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Phase 3 trial of exenatide for Parkinson's disease

Submission date	Recruitment status	[X] Prospectively registered
23/09/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/10/2019	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/06/2025	Nervous System Diseases	

Plain English summary of protocol

Background and study aims

This study is a clinical trial in patients with Parkinson's disease (PD), of a drug called exenatide, which is already licensed for the treatment of patients with type 2 diabetes. There have been several groups that have confirmed that exenatide has beneficial effects on nerve cells when tested in the laboratory, which raises the possibility that exenatide may slow down or stop the degeneration of PD. In an open label trial in patients with PD who self-administered the drug for a period of 48 weeks, the researchers have previously shown that the drug is well tolerated and shows encouraging effects on the movement and non-movement aspects of the disease. A trial was then conducted which indicated that exenatide may be a neuroprotective drug, i.e. one that stops the nerve cells dying in PD. The next step is therefore to confirm this neuroprotective effect and to see whether this effect can be reproduced in multiple centres including a larger number of participants. An important objective is to explore whether any positive effects remain static or increase when the treatment is continued over a 96-week period.

Who can participate?

Patients aged between 25 and 80 years of age with a confirmed diagnosis of Parkinson's disease that responds to dopamine medication.

What does the study involve?

At the baseline visit first thing in the morning (before they take their regular Parkinson's medication) participants have a series of movement tests after which they take their regular Parkinson's medication. They are then asked a further set of questions to assess thinking, memory and other symptoms of Parkinson's disease. One of these tests is video recorded in case the investigators wish to review the responses after the visit. The movement tests are repeated once the medication has started working. All assessments should be completed within two to three hours. Participants are randomly allocated into two groups to receive either exenatide or placebo (dummy drug) once weekly for 96 weeks. Patients in both treatment groups are given their first injection of the trial treatment at the hospital during the baseline visit. During this visit, they are taught how to perform the injections once weekly at home. Injections are given under the skin of the abdomen, arm, thigh or buttocks. All patients continue their regular Parkinson's medications alongside the trial drug throughout the trial. After they have been taking the trial medication for one month, they receive a call from a member of the trial team to

discuss the medications they are taking and how they are feeling. All patients are invited to attend their trial centre for assessments after 12 weeks (Visit 3), 24 weeks (Visit 4), 36 weeks (Visit 5), 48 weeks (Visit 6), 60 weeks (Visit 7), 72 weeks (Visit 8), 84 weeks (Visit 9) and a final visit at 96 weeks (Visit 10). For visits 4, 6, 8 and 10, they are asked to attend without taking their normal morning Parkinson's medications. For all other assessments they take their Parkinson's medication as normal. It is important that they do not take their normal treatment before visits 2, 4, 6, 8 and 10 so that the researchers can look at the severity of their Parkinson's disease in an "OFF medication state" and compare these to when they are taking their medication. This allows a more reliable comparison to be made. Participants are asked to not take their normal medication for 8 hours (overnight) in the case of levodopa, or 36 hours in the case of longer acting agents such as Ropinirole XL, Pramipexole Prolonged Release or Rasagiline, before their appointment. Participants complete a short questionnaire called the "Hauser Diary" at home at the start, middle and end of the study (3 times in total, just after visits 2 and before visits 6 and 10).

