Parkinson's research in Edinburgh: Where are we now?

Gordon W Duncan
NHS Lothian and University of Edinburgh

8 January 2020
Edinburgh Branch Get-together
Bellevue Chapel

Plan

Part 1: Our clinical research programme for Parkinson's

Comfort break & refreshments

Part 2: Growing our clinical research portfolio: past, present & future

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Part 1:

Our clinical research programme for Parkinson's

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My role

- NHS Lothian: Consultant Physician
- University of Edinburgh (Centre for Clinical Brain Sciences): Honorary Clinical Senior Lecturer
- Chief Scientist Office & NHS Research Scotland: Career Research Award (Neuroprogressive & Dementia)

Initiate and Grow *a portfolio of clinical research for Parkinson's in NHS Lothian*

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OUR TOP 10 RESEARCH AREAS FOR IMPROVING EVERYDAY LIFE

Our number 1 priority is to develop better treatments and a cure for Parkinson's, and that is what the majority of our research is working towards.

But finding a cure will take time so we also champion research to improve quality of life for people with the condition and their families.

To help researchers focus on the most important issues, we asked people affected by Parkinson's, carers and health and social care professionals to come up with 10 priority areas for improving everyday life with Parkinson's.

> "The Top 10 enables us to focus on clinical questions that will be of most benefit to people with Parkinson's and their families."
>
> Caroline Rick, Neurosciences Team Leader

The findings were published in December 2014 in The British Medical Journal: read the full open access paper.

Can you help?

It is vital that the top 10 is now used to inform, guide and drive future Parkinson's research.

Here are some ways you can help us address the top 10:

Top 10 priority research areas

1. Balance and falls
2. Stress and anxiety
3. Uncontrollable movements
4. Personalised treatments
5. Dementia
6. Mild thinking and memory problems
7. Monitoring symptoms
8. Sleep
9. Dexterity
10. Urinary problems

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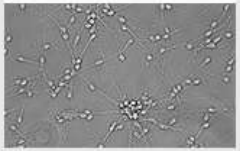
SYNAPSE
for researchers



Be the first to find out about funding opportunities and research news

Delivering clinical research in Lothian

NHS Lothian

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NHS Lothian

Anne Rowling Regenerative Neurology Clinic

THE UNIVERSITY of EDINBURGH

NHS Clinics

PwPs

Research & Development Office

Research Team / Clinical Research Facility

NHS SCOTLAND

NHS RESEARCH SCOTLAND

Neuroprogressive & Dementia Network (NDN)

Supporting Parkinson's Research in Lothian

DELIVERING RESEARCH EXCELLENCE

Lothian Clinical Research Team

Neuroprogressive & Dementia Network (NDN): Multidisciplinary Expertise

Name	Role
Dr Gordon Duncan	Consultant Physician & Geriatrician
Dr David Breen	Consultant Neurologist
Dr Tom Russ	Consultant Old Age Psychiatrist
Ms Jacqui Kerr	Senior Clinical Studies Officer
Ms Maria Dewar	Clinical Studies Officer
Mr Bernie McInally	Clinical Studies Officer
Dr Lewis Killin	Clinical Studies Officer

Dundee – Edinburgh Parkinson's Research Initiative

Dundee and Edinburgh
Parkinson's Research Initiative
Working together to keep on moving

University of Dundee

MRC Protein Phosphorylation and Ubiquitylation Unit

Anne Rowling Regenerative Neurology Clinic

Centre for Regenerative Medicine

Dundee and Edinburgh
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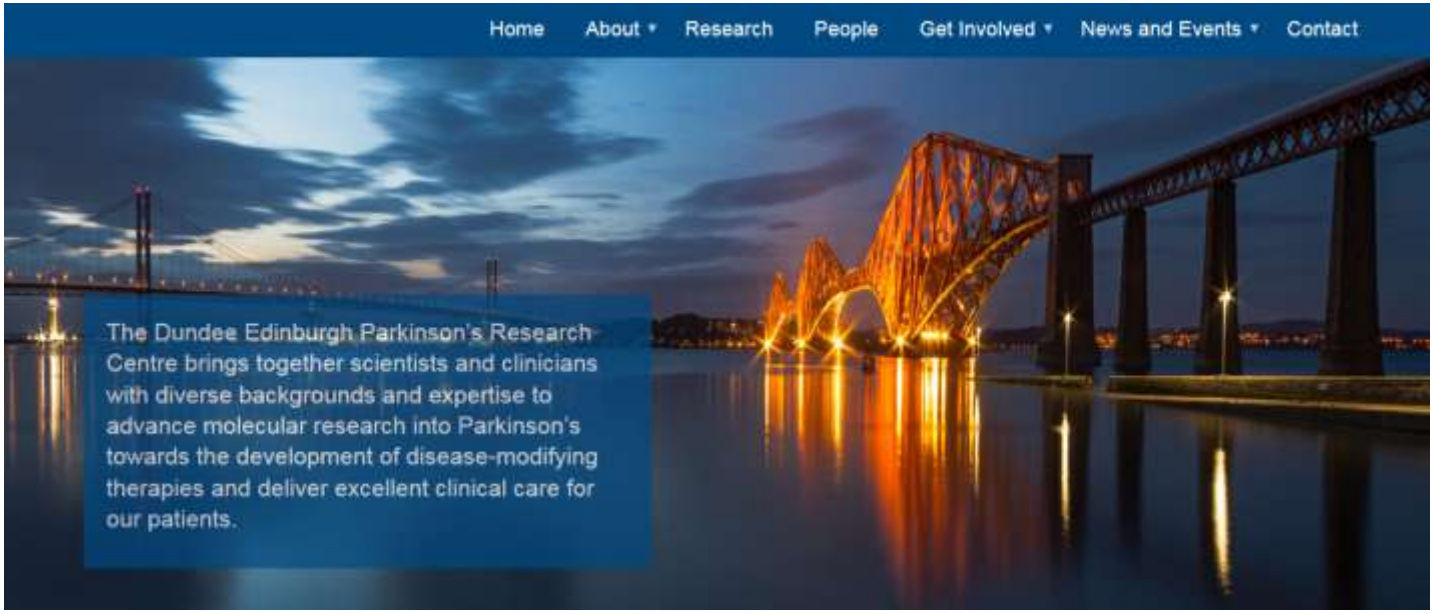
MRC | Protein Phosphorylation and Ubiquitylation Unit

Anne Rowling Regenerative Neurology Clinic

Centre for Regenerative Medicine



Deliver a translational research programme for Parkinson's that integrates innovative laboratory science with clinical research to transform our clinical practice and improve clinical care.

