

Donepezil and memantine in moderate to severe Alzheimer's disease

Submission date 28/03/2007	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 04/04/2007	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 05/12/2017	Condition category Nervous System Diseases	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=50

Study website

<http://neuroscience.iop.kcl.ac.uk/domino/default.aspx>

Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

EudraCT/CTIS number

2007-001172-36

IRAS number

ClinicalTrials.gov number

NCT00866060

Secondary identifying numbers

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

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Patient information can be found at: <http://neuroscience.iop.kcl.ac.uk/domino/docs/patient.pdf>

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 measure

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.

Secondary outcome measures

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.

Overall study start date

01/11/2007

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

Age group

Not Specified

Sex

Not Specified

Target number of participants

800

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

England

United Kingdom

Study participating centre
Old Age Psychiatry, PO70
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Sponsor information

Organisation
Institute of Psychiatry (UK)

Sponsor details
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Sponsor type
Research organisation

Website
<http://www.iop.kcl.ac.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

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**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?
Protocol article	protocol	24/07/2009		Yes	No
Results article	results	08/03/2012		Yes	No
Other publications	secondary analysis	01/12/2015		Yes	No