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Mirtazapine for treatment resistant depression

Submission date	Recruitment status	[X] Prospectively registered
20/09/2012	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/09/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/12/2018	Mental and Behavioural Disorders	

Plain English summary of protocol

Background and study aims

Depression is common and most depressed patients are treated by their general practitioner (GP). Antidepressants are very widely prescribed, but a substantial proportion of those who take them do not get better. There is very little evidence to guide GPs when this happens, and most are unsure what to do when their patients do not respond to the medication. Many patients remain in a depressed state for long periods of time, despite taking antidepressant treatment. We are looking for other ways to help those whose depression does not respond to initial treatment, and we think that it might be useful to use combinations of antidepressant drugs. Combination treatments are used in many areas of medicine, including other common conditions such as hypertension and diabetes. Most of the antidepressants prescribed in the UK as first line treatment are Selective Serotinin Reuptake Inhibitors (SSRIs) like Fluoxetine (Prozac). However, there is another well-established antidepressant called Mirtazapine, that works in a different way from SSRIs and the related noradrenaline reuptake inhibitors (SNRIs). We propose a large study in general practice, where most depression is treated, to examine the effectiveness and cost-effectiveness of the combination of mirtazapine and an SSRI or SNRI.

Who can participate?

Patients from primary care who are depressed and have taken an SSRI or SNRI antidepressant for at least six weeks without substantial benefit. They must be aged between 18 and 75 and must not be suffering from a psychotic disorder or be dependent on drugs and alcohol. They must not be pregnant.

What does the study involve?

Participants who agree will be randomly allocated to receive either mirtazapine treatment or a dummy drug (placebo) that appears identical. Neither the participant, GP, or study investigator will know whether the participant is taking mirtazapine or placebo. They will continue to take their SSRI antidepressant and be treated by their GP in the usual way.

What are the possible benefits and risks of participating?

If it proves effective, this combination has the potential to rapidly make a difference for people with depression that does not respond to usual first line antidepressant treatment. Mirtazapine has been licensed in the UK for the treatment of depression since 1994, and its adverse effect

profile is well known. Its principal effects are increase in appetite, weight gain and drowsiness. Mirtazapine continues to be used in psychiatric settings in combination with other antidepressants without the reporting to date of any unexpected or new adverse events.

Where is the study run from?
Bristol University. The other participating centres are the Universities of Exeter, Manchester and York.

When is study starting and how long is it expected to run for?
The study begins in January 2013 and will run for 42 months

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 11/129/76

Study information

Scientific Title
A double blind placebo-controlled randomised trial of the addition of mirtazapine for patients with depression in primary care who have not responded to at least 6 weeks of treatment with a selective serotonin reuptake inhibitor or serotonin and noradrenaline reuptake inhibitor.

Acronym
MIR

Study objectives
That the addition of mirtazapine will improve outcome in depressed patients from primary care who have not responded to an SSRI antidepressant after at least 6 weeks of treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Wales Research Ethics Committee C, 25/01/2013, ref: 12/WA/0353

Study design
A two parallel group multi-centre pragmatic placebo-controlled randomised trial with allocation at the level of the individual

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
Depression

Interventions
The addition of Mirtazapine to SSRI antidepressants

Added 27/07/2017:
To investigate whether combining mirtazapine with Serotonin-Noradrenaline Reuptake Inhibitor (SNRI) or Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants results in better patient outcomes and more efficient NHS care than SNRI or SSRI therapy alone in Treatment Resistant

Depression (TRD).
Design: MIR is a two-parallel group, multi-centre, pragmatic, placebo controlled, randomised trial with allocation at the level of the individual.
Interventions: Participants are randomised to receive either oral mirtazapine or matched placebo, starting at 15mg daily for two weeks and increasing to 30mg daily thereafter, for up to 12 months to be taken in addition to their usual antidepressant.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Change in Beck Depression Inventory score at 12 weeks (added 27/07/2017: measured using the BDI-I) measured as a continuous variable

Secondary outcome measures
Current secondary outcome measures:
The following are measured at 12, 24, and 52 weeks:
1. Response
2. Remission of depression symptoms
3. Changes in anxiety symptoms
4. Adverse Effects
5. Quality of life
6. Adherence to antidepressant medication
7. Health and social care use
8. Time off work
9. Cost effectiveness
All outcomes are analysed on an intention to treat basis.

Previous secondary outcome measures:
1. 50% improvement in BDI score (remission)
2. A measure of anxiety (GAD7)
3. Quality of life (EQ-5D-5L)
4. Health care utilisation

Overall study start date
01/01/2013

Completion date
30/06/2016

Eligibility

Key inclusion criteria

1. Aged 18-75 years
2. Currently taking any of the following SSRI or SNRI antidepressants, for at least 6 weeks at recommended (BNF) doses:
2.1. Fluoxetine
2.2. Sertraline
2.3. Citalopram
2.4. Escitalopram
2.5. Fluvoxamine
2.6. Paroxetine
2.7. Duloxetine
2.8. Venlafaxine and who have done so for at least 6 weeks at
3. Patients who score 14 or more on the Beck Depression Inventory (BDI)
4. Patients who have adhered to their medication and meet ICD-10 criteria for depression (assessed using the Computerised Interview Schedule Revised version (CIS-R))

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
400

Key exclusion criteria
GPs will be asked to exclude patients who have bipolar disorder, psychosis or alcohol/substance abuse/dependence or who are pregnant. In addition, we will exclude patients who: are not able to complete the study questionnaires or have a past history of an adverse reaction to mirtazapine.

Date of first enrolment
01/01/2013

Date of final enrolment
30/06/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Bristol
Bristol
United Kingdom
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Study participating centre
University Of Exeter Medical School
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Sponsor information

Organisation
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Sponsor type
University/education

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ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date

Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made 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	protocol	03/02/2016		Yes	No
Results article	results	31/10/2018		Yes	No
Results article	results	01/11/2018		Yes	No
Results article	qualitative study results	14/12/2018		Yes	No
HRA research summary			28/06/2023	No	No