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**NATIONAL VA PARKINSON'S DISEASE
CONSORTIUM**
Education · Collaboration · Advocacy

THE TRANSMITTER

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Article Reviews

Prepared by: Debra Dellinger, NP, Mark Baron MD, William Carne PhD, – Southeast PADRECC

Pharmacokinetic drug evaluation of CVT-301 for the treatment of Parkinson's disease.

Levodopa (LD), in combination with a decarboxylase inhibitor, is a mainstay and the most effective therapeutic agent in the treatment of Parkinson's disease (PD). Unfortunately, during chronic treatment with this agent, ON-OFF phenomena and dyskinesia appear. Despite the many medical treatment options available, unpredictable OFF episodes can still occur and be severe and disabling. A rescue therapy that provides a rapid and predictable ON response for patients with OFF periods would be of great value for such patients. CVT-301 is a self-administered dry powder aerosol inhaled formulation of LD that is being developed as a self-administered treatment for OFF periods. CVT-301 may offer several potential advantages including increased systemic bioavailability through pulmonary absorption, rapid onset of action, avoidance of first-pass drug metabolism and less plasma-level variability.

[Expert Opin Drug Metab Toxicol.](#) 2018 Dec;14(12):1189-1195. doi: 10.1080/17425255.2018.1550483.

Sublingual apomorphine (APL-130277) for the acute conversion of OFF to ON in Parkinson's disease.

OFF episodes negatively impact quality of life in patients with Parkinson's disease (PD). There remains a need for an acute, effective, noninvasive treatment. APL-130277 is a sublingually administered apomorphine oral strip. A phase 2, open-label, proof-of-concept study was conducted. Patients presented to clinic in the morning in the practically defined OFF state and were dosed with APL-130277 10 mg. Assessments of OFF or ON state and MDS-UPDRS part III were conducted predose and at 15, 30, 45, 60, and 90 minutes. If a full ON was not achieved within 3 hours, the dose was increased in 5 mg increments until a full ON was achieved or to a maximum dose of 30 mg. Patients could be dosed up to two times a day over 3 days. Patients were pretreated with trimethobenzamide for 3 days, which was continued during the study. Of the 19 patients, 15 (78.9%) achieved a full ON response. All 15 achieved a full-ON response within 30 minutes and 6 of the 15 patients (40.0%) achieved a full ON response within 15 minutes. The mean (SD) duration of ON was 50 (19.4) minutes. Of the 15 patients, 9 (60.0%) remained fully ON for ≥ 90 minutes. There were no discontinuations as a result of an adverse event. The most common adverse events were dizziness (36.8%), somnolence (31.6%), and nausea (21.1%). This was the first study of a new sublingual apomorphine formulation in PD patients. In this open-label study, the authors concluded that APL-130277 appeared to provide a convenient, rapid, and reliable method for treating OFF episodes.

[Mov Disord.](#) 2016 Sep;31(9):1366-72. doi: 10.1002/mds.26697. Epub 2016 Jul 19.

Informant- and Self-Appraisals on the Psychosis and Hallucinations Questionnaire (PsychH-Q) Enhances Detection of Visual Hallucinations in Parkinson's Disease

Clinicians vary in their ability to elicit and interpret hallucinatory symptoms in patients with Parkinson's disease (PD) and patient report is also not well-validated. One hundred sixty-three PD patient-informant pairs were used to test the usefulness of an informant version of the Psychosis and Hallucinations Questionnaire (PsychH-Q) and its relation to clinician estimates of hallucinations. Additionally, three other questionnaires were completed

(Neuropsychiatric Inventory Questionnaire; Parkinson's Psychosis Questionnaire; and Scales for Outcomes in Parkinson's disease–Psychiatric Complications). Self-ratings and informant ratings across analogous subscales for hallucination presence were compared to clinician ratings on the MDS-UPDRS. There was a low level of agreement between dyads (average $\kappa = 0.39$; κ range = 0.32–0.47; $P < 0.001$), and patients indicated the highest prevalence of hallucinations compared to informant or clinician estimates. Clinician interview missed 32% of PsychH-Q hallucinators identified by dyads. Relative to the sample, 22 patients with exclusively clinician-appraised hallucinations had poorer overall quality of life measured by the Parkinson's Disease Questionnaire. The sole use of clinician-rated scales may underestimate prevalence of PD hallucinations, and there is room for introducing self- and informant-report tools. Nonetheless, clinician appraisals are critical in cases when informant and patient insight might be affected by the impact of illness on quality of life. *Mov Disord Clin Pract*, 5: 607-613. doi:[10.1002/mdc3.12683](https://doi.org/10.1002/mdc3.12683)

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Southeast/Richmond PADRECC leads the committee for January/February. The committee meets via conference call the first Tuesday of the month at 12pm (EST)
- **Standardize and Optimize Clinical Care:** The committee continues to discuss latest research on PD, new treatment strategies and a variety of clinical issues to improve patient care and outcomes. It also serves to provide clinical support to the consortium network by focusing on measures to standardize clinical care across the PADRECC network. Recent agenda items have included discussions on:

Update from minutes

1. Clinical experience and discussion on obtaining baseline EKG with QTc monitoring on patients on anti-psychotics and Pimavanserin
2. Continued discussions and progress towards delivering Telehealth to our veterans using Video Connect.
3. VA Tele-Mental Health Parkinson's Disease Expert Consultation Program was developed to assist providers with managing PD patients with complex mental health diagnostic or psychopharmacological questions
4. Discussion about the use of St. Jude, Medtronic or Boston Scientific device for deep brain stimulation.
5. Clinical experience with recently introduced medications for Parkinson's disease, Huntington's disease, and tardive dyskinesia including Rytary, Extended Release Amantadine, Pimavanserin, deutetrabenazine, valbenazine, etc.
6. Continued discussion about referrals, outcomes and target selection trends regarding deep brain stimulation surgery for PD, ET, and dystonia.
7. Continued discussion focused on clinical experience sharing among the group regarding DUOPA™ (carbidopa/levodopa) enteral suspension for the treatment of motor fluctuations in advanced Parkinson's disease
8. Discussion about newer avenues of delivering tele-health within the VA healthcare system including video-connect
9. Discussion about newer clinic models to provide focused treatment for non-motor symptoms of PD (Palliative Care Clinics) and to improve overall health of our patient population (Wellness Clinics)

10. Discussion about the role of kinesiotherapy in Parkinson's disease.
11. Strategies to minimize the impact of reduced workforce at the PADRECC, innovative ideas to improve performance and deliver care
12. Discussion about collaborative research, including involvement in industry supported projects like Apomorphine subcutaneous infusion study
13. The prevalence of vitamin D deficiency in Parkinson's disease, the need to monitor and strategies and outcomes of current replacement strategies
14. Discussion about management of psychogenic/functional movement disorders

Education Committee

- **PADRECC/EES Movement Disorder Series:** The second audioconference for FY 19 was held on January 10, 2019 “**Stimulating Memory in Parkinson's Disease: New Directions in Neuromodulation**” by R. Kathryn Holloway, Chief Neurosurgeon, Richmond/Southeast PADRECC. The audioconferences are archived on the national website www.parkinsons.va.gov under the Movement Disorder Series tab. Please see the **Dates to Remember** section below for a listing of upcoming FY19 audioconferences and mark your calendars.
- **PD at Home:** Monthly PD telephone education/support group conference available nationwide on the 2nd Tuesday of each month: 10am PT, 11am MT, 12p CT, 1pm ET. Monthly flyers will be emailed to all Consortium Members, please advertise to your PD patients.
- **Updating PADRECC Pocket Card:** Committee is exploring updating the pocket card which includes the treatment algorithm and medication list as it is out of date. Project request submitted and approved by EES to help with design and distribution. Prospective project start date, February 2019.
- **National Website Maintenance:** The committee performs maintenance checks of the National Website to ensure information is current and up-to-date.
- **PADRECC Transmitter:** This committee continues to assemble and distribute this *e*-newsletter every other month.
- **VA Pulse- PADRECC is now on VA PULSE-** We invite you to follow us: <https://www.vapulse.net/community/care-topics/parkinsons-disease/overview>

On this page you can view notices of upcoming Movement Disorders Series presentations, links to all recorded webinars and our 20-video VA Parkinson's playlist on YouTube. Also available are a wealth of resources for VA Professionals and Veterans/families, research publications, informational newsletters, and more.

