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ATLAS: Antipsychotic Treatment of very LAte-onset Schizophrenia-like psychosis

Submission date
20/09/2012

Recruitment status
No longer recruiting

Registration date
24/09/2012

Overall study status
Completed

Last Edited
11/12/2018

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Very late-onset schizophrenia-like psychosis is a common mental health condition that affects an estimated 34,000 of the UK population aged over 60. Antipsychotic drugs (e.g., amisulpride) are widely used to treat these patients but this is not evidence-based. The aim of this study is to determine whether amisulpride works better than a placebo (dummy) drug in the treatment of very late-onset schizophrenia-like psychosis, and to find out whether giving 12 weeks of low-dose amisulpride produces sufficient benefit to outweigh potential risks.

Who can participate?
Patients aged 60 or over with very late-onset schizophrenia-like psychosis.

What does the study involve?
Patients will be randomly allocated to receive either 12 weeks of amisulpride or a matching placebo (dummy). Afterwards, patients allocated to placebo will then switch to amisulpride for 24 weeks, whereas those receiving amisulpride will be randomly allocated either to continue taking amisulpride or take the placebo for 24 weeks.

What are the possible benefits and risks of participating?
Your symptoms may improve because of the treatment and the results of this study will also help improve treatment in the future. The risks are the possible side effects of the treatment (e.g., nausea, difficulty sleeping, restlessness, weight gain) and the possibility that your symptoms may get worse.

Where is the study run from?
King's College London Department of Old Age Psychiatry (UK).

When is the study starting and how long is it expected to run for?
The study started in October 2012 and will run until February 2016.

Who is funding the study?
The study is sponsored by King's College London and South London and Maudsley NHS Foundation Trust and coordinated by CTSU.

Who is the main contact?
Prof. Rob Howard

Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2010-022184-35

Protocol serial number
EudraCT: 2010-022184-35

Study information

Scientific Title
ATLAS: A pragmatic randomised double-blind trial of Antipsychotic Treatment of very LAte-onset Schizophrenia-like psychosis

Acronym
ATLAS

Study objectives
To determine whether amisulpride is superior to placebo in the treatment of very late-onset schizophrenia-like psychosis as measured by significant differences between amisulpride and placebo treated groups in changes in BPRS score over 12 weeks. A prior hypothesis is that benefits of amisulpride will be most apparent on the hostility, suspiciousness, hallucinations, tension, uncooperativeness and motor hyperactivity sub-scores.

More details can be found here: http://www.hta.ac.uk/2377

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Surrey Borders Research Ethics Committee, 23/09/2011, ref: 11/LO /1267

Study design
Multicentre study of 300 patients randomised in 2:1 ratio between 12 weeks of amisulpride or placebo. If on placebo switch to amisulpride, if on amisulpride randomised to amisulpride or placebo

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Late onset schizophrenia like psychosis

Interventions
Double-blind placebo-controlled trial, amisulpride vs placebo

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
1. Brief Psychiatric Rating Scale (BPRS), a widely used clinician-rated 24-item instrument for assessing positive, negative and affective symptoms in patients with psychotic disorders (Ventura et al 1993). The BPRS (Appendix D) consists of 18 symptom constructs and takes 20-30 minutes for the interview and scoring. Each item is assessed by the rater on a 7-point scale ranging from 1 (not present) to 7 (extremely severe). The total score is obtained by summing the scores from the 18 items. Scores thus range from 18 to 126, with higher scores indicating greater levels of psychopathology. The BPRS will be administered at baseline, at week 4, then between weeks 10-12 and between weeks 34-36. Changes in BPRS score between baseline and the week 10-12 assessment and between the week 10-12 and week 34-36 assessments are the trials co-primary outcomes.
2. The proportion of patients withdrawn to open treatment with amisulpride by their physicians between Weeks 13 and 36 (Stage 2) because of perceived lack of efficacy, which will be compared in participants randomised to continue amisulpride (arm A) and switch to placebo (Arm B). The difference between groups in the percentage of patients stopping trial treatment because of physician concerns about non-efficacy was used as an outcome measure in the CATIE-AD trial (Schneider et al 2003).