Goals

- Improve clinical care
- Increase participation in clinical research
- Understand the genetic and molecular mechanisms underlying the progression of Parkinson's
- Develop biomarkers
- Translate novel therapies to the clinic

Dundee and Edinburgh Parkinson's Research Initiative
Working together to keep on moving

University of Dundee

MRC

Anne Rowling

Centre for Regenerative Medicine

DEPRI Activity

- Scientific Meetings & Public Events
  - 13 April 2018
  - 22 March 2019
  - **20 March 2020** (details to follow)
- Joint project funding applications
- PhD students
- Support clinical trials / research

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MRC
Anne Rowling
Centre for Regenerative Medicine

Testing new treatments: clinical trials

Disease-modifying therapies

- Stop disease process
- Slow disease process
- Restore function

Symptomatic therapies

- Motor
- Non-motor

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Comfort break & refreshments

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Part 2:

Growing our clinical research portfolio: past, present & future

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Initiate and Grow *a portfolio of clinical research for Parkinson's in NHS Lothian*

- Improve clinical care
- Increase participation in clinical research
- Understand the genetic and molecular mechanisms underlying the progression of Parkinson's
- Develop biomarkers
- Translate novel therapies to the clinic

Dundee and Edinburgh Parkinson's Research Initiative
Working together to keep on moving

University of Dundee

MRC

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Centre for Regenerative Medicine

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Past:
Closed to recruitment & results awaited…

Investigating skin chemicals as a new way to diagnose Parkinson's disease

Molecules of Interest
Eicosane
Perillic aldehyde
Octadecanal
Hippuric acid

PARKINSON'S UK CHANGE ATTITUDES. FIND A CURE. JOIN US.

Sniffing out biomarkers for Parkinson's

Project information	
Lead researcher	Professor Perdita Barran, University of Manchester
Cost	£49,459 over 2 years
Start date	tbc
Type of project	Small grant
Project code	K-1504

Dance for Parkinson's

- CI: Professor Donald Grosset, Glasgow University
- Dancebase, Edinburgh
- Quality of life and movement

Leucine and ACE inhibitors as therapies for sarcopenia: randomised placebo controlled trial

- Can leucine or perindopril improve muscle mass in older people (*age over 70*)?
- UK multi-centre Phase II study
- NIHR £1.4 million

LACE

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The Present: Recruiting NOW

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Regenerative Neurology Clinic

Rowling CARE

Rowling CARE

Title	**Rowling Clinical Audit Research and Evaluation**
Project type	Clinical registry
Funder	Anne Rowling Regenerative Neurology Clinic
Sponsor	University of Edinburgh
CI	Professor Siddharthan Chandran
Aim	To develop a registry for people with neurological disorders to support clinical care, audit and research
Impact	Support audit & improve care delivery Improve equity of access to future research projects Involve people with neurological conditions and their carers/relatives in the design and oversight of research studies Support the use of health data for research

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Inclusion criteria

1. **Living in Scotland with** neurological conditions such as **Parkinson‘s,** motor neurone disease, multiple sclerosis and young onset dementia
2. Carer or relative for either of the above

!!! EVERYONE HERE !!!

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Anne Rowling Regenerative Neurology Clinic

Exclusion

1. Age <16 years (patient participants only)

Anne Rowling
Regenerative Neurology Clinic

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A Multi-Centre Randomised Controlled Trial to Compare the Clinical and Cost Effectiveness of Lee Silverman Voice Treatment *vs.* Standard NHS Speech and Language Therapy *vs.* Control in Parkinson's Disease

NHS
National Institute for Health Research

BCTU
Birmingham Clinical Trials Unit

King's College London

PD COMM

Project type	Phase III randomised controlled trial UK Multicentre
Funder	National Institute for Health Research
Sponsor	University of Birmingham
CI	Prof Catherine Sackley
PI	Dr Gordon Duncan
CSO	Maria Dewar

PD COMM

NHS National Institute for Health Research

BCTU Birmingham Clinical Trials Unit

King's College London

PD COMM

Aim	Determine the clinical and cost effectiveness of LSVT vs. Standard NHS SLT *vs.* Control
Sample size	546
Local target	6 people annually
Duration	12 months
Intervention	SLT will be administered either in the community or in an out-patient setting. 1. LSVT: 4 sessions per week for 4 weeks of pre-determined content with homework. 2. NHS SLT: typically, 1 session weekly for 6 - 8 wks as determined by participant need. 3. Control: no intervention

PD COMM

NHS National Institute for Health Research

BCTU Birmingham Clinical Trials Unit

King's College London

PD COMM: Rationale

"The evidence to support the use of speech and language therapy in PD is limited and yet patients feel that it is effective. The provision of this service in the NHS is patchy with some patients not receiving speech and language therapy when it may be appropriate."