What are the possible benefits and risks of participating?
Exenatide may help to treat Parkinson's disease symptoms. Although there is no promise that this trial will benefit the participants personally, the results generated may help to improve the treatment options of people with Parkinson's disease in the future. The main disadvantage of taking part in this trial is the need to spend several hours without regular Parkinson's medication on five occasions while attending the full assessment trial visits. Before these five visits participants need to stop taking their regular Parkinson's disease medication the night before the visit to the trial centre. However, the trial team will be on hand to support them as much as possible. All medical procedures involve a risk of harm, but this is usually a low risk. In addition, there might be risks associated with this trial that the researchers do not yet know about. Patients taking exenatide may experience nausea, vomiting or diarrhoea. These symptoms usually settle after the first few doses. Weight loss can also occur. If weight loss occurs too quickly this can have harmful consequences. All patients will be weighed at each hospital visit and should monitor their weight at home in between hospital visits. There is also the risk of bruising and/or discomfort at the site of injection. A possible very rare side effect of exenatide is an illness called pancreatitis (which may affect 1 in 1000 patients taking exenatide). This is inflammation of the pancreas gland. This illness causes severe stomach pains, may require hospital treatment, and has even led to patients dying. Recurrent or chronic pancreatitis has been linked to an increase in risk for cancer of the pancreas. The researchers will monitor for any indication of pancreatitis during the course of the trial using blood tests. The only anticipated side effect from taking the placebo treatment is the risk of bruising and/or discomfort at the site of injection. There are some medications that can cause serious side effects when taken with the trial medications. Participants should tell the trial doctor about all medications they are taking before and during the trial. This includes other prescribed medicines, over the counter medicines, recreational drugs, herbal medicines or supplements. Exenatide may pose an unknown risk to a pregnant woman, an unborn baby, or a breastfeeding child. As such, pregnant women are not allowed to take part in this trial. Urine samples from female participants of childbearing potential will be tested at visit 1 to make sure they are not pregnant. All patients, both female and male, will be advised to use adequate contraception for the duration of the trial. Participants will need to have blood tests at each assessment which can be uncomfortable, but rarely results in any serious problems. Reported side effects include feeling light-headed or faint, bruising and/or discomfort at the site of injection. All reasonable efforts are made to make this trial safe. Despite this, some risks might not be possible to predict. New information about the treatment being studied may become available while the trial is running. The researchers will tell the participants about any new findings that might affect whether they want to continue in the trial.

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
The study started in March 2018. The planned start date for recruitment was October 2019, however this was not possible as there were delays waiting for arrival of the drug (exenatide /placebo). The actual start date for recruitment was January 2020. There were several delays faced in screening and recruitment due to Covid-19. Recruitment closed in April 2022 due to the drug expiry date. The last patient week 96 visit 10 is expected to take place in February 2024, and the last 106 week call is expected to take place 10 weeks after this in May 2024. The study end date is 31st July 2024.

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
1. Miss Rachel McComish (Clinical Trial Manager)
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3. Dr Tom Foltynie (Chief Investigator)
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Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04232969

Clinical Trials Information System (CTIS)
2018-003028-35

Integrated Research Application System (IRAS)
263481

Central Portfolio Management System (CPMS)
42305

Study information

Scientific Title
A randomised, double-blind, parallel-group, placebo-controlled, Phase 3 trial of exenatide once weekly over 2 years as a potential disease-modifying treatment for Parkinson's disease

Acronym
Exenatide-PD3

Study objectives
This study is a clinical trial in patients with Parkinson's disease (PD), of a drug called exenatide, which is already licensed for the treatment of patients with type 2 diabetes. There have been several groups that have confirmed that exenatide has beneficial effects of nerve cells when

tested in the laboratory, which raises the possibility that exenatide may slow down or stop the degeneration of PD. In an open-label trial in patients with PD who self-administered the drug for a period of 48 weeks, we have previously shown that the drug is well tolerated and shows encouraging effects on the movement and non-movement aspects of the disease. A double-blind placebo-controlled trial involving 60 participants was then conducted which indicated that exenatide may be a "neuroprotective" drug, i.e. one that stops the nerve cells dying in PD. The next step is therefore to confirm this "neuroprotective" effect and to see whether this effect can be reproduced in a multi-centre setting including a larger number of participants. An important objective is to explore whether any positive effects remain static or increase when the treatment is continued over a 96 week period.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/10/2019, South Central REC- Berkshire (Bristol HRA Centre, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; Tel: +44 (0)20 7104 8270, +44 (0)207 104 8360, +44 (0)2071048046; Email: nrescommittee.southcentral-berkshire@nhs.net), REC ref: 19/SC /0447

Study design
Randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Parkinson’s disease

Interventions
Current interventions as of 03/11/2023:

Initial identification of potential participants:
Patients attending their routine follow up appointments will be informed about the trial by their neurologist and given a participant information sheet.

Screening:
Patients who wish to be considered for inclusion in the trial will be screened for eligibility at their participating trial centre according to inclusion and exclusion criteria. A narrative of what trial participation entails, together with the participant information sheet, will be used to inform potential participants. Each patient will be aware that they have a 50% chance of being allocated active drug or placebo. They will confirm their willingness to attend the clinic after an overnight period without their conventional PD medication. As part of the informed consent, the contact details of the research team will be given to each patient.

Written informed consent will be obtained from each patient prior to enrolment into the trial. All potential patients will be properly informed as to the purposes of the trial and the potential risks/ benefits known, or that can be reasonably predicted or expected, by an Investigator

trained in Good Clinical Practice. The investigator will retain the original copy of the Informed Consent Form signed by the patient, a duplicate will be given to the patient, and a third copy will be
filed in the patient's hospital notes. Only the consent form approved by the relevant trial ethics committee will be used.

At this screening visit, assessments will be performed to confirm that the patient is eligible for participation in the trial:
- Review of PD medication
- Review of past and current medical history
- Clinical examination
- Pregnancy test - for females of childbearing potential (females who are pregnant or lactating will not be eligible to participate)
- Determination of PD severity (Hoehn and Yahr staging)
- ECG
- Blood tests: full blood count, urea and electrolytes, liver function tests, HbA1C, c-peptide, coagulation, serum amylase, thyroid function tests, kidney function tests, blood glucose, insulin and lipid profile
- Patient Health Questionnaire (PHQ-9): This scale is a validated screening to tool for measuring the severity of depression
- Montreal Cognitive Assessment (MoCA): This scale is a validated global measure of cognitive ability

Randomisation/Baseline:
Eligible consenting patients will be randomly allocated into 2 groups to receive either; exenatide 2mg (powder and solvent for prolonged-release, suspension for injection, prefilled pen) subcutaneous injection once weekly for 96 weeks (n=100), or placebo-exenatide (powder and solvent for prolonged-release, suspension for injection, prefilled pen) subcutaneous injection once weekly for 96 weeks (n=100). Randomisation lists will be sufficiently long to enable continued randomisation should any patients drop out within the first 12 weeks of the study (prior to the first follow up visit).

The following assessments will be performed once the patient is confirmed to be eligible for participation in the trial and before the patient has taken their conventional PD medication:
- The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS UPDRS) part 3.
- Timed motor tests - patients will be asked to perform a sit-stand-walk timed test and timed keyboard taps with left and right hand separately, in both the OFF medication and ON medication condition. The timed sit-stand-walk test will incorporate time taken from a seated position to stand and walk 10 metres, turn and return to original seated position. Timed keyboard taps will use online website Braintaptest.com to quantify the number of alternate taps from key "S" to key";" using a conventional QWERTY keyboard in a 30 second period with each hand in turn. The software is validated and records the number of keystrokes, dwell time, accuracy & rhythmicity in an automated fashion, is freely available online, allows for coded repeatable assessments which are pseudo-anonymised, and date/time stamped.

Patients will then take their conventional PD medication and, whilst waiting for these medications to work, patients will self-complete the following:
- MDS-UPDRS parts 1, 2 and 4
- Non-Motor Symptoms (NMS) severity scale. This validated scale is a tool to collect data on the frequency and severity of 30 non-motor symptoms sometimes experienced by PD patients
- Parkinson's disease questionnaire(PDQ-39). This is the standard disease specific measure of quality of life in PD comprising 39 questions. It has been extensively validated in previous studies

- Unified Dyskinesia Rating scale (UDysRS): This is considered to be the most useful and objective way of quantifying dyskinesia severity
- EQ-5D-5L. This is a simple 5 question form and visual analogue scale that allows calculation of quality adjusted life years (QALY) to enable health economic analyses to be performed
- A review of health resource utilisation (using the CSRI questionnaire) will also be performed.

The MDS-UPDRS part 3 and Timed Walk assessments will be repeated 1 hour after the participant has taken their routine medications - the ON medication state.
After completion of the MDS-UPDRS and Timed walk assessments in the ON medication state, each participant will be assessed using the MoCA, and PHQ-9.
Teaching injections: Patients will be taught how to self administer injections using online teaching video with the support of the trained member of the trial team.

4-Week telephone call:
4-Weeks after starting trial medications the patient will be called by a member of their trial centre team to:
- Review any adverse events
- Review medications taken by the patient

Full assessment visits (Off medication assessments):
- Withdrawal of routine PD medications: All patients will continue to have optimal conventional PD medication administered throughout the trial period with the exception of OFF medication assessments to be performed at trial visits at baseline, and weeks 24, 48, 72 and 96, when the patient will attend the research clinic after an overnight withdrawal from their conventional PD medications to allow an objective measurement of their PD disability. Patients unable to tolerate being off medication will not undergo randomisation.

The following assessments will be performed at these OFF medication assessments, before the patient has taken their conventional PD medication, which will take between 2-3 hours to complete:
- Blood tests
- Vital signs and weight
- MDS UPDRS part 3
- Timed motor tests
- Review of adverse events
- Review of medications

Patients will then take their conventional PD medication and, whilst waiting for these medications to work, patients will self-complete the following:
- MDS-UPDRS parts 1, 2 and 4
- NMS severity scale
- PDQ-39
- UDysRS
- EQ-5D-5L
- CSRI
The MDS-UPDRS part 3 and Timed Walk assessments will be repeated 1 hour after the participant has taken their routine medications, i.e. in the ON medication state.

After completion of the MDS-UPDRS and Timed walk assessments in the ON medication state, each participant will be assessed using:
- MoCA
- PHQ-9

Short assessments:
The following assessments will be performed at these short visits at weeks 12, 36, 60 and 84, (at which the patient does not need to have previously stopped taking their conventional PD medication):
- Blood tests
- Vital signs and weight
- Review of adverse events
- Review of medications

Dispensing of trial medication will occur at each trial visit.
10 weeks after the participant stops taking the trial medication, they will receive a telephone call from a site staff member:
- Review of adverse events

Patients will be asked to complete a 3 day Hauser Diary at home at three timepoints in the trial after consent is taken. The first is before baseline and randomisation visit 2, then during the week prior to visit 6 (week 48) and the week prior to visit 10 (week 96).

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Previous interventions:

Initial identification of potential participants:
Patients attending their routine follow up appointments will be informed about the trial by their neurologist and given a participant information sheet.

Screening:
Patients who wish to be considered for inclusion in the trial will be screened for eligibility at their participating trial centre according to inclusion and exclusion criteria. A narrative of what trial participation entails, together with the participant information sheet, will be used to inform potential participants. Each patient will be aware that they have a 50% chance of being allocated active drug or placebo. They will confirm their willingness to attend the clinic after an overnight period without their conventional PD medication. As part of the informed consent, the contact details of the research team will be given to each patient.

Written informed consent will be obtained from each patient prior to enrolment into the trial. All potential patients will be properly informed as to the purposes of the trial and the potential risks/ benefits known, or that can be reasonably predicted or expected, by an Investigator trained in Good Clinical Practice. The investigator will retain the original copy of the Informed Consent Form signed by the patient, a duplicate will be given to the patient, and a third copy will be
filed in the patient's hospital notes. Only the consent form approved by the relevant trial ethics committee will be used.

At this screening visit, assessments will be performed to confirm that the patient is eligible for participation in the trial:
- Review of PD medication
- Review of past and current medical history
- Clinical examination
- Pregnancy test - for females of childbearing potential (females who are pregnant or lactating will not be eligible to participate)

- Determination of PD severity (Hoehn and Yahr staging)
- ECG
- Blood tests: full blood count, coagulation, HBA1C, glucose, insulin, lipid profile, urea and electrolytes, liver function tests, thyroid function tests, serum amylase and saved serum
- Patient Health Questionnaire (PHQ-9): This scale is a validated screening to tool for measuring the severity of depression
- Montreal Cognitive Assessment(MoCA): This scale is a validated global measure of cognitive ability

Randomisation/Baseline:
Eligible consenting patients will be randomly allocated into 2 groups to receive either; exenatide 2mg (powder and solvent for prolonged-release, suspension for injection, prefilled pen) subcutaneous injection once weekly for 96 weeks n=100, or placebo-exenatide (powder and solvent for prolonged-release, suspension for injection, prefilled pen) subcutaneous injection once weekly for 96 weeks n=100. Randomisation lists will be sufficiently long to enable continued randomisation should any patients drop out within the first 12 weeks of the study (prior to the first follow up visit).

The following assessments will be performed once the patient is confirmed to be eligible for participation in the trial and before the patient has taken their conventional PD medication:
- The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS UPDRS) part 3.
- Timed motor tests - patients will be asked to perform a Sit-stand-walk timed test and timed keyboard taps with left and right hand separately, in both the OFF medication and ON medication condition. The timed Sit-stand-walk test will incorporate time taken from a seated position to stand and walk 10 metres, turn and return to original seated position. Timed keyboard taps will use online website Braintaptest.com to quantify the number of alternate taps from key "S" to key
";" using a conventional QWERTY keyboard in a 30 second period with each hand in turn. The software is validated and records the number of keystrokes, dwell time, accuracy & rhythmicity in an automated fashion, is freely available online, allows for coded repeatable assessments which are pseudo-anonymised, and date/time stamped.

Patients will then take their conventional PD medication and, whilst waiting for these medications to work, patients will self-complete the following:
- MDS-UPDRS parts 1, 2 and 4
- Non-Motor Symptoms (NMS) severity scale. This validated scale is a tool to collect data on the frequency and severity of 30 non-motor symptoms sometimes experienced by PD patients
- Parkinson's disease questionnaire(PDQ-39). This is the standard disease specific measure of quality of life in PD comprising 39 questions. It has been extensively validated in previous studies
- Unified Dyskinesia Rating scale (UDysRS): This is considered to be the most useful and objective way of quantifying dyskinesia severity
- EQ-5D-5L. This is a simple 5 question form and visual analogue scale that allows calculation of quality adjusted life years (QALY) to enable health economic analyses to be performed
- A review of health resource utilisation (using the CSRI questionnaire) will also be performed.

The MDS-UPDRS part 3 and Timed Walk assessments will be repeated 1 hour after the participant has taken their routine medications - the ON medication state.
After completion of the MDS-UPDRS and Timed walk assessments in the ON medication state, each participant will be assessed using the MoCA, and PHQ-9.
Teaching injections: Patients will be taught how to self administer injections using online teaching video with the support of the trained member of the trial team.

1-month telephone call:
1 month after starting trial medications the patient will be called by a member of their trial centre team to:
- Review any adverse events
- Review medications taken by the patient

Full assessment visits ("off medication assessments"):
- Withdrawal of medications: All patients will continue to have optimal conventional PD medication administered throughout the trial period with the exception of "off medication assessments" to be performed at trial visits at baseline, and weeks 24, 48, 72 and 96, when the patient will attend the research clinic after an overnight withdrawal from their conventional PD medications to allow an objective measurement of their PD disability. Patients unable to tolerate being off medication will not undergo randomisation.

The following assessments will be performed at these "off medication" assessments which will take between 2-3 hours to complete:
The following assessments will be performed before the patient has taken their conventional PD medication:
- Blood tests
- Vital signs and weight
- MDS UPDRS part 3
- Timed motor tests
- Review of adverse events
- Review of medications

Patients will then take their conventional PD medication and, whilst waiting for these medications to work, patients will self-complete the following:
- MDS-UPDRS parts 1, 2 and 4
- NMS severity scale
- PDQ-39
- UDysRS
- EQ-5D-5L
- CSRI
The MDS-UPDRS part 3 and Timed Walk assessments will be repeated 1 hour after the participant has taken their routine medications - the ON medication state.

