

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

<b>Submission date</b> 10/01/2008	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
<b>Registration date</b> 29/02/2008	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 26/10/2016	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## 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

**Study design**

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

**Primary study design**

Interventional

**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  $\leq 5$  on QIDS-SR16) and remain free from symptomatic relapse by 52 weeks. Depressive relapse is defined as a QIDS-SR16 score  $\geq 10$  on two consecutive weekly ratings and manic relapse as an Altman Self-Rating Mania Scale (ASRM) score of  $\geq 10$  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  $\leq 5$ ).
5. Proportion of time over 12 months when participants were free from depressive symptoms (QIDS-SR16  $\leq 5$ ).
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  $\geq 14$

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  $\geq 11$  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

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## **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, 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?
<a href="#">Results article</a>	results:	01/01/2016		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes