. McLeod, H. Roger, B. Badran, V. Hinson. Medical University of South Carolina, Charleston, South Carolina, USA.

Objective: Design a novel human pilot trial of Transauricular Vagal Nerve Stimulation (taVNS) in Parkinson’s Disease (PD).

Background: Recent MUSC neuroscience laboratory pre-clinical studies indicate potential for symptomatic as well as disease modifying benefit of vagal nerve stimulation (VNS) in PD. Our collaborators have conducted safety, tolerability, and feasibility trials of taVNS and tested optimal stimulation parameters that mimic cervical implanted VNS in both parasympathetic and sympathetic effects.

Methods: Due to the novelty of this treatment approach, administration technique, sham stimulation, dose, site, and duration of treatment had to be carefully chosen. Choice of primary outcome, relevant secondary outcomes, acute versus subacute measures, prediction of placebo effect, recruitment and retention issues were also evaluated in detail.
POSTER 24
Assessing Tele-Health Outcomes in Multimodal Extensions of Parkinson’s Disease Trials (AT-HOME PD): Initiation of a Long-term Observational Study

T.L. Myers,1 R.B. Schneider,1 S. Anthwal,1 E. Kayson,1 L. Ombregt,2 C.G. Tarolli,3 E.A. Macklin,3 M. Daeschler,3 E.R. Dorsey,1 L. Mangravite,3 M.A. Schwarzschild,4 T. Simuni.5 1University of Rochester, Rochester, NY, USA; 2Sage Bionetworks, Seattle, WA, USA; 3Massachusetts General Hospital, Boston, MA, USA; 4Michael J. Fox Foundation, New York, NY, USA; 5Northwestern University, Evanston, IL, USA

Objective: To develop, implement, and evaluate a model for the remote, long-term observation of Parkinson’s disease (PD) clinical trial cohorts. We will 1) establish the infrastructure for a new research model, 2) compare patient- and clinician-driven outcomes, and 3) explore novel biomarkers of PD disability and progression.

Background: Mobile and remote technologies permit frequent data collection and objective assessment in the home setting, may enable the development of digital biomarkers of disease progression, and may improve clinical trial efficiency.

Methods: AT-HOME PD aims to enroll an estimated 420 participants from two active NINDS-funded phase 3 interventional studies of potential disease-modifying therapies for PD (STEADY-PDIII and SURE-PD3). This 24-month observational study will remotely characterize long-term clinical outcomes using three platforms: virtual research visits conducted annually by centralized movement disorder specialists, smartphone-based motor tasks performed quarterly in two-week sessions by participants using mPower, and web-based surveys completed quarterly in an online companion study (Fox Insight). For consented participants, mPower passively collects GPS- and accelerometer-based movement and activity data. Data from the three platforms and the parent studies will be integrated and transferred to the Parkinson’s Disease Biomarkers Program’s Data Management Resource for use by the broader research community.

Results: From the parent studies, 266 STEADY-PDIII and 201 SURE-PD3 participants have thus far consented to contact regarding participation in AT-HOME PD. As of March 4, 2019, 130 individuals have provided eConsent, 85 have completed the baseline visit, 84 enrolled in Fox Insight, and 70 enrolled in mPower. A total of 2222 smartphone-based motor tasks (mean 32/person) have been completed thus far.

Conclusions: Enrollment in AT-HOME PD has been successfully initiated. The study will develop and test novel tele-health metrics of PD progression to improve efficiency of future PD clinical trials.

POSTER 25
Utilization of the emergency department (ED) in Florida among patients with Parkinson’s disease (PD)

B. Patel,1 R. Eisinger,1 S. Jimshleishvili,2 M. Lewin,3 M. Okun,1 A. Ramirez-Zamora1 1University of Florida, Gainesville, FL, USA; 2University of California, San Francisco, CA, USA; 3California Academy of Sciences, San Francisco, CA, USA

Results: tavNS in PD is a 2-week, randomized, sham controlled, double blind trial of tavNS vs sham treatment on motor symptoms in patients with mild to moderate PD. Recruitment goal is 30 patients (15 active tavNS and 15 sham stimulation) to undergo 10 days of 1-hour stimulation session (5 days treatment, 2 days off, 5 days treatment). Non-invasive electrical stimulation to the auricular branch of the vagus nerve is given at 200% perceptual threshold, 500μs pulse width, 25Hz for 60s ON, 30s OFF cycles, with replicated sham stimulation on the earlobe. Primary outcome measure is the videotaped pre and post stimulation modified MDS-UPDRS part III (baseline/mid-point/completion) in OFF PD medication state with rater blinded to group/condition. Secondary outcome measures include non-motor symptom scale, full MDS-UPDRS, multiple cognition and behavioral domains pertinent to PD, serum monitoring of BDNF, TNF-α, and IL-6, as well as tavNS safety and tolerability assessment in PD patients. Study includes an exploratory global composite of motor and cognition outcomes analysis.

Conclusion: The design considerations in this novel tavNS in PD pilot study will provide important guideposts for future trial design.

POSTER 26
Neuropsychiatric complications as key components of Parkinson’s disease: A critical framework for enhancing engagement in PD mental health research

M. Dennin,1 M. St Dennis,1 K. Rodriguez,2 A. Interian,1,2 R.D. Dobkin1 1Rutgers, The State University of New Jersey, Robert Wood Johnson Medical School, Piscataway, NJ, USA; 2VA NJ Health Care System, Lyons, NJ, USA

Objectives: The objectives of the project were to 1) identify barriers and facilitators to participation in Parkinson’s disease (PD) mental health research, 2) describe factors that influence study dropout, and 3) develop tools to enhance accuracy of self-report and participant retention in PD mental health clinical trials.

Background: Common problems affecting mental health clinical trials include reluctance to take part, early termination, and inaccurate, inconsistent, and/or under- reporting of emotional concerns. These problems have the potential to reduce the impact of research, slowing the development of effective mental health treatments for people with PD (PWP). Enhanced understanding of these barriers represents an important step towards optimizing care for PWP.

Method: Three focus groups (N=16 total, 4-6 participants per group) were completed between December 2017 and March 2018 (Phase 1), transcribed, and analyzed via qualitative methods. Specific deliverables were developed in response to key themes, and two additional focus groups (Phase 2) were completed in June and July 2018 to gather further input on revised research tools and procedures. One Phase 1 group and 1 Phase 2 Group focused specifically on the unique needs of Veterans with PD.

Results: Limited knowledge about the context and central role that neuropsychiatric symptoms play in overall PD management was identified as a key barrier to engagement. Perceived stigma was reported to be a major driver of self-report bias. Peer-to-peer research ambassador programs, improved educational materials regarding PD mental health, quarterly wellness newsletters, and mixed-media testimonials from prior study participants were examples of tools that may enhance the longevity and quality of PWP participation in mental health research, based on focus group results.

Conclusions: Deliverables from this project may support the collection of high quality clinical trial data, ultimately improving available mental health care resources for PWP.

Study supported by: Parkinson’s Foundation.
**POSTER 27**

**Telephone-Administered Cognitive Behavioral Therapy for Depression in Parkinson’s Disease: A Randomized Controlled Trial**

R. D. Dobkin,1 M. A. Gara,1 K. Rodriguez,1 A. Interian,2,3 M. Menza,3 1Rutgers, The State University of New Jersey, Robert Wood Johnson Medical School, Piscataway, NJ, USA; 2VA NJ Health Care System, Lyons, NJ, USA.

**Objectives:** There is a critical need for treatments that address depression and barriers to informed mental health care in Parkinson’s disease (PD). This randomized-controlled trial evaluated the efficacy of a 10-session telephone-guided cognitive behavioral treatment (CBT) for depression in PD (dPD), compared to community-based treatment as usual (TAU).

**Background:** Neuropsychiatric complications of PD, like depression, are common and functionally relevant. Yet, there remains much to be learned about effective treatments for dPD and strategies for leveraging access to specialty mental health care.

**Method:** 72 people with PD (PWP) were randomized to receive telephone-based CBT + TAU or TAU only. CBT was tailored to the unique needs of PWP and provided weekly for 3 months, and then monthly thereafter, during the 6-month follow-up phase of the study. CBT targeted negative thoughts (e.g., I have no control; I am helpless) and behaviors (e.g., avoiding friends and family, lack of exercise, excessive worry). It also trained care-partners to help PWP practice healthy habits. No travel was required and CBT participants were from the comfort of home.

**Results:** CBT was associated with significant improvements in depression, after 3 months of acute treatment, compared to TAU, on clinician-administered (Hamilton Rating Scale for Depression) and self-report (Beck Depression Inventory) measures. There were significantly more “treatment responders” in the CBT group (Clinical Global Impression Improvement Scale Score of 1 or 2; p<0.001). Acute treatment gains were maintained over the 6-month follow-up period on all depression measures (p<0.001).

**Conclusions:** Overall, results suggest that PD-informed CBT delivered remotely may be an effective treatment for dPD, that bypasses several barriers to care, such as geographic location and functional limitations. As depression is associated with increased rates of physical, cognitive, and functional decline for PWP, improved depression treatment may also enhance the overall quality and impact of all aspects of PD care.

**Study supported by:** The Michael J. Fox Foundation and the Parkinson’s Unity Walk.

---

**POSTER 28**

**A pooled analysis for 8 randomized controlled trials of istradefylline, an adenosine A2A receptor antagonist: efficacy as adjunct to levodopa in Parkinson’s disease (PD)**

S. H. Isaacson,1 N. Hattori,2 M. Onofrj,3 A. Mori,4 K. Toyama,5 R. Pahwa,6 1Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan; 2IRCCS San Raffaele Pisana, Rome, Italy; 3Guglielmo Regina University, Augusta, GA, USA; 4Kyowa Kirin Pharmaceutical Development, Inc., Princeton, NJ, USA; 5Kyowa Hakko Kirin Co., Ltd., Tokyo, Japan; 6University of Kansas Medical Center, Kansas City, KS, USA.

**Objective:** To examine safety results from pooled analyses of placebo-controlled and open-label long-term studies of istradefylline plus levodopa in patients with PD experiencing motor fluctuations.

**Background:** Istradefylline, a selective adenosine A2A receptor antagonist, acts via the indirect basal ganglia outflow pathway. In 2013, doses of 20 and 40 mg/day were approved in Japan as adjunctive treatment to levodopa-containing products in adults with PD experiencing wearing-off phenomena. In placebo-controlled studies, istradefylline (20 and 40 mg/day) reduced OFF-time and increased ON-time without troublesome dyskinesia, relative to placebo.

**Methods:** Safety was evaluated in 8 randomized, placebo-controlled double-blind 12- or 16-week phase 2b/3 studies and 4 open-label long-term studies. Patients with PD experiencing motor fluctuations during treatment with levodopa-containing products and possibly other standard anti-Parkinson medications received adjunctive istradefylline or placebo. Assessments included treatment-emergent adverse events (TEAEs), physical (including neurologic) examinations, vital signs, weight, laboratory tests, and electrocardiograms.

**Results:** Placebo-controlled studies included patients receiving istradefylline (10-60 mg/day, fixed-dose, no titration; n=2073) or placebo (n=1010). TEAEs occurred in 72.4% of istradefylline-treated patients and 65.4% of placebo-treated patients. Dyskinesia was the most frequently reported TEAE (istradefylline 18%; placebo 10%). Other TEAEs occurring in >5% of istradefylline-treated patients included nausea, dizziness, and constipation. TEAEs led to similar treatment discontinuation rates between the istradefylline (6.5%) and placebo (5.2%) groups, with discontinuation rates due to dyskinesia of 1.3% and 0.7% (istradefylline and placebo, respectively). In long-term open-label studies (n=1893), patients received istradefylline for a median 53.3 weeks, with 62% treated for 21 years. The pattern of TEAEs during long-term treatment was similar to short-term treatment, with no additional adverse drug reactions identified.

**Conclusions:** Istradefylline offers an A2A receptor-mediated, non-dopaminergic mechanism for patients with PD on levodopa and other conventional PD medications and was well-tolerated by patients with PD, with an acceptable safety profile.

**Study supported by:** Kyowa Kirin Pharmaceutical Development, Inc.

---

**POSTER 29**

**Istradefylline, an adenosine A2A receptor antagonist, as adjunct to levodopa in Parkinson’s disease (PD): A safety analysis of 8 randomized controlled trials and 4 open-label long-term studies**

N. Hattori,2 K. Sethi,3 E. Ohta,4 P. M. Salzman,4 A. Mori,5 K. Toyama,5 R. Pahwa,6 1Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan; 2IRCCS San Raffaele Pisana, Rome, Italy; 3Guglielmo Regina University, Augusta, GA, USA; 4Kyowa Kirin Pharmaceutical Development, Inc., Princeton, NJ, USA; 5Kyowa Hakko Kirin Co., Ltd., Tokyo, Japan; 6University of Kansas Medical Center, Kansas City, KS, USA.

**Objectives:** There is a critical need for treatments that address depression and barriers to informed mental health care in Parkinson’s disease (PD). This randomized-controlled trial evaluated the efficacy of a 10-session telephone-guided cognitive behavioral treatment (CBT) for depression in PD (dPD), compared to community-based treatment as usual (TAU).

**Background:** Neuropsychiatric complications of PD, like depression, are common and functionally relevant. Yet, there remains much to be learned about effective treatments for dPD and strategies for leveraging access to specialty mental health care.

**Method:** 72 people with PD (PWP) were randomized to receive telephone-based CBT + TAU or TAU only. CBT was tailored to the unique needs of PWP and provided weekly for 3 months, and then monthly thereafter, during the 6-month follow-up phase of the study. CBT targeted negative thoughts (e.g., I have no control; I am helpless) and behaviors (e.g., avoiding friends and family, lack of exercise, excessive worry). It also trained care-partners to help PWP practice healthy habits. No travel was required and CBT participants were from the comfort of home.

**Results:** CBT was associated with significant improvements in depression, after 3 months of acute treatment, compared to TAU, on clinician-administered (Hamilton Rating Scale for Depression) and self-report (Beck Depression Inventory) measures. There were significantly more “treatment responders” in the CBT group (Clinical Global Impression Improvement Scale Score of 1 or 2; p<0.001). Acute treatment gains were maintained over the 6-month follow-up period on all depression measures (p<0.001).

**Conclusions:** Overall, results suggest that PD-informed CBT delivered remotely may be an effective treatment for dPD, that bypasses several barriers to care, such as geographic location and functional limitations. As depression is associated with increased rates of physical, cognitive, and functional decline for PWP, improved depression treatment may also enhance the overall quality and impact of all aspects of PD care.

**Study supported by:** The Michael J. Fox Foundation and the Parkinson’s Unity Walk.

---

**POSTER 30**

**Design and Implementation of a Quality Improvement Registry for DBS in Parkinson’s Disease**

J. Jimenez-Shahed,1 P.-F. d’Haeze,2 J. Kirk,3 M. York,1 A. Berg,4 L. Shih,5 J. Schwab,6 J. McInerney4 1Baylor College of Medicine, Houston, TX, USA; 2Neurotargeting, LLC, Nashville, TN, USA; 3Patient advocate 4Penn State Health, Hershey, PA, USA; 5Beth Israel Deaconess Medical Center, Boston, MA, USA; 6Henry Ford Hospital, Detroit, MI, USA.

**Objectives:** To assess the clinical impact of a quality improvement registry in Parkinson’s disease (PD), focused on DBS implantation and subsequent care.

**Background:** DBS has revolutionized the treatment of severe motor complications of PD. However, optimal DBS programming continues to be an area of argument and controversy. A quality improvement registry was implemented at a major academic institution to assess the impact of a structured approach to DBS programming.

**Methods:** The registry includes data on all DBS implantation cases, with a focus on implantation and follow-up care. Data collected include patient demographics, medical history, implantation details, and post-implantation outcomes.

**Results:** The registry has been in operation for 2 years, with over 100 patients implanted. The data collected have been used to identify areas for improvement in DBS programming, including the impact of different DBS lead locations on motor response and the effectiveness of different post-implantation management strategies.

**Conclusions:** The registry has provided valuable insights into the clinical impact of DBS in PD, highlighting areas for improvement in DBS programming. The data collected have been used to inform clinical decision-making and improve patient outcomes. The registry is a valuable tool for quality improvement in DBS care.

**Study supported by:** The Michael J. Fox Foundation.
POSTER 32
A Comprehensive Evaluation of Udca Pharmacokinetics, Biological Target Engagement and Mechanism(s) of Action in People with Parkinson’s Disease (PWPs)
A. G. Sathe,1,2 C. Chen,3 W. Chen,4 J. Cloyd,1,2 L. Coles,1,2 W. Low,5 L. Sanders,6 C. J. Steer,7 P. Tuite,8 and X.-H. Zhu.4 1Department of Experimental and Clinical Pharmacology, College of Pharmacy, 2Center for Orphan Drug Research, 3Department of Food Science and Nutrition, 4Department of Experimental and Clinical Pharmacology, College of Pharmacy, 5Department of Medicine and Genetics, Cell Biology and Development and 6Department of Neurology, Medical School at University of Minnesota, Twin Cities, MN; 7Department of Neurology, Duke University Medical Center, Durham, NC, USA.

Background: Mitochondrial dysfunction due to complex I impairments is implicated in the pathogenesis of Parkinson’s Disease (PD) and results in decreased adenosine triphosphate (ATP) levels and loss of dopaminergic neurons. Ursodeoxycholic acid (UDCA) is a naturally-occurring bile acid which has anti-apoptotic and neuroprotective properties and improves mitochondrial function.

Objective: Our objective was to evaluate UDCA tolerability and pharmacokinetics (PK) in PWPs and its effects on brain and blood energetics.

Methods: An open-label, prospective 6-week study of orally administered UDCA in 5 PWPs (4M, 1F) was completed. A blood safety panel, plasma concentrations of UDCA and UDCA-conjugates (measured using HPLC-MS), mitochondrial function in WBC’s, and brain ATP levels were measured before and after therapy (week 1: 15mg/kg/day; week 2: 30mg/kg/day; and weeks 3-6: 50mg/kg/day). ATP levels and ATPase activity were measured using 7-Tesla high-field 31P magnetic resonance spectroscopy (MRS). Secondary measures included Unified Parkinson’s Disease Rating Scale (UPDRS) parts I-IV and Montreal Cognitive Assessment (MoCA).

Results: UDCA was well tolerated. MRS data were obtained in 3 subjects and showed increased ATP levels and decreased ATPase activity after therapy. Non-compartmental PK analysis resulted in Cmax of 8900 μmol/l/putamen. C2 (24 months follow-up) 8.3×10^11 μmol/l/900 μmol/putamen, and C3 (18 months follow-up) 2.6×10^12 μmol/l/900 μmol/putamen.

Conclusion: These preliminary results suggest that UDCA has the potential to normalize brain bioenergetics in PWPs. Further studies are needed to confirm these findings of target engagement.

POSTER 33
Correlation of Electrode Location and Outcomes of Gait and Axial Function in Parkinson’s Disease Patients managed with Subthalamic Nucleus Deep Brain Stimulation
Huang YL,1,2 Spindler M,3 Deik A,2 Ramirez-Zamora A1 1Parkinson’s Disease Research, Education, and Clinical Center, Philadelphia VA Medical Center, Philadelphia, Pennsylvania; 2Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, 3Department of Neurology, Center for Movement Disorders and Neurorestitution, University of Florida, Gainesville, USA.

Objective: To examine the relationship between subthalamic nucleus-deep brain stimulation (STN-DBS) contact activation and gait/axial outcomes in Parkinson’s disease (PD) patients.

Background: Bilateral STN-DBS provides improvement in PD motor symptoms; however, gait disturbance and axial function deficits may arise. Previous studies report that patients had a clinically worsening of gait several years after STN-DBS and changes in programming and medical management allowed for improvement in these symptoms to some degree. Programming settings, electrode localization and stimulation of certain STN areas may be associated with improved gait outcomes.

Methods: We retrospectively reviewed data (MDS-UPDRS III subscores, and DBS settings) from twenty-five PD patients with STN-DBS implanted between 2014 and 2015 and post-operative data for 3 years. Measures of axial function included posture (UPDRS item 28), gait (item 29), postural

1Department of Neurology, University of California, San Francisco, CA; 2Department of Neurological Surgery, University of California, San Francisco, CA, USA; 3Department of Neurology, University of Pittsburgh, PA, USA; 5Praxis Precision Medicines, Cambridge, MA, USA; 6Voyager Therapeutics, Inc., Cambridge, MA, USA; 7Departments of Medicine and Genetics, Cell Biology and Development and 8Department of Neurology, Medical School at University of Minnesota, Twin Cities, MN; 9Department of Neurology, Duke University Medical Center, Durham, NC, USA.

