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A trial of rivastigmine to prevent falls in Parkinson's

Submission date
08/04/2019

Recruitment status
No longer recruiting

Registration date
16/04/2019

Overall study status
Completed

Last Edited
23/08/2024

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Parkinson’s disease is a common condition particularly affecting older people. Falls are a very frequent complication of the disease affecting 60% of people with Parkinson's every year. As the population ages, the number of people living with Parkinson’s disease and the occurrence of complications will increase. The loss of the chemical dopamine in the brain causes walking in Parkinson's to become slower, unsteady and irregular. People with the condition are therefore at a very high risk of falling. To some extent, people can compensate for these changes by paying more attention to their walking. However, Parkinson's also diminishes memory and thinking ability. This decreases people’s ability to pay attention to their walking, especially when doing something at the same time.

Who can participate?
Cholinesterase inhibitor (ChEis) are drugs that are currently used to treat people with memory problems in Parkinson’s. The effect of these drugs on falls in Parkinson’s has been tested to show that treatment has the potential to almost halve the number of falls.
This trial aims to definitively determine whether cholinesterase inhibitors (ChEi), can prevent falls in Parkinson’s and whether this treatment is cost-effective.

What does the study involve?
600 participants with Parkinson’s disease will be enrolled from hospitals throughout the UK. Participants will be randomly assigned to either receive the drug (ChEi) via a patch or receive a placebo (dummy) treatment via a patch. Neither the researchers nor the participants will know which group they are in. Participants will take the medication for 12 months and record any falls that they experience in diaries.

What are the possible benefits and risks of participating?
There are a few possible benefits of taking part in this trial. If allocated to the group that receives the active medication, walking unsteadiness and/or balance may improve and falls may be less likely, but there is no guarantee. The information we get from this study will improve the treatment of people with Parkinson’s disease in the future.
There are also some risks and discomforts of the trial. The assessments are quite detailed and therefore may cause tiredness and fatigue.

Like all medicines, the treatment can cause side effects, although not everybody gets them. Because the medication is already used to treat memory problems we know a lot about the side effects.
Side effects are experienced more frequently when you start your medicine or increase the dose. In most cases, side effects will gradually disappear.

Where is the study run from?
Bristol Medical School, University of Bristol, UK

When is the study starting and how long is it expected to run for?
April 2018 to July 2024

Who is funding the study?
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Who is the main contact?
CHIEF-PD Trial Management Team, Chief-pd@bristol.ac.uk

Study website
https://chiefpd.blogs.bristol.ac.uk/

Contact information

Type(s)
Scientific

Contact name
Dr Emily Henderson

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University of Bristol
G11, 1-5 Whiteladies Road
Bristol
United Kingdom
BS8 1NU
+44 (0)117 4283111
Chief-pd@bristol.ac.uk

Additional identifiers

EudraCT/CTIS number
2018-003219-23

IRAS number
235625

ClinicalTrials.gov number
NCT04226248

Secondary identifying numbers
CPMS 40906, IRAS 235625

Study information

Scientific Title
CHIEF-PD (CHolinesterase Inhibitor to prEvent Falls in Parkinson’s Disease): A phase 3 randomised double-blind placebo-controlled trial of rivastigmine to prevent falls in Parkinson’s disease

Acronym
CHIEF-PD

Study objectives
Cholinesterase inhibitor (ChEi) treatment prevents people with Parkinson's from falling and is cost-effective.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 17/05/2019, Southwest Central Bristol Research Ethics Committee (Health Research Authority, Whitefriars, Level 3 Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0) 2071048046; nrescommittee.southwest-bristol@nhs.net), ref: 19/SW/0043

Study design
Randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Parkinson's Disease

Interventions
Current interventions as of 05/12/2019:
Previous interventions:

600 participants with Parkinson’s disease will be enrolled from hospitals throughout the UK. Participants will be randomly assigned to either receive the drug (ChEi) via a patch or receive a placebo (dummy) treatment via a patch. Participants are allocated to the two treatment arms using a technique that minimises the differences between the groups but still allocated people randomly. Neither the researchers nor the participants will know which group they are in. Participants will take the medication for 12 months and record any falls that they experience in diaries and through monthly telephone calls.

TRIAL ASSESSMENTS OVERVIEW
At baseline (enrolment) and follow-up (12 months) detailed tests of Parkinson's disease are undertaken to determine what effect the treatment has on the motor and non-motor symptoms of the condition. At monthly intervals between visits participants will complete a diary (detailed below).

BASELINE VISIT (2.5 hours)
Eligibility confirmation (10 minutes)
Consent (15 minutes)
Disease and functional measures (approx 1.5 hours)
1. Questionnaires (optionally can be completed pre-visit) (15 minutes):
1.1 Freezing of gait (New Freezing of Gait questionnaire NFOG-Q)
1.2 Fear of falling (Iconographical Falls Efficacy Scale [ICON-FES])
1.3 Mood (Geriatric Depression Scale [GDS])
1.4 Capability of older people (ICEpop CAPability measure for Older people [ICECAP-O])
1.5 Quality of life (EQ-5D-5L)
1.6 Starkstein Apathy Scale (SAS)
1.7 Swallowing (Swallowing Disturbance Questionnaire [SDQ])

2. Sociodemographics, medical and drug history
3. Brief examination: heart rate (+/- electrocardiogram if indicated), blood pressure, height and weight, Movement Disorder Society Unified Parkinson's Disease Scale (MDS-UPDRS) parts 3 and 4, frailty and gait assessment, Short Physical Performance Battery (SPPB).
4. Functional measures:
4.1 Cognition (Montreal Cognitive Assessment [MoCA])

SELF COMPLETION OF MONTHLY DIARY and PHONE CALLS
Falls are recorded in a patient diary which is posted back to the central team on a monthly basis. Participants are telephoned to remind them about the diaries, to identify any side effects that have occurred.
Questionnaire assessments of quality of life and healthcare use are completed in the diary at months 1, 3, 6, 9 and 12 in order to determine whether the treatment, if successful, is also cost-effective.

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Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
Fall rate measured using monthly diaries and telephone calls prospectively over 12 months from the day the IMP is commenced. A fall is defined as “unintentionally coming to rest on the ground or other lower surface without overwhelming external force or a major internal event”

Secondary outcome measures
Current secondary outcome measures as of 05/12/2019:
1. Parkinson's Disease markers assessed via the MDS-UPDRS total score in the practically defined ON state and each individual subscale (1-4) measured at baseline and 12months
2. Freezing of gait assessed via the New Freezing Of Gait Questionnaire (NFOGQ) measured at

baseline and 12months
3. Frailty and physical performance assessed via Short Physical Performance Battery (SPPB), gait speed and frailty status measured at baseline and 12months
4. Cognition assessed via Montreal Cognitive Assessment (MoCA) measured at baseline and 12months
5. Depression assessed via Geriatric Depression Scale (GDS) measured at baseline and 12months
6. Apathy assessed via the Starkstein Apathy Scale (SAS)
7. Fear of falling assessed via the Iconographical Fall Efficacy Scale (ICON-FES) measured at baseline and 12months
8. Dysphagia assessed via the Swallowing Disturbance Questionnaire (SDQ) measured at baseline and 12months
9. Participant health-related quality of life assessed via the EuroQoL 5D-5L health status questionnaire (EQ-5D-5L) measured at baseline, 1 month, 3 months, 6 months, 9 months and 12months
10.Capability of older people assessed via the ICEpop CAPability measure for Older people (ICECAP-O) measured at baseline and 12 months
11. Mortality (all cause and PD related) through Office of National Statistics measured at 12months
12. Cost-effectiveness and NHS resource use through EQ-5D-5L and NHS Episode Statistics (HES) data
Secondary outcome via CHIEF-PD carer study:
12. Care-related quality of life via the Carer Experience Scale (CES) measured at baseline and 12months

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Secondary outcome via CHIEF-PD carer study:
12. Care-related quality of life via the Carer Experience Scale (CES) measured at baseline and 12months

Overall study start date
01/04/2018

Completion date
30/07/2024

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 05/07/2019:
1. Diagnosis of idiopathic Parkinson's disease
2. Modified Hoehn and Yahr stage 1-4 disease
3. Have experienced a fall in the previous year
4. Able to walk ≥10m without aids or assistance
5. 18 years of age or above

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1. Diagnosis of idiopathic Parkinson's disease
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3. Have experienced a fall in the previous year
4. Able to walk ≥10m without aids or assistance

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 600; UK Sample Size: 600

Total final enrolment
600

Key exclusion criteria
Current participant exclusion criteria as of 05/07/2019:
1. Previous ChEi use in 12 months prior to enrolment.
2. Hypersensitivity to rivastigmine
3. Dementia diagnosed according to Movement Disorder Society (MDS) criteria
4. Inability to attend or comply with treatment or follow-up scheduling
5. Non-English-speaking patients (cognitive tests performed in English)
6. Falling ≥ 4x per day

7. Unwillingness to use an acceptable method of contraception for the duration of the trial if they are of childbearing potential
8. Pregnant of breast feeding

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1. Previous ChEi use in 12 months prior to enrolment
2. Hypersensitivity to rivastigmine
3. Dementia diagnosed according to Movement Disorder Society (MDS) criteria
4. Inability to attend or comply with treatment or follow-up scheduling
5. Non-English-speaking patients (cognitive tests performed in English)
6. Falling ≥ 4x per day
7. Unwillingness to use an acceptable method of contraception for the duration of the trial if they are of childbearing potential

Date of first enrolment
02/09/2019

Date of final enrolment
30/04/2023

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

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

Study participating centre
Northern Care Alliance
North Manchester General Hospital
Delaunays Road
Crumpsall
Manchester
United Kingdom
M8 5RB

Study participating centre
Royal Cornwall Hospitals NHS Trust
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LJ

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

Study participating centre
Derby Teaching Hospitals NHS Foundation Trust
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

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

Study participating centre
Imperial College Healthcare NHS Trust
St. Marys Hospital
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
Yeovil District Hospital NHS Foundation Trust
Yeovil District Hospital
Higher Kingston
Yeovil
United Kingdom
BA21 4AT

Study participating centre
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle-upon-Tyne
United Kingdom
NE7 7DN

Study participating centre
Taunton And Somerset NHS Foundation Trust
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre

Royal Devon And Exeter NHS Foundation Trust
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
The Walton Centre NHS Foundation Trust
Lower Lane
Liverpool
United Kingdom
L9 7LJ

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

Study participating centre
Barking, Havering and Redbridge University Hospitals NHS Trust Rom Valley Way, Romford, RM7 0AG
Rom Valley Way
Romford
United Kingdom
RM7 0AG

Study participating centre
Gateshead NHS Foundation Trust
Queen Elizabeth Avenue
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Great Western Hospitals NHS Foundation Trust
Marlborough Road

Swindon
United Kingdom
SN3 6BB

Study participating centre
NHS Tayside
230 Clepington Road
Dundee
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DD2 1UB

Study participating centre
Nottingham University Hospitals NHS Trust
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Nottingham
United Kingdom
NG5 1PB

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

Study participating centre
Cwm Taf Morgannwg University Health Board
Princess of Wales Hospital
Coity Rd
BrIdgend
United Kingdom
CF31 1RY

Study participating centre
University Hospitals Dorset NHS Foundation Trust
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
Clifford Bridge Rd
Coventry
United Kingdom
CV2 2DX

Study participating centre
Northumbria Healthcare NHS Foundation Trust
Unit 7-8 Silver Fox Way Cobalt Business Park
Silver Fox Way
Newcastle upon Tyne
United Kingdom
NE27 0QJ

Study participating centre
Leeds Teaching Hospitals NHS Trust
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Barnsley Hospital NHS Foundation Trust
Gawber Road
Barnsley
United Kingdom
S75 2EP

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Ln
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre

North Bristol NHS Trust
Southmead Hospital
Southmead Road
Bristol
United Kingdom
BS10 5NB

Study participating centre
Homerton University Hospital NHS Foundation Trust
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
Betsi Cadwaladr University Health Board
Betsi Cadwaladr University Health Board
Ysbyty Gwynedd
Penrhosgarnedd
Bangor
United Kingdom
LL57 2PW

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
University Hospitals Of Leicester NHS Trust
University Hospitals of Leicester Headquarters
Level 3, Balmoral Building
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Sponsor information

Organisation
University of Bristol

Sponsor details
Research and Enterprise Development
One Cathedral Square
Bristol
England
United Kingdom
BS1 5DD
+44 (0)117 42 84021
research-governance@bristol.ac.uk

Sponsor type
University/education

Website
https://www.bristol.ac.uk/

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Government

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

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal, conference presentation, publication on website, submission to regulatory authorities

Intention to publish date
28/02/2025

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		29/10/2021	15/02/2023	Yes	No
HRA research summary			26/07/2023	No	No