After completion of the MDS-UPDRS and Timed walk assessments in the ON medication state, each participant will be assessed using:
- MoCA
- PHQ-9

Short assessments:
The following assessments will be performed at these short visits at weeks 12, 36, 60 and 84, (at which the patient does not need to have previously stopped taking their conventional PD medication):
- Blood tests
- Vital signs and weight
- Review of adverse events
- Review of medications

Dispensing of trial medication will occur at each trial visit.
10 weeks after the participant stops taking the trial medication, they will receive a telephone

call from a site staff member:
- Review of adverse events

Patients will be asked to complete a 3 Hauser Diary at home after randomisation and during the week prior to visit 6 (week 48) and the week prior to visit 10 (week 96).

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Motor and non-motor symptoms associated with Parkinson's measured by comparison of MDS-UPDRS part 3 motor sub-score in the practically defined OFF medication state at 96 weeks between participants according to treatment allocation. Assessments completed every 24 weeks for a total of 96 weeks.

Key secondary outcome(s))
Measured at 48 and 96 weeks:
1. MDS-UPDRS part 3 motor score in the practically defined OFF medication state at 48 weeks. Whereas the analysis of the 96-week scores according to randomisation group will represent the primary outcome for this trial, differences emerging at the end of the 48-week treatment period and also the difference between scores at 48 and 96 weeks will be important secondary outcomes.
2. MDS-UPDRS part 1, 2, 3 and 4 ON medication scores. Part 3 of the MDS-UPDRS as well as the other elements (Part 1, 2 & 4) of the scale will also be evaluated in the presence of conventional PD medication (ON state) to evaluate any change in some of the non-motor symptoms of PD, activities of daily living and the complications of chronic PD treatment
3. Cognitive ability assessed using MoCA in the ON medication state
4. Safety and tolerability of exenatide as indicated by changes in vital signs, weight, clinical laboratory measures and adverse events. Each patient will have pulse, blood pressure and weight documented at screening and at each follow-up visit. Their height will be recorded at screening to enable calculation of body mass index. Exenatide is known to cause weight loss. Each patient will be questioned about adverse events at each visit using open-ended questions and responses documented on their Exenatide-PD3 Adverse Event Log. This will be done by an individual separate from the individual performing the primary outcome measurement to avoid inadvertent potential treatment allocation unblinding of staff performing assessments at each site. In the absence of any such individual being available, the patient will be asked to telephone a clinical staff member centrally to report their weight and adverse events. The known complications of PD and its treatment will be quantitatively captured on the PD related scales and therefore will not be additionally routinely logged as adverse events.
5. Timed tests: Participants will be asked to perform a sit-stand-walk timed test in both the OFF medication and ON medication state. The timed Sit-stand-walk test will incorporate time taken from a seated position to stand and walk 10 metres, turn and return to the original seated position. At selected centres participants will also wear electromagnetic sensors during the assessment of the MDS-UPDRS part 3 motor scores. These sensors will allow objective quantification of movement speed/fluidity and will be uploaded to a secure server to allow

central analysis for e.g. speed and rhythmicity in an automated fashion (see Appendix 4 for details of this sub-study).
6. Dyskinesia severity assessed using UDysRS in the ON medication state
7. Depression severity assessed using PHQ-9 in the ON medication state
8. Frequency and severity of non-motor symptoms assessed using NMSS in the ON medication state
9. Quality of life assessed using PDQ-39

Completion date
31/07/2024

Eligibility

Key inclusion criteria
1. Diagnosis of Parkinson's disease. PD is a clinical diagnosis and is based on the opinion of the PI or delegate on site after review of the clinical history, examination findings and response to PD medication. The Queen Square brain bank criteria MAY be used to help assist in the diagnosis, although this need not be a formal inclusion criteria, and the relevance of a positive family history of PD, or a confirmed genetic basis for an individual's symptoms will be evaluated in the context of other clinical features in determining diagnosis and eligibility
2. Hoehn and Yahr stage < = 2.5 in the ON medication state. This implies that all patients will be mobile without assistance during their best "ON" medication periods
3. Between 25 and 80 years of age
4. On dopaminergic treatment for at least 4 weeks before enrolment. All participants must have had previous or ongoing exposure to dopaminergic treatment either as L-dopa or a dopamine agonist. If L-dopa has been stopped due to side effects or lack of response, the local PI should further confirm that the participant has clinical symptoms and signs and/or radiological investigations consistent with a diagnosis of Parkinson's disease
5. Ability to self-administer, or to arrange carer administration of trial medication
6. Documented informed consent to participate