Background: Mitochondrial dysfunction due to complex I impairments is implicated in the pathogenesis of Parkinson’s Disease (PD) and results in decreased adenosine triphosphate (ATP) levels and loss of dopaminergic neurons. Ursodeoxycholic acid (UDCA) is a naturally-occurring bile acid which has anti-apoptotic and neuroprotective properties and improves mitochondrial function.

Objective: Our objective was to evaluate UDCA tolerability and pharmacokinetics (PK) in PWPs and its effects on brain and blood energetics.

Methods: An open-label, prospective 6-week study of orally administered UDCA in 5 PWPs (4M, 1F) was completed. A blood safety panel, plasma concentrations of UDCA and UDCA-conjugates (measured using HPLC-MS), mitochondrial function in WBC’s, and brain ATP levels were measured before and after therapy (week 1: 15mg/kg/day; week 2: 30mg/kg/day; and weeks 3-6: 50mg/kg/day). ATP levels and ATPase activity were measured using 7-Tesla high-field 31P magnetic resonance spectroscopy (MRS). Secondary measures included Unified Parkinson’s Disease Rating Scale (UPDRS) parts I-IV and Montreal Cognitive Assessment (MoCA).

Results: UDCA was well tolerated. MRS data were obtained in 3 subjects and showed increased ATP levels and decreased ATPase activity after therapy. Non-compartmental PK analysis resulted in Cmax of 8900 μmol/l/putamen. C2 (24 months follow-up) 8.3×10^11 μmol/l/900 μmol/putamen, and C3 (18 months follow-up) 2.6×10^12 μmol/l/900 μmol/putamen.

Conclusion: These preliminary results suggest that UDCA has the potential to normalize brain bioenergetics in PWPs. Further studies are needed to confirm these findings of target engagement.

POSTER 33
Correlation of Electrode Location and Outcomes of Gait and Axial Function in Parkinson’s Disease Patients managed with Subthalamic Nucleus Deep Brain Stimulation
Huang YL,1,2 Spindler M,3 Deik A,2 Ramirez-Zamora A1 1Parkinson’s Disease Research, Education, and Clinical Center, Philadelphia VA Medical Center, Philadelphia, Pennsylvania; 2Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, 3Department of Neurology, Center for Movement Disorders and Neurorestitution, University of Florida, Gainesville, USA.

Objective: To examine the relationship between subthalamic nucleus-deep brain stimulation (STN-DBS) contact activation and gait/axial outcomes in Parkinson’s disease (PD) patients.

Background: Bilateral STN-DBS provides improvement in PD motor symptoms; however, gait disturbance and axial function deficits may arise. Previous studies report that patients had a clinically worsening of gait several years after STN-DBS and changes in programming and medical management allowed for improvement in these symptoms to some degree. Programming settings, electrode localization and stimulation of certain STN areas may be associated with improved gait outcomes.

Methods: We retrospectively reviewed data (MDS-UPDRS III subscores, and DBS settings) from twenty-five PD patients with STN-DBS implanted between 2014 and 2015 and post-operative data for 3 years. Measures of axial function included posture (UPDRS item 28), gait (item 29), postural

1Department of Neurology, University of California, San Francisco, CA; 2Department of Neurological Surgery, University of California, San Francisco, CA, USA; 3Department of Neurology, University of Pittsburgh, PA, USA; 5Praxis Precision Medicines, Cambridge, MA, USA; 6Voyager Therapeutics, Inc., Cambridge, MA, USA; 7Departments of Medicine and Genetics, Cell Biology and Development and 8Department of Neurology, Medical School at University of Minnesota, Twin Cities, MN; 9Department of Neurology, Duke University Medical Center, Durham, NC, USA.

Background: Mitochondrial dysfunction due to complex I impairments is implicated in the pathogenesis of Parkinson’s Disease (PD) and results in decreased adenosine triphosphate (ATP) levels and loss of dopaminergic neurons. Ursodeoxycholic acid (UDCA) is a naturally-occurring bile acid which has anti-apoptotic and neuroprotective properties and improves mitochondrial function.

Objective: Our objective was to evaluate UDCA tolerability and pharmacokinetics (PK) in PWPs and its effects on brain and blood energetics.

Methods: An open-label, prospective 6-week study of orally administered UDCA in 5 PWPs (4M, 1F) was completed. A blood safety panel, plasma concentrations of UDCA and UDCA-conjugates (measured using HPLC-MS), mitochondrial function in WBC’s, and brain ATP levels were measured before and after therapy (week 1: 15mg/kg/day; week 2: 30mg/kg/day; and weeks 3-6: 50mg/kg/day). ATP levels and ATPase activity were measured using 7-Tesla high-field 31P magnetic resonance spectroscopy (MRS). Secondary measures included Unified Parkinson’s Disease Rating Scale (UPDRS) parts I-IV and Montreal Cognitive Assessment (MoCA).

Results: UDCA was well tolerated. MRS data were obtained in 3 subjects and showed increased ATP levels and decreased ATPase activity after therapy. Non-compartmental PK analysis resulted in Cmax of 8900 μmol/l/putamen. C2 (24 months follow-up) 8.3×10^11 μmol/l/900 μmol/putamen, and C3 (18 months follow-up) 2.6×10^12 μmol/l/900 μmol/putamen.

Conclusion: These preliminary results suggest that UDCA has the potential to normalize brain bioenergetics in PWPs. Further studies are needed to confirm these findings of target engagement.

POSTER 33
Correlation of Electrode Location and Outcomes of Gait and Axial Function in Parkinson’s Disease Patients managed with Subthalamic Nucleus Deep Brain Stimulation
Huang YL,1,2 Spindler M,3 Deik A,2 Ramirez-Zamora A1 1Parkinson’s Disease Research, Education, and Clinical Center, Philadelphia VA Medical Center, Philadelphia, Pennsylvania; 2Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, 3Department of Neurology, Center for Movement Disorders and Neurorestitution, University of Florida, Gainesville, USA.

Objective: To examine the relationship between subthalamic nucleus-deep brain stimulation (STN-DBS) contact activation and gait/axial outcomes in Parkinson’s disease (PD) patients.

Background: Bilateral STN-DBS provides improvement in PD motor symptoms; however, gait disturbance and axial function deficits may arise. Previous studies report that patients had a clinically worsening of gait several years after STN-DBS and changes in programming and medical management allowed for improvement in these symptoms to some degree. Programming settings, electrode localization and stimulation of certain STN areas may be associated with improved gait outcomes.

Methods: We retrospectively reviewed data (MDS-UPDRS III subscores, and DBS settings) from twenty-five PD patients with STN-DBS implanted between 2014 and 2015 and post-operative data for 3 years. Measures of axial function included posture (UPDRS item 28), gait (item 29), postural...
PACULATION RESULTS (NEW) 

Stability (item 30), and PGID (items 27–30). Wilcoxon’s test and Two-way ANOVA were used according to data distribution. Lead localization was verified using a postoperative CT scan fused with preoperative stereotactic MRI. Contact 0 and 1 were considered as ventral contact. Contact 2 and 3 were considered as dorsal contact.

Results: Posture, gait and PGID MDS-UPDRS III subscores in STN-DBS patients significantly improved from baseline off medication (P<0.05, P<0.01 and P<0.05 individually). There is no significant difference of stimulation frequency and pulse width between year 1, year 2 and year 3. Stimulation of ventral contact showed consistent improvement of gait and axial functions as compared to stimulation of dorsal contact at year 3 (P<0.05). There was significant and consistent improvement of motor functions after STN-DBS (51% at MDS-UPDRS motor score year 1 compared with baseline off medication, P<0.01; 42% at year 3, P<0.01).

Conclusion: Our study indicates gait and axial functions improve following STN-DBS implantation. Ventral contact stimulation might be associated with consistently improved outcomes in gait and axial functions after STN-DBS.

POSTER 34
Population Pharmacokinetics Model of Apomorphine/Apomorphine-Sulphate Administered as a Sublingual Film or Subcutaneously in Healthy Subjects and Patients With Parkinson’s Disease

F. Agbo,1 H. Bockbrader,2 Y-Y. Chiu,3 S. Chapel,3 G. Galluppi,1 B. Navia,1 D. Blum1 Sunovion Pharmaceuticals, Inc., Fort Lee, New Jersey, and Marlborough, Massachusetts, USA; 2Ann Arbor Pharmacometrics Group, Inc., Ann Arbor, Michigan, USA.

Objective: A population pharmacokinetics (popPK) model was developed to characterize the PK of apomorphine and its major metabolite, apomorphine-sulfate, in healthy subjects and patients with Parkinson’s disease (PD) following administration of apomorphine sublingual film (APL-130277; APL) and subcutaneously injected apomorphine.

Background: APL was found to be safe, well tolerated, and effective as an acute, intermittent treatment for “OFF” episodes in patients with PD in a controlled phase 3 trial.

Methods: 2302 PK samples from 87 healthy subjects and 60 patients with PD and 1012 samples from 9 healthy subjects/patients with PD were analyzed for apomorphine/apomorphine-sulfate from 9 studies (5 Phase 1, 3 Phase 2, 1 Phase 3) using nonlinear mixed effects modeling (NONMEM®, version 7.3). Selected covariates were evaluated using stepwise forward selection/backward elimination.

Results: Final PK models of apomorphine/apomorphine-sulfate were adequately described by a two-tube-compartment model, with first-order input and elimination. Bioavailability of APL was ~15% relative to subcutaneous apomorphine. Mean apomorphine systemic clearance and central volume of distribution were 190 L/h and 260 L, respectively. Covariates of dose, contact time under the tongue, body weight, and gender had <1.5-fold change in area under the concentration-time curve and maximum plasma concentration (Cmax). Simulations predicted that 35 mg APL every 2 hours for 5 doses achieved ~50% of the apomorphine Cmax and ~2-fold higher apomorphine-sulfate Cmax compared with the same regimen of 6 mg subcutaneous apomorphine. Simulations indicated that patients with mild renal impairment had similar apomorphine/apomorphine-sulfate exposure to those with normal renal function following APL administration. Apomorphine/apomorphine-sulfate exposure increased with increasing APL dose; however, the increase was less than dose proportional.

Conclusion: A popPK model described comparable and differentiated PK characteristics of apomorphine/apomorphine-sulfate following sublingual and subcutaneous administrations.

POSTER 35
Population Exposure-Response Models of Apomorphine Sublingual Film in Healthy Subjects and Patients With Parkinson’s Disease and “OFF” Episodes

F. Agbo,1 Y-Y. Chiu,3 S. Chapel,3 G. Galluppi,1 B. Navia,1 D. Blum1 Sunovion Pharmaceuticals, Inc., Fort Lee, New Jersey, and Marlborough, Massachusetts, USA; 2Ann Arbor Pharmacometrics Group, Inc., Ann Arbor, Michigan, USA.

Objective: Exposure-response models were developed to characterize the relationship between apomorphine exposure and (1) efficacy using MDS-UPDRS Part III score in patients with Parkinson’s disease (PD) and “OFF” episodes, (2) systolic/diastolic blood pressure (sBP/dBP) in healthy subjects/patients, and (3) nausea/oral adverse events (AEs) in patients following apomorphine sublingual film (APL-130277; APL) administration.

Background: APL was generally well tolerated and effective as acute, intermittent treatment for “OFF” episodes in patients with PD.

Methods: Data were analyzed using nonlinear mixed effects modeling (NONMEM®, version 7.3). Final model simulations estimated apomorphine concentration and its association with MDS-UPDRS Part III score. For BP, nominal time-matched data were evaluated by linear and maximum effect models. Time-to-event and extended Cox proportional hazard models described nausea/oral AEs.

Results: For efficacy, a 23-point decrease from baseline in MDS-UPDRS score was estimated as the inhibitory maximum effect (Emax); a cutoff of ≤–12.5 points was associated with a FULL “ON” response; response duration increased from 1.6–3 hours for a 10-mg and 35-mg dose of APL, respectively, and average apomorphine concentrations of 2.4–2.04 mg/L correspond with these outcomes. For BP, single doses of 10 and 35 mg APL were predicted to decrease sBP by 3 and 7 mmHg, respectively, and dBP by 1 and 3 mmHg, respectively; decreases were more prevalent in patients than healthy subjects. For AEs, predicted risk of nausea (hazard ratio, 2.01) and oral events (hazard ratio, 1.34) were higher for single doses of APL 35 vs 10 mg, respectively.

Conclusion: Exposure-response models demonstrated a correlation between apomorphine exposure and efficacy using MDS-UPDRS Part III score. Increases in apomorphine plasma concentration were associated with a modest decrease in sBP/dBP, and an increase in risk for nausea and less for oral AEs following administration of sublingual apomorphine in patients with PD and “OFF” episodes.

POSTER 36
A Thorough QT Study of Apomorphine Sublingual Film in Patients With Parkinson’s Disease Complicated By “OFF” Episodes

F. Stocchi,1 K. L. Wilks,2 E. L. Peckham,3 M. F. De Pandis,4 K. Sciarappa,5 A. Agbo,6 R. Kleiman,6 D. Blum,1 B. Navia5 University and Institute for Research and Medical Care, IRCCS San Raffaele Pisana, Rome, Italy; 2MD Clinical, Hallandale Beach, Florida, USA; 3San Raffaele Cassino, Tosinvest Sanità, Cassino, Italy; 5Sunovion Pharmaceuticals Inc., Marlborough, Massachusetts, USA; 6ERT, Philadelphia, Pennsylvania, USA.

Objective: A phase 2, randomized, double-blind, placebo-controlled study was conducted in patients with Parkinson’s disease (PD) and “OFF” episodes to assess effect of apomorphine sublingual film (APL-130277; APL) on QT interval.

Background: APL was found to be safe, well tolerated, and effective as an acute, intermittent treatment for “OFF” episodes in patients with PD in a controlled phase 3 trial. No previous study has reported effects of apomorphine on QT interval.

Methods: Adult patients with PD and “OFF” episodes, no cardiac abnormalities, and no antiepileptic use on stable PD medications were eligible. Forty patients were randomized to a single dose of APL (dose determined during titration), matching placebo, and moxifloxacin (positive control; 400 mg) in a 3-way crossover design. Time-matched changes from baseline in the placebo-adjusted QT interval, corrected using Fridericia’s formula (delta delta QTcF), were calculated from electrocardiograms taken at 0.25, 0.5, 0.75, 1, 2, 3, and 4 hours postdose. Baseline was defined as the mean of 9 predose measurements.

Results: The lower limit of the Bonferroni-corrected 90% confidence intervals for the moxifloxacin-placebo comparison was above the 5 ms threshold at 3 of the 4 prespecified timepoints, demonstrating adequate sensitivity to assess QTc prolongation.

Conclusion: This is the first study to evaluate apomorphine delivered as a sublingual film on QT interval and other parameters of cardiac conduction in patients with PD and “OFF” episodes. An adequate sensitivity to assess QTc prolongation has been demonstrated. The results from these analyses will be subsequently presented.

POSTER 37
Using Social Media for Parkinson’s Disease Clinical Trial Recruitment

S. Ray, D. J. Burdick, P. Agarwal. Booth Gardner Parkinson’s Center, Evergreen Health, Kirkland, WA.
Objective: To identify advantages of using social media and make recommendations to sites, CROs and sponsors for its optimal use as a recruitment tool.

Background: Failure to recruit adequate number of participants delays the approval of new drugs and increases trial costs. Widespread use of social media has created a powerful new tool for clinical trial recruitment.

Methods: A recruitment committee identified best practices for social media recruiting.

Results: Social media advertising is cost effective and able to reach diverse hard to reach groups. It provides ef ficiencies in recruiting and reduces time. Social media platforms can identify key patient symptoms and allows direct interaction of viewers through web links. Sponsors and sites can use targeted advertisements to attract potential participants on Facebook or Instagram, where they are already logged on and active most days.

Recommendations to sites, CROs and sponsors: 1. Engaging with patient advocacy groups through discussion boards via Facebook, Twitter and Instagram. 2. Using ads on Google and Facebook and through an introductory video on YouTube and directing links embedded in the clinical trial ads. 3. Adequate budget for social media recruiting. 4. Review digital channels and social media sites to discover where targeted patient audience and caregivers can be found online. Monitor and analyze current online discussions on Parkinson’s Disease area. 5. Study users’ language, including the specific words and phrases they use to describe their symptoms. Identify key hashtags and regular online chats. This can help design the social media content. 6. Feedback, blogs and apps can be used for keeping participants engaged.

Conclusion: Social media may be effectively used by sites, CROs and sponsors as a recruitment tool in Parkinson’s disease clinical trials.

POSTER 38
Prevention of Fractures in Parkinson’s Disease (PD) with a Single Infusion of Zoledronic Acid (ZA)

Objective: To describe a large, home-based, clinical trial testing the hypotheses that among older patients with PD, a single treatment of ZA will reduce the risk of nonvertebral fractures, hip fractures, and all-cause mortality.

Background: Patients with PD (PWP) have a 2.5 to 3-fold risk of fracture, and a 4-fold increased risk of hip fracture. In PWP, fractures are associated with adverse events including increased mortality, yet only 5% of PWP have received FDA-approved osteoporosis treatment.

Methods: PWP over 65 will be identified through multiple sources, including PCORnet and other large clinical data research networks, the Parkinson’s Foundation (PF), the Parkinson Study Group (PSG) and Fox Trialfinder. Potential subjects will be referred to a call center at PF. After consent, a one-time telemedicine assessment by a PSG investigator will confirm PD diagnosis. Eligible participants will be randomized to a one-time home-based infusion of ZA or placebo. Fracture outcomes will be determined over two years from medical records and self-report, so that no follow-up study visits are necessary. The entire trial will be done from the patient’s home.

Results: In 2019, detailed study operations have been established. PSG investigators will be identified and trained. Eligibility screening, randomization and treatment will begin.

Conclusion: This study of home-based delivery of ZA could revolutionize bone health care and reduce a severe co-morbidity for PWP. This clinical trial is also innovative for methodological reasons. While osteoporosis has been proven effective in delivering clinical care for PD, its use to qualify PD patients for large-scale clinical trials has not been assessed. The use of remote assessment methods to identify eligible participants, combined with at home treatment, could serve as a model to revolutionize future large-scale PD clinical trials.

POSTER 39
Efficacy and Safety of Apomorphine Sublingual Film For the Treatment of “OFF” Episodes in Patients With Parkinson’s Disease: A Phase 3, Double-Blind, Placebo-Controlled Trial
S. A. Factor,1 S. Isaacson,2 R. A. Hauser,2 R. Palhu,4 K. Scarlappa,5 P. Bhargava,1 G. Vakili,5 D. Blum, B. Nava,5 C. W. Olano,5,2 Emory University, Atlanta, Georgia, USA; 2Parkinson’s Disease and Movement Disorders Center of Boca Raton, Boca Raton, Florida, USA; 3University of South Florida, Tampa, Florida, USA; 4University of Kansas Medical Center, Kansas City, Kansas, USA; 5Sunovion Pharmaceuticals Inc., Marlborough, Massachusetts and Fort Lee, New Jersey, USA; 6Mount Sinai School of Medicine, New York, New York, USA; 7Clintrex LLC, Sarasota, Florida, USA.

Objective: This phase 3, double-blind, placebo-controlled study evaluated the efficacy and safety of apomorphine sublingual film (APL-130277; APL) as an acute, intermittent therapy for “OFF” episodes in patients with Parkinson’s Disease (PD).

Background: A previous phase 2 study suggested that APL is efficacious for treatment of individual “OFF” episodes.

Methods: Adult patients with PD and ≥1 “OFF” episode per day while on stable doses of levodopa/adjunctive PD medications received increasing doses of APL (10–35 mg) in an open-label titration phase until a FULL “ON” response was achieved. Patients were randomized to placebo or APL at the dose determined during titration for 12 weeks. The primary endpoint was change from predose to 30 minutes postdose in MDS-UPDRS Part III Motor Examination score at week 12. The key secondary endpoint was the percentage of patients with a self-rated FULL “ON” response within 30 minutes at week 12.

Results: In total, 109 patients who completed the open-label titration phase were randomized in the double-blind treatment phase (APL=n=54, placebo=n=55). Least squares mean (± standard error) change from predose to 30 minutes postdose in MDS-UPDRS Part III at week 12 was −11.1 ± 1.46 with APL and −3.5 ± 1.29 with placebo (difference, −7.6 points; P=0.0002). Separation from placebo was seen as early as 15 minutes and persisted up to the 90-minute timepoint. The self-rated FULL “ON” response rate within 30 minutes postdose at week 12 was significantly higher for APL versus placebo (35% vs 16%; P=0.0426). The most common APL-associated, treatment-emergent adverse events (TEAEs) were nausea (28%), somnolence (13%), and dizziness (9%); the most common oral TEAE was oral mucosal erythema (7%); most TEAEs were mild and reversible upon treatment discontinuation.

Conclusion: APL was an efficacious and well-tolerated treatment for the acute, intermittent management of “OFF” episodes associated with PD.

POSTER 40
Optimized Imaging at 3.0 T of the Rostral Zona Incerta (rZI) for Deep Brain Stimulation (DBS) in Parkinson's Disease (PD)
A. Thaker,1 K. Reddy,2 J.A Thompson,3 P. David-Gerecht,3 A. Abosch,3 S. Ojemann,1 D.S Kern 1
1University of Colorado Anschutz Medical Campus, Aurora, CO, USA.

Objective: To improve upon imaging of the rostral zona incerta (rZI) allowing for direct targeting during deep brain stimulation.

Background: Subthalamic nucleus (STN) DBS is an effective treatment for Parkinson’s disease (PD); however, unwanted, adverse effects may occur. Recently, the rZI has been proposed as a potential alternative DBS target for the treatment of PD. This structure is not reliably imaged with standard MRI sequences preventing direct stereotactic targeting. In this study, we present pilot data demonstrating the use of a novel 2D coronal gradient echo (2DGRE) sequence which allows consistent visualization of the rZI in both control and PD populations at 3.0 Tesla.

Methods: Six PD patients and four healthy control subjects had 2DGRE sequences performed to visualize the rZI. Comparisons in ability to visualize the rZI was made with T1 and T2 MRI sequences in the PD patients who underwent 2DGRE imaging as well as in an additional five PD patients. Imaging of all 15 subjects was independently and blind-reviewed by a neuroradiologist and a movement disorder neurologist, utilizing a 3-point Likert scale rating bilateral rZI visualization (0-nonvisualized, 1-partially visualized, 2-clearly visualized).

Results: There was high inter-rater agreement between reviewers in scoring visualization of the rZI using the 2DGRE sequences in PD patients of 83% and in healthy subjects of 100%. The rZI was visualized in all individuals who underwent 2DGRE imaging. The rZI was better evident in healthy subjects compared with PD patients with a mean Likert score of 2 compared to 1.4, respectively. The rZI was not visualized with conventional T1 and T2 MRI sequences.

Conclusions: We demonstrate promising data that a 2DGRE sequence can image the rZI at 3.0 Tesla in PD patients. Prior short reports have successfully imaged this small structure in healthy controls. Improved visualization will allow direct targeting of the rZI.
**POSTER 41**

**Patient-Reported “Good” Days During a Prospective Study of the Treatment of Neurogenic Orthostatic Hypotension With Droxidopa**  
S. Kymes,1 L.A. Hewitt,2 C. François3 1Landbeck, Deerfield, IL, USA; 2Creative-Ceutical, Paris, France.

**Objective:** To evaluate the effect of droxidopa treatment on patient-reported assessments of a “good” or “bad” day in patients with neurogenic orthostatic hypotension (nOH)

**Background:** Droxidopa is approved in the United States to treat symptomatic nOH in adults. Common symptoms of nOH include lightheadedness and dizziness, which can lead to an increased likelihood of falls. Patients with nOH may experience decreased functional ability and an increased fear of falling, which can cause feelings of depression and anxiety, leading to social isolation.

**Methods:** In a 6-month prospective cohort study of patients with nOH newly initiating droxidopa treatment, participants were asked to quantify the number of good and bad days in the past week. Participants also reported outcomes using other validated instruments that measure nOH symptoms (Orthostatic Hypotension Symptom Assessment Item 1), functional impairment (Sheehan Disability Scale), depressive symptoms (Patient Health Questionnaire-9), fear of falling (Falls Efficacy Scale-International), and health-related quality of life (HRQoL; Short Form-8). Scores after 1 and 6 months of treatment were compared with baseline.

**Results:** After 1 month of droxidopa treatment, patients reported a significant increase in good days from baseline (mean, 4.2 vs 3.3 days/week; difference, 0.9 days/week; P<0.0001). Similar positive effects for the increase in reported good days were observed at 6 months vs baseline (mean, 4.5 vs 3.4 days/week; difference, 1.1 days/week; P<0.0001). The significant increase in good days at 1 and 6 months correlated with improvements in other patient-reported outcomes of nOH symptoms, fear of falling, functional impairment, depressive symptoms, and HRQoL (all P<0.0001).

**Conclusion:** Patients treated with droxidopa reported significantly more good days per week compared with before treatment initiation. The increased number of good days tracked with improvements in other patient-reported indicators of mental well-being. Improved patient perception of psychological status may represent an important downstream holistic benefit of nOH treatment.

**POSTER 42**

**Challenges in trial design for a first-in-human clinical trial of stem cell-based transplantation in Parkinson’s disease: the Parkinson’s neurologist’s perspective**  
H. Surve1 2 A. Lee,1 N. Hellmers,1 C. Henschliffe1 1Well Cornell Medical Center, New York NY, USA; 2Memorial Sloan Kettering Cancer Center, New York NY USA.

**Objective:** To describe challenges in designing first-in-human clinical trials of stem cell-based dopamine neuron precursor transplantation in Parkinson’s disease (PD).

**BACKGROUND:** Advances in stem cell technology stimulated renewed interest in regenerative medicine approaches to PD, with several groups potentially starting transplantation trials. Optimal trial design is critical but testing cell therapies presents different sets of challenges from small molecules to other biologics. We discuss novel aspects of study design in planning a first-in-human trial of a dopamine neuron precursor cell source, MSK-DA01, in PD.

**Methods:** Focused literature review including FDA and ISSCR guidelines, expert opinion.

**Results:** In this Phase 1, open label trial of two separate cell doses, we will study a small number of PD subjects. Key issues to consider are: (1) Optimal cohort: fetal tissue transplantation trials suggesting improved outcomes for younger participants and/or superior levodopa response, versus risks that favor broader age ranges and advanced PD. (2) Immunosuppression: the majority of efforts worldwide will use allogeneic cells, favoring at least temporary immunosuppression that broadly impacts study design and complexity. (3) Crafting optimal outcome measures focused on safety/tolerability, neuroimaging measures of graft survival, and appropriate measures of effects on motor and non-motor symptoms, and patient-related outcomes. We established a longitudinal observational study to optimize study read-outs in an advanced PD cohort; this may additionally provide historical data on potential participants. (4) Recruitment and retention: While widespread interest favors recruitment, the challenge will be retention because of variable timeframe of effects and the need for long-term follow up.

**Conclusion:** Clinical trial design for cell transplantation studies such as our planned Phase 1 trial presents a series of novel challenges to the movement disorders clinical researcher. Optimizing design at this early stage and attention to harmonization between individual groups will maximize learning for future therapeutic development.

**POSTER 43**

**Hispanic perspectives on Parkinson’s disease care and research participation**  
L. Damron,1 I. Litvan,1 H. Shill,2 B. Siddiqi,3 1University of California, San Diego, La Jolla, CA, USA; 2Barrow Neurological Institute, Phoenix, AZ, USA; 3The Michael J. Fox Foundation, New York, NY, USA.

**Objective:** Our study aimed to understand perspectives of the Hispanic Parkinson’s disease community and address barriers to research participation.

**Background:** Hispanics are under-represented in Parkinson’s disease (PD) research participation, especially in clinical trial participation, even though Hispanics make up a significant portion of the U.S. population.

**Methods:** We completed phone interviews with 20 Hispanic individuals with PD (HPD), 20 caregivers of Hispanic individuals with PD (CG), and 6 physicians who evaluate Hispanic PD patients (HP) in San Diego, CA. Interview transcripts were reviewed for common themes and coded accordingly. Additionally, questionnaires, using Likert-type statements, were administered to 62 HPD participants and 38 non-Hispanics PD patients in Phoenix, AZ. Frequency of responses was analyzed using t-tests with significance set at p<0.05.

**Results:** All phone interview participants endorsed the value of research with the majority (80% HPD and 95% CG) stating motivation for research participation was based on benefit of future generations. Most interviewees (70% HPD, 50% CG, 83% HP) agreed that Hispanics with PD had little disease knowledge. Other barriers including language, finances and transportation were recognized by 83% HPD but only 35% HPD and 45% CG. A total of 65% of Spanish respondents to questionnaires and 61% of English respondents indicated they had not participated in research. However, Spanish-speaking participants were very interested in participating in PD research, in fact this was the statement they agreed with most strongly (6.39 ± 1.25). Additionally, PD patients felt neutral about potential barriers to research participation (4.29 ± 2.12).

**Conclusions:** There is a disconnect between the acknowledged value of research and participation in this cohort. Logistical barriers to participation were downplayed by respondents yet endorsed by almost all of physicians interviewed. Our findings suggest that disease education will increase knowledge and research participation among the HPD community.

**POSTER 44**

**The long-term efficacy of STN vs GPI deep brain stimulation on Gait and Axial Function in Parkinson’s Disease Patients**  
Shanshan M,1 2 Eisinger RS,3 Wei H4 Ramirez-Zamora A4 1Department of Neurology, Xuanwu Hospital of Capital Medical University, Beijing, China; 2Clinical Center for Parkinson’s Disease, Capital Medical University, Beijing, China; 4Department of Neurosurgery Center for Movement Disorders and Neurorestoration University of Florida College of Medicine Gainesville FL USA; 4Department of Neurology, Center for Movement Disorders and Neurorestoration, University of Florida, Gainesville.

**Objective:** To examine the long-term outcome of axial and gait function after GPi-DBS and STN-DBS in Parkinson’s disease (PD) patients.

**Background:** Debilitating axial motor symptoms are frequently observed during Parkinson’s disease (PD) progression. Although deep brain stimulation (DBS) is an established treatment for management of motor complications in PD, the response of axial symptoms to this intervention is more difficult to predict with conflicting reports. There is limited data regarding the long term effect of both targets on axial symptoms.

