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Donepezil in early dementia associated with Parkinson's disease

Submission date	Recruitment status	[X] Prospectively registered
08/07/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
07/08/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/06/2019	Nervous System Diseases	

Plain English summary of protocol

Background and study aims

Every day in the UK, between 30 and 40 people are told they have Parkinson's disease. Of these, nearly four-fifths will go on to develop dementia. The symptoms of dementia, which include hallucinations, also put a huge additional strain on the person's family. Parkinson's disease is a very costly disease in the UK and when dementia occurs it is likely to increase the healthcare costs even further. Whilst drug treatments have made a big impact in treating the motor symptoms of Parkinson's disease (slowness, stiffness and tremor), the management of dementia is woefully inadequate. We wish to test the effectiveness of a drug called donepezil in people with dementia associated with Parkinson's disease. Donepezil and similar drugs cost the NHS around £1200 per year to prescribe for each patient. It is therefore important to learn whether donepezil produces benefits that are truly meaningful to patients and their families, whilst also being good value for money. In this study the participants will have only mild symptoms of dementia when they are approached to consider taking part. By treating at this stage, we will be able to assess the effect of early intervention.

Who can participate?

Patients aged 18 or over with Parkinson's disease and mild dementia

What does the study involve?

Participants are randomly allocated to receive either donepezil or an identical tablet, called a placebo, which contains no active drug. Participants take the tablets for up to two years. The results are then compared to see if one treatment is better than the other. We measure cognition (memory and attention), psychiatric disturbances (for example, visual hallucinations) and changes in patient and carer quality of life. We also look at the services people use, their costs, and the time spent by family members providing unpaid care, so that we can determine whether the treatment is good value for money.

What are the possible benefits and risks of participating?

Not provided at time of registration

Where is the study run from?

Newcastle University (UK)

When is the study starting and how long is it expected to run for?
November 2009 to October 2014

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Prof. David Burn
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2009-015170-35

IRAS number

ClinicalTrials.gov number
NCT01014858

Secondary identifying numbers
HTA 08/14/13; Protocol 1.0

Study information

Scientific Title
Multicentre UK study of the acetylcholinesterase inhibitor donepezil in early dementia associated with Parkinson's disease

Acronym
MUSTARDD-PD

Study objectives
Primary hypothesis:
That donepezil is superior to placebo in improving cognitive function, neuropsychiatric burden and functional ability in people with Parkinson's disease and mild dementia after 24 months of treatment.

Secondary hypotheses:
1. That donepezil is superior to placebo in improving patient and carer quality of life
2. That donepezil is a cost-effective treatment option

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/081413
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0003/81372/PRO-08-14-13.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised double-blind placebo-controlled study

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Parkinson's disease with mild dementia

Interventions
Treatment group: donepezil orally, 5 mg once a day for 8 weeks, then 10 mg once a day (presented in both cases as 1 capsule) for up to 96 weeks.
Control group: matched placebo orally, 1 capsule daily for up to 104 weeks.

Total duration of treatment: maximum of 2 years (104 weeks). Total duration of follow-up: 2 years (i.e. to end of treatment period).

Intervention Type

Drug

Phase
Phase III

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

Primary outcome measure
1. Mattis Dementia Rating Scale (DRS-2)
2. Neuropsychiatric Inventory
3. Bristol Activity of Daily Living Scale

All primary and secondary outcome measures will be measured at baseline (commencement of treatment), 26 weeks, 52 weeks, 76 weeks and 104 weeks (+/- 7 days for each visit). The primary analysis will focus on outcomes at 104 weeks.

Secondary outcome measures
1. Quality of life via:
1.1. European Quality of Life questionnaire (EQ5D)
1.2. Dementia Quality of Life (DEMQOL)
1.3. DEMQOL-proxy
2. Costs via Client Service Receipt Inventory

All primary and secondary outcome measures will be measured at baseline (commencement of treatment), 26 weeks, 52 weeks, 76 weeks and 104 weeks (+/- 7 days for each visit). The primary analysis will focus on outcomes at 104 weeks.

Overall study start date
01/11/2009

Completion date
31/10/2014

Eligibility

Key inclusion criteria
1. Aged greater than or equal to 18 years, no upper age limit, either sex
2. A diagnosis of Parkinson's disease according to UK Parkinson's Disease Society Brain Bank Criteria
3. People with mild dementia associated with PD, where the patient and/or their family have become aware of cognitive with or without behavioural symptoms that are causing functional impairment. "Dementia" will be defined according to recently published Movement Disorder Society Task Force criteria for dementia associated with Parkinson's disease and "operationalised" using the Addenbrooke's Cognitive Examination (ACE-R). Participants will have an ACE-R of 88 or less. If this criterion is met, subjects will be further assessed using the Mattis Dementia Rating Scale (DRS-2). An age- and education-corrected total DRS-2 score of less than 8 but greater than 6 (corresponding to between the 6th and 28th percentile) will be used to define "mild" dementia.
4. Community-living and a spouse, close relative or well established informal carer to accompany the subject to act as an informant

5. Where relevant, women of child bearing potential must be using adequate contraception for duration of study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
500

Key exclusion criteria
1. Dementia that develops within one year of the onset of motor symptoms. The reason for this "one year rule" is to specifically exclude participants with Dementia with Lewy Bodies (DLB).
2. People with such severe motor disability, or who are so impaired in their activities of daily living from other aspects of their PD, that it would interfere with cognitive and global assessments
3. Severe current depressive episode. This will be operationalised using the self-completed Beck Depression Inventory and a cut-off score of 13/14.
4. Unstable significant medical co-morbidity
5. Patient receiving an anticholinergic drug for control of parkinsonian motor symptoms
6. Previous exposure to a cholinesterase inhibitor
7. Presence of a condition that is contraindicative to use of donepezil (including a clinically significant cardiac conduction defect)
8. Allergy/hypersensitivity to excipients of donepezil or placebo
9. Patient receiving the N-methyl-d-aspartate antagonist memantine
10. Previous neurosurgery for Parkinson's disease

Date of first enrolment
01/11/2009

Date of final enrolment
31/10/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

Clinical Ageing Research Unit
Newcastle upon Tyne
United Kingdom
NE4 5PL

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

Sponsor details
Joint Research Office
4th Floor, Leazes Wing
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
England
United Kingdom
NE1 4LP

Sponsor type
Hospital/treatment centre

Website
http://www.newcastle-hospitals.org.uk/about-us/staff-information_research-development.aspx

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/08/2015

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No