Adjunct Zonisamide to Levodopa for DLB Parkinsonism: a Randomized, Double-blind Phase 2 study

Previous studies have shown that low-dose zonisamide can improve motor symptoms of Parkinson’s Disease (PD) when used as an adjunct to levodopa. In this study, 158 patients with probable Dementia with Lewy Bodies (DLB) on stable levodopa treatment were randomized to receive zonisamide 25 mg/day, 50 mg/day or placebo. The primary outcome measure was change in Unified Parkinson’s Disease Rating Scale (UPDRS) part 3, which measures motor symptoms of PD, from baseline to follow-up at 12 weeks. Subjects who received zonisamide 50 mg/day were shown to have a significant improvement in UPDRS part 3 score when compared to placebo. Zonisamide did not worsen cognitive function, behavioral and psychological symptoms of dementia, or caregiver burden. Similar rates of adverse events were observed among all groups, and the adverse events were similar to what the PD studies have shown, namely anorexia and weight loss. This study provides Class I evidence that zonisamide, adjunctive to levodopa, improves motor symptoms in patients with DLB without worsening their neuropsychiatric symptoms.

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Using Smartphones and Machine Learning to Quantify Parkinson Disease Severity: The Mobile Parkinson Disease Score.

Having a tool to objectively assess On/Off motor state in Parkinson's disease (PD) in the real-life environment has long been a goal of PD clinical research, especially since subjective "motor diaries" are notoriously inaccurate. Currently, many researchers are using mobile technology as a means of achieving this goal. In this study, Zhan et al., at Johns Hopkins University, performed smartphone app activity assessments (comprised of 5 tasks: voice, finger tapping, gait, balance, and reaction time) in 129 individuals, and used machine learning to generate a novel "mobile PD score" (mPDS). The mPDS correlated well with motor fluctuations measured by standard in-clinic MDS-UPDRS assessments on 40 individuals. The researchers concluded that the assessments could be "performed frequently in real-world settings", not impacted by interrater variability. Hopefully, upon further validation, this will be a useful tool in objectively measuring motor state in real-life environment, which might help in clinical treatment decision-making, and clinical trials research.


Effect of High Intensity Treadmill Exercise on Motor Symptoms in Patients with De Novo Parkinson Disease: A Phase 2 Randomized Clinical Trial

Previous studies have shown that endurance exercise is beneficial for symptom modification, health benefits and possibly neuroprotection in Parkinson’s Disease (PD), but there is limited evidence that endurance exercise modifies disease severity, particularly high-intensity exercise. The SPARX study (The Study in Parkinson’s Disease of Exercise) was a phase 2 multi-center randomized clinical trial designed to examine the feasibility and safety of high-intensity treadmill exercise in patients with de novo PD not on medication. It evaluated 128 PD patients randomly assigned to 1 of 3 groups including high-intensity endurance exercise (80-85% maximum
heart rate, 4 days per week), moderate-intensity endurance exercise (60-65% maximum heart rate, 4 days per week) or control (usual exercise). Feasibility measures included adherence to prescribed heart rate and exercise frequency of 3 days per week. Clinical outcomes included 6-month change in UPDRS motor score.

Feasibility was determined with both high and moderate-intensity exercise groups meeting the targeted heart rate intensity and exercise frequency. A futility analysis was conducted using UPDRS motor scores, revealing that the high-intensity group 6-month change of 0.3 compared to a change of 3.2 in the usual care/control group did not reject the null hypothesis, reaching the non-futility threshold. This was not the case for the moderate intensity group.

The authors concluded that high intensity endurance exercise is feasible and attenuates worsening on the UPDRS motor score over 6 months. It can be safely conducted, with adverse musculoskeletal events as expected with endurance exercise, which was reflected in the low attrition rate. The futility analysis indicated that high-intensity treadmill warrants further investigation as a potential intervention for motoric symptoms in de novo PD.


Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Philadelphia PADRECC leads the committee for May/June. 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:
  1. New medications deutetrabenazine and valbenazine for Huntington’s chorea and tardive dyskinesia.
  2. The management of orthostatic hypotension including the role of the newly FDA-approved agent droxidopa (Northera).
  3. Continued discussion focused on clinical experience sharing among the group regarding DUOPA™ (carbidopa and levodopa) enteral suspension delivered directly into the small intestine for the treatment of motor fluctuations for people with advanced Parkinson's disease
  4. The prevalence of vitamin D deficiency in Parkinson’s disease and the need to monitor and adequately replete levels for bone and cognitive health.
  5. Practical aspects regarding the use of DAT scans; applications and pitfalls, including the issue of drug interference
  6. Continued discussion on the use of Pimavaserin (Nuplazid) in the treatment of psychosis associated with PD, compared to quetiapine and clozariil.
  7. Continued discussion of Rytary and conversion and titration dosing strategies. Consensus that often more than a three times/day dosing is needed.
  8. Discussion of the possible role for levodopa-induced hyperhomocystinemia in Parkinson’s disease and the strategies to monitor and manage this problem

Education Committee

- **PADRECC/EES Movement Disorder Series:** The fourth audioconference for FY 18 was held on May 10th, 2018, “Psychiatric Issues in PD” by Joel Mack, MD, Portland PADRECC. The audioconferences are archived on the National website [www.parkinsons.va.gov](http://www.parkinsons.va.gov) under the Movement Disorder Series tab. Please see the Dates to Remember section below for a listing of upcoming FY17 audioconferences and mark your calendars.

- **National VA PD Newsletter:** Currently accepting articles for the 2018 VA Parkinson Report. Articles should be on cutting edge research or treatment pertaining to PD and be limited to 1 - 1.5 pages including references. In order to avoid duplication, the topic needs to be pre-approved by Dr. Sarwar. If you are interested in submitting an article for the newsletter please email Suzanne Moore ([Suzanne.Moore@va.gov](mailto:Suzanne.Moore@va.gov)). Deadline for submission is **June 1st, 2018**

- **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.

- **National Website Maintenance:** The committee performs monthly 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.

- **Resources available on the National Website—Please share with your patients**
  - Updated Patient Education Brochures- [https://www.parkinsons.va.gov/patients.asp](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](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](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 and complete the Resource Request Form and mail or fax to address listed: [https://www.parkinsons.va.gov/clinicians.asp](https://www.parkinsons.va.gov/clinicians.asp)
Dates to Remember

September 13, 2018

*EES/PADRECC Movement Disorders Series*

Topic: Neurotoxin use for treating PD Symptoms

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

October 5-9, 2018

*International Parkinson and Movement Disorder Society (MDS)~International Congress*

Hong Kong

http://www.mdscongress.org/Congress-2018.htm

June 2-7, 2019

*5th World Parkinson Congress*

Kyoto, Japan

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