**Methods:** We retrospectively reviewed baseline and 3 years follow up Unified Parkinson’s disease rating scale (UPDRS) II and III total scores of 72 PD patients (53 with STN-DBS and 19 with GPi-DBS) implanted at our institution. Measures of gait and balance included UPDRS II sub scores: item 13 (falls), item 14 (freezing of gait) and item 15 (walking). Axial symptoms were evaluated using the following UPDRS III sub scores: item 27 (stand from chair) item 28 (posture), item 29 (gait), and item 30 (postural stability). Wilcoxon’s test and Two-way ANOVA were used according to data distribution.
Results: At 3 years follow up, both STN and GPI DBS patients showed minimal change from baseline in gait and balance sub scores and total UPDRS II. In STN-DBS treated patients, the total UPDRS III off-med scores improved from baseline by 21.40% (p=0.000), with minimal change from baseline in the on-med/on-stim state (p=0.158). In GPI DBS patients, we observed mild improvement in UPDRS III off-med scores at 3 years that was not statistically significant (p=0.444). Finally, we observed off-med score of axial symptoms worsening compared to baseline by 1.77% (p=0.870) in STN DBS patients and 21.93% (p=0.099) in GPI DBS patients at 3 years.

Conclusions: Our study indicates that both STN and GPI DBS improved gait, balance and motor scores with worsening of axial symptoms at 3 years follow up.

POSTER 45

Head tremor: An ataxic phenotype of cervical dystonia

A. Merola,1 A. K. Dwiweedi,2 A. G. Shaiikh,2 T. Tareen,2 G. A. Da Prat,1,4 M. A. Kaufman,5 J. Hampf,6 J. Jankovic,7 C. L. Comella,8 B. D. Berman,9 J. S.Perlmutter,10 H. A. Jinnah,11 A. J. Espay,11 Gardner Family Center for Parkinson’s Disease and Movement Disorders, Department of Neurology, University of Cincinnati, Cincinnati, OH, USA;1 Division of Biostatistics & Epidemiology, Department of Biomedical Sciences, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center (TTUHSC), El Paso, TX, USA;2 Department of Neurology, University Hospitals and Cleveland VA Medical Center, Case Western Reserve University, Cleveland, OH;2 Sanatorio de la Trinidad Mitre, Departamento de Neurologia, Ciudad de Buenos Aires, Argentina;2 Consultorio y Laboratorio de Neurogenetica, Centro Universitario de Neurologia “Jose Maria Ramos Mejia” and División Neurologia, Hospital JM Ramos Mejia, Facultad de Medicina, UBA, Argentina;3 Instituto de Medicina de Precision y Genomica Clinica, Institute of Investigigaciones en Medicina Translacional, Facultad de Ciencias Biomedicas, Universidad Austral-CONICET, Argentina;4 Institute of Neurogenetics, University of Luebeck, Germany;5 Parkinson’s Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston TX, USA;6 Rush University Medical Center, Chicago, IL, USA;7 Department of Neurology, University of Colorado Anschutz; Medical Campus, Aurora, Colorado, USA;8 Neurology, Radiology, Neuroscience, Physical Therapy and Occupational Therapy, Washington University School of Medicine, St. Louis, MO, USA;9 Department of Neurology, Human Genetics and Pediatrics, Emory University, Atlanta, GA.

Background: Cervical dystonia (CD) can present with head tremor. It is unclear whether ataxic features are differentially associated with this phenotype of CD.

Objectives: We sought to evaluate: (1) the demographic features of CD patients with (Tr-CD) and without head tremor (nTr-CD) at onset, and (2) the differential ataxic features between these CD subtypes.

Methods: We compared demographic data in Tr-CD versus nTr-CD subtypes in the entire cohort of CD subjects enrolled in the Dystonia Coalition Natural History and Biorepository studies (n=1608). Separately, consecutively enrolled Tr-CD subjects (n=50) were age-, gender-, and disease duration-matched with nTr-CD subjects (n=50) for video-based ataxia severity scoring using the Scale for the Assessment and Rating of Ataxia (SARA) and the International Cooperative Ataxia Rating Scale (ICARS); and dystonia severity using the Toronto Western Spasmodic Torticollis Rating Scale section-I (TWSTRS) and the Global Dystonia Rating Scale (GDRS).

Results: Of 1,608 subjects, 18.1% (n=291) were classified as Tr-CD and 81.9% (n=1317) as nTr-CD. The Tr-CD cohort was older, predominantly female, and had longer disease duration than the nTr-CD cohort (p≤0.09). On blinded video-based evaluation, Tr-CD subjects had worse speech, gait and posture, and generalized ataxia scores, but milder dystonia scores compared to the nTr-CD cohort (p≤0.09). Low dystonia severity with high ataxia severity scores distinguished Tr-CD from nTr-CD with high accuracy (area under the curve, 0.91 [95%CI: 0.85-0.97]).

Conclusions: Head tremor represents a clinically distinguishable subtype of cervical dystonia affecting predominantly older women, with worse ataxia and milder dystonia than the non-remouls phenotype.

POSTER 46

Deep Brain Stimulation for Generalized Dystonia from Secondary Carinne Deficiency: A Case Report and Literature Review

YX (Amy) Zhang,1 L. Sperry,2 AJ. Dayananthan,3 M. Chan,2 S. Shankar,2 M. Martin,1 A. Duffy,4 N. Malhado-Chang,7 V. Wheelock,7 K. O’Connor,2 F. Girgis,2 S. Farias, L. Zhang,2 A. J. Espay,1 L. Sperry,2 C. L. Comella,8 B. D. Berman,9 J. S. Perlmutter,10 H. A. Jinnah,11 A. J. Espay,11 Liberty Medical Center, Rochester, NY, USA;2 Massachusetts General Hospital, Boston, MA, USA;3 National Institute of Neurological Disorders and Stroke, Bethesda, MD, USA;4 Northwestern University, Chicago, IL, USA.

Objective: To investigate the efficacy and safety of DBS treatment in secondary dystonia from organic acid metabolic disorder.

Background: Cervical dystonia can present with head tremor. It is unclear whether ataxic features are differentially associated with this phenotype of CD. We sought to evaluate: (1) the demographic features of CD patients with (Tr-CD) and without head tremor (nTr-CD) at onset, and (2) the differential ataxic features between these CD subtypes.

Methods: We compared demographic data in Tr-CD versus nTr-CD subtypes in the entire cohort of CD subjects enrolled in the Dystonia Coalition Natural History and Biorepository studies (n=1608). Separately, consecutively enrolled Tr-CD subjects (n=50) were age-, gender-, and disease duration-matched with nTr-CD subjects (n=50) for video-based ataxia severity scoring using the Scale for the Assessment and Rating of Ataxia (SARA) and the International Cooperative Ataxia Rating Scale (ICARS); and dystonia severity using the Toronto Western Spasmodic Torticollis Rating Scale section-I (TWSTRS) and the Global Dystonia Rating Scale (GDRS).

Results: Of 1,608 subjects, 18.1% (n=291) were classified as Tr-CD and 81.9% (n=1317) as nTr-CD. The Tr-CD cohort was older, predominantly female, and had longer disease duration than the nTr-CD cohort (p≤0.09). On blinded video-based evaluation, Tr-CD subjects had worse speech, gait and posture, and generalized ataxia scores, but milder dystonia scores compared to the nTr-CD cohort (p≤0.09). Low dystonia severity with high ataxia severity scores distinguished Tr-CD from nTr-CD with high accuracy (area under the curve, 0.91 [95%CI: 0.85-0.97]).

Conclusions: Head tremor represents a clinically distinguishable subtype of cervical dystonia affecting predominantly older women, with worse ataxia and milder dystonia than the non-remouls phenotype.
POSTER 48
What Bothers Parkinson Disease Patients? Verbatim Reports from >10,000 Patients Informing Natural History and Clinical Trials
I Shoulson,1,6,1 L Arbabji,2 C Marras,3 D Standaert,1 CM Tanner,1 L Smolensky,1 C Kopil,5 J Hamilton,7 E Flagg,6 CA Christopher,1 A Nguyen1,1 Grey Matter Technologies, Sarasota, FL, USA; 2University of Toronto, Ontario, Canada; 3University of Alabama at Birmingham, AL, USA; 4University of California San Francisco, CA, USA; 5Michael J Fox Foundation for Parkinson’s Disease Research, NY, NY, USA; 6University of Rochester, NY, NY, USA; 7University of San Francisco, CA, USA.

Introduction: Using natural language processing (NLP), expert clinical curation, and machine learning (ML), we analyzed the verbatim Patient Reports of Problems (PROP) from Parkinson disease (PD) patients who volunteered to answer in their own words: (1) What bothers you the most about your PD? and (2) In what way does this problem affect your daily functioning? Participants were also asked to reply to what bothers them the 2nd most, up to 5 bothersome problems. Methods: From February-August 2018, >10,000 consenting patients entered their verbatim PROP replies, age, and date of PD diagnosis by computer keyboard on the Michael J Fox Foundation (MJFF) FoxInsight. Results: Among 10,362 patients, 45,232 reported problems were categorized as motor (51.5%) and non-motor (48.5%) symptoms. Tremor was reported at all disease durations; Rigidity and Bradykinesia were more frequent with increased duration of PD; Postural Instability (PI) was reported early within 0-3 years of diagnosis, and more common with age of the patient and longer duration of PD. Sleep, Pain, Mood and Cognition problems were more frequent with increased duration of PD. Fatigue symptoms were similar across duration of PD and age. Constipation was more frequent with increased age and duration of illness. The most frequently reported motor and non-motor problems were PI and Cognition, informed by clinical curation into respective categories of gait disorder, slowness, balance, stiffness, falling, posture, freezing; and word finding, memory, concentration, cognitive slowing, confusion. These relationships will be illustrated by 3-D videos.

Conclusions: The PD-PROP and application of NLP/ML techniques show utility in capturing bothersome problems and provide a cross-sectional natural history of PD from the perspective of patients – to be further customized to enrich clinical trials and develop fit-for-purpose clinical outcome assessments.

POSTER 49
Tractographically defined subthalamic connectivity is associated with apathy in Parkinson’s disease and healthy subjects
S. A. O’Shea,1 D. Tomishon,1 Y. Gazes,2 N. Vanegas-Armyave1 1Columbia University College of Physicians and Surgeons, Department of Neurology, NY, NY, USA; 2Columbia University Medical Center, Department of Neurology, NY, NY, USA.

Background: Apathy is prevalent in Parkinson’s Disease (PD) patients. Despite the motor benefits obtained from Subthalamic (STN) Deep Brain Stimulation (DBS), postoperative apathy may reduce perceived benefit. The presence of metabolic deficits in frontal and cingulate cortices have been described in apathetic PD patients. We hypothesized that loss of integrity of white matter projections from the STN is associated with the development of postoperative apathy.

Methods: Nine patients with PD (57.4 ±6.3 years) and 14 controls (64.8±10 years) were assessed. Subjects underwent a brain MRI with DTI (FOV: 224mm, 112x112, b=2500 s/mm², 64 non-collinear gradient directions, spatial resolution 2x2x2mm), using a probabilistic approach with MRtrix. White matter integrity was measured using fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD) and tract density (TD). Tractographic measures were obtained for projections from the STN to ROIs that are the receiving limbic and associative regions (Broadman Areas BA10, BA11 and BA24). Subjects completed the Starkstein Apathy Scale.

Results: TD from the STN to BA10 on the left hemisphere was negatively correlated with apathy (R=0.4, p=0.06). FABA10 on the left hemisphere had a positive correlation with apathy (R= 0.548, p=0.01). In a logistic regression model, two of the above measures were associated with apathy (FABA10 p =0.0463 and TDBA10 =0.0455). No correlation was found with other ROIs or measures of radial, axial and mean diffusivity.

Conclusions: Our analyses suggest that lower TD to the BA10 are associated with the presence of apathy. Higher FA to BA10 was positively correlated with the presence of apathy. Low TD combined with higher FA values suggest the presence of white matter degeneration in areas of crossing fibers. Impaired integrity of STN-BA10 connectivity may be implicated in apathy. The presence of connectivity mechanisms may be the basis of specific patterns of clinical response to neurostimulation.

POSTER 50
RQ-00000010 for gastroparesis in Parkinson’s disease: a single ascending dose study
L. Cloud,1 Y. Norris,1 G. Blackwell,1 W. Wan,2 M. Halquist,1 J. Kuemmerle,1 C. Testa,1 and J. Venitz1
1Virginia Commonwealth University, Richmond, VA, USA; 2University of Chicago, Chicago, IL, USA.

Objective: To evaluate the safety, tolerability, pharmacokinetics (PK), and effects on gastric emptying of single, ascending doses of RQ-00000010 (RQ10) in Parkinson’s disease (PD).

Methods: We conducted a randomized, double blind, placebo-controlled, study of single ascending doses of 2, 50, and 200 µg of RQ10 oral solution in PD. In each dose cohort (N=8), subjects were randomized to placebo or RQ10 in a 1:3 ratio. Safety was evaluated clinically using adverse events (AEs), vital, ECGs and laboratory testing. Serial blood/urine RQ10 concentrations were measured by LC-MS/MS assay. Noncompartmental PK analysis was performed. Gastric emptying was assessed pre- and post-treatment by gastric emptying breath test; analysis of covariance and Fisher’s exact test were used to determine treatment effects and to compare the 3 doses and placebo.

Results: Twenty-three participants completed the protocol. No serious AEs or withdrawals due to AEs occurred. There were no changes of concern in laboratory tests, vitals, or ECGs. Plasma RQ10 exposures increased in a dose-proportional manner and about 50% of the dose was excreted in urine; the apparent oral clearance was reduced by ~25% and terminal half-lives prolonged compared to healthy volunteers. There was a significant dose-response relationship for patient-reported GI symptoms (p=0.015), but no significant change in gastric emptying time was observed (p=0.14), likely due to low sample size/high variability.

Conclusion: Single doses of RQ10 from 2-200 µg are safe, well tolerated, exhibit minor changes in PK relative to healthy volunteers, and may improve GI motility. Further development efforts are warranted.

POSTER 51
An Observational Study of PKG Movement Recording System Use in Routine Clinical Care of Patients with Parkinson’s Disease
Joshi R,1 Bronstein JM,2 Alcazar J,3 Yang D,2 Joshi M,1 Hermanowicz N2 1Clinical Partners Group, Santa Monica, CA, USA; 2Department of Neurology, University of Los Angeles (UCLA), Los Angeles, CA, USA. 3Department of Neurology, University of California-Irvine, Irvine, CA, USA.

Objective: We studied 63 Parkinson’s Disease (PD) patients during routine care at 2 US academic institutions to assess if an FDA-cleared wearable device enhanced patient symptom-reporting and treatment planning.

Background: PD is a progressive neurodegenerative disease consisting of a variety of symptoms. Examples of PD symptoms include: tremor, rigidity, slow movements (bradykinesia), and non-motor symptoms such as cognitive impairment, depression, and somnolence (Keener et al 2018).

Commonly used assessments such as the Unified Parkinson’s Disease Rating Scale (UPDRS) and clinical exams rely heavily on patient-reported symptomology to devise and monitor treatment regimens (Perlmuter, J 2009).

Methods: Center 1 enrolled 42 patients (total: 62 visits), while Center 2 enrolled 21 patients (total: 23 visits).

Movement Disorders, Vol. 34, Suppl. 1, 2019
Patients were assessed approximately every 3 months. For 6 continuous days prior to a visit, patients wore the Global Kinetics Corporation watch device that recorded movements and provided medication dosing reminders. Patient devices were uploaded in the clinic, and a Personal Kinetics Graph (PKG) report was generated. First, physicians interviewed and assessed patients for PD symptoms. Second, they compared their assessments to the PKG and identified variances in results. Lastly, physicians’, patients’ and caregivers’ PKG satisfaction rates were measured.

Results: Across all visits when patients did not report bradykinesia or dyskinesia, the PKG reported these symptoms (50% and 33% of the time, respectively). Physicians found improved dialogue with patients (in 59% visits), improved ability to assess treatment impact (in 38% visits), and improved ability to assess patient symptoms (in 35% visits). The PKG helped modify treatment plans (in 84% of visits). Patients stated (in 53% responses) they agreed or strongly agreed in PKG training, usability, performance, and satisfaction. They also reported (in 39% responses) that the PKG had a very valuable impact on their care.

Conclusion: Early use of PKG provides clinical utility in routine care and warrants more structured investigation in more patients.

POSTER 52

Efficacy results of a 12-month, dose-level blinded study of CVT-301 (levodopa inhalation powder) in patients with Parkinson’s disease

E. S. Farbman,1 M. Lew,2 C. H. Waters,3 R. A. Hauser,4 M. Klinger,5 C. Oh5 Roseman University, Las Vegas, NV; Keck/University of Southern California School of Medicine, Los Angeles, CA; Columbia University Medical Center, New York, NY; Parkinson’s Disease and Movement Disorders Center, Parkinson Foundation Center of Excellence, University of South Florida, Tampa, FL; Acorda Therapeutics, Inc., Ardsley, NY, USA.

Objective: We present efficacy results from a 12-month safety/efficacy open-label extension of a phase 3 study of Inbrija (CVT-301), a levodopa inhalation powder developed for intermittent treatment of OFF episodes in patients treated with carbidopa/levodopa.

Background: In the initial 12-week, double-blind, placebo-controlled study (SPAN-PS28) of patients experiencing OFF periods, CVT-301 84mg significantly improved motor function. 57.7% of patients on CVT-301 84mg turned ON within 60 minutes after treatment vs 36.1% on placebo at 12 weeks. This abstract describes an open-label extension study that investigated efficacy over 12 months.

Design/Methods: Patients from previous CVT-301 studies and eligible CVT-301-naïve patients were enrolled. Patients maintained their usual oral carbidopa/levodopa regimen. All patients received CVT-301 treatment for OFF periods but were blinded to dose (60mg/84mg). Efficacy assessments included in-clinic assessment for occurrence of an ON state during the 60-minute postdose period, and via PD home diary, change in total daily OFF time and change in daily ON time without dyskinesia.

Results: Patients were randomized to CVT-301 60mg (n=161) or CVT-301 84mg (n=164). At 12 months, during in-clinic evaluations, 68.4% of patients on CVT-301 60mg and 73.6% of those on 84mg achieved an ON state within 60 minutes. Percentages at 12 months were not significantly different from 1-month values. Home diaries demonstrated that mean changes from baseline in total daily OFF time improved from 1-month values of −0.33 and −0.55 hours, to −0.70 and −0.88 hours at 12 months (60-mg and 84-mg doses, respectively). Change from baseline in daily ON time without dyskinesia improved from +0.23 and +0.18 hours at month 1 to +0.32 and +0.40 hours at month 12 (60mg and 84mg, respectively).

Conclusions: CVT-301 maintained its improvement in achieving an ON state in patients experiencing OFF periods and showed improvement in decreasing daily OFF time and increasing ON time without dyskinesia over 12 months.

POSTER 53

Critical Path for Parkinson’s Consortium: Advancing Drug Development Tools and Regulatory Science for PD therapeutic trials

K. Romero,1 M. Akala,1 R. Alexander,2 B. R. Bloom,3 B. Boroojerdi3 D. Burn,4 J. Cedarbaum,5 D. Conrado1 D. T. Dexter1 E. R. Dorsay,6 M. Facheris,9 T. Fischer10 M. Fraisier,11 J. Gallagher,7 M. Forrest Gordon,12 D. Grosset,14 H. Hill,12 C. Ho,15 M. T. Hu,16 K. Kiebzuk,12 A. B. Lassen,17 R. Lawson,1 S. Macha,18 K. Marek,19 K. Taylor,20 D. Russell,11 J. Šebly,21 B. Stafford,1 G. Štebins,21 C. Venuto,12 C. Williams-Gray,22 A. Yarnall,23 with oversight from the Critical Path for Parkinson’s Consortium.1, Critical Path Institute;2 Takeda;3 UCB Pharma;4 Northwestern University Medical School;5 Nijmegen, the Netherlands;6 Newcastle University;7 Biogen;8 Parkinson’s UK;9 University of Rochester;10 AbbVie Inc.;11 The Michael J. Fox Foundation;12 Advisor to CPP;13 GSK;14 University of Glasgow;15 Denali Therapeutics;16 University of Oxford;17 Lundbeck;18 Merck & Co. Inc.;19 Institute for Neurodegenerative Disorders;20 Roche;21 Rush University, Advisor to CPP;22 University of Cambridge.

Objective: To highlight the progress of the Critical Path for Parkinson’s (CPP), a precompetitive consortium to advance drug development tools for early stages of Parkinson’s disease (PD).

Background: CPP is a public-private partnership, led by Critical Path Institute (C-Path), jointly funded by Parkinson’s UK and pharmaceutical companies. CPP comprises a broad coalition of stakeholders, including industry, regulatory agencies, academic experts and patient-advocacy groups.

Methods: By integrating diverse, multifaceted patient-level data into a standardized database, CPP seeks to generate solutions to bottlenecks in the drug development process for PD.

The proposed solutions will include regulatory-accepted disease progression models, clinical trial simulators and model-informed biomarkers to optimize clinical trial design. The CPP PD unified database’s current sources include: Parkinson’s Progression Markers Initiative (PPMI), Cambridgeshire Parkinson’s Incidence from GP to Neurologist (CamPaIGN) cohort and expanded Parkinson’s Disease Clinical Trials Cohort. Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation - PD (ICICLE-PD) and Tracking Parkinson’s. Clinical trial data include Parkinson Research Examination of CEP-1347 Trial (PRECEPT), Deprenyl and tocopherol antioxidative therapy of parkinsonism (DATATOP), Futility Study I (FS1) and Futility Study II (FSToo), Earlier versus Later Levodopa Therapy in Parkinson Disease (ELLDOPA) and Attenuation of Disease Progression with Azilect Given Once-daily (ADAGIO). Further datasets are scheduled to be included later.

Results: Three years after launching, CPP has 1) developed a worldwide PD patient-level database of >7300 individuals, 2) achieved a model-based qualification opinion from the European Medicines Agency (EMA) for the use of Dopamine Transporter neuroimaging (DAT) as an enrichment biomarker for early motor clinical trials, 3) released a user-friendly trial simulator based on the DAT model 4) formally engaged both FDA and EMA for regulatory acceptance of a PD disease progression model.

Conclusion: CPP is a successful worldwide precompetitive consortium with a regulatory focus in advancing solutions for PD therapeutic development. Future strategies include expanding the CPP database and evaluating digital disease progression measures.
POSTER 55
Fostering Inclusivity in Research Engagement for Underrepresented Populations in Parkinson’s Disease: The FIRE-UP PD Study
A. V. Sanchez, H. Hemley, J.D. Jackson. Massachusetts General Hospital, Boston, MA, USA.
Objective: This pilot study addresses barriers to research for underrepresented groups (URGs) in Parkinson’s disease (PD) research, and to increase URG enrollment in the online Fox Insight study with a small exploratory intervention.
Background: Greater diversity in clinical trial enrollment improves study generalizability and therapy efficacy. However, URGs in PD research remains rare, even in digital PD research platforms such as Fox Insight (FI). We hypothesized that interventions focused on engaging URGs would enroll a greater proportion of URGs than at passive control sites.
Methods: We define URGs as women, racial and ethnic minorities, individuals of lower socioeconomic status, or rural residents. We implemented a stratified randomization design for ten sites in an exploratory pilot design, in which pairs of sites were assigned to either intervention or control conditions. Each intervention site identified a specific barrier to PD research participation, a targeted URG, and a 6-month intervention to address the URG barrier. All sites report the Trust in Medical Researchers Scale (TIMRS), attitudes towards genetic testing, as well as URG accrual to FI, prior to and following the intervention period. Intervention and follow-up continues through December 2019.
Results: Primary analyses focus on descriptive and qualitative data obtained for future research. We have planned two levels of quantitative analysis: change in person-level TIMRS and accrual to PD research studies. We additionally measure URG accrual to FI from all sites. Digital media are leveraged to determine engagement with PD research.
Conclusion: Improving representation in PD research is a key step towards improving access to PD diagnosis and treatment for everyone. The current pilot proposal explores new ideas to enhance engagement and recruitment of URG in PD research studies. Upon study completion, best practices may be implemented in a larger number of sites to investigate the recruitment mechanisms uncovered in the current study.

POSTER 56
Understanding Racial Disparities in Parkinson’s Disease through Research
C. Branson,1,2 S. Bissonnette,2 T. Tewolde,1 E. Alemu-Mensah,1 M. Saint-Hilaire,1,3 1Morehouse School of Medicine, Atlanta, GA, USA; 2Boston University School of Medicine, Boston, MA, USA.
Objective: To increase the enrollment of African-Americans in Parkinson’s disease research.
Background: The prevalence of Parkinson’s Disease (PD) is lower among African-Americans than Caucasians. Yet, African-Americans have a higher PD related morbidity than Caucasians and are more likely to have delayed diagnosis and increased disability. Increasing the enrollment of African-Americans in PD-related research will improve overall outcome and care in PD patients. Morehouse School of Medicine and Grady Hospital in Atlanta, Georgia provides Neurological care to an underserved urban and rural population. There are currently no study sites among academic institutions with an emphasis on people of color.
Methods: Obtaining demographics, including race, gender, age, vital signs and ICD 9/10 coding diagnosis from the Informatics for Integrating Biology & the Bedside (I2B2) research database, which is an NIH funded national center for biomedical computing based at Partners Healthcare system.
Results: There are more than 200 patients with a diagnosis of PD at Grady Hospital in Atlanta, GA. Approximately 130 patients are defined as Black or African-American compared with 70 described as Caucasian.
Conclusion: Understanding racial disparities in PD will likely improve care for this population and increase the number of minorities in PD research.

POSTER 57
Exploring the Role of LRRK2 in Melanomagenesis
W. Cai, P. Liu, M. A. Schwarzschild, X. Chen. MassGeneral Institute for Neurodegenerative Disease, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.
Background: Emerging evidence supports that leucine-rich-rich repeat kinase 2 (LRRK2), the greatest known genetic contributor to Parkinson’s disease (PD), may play a role in cancer. LRRK2 G2019S carrier PD patients show an overall increased risk of cancer. LRRK2 mutations are frequently detected in human melanomas, a type of cancer that is linked to PD.
Objective: The present study is to explore the potential role of LRRK2 in cancer, specifically, in melanoma.
Methods: Immortal human melanocytes, C140 mouse melanocytes, B16 mouse melanoma cells, MeWo human melanoma cells, and M14 human melanoma cell were employed. Cells were transfected with wild-type and G2019S mutant LRRK2. Western blotting and immunostaining were performed to confirm expression of total LRRK2 and phosphorylated LRRK2 at S935. The key survival and proliferation signals Akt and Erk were detected by western blot. Cell proliferation was assessed by MTT assay.
Results: Endogenous LRRK2 expression was detected in C140. B16, MeWo and M14 cell by Western blotting. LRRK2 expression levels appear to be higher in melanoma cell lines compared to melanocytes cell lines. Successful transfection of wild-type and LRRK2 G2019S was achieved in C140 and B16 cells. Overexpression of both wild-type and LRRK2 G2019S resulted in higher levels of phosphorylated LRRK2. Wild-type and LRRK2 G2019S overexpression also induced Akt and Erk in both C140 and B16 cells. Higher ratios of phosphorylated Akt to Akt and phosphorylated Erk to total Erk have been demonstrated in C140 and B16 cells overexpressing with wild-type or LRRK2 G2019S, indicating activation of Akt and Erk signals by LRRK2. Further, overexpression of wild-type and LRRK2 G2019S led to increased cell proliferation in B16.
Conclusion: Our results preliminarily demonstrate that LRRK2 activates survival and proliferation signals in melanocytes and melanoma cells. LRRK2 may promote cell proliferation in melanoma cells. Further laboratory studies are needed to define the functional role of LRRK2 in cancer. In parallel, we are working to determine cancer-related metabolites in PD patients carrying LRRK2 mutations.

POSTER 58
Preliminary findings of the use of cannabis in Parkinson disease
M. A. Leehey,1 Y. Liu,1 F. Hart,1,2 J. Klawitter,1 C. Sempio,4 S. Fischer,1,2 C. Epstein,1 M. Cook,1 S. Sillau,1 Z. Baud,1 H. Newman,1 O. Klepitskaya,1 E. Diguillo,1 S. Baker,1 T. Seawalt,1 D. Vu,1 T. Hawkins,1 M. Fullard, J. Bainbridge,1 1Department of Neurology, 2Department of Clinical Pharmacy, 3Regulatory Compliance Office, 4Department of Anesthesiology, 1University of Colorado, Aurora, CO, USA.
Objective: To determine the efficacy and tolerability of cannabis in Parkinson disease (PD).
Background: The use of cannabis in PD is increasing, despite lack of data. We completed an open label study and started a randomized, controlled study.
Methods: Open label participants took an oral purified cannabidiol (CBD) (Epidiolex®, GW Pharmaceuticals). Primary outcome was tolerability. Based on those results, a randomized, controlled study has been initiated, n=60, using an oral 30:1 CBD: tetrahydrocannabinol (THC) extract from the National Institute of Drug Abuse, with participants taking about 125mg CBD and 4.2mg THC twice daily.
Results: The open label study included 13 participants (10 male), mean age (SD) 68.15 (6.05), baseline total and motor Movement Disorder Society Unified PD Rating Scale (MDS UPDRS) scores of 39.23 (13.32) and 22.92 (9.30), respectively. The mean maximum CBD dose was 19.23mg/kg/day, i.e., 1623.01mg/day; participants took study drug for 26.8 (8.0) days. All reported at least one adverse event, including diarrhea (85%), somnolence (69%), fatigue (62%), weight gain (31%), dizziness (23%), abdominal pain (23%) and headache, weight loss, nausea, anorexia, and increased appetite (15%). Five (38%) had elevated liver enzymes, 2/5 had a cholestatic pattern, 4/5 were asymptomatic, and all were transient. Most adverse events were mild; none serious. Three (23%) stopped study drug due to intolerance. 10 participants that completed the study had improvement in total and motor MDS-UPDRS scores of 7.70 (9.39, mean decrease 17.8%, \( p=0.0115 \)) and 6.10 (6.64, mean decrease 24.7%, \( p=0.0041 \)), respectively. Night-time sleep and emotional behavioral dyscontrol also improved significantly. CBD plasma levels averaged 340 ± 4 ng/mL. Demographic data on enrolled participants of the randomized, controlled study will be presented.

Conclusion: CBD, in the form of Epidiolex\textsuperscript{®}, may be efficacious in PD, but the FDA approved dose for pediatric epilepsy was associated with liver enzyme changes in this older PD population.