The Personalized Parkinson Project - de novo cohort

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON49224

Source
ToetsingOnline

Brief title
PPP NOVO

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: UCB Biopharma SPRL,UCB Pharma

Intervention

Keyword: Big data, Biomarkers, Parkinson's disease, Wearable sensors

Outcome measures

Primary outcome

Digitale biomarkers, calculated from the Verily Study Watch data, i.e.,

. Pulse rate

. Skin temperature, Electrodermal activity (sweat)

. Movement data (Accelerometer)

. Electrocardiogram (ECG)

. Altitude, pressure, relative humidity

. Environment temperature

. Ambient light level

. Sound pressure level

The development of these digital biomarkers is part of the study. Selection of the digital biomarker is based on it's sensitivity to detect disease progression.

Secondary outcome

Clinimetrics (on site, by assessor)

- Motor Assessment Subset ON Medication: Hoehn & Yahr stage; UPDRS-II; UPDRS-III (Including timed up-and-go tests to assess gait); UPDRS-IV; Freezing of Gait Questionnaire; Standing leg / flamingo Test; Pirouette Test;

Pegboard Test; Grip strength.

- Neuropsychological Symptoms: UPDRS-I; Montreal Cognitive Assessment; Phonemic Fluency Semantic Fluency; 15

Words Test; Benton Judgment of Line Orientation; Letter Number Sequencing;

Symbol Digit Modalities Test.

Questionaires:

- Neuropsychological symptoms: Beck Depression lnventoryi Quip- RS (impulsive compulsive disorder); Apathy scale;

Trait Anxiety lnventory for Adults;

- Other UPDRS-ll;: SCOPA- autonomic; SCOPA- sleep; RBD questionnaire; Epworth sleep questionnaire; SF-12; PDQ-39

Wearing-off questionnaire; Radboud Oral Motor lnventory; Screening Questionnaire on Visual lmpairment; PASE (Physical Activity Scale for the Elderly).

Biomarkers

* lmaging

- ECG: heart rate variability

* Biospecimens

- Blood: Plasma / PBMCs serum, EDTA plasma (DNA), PAXgene (RNA)

Study description

Background summary

Parkinson's disease (PD) is the second most prevalent degenerative brain disease. Our understanding of the basic pathology, etiology, and progression of PD has stagnated, partly due to the limited patient diversity captured in study cohorts. Additionally, we lack sufficient biological insight into the underlying etiologies and pathophysiological mechanisms to develop new interventions that can slow down or arrest dìsease-progression. As a result, patients do not receive the best care they deserve, leading to unnecessary disability, and to mounting costs for society.

This PPP NOVO cohort aims to validate novel digital biomarkers for disease progression, fostering the unique research infrastructure and data collection protocol that are available. The PPP NOVO cohort consists of patients with de novo (i.e., newly diagnosed and previously untreated) Parkinson*s disease who will be followed longitudinally for two years. De novo patients create the opportunity to study disease progression without interference of pharmacological treatment. The observation of this natural process in the earliest course of the disease is highly relevant for the development disease modifying interventions, which are likely to have the biggest potential in the earliest phases of the disease, when the loss of substantia nigra cells is minimal. In particular, we will deploy the PPP NOVO cohort for the development of digital biomarkers that could serve as a surrogate or, with time, possibly as key secondary or even a primary outcome in future clinical trials of disease-modifying interventions. Digital biomarkers hold great promise in this regard, as they provide a means to objectively track patients and measure their function in their own living environment, unobtrusively, and over long periods of time. The outcomes are potentially more sensitive than currently available clinical scales, which also be included in the protocol and perhaps also more relevant as they provide an insight into daily life functioning over extended periods of time.

Study objective

The first objective is to validate novel digital biomarkers for disease progression in de novo Parkinson*s disease patients. The biomarkers can eventually serve as a primary clinical endpoint in additional future clinical studies. As part of this present proposal, we will longitudinally collect wearable sensor data using the Verily Study Watch from a large cohort of de novo Parkinson patients. Our hypothesis is that digital progression biomarkers will have greater sensitivity and greater power for detecting disease progression than conventional scales. For the MDS-UPDRS, which is such a conventional scale and often used as the primary endpoint in clinical trials in PD, we recently demonstrated its inability to track individual disease progression (Evers et al, 2019a). We will collect multi-dimensional data, including digital data from the Verily Study Watch, to track the progression of

the earliest phase of Parkinson*s disease. Specific outcomes will focus on tracking the progression of bradykinesia, gait impairment, postural sway, tremor, physical activity, sleep quality, and autonomic dysfunction. Data will consist of both the unstructured passive monitoring, as well as the intermittent scheduled active tasks that patients will complete at home. As the data analysis is heavily relying on a machine/deep learning approach, the digital signatures collected in the PPP NOVO cohort will instruct the analysis of the POC data, both as a standalone analysis (by potentially identifying novel digital signatures and validating findings from the POC). Moreover the PPP NOVO data will serve as a training data set to improve the yield of the machine learning procedures applied to the POC data.

Testing the feasibility of the study protocol is defined as the second objective of this study. The PPP NOVO cohort is considered instrumental in optimizing planning, data acquisition, analysis and interpretation of the digital data collected in the POC. To this aim, the entry criteria, as well as all data collection routines, clinical protocols and the technical infrastructure of the PPP NOVO cohort accurately mirror the planned POC study. Thereby, we will collect critical information on potential handling and analysis issues before actually engaging in an interventional study. This will ultimately de-risk the overall endeavor, both in terms as investments as well as in terms of strategic decisions. Observations on patient experience, technical handling, support and adherence in the PPP NOVO cohort will be critical to anticipate and counteract potential issues in the POC study and thereby increase the chance of success.

The third objective of this study is to create an extensive longitudinal dataset describing the clinical and functional characteristics of a representative Parkinson*s disease de novo cohort to allow researchers to investigate important unanswered questions in PD.

Study design

Prospective, longitudinal, single-center cohort study.

Study burden and risks

Nature and extent of the burden to patients
Participants are invited to come to the study site in Nijmegen for a full (up to 1.0) day of data collection three times during the 2-year study duration. If needed, they can come to Nijmegen one day ahead of the day they have their appointment at the study site. All study assessments are routine exams done in standard clinical practice and are generally well tolerated. The Verily Study Watch will be worn daily for up to 23 hours. This small, unobtrusive electronic device is easily applied and poses no significant safety issues. Data collection does not require patient intervention, and data transfer does not

require connection to a mobile phone or computer. The Study Watch requires minimum care (daily charge and sync, remove when near water). Furthermore, participants will be asked to fill in a questionaire which can take up to 100 minutes. However, the questionaire can be saved during and participants get 4 weeks to complete the entire questionaire. Participants will be asked to perform once a week two sets of eight motor tasks with the Study Watch.

Risks
There are limited risks for the patients during the data collection. The diagnostic measurements (12-lead ECG and Holter ECG) are standard non-invasive tests that are routinely performed in clinical practice.
Tests that may lead to discomfort / risk are the following:
. Local hematoma can occur related to the venipuncture for blood collection.
. The Verily Study Watch is a low risk non-invasive device (class lla) used as an adjunct tool and not to guide diagnosis
or therapy, therefore it does not pose significant risks.

Benefits
Because data collection is not performed for immediate diagnostic or therapeutic purposes, there will be no direct
benefits for the subjects enrolled in this study. As a service in return for their efforts for research, participants will be
offered an educational program (voluntarily) on Parkinson's disease and how to handle the disease in daily life.
Moreover, patients will indirectly benefit from the study, as their data contribute to gain novel etiological insights for
improvement of existing treatments, development of new therapeutic approaches, and more precise and personalized
disease management. This will provide future benefit for all patients affected by the disease.

The Study Watch supplements and enhances the information available to the physician, providing continuous
measurement and quantitative (rather than subjective) data. The device detects important physiologic parameters that
are expected to change with disease conditions or behavioral patterns (e.9., electrodermal activity [EDA], physical
movement of the body in three dimensions [acceleration], skin temperature, heart rhythm). As such, by wearing the
Study Watch, patients are providing unprecedented insight into the evolution of PD and potentially allowing to identify
better ways to treat the disease. ln addition to collecting data, the device also functions as a wristwatch.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Prior to enrollment in this clinical investigation, candidates must meet ALL of the following criteria:
* Subject has never been treated before with any symptomatic dopaminergic drug treatment for Parkinson*s disease and is not expected to start treatment for motor symptoms of PD within 52 weeks from baseline.
* Subject has Parkinson*s disease of <=2 years of duration, defined as the time since the diagnosis was made by a neurologist.
* Subject is an adult, at least 18 years of age.
* Subject can read and understand Dutch.
* Subject has completed the CMO-approved Informed Consent.
* Subject is willing, competent, and able to comply with all aspects of the

protocol, including follow-up schedule and biospecimen collection.

Exclusion criteria

Candidates must be excluded from this study if ANY of the following criteria are met:
* Subject is pregnant or breastfeeding.
* Subject has co-morbidities that would hamper interpretation of parkinsonian disability, such as coincident musculoskeletal abnormalities, in the opinion of the Investigator.
* Subject is allergic to nickel.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-08-2020
Enrollment:	144
Type:	Actual

Medical products/devices used

Generic name:	Verily Study Watch
Registration:	No

Ethics review

Approved WMO

Date:	20-04-2020

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-03-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-05-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-02-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL72631.091.20