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Are antidepressants more effective than placebo, when given in combination with mood stabilisers, in preventing mood episodes in people with bipolar I disorder?

Submission date
04/08/2009

Registration date
26/11/2009

Last Edited
26/11/2009

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

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
MCT-94835

Study information

Scientific Title
Mood stabiliser plus antidepressant versus mood stabiliser plus placebo in the maintenance treatment of bipolar disorder

Study objectives
We hypothesise that in clinically representative patients with bipolar disorder (BD) who respond to acute treatment with a newer antidepressant medication in conjunction with a mood stabilising medication, continuing the antidepressant for 12 months will reduce the risk of relapse into any mood episode, including depression, mania, and hypomania, compared to stopping the antidepressant after 8 weeks.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The University of British Columbia Office of Research Services Clinical Research Ethics Board approved on the 25th of August 2009 (UBC CREB NUMBER: H09-01017)

Study design
Two-part interventional open label randomised multicentre study

Primary study design
Interventional

Study type(s)
Prevention

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

Interventions
Open label acute treatment phase:
1. Escitalopram will be initiated at a dose of 10 mg daily:
1.1. The dose may be increased in increments of 10 mg at the discretion of the study psychiatrist, until remission of the index depression
1.2. In patients who develop intolerable side effects, the dose may be decreased in 10 mg increments
1.3. The total dose must remain within the range of 10 - 30 mg daily. Patients who are unable to tolerate a minimum dose of 10 mg daily will be discontinued from the study.
2. Bupropion XL will be initiated at a dose of 150 - 450 mg daily:
2.1. The dose may be increased in increments of 150 mg, at the discretion of the study psychiatrist, until remission of the index depression
2.2. In patients who develop intolerable side effects, the dose may be decreased in 150 mg increments
2.3. The total dose must remain within the range of 150 - 450 mg daily. Patients who are unable to tolerate a minimum dose of 150 mg daily will be discontinued from the study.

Double-blind maintenance treatment phase:
1. Escitalopram will be prescribed in the dose range 10 - 30 mg daily:
1.1. In patients randomised to the "8-week group", escitalopram will be tapered, discontinued, and replaced with placebo over a period of 2 weeks, beginning at the week 6 study visit.
1.2. The dose of escitalopram (or matching placebo) may be decreased in 10 mg increments only in the case of intolerable side effects. The dose must remain within the protocol-defined range of 10 - 30 mg daily at all time points.
2. Bupropion XL will be prescribed in the dosage range 150 - 450 mg daily:

2.1. In patients randomised to the "8-week group", bupropion XL will be tapered, discontinued, and replaced with placebo over a period of 2 weeks, beginning at the week 6 study visit.
2.2. The dose of bupropion XL (or matching placebo) may be decreased in 150 mg increments only in the case of intolerable side effects. The dose must remain within the protocol-defined range of 150 - 450 mg daily at all time points.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Escitalopram, Bupropion XL

Primary outcome(s)
Open-Label Phase:
The primary outcome for the open-label phase is mean improvement in Montgomery Asberg Depression Rating Scale (MADRS) score from baseline to endpoint.
The MADRS will be completed at all study visits in the open label phase.

Double-Blind Phase:
1. MADRS
2. Young Mania Rating Scale (YMRS)
3. Clinical Global Impression: Bipolar Severity Scale (CGI BP Severity)
4. Hospitalization
5. Requirement for additional treatment for mood episode.
These measures will be completed at all visits in the double-blind phase.

Key secondary outcome(s))
Open-Label Phase:
1. MADRS
2. Inventory of Depressive Symptomatology (Clinician- Rated) Scale (IDS-CEnglish[1])
3. Inventory of Depressive Symptomatology (Self-Rated) Scale (IDS-SREnglish[1]
4. YMRS
5. CGI BP - Severity
6. Clinical Global mpression: Bipolar Change Scale (CGI BP Change)
7. Quality of Life scale (Q-LES-Q)
8. MDC Side Effect Scale (MDCSES).
The MADRS, IDS-CEnglish[1], IDS-SREnglis[1], YMRS, CGI BP Severity and the MDCSES scales will be completed at all study visits.
The CGI BP Change will be completed at every visit starting at Week 2 and the Q-LES-Q will be completed at Baseline and Week 16/ Termination.

Double-Blind Phase:
1. Time to manic or hypomanic episode
2. Time to depressive episode
3. Time to study discontinuation for any reason (eg. onset of mood episode, intolerable side effects, patient or clinician decision)
4. Percentages of patients who experience any mood episode, a manic or hypomanic episode, or a depressive episode

5. Percentage of patients who experience subsyndromal symptoms and the percentage of time spent with subsyndromal symptoms
6. Rates of adverse events and serious adverse effects (SAEs)
7. Mean endpoint scores on the clinical rating scales.
These will be assessed using the MADRS, IDS-CEnglish[1], IDS-SREnglish [1], YMRS, CGI BP Severity; CGI BP Change; MDCSES scales and will be completed at all visits in the double-blind phase.