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 years

Upper age limit
80 years

Sex
All

Total final enrolment

Key exclusion criteria

1. Diagnosis or suspicion of other cause for Parkinsonism. Patients with clinical features indicating a diagnosis of Progressive Supranuclear Palsy, Multiple Systems Atrophy, Drug-induced Parkinsonism, Dystonic tremor or Essential tremor will not be recruited.
2. Patients unable to attend the clinic visits in the practically defined OFF medication state.
3. Body mass index < 18.5. (Exenatide is known to cause weight loss therefore individuals that may not tolerate further weight loss will not be recruited).
4. Known abnormality on CT or MRI brain imaging considered likely to compromise compliance with trial protocol.
5. Significant cognitive impairment defined by a score < 21 on the Montreal Cognitive Assessment.
6. Concurrent severe depression defined by a score > = 16 on the Patient Health Questionnaire (PHQ-9).
7. Prior intra-cerebral surgical intervention for Parkinson’s disease. Patients who have previously undergone Deep Brain Stimulation, intra-cerebral administration of growth factors, gene therapy or cell therapies will not be eligible.
8. Previous participation in one of the following Parkinson’s disease trials (Biogen SPARK trial, Prothena Pasadena trial, Sanofi Genzyme MOVES-PD trial, UDCA-PD UP Study or any other trial still considered to involve a potentially PD modifying agent).
9. Participation in another clinical trial of a device, drug or surgical treatment within the last 30 days.
10. Previous exposure to exenatide.
11. Impaired renal function with creatinine clearance < 50 ml/min.
12. History of pancreatitis. Baseline serum amylase value must fall within laboratory normal range +/- 50%.
13. Type 1 or Type 2 Diabetes mellitus.
14. Severe gastrointestinal disease (e.g. gastroparesis)
15. Hyperlipidaemia. A lipid profile will be tested at the screening visit. Cholesterol or Triglyceride levels greater than 2 x the upper limit of normal will raise suspicion of a familial or acquired hyperlipidaemia and will prompt referral to a relevant specialist for investigation and treatment.
16. History or family history of medullary thyroid cancer (MTC). Undiagnosed neck lump, hoarse voice or difficulty swallowing (not attributable to PD diagnosis).
17. Multiple endocrine neoplasia 2 (MEN2) syndrome.
18. Hypersensitivity to any of exenatide's excipients.
19. Females that are pregnant or breastfeeding. There are no safety data regarding Exenatide use in pregnancy.
20. WOCBP who are unwilling or unable to use an acceptable method to avoid pregnancy for the entire trial period and up to 3 months after the last dose of trial medication. Female participants who are able to become pregnant (defined as women of childbearing potential) will undergo a pregnancy test prior to randomisation and will be asked at each visit to confirm regular use of an effective method of contraception.
21. Participants who lack the capacity to give informed consent.
22. Any medical or psychiatric condition or previous conventional/experimental treatment which in the investigator’s opinion compromises the potential participant’s ability to participate.

Date of first enrolment

01/01/2020

Date of final enrolment
23/04/2022

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
Plymouth
United Kingdom
PL6 8DH

Study participating centre
NHS Lothian, Western General Hospital
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Oxford University Hospitals NHS Foundation Trust, John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Salford Royal NHS Foundation Trust, Salford Royal
Stott Lane
Salford
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M6 8HD

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 16/167/19

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		04/02/2025	10/02/2025	Yes	No
Protocol article		28/05/2021	01/06/2021	Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version 9.0	21/05/2024	06/06/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes