

# Simvastatin as a neuroprotective treatment for m

<b>Submission date</b> 19/11/2015	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 19/11/2015	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 21/12/2023	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Parkinson's disease (PD) is a long-term medical condition which is caused by the gradual loss of nerve cells (neurons) in a part of the brain called the substantia nigra. These neurons are normally responsible for producing dopamine, a chemical messenger (neurotransmitter) which carries signals around the brain that help to coordinate movement. In people suffering from PD, these neurons gradually die over time, causing the level of dopamine in the brain to gradually fall. As the levels of dopamine become lower, the brain is unable to coordinate movement as effectively, causing abnormal movements such as stiffness, tremor (uncontrollable shaking) and slowness of movement (bradykinesia). Currently, PD affects more than 127,000 people in the UK alone, with a further 10,000 diagnosed each year. Unfortunately, there is no cure for PD and so current therapies are only able to help relieve the symptoms, such as by artificially replacing dopamine or preventing the body from breaking it down. These treatments ultimately fail however, as they are unable to prevent the overall loss of neurons in the brain. Neuroprotection is an area of research which aims to protect nerves from damage. Studies have shown that statins (a group of medications which lower cholesterol) are potentially neuroprotective. The way this works is still only partly understood however, and so more research is needed to find out if statins have the potential of being neuroprotective. The aim of this study is to find out whether simvastatin has potential as a neuroprotective therapy in PD.

### Who can participate?

Adults aged between 40 and 90 years old who have been diagnosed with idiopathic PD (i.e. the cause is unknown), with no current or previous use of statins.

### What does the study involve?

Participants are randomly allocated to one of two treatment groups. In one group, participants are given capsules of simvastatin to take orally (by mouth) for 24 months. In the other group, participants are given placebo (dummy) capsules to take orally for 24 months. At the start of the study, when they receive their medication, participants complete a number of questionnaires and motor (movement) tests (a walking test and a finger tapping test). Participants in both groups also attend a further 6 clinic visits after 1, 6, 12, 18 and 24 months, where they are asked about their health and any medication they are taking, as well as repeating the questionnaires and motor tests. For 4 of these clinic visits, the participants will be asked to attend in the 'OFF medication' state (having omitted their usual PD medication) so that the researchers can get a true picture of their disease without it being masked by their normal medication.

What are the possible benefits and risks of participating?

Participants may or may not benefit directly from taking part in the study, but by taking part they will be contributing to a study which could potentially bring future benefit to large numbers of people with PD. There are no significant risks of taking part, however participants may experience side effects from the medication (such as muscle aches and pains) and could experience pain or bruising from blood testing.

Where is the study run from?

24 NHS hospitals in England (UK)

When is the study starting and how long is it expected to run for?

January 2015 to September 2020

Who is funding the study?

1. Cure Parkinson's Trust (UK)
2. The JP Moulton Charitable Foundation (UK)

Who is the main contact?

Mr Doug Webb

## Contact information

### Type(s)

Public

### Contact name

Mr Doug Webb

### Contact details

Peninsula Clinical Trials Unit  
Plymouth University Peninsula Schools of Medicine and Dentistry  
Room N16  
ITTC Building 1  
Plymouth Science Park  
Plymouth  
United Kingdom  
PL6 8BX

## Additional identifiers

### ClinicalTrials.gov (NCT)

NCT02787590

### Clinical Trials Information System (CTIS)

2015-000148-40

### Central Portfolio Management System (CPMS)

19666

# Study information

## Scientific Title

Simvastatin as a neuroprotective treatment for Parkinson's disease: a double-blind, randomised, placebo-controlled futility study in patients of moderate severity

## Acronym

PD STAT

## Study objectives

The aim of this study is to establish whether the cholesterol-lowering drug, simvastatin, has potential as a neuroprotective therapy in Parkinson's disease.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Newcastle and North Tyneside 2 Research Ethics Committee, 12/10/2015, ref: 15/NE/0324

## Study design

Double-blind placebo-controlled multi-centre randomized futility study

## Primary study design

Interventional

## Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Topic: Dementias and neurodegeneration; Subtopic: Parkinson's Disease; Disease: Parkinson's disease

## Interventions

Participants in this study will be randomly allocated to one of two treatment groups in a 1:1 ratio:

Intervention group: Participants will receive oral simvastatin capsules to take daily for 24 months.

