FULL PROTOCOL TITLE

A Dose Selection Trial of Light Therapy for Impaired Sleep in Parkinson's Disease

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SHORT PROTOCOL TITLE
ENLITE PD

Protocol Principal Investigator (PPI):

Aleksandar Videnovic, MD, MSc
Director, Program on Sleep, Circadian Biology, and Neurodegeneration
Director, Division of Sleep Medicine
Massachusetts General Hospital

Associate Professor of Neurology
Harvard Medical School

MGH Neurological Clinical Research Institute
165 Cambridge Street, Suite 600
Boston, MA 02114

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n/a

SYNOPSIS

Study Title

A Dose-selection Trial of Light Therapy for Impaired Sleep in Parkinson's Disease

Primary Objectives

The primary aims of this trial are to (i) determine whether once- or twice-daily bright-white light therapy (BWLT) improves sleep in Parkinson's disease (PD) sufficiently to carry forward in a phase III efficacy trial and, if so, (ii) to select the superior dose frequency to carry forward. Only dose frequencies judged to be safe will be considered for selection.

Secondary Objectives

The key secondary aim is to determine whether once-weekly BWLT is a non-inferior control condition relative to twice-daily dim-red light therapy (DRLT). Additional secondary aims will (i) estimate the effect of daily BWLT on fatigue in PD, and (ii) determine whether patients adhere to light therapy (LT).

Design and Outcomes

This is a 16-week, randomized, phase II, parallel-group, placebo-controlled, dose-selection clinical trial of LT in participants with PD and co-existing sleep disruption using a comparative selection trial design.

At baseline, the mid-treatment visit, and at completion of the treatment and wash-out periods, the following assessments/instruments will be completed: Parkinson's Disease Sleep Scale, 2nd version (PDSS-2), Parkinson's Disease Fatigue Scale (PFS-16), Epworth Sleepiness Scale (ESS), Non-Motor Symptoms Scale (NMSS), MDS Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Parkinson's Disease Questionnaire-39 (PDQ-39), Geriatric Depression Scale (GDS-15), and Montreal Cognitive Assessment (MoCA). Participants will complete daily sleep logs and wear a wrist activity and light exposure monitor throughout the study. The PDSS-2 will be the primary outcome variable

Interventions and Duration

After a 4-week baseline period that will incorporate sleep hygiene education, eligible participants will be randomized 1:1:1:1 to 8 weeks of one of four treatment conditions: (i) BWLT twice daily (morning and evening), (ii) BWLT once daily (evening only), (iii) BWLT once weekly (evening only), and (iv) DRLT twice daily (morning and evening). Participants randomized to the once-weekly BWLT and twice-daily DRLT groups will serve as controls of dose frequency and of wavelength and illuminance, respectively. Participants randomized to BWLT will receive one hour of full-spectrum white light (10,000 lux) in direction of gaze, in the morning and evening (twice daily) or in the evening only, daily or weekly, for eight weeks. Participants randomized to DRLT will receive one hour of filtered red light (300 lux) in direction of gaze, in the morning and evening (twice daily), for eight weeks. *SunRay* light boxes (The SunBox Co., Gaithersburg, MD, USA) will be used for LT administration. Dimensions of the box are 15.5" (H) x 23" (W) x 3.25" (D). *SunRay* light boxes are equipped with a spectrally transparent prismatic diffuser or a red filter, both of which block UV rays. After the intervention period, all participants will complete a 4-week wash-out period to assess carry-over effects of LT. Each participant will be on-study for

16 weeks. Total enrollment time is estimated to be 20 months. Estimated time from enrollment to the completion of data analysis is 30 months.

Sample Size and Population

Approximately up to 158 participants with PD will be randomized from 25 PD and Movement Disorders Centers in the United States.

Inclusion Criteria:

1) Diagnosis of idiopathic PD as defined by the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease;
2) PD Hoehn and Yahr stage 2-4;
3) A score of 2 (mild) or above on the Sleep Problems question of the MDS-UPDRS Part 1;
4) Stable dose of all PD medications for at least 30 days prior to randomization;
5) Willingness to wear an Actiwatch and complete daily sleep logs;
6) Age 45 or above

Exclusion Criteria:

1) Atypical or secondary forms of parkinsonism;
2) Co-existent significant sleep apnea at screening, as determined by the PI's clinical assessment; adequately treated sleep apnea, as assessed by sleep apnea machine download (CPAP download) will be permitted;
3) Co-existent symptomatic restless legs syndrome (RLS) (as assessed by the International Classification of Sleep Disorders (ICDS) diagnostic criteria for RLS) at screening;
4) Cognitive impairment as determined by a Mini Mental State Examination score <25 at screening;
5) Presence of moderate depression defined as a Beck Depression Inventory II (BDI-II) score ≥20 at screening;
6) Current untreated hallucinations or psychosis (drug-induced or spontaneous) with a score of 2 or above on the Hallucinations and Psychosis question of the MDS-UPDRS Part 2;
7) Use of hypno-sedative drugs or melatonin for sleep or stimulants, unless the participant has been on a stable dose for at least 60 days prior to the screening;
8) Ongoing or recent (within 30 days prior to screening) Cognitive Behavioral Therapy for Insomnia;
9) Use of antidepressants, unless the participant has been on a stable dose for at least 60 days prior to the screening;
10) Work hours between 10 PM and 6 AM, within 60 days prior to randomization or anticipated during the 16 weeks after screening;
11) Travel between 3 or more time zones within 45 days prior to study screening or anticipated such travel during the 16 weeks after screening;
12) Unstable or serious medical illness;
13) History of significant eye trauma or disease, retinopathy, or cataract Grade 4 that would significantly affect transmission or processing of light through either eye;
14) Current use, use at any time during study participation, or use within the 30 days prior to screening of photosensitizing or other medications that in the opinion of the investigator would interfere with the safety of the participant during the trial, including: amiodarone, porfimer, psoralens, chlorpromazine, quinidine, demeclocycline, temoporfin, tetracycline, fleroxacin, oral isoretinoin, voriconazole, nalidixic acid, thioridazine, St. John's wort, ofloxacin, and piroxicam;

15) Pregnant women will be excluded from participation; if a participant is pre-menopausal, a urine pregnancy test will be conducted at randomization to determine eligibility.
16) Individuals currently enrolled in another interventional trial will be excluded from participation; individuals may be screened for the study after a 12-week washout period following their completion of the other trial. Individuals currently enrolled in an observational study may be enrolled if in the opinion of the investigator the observational study will not impact the participant's ability to meet the requirements of this trial.

Schedule of Activities

Evaluation	Screening/ Sleep Hygiene Education	Baseline/ Randomization	Mid-Treatment Assessment	End of Intervention Assessment	Wash-out Assessment
	V1 Screening	V2 Week 0	V3 Week 4	V4 Week 8	V5 Week 12
Written Informed Consent	x				
Inclusion/Exclusion Review	x	x			
Medical History/ Demographics	x				
HT, WT, Vital Signs (HR,BP)	x				
Physical Examination	x				
Neurological Examination	x				
BDI-II	x				
MMSE	x				
Berlin questionnaire	x				
Eye Exam	x				
Concomitant Medication Review	x	x	x	x	x
MDS-UPDRS (I-IV)	x[1]	x	x	x	x
PDSS-2		x	x	x	x

PFS-16		x	x	x	x
NMSS		x	x	x	x
PDQ-39		x	x	x	x
GDS-15		x	x	x	x
MoCA		x	x	x	x
Randomization		x			
Dispense / Return Study Device		x		x	
Dispense / Collect LT Log	x	x	x	x	x
Dispense / Collect Actiwatch	x	x	x	x	x
Mail Actiwatch to Actigraphy Core		x	x	x	x
Dispense / Collect Sleep Logs	x	x	x	x	x
Adverse Event Review		x	x	x	x

[1]Only the Sleep question of the MDS-UPDRS Part 1 will be administered at the Screening visit.