Key secondary outcome(s))
1. Extrapyramidal side-effects (EPSE) measured with the Simpson-Angus Scale (SAS). The modified SAS being used in ATLAS measures nine extrapyramidal signs: gait, arm dropping,

shoulder shaking, elbow rigidity, wrist rigidity, leg pendulousness, glabellar tap, tremor, and salivation, all of which are assessed by direct examination. The head dropping item is omitted because of difficulties with this assessment in home visits. Each item is rated on a scale of 0-4, with higher scores indicating greater severity of EPSE. The scale range of the modified SAS is thus from 0-36. A standardised description is given of each item to optimise reliability. The SAS has been widely used to measure EPSE within clinical trials and will be administered at baseline, 4, 10-12 and 34-36 weeks. The change in SAS between Baseline and Week 10-12 and between Week 10-12 and Week 34-36 will be compared between groups to assess EPSE.
2. Compliance expressed as treatment discontinuation rates and as percentage of prescribed trial medication taken between Weeks 1 and 12 and between Weeks 13 and 36 will be compared in patients allocated to receive amisulpride and those allocated placebo.
3. Quality of life measured with the self-rated, short, 26-item, WHO Quality of Life Scale (WHOQOL-BREF) at baseline, 10-12 and 34-36 weeks. The WHOQOL-BREF includes two items about an individuals overall perception of their quality of life and health and questions assessing four domains: physical, psychological, social and environmental well-being, with higher scores denoting a better quality of life. This instrument has been previously used in studies of older people with schizophrenia and psychosis patients in residential care settings (Picardi et al 2006).
4. Cost-effectiveness calculated by attaching nationally applicable unit cost measures to health and social service use and medication data collected for each patient with a modified version of the Client Service Receipt Inventory (CSRI) at 10-12 and 34-36 and the EQ-5D (EuroQol) at baseline, 10-12 and 34-36 weeks. We will also collect data on informal carer inputs, and attach imputed values.
The cost-effectiveness of oral amisulpride versus placebo over 12 weeks and the cost-effectiveness of treatment continuation for a further 24 weeks versus discontinuing amisulpride treatment at 12 weeks will be investigated. The differences between patient groups in the costs for each Stage (covering health and social care service use, medication and carer support) will be calculated, and an incremental cost-effectiveness ratio estimated using QALYs computed from EQ-5D. We will also examine cost-effectiveness by plotting a cost-effectiveness acceptability curve (CEAC) generated from the net benefit approach using bootstrap regression for a range of hypothesised values for willingness to pay for incremental improvements in psychiatric symptoms measured on the BPRS. Each cost-effectiveness analysis will be conducted from the perspective of (a) the NHS and social services, and (b) society as a whole, the main difference being the exclusion of formal and informal carer costs and out-of-pocket patient or carer payments

Completion date
29/02/2016

Eligibility

Key inclusion criteria
1. Diagnosis of very late-onset schizophrenia-like psychosis (defined by International Consensus Group criteria, Howard et al 2000), including onset of delusions and/or hallucinations after the age of 60 years
2. BPRS score ≥30, or active psychotic symptoms of a nature and severity that would be consistent with a BPRS score of 30 or greater
3. Capacity to give informed consent to inclusion in trial (in the view of the responsible clinician)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Evidence of significant cognitive impairment and MMSE score <25
2. Uncontrolled serious concomitant physical illness
3. Primary diagnosis of affective disorder
4. Prescribed amisulpride in previous 28 days. (Patients who have been treated with other antipsychotic agents in the previous 28 days but still satisfy the eligibility criteria, and stopping current antipsychotic is considered appropriate, can participate and this will be included as a stratification factor at randomisation)
5. Contraindication to amisulpride (e.g. phaeochromocytoma, prolactin dependent tumour or potential drug interactions: e.g. with levodopa - see most recent Summary of Product Characteristics http://emc.medicines.org.uk/)
6. Participation in another Clinical Trial of an Investigational Medicinal Product (IMP) in the previous 28 days

Date of first enrolment
01/10/2012

Date of final enrolment
29/02/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College London Department of Old Age Psychiatry,
London
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SE5 8AF

Sponsor information

Organisation

Kings College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK) ref: 09/55/06

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	01/07/2018		Yes	No
Results article	results	01/11/2018		Yes	No
HRA research summary			28/06/2023	No	No