Control group: Participants will receive oral matched-placebo capsules to take daily for 24 months.

Trial treatment will be provided to the participants at the baseline, 1 month, 6 month, 12 month and 18 month clinic visits; the maximum supply provided will be a 6 month supply. Bottles containing 100 capsules of either 40mg simvastatin or matched placebo will be issued to the participants.

Over a 26 month period, participants in both treatment groups will attend scheduled study clinic visits, complete a number of validated assessments and receive telephone contacts.

## Intervention Type

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Simvastatin

**Primary outcome(s)**

Patient motor skills are determined using the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS Part III) in the OFF state at 12 and 24 months.

**Key secondary outcome(s)**

1. The overall impact of PD on the participant is assessed using the MDS-UPDRS total score in the practically defined ON state at 12 and 24 months
2. The impact of PD on activities of daily living is assessed using the MDS-UPDRS part II subscale score in the practically defined ON state at 12 and 24 months
3. Motor skills are assessed using timed motor tests (finger tapping and timed walk test (10MWT)) in the OFF state at 12 and 24 months
4. Depression is assessed using the Montgomery and Asberg Depression Rating Scale (MADRS) at 12 and 24 months
5. Cognition is assessed using the Addenbrooke's Cognitive Assessment-III (ACE-III) at 12 and 24 months
6. The presence of the non-motor features of PD is captured using the Non-Motor Symptom assessment scale (NMSS) at 12 and 24 months
7. A PD-specific health status is assessed using the Parkinson's disease Questionnaire (PDQ-39) at 12 and 24 months
8. Changes in PD medication are measured by capturing a levodopa-equivalent dose (LED) at 12 and 24 months
9. Cholesterol levels are captured using total, HDL, LDL, and total/HDL ratio results at 12 and 24 months
10. The presence of PD-specific pain is captured using the King's PD pain scale (KPPS) at 12 and 24 months
11. A current overall health status is captured using the EuroQoL 5D-5L (EQ-5D-5L) health status questionnaire at 12 and 24 months
12. The safety and tolerability of trial medication is assessed by adverse events (AEs) review at 12 and 24 months
13. The incidence of diabetes mellitus is assessed at 24 months using a glycated haemoglobin (HbA1c) level of 6.5% (48mmol/mol) as diagnostic of diabetes mellitus (WHO 2011)

**Completion date**

30/09/2020

**Eligibility****Key inclusion criteria**

1. Diagnosis of idiopathic PD
2. Modified Hoehn and Yahr stage  $\leq 3.0$  in the ON medication state
3. Age 40-90 years
4. On dopaminergic treatment with wearing-off phenomenon
5. Able to comply with study protocol and willing to attend necessary study visits

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

40 years

**Upper age limit**

90 years

**Sex**

All

**Total final enrolment**

235

**Key exclusion criteria**

1. Diagnosis or suspicion of other cause for parkinsonism
2. Known abnormality on CT or MRI brain imaging considered to be causing symptoms or signs of neurological dysfunction, or considered likely to compromise compliance with study protocol
3. Concurrent dementia defined by MoCA score <21
4. Concurrent severe depression defined by MADRS score >31
5. Prior intracerebral surgical intervention for PD including deep brain stimulation, lesional surgery, growth factor administration, gene therapy or cell transplantation
6. Already actively participating in a research study that might conflict with this trial
7. Prior or current use of statins as a lipid lowering therapy
8. Intolerance to statins
9. Untreated hypothyroidism
10. End stage renal disease (creatinine clearance <30 mL/min) or history of severe cardiac disease (angina, myocardial infarction or cardiac surgery in preceding two years)
11. eGFR <30 mL/min
12. History of alcoholism or liver impairment
13. Creatine kinase (CK) >1.1 x upper limit of normal (ULN)
14. Aspartate transaminase (AST) or alanine transaminase (ALT) >1.1 x ULN
15. Females who are pregnant or breast feeding or of child-bearing potential and unwilling to use appropriate contraception methods whilst on trial treatment
16. Currently taking any medication contraindicated with simvastatin use
17. Any requirement for statin use
18. Regular participation in endurance or high -impact sports
19. Unable to abstain from consumption of grapefruit -based products

**Date of first enrolment**

01/12/2015

**Date of final enrolment**

31/03/2018

# Locations

## Countries of recruitment

United Kingdom

England

## Study participating centre

### Royal Cornwall Hospital

2 Penventinnie Lane

Treliske

Cornwall

United Kingdom

TR1 3LQ

## Study participating centre

### Derriford Hospital

Derriford Road

Plymouth

United Kingdom

PL6 8DH

## Study participating centre

### Musgrove Park Hospital

Parkfield Drive

Taunton

United Kingdom

TA1 5DA

## Study participating centre

### Yeovil District Hospital

Higher Kingston

Yeovil

United Kingdom

BA21 4AT

## Study participating centre

### Christchurch Hospital

Fairmile Road

Christchurch

United Kingdom  
BH23 2JX

**Study participating centre**  
**Royal United Hospital Bath**  
Combe Park  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**  
**St Peter's Hospital**  
Guildford Road  
Chertsey  
United Kingdom  
KT16 0PZ

**Study participating centre**  
**Charing Cross Hospital**  
Fulham Palace Road  
London  
United Kingdom  
W6 8RF

**Study participating centre**  
**Royal Free Hospital**  
Pond Street  
London  
United Kingdom  
NW3 2QG

**Study participating centre**  
**Queen's Hospital**  
Rom Valley Way  
Romford  
United Kingdom  
RM7 0AG

**Study participating centre**

**John Radcliffe Hospital**

Headley Way  
Oxford  
United Kingdom  
OX3 9DU

**Study participating centre**

**Luton and Dunstable University Hospital**

The L&D Hospital NHS Foundation Trust  
Lewsey Road  
Luton  
United Kingdom  
LU4 0DZ

**Study participating centre**

**Addenbrookes Hospital**

Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**

**Salford Royal Hospital**

Stott Lane  
Salford  
United Kingdom  
M6 8HD

**Study participating centre**

**Fairfield General Hospital**

Rochdale Old Road  
Bury  
United Kingdom  
BL9 7TD

**Study participating centre**

**Royal Preston Hospital**

Sharoe Green Lane North  
Preston  
United Kingdom  
PR2 9HT

**Study participating centre**

**Leeds General Infirmary**

Great George Street

Leeds

United Kingdom

LS1 3EX

**Study participating centre**

**Clinical Ageing Research Unit**

Campus for Ageing and Vitality

Newcastle upon Tyne

United Kingdom

NE4 5PL

**Study participating centre**

**Royal Devon and Exeter Hospital**

Barrack Road

Exeter

United Kingdom

EX2 5DW

**Study participating centre**

**King's College Hospital**

Denmark Hill

Brixton

London

United Kingdom

SE5 9RS

**Study participating centre**

**Royal Hallamshire Hospital**

Glossop Road

Sheffield

United Kingdom

S10 2JF

**Study participating centre**

**Norfolk and Norwich University Hospital**  
Colney Lane  
Norwich  
United Kingdom  
NR4 7UY

**Study participating centre**  
**Rotherham General Hospital**  
Moorgate Road  
Rotherham  
United Kingdom  
S60 2UD

**Study participating centre**  
**Royal Stoke University Hospital**  
Newcastle Road  
Stoke-on-Trent  
United Kingdom  
ST4 6QG

## **Sponsor information**

**Organisation**  
Plymouth Hospitals NHS Trust

**ROR**  
<https://ror.org/05x3jck08>

## **Funder(s)**

**Funder type**  
Charity

**Funder Name**  
Cure Parkinson's Trust

**Funder Name**  
The JP Moulton Charitable Foundation

# Results and Publications

## Individual participant data (IPD) sharing plan

The researchers intend to deposit anonymised patient-level data in the Critical Path for Parkinson's Consortium.

## IPD sharing plan summary

Stored in repository

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		31/10/2022	01/11/2022	Yes	No
<a href="#">Protocol article</a>	protocol	07/10/2019	23/07/2020	Yes	No
<a href="#">Basic results</a>		03/06/2021	16/06/2022	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol (other)</a>		31/10/2022	21/12/2023	No	No
<a href="#">Statistical Analysis Plan</a>		24/08/2020	07/01/2022	No	No
<a href="#">Statistical Analysis Plan</a>		31/10/2022	21/12/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes