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Donepezil and memantine in moderate to severe Alzheimer's disease

Submission date	Recruitment status	[X] Prospectively registered
28/03/2007	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
04/04/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
05/12/2017	Nervous System Diseases	

Plain English summary of protocol
http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=50

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2007-001172-36

ClinicalTrials.gov (NCT)
NCT00866060

Protocol serial number
2006/123

Study information

Scientific Title
DOnepezil and Memantine IN mOderate to severe Alzheimer's Disease

Acronym
DOMINO - AD

Study objectives
The trial will test a number of hypotheses in patients who have declined in terms of cognitive function to reach the transition point to moderate-to-severe Alzheimer's Disease (AD):
1. Patients with AD who continue donepezil beyond the moderate to severe transition point will show a significantly smaller decline on ratings of cognitive function and activities of daily living over the following 12 months than those discontinuing donepezil
2. Patients with AD who commence memantine therapy will show a significantly smaller decline on ratings of cognitive function and activities of daily living over the following 12 months than those who do not
3. Patients given the combination of memantine and donepezil will show additive or synergistic significant benefits on measures of activities of daily living and cognitive function after 12 months compared to those patients continuing on either monotherapy
4. Treatment of patients with donepezil beyond the moderate to severe transition point will be more cost-effective than discontinuing donepezil. Memantine therapy will be more cost-effective than placebo. The combination of memantine and donepezil will be more cost-effective than monotherapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A Research Ethics Committee on 28/05/2007 (ref: 07/MRE00/52).

Study design
Pragmatic multi-centre double-blind randomised placebo-controlled (double-dummy) parallel group 2 x 2 factorial clinical trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
There will be four arms being assessed (all patients will be on donepezil when entering the trial):
Arm one: combination of donepezil 10 mg plus memantine 20 mg
Arm two: withdrawal of donepezil and prescription of memantine 20 mg
Arm three: continued prescription of donepezil 10 mg
Arm four: withdrawal of donepezil

The patients on each arm will receive the appropriate treatment once daily for 52 weeks.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
1. Cognitive function measured by the Standardised Mini Mental State Exam (SMMSE)
2. Activities of daily living measured using the Bristol Activities of Daily Living Scale (BADLS)

All measures will be taken at zero, six, 18, 30 and 52 weeks.

Key secondary outcome(s))
1. Non-cognitive dementia symptoms measured using the neuropsychiatric inventory
2. Health related quality of life measured by Euro Quality of Life (EQ-5D) questionnaire and Demential Quality of Life (DEMQOL)-proxy
3. Care giver burden measured by the 12-item General Health Questionnaire (GHQ-12)
4. Cost effectiveness measured using the client service receipt inventory in conjunction with SMMSE and BADLS results

All measures will be taken at zero, six, 18, 30 and 52 weeks.

Completion date
31/08/2013

Eligibility

Key inclusion criteria
Participants will be patients who meet National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable or possible AD and in addition will meet all of the following criteria:
1. Continuously prescribed donepezil for at least three months
2. No change in dosage of donepezil in previous six weeks
3. No changes in prescription of any psychotropic (antipsychotic, antidepressant, benzodiazepine) medication in previous four weeks
4. Prescribing clinician considers (based on National Institute of Clinical Excellence [NICE] guidance, discussions with patient and carer and clinical judgement) that change of drug treatment (i.e. stop donepezil or introduce memantine) may be appropriate and Standardised Mini Mental State Exam (SMMSE) = 5 to 13 (13 chosen as NICE threshold of 10 plus 1 SD on SMMSE score)
5. Patient is community resident and has family or professional carer or is visited on at least a daily basis by carer
6. Patient agrees to participate where possible
7. Main carer (informal or institutional) consents to their own involvement

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Sex
Not Specified

Key exclusion criteria
1. Patient has severe, unstable or poorly controlled medical conditions apparent from physical examination or clinical history
2. Patient is already prescribed memantine
3. Patient is unable to take trial medications
4. Patient is involved in another clinical trial
5. Patient has absolute contraindication to either donepezil or memantine
6. Clinician considers patient would not be compliant with medication

Date of first enrolment
01/11/2007

Date of final enrolment
31/08/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Old Age Psychiatry, PO70
London
United Kingdom
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Sponsor information

Organisation
Institute of Psychiatry (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (UK) (grant ref: G0600989)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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?
Results article	results	08/03/2012		Yes	No
Protocol article	protocol	24/07/2009		Yes	No
Other publications	secondary analysis	01/12/2015		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes