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Efficacy of add-on mirtazapine on clinical and neuropsychologic parameters in schizophrenic patients treated with conventional antipsychotics: a double-blind, placebo-controlled trial with an open-label extension phase

Submission date
19/09/2005

Recruitment status
No longer recruiting

Registration date
25/05/2006

Overall study status
Completed

Last Edited
20/11/2012

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
7183

Study information

Scientific Title

Study objectives
Mirtazapine will improve negative, possibly positive and extrapyramidal symptoms, as well as neurocognition, if added to a conventional antipsychotic.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved by the Republican Commision on Medical Ethics, Petrozavodsk (Session #6, Sept 9, 2004)

Study design
Double-blind, placebo-controlled trial with an open-label extension phase

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
Schizophrenia

Interventions
Add-on mirtazapine versus placebo.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
Positive and negative syndrome scale (PANSS) total scores.

Secondary outcome measures
1. Number of responders (20% or more decline on PANSS total or subscores)
2. Change in standard neurocognitive tests

Overall study start date
10/10/2004

Completion date
31/12/2006

Eligibility

Key inclusion criteria
Male or female in- or out-patients will be recruited if:
1. They are aged 18-65 years
2. Have schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition (DSM-IV) (APA, 1994); defined schizophrenia (disorganized, catatonic, paranoid, residual, or undifferentiated) or schizo-affective disorder, depressive type
3. Receiving one or more conventional antipsychotics at cumulative daily dose of at least 400 mg chlorpromazine equivalents (e.g. haloperidol 12 mg daily) (see Table of Antipsychotic Equivalents), which has remained unchanged (also in terms of dosage) during at least 6 last weeks prior to screening baseline (8 weeks for depot antipsychotics).
Table of antipsychotic equivalents (Basire, 2000) oral mg/day: chlorpromazine 100 mg (= 25-50 mg intramuscular (IM) or 250 mg rectal), fluphenazine 2 mg, levomeptromazine - not known, pericyazine 24 mg, perphenazine 8 mg, prochlorperazine 15 mg, promazine 100 mg, thioridazine 100 mg, trifluoperazine 5 mg, benperidol 2 mg, droperidol 4 mg (Short t1/2) or 3 mg IM /intravenous (IV), haloperidol 3 mg or 1.5 mg IM/IV for doses up to 150 mg/day, trifluoperidol 2 mg, flupentixol 2 mg, zuclopentixol 25 mg up to 150 mg/day, pimozide 2 mg (Long t1/2), remoxiprid 75 mg, amisulpride 100 mg, sulpiride 200 mg, loxapine 10 mg depot (mg/week), fluphenazine 5-10 mg (1-12.5 mg), pipothiazine 10 mg (5-12.5 mg), haloperidol 15 mg (5-12.5 mg), flupentixol 10 mg (8-20 mg), zuclopentixol 100 mg (40-100 mg), fluspirilene 2 mg - not fully established.
4. Demonstrating less than optimal clinical outcome i.e. experiencing either positive or negative symptoms (disability due to only general symptoms will be insufficient for inclusion) resulting in the illness of at least moderate severity (i.e. 4, moderately ill, or more on the clinical global impression (CGI), severity item) (Guy, 1970)
5. The clinical condition has remained stable during the last 6 weeks prior to the baseline visit
6. The patient has a level of understanding that enables reasonable cooperation with the investigator and the ability to fulfil the neurocognitive tests
7. The patient has given written informed consent

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
40

Key exclusion criteria
1. History of allergy or serious adverse events due to mirtazapine
2. Previous lack of response to a trial with mirtazapine in daily doses of 30 mg or more during four or more weeks, added to the patients current or earlier conventional antipsychotic medication
3. Previous lack of response to another antidepressant with affinity to postsynaptic (5-hydroxytryptamine) 5HT2 receptors (e.g. mianserine, trazodone, or nefazodone) used in adequate doses during four or more weeks
4. Current atypical antipsychotic medication (e.g. clozapine, risperidone, olanzapine, sertindole, quetiapine, zotepine, ziprasidone, etc.)
5. History of non-response to either clozapine or other atypical antipsychotics
6. Medical or neurological condition or drug treatment that might put patients at serious risk or bias the assessment of their clinical or mental status (e.g. serious unstable physical illness, epilepsy, organic brain syndrome etc.)
7. History of or current bipolar disorder or schizoaffective disorder, bipolar type (patients with schizoaffective disorder, depressive type can participate in the study)
8. Substance addiction or abuse within the last three months prior to screening
9. Clearly predictable poor compliance
10. For females of child-bearing potential: pregnancy, lactation, or inability or unwillingness to use medically acceptable methods of contraception during the study
11. Treatment with any antidepressant, mood stabilizer, regular (i.e. four or more times within 1 week) use of sumatriptan, naratriptan, zolmitriptan, or drugs with similar mechanism of action, or buspiron or drugs with similar mechanism of action - within four weeks (for fluoxetine, six weeks) prior to baseline. Accidental use of the drugs for treatment of migraine listed above is forbidden on the day of clinical assessment before the assessment.
12. Treatment with antipsychotics other than those currently in use within six weeks prior to baseline
13. Treatment with benzodiazepines as follows:
a. Regular use (i.e. four or more times weekly) of any benzodiazepines at any doses during any of the last four weeks prior to baseline, if they have being received for less than two months. However, regular use of benzodiazepines is permitted if they are absolutely necessary and have been received during two or more months prior to baseline in stable daily doses not exceeding 30 mg of diazepam or comparable doses of other benzodiazepines, as determined by the table of equivalents (Bazire, 2000).
b. Accidental use (i.e. three or less times weekly) of benzodiazepines in daily doses exceeding 30 mg of diazepam or comparable doses of other benzodiazepines (see table of equivalents) (i.e. accidental use of 30 mg or less of diazepam or comparable doses of other benzodiazepines is

not a criterion for exclusion). Use of benzodiazepines on the day of clinical assessment is forbidden before the assessment.
14. Electroconvulsive therapy (ECT) within three months prior to baseline
15. Any clinically relevant abnormality detected during the physical examination or laboratory screening tests and likely to interfere with the conduct of the study

Date of first enrolment
10/10/2004

Date of final enrolment
31/12/2006

Locations

Countries of recruitment
Finland

Study participating centre
Hospital of Kellokoski
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Sponsor type
Research organisation

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ROR
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Funder(s)

Funder type
Research organisation

Funder Name
Stanley Medical Research Institute

Alternative Name(s)
The Stanley Medical Research Institute, SMRI

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United States of America

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	01/01/2013		Yes	No