NICE Guidance

PD COMM

NHS National Institute for Health Research

BCTU Birmingham Clinical Trials Unit

King's College London

Inclusion criteria

1. Idiopathic PD defined by UK Brain Bank Criteria

2. PwP or carer report problems with their speech or voice when asked

The inclusion criteria are broad to allow the inclusion of a wide spectrum of typical people with Parkinson's

PD COMM

NHS National Institute for Health Research

BCTU Birmingham Clinical Trials Unit

King's College London

Exclusion criteria

1. Dementia

2. Laryngeal disease e.g. vocal nodules, history of vocal strain or previous laryngeal surgery

3. Received SLT for PD speech or voice problems in the preceding 2 years

PD COMM

NHS National Institute for Health Research

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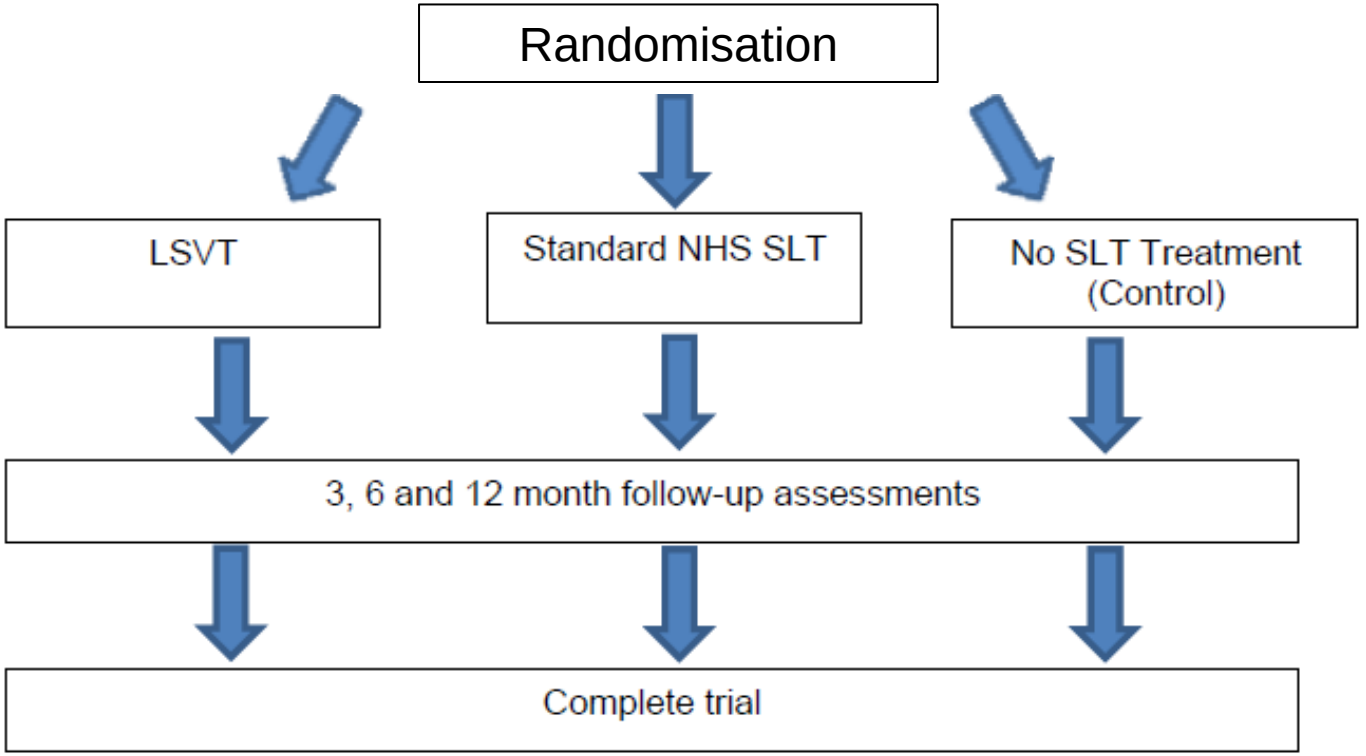
KING'S College LONDON

PD COMM



PD COMM

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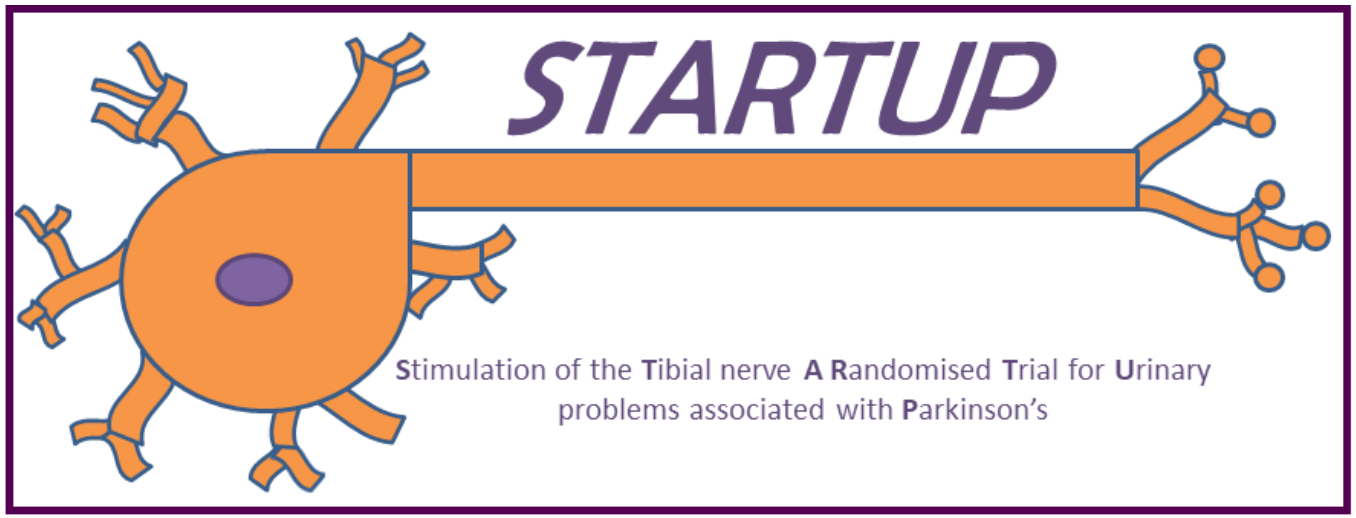
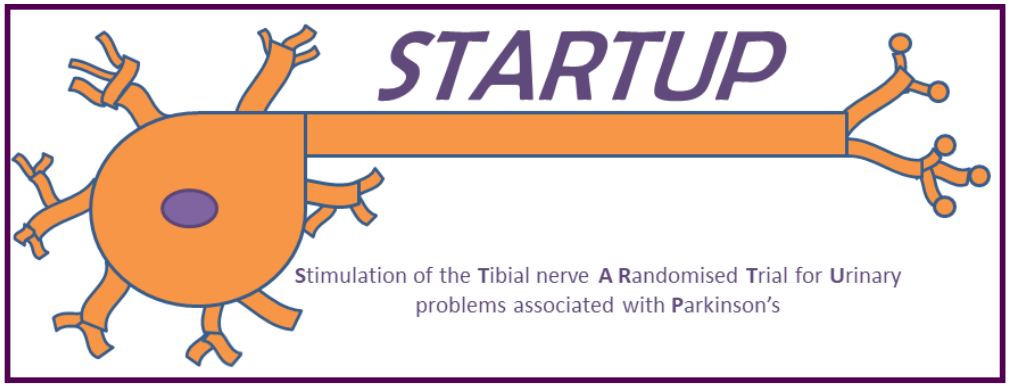
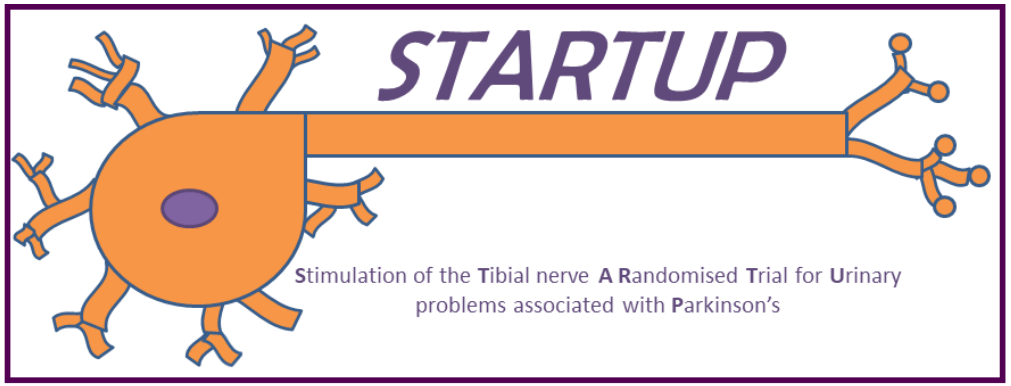