Completion date
01/03/2014

Eligibility

Key inclusion criteria
Patients meeting all of the following criteria will be eligible for inclusion in the open-label study phase:
1. Diagnosed with BD, current episode depressed, with a Montgomery Asberg Depression Rating Scale (MADRS) score greater than or equal to 20 at both the screening and baseline assessments
2. The duration of the current depressive episode is greater than or equal to 2 weeks but less than or equal to 52 weeks
3. Taking or initiating treatment with a mood stabilising medication at a therapeutic dose. Mood stabilising medications and therapeutic doses are: lithium, serum level 0.6 - 1.4 mEq/L; divalproex, serum level 350 - 700 mM; risperidone 1 - 6 mg/day; olanzapine 5 - 30 mg/day; quetiapine IR or XR 300 - 900 mg/day; aripiprazole 10 - 30 mg/day; and ziprasidone 80 - 160 mg /day.
4. If taking any other psychoactive medication (other than lorazepam less than or equal to 4 mg /day or equivalent), is agreeable to tapering and discontinuing it over a period of less than or equal to 4 weeks
5. If female and of childbearing potential, is using an adequate method of contraception. Adequate methods of contraception include abstinence; oral contraceptive pill or surgically implanted device; intra-uterine device; condom plus spermicidal foam or jelly; or tubal ligation.
6. Aged 18 - 70 years, inclusive, either sex
7. Fluent in English and capable of providing informed consent

Patients meeting all of the following criteria will be eligible to be included in the double-blind study phase:
1. Taking escitalopram 10 - 30 mg/day or bupropion XL 150 - 450 mg/day, in addition to either a mood stabilising medication (lithium, serum level 0.8 - 1.2 mEq/L or divalproex, serum level 350 - 700 mM), an SGA (risperidone 1 - 6 mg/day; olanzapine 5 - 30 mg/day; quetiapine IR or XR 150 - 900 mg/day; aripiprazole 10 - 30 mg/day; or ziprasidone 80 - 160 mg/day), or a mood stabiliser plus a second-generation antipsychotic (SGA).
2. Has adequately tolerated the combination of antidepressant plus mood stabiliser, and is currently in remission for greater than or equal to 2 weeks and less than or equal to 8 weeks
3. If female and of childbearing potential, is using an adequate method of contraception

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Patients meeting any of the following criteria will be excluded from the open-label study phase:
1. Has a history of rapid cycling, defined as greater than or equal to 4 mood episodes in the preceding 12 months
2. Has current manic, hypomanic, or subsyndromal hypomanic symptoms, defined as a Young Mania Rating Scale (YMRS) score greater than or equal to 8 at the screening or baseline visits
3. Has previously been refractory to treatment with both escitalopram and bupropion XL, or has been unable to tolerate both medications due to intolerable side effects or an allergic reaction
4. Has active substance dependence, other than caffeine or nicotine dependence, in the preceding 3 months. Otherwise, patients with comorbid substance abuse or other comorbid psychiatric illnesses will be eligible to participate in the study.
5. Is at high risk for suicide, as defined by a score of greater than or equal to 3 on the suicide item of the Hamilton Depression Rating Scale (HAM-D), or in the opinion of the investigator
6. Has an unstable medical illness, as defined by a change in medication or other treatment in the past 4 weeks, or in the opinion of the investigator
7. Is pregnant or lactating

Patients meeting any of the following criteria will be excluded from the double-blind study phase:
1. Has a history of rapid cycling, defined as greater than or equal to 4 mood episodes in the preceding 12 months
2. Has current manic, hypomanic, or subsyndromal hypomanic symptoms, defined as a YMRS score greater than or equal to 8 at the screening or baseline visits
3. Has active substance dependence, other than caffeine or nicotine dependence, in the preceding 3 months. Otherwise, patients with comorbid substance abuse or other comorbid psychiatric illnesses will be eligible to participate in the study.
4. Is at high risk for suicide, as defined by a score of greater than or equal to 3 on the suicide item of the HAM-D, or in the opinion of the investigator
5. Has an unstable medical illness, as defined by a change in medication or other treatment in the past 4 weeks, or in the opinion of the investigator
6. Is pregnant or lactating
7. Has experienced an episode of mania, hypomania, or a mixed episode during antidepressant treatment of the acute depression, defined as a YMRS score of greater than or equal to 16 at any open-label study visit, or in the opinion of the study psychiatrist

Date of first enrolment
05/10/2009

Date of final enrolment
01/03/2014

Locations

Countries of recruitment
Canada

Study participating centre
Rm 2C1 2255 Wesbrook Mall
Vancouver
Canada
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Sponsor information

Organisation
University of British Columbia (Canada)

ROR
https://ror.org/03rmrcq20

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: MCT-94835)

Funder Name
GlaxoSmithKline/Biovail (Canada) - medication support

Funder Name
Lundbeck Canada Inc. (Canada) - medication support

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes