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Concomitant administration of quetiapine (Seroquel®) in cognitive-behavioural therapy for refractory depression: a 12-week placebo-controlled study

Submission date
12/10/2007

Recruitment status
No longer recruiting

Registration date
19/10/2007

Overall study status
Completed

Last Edited
31/12/2020

Condition category
Mental and Behavioural Disorders

[ ] 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

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
5077-9016

Study information

Scientific Title
Concomitant administration of quetiapine (Seroquel®) in cognitive-behavioural therapy for refractory depression: a 12-week placebo-controlled study

Study objectives
1. To assess whether Cognitive Behavior Therapy (CBT) is effective (pharmacologically) for refractory depression
2. To assess whether the addition of a sedative medication, in the form of an atypical neuroleptic at low doses, can increase the efficacy of CBT

Ethics approval required
Old ethics approval format

Ethics approval(s)
Two ethics approvals were obtained as this study was carried out at two sites:
1. The Notre-Dame Hospital Ethics Board, the University of Montreal, Quebec, Canada. Approved on 7 January 2002.
2. Ethics Committee at the Ethica Clinical Research Inc. Approved on 24 September 2002

Study design
Randomized, double-blind, placebo-controlled trial.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
The participants were recruited at the following two sites:
1. The Notre-Dame Hosptial, the University of Montreal, Quebec, Canada
2. The city of Saint-Jean-sur-Richelieu, Quebec, Canada

In order to confirm that patients are indeed refractory all candidates will undergo an initial open phase of antidepressant potentiation using lithium carbonate (at least 600 mg per day) for three weeks. The antidepressant dose of patients currently receiving either TCAs, venlafaxine or SSRIs will be set as close as possible to the maximum recommended therapeutic dose for the three week period. Primary assessment variables will be reassessed at day 21 (HAMD and the Clinical Global Impression of Severity [CGI-S]/ Clinical Global Impression of Improvement [CGI-I]). A reduction equal or greater than 40% of the initial HAMD score will classify the patient as a responder. Responders will be tapered off lithium and referred back to their attending physicians following this three week period. Treatment with lithium for three weeks should be sufficient to maintain response in these patients now taking their initial antidepressant only. As lithium potentiation has not been extensively investigated with the newer atypical antidepressants, patients currently receiving buproprion, nefazodone or moclobemide who nevertheless wish to participate in the study will be switched to venlafaxine XR for a period of five weeks prior to the three week lithium potentiation.

Following this initial phase, non-responders will be tapered of their medication (lithium and antidepressant) during a one week period and subsequently randomized to one of two treatment groups; CBT and placebo or CBT and quetiapine. CBT will be administered in 12 weekly two hour CBT sessions given in an individual setting. Individual, rather than group CBT treatment is chosen as there is evidence to suggest that group CBT may be less efficacious in alleviating depressive symptomatology than individually administered CBT. The CBT paradigm will be based upon the Beck cognitive therapy model with its associated behavioral techniques. In addition, social skills training and, when warranted, applied relaxation training were also administered. In addition, modifications of the Cognitive Behavioral Analysis System will be integrated into the CBT paradigm as these have been shown to be particularly useful in the treatment of MD. Homework assignments will be kept in record form and monitored by the therapist at each session. All CBT sessions will be performed by the same therapist.

All medications will be administered orally, with an initial dose of 25 mg/twice a day (bid) for quetiapine and placebo bid. Doses will be titrated up to a maximum of 200 mg/bid for quetiapine within the first 14 days of the study using a flexible dose schedule dependent upon the patient's clinical response and the side-effects profile of the medication. Doses will remain stable thereafter.

At the end of the study, patients will be tapered off study drug. Down titration will be accomplished by decreasing the dose level every fourth day until complete cessation of drug results. Duration of the taper, therefore, will depend on the patient's dose level at study completion. During this time, patients will be treated according to local practice and appropriate treatments will be initiated as required.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Quetiapine (Seroquel®)

Primary outcome measure

Primary efficacy variables will be reassessed (HAMD, the Montgomery-Asberg Depression Rating Scale [MADRS] and CGI-S/CGI-I) on day 21 and 28 as well as every two weeks thereafter by raters blind to the treatment.

Secondary outcome measures
Assessment of the secondary variables (Extrapyramidal Symptom Rating Scale [ESRS], the Barnes' Akathisia Rating scale and the Heinrich Quality of Life Scale [HQL]) will be performed again at day 112.

Overall study start date
23/05/2002

Completion date
15/07/2003

Eligibility

Key inclusion criteria
1. Males and females between the ages of 18 and 70.
2. Signed an informed consent form and have the capacity to follow the course of the study.
3. Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition (DSM-IV) criteria for depression (unipolar) as well as a Hamilton depression rating scale (HAMD, 21 items) score of 20 or greater at screen (day 0) and 18 or over at randomization (day 28).
4. A Clinical Global Impression (severity scale) score of 4 or greater.
5. Patients will be required to have a diagnosis of refractory major depression as determined by having had;
5.1. At least two sequential 8 week treatments with two different classes of antidepressants. For instance, an 8 week treatment with a Selective Serotonin Reuptake Inhibitor (SSRI) + an atypical antidepressant or alternatively, a SSRI + a TriCyclic Antidepressant (TCA) (this latter class would include venlafaxine) or alternatively, a SSRI + a monoamine oxidase inhibitor. All antidepressants would have had to be administered at the following doses:
a. Venlafaxine (regular venlafaxine 300 mg/day; venlafaxine 'Extended Release' (venlafaxine XR) 225 mg/day, for at least 3 of the 8 weeks)
b. A tricyclic antidepressant (minimum dose of 150 mg/day equivalent of imipramine for 3 of the 8 weeks)
c. A SSRI (at a minimum 40 mg/day for fluoxetine, 30 mg/day for paroxetine and citalopram, 150 mg/day of sertraline and 250 mg/day for fluvoxamine for 3 of the 8 weeks)
d. Moclobemide (600 mg/day for 3 of the 8 weeks)
e. Nefazodone (500 mg/day for 3 of the 8 weeks)
f. Bupropion (250 mg/day for 3 of the 8 weeks)
g. An irreversible monoamnie oxidase inhibitor (at maximum posology for 3 of the 8 weeks)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
32

Total final enrolment
31

Key exclusion criteria
1. Patients who in the investigator's opinion pose a current risk of suicide.
2. Women of childbearing potential who are pregnant, planning pregnancy in the next 6 months, breast-feeding, or not using medically adequate means of birth control (abstinence, hormonal treatment, Intrauterine Device [IUD]).
3. Any of the following DSM-IV diagnoses: schizophrenia or any other chronic psychotic disorder, personality disorder, panic disorder, generalized anxiety disorder, obsessive-compulsive disorder, somatoform disorder, anorexia nervosa, bulimia, organic mental disorder.
4. Definite or suspected substance abuse in the past 12 months.
5. Serious or unstable medical illness or any co-existing disease or treatment that in the opinion of the investigator contraindicates the use of study drug.
6. Treatment with other psychotropic drugs (prescription or not) other than zopiclone 7.5 mg or temazepam, 15 to 30 mg on a prn ("when necessary") basis for insomnia.
7. Clinically significant laboratory abnormalities at screen.
8. Positive urine screen for drugs of abuse.
9. Known or suspected allergies to psychotropic drugs.
10. Use of any of the following potent cytochrome P450 inhibitors in the 14 days preceding randomization (Day 1) e.g. ketoconazole, itraconazole, fluconazole, erythromycin, clarithromycin, troleandomycin, indinavir, nelfinavir, tironavir, and saquinavir.
11. Use of potent P450 inducers (e.g. phenytoin, carbamazepine, barbiturates, rifampin, glucorticoids) in the 14 days preceding randomization (Day 1).
12. Thyroid-stimulating hormone concentration more than 10% above the upper limit of the normal range, regardless of treatment for hypothyroidism or hyhperthyroidism.

Date of first enrolment
23/05/2002

Date of final enrolment
15/07/2003

Locations

Countries of recruitment
Canada

Study participating centre

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Sponsor information

Organisation
Astra Zeneca Canada Inc.

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Sponsor type
Industry

Website
http://www.astrazeneca.ca

ROR
https://ror.org/04r9x1a08

Funder(s)

Funder type
Industry

Funder Name
Astra Zeneca Canada Inc. (Investigator initiated trial)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	28/08/2008	31/12/2020	Yes	No