Stimulation of the tibial nerve: A randomised trial for urinary problems associated with Parkinson's



Project type	Phase III randomised controlled trial UK Multicentre
Funder	Parkinson's UK & Dunhill Medical Trust
Sponsor	Glasgow Caledonian University
CI	Prof Doreen McLurg
PI	Dr Gordon Duncan
CSO	Maria Dewar



Aim	To determine if transcutaneous tibial nerve stimulation will reduce lower urinary tract symptoms in people with Parkinson's significantly more than placebo stimulation
Sample size	208
Local target	10 people annually
Duration	12 weeks
Intervention	Participants will be randomised to use the stimulator for 2 sessions / week for 6 weeks (total 12 sessions) Each session is 30 minutes in length Active *vs*. placebo

Inclusion criteria

1. Parkinson's and self-reported problematic lower urinary tract symptoms
2. Able to apply nerve stimulator independently or has carer who can apply for duration
3. Stable Parkinson's medication for 3 months

STARTUP

Stimulation of the Tibial nerve A Randomised Trial for Urinary problems associated with Parkinson's

Exclusion criteria

1. Pacemaker or implanted electrical device
2. Ulceration or broken skin in the area of pad placement
3. History of peripheral vascular disease or epilepsy
4. Current urinary tract infection
5. Receipt of *botox* for bladder symptoms or PTNS within the last year

STARTUP

Stimulation of the Tibial nerve A Randomised Trial for Urinary problems associated with Parkinson's

Living well and enhancing active life: The IDEAL-2 study

IDEAL 2

Title	**IDEAL 2: Improving the experience of dementia and enhancing active life: a longitudinal perspective on living well with dementia**
Project type	UK Multicentre Observational study
Funder	Alzheimer's Society
Sponsor	University of Exeter
CI	Professor Linda Clare
PI	Dr Lewis Killin

Living well and enhancing active life: The IDEAL-2 study

Aim	To provide evidence about living well with dementia, service use and areas of unmet need for people living with dementia.
Sample size	250
Local target	10 people with Parkinson's disease dementia or dementia with Lewy bodies
Duration	2 years
Intervention	Participants are seen at their home to complete baseline visits, which involve taking consent and completing questionnaires.

UNIVERSITY OF EXETER

Inclusion criteria

1. Diagnosis of dementia with Lewy bodies or Parkinson's disease dementia
2. Capacity to consent
3. Living in the community
4. MMSE greater than or equal to 15

Exclusion criteria

1. Presence of a co-morbid terminal illness at point of approach
2. Living in a care home
3. Unable to give informed consent

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The Future: Recruiting in 2020

Exenatide-PD3

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

ARTICLE

Association between diabetes and subsequent Parkinson disease

A record-linkage cohort study

Eduardo De Pablo-Fernandez, MD, Raph Goldacre, MSc, Julia Pakpoor, BM BCh, Alastair J. Noyce, MRCP, PhD,* and Thomas T. Warner, FRCP, PhD*

Correspondence
Prof. Warner
t.warner@ucl.ac.uk

Neurology® 2018;91:e139-e142. doi:10.1212/WNL.0000000000005771

Table HRs and associated 95% CIs in the exposed T2DM cohort compared with the reference cohort[a]

	PD observed	HR	95% CI	*p* Value
T2DM cohort (N = 2,017,115)	14,252	1.32	1.29–1.35	<0.001
Age group				
25–44 y (n = 130,728)	58	3.81	2.84–5.11	<0.001
45–64 y (n = 650,387)	1,711	1.71	1.61–1.81	<0.001
65–74 y (n = 571,291)	5,112	1.40	1.35–1.45	<0.001
≥75 y (n = 664,709)	7,371	1.18	1.14–1.21	<0.001

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Diabetes mellitus is independently associated with more severe cognitive impairment in Parkinson disease

Nicolaas I. Bohnen [a, b, c, *], Vikas Kotagal [b], Martijn L.T.M. Müller [a], Robert A. Koeppe [a], Peter J.H. Scott [a], Roger L. Albin [b, c, d], Kirk A. Frey [a, b], Myria Petrou [a]

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Dementia is associated with Insulin Resistance in patients with Parkinson's Disease

Domenico Bosco[a,*], Massimiliano Plastino[a], Dario Cristiano[a], Carmela Colica[b], Caterina Ermio[c], Matteo De Bartolo[d], Pasquale Mungari[e], Giulia Fonte[f], Domenico Consoli[g], Arturo Consoli[h], Antonietta Fava[i]

Contents lists available at SciVerse ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Diabetes is associated with postural instability and gait difficulty in Parkinson disease

Vikas Kotagal[a,*], Roger L. Albin[a,b], Martijn L.T.M. Müller[c], Robert A. Koeppe[c], Kirk A. Frey[a,c], Nicolaas I. Bohnen[a,b,c]

Exenatide-PD2

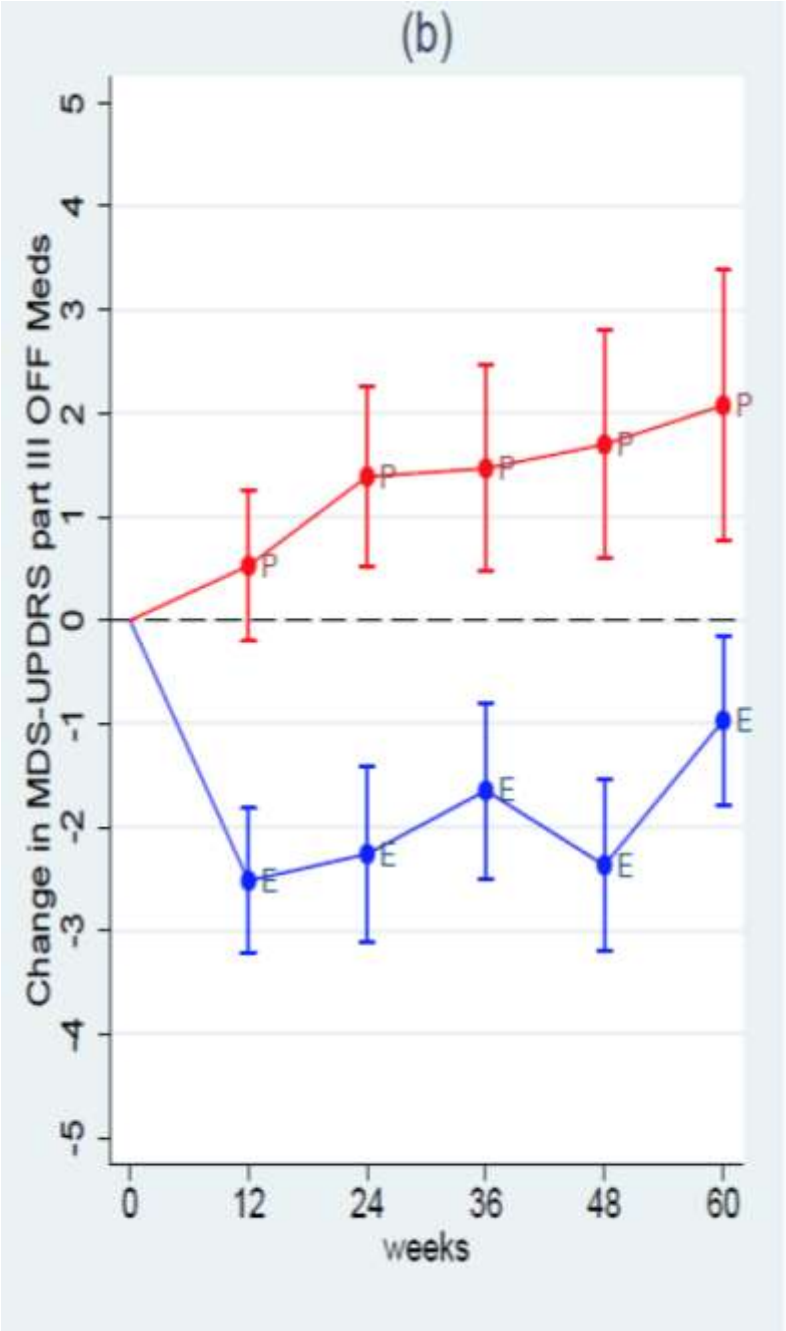
Project type	Phase II, randomised, placebo controlled, double blind UK single centre
Funder	CPT / MJFF
Sponsor	University College London
CI	Prof Tom Foltynie
Sample size	60
Duration	48 weeks of CTIMP 60 week assessment
Intervention	Participants randomised into two groups to self-inject a long acting form of exenatide (Bydureon 2mg) once weekly, or placebo for 48 weeks Final assessment at the 60 week time point to explore any lasting effects following washout of the trial medication

Exenatide once weekly versus placebo in Parkinson's disease: a randomised, double-blind, placebo-controlled trial

Dilan Athauda, Kate Maclagan, Simon S Skene, Martha Bajwa-Joseph, Dawn Letchford, Kanjifa Chowdhury, Steve Hibbert, Natalia Budnik, Luca Zampedri, John Dickson, Yuzhou Li, Ieir Aviles-Olmos, Thomas T Warner, Patricia Limousin, Andrew J Lees, Nigel H Greig, Susan Tebbs, Thomas Foltynie

- Participants randomised to receive exenatide had an adjusted mean 3.5 point advantage in their MDS-UPDRS part 3 OFF medication scores at the 60 week time-point of the trial

- This was statistically significant (p=0.03) even following adjustment for possible confounders including baseline MDS-UPDRS part 3 scores, and Levodopa equivalent dose (LED)



THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

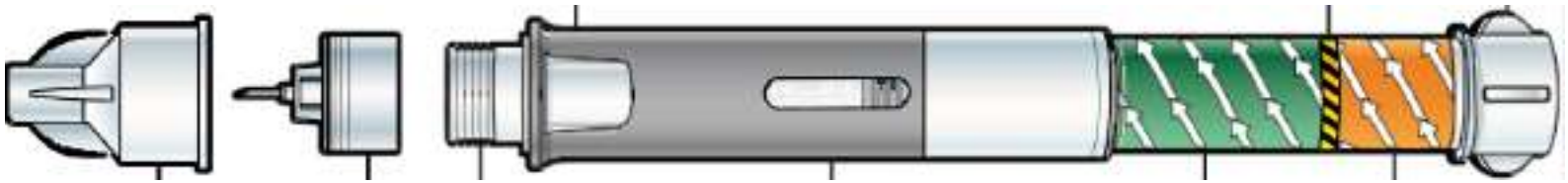
Exenatide-PD3

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**
Project type	Phase III, randomised, placebo controlled, double blind UK Multicentre (6 sites)
Sites	UCL, KCL, Oxford, Salford, Plymouth, Edinburgh
Funder	NIHR - EME
Sponsor	University College London
CI	Prof Tom Foltynie
PI	Dr Gordon Duncan

Exenatide-PD3

Aim	To compare the effectiveness of exenatide once weekly vs. placebo on the MDS-UPDRS part 3 motor sub-score in the “practically defined OFF medication state” in patients with PD
Sample size	200
Local target	16 – 20
Duration	2 years (10 study visits)
Recruitment	21 months
Intervention	ACTIVE: Exenatide extended release 2mg subcutaneous injection (Bydureon) once weekly for 96 weeks (n=100) PLACEBO: Exenatide extended release placebo subcutaneous injection once weekly for 96 weeks (n=100)

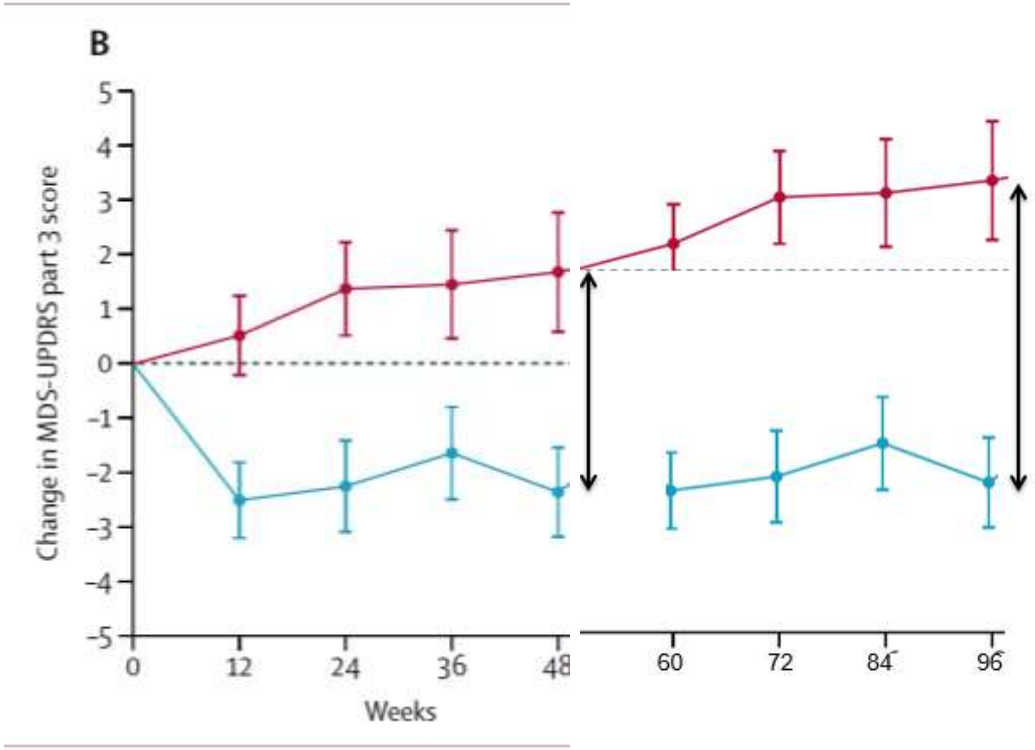
Exenatide-PD3



Ref: IMP Management Plan

Primary Objective

MDS-UPDRS part 3 motor sub-score in the practically defined OFF medication state at **96 weeks** between participants according to treatment allocation.



Secondary Outcomes

- Movement Disorder Society Unified Parkinson's Disease Rating Scale part 1,2,3 and 4 ON medication scores
- Timed Walk assessment ON and OFF medication
- Montreal Cognitive Assessment
- Safety and tolerability of exenatide as indicated by changes in vital signs, weight, clinical laboratory measures and adverse events
- Unified Dyskinesia Rating Scale
- Patient Health Questionnaire (PHQ-9)
- Parkinson's Disease 39 item Quality of life questionnaire
- Non-Motor Symptoms scale
- Levodopa equivalent dose
- 3 day Hauser diary of PD state (Time-On, Off, Non troublesome Dyskinesia, Troublesome dyskinesia, Asleep)

SHORT VISITS (5): 1, 3, 5, 7 & 9

- Screening / baseline
- Height, weight, pulse, BP
- Blood tests
- Concomitant medication review
- Adverse event review
- IMP dispensed (not visit 1)

LONG VISITS (5): 2, 4, 6, 8 & 10

- Blood pressure
- Weight
- Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I,II,III,IV
- Timed Sit-Stand-Walk
- Client Service Receipt Inventory (CSRI)
- EQ-5D-5L
- Montreal Cognitive Assessment (MoCA)
- Patient Health Questionnaire 9 (PHQ-9)
- Non Motor Symptoms Scale (NMS Scale)
- Parkinson's Disease Questionnaire 39 (PDQ-39)
- Unified Dyskinesia Rating Scale (UDysRS)
- Levodopa Equivalent Dose (LED)
- Research Blood samples (plasma) for storage

Inclusion Criteria

1. Diagnosis of Parkinson's disease.
2. Hoehn & Yahr stage ≤2.5 in the ON medication state.
   - All participants 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.
5. Ability to self-administer, or to arrange carer administration of trial medication.
6. Documented informed consent to participate.

Exclusion Criteria (1)

1. Diagnosis or suspicion of other cause for Parkinsonism.
2. 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. Severe depression defined by a score ≥16 on the Patient Health Questionnaire (PHQ-9).
7. Prior intra-cerebral surgical intervention for Parkinson's. People who have previously undergone Deep Brain Stimulation, intra-cerebral administration of growth factors, gene therapy or cell therapies will not be eligible.

Exclusion Criteria (2)

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 <50ml/min.
12. History of pancreatitis. Screening 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.

Exclusion Criteria (3)

16. History or family history of medullary thyroid cancer. Undiagnosed neck lump, hoarse voice or difficulty swallowing (not attributable to PD).
17. Multiple endocrine neoplasia 2 (MEN2) syndrome
18. Hypersensitivity to any of exenatide's excipients.
19. Females that are pregnant or breast feeding. 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.
21. Patients who lack capacity to give informed consent
22. Any medical or psychiatric condition or previous conventional/experimental treatment which compromises the potential participant’s ability to participate.

Royal United Hospitals Bath
NHS Foundation Trust

CHIEF PD

CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

A phase 3 randomised control trial of rivastigmine to prevent falls in Parkinson's disease

BTC

University of BRISTOL

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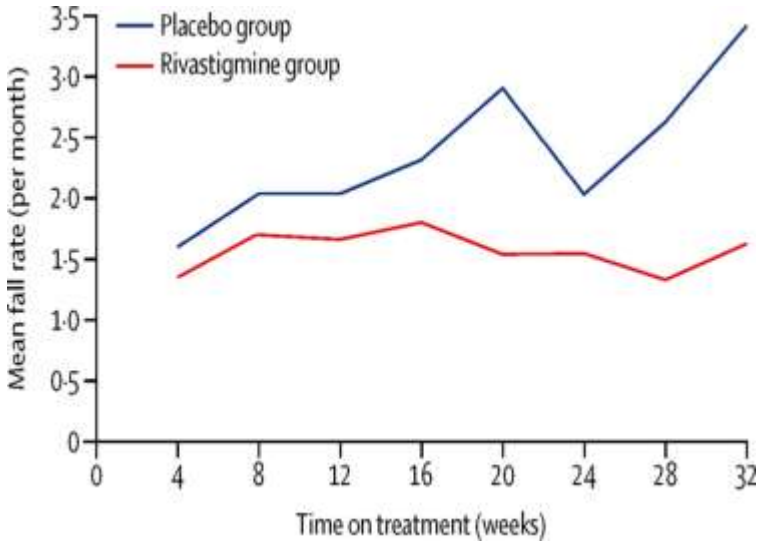
CHIEF PD
CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

Phase 2 trial: RESPOND

Royal United Hospitals Bath
NHS Foundation Trust

- 130 PwPs
- 45% reduction in falls
- More stable walking
- Better balance



The Lancet Neurology 2016 15, 249-258DOI: (10.1016/S1474-4422(15)00389-0)

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CHIEF PD
CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

CHIEF PD

CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

Title	**A phase 3 randomised control trial of rivastigmine to prevent falls in Parkinson's disease**
Project type	Phase III, randomised, placebo controlled, double blind UK Multicentre
Funder	National Institute for Health Research - Health Technology Assessment Programme
Sponsor	University of Bristol
CI	Dr Emily Henderson
PI	Dr Gordon Duncan

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CHIEF PD

CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

CHIEF PD

CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

Aim	To determine the difference in fall rate between people with Parkinson's treated for 12 months with a Rivastigmine patch and those treated with placebo.
Sample size	600
Local target	20
Duration	1 year
Intervention	Transdermal Rivastigmine versus placebo

BTC

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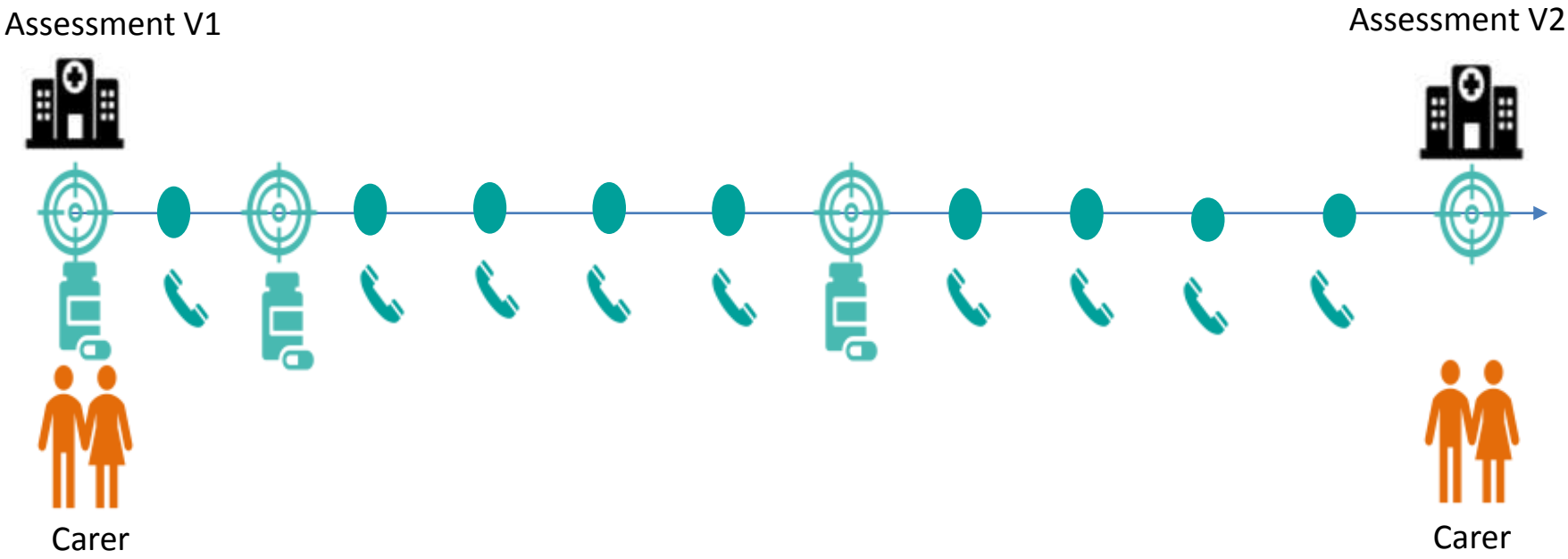
SUPPORTED BY NIHR | National Institute for Health Research

CHIEF PD

CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

Participant Experience



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CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

Inclusion Criteria

- Idiopathic Parkinson's disease
- Hoehn and Yahr stage 1 - 4
- 1 or more falls in the past year
- Able to walk >10m

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CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

Exclusion Criteria

- Dementia
- Already prescribed a cholinesterase inhibitor
- Inability to undertake assessments or apply patch
- Non-English speaking
- >4 falls per day
- Contraception

BTC
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SUPPORTED BY NIHR | National Institute for Health Research
CHIEF PD | CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

ADepT-PD

UCL COMPREHENSIVE CLINICAL TRIALS UNIT

Anti**Dep**ressants **T**rial in **P**arkinson's **D**isease:
A Randomised Controlled Trial of Escitalopram and Nortriptyline compared to placebo, together with standard psychological care, for depression in Parkinson's disease

ADepT-PD

UCL COMPREHENSIVE CLINICAL TRIALS UNIT

Project type	Phase III, randomised, placebo controlled, double blind UK Multicentre
Funder	National Institute for Health Research - Health Technology Assessment Programme Cure Parkinson's Trust
Sponsor	University College London
CI	Prof Anette Schrag
PI	Dr Gordon Duncan
CSO	Maria Dewar

ADepT-PD

UCL COMPREHENSIVE CLINICAL TRIALS UNIT

Aim	1. Establish the clinical and cost-effectiveness of **escitalopram** at 8 weeks compared to placebo in the treatment of depression in addition to standard psychological care in the NHS. 2. Establish the clinical and cost-effectiveness of **nortriptyline** at 8 weeks compared to placebo in the treatment of depression in addition to standard psychological care in the NHS.
Sample size	408
Local target	10 - 15
Duration	12 months
Intervention	In addition to available standard psychological care: 1. Nortriptyline ***or*** 2. Escitalopram ***or*** 3. Placebo

Inclusion criteria

- Diagnosis of idiopathic Parkinson's
- Age 18 to 85 years
- At least 2 depression features, one of which has to be low mood or lack of enjoyment
- Beck Depression Inventory-II (BDI-II) score ≥14

Exclusion criteria (1)

- Women who are pregnant, breastfeeding or of childbearing potential without effective contraception.
- Patients who do not have sufficient understanding of the English language to be able to read and understand the self-completed questionnaires or patients who are unable to communicate answers to the self-rating questionnaires.
- Patients with Montreal Cognitive Assessment (MoCA) score <16
- Patients without capacity to consent.
- Treatment with an antidepressant within 4 weeks of enrolment (except for a small dose of amitriptyline up to 30 mg for indications other than depression).
- Known severe liver failure.
- Active suicidal ideation or intent on the BDI-II item 9.

Exclusion criteria (2)

- Absolute contraindications to escitalopram or nortriptyline:
  - QT-interval prolongation (defined as >420ms) or congenital long QT syndrome.
  - Recent myocardial infarction, any degree of heart block or other cardiac arrhythmias.
- Medications contraindicated with nortriptyline or escitalopram:
  - Non-selective and selective irreversible monoamine oxidase inhibitors (MAOIs) within 14 days (rasagiline, selegiline and safinamide are not contraindicated)
  - Concomitant QT prolonging drugs, including domperidone, apomorphine at high doses (single dose or hourly rate of >6mg), certain neuroleptics, quinine, amiodarone, dronedarone, moxifloxacin, erythromycin IV and others...
- Treatment with antiparkinsonian medication is not optimised and stable within 4 weeks of receiving the trial medication and there are plans to change up to primary endpoint (8 weeks).
- Participation in another clinical trial of an investigational medicinal product or device within the last 30 days.

NHS Lothian

Anne Rowling Regenerative Neurology Clinic

THE UNIVERSITY of EDINBURGH

Work in progress

In development

Rostock International Parkinson's Disease Study – ROPAD

Title	**LRRK2 Rostock International Parkinson's Disease Program - ROPAD**
Project type	International epidemiological observational non-interventional
Funder	Centogene AG Rostock
CI	Prof Peter Bauer
PI	Dr David Breen
Aim	Identification of 1500 LRRK2-positive patients and 1500 non-LRRK2 PD patients Establishment of a candidate biomarker in the LRRK2-positive cohort
Sample size	10,000 participants with PD 1,500 LRRK2-positive patients 1,500 non-LRRK2 PD patients (including a subset of ~500 patients with monogenic PD patients other than LRRK2
Duration	2 years
Intervention	Blood tests

Inclusion criteria

- Informed consent
- Clinical diagnosis of Parkinson‘s disease
- Family member of a participant with LRRK2 parkinsonism
- Participant is 18 years or older

Exclusion criteria

- Does not have Parkinson‘s disease
- Inability to provide informed consent
- Younger than 18 years old

Prasinezumab - Phase 3

Title	A Phase III, Randomised, Double-Blind, Placebo-Controlled, Multicentre, 104-week Trial to Evaluate the Efficacy and Safety of Intravenous Prasinezumab in Patients with Early Parkinson disease
Project type	Phase III, randomised, placebo controlled, double blind Global Multicentre
Funder	Roche
Sponsor	Roche
PI	Dr David Breen
Aim	To evaluate the efficacy, safety, and pharmacokinetics of prasinezumab compared with placebo in patients with early Parkinson on background therapy, with or without other symptomatic therapies.
Sample	1316

More details to follow...

Dundee and Edinburgh
Parkinson's Research Initiative
Working together to keep on moving

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Centre for Regenerative Medicine

Clinical Audit Research and Evaluation – PD (CARE-PD):

An integrated health informatics platform for Parkinson's

Care, Research and Clinical Trials

- Deliver better clinical care
- Stratify the different subtypes of Parkinson's
- Increase patient participation
- Validate biomarkers
- Tissue banking
- Develop a platform for clinical trials

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Thank you
&
Questions