- **Resources available on the National Website-** *Please share with your patients*
 - **Patient Education Brochures-** <https://www.parkinsons.va.gov/patients.asp>
 - Exercise and Physical Activity
 - Fall Prevention
 - PD Medications
 - Motor Symptoms
 - Non-Motor Symptoms
 - Agent Orange and Toxic Exposures and PD
 - **My Parkinson's Story-**<https://www.parkinsons.va.gov/patients.asp>
A series of short videos prepared by the VA PADRECCs addressing various aspects of Parkinson's

disease.

- **Suggested Education Essentials for Veterans with PD** <https://www.parkinsons.va.gov/patients.asp>
- **PADRECC Support Group Listings** <https://www.parkinsons.va.gov/patients.asp>
- **Updated Resource Request Form**-PADRECC staff and consortium members can order bulk supply of FREE educational materials from PF and APDA. Please click on the following website link and complete the *Resource Request Form* and mail or fax to address listed: <https://www.parkinsons.va.gov/clinicians.asp>

Southeast PADRECC Service Area Updates

Southeast PADRECC

Acting Director: Dr. Jessica Lehosit

Research Update:

Research at the Southeast Richmond PADRECC has undergone a rapid expansion over the past year. With more flexibility and many pending collaborative efforts, we hope to expand research even further next year. For more information on any of these studies, please contact George Gitchel PhD, at george.gitchel@va.gov, or 804-675-6300.

Oculomotor functions in movement disorders:

This ongoing study has been enrolling subjects for 10 years, and has become a part of every willing participant's initial visit to our clinic. Eye movements are recorded for 5 minutes while subjects follow basic stimuli. Specific, unique, repeatable eye movement abnormalities have been correlated with different movement disorders, strongly suggesting the ability to assist in differential diagnosis. George Gitchel PhD, Mark Baron MD, and their collaborator from the local university have filled for a patent on the technology, and have licensed the intellectual property to a company. Tremendous progress has been made in writing algorithms and coding to automate data analysis as well as differential classification of each disorder. Royalties from this collaboration have already come back into the VA system, and we believe this will substantially increase when a commercially viable product is released within the next year. The company announced the release of this new product at the Consumer Electronic Show (CES), where it was awarded as an Innovation Awards Honoree, for "Tech for a Better World."

(<https://www.businesswire.com/news/home/20180107005112/en/Eyes-Health-CES-2018-Innovation-Awards-Honoree>)

Eye movements as a clinical and prodromal biomarker in Parkinson's disease:

Funded by the Michael J Fox Foundation for \$1M, this study expands upon our longstanding aforementioned protocol investigating the oculomotor behavior of movement disorders. This blinded multisite study (Richmond PADRECC, VCU, Emory, University of Iowa) is recruiting controls, PD subjects, those with "Other" movement disorders, and subjects with REM behavior disorder (RBD). Enrollment is over halfway complete, and interim analysis is promising; with the data suggesting that blinded eye movement recordings could potentially effectively differentiate clinically manifest disease states. Excitingly, preliminarily, the data from RBD subjects strongly suggest the ability to detect preclinical stages of PD, perhaps a decade or more before clinical conversion.

BOSS-PD:

The Richmond PADRECC is serving as a site for this MERIT funded study at the Atlanta VA. The purpose is to investigate the equivalence (or at least non-inferiority) of behavioral therapy versus Solifenacin for urinary

incontinence in PD subjects. Jessica Lehosit DO, Debra Dellinger NP, and George Gitchel PhD, are actively enrolling subjects in this study.

TMS for cognition in TBI subjects:

George Gitchel (PI) was awarded \$500k for this study to investigate the possibility of improving cognition in a population of TBI subjects with cognitive complaints. The PADRECC owned TMS system is being utilized in this double blind, sham controlled crossover study, and enrollment is more than 1/3 complete. If findings are positive, this protocol will be expanded and submitted for funding in a population of PD subjects.

RRRSC:

The Richmond Rehabilitation Research Steering Committee (RRRSC) was formed within the last year, with George Gitchel PhD as a founding member. The purpose of this committee is to foster collaboration between many related but independent services in the hospital. As a result of the RRRSC, 3 grant applications have been submitted that will involve PD subjects. We have identified investigators in pain, psychiatry, vestibular, and cognitive therapy who have all expressed interest in submitting collaborative grants with PADRECC involvement.

Bile Acids and Gut Microbiome:

This is a MERIT funded study at the Richmond VAMC in the hepatology clinic. PADRECC is a collaborative partner, recruiting and assessing PD subjects to compare with other conditions affecting the gut. Enrollment is currently open for this study.

AP2-3000:

Richmond PADRECC has been selected as a site for this study involving the Apokyn subcutaneous continuous infusion pump. Currently pending IRB approval.

P2B001/003:

Richmond PADRECC has been selected as a site for this study investigating this new drug that contains rasagiline and pramipexole in a single pill. Currently pending IRB approval.

RESTORE-402:

Richmond PADRECC has been selected as a site for this study investigating droxidopa for neurogenic orthostatic hypotension. We have not yet received regulatory paperwork for this study, but anticipate starting in the coming months.

PASSPORT STUDY:

We have been selected as a back-up site for this study which involves a possible tau antibody for the treatment of PSP.

Alpha-stim Cranial Electrotherapy Stimulation (CES):

Dr. Abu Qutubuddin MD, MBBS PADRECC Associate Director of Rehabilitation and William Carne PhD PADRECC Neuropsychologist.

Sleep disorders are very common in patients with Parkinson's Disease. Dr. Qutubuddin and Dr. Carne are in the process of starting research using Alpha-Stim to treat sleep disorders in Parkinson's patients, mainly insomnia.

The Alpha-Stim CES is a device used in the treatment of depression, anxiety, sleep and pain. The exact mechanism and how it produces its effect is not fully known. It appears that the Alpha-Stim's microcurrent waveform activates a groups of nerve cells that are located at the brainstem. These nerve cells produce the

neurotransmitters serotonin and acetylcholine, which can affect the chemical activity of the nerve cells that are both nearby and at a distant site. Alpha-Stim appears to amplify or diminishes the activities of these cells called modulation, and occurs either because of, or together with the production of a certain type of electrical activity pattern in the brain known as an alpha state which can be measured on brain wave recordings. Such alpha rhythms are accompanied by feelings of calmness, relaxation and increased mental focus. The neurological mechanisms that are occurring during the alpha state appear to decrease stress-effects, reduce agitation and stabilize mood, and control both sensations and perceptions of types of pain.

These effects can be produced after a single treatment, and repeated treatments have been shown to increase the relative strength and duration of these effects. In some cases, effects have been stable and permanent, suggesting that the electrical and chemical changes evoked by Alpha-Stim have led to a durable re-tuning back to normal function. Electromedical Products International, Inc. is dedicated to using exciting new research technology and advanced, innovative methods to study the exact mechanisms through which Alpha-Stim can be beneficial to patients with pain, anxiety, depression and sleep disorders.

Clinical/Education News

Telehealth Update:

The Richmond PADRECC continues to expand telehealth services to those veterans unable to travel to the Richmond PADRECC for face to face clinical visits. Richmond PADRECC has consistently seen over 400 TH visits/year for the last 2 years. We are currently projected to increase by 10-15% for this fiscal year.

TH continues to be utilized by our Neurosurgery DBS team. Neurosurgeon, Dr. Kathryn Holloway and DBS coordinator, Miriam Hirsch BSN, RN provide DBS evaluations and off/on medications testing via TH as part of the preliminary evaluations for DBS.

Speech Therapy:

Richmond PADRECC - Moving forward with Speech Therapy – Adding CVT to Home, Pre- and Post DBS evaluation and Utilizing the Speech Vive.

Caitlin Kane, M.Ed. CCC-SLP has recently transitioned to serve as the primary Speech-language Pathologist for the Richmond PADRECC treating patients who have impairment in speech, voice, swallowing or cognition. She has established pre- and post-operative speech screening tools for patients undergoing deep brain stimulation (DBS) surgery.

In addition, Collaborative efforts from the speech pathology department and PADRECC team have recently brought the Speech Vive, an effective tool to improve vocal loudness, to the Richmond VAMC. Caitlin is also working to help increase utilization of interdisciplinary therapy through Clinical Video Telehealth allowing the veteran to be seen and treated in the convenience of their own home

Wellness Workshop:

Richmond PADRECC Providers collaborated with a community Assisted Living facility offering a Wellness Workshop to PD patients in the community. Topics included a Holistic Approach to Managing Parkinson's, atypical Parkinsonism, fatigue and GI complications. The wellness workshop was well attended.

Rehabilitation Services:

During Parkinson's Awareness month in April, the Richmond PADRECC in collaboration with PM&R held an educational awareness event covering Rehabilitation services available at the Richmond VA for our Parkinson's patients. Each department including Physical Therapy, Occupational Therapy, Speech Therapy, Kinesiotherapy and Music Therapy presented information about their discipline, demonstrated equipment and answered questions. The event was led by Dr. Abu Qutubuddin MD, MBBS PADRECC Associate Director of Rehabilitation and Lynn Klanchar RN, MSN associate director of education for the Richmond PADRECC.

Southeast Consortium Center Updates:

- From Burton Scott, MD, PhD, Director at **Durham, NC**: Durham Consortium Center provides care for about 100 veterans with Parkinson's disease (PD). Our PD clinics meet 10 times a month and are staffed by two movement disorders neurologists, Dr. Burton Scott and Dr. Jeff Cooney, in addition to Anna Cotton, PA and a variety of Duke Neurology residents who rotate through the clinic. Physical therapy, occupational therapy, speech therapy, and social work support are available at our facility. The VA neurosurgeons, Dr. Dennis Turner and Dr. Nandan Lad perform about 6 Deep Brain Stimulation (DBS) surgeries at the Durham VAMC per year, and about 100 DBS surgeries per year at Duke University Medical Center across the street from the VA. Initial DBS programming is performed by Dr. Turner's group, and maintenance programming is done in our movement disorders clinics. In addition, Veterans are offered the opportunity to participate in multiple Parkinson's disease clinical trials at Duke University if they choose to, including trials sponsored by Biogen, Biotie, and the Parkinson Study Group.
- From Michael Hoffman, Director and Lourdes Benes Lima MD Movement Disorder Specialist and Behavioral Neurology at Orlando, FL: continues with intestinal carbidopa levodopa program and botulinum toxins for all dystonia's and sialorrhea.

Dates to Remember

March 14, 2019

EES/PADRECC Movement Disorders Series

Topic: Pain in PD

<http://www.parkinsons.va.gov/>

May 4-10, 2019

American Academy of Neurology (AAN) Annual Meeting

Philadelphia, PA

<https://www.aan.com/conferences-community/annual-meeting/>

May 9, 2019

EES/PADRECC Movement Disorders Series

Topic: Sleep Issues and PD

<http://www.parkinsons.va.gov/>

June 2-7, 2019

5th World Parkinson Congress

Kyoto, Japan

<https://www.worldpdcoalition.org/default.aspx>

September 12, 2019

EES/PADRECC Movement Disorders Series

Topic: Parkinson's 101

<http://www.parkinsons.va.gov/>