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Comparative Evaluation of QUEtiapine-Lamotrigine combination versus quetiapine monotherapy (and folic acid versus placebo) in people with bipolar depression

Submission date
10/01/2008

Recruitment status
No longer recruiting

Registration date
29/02/2008

Overall study status
Completed

Last Edited
26/10/2016

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 John Geddes

Contact details
Department of Psychiatry
Warneford Hospital
Oxford
United Kingdom
OX3 7JX
+44 (0)1865 226480
john.geddes@psych.ox.ac.uk

Additional identifiers

Protocol serial number
MRC ref: 81651; OCTUMI-02:CEQUEL

Study information

Scientific Title
Comparative Evaluation of QUEtiapine-Lamotrigine combination versus quetiapine monotherapy (and folic acid versus placebo) in people with bipolar depression

Acronym
CEQUEL

Study objectives
The combination of quetiapine and lamotrigine will be more effective than quetiapine alone as treatment for acute bipolar depression.

Please note that this trial has been updated since the original submission. All changes can be found in the relevant field under the update date of 28/04/2008. The previous title of this trial was 'Comparative Evaluation of QUEtiapine-Lamotrigine combination versus quetiapine monotherapy (and folic acid versus placebo) in patients with bipolar depression', and the previous anticipated start date of this trial was 01/04/2008.

More details can be found at:
http://www.mrc.ac.uk/ResearchPortfolio/Grant/Record.htm?GrantRef=G0700477&CaseId=9701

On 20/12/2013 the anticipated end date was changed from 31/03/2012 to 05/05/2013 and the target number of participants field was changed from 584 to 202.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire Research Ethics Committee B, 09/04/2008, ref: 08/H0605/39

Primary study design
Interventional

Study design
Multicentre double-blind randomised placebo-controlled parallel-group, 2 x 2 factorial clinical trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bipolar depression

Interventions
1. Open-label quetiapine (oral) plus
2. Lamotrigine (oral) or placebo plus
3. Folic acid (oral) or placebo

The recommended dose of quetiapine is 300 mg/day but this can be reduced if the higher dose is not tolerated. Minimum dose 150 mg/day. Quetiapine will be taken for about 54 weeks (1-2 week run-in phase and 12 month randomised phase).

The recommended dose of lamotrigine is 200 mg/day (reduced to 100 mg/day for participants taking concurrent valproic acid preparations). Lamotrigine will be taken for the 12 months randomised phase.

Dose of folic acid: 500 µg/day. Folic acid will be taken for the 12 months randomised phase.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Quetiapine, lamotrigine

Primary outcome(s)
Remission of depressive symptoms at 12 weeks post-randomisation.

Key secondary outcome(s)
1. The proportion of participants who both achieve remission by 12 weeks following randomisation (defined as a score of <= 5 on QIDS-SR16) and remain free from symptomatic relapse by 52 weeks. Depressive relapse is defined as a QIDS-SR16 score >= 10 on two consecutive weekly ratings and manic relapse as an Altman Self-Rating Mania Scale (ASRM) score of >=10 on a single weekly rating.
2. New intervention (admission or drug treatment) for manic episode by 52 weeks.
3. New intervention (admission or drug treatment) for depressive episode by 52 weeks.
4. Proportion of time over 12 months when participants were free from manic symptoms (ASRM <= 5).
5. Proportion of time over 12 months when participants were free from depressive symptoms (QIDS-SR16 <= 5).
6. Death (all cause and cause-specific including suicide).
7. Deliberate self-harm.
8. Quality of life will be assessed 4-weekly over 52 weeks (timepoints added 28/04/2008)
9. Unexpected adverse events.
10 Withdrawal from quetiapine or lamotrigine due to adverse effects.
11. Use of health and social care service resources.
12. Social costs/benefits.

Completion date
05/05/2013

Eligibility

Key inclusion criteria
For the active run-in phase:
1. Primary diagnosis of bipolar disorder type I or II (based on Diagnostic and Statistical Manual of Mental Disorders, 4th edition [DSM-IV] criteria for a hypomanic or manic episode)
2. Consent to participate in the trial
3. Aged 16 or over

4. Current depressive episode requiring new pharmacological treatment (either as add-on therapy or as a change of treatment)
5. Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR16) Score >= 14

Please note that, as of 15/09/2008, inclusion criterion "1. Diagnosis of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) bipolar disorder type I or II (assessed using the Mini-International Neuropsychiatric Interview [MINI])" has been replaced with "1. Primary diagnosis of bipolar disorder type I or II (based on Diagnostic and Statistical Manual of Mental Disorders, 4th edition [DSM-IV] criteria for a hypomanic or manic episode)"

For the randomised phase:
1. Able to tolerate quetiapine at a dose of at least 150 mg/day
2. Uncertainty whether quetiapine plus lamotrigine would be more effective than quetiapine monotherapy
3. Acceptable adherence to quetiapine (>90%) and to self-report SMS text-messages satisfactory
4. QIDS-SR16 score of >=11 on day of randomisation
5. Willing to accept random allocation of treatments
6. In the opinion of the investigator, not currently experiencing manic or mixed episode

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Current exclusion criteria as of 15/09/2008:
1. Definite indications or contraindications to lamotrigine, quetiapine or folic acid (Including pregnancy or planned pregnancy)
2. New course of specific psychosocial intervention started in the past four weeks
3. First appointment for specific psychosocial intervention booked within the next 14 weeks
4. Primary diagnosis of schizophrenia

Plus, for women of child-bearing potential:
5. Currently breast feeding or not using adequate contraception

Current exclusion criteria as of 28/04/2008:
1. Definite indications or contraindications to lamotrigine, quetiapine or folic acid (Including pregnancy or planned pregnancy)
2. New course of specific psychosocial intervention started in the past four weeks
3. First appointment for specific psychosocial intervention booked within the next 14 weeks
4. Currently meeting criteria for (hypo)mania (based on MINI)
5. Currently meeting criteria for schizophrenia
6. Eight or more mood episodes in the past year

Plus, for women of child-bearing potential:
7. Not using adequate contraception

Initial exclusion criteria:
1. Definite indications or contraindications to lamotrigine, quetiapine or folic acid (Including pregnancy or planned pregnancy)
2. New course of structured psychotherapy started in the past four weeks
3. First appointment for structured psychotherapy booked within the next 14 weeks
4. Currently meeting criteria for (hypo)mania (based on MINI)
5. Eight or more mood episodes in the past year

Plus, for women of child-bearing potential:
6. Not using adequate contraception

Date of first enrolment
01/06/2008

Date of final enrolment
05/05/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Psychiatry
Oxford
United Kingdom
OX3 7JX

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type

Government

Funder Name
Medical Research Council (MRC) (UK) (ref: 81651)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory 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:	01/01/2016		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes