ISRCTN88882979 https://doi.org/10.1186/ISRCTN88882979

HTA Study of Antidepressants for Depression in Dementia: A definitive multi-centre pragmatic randomised controlled double-blind trial of the clinical and cost effectiveness of mirtazapine and sertraline versus placebo for the treatment of depression in dementia presenting in secondary care

Submission date
27/02/2006

Recruitment status
No longer recruiting

Registration date
02/03/2006

Overall study status
Completed

Last Edited
11/07/2013

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Sube Banerjee

Contact details
Professor of Mental Health and Ageing
Unit PO26, Section of Mental Health and Ageing
Health Services Research Department
The Institute of Psychiatry
Kings College London
De Crespigny Park
London
United Kingdom

SE5 8AJ
+44 (0)20 7848 0012
s.banerjee@iop.kcl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2006-000105-38

Protocol serial number
HTA 04/11/02, EudraCT Number: 2006-000105-38

Study information

Scientific Title

Acronym
HTA-SADD

Study objectives
Primary Objective
1. To determine the clinical and cost effectiveness of two classes of antidepressants for depression in dementia (compared with placebo)
a. To determine whether a selective serotonin reuptake inhibitor (SSRI) (sertraline) is i) more clinically effective and ii) more cost effective than placebo in reducing Cornell depression score 13 weeks post randomisation
b. To determine whether a noradrenergic and specific serotonergic antidepressant (NaSSA) (mirtazapine) is i) more clinically effective and ii) more cost effective than placebo in reducing Cornell Depression score 13 weeks post-randomisation

Secondary Objectives
2. To investigate differences in the clinical and cost effectiveness, and in terms of adverse events, withdrawals from treatment and adherence to treatment between mirtazapine and sertraline for depression in dementia at 13 and 39 weeks post-randomisation
3. To investigate differences in the clinical and cost effectiveness of mirtazapine/sertraline and placebo on patient (e.g. quality of life, cognition) and family carer (e.g. carer burden, carer quality of life) outcomes at 13 and 39 weeks post-randomisation
4. To investigate the influence on clinical and cost effectiveness of clinical characteristics including: dementia severity, dementia type, depression type, depression severity, care arrangements, neuropsychiatric symptoms, and physical illness

As of 30/07/09 this record has been updated. All updates can be found in the relevant field with the above update date. Please also note that the sponsor of this trial has been changed.
Initial sponsor at time of registration:
Department of Health (UK)
Quarry House
Quarry Hill
Leeds
LS2 7UE

United Kingdom
Sheila.Greener@doh.gsi.gov.uk
http://www.dh.gov.uk/en/index.htm

Please note that, as of 04/09/2009, the anticipated end date of this trial has been updated from 30/11/2008 to 31/05/2010.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Added on 29/07/09: Ethics approval received on the 12th of July 2006

Study design
A multi-centre double-blind placebo-controlled randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Depression in dementia

Interventions
The randomised interventions are:
1. Mirtazapine (a NaSSA) + sertraline placebo with normal clinical care
2. Sertraline (an SSRI) + mirtazapine placebo with normal clinical care
3. Mirtazapine placebo + sertraline placebo with normal clinical care

Interventions will be available in 15 mg tables for mirtazapine and 50 mg capsules for sertraline. The protocol will therefore require each subject to take six tablets per day. This is a double dummy design.

For the first two weeks of treatment, participants will receive:
1. Sertraline 50 mg plus a placebo mirtazapine tablet
2. Mirtazepine 15 mg plus a placebo sertraline tablet
3. A placebo sertraline tablet and a placebo mirtazapine tablet

For the second two weeks, participants will receive:
1. Sertraline 100 mg (2 tablets) plus two placebo mirtazapine tablets
2. Mirtazapine 30 mg (2 tablets) plus two placebo sertraline tablets
3. Two placebo sertraline tablets and two placebo mirtazapine tablets

From week 4 until the end of the trial (ten months in total), participants will receive:
1. Sertraline 150 mg (3 tablets) plus three placebo mirtazapine tablets
2. Mirtazapine 45 mg (3 tablets) plus three placebo sertraline tablets
3. Three placebo sertraline tablets and three placebo mirtazapine tablets

Dose adjustments can be made by reducing back to 2 of each tablet daily or to 1 of each tablet daily in participants experiencing troublesome side effects.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Mirtazapine and sertraline

Primary outcome(s)
1. Depression in dementia - CSDD (Alexopoulos et al 1988)
2. Costs - Client Service Receipt Inventory (CSRI; Beecham et al 2001)

Key secondary outcome(s))
1. Disease specific quality of life - DEMQOL and DEMQOL-Proxy (Smith et al 2005)
2. Generic measure of quality of life - interview administered to carer (Coucill et al 2001) EQ-5D (EuroQoL Group 1990)
3. Withdrawal from treatment arm
4. Cognitive impairment - MMSE (Folstein et al 1975)
5. Medication adherence
6. Adverse events
7. Carer mental health - General Health Questionnaire - 12 (GHQ-12; Goldberg et al 1988)
8. Carer quality of life - SF-12 v2 (Ware et al 1996)
9. Carer burden - Zarit Carer Burden Scale (Zarit 1980)

Completion date
31/05/2010

Eligibility

Key inclusion criteria
We have designed this study as a pragmatic trial of effectiveness in routine clinical practice. We wish to minimise exclusions from the study in order to maximise the generalisability of the data generated.

The criteria for inclusion are set to be as close to clinical practice as possible. For this reason we do not specify the use of anything other than clinical diagnoses of dementia and depression since standardised instruments (other than the Mini-Mental State Examination [MMSE] as a measure of severity) are not used in routine practice. A detailed characterisation of cases using standardised tools will be completed at the research assessment. We will recruit those in whom a secondary care doctor makes at the point of referral to the RW:
1. A clinical diagnosis of mild to moderate probable or possible Alzheimer's Disease
2. A co-existing depressive illness likely to need treatment with antidepressants
3. Depression should have a duration of more than four weeks

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria
We wish to minimise exclusions. We will exclude from the trial those in whom a secondary care doctor finds at the point of referral to the RW are:
1. Currently taking antidepressants
2 Those with severe dementia (defined as MMSE >7)
3. The case is considered as being too critical to be randomised (e.g. because of suicide risk)
4. Displays absolute contraindications to one or more of the trial treatments
5. Not in another trial
6. Those where there is no identifiable family carer or other informant (e.g. a formal /professional carer who spends sufficient time with the person with dementia to be able to give an informed opinion) to give collateral information

We will further exclude from the trial those in whom the RW finds have a Cornell score <8 at the point of randomisation.

Date of first enrolment
01/09/2006

Date of final enrolment
31/05/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Professor of Mental Health and Ageing
London
United Kingdom
SE5 8AJ

Sponsor information

Organisation
King's College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

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

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	30/07/2011		Yes	No
Results article	results	01/02/2013		Yes	No
Other publications	cost-effectiveness analysis	01/02/2013		Yes	No